AN INVESTIGATION OF THE SYSTEMIC INFLAMMATORY RESPONSE IN THE PERI-OPERATIVE PERIOD IN PATIENTS UNDERGOING POTENTIALLY CURATIVE SURGERY FOR COLORECTAL CANCER

by

JOSEPH E.M.CROZIER

M.B.Ch.B., M.R.C.S. (Ed)

A THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

to

THE UNIVERSITY OF GLASGOW

from RESEARCH CONDUCTED IN THE UNIVERSITY DEPARTMENT OF SURGERY,

GLASGOW ROYAL INFIRMARY

MAY 2008

CONTENTS

DEDICATION

To my wife.

I dedicate this work for her help, encouragement and support during the writing of this thesis. I also dedicate this to my son Adam who was born early on in my studies and my daughter Ella who was born just after the thesis was submitted, giving me the final motivation to cross the finishing line.

ACKNOWLEDGEMENTS

I owe a large debt to the following people who helped and advised me through my research

Dr Donald McMillan	University Department of Surgery Glasgow Royal Infirmary
Dr Ruth McKee	University Department of Surgery Glasgow Royal Infirmary
Prof Colin McArdle	University Department of Surgery Glasgow Royal Infirmary
Mr John Anderson	University Department of Surgery Glasgow Royal Infirmary
Dr Wilson Angerson	University Department of Surgery Glasgow Royal Infirmary

DECLARATION

The work presented in this thesis was carried out in the University Department of Surgery, Royal Infirmary, Glasgow. It was undertaken while working as a surgical research fellow in 2003 in the University Department of Surgery at Glasgow Royal Infirmary. The recruitment period and also the patient numbers varied between different studies in the thesis for a number of reasons. The thesis work was carried out over the period 2003-2007 and to maximise the numbers of patients with a minimum follow-up period of 12 months that were studied, different recruitment periods were required.

I declare that the work presented in this thesis has been carried out by me except where indicated below.

C-reactive protein and albumin were measured by the routine hospital laboratory service.

The statistical analysis was performed under the supervision of Dr DC McMillan (Senior Lecturer) and Dr WJ Angerson (Reader: Biostatistician), Department of Surgery, Royal Infirmary, Glasgow

The work presented in this thesis has resulted in the following publications.

Joseph EM Crozier, Ruth F McKee, Colin S McArdle, Wilson J Angerson, John H Anderson, Paul G Horgan, Donald C McMillan. (2006) The presence of an elevated

C-reactive protein concentration preoperatively predicts poorer survival in patients receiving adjuvant 5-FU chemotherapy following potentially curative resection for colorectal cancer. British Journal of Cancer 94, 1833-1836

J. E. M. Crozier, R. F. McKee, C. S. McArdle, W. J. Angerson, J. H. Anderson, P. G. Horgan and D. C. McMillan (2007) Preoperative but not postoperative systemic inflammatory response correlates with survival in colorectal cancer. British Journal of Surgery 94;8, 1028-1032

Joseph EM Crozier, Donald C McMillan, Colin S McArdle, John H Anderson, Paul G Horgan, Ruth F McKee (2007) Tumour size is directly proportional to the pre-operative systemic inflammatory response in patients with primary operable colorectal cancer.
Accepted for publication in the Journal of Gastroenterology and Hepatology.

Donald C McMillan, Joseph EM Crozier, Khalid Canna, Wilson J Angerson, Colin S McArdle (2007). Evaluation of an inflammation-based prognostic score (GPS) in patients undergoing resection for colon and rectal cancer. International Journal of Colorectal Disease 22;8, 881-886

Joseph EM Crozier, Donald C McMillan, Colin S McArdle, John H Anderson, Paul G Horgan, Ruth F McKee. The relationship between emergency presentation, the systemic inflammatory response and cancer specific survival in patients undergoing potentially curative surgery for colorectal cancer. American Journal of Surgery, in press.

LIST OF TABLES

LIST OF FIGURES

SUMMARY OF THESIS

Colorectal cancer remains the second commonest cause of cancer death in Western Europe and North America. Each year in the UK, there are approximately 35,000 new cases and 16,000 deaths attributable to the disease. Despite a trend towards earlier presentation and improvements in the quality of surgery many patients still die of their disease. Overall about a third of patients undergoing surgery for potentially curative disease will die within five years.

Recent work has meant that it is now recognised that it is not only the tumour characteristics that are responsible for cancer specific survival but also the host immune response. Part of this host response is the non-specific systemic inflammatory response. There is now a body of work examining the relationship between the systemic inflammatory response and cancer specific survival. Indeed, there is evidence that the systemic inflammatory response, as evidenced by an elevated C-reactive protein, predicts overall and cancer specific survival independent of tumour stage in a number of solid tumours including colorectal cancer.

The aim of this thesis was to investigate the following in patients undergoing potentially curative surgery for colorectal cancer:

1. To establish the prognostic value of the pre-operative compared with the post-operative systemic inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.

2. To examine the pre-operative inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.
3. To examine the utility of the systemic inflammatory response as a guide to treatment in patient undergoing potentially curative surgery for colorectal cancer.

Chapter 3 examines the relationship between the systemic inflammatory response in the preoperative period and the immediate post operative period. This chapter confirmed that an elevated C-reactive protein concentration, prior to but not immediately after surgery, was associated with poor cancer specific survival in patients undergoing curative open resection for colorectal cancer. This might suggest that approaches that focus on reducing the magnitude of the immediate post-operative systemic inflammatory response are unlikely to improve long term outcomes.

Chapter 4 examines the relationship between the tumour size and the systemic inflammatory response. This chapter shows that the maximal tumour diameter is associated with an elevated pre-operative C-reactive protein concentration but not survival in patients with primary operable colorectal cancer. This would suggest that the direct relationship between CRP and tumour diameter may be due to a compromised immune response promoting tumour growth.

Chapter 5 examines how the patients presented for their surgery. The results of this study suggest that as well as being prognostic in patients undergoing elective surgery C-reactive protein and the modified Glasgow prognostic score (mGPS) are prognostic in patients who present as an emergency which is the first time this has been shown.

Chapter 6 examines the relationship between the systemic inflammatory response, interleukin-6 and 10 and lymphocyte subpopulations in patients with colorectal cancer. The results of this study suggest that the presence of a systemic inflammatory response is associated with upregulation of immunomodulatory cytokines but not with down regulation of lymphocyte derived immune status.

Chapter 7 examines the relationship between the systemic inflammatory response and outcome in those patients receiving post-operative adjuvant chemotherapy. This shows that the presence of a systemic inflammatory response appears to be an independent predictor of poor outcome in patients receiving adjuvant 5FU-based chemotherapy following potentially curative resection for colorectal cancer.

Chapter 8 is a pilot study examining the relationship between node negative colon cancer patients and the systemic inflammatory response. This chapter suggests that an elevated C-Reactive protein might predict cancer specific survival, independent of recommended pathological criteria, in patients undergoing resection for node negative colon cancer. However this does need a further, much larger study to confirm this trend.

Taken together, the studies in the present thesis would indicate that an elevated pre-operative systemic inflammatory response is a prognostic factor independent of stage of disease.

1 INTRODUCTION

1.1 Epidemiology of colorectal cancer

Colorectal cancer is one of the most common forms of cancer. Worldwide there were approximately 945,000 new cases diagnosed in 2000 [Parkin, 2001]. It is more common in developed countries such as North America, Australia and Western Europe [Parkin et al., 1999]. In Europe it is the second most common cancer with almost 334,000 new cases diagnosed in 1995 accounting for 12.8% of the cancer burden. Within developed countries the incidence is highest in urban areas and within Europe higher incidences occur in the more Northern Latitudes. The age standardised ratios for colorectal cancer in Europe are 49.6 per 100,000 for males and 33.9 per 100,000 for females and the mortality is 27.9 per 100,000 for males and 18.5 per 100,000 in females. The figures for the United Kingdom in 1995 are almost identical to these European averages [Bray et al., 2002].

In the United Kingdom colorectal cancer is the second most common cancer to breast cancer with an overall incidence of 35,300. This breaks down to an incidence of 18,960 in men and 16,340 in women. In Scotland there were 1,842 new cases in men and 1,669 in women in the year 2000. The numbers of colon cancer are similar for both males and females but there are a greater number of rectal cancers in males (1.44:1 male: female). In 2002 there were 16,220 deaths from colorectal cancer in the United Kingdom [Cancer research UK, 2004]. However the incidence varies between regions in the United Kingdom. For example in London the population risk is in the

order of 1 in 50 compared with a risk in Scotland of between 1 in 23(males) and 1 in 33(females) [Dunlop, 1992].

Colorectal cancer is a disease of old age with more than 80% of cases arising in patients who are 60 years or older [Cancer research UK, 2004]. Up to the age of 40 years, men and women have similar rates of bowel cancer but in later life the rates are higher in males. However, because of a larger female population at risk the actual number of females with colorectal cancer is greater in old age.

The incidence trends of colorectal cancer for men and women differ. Male bowel cancer incidence rates rose slowly by an average of 1% each year between 1979 and 1999, since when there has been a slight decrease. Over the same time period female rates have remained relatively constant [Cancer research UK, 2004;ISD Online, 2007].

1.2 Aetiology of colorectal cancer

The majority of colorectal cancers are sporadic. About 5-10% of colorectal cancers are found in the setting of defined hereditary cancer syndromes, but about 20% of all colorectal cancers are thought to arise in patients with some component of family risk [Lynch and de la Chapelle, 2003].

1.2.1 Hereditary colorectal cancer

The two major forms of hereditary colorectal cancer are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). A diagnosis of hereditary colorectal cancer is based on a thorough family history looking at identifying cancers of all types, age of onset of the cancer, multiple primary cancers, specific phenotypic features such as adenomas that are associated with cancers and pathological findings [Lynch and de la Chapelle, 2003].

1.2.2 Hereditary non-polyposis colorectal cancer (HNPCC)

This is the most common form of hereditary colorectal cancer accounting for at least 50% of hereditary cases [Lynch and de la Chapelle, 1999]. Patients with the HNPCC gene are at very high lifetime risk of developing a cancer before the age of 70 (90% risk in males and 69% risk in females). Forty percent of those patients with colorectal cancer under the age of 30 will have the HNPCC gene [Cancer research UK, 2004]. Despite this HNPCC patients have a better prognosis than sporadic colorectal adenocarcinomas [Lynch and de la Chapelle, 1999].

The main clinical features are multiple generations affected with colorectal cancer at an early age with a predominance of right-sided tumours. There is also a higher proportion of both synchronous and metachronous colorectal cancer. There are also associated extra colonic tumours – endometrium, ovary, stomach, small bowel, pancreas, hepatobiliary tract, brain and upper uroepithelial tract [Watson and Lynch, 1994;Aarnio et al., 1999].

HNPCC tumours are generally more often poorly differentiated, with excess mucoid and signet ring features, a Crohn's like reaction and the presence of infiltrating lymphocytes within the tumour [Jass and Stewart, 1992;Jass et al., 1998;Smyrk et al., 2001].

HNPCC is thought to result from a DNA mismatch repair gene deficiency of which five have been identified and mutations in two of these results in the majority of HNPCC families.

In 1990, the International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC) proposed the Amsterdam criteria as a means to help identify families likely to be harbouring HNPCC. These criteria were further modified in 1999 to include HNPCC-associated cancers other than colorectal cancer [Vasen et al., 1999]. The Amsterdam Criteria for colorectal cancer are as follows;

- At least three relatives with colorectal cancer, one of whom should be a first degree relative of the other two
- At least two successive generations should be affected

- At least one colorectal cancer should be diagnosed before age 50 years FAP should be excluded
- Tumours should be verified by pathological examination

1.2.3 Familial Adenomatous Polyposis (FAP)

FAP accounts for about 1% of all colorectal cancers. It is an autosomal dominant, hereditary colon cancer syndrome that is characterized by the presence of hundreds of adenomatous polyps in the colon and rectum at a young age. It is also associated with duodenal adenomatous polyps and multiple extracolonic manifestations including desmoid tumours osteomas, epidermoid cysts, various soft tissue tumours, and a predisposition to thyroid and periampullary cancers.

Mutations of the adenomatous polyposis coli (APC) gene on chromosome 5q have been identified as an early change in colorectal cancer and these mutations are found in about 80% of FAP patients [Bisgaard et al., 1994].

1.2.4 Genetic basis of colorectal cancer

Histopathological and epidemiological studies have shown that the majority of colorectal adenocarcinomas originate from premalignant adenomatous polyps. This multi-step process involving complex genetic mutations, which develop benign disease to a malignant state, is known as the adenoma-carcinoma sequence. This multistep model of carcinogenesis proposes that neoplasia results from accumulation of a series of genetic abnormalities [Vogelstein et al., 1988]. These genetic

abnormalities lead to changes in the colonic mucosa from normal, to dysplasia, to carcinoma in-situ and finally invasive carcinoma (Figure 1). This adenoma-carcinoma sequence was developed from a number of clinical observations. Firstly age distribution curves for adenomas and carcinomas show that the prevalence of both increases with increasing age, but adenomas are recognized and their prevalence peaks at least 5 years earlier than that of colorectal cancers [Muto et al., 1975]. Furthermore, the varying prevalence of adenomas in different geographical regions correlates with the colorectal cancer incidence in those regions [Clark et al., 1985].

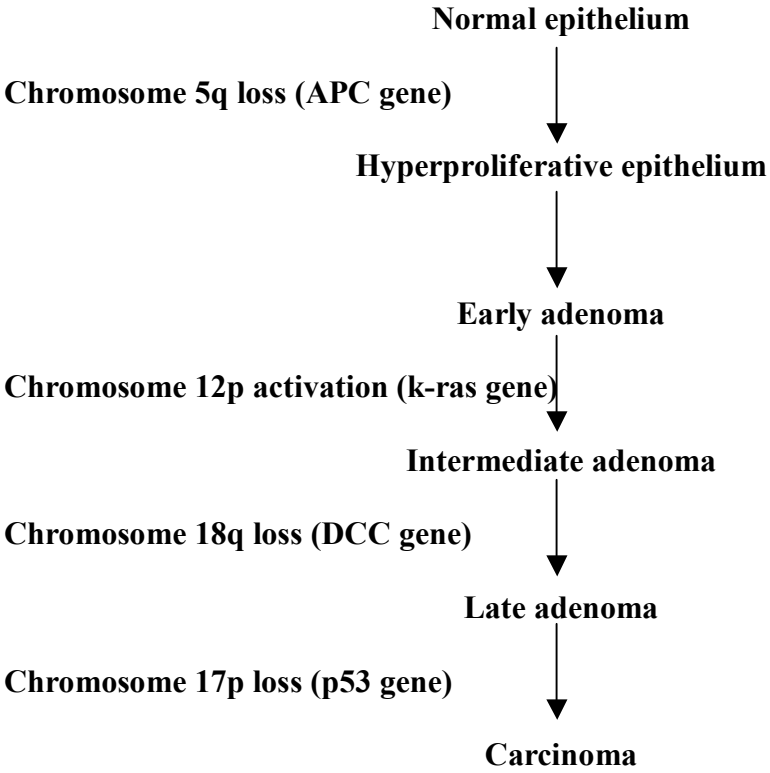

Figure 1.1 the adenoma-carcinoma sequence [Fearon and Vogelstein, 1990]

1.2.5 Sporadic colorectal cancer

Approximately 90% of colorectal cancers are sporadic in nature and the genetic damage that occurs as part of the adenoma-carcinoma sequence are mainly due to lifestyle factors. These include diet, physical activity, smoking and alcohol intake.

The main association between colorectal cancer and diet is the lack of dietary fibre in the Western diet, as was first suggested by Burkett in 1971. Burkett hypothesised that dietary fibre reduces intestinal transit time and acts as a dilutent. These factors could reduce the exposure of the large intestine mucosa to carcinogens [Burkitt, 1971]. This hypothesis has been strengthened by epidemiological studies [Modan et al., 1975] and two questionnaire studies which have indicated a strong association between intake of dietary fibre and decreased colorectal cancer risk [Bingham et al., 2003;Peters et al., 2003].

However, other studies since Burkitt's initial observation have been unable to find such a link between colorectal cancer and dietary fibre [Platz et al., 1997]. In a study of 88,757 women, Fuchs and co-workers followed the intake of dietary fibre and incidence of colorectal cancer for 16 years. During this period, 787 cases of colorectal cancer and 1012 cases of adenomas of the distal colon and rectum were found in 27,530 of the participants who underwent colonoscopy investigation. This prospective study failed however to find an association with dietary fibre and protection from colorectal cancer or adenoma [Fuchs et al., 1999].

Other dietary links to colorectal cancer include a diet lacking in vegetables [Burkitt, 1971] and diets rich in animal fats. There has been a longstanding hypothesis that dietary fat increases the risk of colorectal cancer but epidemiologic studies have not supported the hypothesis that dietary fat increases risk independently of its contribution to overall energy intake [Willett et al., 1990;Bostick et al., 1994].

However there is good evidence that obesity and increased energy intake are linked to colorectal cancer [Bostick et al., 1994;Giovannucci et al., 1995a]. In a large study looking at obesity and cancer in Europe it has been suggested that about 10 – 11% of colorectal cancer cases can be attributed to being overweight or obese [Bergstrom et al., 2001].

Another dietary factor associated with colorectal cancer is alcohol. Research has shown that higher consumption of alcohol, when combined with low micronutrient intake, may considerably increase the risk of colorectal cancer [Jedrychowski et al., 2002]. Linked to this there is also good evidence that smokers have a greater incidence of colorectal cancer [Giovannucci, 2001].

There is also good evidence that inflammation of the large bowel is a risk factor for colorectal cancer. In patients with inflammatory bowel disease (IBD), ulcerative colitis or Crohn's disease there is an approximately fivefold overall relative risk in colorectal cancer compared with the age-matched general population [Ekbom et al., 1990a]. This increased risk of colorectal cancer in IBD patients is a result of the disease rather than an inherited phenomenon, and is associated with the site, extent and duration of inflammation [Ekbom et al., 1990b]. However, the presence of a family history of colon cancer does increase this risk still further for the individual

with IBD; this shows that, as for sporadic colon cancer, both genetic and acquired factors are important [Askling et al., 2001].

1.2.6 Non-steroidal anti-inflammatory drugs and colorectal cancer

In 1977, Bennett and co-workers found there were increased concentrations of prostaglandins in colorectal cancer tissue when compared with normal colorectal mucosa [Bennett et al., 1977]. Non steroidal anti-inflammatory drugs (NSAIDs) inhibit the cyclooxygenase (COX-1) enzyme and thereby block prostaglandin synthesis. Several studies have shown that NSAIDs could prevent and reverse colorectal adenomas and carcinomas [Kudo et al., 1980;Kune et al., 1988]. Clinical experience with non steroidal anti-inflammatory drugs included a series of case reports [Waddell and Loughry, 1983;Waddell et al., 1989] and randomised trials [Labayle et al., 1991;Giardiello et al., 1993], which demonstrated the ability of sulindac to reduce the size and number of colorectal polyps occurring in patients with familial adenomatous polyposis (FAP). It is felt that the adenoma-carcinoma sequence in FAP and the general population are similar, therefore these findings are important not just for FAP patients but possibly also for the general population. Recent epidemiological findings have shown a 40-50% reduction in colorectal cancer mortality among patients regularly taking NSAIDs compared to the general population not taking these drugs [Kune et al., 1988;Rosenberg et al., 1991;Thun et al., 1991;Thun et al., 1993;Giovannucci et al., 1994;Cotton et al., 1996;Smalley and DuBois, 1997].

It is felt that the ability of NSAIDs to inhibit cyclooxygenase 2 (COX 2) enzymes is the probable mechanism of chemoprevention in colorectal adenomas and carcinomas but it is not clear. However controversy exists about the safety, efficacy and optimal treatment regimen of NSAIDs as long term chemopreventative agents in the general population [Herendeen and Lindley, 2003].

Epidemiological studies have looked at the chemopreventive effect of NSAID's, especially aspirin, with regards to colorectal cancer. A large study in women found that regular aspirin use, at doses similar to those recommended for the prevention of cardiovascular disease, substantially reduces the risk of colorectal cancer. However, this benefit may not be evident until after at least a decade of regular aspirin consumption [Giovannucci et al., 1995b]. More recent work has shown that this reduction is in the risk of colorectal cancers that overexpress COX-2 but not the risk of colorectal cancers with weak or absent expression of COX-2[Chan et al., 2007]. However the optimal chemoprevention for colorectal cancer requires long-term use of aspirin doses substantially higher than those recommended for prevention of cardiovascular disease, but the dose-related risk of gastrointestinal bleeding must also be considered [Chan et al., 2005].

Taking all this together it can be summarised that inflammation in the colon and rectum appears to be an important aetiological factor in the development of colorectal cancer.

1.3 Clinical features of colorectal cancer

Colorectal carcinoma usually occurs in patients over 60 years of age. The cardinal symptoms of colorectal cancer are alteration of bowel habit and rectal bleeding, however the symptoms depend on location of the tumour, type of growth and the presence or the absence of metastasis.

Traditionally the majority of colorectal cancers occurred either in the rectum or the left side of the colon but more recently there has been a proximal shift. In the 1970s about a quarter of tumours were found proximal to the splenic flexure but this figure has increased to approximately a third of tumours [Ikeda et al., 1996;McCallion et al., 2001]. Over the last 30 years the average age of patients with colorectal cancer has been increasing [Kotake et al., 2003] and with this there has been an increase in the proportion of proximal tumours [Ikeda et al., 1996].

Caecal and ascending colon cancer may present with iron deficiency anaemia, the presence of a mass in the right iliac fossa, distal small bowel obstruction or weight loss. These tumours are more likely to be polypoidal. Left sided colon cancers present in a different way; the tumours are more likely to be annular and the bowel contents are more solid. This means that left sided tumours present with constipation, colicky pain and obstruction. About a third of colon cancers present as an emergency with either obstruction or perforation [McArdle and Hole, 2004].

Rectal cancers present with fresh rectal bleeding, mucus discharge and tenesmus. Tenesmus is the latest of these symptoms and usually indicates an advanced rectal tumour.

Some patients present at a later stage with symptoms attributable to local or distant spread. Symptoms of local spread depend upon which organ has been invaded by the tumour. These can include urinary tract symptoms if invasion of the ureters, bladder or prostate have occurred, back pain if the sacral plexus has been invaded or symptoms of a fistula with invasion of the vagina or other parts of the intestines. Metastatic spread of colorectal cancer is most commonly to the liver. Symptoms such as pain in the right upper quadrant, ascities, jaundice and fatigue can occur but sometimes liver metastases are asymptomatic. Other sites of metastatic spread include the peritoneum, lungs and brain.

1.4 Clinical investigation of colorectal cancer

As with all aspects of clinical medicine a good history and clinical examination are important. The clinical examination should include a rectal examination as well as an abdominal examination. Once these have been performed there are a number of investigations that are employed to help diagnose and stage colorectal cancer.

1.4.1 Faecal occult blood tests

The faecal occult blood (FOB) test is a cheap investigation that detects blood in faeces. It can detect blood from colorectal cancers and polyps that tend to bleed more than normal colonic mucosa. Hemoccult II is most widely used of the many different types of FOB tests available. This test detects the pseudoperoxidase activity found in haemoglobin when it interacts with a guaiac-impregnated card in the presence of a hydrogen peroxide developer. A positive result is indicated by the immediate appearance of a blue colour on addition of the hydrogen peroxide developer. The test detects peroxidase or pseudoperoxidase activity in stool, and is not specific for human haemoglobin. This means that dietary substances can result in false positive (e.g., rare red meat, turnips, horseradish) or false negative (e.g., vitamin C) results. Faecal occult blood has been used as a method of screening for colorectal cancer and screening using FOB and colonoscopy has been shown to reduce mortality from colorectal cancer by 16% for those allocated to screening and by 23% for those who were actually screened [Towler et al., 1998]. However the main disadvantage of FOB testing is the low sensitivity. It has been shown that about 40% of cancers and 80% of adenomas are missed by FOB screening [Rozen et al., 1987;Steele, 2006].

1.4.2 Flexible / Rigid sigmoidoscopy

The rigid sigmoidoscope is a plastic tube 20-25cm long attached to a light source and insufflation. It can be used in the outpatient setting to examine the lower part of the rectum and sigmoid colon. Biopsies can be taken at the time of rigid sigmoidoscopy. The flexible sigmoidoscope is a fibre optic instrument about 60 cm long and is used to examine most of the left side of the colon. The colon needs to be prepared with a phosphate enema but the patient does not require sedation. It has the advantage of being a therapeutic instrument as well as a diagnostic instrument.

Because about 2/3rds of colorectal cancer occur within the reach of the flexible sigmoidoscope it has been used as a screening tool. Small studies have shown a reduction in colorectal cancer incidence and mortality with screening sigmoidoscopies [Muller and Sonnenberg, 1995] but no randomised controlled trials have been published yet.

The disadvantage of flexible sigmoidoscopy is that the right side of the colon is not visualised. It has been shown that up to 30% of subjects with distal colonic neoplasms had synchronous proximal lesions at colonoscopy and up to 20% of subjects had advanced proximal lesions [Collett et al., 1999]. However the main aim of screening colonoscopies is to identify patients with pathology such as polyps on the left side of the bowel who will then go on to undergo a full colonoscopy. This is because left sided polyps are markers for polyp formation throughout the rest of the colon.

1.4.3 Colonoscopy

Colonoscopy has the capacity to visualise the whole of the large bowel and is therefore able to diagnose the tumour as well as detect synchronous polyps or carcinomas. Colonoscopy should also be used when pathology has been found at sigmoidoscopy. In experienced hands caecal intubation rates should be in excess of 90%. Even though colonoscopy has the advantage of being therapeutic as well as diagnostic there are well recognised complications. The main complications are bleeding, perforation and even death. The rates of these complications are reported as between 0.24% and 0.33% for significant bleeding following colonoscopy and between 0.08% and 0.19% for perforation. The mortality rate is between 0.0% and 0.02% (1 in 5000) [Viiala et al., 2003].

1.4.4 Barium Enema

Double contrast barium enema uses combination of both barium and air to image the large bowel. It is used to complete the visualisation of the bowel following sigmoidoscopy or when colonoscopy was not completed. Barium enema has the advantages that it is widely available, safe and inexpensive. However the sensitivity of barium enema especially for small polyps has been questioned. Complications associated with barium enema are very rare [Blakeborough et al., 1997].

1.4.5 Ultrasound

Two types of ultrasound are used in the staging of colorectal cancer patients. These are transabdominal ultrasound and endorectal ultrasound. Endorectal ultrasound is used to aid the preoperative staging of low rectal tumours by assessing the extent of growth through the bowel wall and if any preoperative radiotherapy is indicated to achieve a curative resection. Endorectal ultrasound has been shown to have an accuracy of between 80 and 90% for assessing the extent of tumour invasion [Beynon et al., 1986;Meyenberger et al., 1995;Barbaro et al., 1999].

1.4.6 Computed tomography

Computed tomography is used mainly for staging but not diagnosis of colorectal cancer. However, recently virtual or CT colonoscopy has been increasingly used for the diagnosis of colorectal cancer. The advantages over conventional colonoscopy are that it is safe, there is a high patient acceptance, and it has an ability to provide a full structural evaluation of the entire colon [Pijl et al., 2002]. Early studies seemed to suggest that the accuracy of CT colonography exceeds barium enema and approaches that of conventional colonoscopy [Fenlon et al., 1999].

Presently the role of CT colonography is in those patients who have had an incomplete or failed colonoscopy and also in the preoperative assessment of the colon proximal to an occlusive cancer that cannot be passed at colonoscopy.

1.4.7 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is used for the staging of rectal tumours. It can accurately stage rectal tumours and again help in the decision making about preoperative radiotherapy [Meyenberger et al., 1995]. It also provides information about extra colonic spread of the tumour.

1.5. Staging and prognosis

The International Union against Cancer (UICC) states that the main aims of staging cancers are as an aid to planning of treatment, an indication of prognosis, allow results to be compared, contribute to continuing investigation and to allow the exchange of information between centres.

Colorectal cancer either spreads by direct extension through the bowel wall or by lymphatic or venous spread. There are a number of different staging systems for colorectal cancer however Dukes stage and TNM stage are used in the main.

1.5.1 Dukes' Stage

Dr Cuthbert Dukes produced a simple and reproducible classification in 1932. This was designed initially as a clinically helpful prognostic classification for rectal cancers. Dukes initially divided rectal cancers into three groups; A, B and C, based upon direct and lymphatic spread of the tumour from the pathological specimen. Stage A meant that the tumour was limited to the bowel wall, B meant that the tumour spread through the bowel wall but there was no metastatic spread to the regional lymph nodes and Stage C meant that there was spread to regional lymph nodes [Dukes, 1932].

Since it was first introduced Dukes' classification has undergone many modifications. Stage C has been broken down into two groups; C1 for those tumours with direct lymphatic spread in continuity with the bowel wall and stage C2 for those tumours

where the apical node contains metastatic tumour. Stage D was introduced in 1967 for patients who had distant metastatic disease. Finally Dukes' stage has been used to classify colonic tumours.

Prognosis of colorectal cancer depends upon the stage of the tumour. Five year survival rates are 90-94% for Dukes' stage A, 75%-85% for Dukes' stage B, 52%-57% for Dukes' stage C, and up to 2% for Dukes' stage D [Mandel et al., 1993;Rae and Gibberd, 2000].

1.5.2 TNM Stage

Dukes' stage has a lack of precision mainly because it does not assess the extent of tumour penetration or the number of involved lymph nodes. For this reason the TNM classification has been widely adopted. There have been a number of updates to TNM staging and the latest version used is the sixth version. This can lead to some confusion in patients who were staged on previous versions because of subtle differences between the definitions.

The basis for TNM classification includes assessment of tumour size and depth of penetration ('T'); nodal involvement ('N'); and the presence of distant metastases ('M'). Five year survivals based on TNM stages I-IV are similar to Dukes' stage A-D.

Table 1.1 shows the breakdown of the various components of the TNM classification and Table 1.2 demonstrates the interaction between Dukes' stage and TNM stage.

TNM Category	Description
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ (intraepithelial or intramucosal, with invasion of lamina propria
T1	Tumour invades submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues
T4	Tumour directly invades other organs or structures and/or perforates visceral peritoneum
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis to 1-3 regional lymph nodes
N2	Metastasis to 4 or more regional lymph nodes
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Table 1.1 TNM categories

TM Stage	TNM classification	Dukes' classification
Stage 0	Tis N0 M0	
Stage I	T1-T2 N0 M0	A
Stage IIA	T3 N0 M0	B
Stage IIB	T4 N0 M0	B
Stage IIIA	T1-T2 N1 M0	C
Stage IIIB	T3-T4 N1 M0	C
Stage IIIC	Any T N2 M0	C
Stage IV	Any T any N M1	D

Table 1.2 TNM stage and Dukes' Stage

1.6 Treatment

1.6.1 Elective Surgery

The best chance of a permanent cure of colorectal cancer is surgery. Resection of the primary tumour is a valid palliative option to alleviate symptoms such as obstruction and prevent complications, such as perforation.

At the time of presentation about a quarter of patients will have extensive hepatic metastases and about one fifth will have locally advanced tumours [McArdle et al., 1990].

In the 75 to 80% of patients who present electively, diagnosis is confirmed preoperatively by histology of biopsy specimens. Patients are then staged as discussed in earlier sections with CT scanning (and MRI or ultrasound as indicated). Ideally patients should have preoperative imaging of the entire colon by colonoscopy or barium enema to rule out the presence of synchronous lesions (4-5%). However, in the presence of an obstructing tumour this may not be possible.

Surgical Resection

Traditionally surgical resection was performed via a large laparotomy incision. The abdomen is inspected to rule any evidence of metastatic spread of the tumour, which might not have been found on preoperative staging. Also resectability of the tumour is

assessed. Recently there has been a trend to perform colorectal resections laparoscopically [Braga et al., 2002;Lacy et al., 2002].

Whether the operation is performed laparoscopically or via an open incision the same principles apply. This is to ensure an enbloc oncological resection removing the tumour and also the draining lymph nodes. It should be an anatomical resection based upon the blood supply to enable anastomosis of the colon.

Tumours of the caecum and ascending colon are removed by right hemicolectomy, removing as little as possible of the terminal ileum and as much as the ileo-caecal artery as is possible, while still maintaining the blood supply to the terminal ileum. More terminal ileum may need to be removed for tumours near the ileo-caecal valve, but vitamin B12 deficiency and bile salts diarrhoea are common complications if more than 50 cm is resected. Transverse colon tumours are removed by performing an extended right hemicolectomy. Tumours of the descending colon are removed by performing a left hemicolectomy and a sigmoid colectomy is performed for sigmoid tumours.

Rectal tumours are removed either by an anterior resection or an abdomino-perineal excision depending on the level of the tumour. The introduction of the circular stapling gun has allowed lower anastomosis to be performed and reduced the abdominal perineal resection rate.

Over the last 20 years rectal cancer surgery has improved with the introduction of the total mesorectal excision (TME). This technique improves rates of complete resection

and reduces local recurrence rates [Heald and Ryall, 1986]. The usual field of spread of rectal cancer is confined within the mesorectum which means that TME increases the probability of cure of rectal cancer. The local recurrence rate of TME is in the region of 4-5% with an overall recurrence rate of 18% at 5 years [MacFarlane et al., 1993].

Colorectal cancer can also be treated by local excision. This can either be performed via colonoscopy or via a transanal approach. Indications for potentially curative local excision include mobile tumours, T1 tumours (assessed by ultrasonography), well or moderately differentiated histology (determined by biopsy) and tumour size less than three cm. Relative indications include T2 and T3 tumours (by ultrasonography), and tumour size greater than three cm depending on patient fitness [Banerjee et al., 1995].

1.6.1 Emergency surgery

Approximately 30% of patients present as emergencies e.g. obstruction, perforation or bleeding. These patients tend to be old, have concomitant disease, spend longer in hospital and are more likely to have a permanent stoma. Therefore, postoperative morbidity and mortality (19% vs. 8%) is higher and survival is poorer (29% vs. 39% at five years) compared with patients presenting electively [Anderson et al., 1992;Scott et al., 1995;McArdle and Hole, 2004].

Historically, 20-30 years ago emergency operations were performed as a three stage procedure (colostomy then resection then closure of colostomy) but with improvements in operative technique and peri-operative care this approach has been

replaced by a two stage (Hartmann's) procedure or a resection and primary anastomosis. Studies fail to show a survival benefit from the one stage approach but there was a shorter hospital stay [Phillips et al., 1985;Buechter et al., 1988]. The SCOTIA study was a randomised trial comparing segmental resection to subtotal colectomy in obstructed distal colon cancers. It found that segmental resection provided better long term results especially in terms of function. They concluded that segmental resection following intraoperative irrigation is the preferred option except when there is caecal perforation or if synchronous neoplasms are present in the colon, when subtotal colectomy is more appropriate [SCOTIA., 1995].

1.6.3 Adjuvant Chemotherapy

The aim of giving adjuvant chemotherapy is to eradicate micrometastases and increase the rates of cure. In those patients who have Dukes C disease adjuvant chemotherapy with 5-flurouracil has been shown to have a 22% reduction in mortality [IMPACT, 1995;O'Connell et al., 1997]. This has lead to the recommendation that all patients with Dukes C disease should be offered adjuvant chemotherapy. However studies have shown that only about 45% of these patients receive chemotherapy because of comorbidities and patient choice [Schrag et al., 2001]. The value of adjuvant chemotherapy in patients with Dukes' B disease is less clear [IMPACT, 1999;Benson, III et al., 2004]. However in the subgroup of Dukes' B patients with high risk tumours some clinicians would advocate chemotherapy as they have a higher risk of relapse. There is however little hard evidence to support this.

Chemotherapy with fluorouracil and levamisole or fluorouracil and folinic acid is not without toxicity, but this usually consists only of mild nausea, mucositis, diarrhoea, and lethargy. Most of these toxicities are mild and can be controlled with modern antiemetic and antidiarrhoeal drugs [Slevin, 1996].

1.7 Prognostic factors in colorectal cancer

Traditionally prognosis of colorectal cancer was dependent on Dukes' stage and then subsequently TNM staging of the primary tumour. However it has been shown that there are a number of other prognostic factors which are used in decision making for adjuvant chemotherapy especially in those patients with stage II disease. Indeed current recommendations in the UK and USA suggest that those patients with stage II disease and poor prognostic factors should be considered for chemotherapy [NIH consensus conference, 1990;Association of Coloproctology for Great Britain and Ireland, 2001].

These prognostic factors include perforation or obstruction at presentation, Stage T4, poor differentiation, vascular invasion and inadequate node sampling [Burdy et al., 2001;Petersen et al., 2002].

There has also been a lot of work looking at biomarkers and their role in prognosis of colorectal cancer (especially stage II disease). A large review in 2003 split these biomarkers into six groups. These were cell proliferation indices (Ki-67, MIB-1, proliferating cell nuclear antigen); oncogenes/tumor suppressor genes (p53, K-ras, Deleted in Colorectal Cancer (DCC), Bcl-2, c-erbB2); DNA repair (microsatellite instability); markers of angiogenesis (vascular count, vascular endothelial growth factor); markers of invasion or metastasis (plasminogen-related molecules, matrix metalloproteinases); and biochemical markers (thymidylate synthase) [Graziano and Cascinu, 2003]. They concluded that current data did not provide sufficient evidence for the incorporation of available prognostic biomarkers into clinical practice.

However markers of altered DCC function have shown promising prognostic role and sufficient prevalence in retrospective investigations and they deserve further assessment in prospective studies.

Carcino Embryonic Antigen (CEA)

Carcino Embryonic Antigen (CEA) is a tumour marker which was first described in 1965 by Gold and Freedman [Gold and Freedman, 1965]. It is a member of the immunoglobulin superfamily with a role as an intracellular adhesion molecule. It has a role as a useful tumour marker in colorectal cancer.

Preoperatively there have been studies looking at its role as a prognostic factor. A large multivariate analysis of over 550 patients with node negative colorectal cancer showed that CEA is an independent prognostic factor. Indeed the conclusion was that an elevated CEA identifies a group of patients with a poorer prognosis and defines a subset who may benefit from chemotherapy [Harrison et al., 1997]. This observation has also been seen in node positive (Dukes' C) cancers [Wang et al., 2000]. However further studies have shown that an elevated CEA is associated with advanced disease but when controlled for stage, CEA is not a predictor of survival [Chapman et al., 1998].

Overall the various studies looking at preoperative CEA as a prognostic factor are conflicting and for this reason it is not used routinely. However, postoperatively CEA is used in two clinical situations. In patients receiving chemotherapy for metastatic colorectal cancer, CEA levels can help indicate disease progression or regression.

However there is no convincing evidence that CEA monitoring significantly affects either survival or quality of life [Macdonald, 1999].

The other situation when CEA is measured, and the area of most interest for CEA monitoring has been the potential for its use after curative resection. The aim of using CEA measurements is to detect cancer recurrence at an earlier stage when it might be more amenable to curative therapy. There is good evidence that routine CEA monitoring post resection of colon cancer detects metastatic disease on average 5 months before routine follow-up evaluation without CEA monitoring detects recurrence [McCall et al., 1994]. However, the overall cost-effectiveness of this approach is not clear, and convincing definition of the role of postoperative CEA monitoring awaits the results of large randomized clinical trials [Macdonald, 1999].

1.8 Host response to colorectal cancer

1.8.1 The acute phase response,

The systemic inflammatory response or acute phase response is a complex, non-specific rapid response to many types of tissue damage including tumour growth. It incorporates both systemic and local modifications of the normal physiology in an aim to control damage, clean up debris and start repair.

1.8.2 Inflammation

The four cardinal signs of inflammation are redness, swelling, heat and pain. These signs occur in the acute phase of the inflammatory response because of local release of inflammatory mediators resulting in an increase in capillary flow, leakage of plasma into the surrounding tissues and pain. This acute phase can be split into three separate phases: hyperaemia, exudation and emigration of leucocytes.

Following tissue injury, vasoactive mediators are released from tissue mast cells and parts of the vascular wall which cause vasoconstriction. This is followed by dilatation of precapillary arterioles, which increases the blood flow to the capillary beds. This causes the redness. Fluid then leaks into the intravascular space because of an increase in the permeability of the postcapillary venules which results in oedema and swelling.

These changes cause a relative increase in the concentration of blood cells in the vasculature, which causes a slowing of blood flow in the venules. This facilitates marginalisation of the lymphocytes and adherence of neutrophils to the vessel walls.

1.8.3 The acute phase response

The acute phase response is a term that has been used to encompass some or all of the physiological events that follow tissue damage and inflammation. In the acute phase response the synthesis of certain liver-derived proteins (the acute phase proteins) changes. The acute phase proteins have been defined as plasma proteins which increase in concentration by 25% or more in the first seven days following tissue damage [Kushner, 1982]. The measurement of these changes is important clinically in indicating the presence and severity of inflammation. Interleukin-6 (IL-6), interleukin-1 (IL-1) and tumour necrosis factor (TNF) have been shown to be the prime inducers of the hepatic acute phase proteins [Thompson et al., 1992]. The level of this inflammatory response is usually best seen by measuring C-reactive protein (CRP) because of large changes from its initial concentration in the presence of inflammation [Aronsen et al., 1972].

The development of this acute phase protein response in patients with cancer relates to the concentrations of circulating cytokines [Pepys and Baltz, 1983;Perlmutter et al., 1986]. Cytokines are polypeptides produced by blood monocytes and tissue macrophages in response to sepsis, trauma, and other inflammatory conditions such as Crohn's disease [Dinarello, 1984].

1.8.4 C-Reactive protein

C-reactive protein was first described in 1930 and was named due to its ability to bind to the C-polysaccharide in the pneumococcal cell wall. It is a non-specific positive acute phase protein which is secreted by the liver in response to a variety of inflammatory cytokines, mainly interleukin-6 (IL-6), interleukin-1 (IL-1) and tumour necrosis factor (TNF) [Du Clos, 2000]. Thus, the serum measurement of C-reactive protein is widely used to monitor the systemic inflammatory response and therefore the extent, activity and prognosis of various disease [Kolb-Bachofen, 1991].

C-reactive protein is a protein consisting of five non-glycosylated subunits which are encoded by a single gene on chromosome 1. C-reactive protein is upregulated by the local and systemic release of the pro-inflammatory cytokines especially interleukin-6. In the presence of calcium, C-reactive protein undergoes specific ligand binding to phosphocholine in autologus phospholipids and microbial polysaccharides. This activates the classical complement pathway opsonising ligands for phagocytosis. C-reactive protein also neutralises platelet –activating factor which is a potent inflammatory mediator having a down-regulatory effect on neutrophil function. It is thought that C-reactive protein may therefore contribute to host defence, modulation of inflammation and lipid metabolism [Pepys and Baltz, 1983;Pepys and Hirschfield, 2003].

The function of C-reactive protein is felt to be related to its role in the innate immune system. It activates complement, binds to Fc receptors and acts as an opsonin for various pathogens. Interaction of C-reactive protein with Fc receptors leads to the

generation of proinflammatory cytokines that enhance the inflammatory response. It is thought to act as a surveillance molecule for altered self and certain pathogens. This recognition provides early defence and leads to a proinflammatory signal and activation of the humoral, adaptive immune system [Du Clos, 2000;Pepys and Hirschfield, 2003].

The plasma concentration of C-reactive protein is mainly determined by its synthesis rate. In normal subjects the serum C-reactive protein concentrations are barely detectable with 99% of the normal population having levels below 10mg/l. Higher levels of C-reactive protein are abnormal. Levels of C-reactive protein increase very rapidly in response to trauma, inflammation, and infection and decrease just as rapidly with the resolution of the condition. After the onset of inflammation, C-reactive protein production increases within four to six hours, doubling every eight hours thereafter and peaks at approximately thirty six to fifty hours. Levels remain raised with continual inflammation and quickly return to normal once inflammation is resolved [Gabay and Kushner, 1999]. The sensitivity and rapid response of C-reactive protein to inflammation has lead to it becoming a useful tool in the monitoring of patients with inflammatory diseases [Werner et al., 2003;Vermeire et al., 2006].

Work, both recently and historically has looked at the link between the acute phase protein response and neoplasias including colorectal cancer. Activated white blood cells usually produce pro-inflammatory cytokines [Pepys and Baltz, 1983;Gabay and Kushner, 1999;Whiteside, 2003] and may act as growth factors for neoplasia [Dunlop

and Campbell, 2000]. There is also evidence that cancer cells themselves may produce pro-inflammatory cytokines as well [Balkwill and Mantovani, 2001;Whiteside, 2003].

It has also been shown the systemic inflammatory response is a strong predictor of tumour progression and survival independent of tumour stage in colorectal, gastric, pancreatic and lung cancer [Falconer et al., 1995;Nozoe et al., 1998;Fujita et al., 1999;Scott et al., 2002;Forrest et al., 2003;McMillan et al., 2003]. Also the presence of a systemic inflammatory response is associated with weight loss and a reduction in performance status in patients with lung cancer [Scott et al., 2002].

Specifically in colorectal cancer there have been numerous studies looking at the role of the systemic inflammatory response. The presence of a systemic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein, is associated with increased recurrence and poor survival, independent of Dukes' stage, in patients undergoing potentially curative surgery for colorectal cancer [McMillan et al., 1995;Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003].

1.8.5 Albumin

Albumin is a single polypeptide consisting of 585 amino acids with a molecular weight of approximately 66 248. It is a major negative acute phase protein. Serum albumin concentration is about 40g/l but the total albumin pool being in the region of 4-5g/kg of body weight [Margarson and Soni, 1998].

The main functions of albumin are maintenance of colloid osmotic pressure, as a result of its relatively low molecular weight compared to the other major intravascular proteins such as immunoglobulin, binding and transport, free radical scavenging, platelet function inhibition and antithrombotic effects and its effects on capillary membrane permeability [Margarson and Soni, 1998].

Traditionally the serum albumin level was seen as the standard way of assessing a patient's nutritional status. However, in diseased patients a decreased serum albumin is inevitably found and persisting changes are generally associated with a poor prognosis [Margarson and Soni, 1998]. It appears to be primarily mediated in the acute phase response by the altered protein and energy metabolism that occurs. In the acute phase response there is an increased demand for specific amino acids for mediator and acute phase protein synthesis and immune and antioxidant defences. This promotes the progressive loss of the available protein components including albumin. As the albumin pool size is modest in relation to body cell mass its loss is noticeable at an earlier stage [Fearon et al., 1998;Fearon et al., 1999;McMillan et al., 2001b].

It has long been recognised that there is an association between reduced serum albumin and elevated C-reactive protein concentrations with severity of illness and poor outcome. In malignant disease low albumin concentration and elevated C-reactive protein concentrations were more likely to occur in patients with inoperable or metastatic cancers than in patients with potentially curable early stage disease. This most probably reflects a larger tumour burden and subsequent poorer prognosis [Goransson et al., 1996;McMillan et al., 2001b].

In colorectal cancer it has been recognized that low serum albumin concentrations (<35g/l) are associated with a poorer outcome [Heys et al., 1998;Longo et al., 1998;Longo et al., 2000]. Of these studies Heys and colleagues looked at a cohort of over 400 patients and they showed that the presence of a low circulating concentration of albumin prior to surgery and the magnitude of the decrease were associated with poorer overall survival [Heys et al., 1998].

1.8.6 Interleukin-6

Interleukin-6 is a multifunctional proinflammatory cytokine which plays a major role in regulating the immune and inflammatory responses via the synthesis of most acute phase proteins including C-reactive protein. Elevated interleukin-6 production is seen in infectious disease, inflammatory diseases and malignant disease. It is produced by a number of different types of cells including immune cells, polymorphonuclear neutrophils, monocytes, B and T lymphocytes, mast cells, endothelial and mesothelial cells, fibroblasts, keratinocytes, some nerve cells and certain tumour cells [Gabay and Kushner, 1999].

In patients with colorectal cancer increased concentrations of serum interleukin-6 has been shown to reflect disease status and correlates with cancer stage. It is believed to be associated with malignant transformation and tumour progression by a paracrine or autocrine mechanism [Chung and Chang, 2003b].

1.8.7 Interleukin-10

Interleukin-10 (IL-10 or IL10), also known as human cytokine synthesis inhibitory factor (CSIF), is an anti-inflammatory cytokine, capable of inhibiting synthesis of pro-inflammatory cytokines like IFN-gamma, IL-2, IL-3, TNFα and GM-CSF by cells such as macrophages and Th1 cells. However, it is also stimulatory towards certain T cells, mast cells and B cells.

Recently, interleukin-10 has been recognised to be an important immunosuppressive cytokine for the Th1 anti-tumour response and may be important in determining tumour growth and metastases [Mocellin et al., 2005]. It has also been reported that interleukin-10 concentrations were increased in patients with primary operable colorectal cancer compared with age and sex matched normal subjects [Ordemann et al., 2002].

2.0 SUMMARY AND AIMS OF PROJECT

2.1 Summary

Colorectal cancer remains the second commonest cause of cancer death in Western Europe and North America. Overall survival is poor, even in those patients who undergo potentially curative resection, more than one third die within 5 years.

Traditionally colorectal cancer prognosis is predicted by looking at the pathology of the primary tumour. However, even in the cohort of patients who have had potentially curative surgery, a significant proportion will get recurrence of their disease.

Recent work has shown that there seems to be a relationship between cancer specific survival and the presence or absence of a systemic inflammatory response.

2.2 Aims of thesis

The aim of this thesis is to investigate the following in patients undergoing potentially curative surgery for colorectal cancer:

1. To establish the prognostic value of the pre-operative compared with the post-operative systemic inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.
2. To examine the pre-operative inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.

3. To examine the utility of the systemic inflammatory response as a guide to treatment in patient undergoing potentially curative surgery for colorectal cancer.

3.0 PRE- BUT NOT POST-OPERATIVE SYSTEMIC INFLAMMATORY RESPONSE CORRELATES WITH COLORECTAL CANCER SURVIVAL

3.1 Introduction

Colorectal cancer remains the second commonest cause of cancer death in Western Europe and North America. Each year in the UK, there are approximately 35,000 new cases and 16,000 deaths attributable to the disease [Cancer research UK, 2004]. Overall survival is poor. Many patients have evidence of locally advanced or metastatic disease at the time of presentation; even in those who undergo potentially curative resection, only half survive five years [McArdle and Hole, 2002].

In patients who undergo potentially curative resection there are a number of factors such as age, sex, deprivation, surgeon specialisation, tumour stage and post-operative complications which have been recognised to predict long term survival in colorectal cancer [Hodgson et al., 2001].

There is increasing evidence to show that the presence of a systemic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein, measured prior to surgery is associated with poor survival independent of Dukes' stage [Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003] and adjuvant therapy (Chapter 7), in patients undergoing potentially curative surgery for colorectal cancer. There is also evidence to suggest that elevated C-reactive protein concentration 4-6 months following surgery is associated with poor outcome in these patients [McMillan et al., 1995;McMillan et al., 2003].

There has also been a long-standing interest in whether the systemic inflammation as a result of surgery or bowel manipulation may act to enhance implantation and growth of circulating tumour cells or the growth of micrometastatic disease in colorectal cancer [DerHagopian et al., 1978;Nowacki and Szymendera, 1983;Mynster et al., 2000].

More recently there has been considerable interest in whether reducing the systemic inflammatory response immediately following colorectal cancer surgery either by minimally invasive surgical techniques [Stocchi and Nelson, 2005] or enhanced recovery protocols [Fearon et al., 2005] may not only improve post-operative outcome but also long term survival for cancer patients. However, the relationship between the magnitude of the immediate post-operative systemic inflammatory response and cancer specific survival has not been established. Moreover, the relationship between the pre- and immediate post-operative systemic inflammatory response has not, to our knowledge, been previously examined.

The aim of the present study was to examine the relationship between the pre- and the immediate post-operative C-reactive protein concentrations and long term survival in patients undergoing potentially curative resection for colorectal cancer.

3.2 Patients and Methods

Patients with histologically proven colorectal cancer who, on the basis of laparotomy findings and pre-operative abdominal computed tomography, were considered to have undergone a potentially curative resection between March 1999 and June 2004 in a single surgical unit at Glasgow Royal Infirmary and in whom C-reactive protein was measured in the pre and the immediate post-operative period were studied prospectively. The tumours were staged using the conventional TNM classification [Greene Fl et al., 2002]. Patients who had non-elective surgery or pre-operative radiotherapy or showed clinical evidence of infection or other inflammatory conditions were excluded from the study.

Blood samples were taken for routine laboratory measurement of C-reactive protein immediately prior to surgery and on post-operative days 1-4. The limit of detection of the assay was a C-reactive protein concentration lower than 5 mg/l. The coefficient of variation, over the range of measurement, was less than 5 per cent, as established by routine quality-control procedures.

Patient survival was defined as the time from surgery to the date of death. All patients were followed-up at a specialist colorectal cancer clinic. Information on date and cause of death was checked with that received by the Cancer Registry (Scotland).

The study was approved by the Research Ethics Committee, Royal Infirmary, Glasgow.

3.3 Statistics

Comparisons between groups of patients were carried out using contingency table analysis (X^2) as appropriate. The level for statistical significance was taken as a p-value <0.05. Grouping of the variables age and C-reactive protein was carried out using standard thresholds [O'Gorman et al., 2000;Scottish Cancer Intelligence Unit, 2000]. Survival analysis of the group variables was performed using the Cox proportional hazard model. Follow up continued until the close of the present study at the end of April, 2006. The proportional hazards assumption was tested by visual inspection of log minus log curves, and was found to be satisfied for all covariates. Multivariate survival analysis was performed using a stepwise backward procedure to derive a final model of the variables that had a significant independent relationship with survival. To remove a variable from the model, the corresponding p-value had to be >0.05. Correlations between two variables were calculated using Spearman's rank correlation test. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

3.4 Results

The baseline characteristics of the 180 patients who underwent potentially curative resection for colorectal cancer are shown in Table 3.1. The majority of patients were male, aged 65 years or more, had colonic tumours and had TNM stage I or II disease. Eighty (44%) patients had an elevated C-reactive protein concentration (>10 mg/l) and 16 (9%) patients had hypoalbuminaemia prior to surgery. Of the 16 patients with hypoalbuminaemia 15 (94%) had an elevated C-reactive protein concentration. Forty nine (27%) patients received adjuvant 5FU- based chemotherapy.

The C-reactive protein concentrations prior to surgery and during the post-operative period (days 1-4) are shown in Figure 3.1. The peak C-reactive protein concentration was on day 2 ($p<0.001$) and therefore was used in the survival analysis.

The minimum follow-up was 22 months; the median follow-up of the survivors was 40 months. During the course of the study 59 patients died, 30 patients of their cancer and 29 of intercurrent disease. Day 2 C-reactive protein concentrations were dichotomised; the median day 2 concentrations were 133 and 202mg/l respectively.

On univariate analysis, age ($p<0.01$), TNM stage ($p<0.01$) and pre-operative C-reactive protein concentration ($p<0.001$) were associated with overall survival (Table 3.1). On univariate analysis, TNM stage ($p<0.01$), pre-operative C-reactive protein concentration ($p<0.001$) and hypoalbuminaemia ($p<0.05$) were associated with cancer specific survival (Table 3.1). Postoperative C-reactive protein concentration was not associated with either overall or cancer-specific survival.

On multivariate analysis, age (p=0.044), TNM stage (p=0.003) and pre-operative C-reactive protein concentration (p=0.001) were independently associated with overall survival. On multivariate analysis, both TNM stage (p=0.002) and pre-operative C-reactive protein concentration (p<0.001) were independently associated with cancer specific survival.

The relationship between day 2 C-reactive protein concentrations and clinicopathological characteristics is shown in Table 3.2. The dichotomised groups of day 2 C-reactive protein were similar in terms of age, tumour site, TNM stage and hypoalbuminaemia. In contrast, with an increasing day 2 C-reactive protein there was an increase in the proportion of male patients (p<0.05) and patients with an elevated pre-operative C-reactive protein (p<0.10). Day 2 C-reactive protein concentrations were associated with pre-operative C-reactive protein concentrations (r^s=0.155, p=0.038).

With respect to the dichotomised day 2 C-reactive protein concentrations, the present study had approximately 80% power to detect hazard ratios of 2.0 for overall survival and 3.0 for cancer-specific survival [Lachin and Foulkes, 1986].

3.5 Discussion

In the present study, increasing TNM stage and an elevated pre-operative C-reactive protein concentration (>10mg/l) prior to surgery were independently associated with poorer cancer specific survival in patients undergoing potentially curative surgery for colorectal cancer. These results are consistent with previous studies that showed that an elevated C-reactive protein concentration had prognostic value independent of Dukes stage [Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003].

In contrast, in the present study the peak systemic inflammatory response to surgery, as defined by day 2 C-reactive protein, had no significant prognostic value. Also, although statistically significant, the correlation between pre- and post-operative C-reactive protein was low. This is perhaps unexpected since there is a general view that pre- and post-operative systemic inflammatory responses are linked and that the reduction of the magnitude of the systemic inflammatory response in the immediate post-operative period might improve long term survival [Lacy et al., 2002;Ng et al., 2005]. Our results do not preclude such an effect but suggest that it is likely to be much smaller than that of the pre-operative systemic inflammatory response.

The basis of the independent relationship between an elevated C-reactive protein concentration prior to surgery and poor survival in patients with primary operable colorectal cancer is not clear. A plausible explanation is that an elevated C-reactive protein concentration may reflect compromised cell mediated immunity since C-reactive protein is associated with lymphocytopenia [Nozoe et al., 2000;Crumley et al., 2006a] and an impaired T-lymphocytic response in the colorectal tumour [Canna et

al., 2005]. Alternatively, C-reactive protein is also associated with components of innate immune system including complement and this response may also be compromised [Du Clos and Mold, 2004;Ytting et al., 2006]. Therefore, the results of the present study would suggest that compromised immune function may occur prior to surgery and influences long term survival.

It is of interest that recently a number of workers have demonstrated a relationship between elevated C-reactive protein concentrations and increased cancer incidence, in particular colorectal cancer in apparently healthy individuals [Erlinger et al., 2004;Gunter et al., 2006;Otani et al., 2006]. Although it is not clear from these data whether elevated C-reactive protein concentrations give rise to or stimulate progression of colorectal cancer they suggest an important chronic role for C-reactive protein in the outcome of patients who develop colorectal cancer.

In summary, the results of the present study confirm that an elevated C-reactive protein concentration, prior to but not immediately after surgery, is associated with poor cancer specific survival in patients undergoing curative resection for colorectal cancer.

Table 3.1. Clinicopathological characteristics in patients undergoing potentially curative surgery for colorectal cancer: univariate survival analysis

		Patients	Survival Overall	p-	Survival Cancer specific	p-value
		180 (%)	HR (95% CI)	value	HR (95% CI)	
Age group	<65	56 (31)				
	65-74	58 (32)				
	≥75	66 (37)	1.55 (1.12-2.14)	0.009	1.47 (0.93-2.31)	0.096
Sex	Male	99 (55)				
	Female	81 (45)	1.03 (0.61-1.71)	0.925	1.04 (0.51-2.14)	0.905
Site	Colon	102 (57)				
	Rectum	78 (43)	1.13 (0.68-1.88)	0.642	0.57 (0.26-1.24)	0.158
Tumour	T1	7 (4)				
	T2	28 (15)				
	T3	102 (57)				
	T4	43 (24)	1.59 (1.09-2.31)	0.016	3.00 (1.65-5.47)	<0.001
Nodal involvement	N0	100 (56)				
	N1	62 (34)				
	N2	18 (10)	1.51 (1.08-2.12)	0.017	1.93 (1.21-3.07)	0.006
TNM stage	I	23 (13)				
	II	77 (43)				
	III	80 (44)	1.89 (1.23-2.91)	0.004	3.06 (1.52-6.20)	0.002
Pre-operative CRP						
	≤10mg/l	100 (56)				
	>10mg/l	80 (44)	2.57 (1.52-4.36)	<0.001	4.98 (2.13-11.6)	<0.001
Pre-operative Albumin	≥35g/l	155 (86)				
	<35g/l	16 (9)	1.88 (0.85-4.17)	0.119	2.72 (1.03-7.17)	0.043
Day 2 CRP (mg/l) dichotomised/ median (range)		133 (36-163) 202 (164-281)	1.29 (0.77-2.16)	0.326	1.33 (0.65-2.74)	0.431
Chemotherapy	No	131 (73)				
Yes		49 (27)	1.15 (0.65-2.02)	0.627	1.43 (0.67-3.05)	0.357

Table 3.2. The relationship between increasing day 2 C-reactive protein and clinicopathological characteristics in patients undergoing potentially curative resection for colorectal cancer.

	Day 2 C-reactive protein dichotomised (mg/l)		
	Median 133 (n= 92)	Median 202 (n= 88)	p-value
Age group (<65/ 65-74/ ≥75)	28/ 24/ 40	28/ 34/ 26	0.212
Sex (male/ female)	44/ 48	55/ 33	0.049
Site (colon/ rectum)	54/ 38	48/ 40	0.575
Tumour (T1/ T2/ T3/ T4)	4/ 14/ 54/ 20	3/ 14/ 48/ 23	0.615
Nodal involvement (N0/ N1/ N2)	48/ 39/ 5	52/ 23/ 13	0.809
TNM stage (I/ II/ III)	12/ 36/ 44	11/ 41/ 36	0.535
Pre-operative C-reactive protein (≤10/ >10mg/l)	57/ 35	43/ 45	0.078
Pre-operative Albumin (≥35/ <35g/l)	78/ 8	77/ 8	0.980
Adjuvant chemotherapy (No/ Yes)	68/ 24	63/ 25	0.727

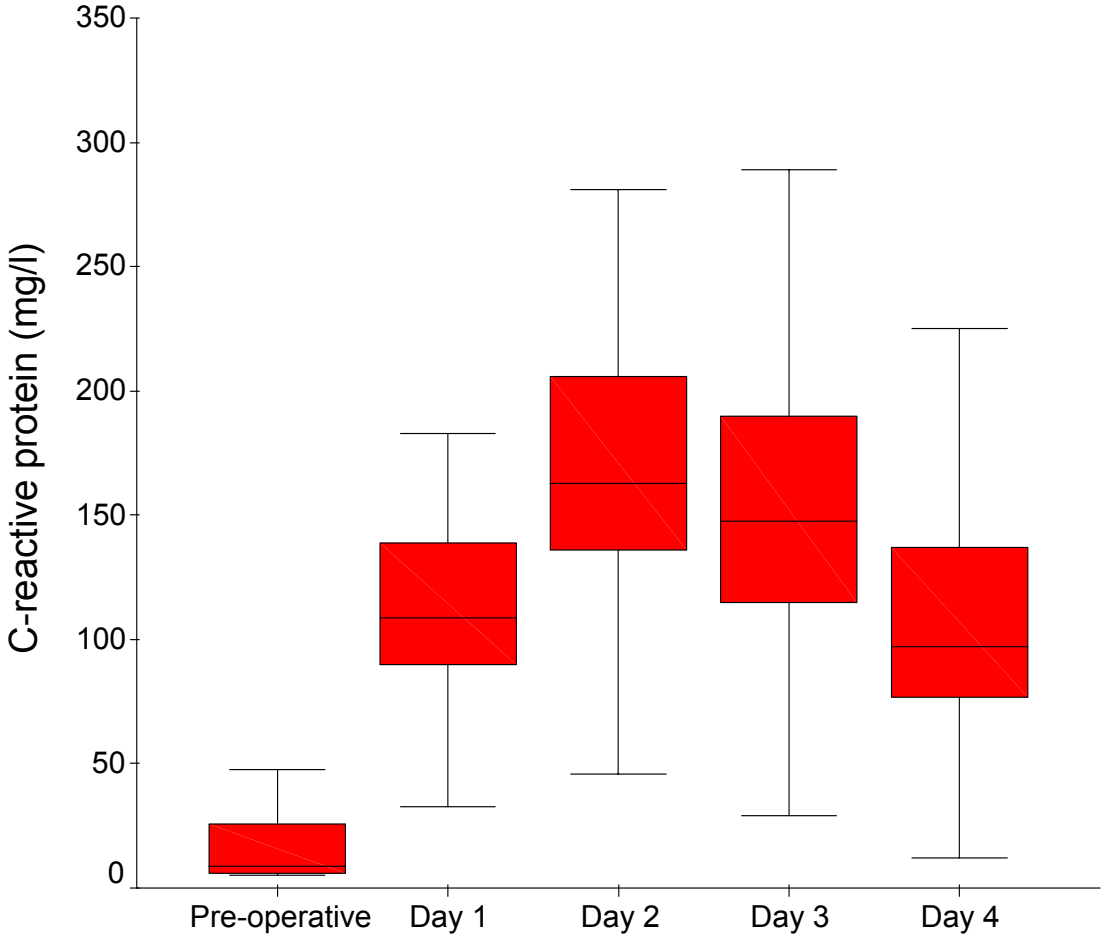

Figure 3.1. The peri-operative profile of circulating C-reactive protein concentrations in patients undergoing potentially curative resection for colorectal cancer.

4.0 TUMOUR SIZE IS ASSOCIATED WITH THE SYSTEMIC INFLAMMATORY RESPONSE BUT NOT SURVIVAL IN PATIENTS WITH PRIMARY OPERABLE COLORECTAL CANCER

4.1 Introduction

At present, predicting the likely outcome following surgery with curative intent for patients with colorectal cancer is based predominantly on examination of the primary tumour and associated lymph nodes. However, whilst TNM stage is widely used, it fails to provide clear separation between those patients who will eventually succumb to the disease from those who are cured. It is therefore of interest that it has been shown that the presence of a systemic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein pre-operatively, is associated with increased recurrence and poor survival in patients undergoing potentially curative surgery for colorectal cancer [Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003;Canna et al., 2004].

Pre-operatively, there are two possible explanations of the relationship between the systemic inflammatory response and the malignant potential of the tumour. Firstly, that the systemic inflammatory response is associated with a compromised immune response or secondly that the tumour expresses factors which stimulate growth and dissemination of tumour cells. If the latter were the case then it might be expected that C-reactive protein concentrations would be directly related to tumour size.

It is therefore of interest that age, tumour site and tumour diameter have all been reported to be associated with elevated C-reactive protein concentrations prior to surgery [Nozoe et al., 1998;Chung and Chang, 2003a]. However, these studies included patients with metastatic disease and this may have been a confounding factor in their observations. The aim of the present study was therefore to examine the relationship between tumour diameter, C-reactive protein concentrations and survival in patients undergoing potentially curative surgery for colorectal cancer.

4.2 Patients and Methods

Patients with histologically proven invasive colorectal cancer who presented electively and who on the basis of laparotomy findings and pre-operative abdominal computed tomography, were considered to have undergone a potentially curative resection between January 1999 and June 2004 in a single surgical unit at Glasgow Royal Infirmary were included in the study. Patients who had pre-operative radiotherapy were excluded from the study.

Tumours were classified according to site; carcinomas arising at the rectosigmoid junction were classified as rectal cancers. Tumour size was determined by the maximal diameter of the fixed tumour specimen at the time of pathological reporting. The extent of tumour spread was assessed by TNM stage based on histological examination of the resected specimen [Greene Fl et al., 2002].

A blood sample was taken for routine laboratory measurement of C-reactive protein measurement immediately prior to surgery. At this time no patient showed clinical evidence of infection or other inflammatory condition. The limit of detection of the assay was a C-reactive protein concentration lower than 5 mg/l. The coefficient of variation, over the range of measurement, was less than 5 per cent, as established by routine quality-control procedures.

The study was approved by the Research Ethics Committee, Royal Infirmary, Glasgow.

4.3 Statistics

Comparisons between groups of patients were carried out using contingency table analysis (X^2) for trend. Grouping of the variables, age and C-reactive protein, was carried out using standard thresholds [O'Gorman et al., 2000;Scottish Cancer Intelligence Unit, 2000]. Survival (cancer-specific) analysis was performed using the Cox proportional hazard model. Deaths up to May 2005 have been included in the analysis. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

4.4 Results

Two hundred and twenty seven patients undergoing potentially curative resection for colorectal cancer were studied. The majority of patients were aged 65 years or more, had colonic tumours and had TNM stage I/ II disease. Ninety six (42%) patients had an elevated C-reactive protein concentration (>10 mg/l) prior to surgery. A total of 58 patients received 5-FU-based chemotherapy.

Patients were grouped according to tertiles of the tumour diameter (Table 4.1). The groups were similar in terms of age (p=0.477), sex (p=0.802), tumour site (p=0.281), presence of ulceration (p=0.961), degree of differentiation (p=0.148), the presence of venous invasion (p=0.556), nodal involvement (p=0.448), TNM stage (p=0.870) and adjuvant therapy (p=0.609). Increasing tumour diameter was associated with T stage (p<0.001), and an elevated C-reactive protein concentration (p<0.001). The relationship between tumour diameter and C-reactive protein concentration was similar in the colon (r_s= 0.53, p<0.001) and rectum (r_s= 0.36, p<0.001, Figure 4.1).

The minimum follow-up was 12 months; the median follow-up of the survivors was 33 months. During this period 55 patients died, 30 patients of their cancer and 25 of intercurrent disease. On univariate survival analysis, increased age (p=0.050), TNM stage (p=0.005) and elevated circulating C-reactive protein concentrations (p<0.001, Figure 4.2) were associated with poorer cancer-specific survival. Tumour diameter (tertiles) was not associated with cancer specific survival (p=0.998, Figure 4.3).

4.5 Discussion

The results of the present study show that maximal tumour diameter is directly associated with circulating concentrations of C-reactive protein prior to curative surgery in patients with colorectal cancer. This observation was independent of age, sex, site of disease and the tumour histological characteristics. This is in contrast to previous reports that have shown that such elevated circulating C-reactive protein concentrations in colorectal cancer were not only associated with increased tumour diameter but also venous invasion and lymph node metastases [Nozoe et al., 1998;Chung and Chang, 2003a]. However, these previous studies included patients with metastatic disease.

In the present study increasing tumour diameter was not significantly associated with poor survival. This probably reflects the fact that tumour diameter was not associated with either venous invasion or nodal involvement which are recognised to be major determinants of cancer survival in patients undergoing potentially curative resection for colorectal cancer [Greene Fl et al., 2002].

Although the results of the present study are consistent with the concept that the tumour expresses factors which stimulate C-reactive protein production, they do not appear to be consistent with the hypothesis that the increased production of such factors by larger tumours increase the malignant potential of the tumour, since an elevated pre-operative C-reactive protein concentration has prognostic value whereas tumour diameter has not.

It may be that the relationship between increasing tumour diameter and elevated concentrations of C-reactive protein may simply reflect, in general, a more profound failure of the immunological response in patients with large tumours. Indeed, this would be consistent with the observations that an elevated C-reactive protein concentration several months after curative surgery for colorectal cancer is also associated with poor outcome [McMillan et al., 1995;McMillan et al., 2003]. Moreover, that elevated concentrations of C-reactive protein appear to be associated with a compromised immune response in such patients [Nozoe et al., 2000;Canna et al., 2005]. Therefore, a plausible explanation of the results of the present study is that the compromised immunological response is more closely related to subsequent cancer dissemination and thus poor cancer specific survival than large tumour size.

In the present study the relationship between pre-operative C-reactive protein and tumour diameter was similar in patients with colon cancer and those with rectal tumours that had not been irradiated. The reasons for excluding patients who had irradiated rectal tumours were that tumour size could not be assessed in most of the post radiotherapy specimens and that the relationship between C-reactive protein and tumour diameter was likely to have been altered.

In summary, the results of the present study show that, prior to surgery, the maximal tumour diameter is associated with an elevated pre-operative C-reactive protein concentration but not survival in patients with primary operable colorectal cancer.

Table 4.1. The relationship between tumour diameter, clinicopathological characteristics and C-reactive protein in patients undergoing curative resection for colorectal cancer.

	Tumour diameter (mm)			
	Tertile 1 Median= 30 (n= 76)	Tertile 2 Median= 45 (n= 76)	Tertile 3 Median= 60 (n= 75)	p-value
Age group (<65/ 65-74/ ≥75)	21/ 29/ 26	25/ 25/ 26	20/ 23/ 32	0.477
Sex (male/ female)	41/ 35	40/ 36	42/ 33	0.802
Site (colon/ rectum)	45/ 31	34/ 42	51/ 24	0.281
Tumour characteristics				
Ulceration (No/ yes)	57/ 19	53/ 23	56/ 19	0.961
Differentiation (well/ moderate/ poor)	43/ 25/ 8	46/ 21/ 9	34/ 29/ 12	0.148
Venous invasion (No/ yes)	55/ 21	55/ 21	51/ 24	0.556
Tumour (T1/ T2/ T3/ T4)	8/ 13/ 43/ 12	1/ 14/ 39/ 22	0/ 2/ 51/ 22	<0.001
Nodal involvement (N0/ N1/ N2)	41/ 30/ 5	39/ 24/ 13	50/ 17/ 8	0.448
TNM stage (I/ II/ III)	13/ 28/ 35	9/ 30/ 37	2/ 48/ 25	0.870
Adjuvant therapy (no/ yes)	56/ 20	55/ 21	58/ 17	0.609
C-reactive protein (mg/l)[a]	6 (<5-31)	6 (<5-120)	29 (<5-209)	<0.001[b]
C-reactive protein (≤10/ >10mg/l)	62/ 14	52/ 24	17/ 58	<0.001

[a] median (range), [b] Kruskal-Wallis test

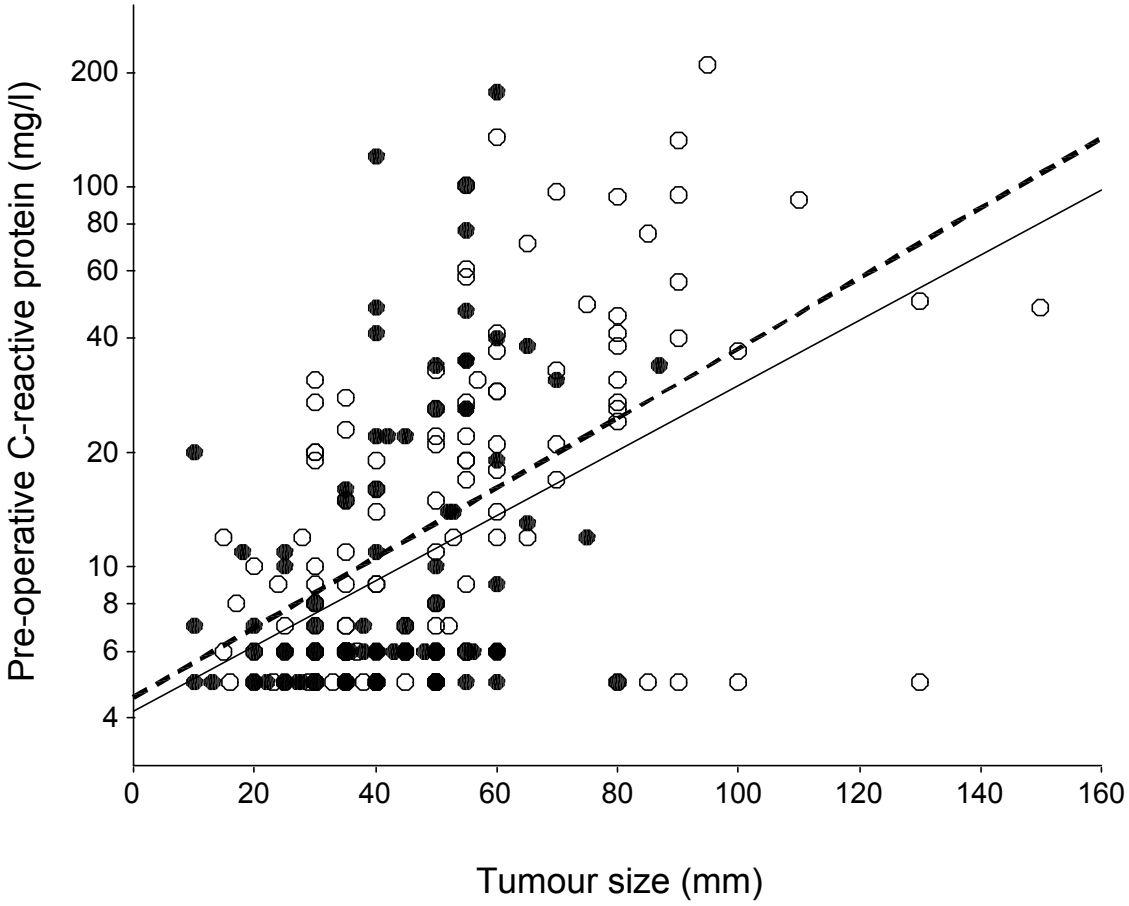

Figure 4.1. The relationship between tumour diameter and pre-operative C-reactive protein concentrations in patients undergoing potentially curative surgery for cancer of the colon (unfilled) and rectum (filled) with lines of best fit for colon (—) and rectum (- - -).

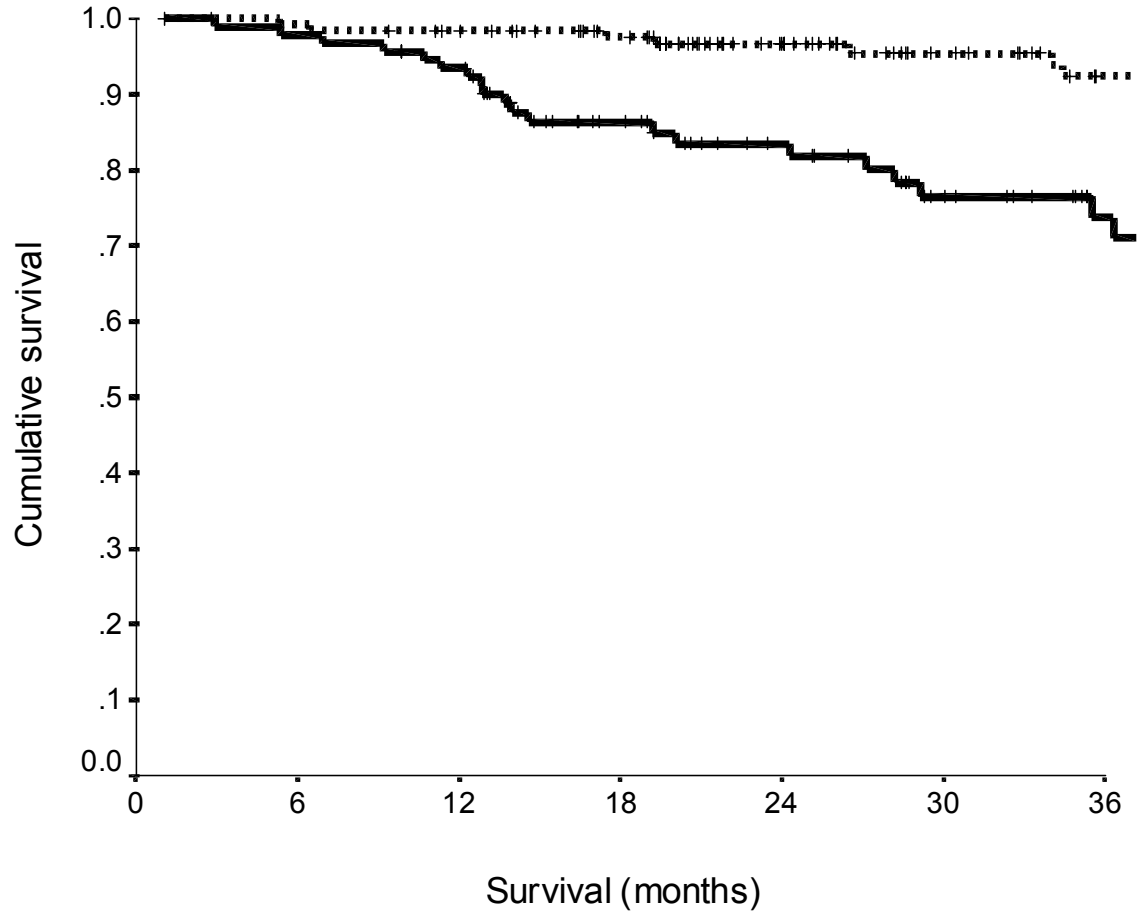

Figure 4.2. The relationship between pre-operative C-reactive protein concentrations (≤10/ >10mg/l from top to bottom) and survival in patients undergoing potentially curative surgery for colorectal cancer.

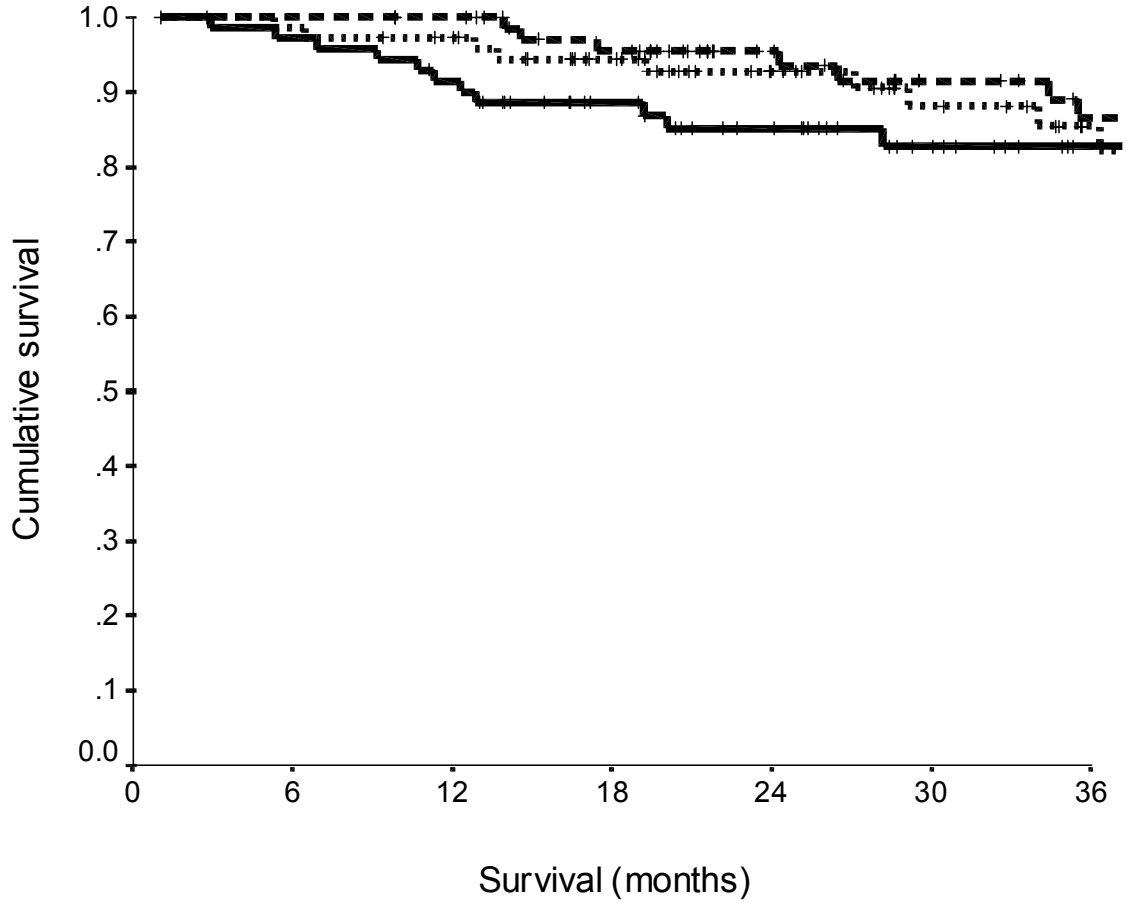

Figure 4.3. The relationship between tumour diameter (tertiles 2, 1, 3 from top to bottom) and survival in patients undergoing potentially curative surgery for colorectal cancer.

5.0 THE RELATIONSHIP BETWEEN EMERGENCY PRESENTATION, THE SYSTEMIC INFLAMMATORY RESPONSE AND CANCER SPECIFIC SURVIVAL IN PATIENTS UNDERGOING POTENTIALLY CURATIVE SURGERY FOR COLORECTAL CANCER

5.1 Introduction

It has long been recognized that emergency presentation is associated with high postoperative mortality rate [Phillips et al., 1985;Scott et al., 1995;McArdle and Hole, 2004]. Furthermore, not only is emergency presentation associated with higher post-operative mortality but, compared to those who undergo elective curative resection, there is also a reduction in overall and cancer specific survival [Scott et al., 1995;McArdle and Hole, 2004].

The reasons for the increase in cancer specific mortality in those who present as an emergency are not clear. However, the presence of a systemic inflammatory response prior to surgery, as evidenced by an elevated C-reactive protein concentration or hypoalbuminaemia, predicts overall and cancer specific survival, independent of stage, in patients undergoing potentially curative resection for colorectal cancer [Heys et al., 1998;Nielsen et al., 2000;McMillan et al., 2003;McMillan et al., 2007].

We have recently combined C-reactive protein and albumin to form a new score, the Glasgow Prognostic score (GPS, recently modified to mGPS), which has prognostic value, independent of stage, in patients with advanced or primary operable cancer [Forrest et al., 2003;McMillan et al., 2007]. Since it is likely that emergency

presentation would be associated with a pre-operative systemic inflammatory response, it may be that the mGPS might explain the impact of emergency presentation on cancer specific survival [McArdle et al., 2006].

To our knowledge this relation has not been previously examined. Therefore, the aim of the present study was to examine the relationship between emergency presentation, the pre- operative mGPS and cancer specific survival in patients undergoing curative resection for colorectal cancer.

5.2 Patients and Methods

Patients with histologically proven colorectal cancer who, on the basis of laparotomy findings and preoperative abdominal computed tomography, were considered to have undergone a potentially curative resection between March 1999 and May 2005 in a single surgical unit at Glasgow Royal Infirmary and in whom C-reactive protein and albumin were measured prior to surgery were included in the study.

For the purpose of this analysis, outcome in patients who presented as an emergency with evidence of blood loss, obstruction or perforation was compared with those patients admitted for elective surgery [McArdle et al., 2006].

The extent of deprivation was defined using the Carstairs deprivation index [Carstairs and Morris, 1991]. This is an area-based measure derived from the 1991 census, using the postcode of residence at diagnosis, which divides the score into a seven-point index. For illustrative purposes, the results are presented by amalgamating the seven categories into three groups: affluent (categories 1 and 2), intermediate (categories 3–5) and deprived (categories 6 and 7). The Carstairs deprivation index has been extensively utilised in cancer patients and is particularly appropriate for use in the central belt of Scotland [Hole and McArdle, 2002].

The tumours were staged using the conventional TNM classification [Greene Fl et al., 2002]. Patients who had neo-adjuvant therapy or who died within 30 days of surgery were excluded from the study. The study was approved by the Research Ethics Committee, Royal Infirmary, Glasgow.

Methods

Routine laboratory measurements of C-reactive protein and albumin at the time of diagnosis were carried out. The limit of detection of the C-reactive protein assay was <6mg/l and a value greater than 10mg/l was considered to indicate the presence of a systemic inflammatory response [McMillan et al., 2003]. The coefficients of variation of these methods, over the range of measurements, was less than 5% as established by routine quality control.

The GPS was constructed as previously described [Forrest et al., 2003]. Briefly, patients with both an elevated C-reactive protein (>10 mg/l) and hypoalbuminaemia (<35g/l) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0.

Recently, this has been modified based on evidence that hypoalbuminaemia, in patients without an elevated C-reactive protein concentration, had no significant association with cancer specific survival. Therefore, patients with an elevated C-reactive protein were assigned a modified GPS score (mGPS) of 1 or 2 depending on the absence or presence of hypoalbuminaemia [McMillan et al., 2007].

5.3 Statistics

Comparisons between groups of patients were carried out using contingency table analysis (X^2) as appropriate. Survival analysis of the group variables was performed using the Cox proportional hazard model. Deaths to the end of November 2006 were included in the analysis. Multivariate survival analysis was performed using a stepwise backward procedure to derive a final model of the variables that had a significant independent relationship with survival. To remove a variable from the model, the corresponding p-value had to be >0.10. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

5.4 Results

The baseline characteristics of the 261 patients who underwent potentially curative resection for colorectal cancer are shown in Table 5.1. The majority of patients were male, aged 65 years or more, were deprived, had colonic tumours and had TNM stage I or II disease.

One hundred and twenty one (46%) patients had an elevated C-reactive protein concentration (>10 mg/l) and 31 (12%) patients had hypoalbuminaemia prior to surgery. Of the 31 patients with hypoalbuminaemia, 27 (87%) had an elevated C-reactive protein concentration. Seventy three (28%) patients received adjuvant 5FU-based chemotherapy.

Thirty eight patients (15%) presented as emergencies. Of those patients who presented as an emergency, 11 patients presented with blood loss, 15 patients with obstruction and 12 patients presented with perforation. In the emergency group, there were fewer rectal tumours ($p<0.001$), tumour stage was greater ($p<0.01$), more patients had an elevated mGPS ($p<0.001$) and more patients received adjuvant therapy ($p<0.05$).

The minimum follow-up was 18 months; the median follow-up of the survivors was 40 months. In those patients who presented electively, 32 died of their cancer and 28 of intercurrent disease. In those patients who presented as an emergency, 16 died of their cancer and none of intercurrent disease ($p<0.001$).

On univariate analysis, emergency presentation ($p<0.001$), age ($p<0.01$), tumour site ($p<0.05$), TNM stage ($p<0.001$), C-reactive protein ($p<0.001$), albumin ($p<0.001$) and the mGPS ($p<0.0001$) were associated with cancer specific survival (Table 5.2).

On multivariate analysis including emergency presentation, age, sex, deprivation, tumour site, TNM stage, the mGPS and adjuvant chemotherapy as covariates, emergency presentation ($p<0.05$), age ($p<0.05$), TNM stage ($p<0.001$) and the mGPS ($p<0.001$) were independently associated with cancer specific survival (Table 5.2). When the mGPS was excluded from the multivariate analysis, emergency presentation (HR 2.47, 95%CI 1.32-4.63, p=0.0046), increased age (HR 1.71, 95%CI 1.20-2.46, p=0.0034) and more advanced TNM stage (HR 2.57, 95%CI 1.50-4.41, p=0.0006) were independently associated with poorer cancer specific survival.

Using cancer-specific mortality as an endpoint, the area under the receiver operator curve was 0.651 (95% CI, 0.570–0.731; p=0.001) for TNM stage and 0.665 (95% CI, 0.576–0.753; $p<0.001$) for the mGPS.

5.5 Discussion

In the present study, in patients undergoing potentially curative surgery for colorectal cancer, emergency presentation was associated with poorer cancer specific survival, independent of TNM stage. These results are consistent with our previous study of 3,200 patients which showed that, even after excluding deaths within 30 days of surgery, emergency presentation was independently associated with a two fold decrease in cancer specific survival [McArdle and Hole, 2004].

We have also shown, for the first time, that emergency presentation is associated with the presence of a systemic inflammatory response prior to surgery, as evidenced by elevated concentrations of C-reactive protein, hypoalbuminaemia and therefore an elevated mGPS.

Furthermore, on multivariate survival analysis, an elevated mGPS weakened emergency presentation as a significant predictor of survival. This would be consistent with the hypothesis that the deleterious impact of emergency presentation on cancer specific survival, in patients undergoing potentially curative surgery for colorectal cancer, is in part due to and associated with the presence of a systemic inflammatory response prior to surgery [McArdle and Hole, 2004;McArdle et al., 2006].

The basis of the independent relationship between an elevated mGPS prior to surgery and poor survival in patients with primary operable colorectal cancer is not clear. A plausible explanation is that an elevated mGPS may reflect compromised cell

mediated immunity since an elevated C-reactive protein and hypoalbuminaemia are associated with lymphocytopenia [Nozoe et al., 2000] and an impaired T-lymphocytic response in the tumour [Canna et al., 2005]. Furthermore, the presence of an elevated C-reactive protein concentration and hypoalbuminaemia have also been shown to be associated with upregulation of components of innate immune system, including complement and macrophage function [Du Clos and Mold, 2004;Ytting et al., 2006]. Therefore, these results would suggest that immune function is compromised prior to surgery, resulting in disease progression and poorer long term survival. Moreover, we have shown that the mGPS compares favourably with TNM stage in predicting cancer specific survival and therefore the systemic inflammatory response should also be assessed in patients undergoing potentially curative surgery for colorectal cancer.

It is of interest to speculate on the temporal relationship between these events. Does the pathophysiology of emergency presentation lead to a systemic inflammatory response which in turn results in poor cancer specific survival? Alternatively, does an impaired immune response lead to emergency presentation and poor survival? In the present study, emergency presentation was associated with increased T stage but not nodal involvement. It would therefore appear that the former explanation is more likely; namely that emergency presentation leads to a systemic inflammatory response, impaired immune response and poor cancer specific survival.

In summary, the results of the present study suggest that the presence of systemic inflammatory response prior to surgery may account for the deleterious effect of emergency presentation on cancer specific survival in patients undergoing potentially curative surgery for colorectal cancer.

Table 5.1. Clinicopathological characteristics in patients undergoing potentially curative surgery for colorectal cancer according to mode of presentation (n= 261).

		Elective	Emergency	p-value
		n= 223 (%)	n= 38 (%)	
Age group	<65 years	70 (31)	14 (36)	
	65-74 years	76 (34)	11 (30)	
	≥75 years	77 (35)	13 (34)	0.688
Sex	Male	121 (54)	23 (61)	
	Female	102 (46)	15 (39)	0.474
Deprivation	Affluent (1, 2)	8 (4)	0 (0)	
	Intermediate (3, 4, 5)	93 (42)	13 (34)	
	Deprived (6, 7)	122 (55)	25 (66)	0.134
Site	Colon	133 (60)	34 (90)	
	Rectum	90 (40)	4 (10)	<0.001
Tumour	T1	10 (4)	1 (3)	
	T2	35 (16)	1 (3)	
	T3	125 (56)	19 (50)	
	T4	53 (24)	17 (44)	0.005
Nodal involvement	N0	130 (58)	18 (47)	
	N1	68 (31)	15 (40)	
	N2	25 (11)	5 (13)	0.289
TNM stage	I	33 (15)	0 (0)	
	II	97 (43)	18 (47)	
	III	93 (42)	20 (53)	0.032
C-reactive protein	≤10mg/l	130 (58)	10 (26)	
	>10mg/l	93 (42)	28 (74)	<0.001
Albumin	≥35g/l	201 (90)	29 (76)	
	<35g/l	22 (10)	9 (24)	0.015
mGPS	0	130 (58)	10 (26)	
	1	74 (33)	20 (53)	
	2	19 (8)	8 (21)	<0.001
Adjuvant therapy	No	167 (75)	21 (55)	
	Yes	56 (25)	17 (45)	0.013

Table 5.2. Clinicopathological characteristics and cancer specific survival in patients undergoing potentially curative surgery for colorectal cancer

	Survival analysis			
	Univariate Hazard ratio (95% CI)	p-value	Multivariate Hazard ratio (95% CI)	p-value
Presentation (elective/ emergency)	2.90 (1.59-5.29)	0.0005	1.93 (1.02-3.66)	0.0422
Age group (<65/ 65-74/ ≥75)	1.70 (1.18-2.45)	0.0041	1.53 (1.08-2.18)	0.0173
Sex (male/ female)	0.85 (0.48-1.51)	0.5745		0.1793
Deprivation (affluent/ intermediate/ deprived)	0.95 (0.80-1.13)	0.5835		0.3852
Site (colon/ rectum)	0.45 (0.22-0.90)	0.0244		0.2859
TNM stage (I/ II/ III)	2.48 (1.49-4.14)	0.0005	3.07 (1.73-5.44)	0.0001
mGPS (0/ 1/ 2)	2.33 (1.59-3.41)	<0.0001	2.22 (1.43-3.46)	0.0004
Adjuvant therapy (no/ yes)	1.11 (0.60-2.05)	0.7030		0.7644

6.0 THE RELATIONSHIP BETWEEN C-REACTIVE PROTEIN, INTERLEUKIN-6, INTERLEUKIN-10 AND LYMPHOCYTE SUBPOPULATIONS IN PATIENTS UNDERGOING POTENTIALLY CURATIVE RESECTION FOR COLORECTAL CANCER

6.1 Introduction

It has recently become clear that the systemic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein, prior to surgery, is an important prognostic factor independent of tumour stage in patients undergoing potentially curative surgery for colorectal cancer [Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003;Canna et al., 2004;Miki et al., 2004] (see Chapter 3).

The basis of the independent relationship between an elevated C-reactive protein concentration and poor cancer specific survival in colorectal cancer is not clear. Specifically, it is not clear whether the systemic inflammatory response arises from the tumour per se or as a result of an impaired immune cytokine response. However, given the prognostic value of an elevated C-reactive protein concentration remains following potentially curative resection for colorectal cancer [McMillan et al., 1995;McMillan et al., 2003] this would suggest an impaired immune cytokine response.

Interleukin-6 and interleukin-10 are likely to be key cytokines in such a response as they appear to have key stimulant and suppressive actions, on T-lymphocytes and macrophages [Gabay and Kushner, 1999;Jee et al., 2001;Trikha et al., 2003a].

Moreover, interleukin-6 is recognised as an autocrine growth factor for a number of common solid tumours [Trikha et al., 2003b]. Recently, interleukin-10 has been recognised to be an important immunosuppressive cytokine for the Th1 anti-tumour response and may be important in determining tumour growth and metastases [Mocellin et al., 2005]. Therefore, it is of interest that Ordemann and co-workers reported that interleukin-6 and interleukin-10 concentrations were increased in patients with primary operable colorectal cancer compared with age and sex matched normal subjects [Ordemann et al., 2002].

In colorectal cancer patients it has long been recognised that, on simple staining of tumour sections, the presence of a pronounced lymphocytic infiltration within the tumour is associated with improved survival [Jass et al., 1987;Ropponen et al., 1997;Nielsen et al., 1999]. More recently, the ability to identify lymphocyte subsets by immunohistochemistry has led to renewed interest in the relationship between the tumour inflammatory infiltrate and outcome. Indeed, increased infiltration of the tumour by CD8+ [Naito et al., 1998] and CD4+ T-lymphocytes [Ali et al., 2004] has been shown to be associated with increased survival in patients with colorectal cancer. Recently, it has been reported that a low tumour CD4+ lymphocyte infiltration was weakly associated with an elevated circulating C-reactive protein concentration, both predicted poor cancer-specific survival on univariate analysis but only C-reactive protein on multivariate analysis [Canna et al., 2005].

It is therefore of interest that poor cell mediated immunity [Berghella et al., 1996;King et al., 1997] and specifically lower circulating CD4+ T-lymphocytes numbers were associated with metastatic colorectal cancer compared with primary operable disease

[Arista et al., 1994]. Furthermore, following curative resection of primary operable colorectal cancer lower circulating CD4+ T-lymphocytes were associated with increased recurrence [McMillan et al., 1997]. There is also some evidence that circulating lymphocytes numbers are lower in colorectal cancer patients with an elevated C-reactive protein concentration [Nozoe et al., 2000]. However to date, the relationship between the systemic inflammatory response, circulating concentrations of interleukin-6 and interleukin-10 and circulating lymphocyte subsets in patients with colorectal cancer does not appear to have been reported.

The aim of the present study was to examine these interrelationships in patients undergoing potentially curative resection for colorectal cancer.

6.2 Patients and Methods

Patients with histologically proven colorectal cancer who, on the basis of laparotomy findings and preoperative abdominal computed tomography, were considered to have undergone a potentially curative resection between April 2004 and November 2006 in a single surgical unit at Glasgow Royal Infirmary were studied prospectively. The tumours were staged using the International Union Against Cancer tumour node metastasis (TNM) classification [Greene Fl et al., 2002]. Patients who had non-elective surgery or preoperative radiotherapy, or who showed clinical evidence of infection or other inflammatory conditions were excluded from the study.

Experimental design

Blood samples were collected, prior to surgery for routine laboratory analysis of white cell and lymphocyte counts, albumin and C-reactive protein. The limit of detection of the assay was a C-reactive protein concentration lower than 6mg/l. The coefficients of variation of these methods, over the range of measurements, were less than 10% as established by routine quality control procedures.

A further blood sample was taken, centrifuged, and the serum stored at $-80^{o}C$ prior to analysis of interleukin-6 and interleukin-10. Circulating concentrations of these cytokines were measured using an enzyme linked immunosorbent assay (ELISA) technique. The minimum detectable concentrations were 2 pg/ml for interleukin-6 and 4pg/ml for interleukin-10 (Quantikine ELISA, R&D Systems Europe Ltd, Abingdon, UK). Inter- and intra-assay variability was less than 10% for both assays. Cytokine

concentrations below the threshold of sensitivity of the respective assays were expressed as equal to this threshold.

A pre-operative blood sample was also taken for analysis of circulating T-lymphocyte subset populations. The T-lymphocyte subsets were analysed on a FACScanto flow cytometry (BD Bioscience, Oxford, UK) equipped with a 488-nm argon laser and a 635-nm red diode laser using FACScanto software. The monoclonal antibodies used were CD3 FITC / CD4 PE / CD3 PenCPCy 5.5 / CD8 APC and CD3 FITC / CD19 PE / CD16+ 56 PenCPCy 5.5 / CD45 APC (BD Bioscience Oxford, UK). Absolute counting was performed on a single platform using TruCOUNT tubes.

The Research Ethics Committee of North Glasgow NHS Trust approved the study.

6.3 Statistics

Data are presented as median and range. Comparisons between groups of patients were carried out using contingency table analysis (X^2) for trend. Grouping of the variables, age, C-reactive protein, albumin, interleukin-6, and interleukin-10 was carried out using standard thresholds [Scottish Cancer Intelligence Unit, 2000;McMillan et al., 2001a;Ramsey et al., 2006]. Lymphocyte subsets were grouped according to the laboratory defined lower limit of the normal reference range. Cytokine concentrations below the threshold of sensitivity of the respective assays were expressed as equal to this threshold. Where appropriate, data were tested for statistical significance using Mann–Whitney U test. As the distribution of C-reactive protein and the cytokines were skewed, they were logarithmically transformed before stepwise multiple regression analysis for the examination of independent associations with C-reactive protein. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

6.4 Results

The pre-operative characteristics of patients (n= 53) who underwent potentially curative resection for colorectal cancer, according to the presence of a systemic inflammatory response are shown in Table 6.1. The majority of patients were male, aged 65 years or more, had colonic tumours, had TNM stage I or II disease and had a C-reactive protein concentration in the normal range. The majority of patients had albumin, interleukin-6 and interleukin-10 concentrations in the normal range. Also, the majority of patients had white cell, lymphocyte and lymphocyte subpopulation counts in the normal range.

The patients were grouped according to TNM stage (Table 6.1). The groups were similar in terms of age, sex, site, C-reactive protein, albumin, interleukins 6 and 10, white cell count and lymphocyte subpopulation counts between the groups.

The patients were grouped according to the absence or presence of a systemic inflammatory response (C-reactive protein $\leq$10/ >10mg/l, Table 6.2). There were less males ($p<0.01$) and more colonic tumours ($p<0.05$), higher interleukin-6 ($p<0.001$) and higher interleukin-10 ($p<0.01$) concentrations in the inflammatory group. The white cell and lymphocyte subpopulation counts were similar between the groups. Log-transformed concentrations of C-reactive protein were significantly correlated with interleukin-6 ($r^2=0.51$, $P<0.001$, Figure 1) but not interleukin-10 ($r^2=0.02$, $P=0.311$).

6.5 Discussion

In the present study, in patients with primary operable colorectal cancer prior to surgery, both interleukin-6 and interleukin-10 concentrations were greater in those patients with an elevated C-reactive protein. In contrast, lymphocyte and lymphocyte subpopulation counts were not altered with evidence of a systemic inflammatory response. Therefore, the results of the present study suggest that the presence of an elevated C-reactive protein concentration is associated with an increase in interleukin-6 and interleukin-10 concentrations, but is not associated with significant differences in the lymphocyte subpopulations measured.

These results, in terms of total lymphocyte numbers, appear to contradict those of Nozoe and coworkers who reported that an elevated C-reactive protein concentration was associated with a reduction [Nozoe et al., 2000]. However, their study included patients with liver metastases and therefore the reduction in circulating lymphocytes may have confounded by the presence of disseminated disease. Given the little change (non-significant) in lymphocyte subsets associated with an elevated C-reactive protein it is likely that other host inflammatory cell types such as macrophages are important in the increased production of interleukin-6 and the consequent increase C-reactive protein concentrations.

The results of the present study are consistent with a number of studies which have shown that interleukin-6 and interleukin-10 concentrations [Galizia et al., 2002;Ordemann et al., 2002] are elevated in patients with colorectal cancer. In the

present study we have shown that, of these cytokines, interleukin-6 is predominantly associated with an increased in C-reactive protein concentrations. These results are consistent with previous observations in patients with primary operable renal cancer [Ramsey et al., 2006].

As part of further investigations it would be important to establish whether macrophage numbers and their activation were increased in colorectal cancer patients with evidence of a systemic inflammatory response. If this were to prove to be the case then macrophage production of interleukin-6 would be an important pre- and post-operative target in patients with primary operable colorectal cancer.

In summary, the results of the present study show that, in patients undergoing curative resection for colorectal cancer, an elevated C-reactive protein concentration is primarily associated with increased circulating interleukin-6 concentrations. Furthermore, circulating lymphocytes subpopulations do not appear to be associated with an elevated C-reactive protein concentration.

Table 6.1. The relationship between the tumour stage, the systemic inflammatory response, interleukin-6 and interleukin-10 and lymphocyte subpopulations in patients with colorectal cancer (n=53).

	TNM stage I (n= 9)	TNM stage II (n= 24)	TNM stage III (n= 20)	P-value
Age (<65/ 65-74/ >75yrs)	2/ 2/ 5	10/ 9/ 5	5/ 7/ 8	0.961
Sex (male/ female)	5/ 4	15/ 9	8/ 12	0.280
Site (colon/ rectum)	4/ 5	15/ 9	12/ 8	0.542
C-reactive protein (≤10/ >10mg/l)	8/ 1	17/ 7	12/ 8	0.125
Albumin (≥35/ <35g/l)	7/ 2	19/ 5	11/ 9	0.125
Interleukin-6 (pg/ml)*	2 (<2-32)	3 (<2-20)	4 (<2-16)	0.071
Interleukin-6 (≤4/ >4pg/ml)	6/ 3	17/ 7	8/ 12	0.085
Interleukin-10 (pg/ ml)*	9 (7-27)	9 (7-17)	10 (7-218)	0.443
Interleukin-10 (≤10/ >10pg/ml)	5/ 3	16/ 8	9/ 9	0.544
White cell count (10^9/l)*	7.9 (4.4-12.0)	7.6 (4.7-16.1)	7.8 (5.1-15.5)	0.941
White cell count (≤11/ >11 10^9/l)	8/ 1	22/ 2	16/ 4	0.381
Lymphocytes (10^9/l)*	1.61 (0.87-2.61)	1.69 (0.61-3.11)	1.88 (0.92-5.53)	0.538
Lymphocytes (≥1/ <1 10^9/l)	8/ 1	22/ 2	18/ 2	0.980
CD3+ (10^9/l)*	1.10 (0.55-1.83)	1.28 (0.39-2.59)	1.32 (0.52-3.34)	0.388
CD3+ (≥0.96/ <0.96 10^9/l)	6/ 3	15/ 9	17/ 3	0.185
CD4+ (10^9/l)*	0.65 (0.46-0.98)	0.77 (0.28-1.73)	0.78 (0.34-1.80)	0.701
CD4+ (≥0.54/ <0.54 10^9/l)	5/ 4	16/ 8	17/ 3	0.080
CD8+ (10^9/l)*	0.29 (0.07-0.91)	0.44 (0.05-1.59)	0.54 (0.16-1.64)	0.340
CD8+ (≥0.27/ <0.27 10^9/l)	5/ 4	17/ 7	15/ 5	0.333
CD19+ (10^9/l)*	0.28 (0.05-0.45)	0.19 (0.07-0.72)	0.20 (0.07-1.49)	0.734
CD19+ (≥0.12/ <0.12 10^9/l)	8/ 1	19/ 5	16/ 4	0.651

*median (range)

Table 6.2. The relationship between the systemic inflammatory response, interleukin-6 and interleukin-10 and lymphocyte subpopulations in patients with colorectal cancer (n=53).

	C-reactive protein ≤10mg/l (n= 37)	C-reactive protein >10mg/l (n= 16)	P-value
Age (<65/ 65-74/ >75yrs)	16/ 8/ 13	1/ 10/ 5	0.177
Sex (male/ female)	24/ 13	4/ 12	0.008
Site (colon/ rectum)	18/ 19	13/ 3	0.029
TNM stage (I/ II/ III)	8/ 17/ 12	1/ 7/ 8	0.125
Albumin (g/l)	39 (21-47)	36 (12-42)	0.097
Albumin (≥35/ <35g/l)	27/ 10	10/ 6	0.450
Interleukin-6 (pg/ml)*	2 (<2-6)	7 (<2-32)	<0.001
Interleukin-6 (≤4/ >4pg/ml)	29/ 8	2/ 14	<0.001
Interleukin-10 (pg/ ml)*	9 (7-218)	12 (8-33)	0.006
Interleukin-10 (≤10/ >10pg/ml)	25/ 10	5/ 10	0.013
White cell count (10^9/l)*	7.5 (4.4-15.5)	8.3 (4.7-16.1)	0.438
White cell count (≤11/ >11 10^9/l)	34/ 3	12/ 4	0.099
Lymphocytes (10^9/l)*	1.6 (0.6-5.5)	1.8 (1.0-2.7)	0.779
Lymphocytes (≥1/ <1 10^9/l)	33/ 4	15/ 1	0.605
CD3+ (10^9/l)*	1.15 (0.39-3.34)	1.30 (0.61-2.14)	0.608
CD3+ (≥0.96/ <0.96 10^9/l)	24/ 13	14/ 2	0.096
CD4+ (10^9/l)*	0.81 (0.28-1.80)	0.62 (0.47-1.73)	0.581
CD4+ (≥0.54/ <0.54 10^9/l)	26/ 11	12/ 4	0.728
CD8+ (10^9/l)*	0.35 (0.05-1.64)	0.54 (0.16-0.85)	0.121
CD8+ (≥0.27/ <0.27 10^9/l)	23/ 14	14/ 2	0.068
CD19+ (10^9/l)*	0.21 (0.05-1.49)	0.19 (0.07-0.39)	0.278
CD19+ (≥0.12/ <0.12 10^9/l)	30/ 7	13/ 3	0.989

*median (range)

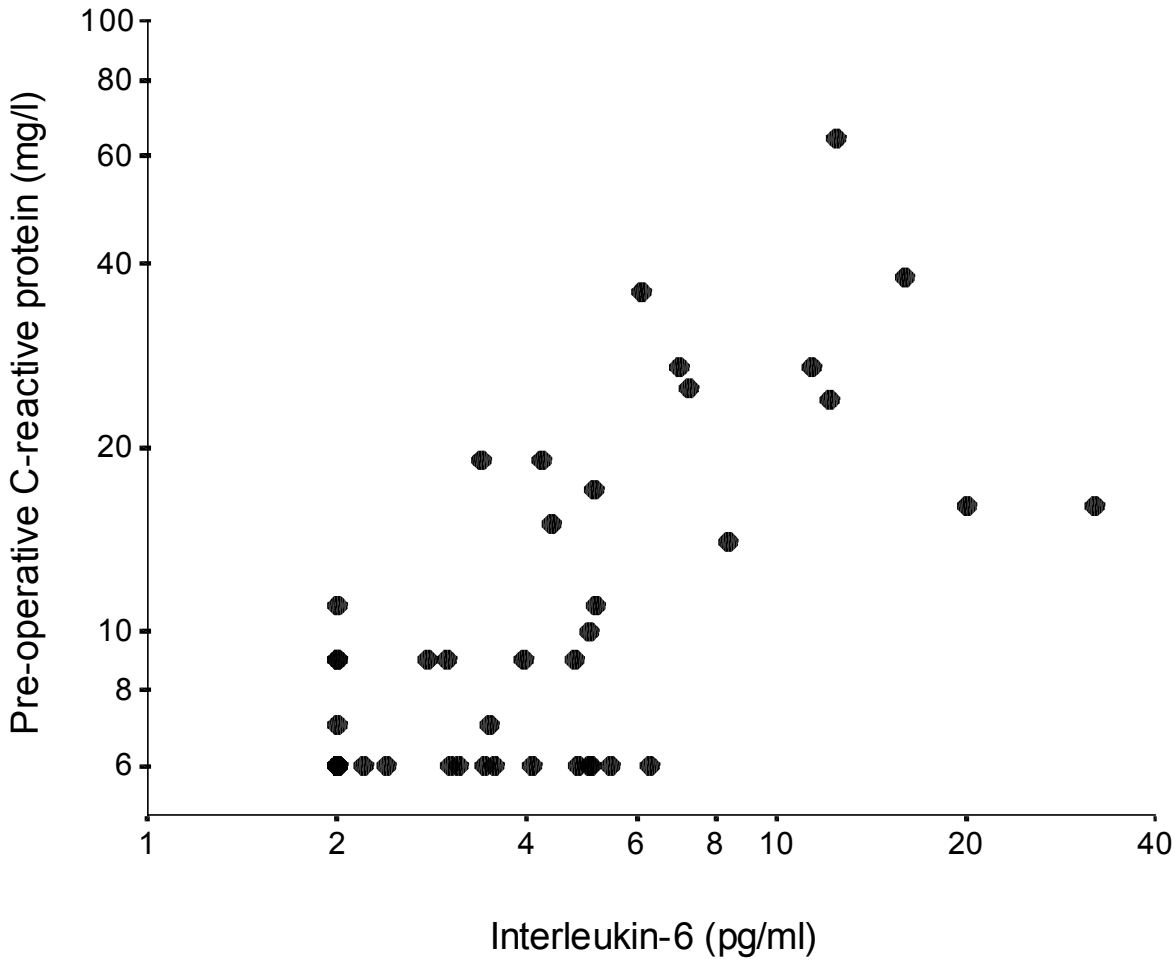

Figure 6.1. Relationship between circulating concentrations of interleukin-6 and C-reactive protein in patients with primary operable colorectal cancer.

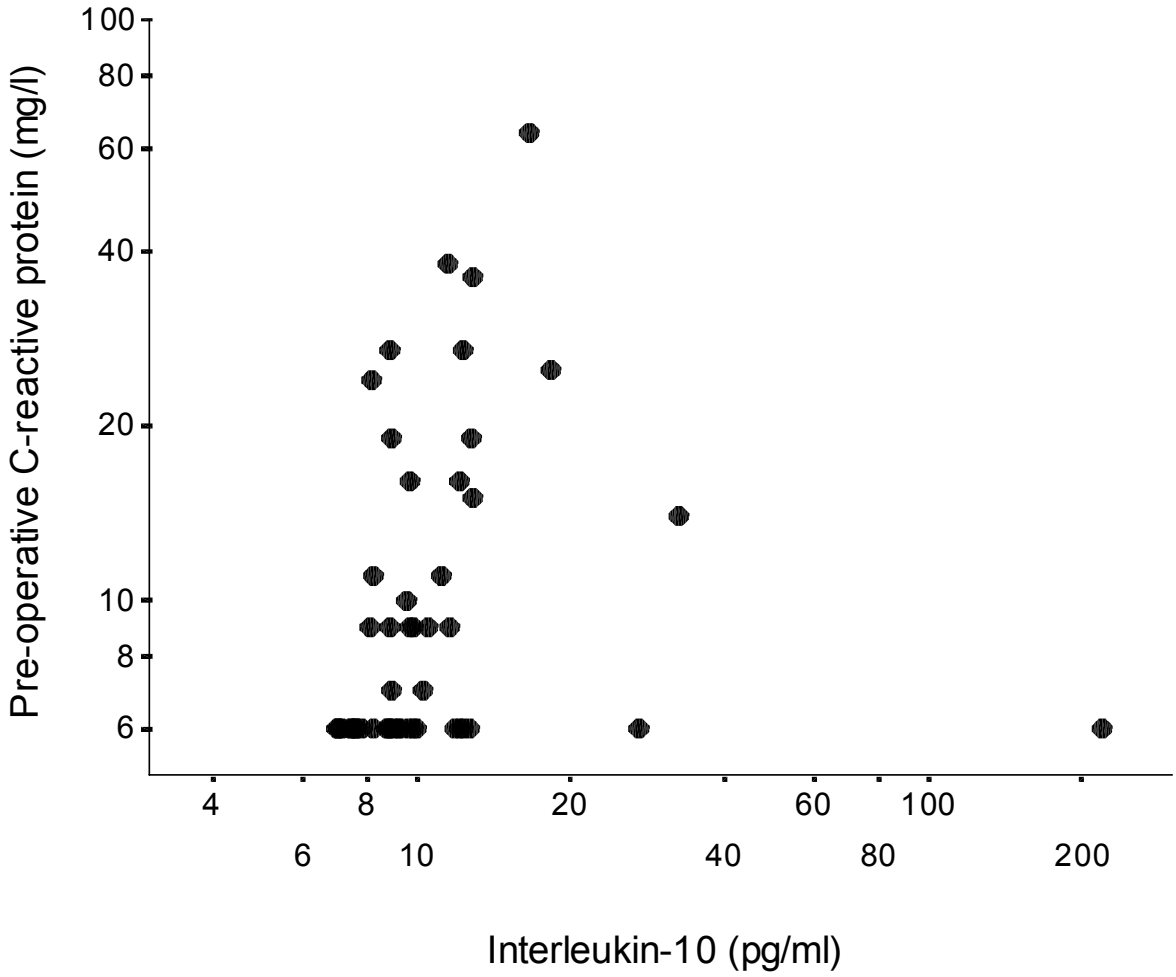

Figure 6.2. Relationship between circulating concentrations of interleukin-10 and C-reactive protein in patients with primary operable colorectal cancer.

7.0 THE PRESENCE OF A SYSTEMIC INFLAMMATORY RESPONSE PREDICTS POORER SURVIVAL IN PATIENTS RECEIVING ADJUVANT 5-FU CHEMOTHERAPY FOLLOWING POTENTIALLY CURATIVE RESECTION FOR COLORECTAL CANCER.

7.1 Introduction

Conventionally, in patients with primary operable colorectal cancer, the decision whether or not to offer adjuvant 5-Flurouracil-based chemotherapy is primarily based on the patient's age, pathological stage and fitness to tolerate chemotherapy. However, even in this selected cohort, the impact of chemotherapy on outcome is unpredictable. Therefore, there is continuing interest in prognostic factors that better reflect clinical outcome [Cascinu et al., 2003;Benson, III et al., 2004].

It has been demonstrated that the presence of a systemic inflammatory response, as evidenced by elevated circulating concentrations of C-reactive protein, is associated with increased recurrence and poor survival, independent of Dukes' stage, in patients undergoing potentially curative surgery for colorectal cancer [McMillan et al., 1995;Nielsen et al., 2000;McMillan et al., 2003]. However, in these studies, few patients had received adjuvant chemotherapy.

It is therefore of considerable interest to examine whether this poor outcome might also be found in patients receiving adjuvant chemotherapy. Indeed, an elevated C-reactive protein has recently been shown to be associated with poorer survival in patients

receiving chemotherapy for advanced lung cancer [Forrest et al., 2004] and renal cancer patients [Bromwich et al., 2004].

Therefore, the aim of the present study was to evaluate the relationship between the systemic inflammatory response and survival in a prospective cohort of patients receiving adjuvant 5-FU chemotherapy following potentially curative resection for colorectal cancer.

7.2 Patients and Methods

Patients with histologically proven colorectal cancer who, on the basis of laparotomy findings and preoperative abdominal computed tomography (CT), were considered to have undergone a potentially curative resection between January 1999 and June 2004 at Glasgow Royal Infirmary were included in the study. The tumours were staged using conventional Dukes' classification [Dukes and Bussey, 1958]. Patients who had pre-operative radiotherapy were excluded from the study since radiotherapy has been reported to evoke a systemic inflammatory response [Cengiz et al., 2001;Koc et al., 2003].

Patients were selected for 5-FU-based chemotherapy following discussion in the multidisciplinary group and taking into account tumour pathology, comorbidity and also patients' wishes. This was predominantly administered using the Mayo regimen for 6 cycles [O'Connell et al., 1997].

A blood sample was taken for routine laboratory measurement of C-reactive protein measurement immediately prior to surgery. The limit of detection of the assay was a C-reactive protein concentration lower than 6 mg/l. The coefficient of variation, over the range of measurement, was less than 5 per cent, as established by routine quality-control procedures. At this time no patient showed clinical evidence of infection or other inflammatory condition.

The study was approved by the Research Ethics Committee, Royal Infirmary, Glasgow.

7.3 Statistics

Comparisons between groups of patients were carried out using contingency table analysis (X^2) as appropriate. Grouping of the variables age and C-reactive protein was carried out using standard thresholds [O'Gorman et al., 2000;Scottish Cancer Intelligence Unit, 2000]. Survival analysis of the group variables was performed using the Cox proportional hazard model. Deaths up to 31st August 2005 were included in the analysis. Multivariate survival analysis, including all covariates was performed using a stepwise backward procedure to derive a final model of the variables that had a significant independent relationship with survival. To remove a variable from the model, the corresponding P-value had to be greater than 0.10. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

7.4 Results

Two hundred and twenty two patients undergoing potentially curative resection for colorectal cancer were studied (Table 7.1). The majority of patients were aged 65 years or more, had colonic tumours and had C-reactive protein concentration in the normal range ($\leq$10 mg/l) prior to surgery.

Of the 222 patients, 50 received adjuvant 5-FU based chemotherapy (Table 7.1). Those patients who received chemotherapy were younger ($p<0.001$), more likely to be male ($p<0.10$), were more likely to have Dukes C disease ($p<0.001$) and did not have hypoalbuminaemia ($p\leq0.01$). The groups were similar in terms of site and C-reactive protein concentration.

The minimum follow-up was 15 months; the median follow-up of the survivors was 38 months. During this period 61 patients died, 32 patients of their cancer and 29 of intercurrent disease. On univariate survival analysis, in those patients who did not receive adjuvant chemotherapy, age ($p<0.001$), Dukes stage ($p<0.05$) and an elevated C-reactive protein ($p<0.01$) were significantly associated with survival (Table 7.2). In those patients who did receive adjuvant chemotherapy, an elevated C-reactive protein concentration ($p<0.01$) was significantly associated with survival. On multivariate survival analysis, in those patients who did not receive adjuvant chemotherapy, age ($p<0.05$) and an elevated C-reactive protein ($p<0.05$) were independently associated with survival (Table 7.2). In those patients who did receive adjuvant chemotherapy, an elevated C-reactive protein concentration ($p<0.05$) was independently associated with survival.

7.5 Discussion

In the present study, an elevated C-reactive protein concentration was associated with poorer survival, independent of age and Dukes stage, in patients receiving adjuvant chemotherapy following potentially curative resection for colorectal cancer. These results would suggest that the systemic inflammatory response, as evidenced by an elevated C-reactive protein concentration, is an important factor in determining outcome in patients receiving adjuvant 5FU-based chemotherapy.

The basis of the relationship between the systemic inflammatory response and poor survival in patients undergoing potentially curative resection for colorectal cancer is not clear. The presence of an elevated C-reactive protein concentration may simply reflect a non-specific inflammatory response secondary to tumour necrosis or local tissue damage. However, these elevated C-reactive protein concentrations do not appear to resolve following potentially curative surgery in the majority of patients [McMillan et al., 2003]. Also, an elevated C-reactive protein concentration 3-6months following curative resection also has independent prognostic value [McMillan et al., 1995;McMillan et al., 2003]. Therefore, these data suggest that the systemic inflammatory response participates in the progression of metastatic disease in patients with colorectal cancer.

There are a number of possible mechanisms by which this could occur. Firstly, that an elevated C-reactive protein identifies those patients with an impaired T-lymphocytic response, since poor infiltration of gastrointestinal tumours appears to be associated

with poor outcome [Jass et al., 1987;Nielsen et al., 1999] and an elevated C-reactive protein concentration has recently been shown to be inversely associated with T-lymphocyte subset infiltration [Canna et al., 2005]. An alternative explanation is that an elevated C-reactive protein concentration may identify those patients with a pro-angiogenic environment, since increased angiogenesis is associated with poor outcome in patients with colorectal cancer [Salmon et al., 2005] and circulating concentrations of vascular endothelial growth factor are directly associated with C-reactive protein [Xavier et al., 2006]. Clearly, both these inflammatory mechanisms may be related and promote unrestrained tumour growth and the dissemination required for the greater malignant potential associated with an elevated C-reactive protein concentration

In the present study an elevated C-reactive protein concentration also predicted poor outcome in those patients receiving adjuvant 5FU-based chemotherapy. However, it has long been recognised that progressive weight loss is associated with poor tolerance to chemotherapy. For example, Andreyev and coworkers in a study of over 1500 patients who were to receive chemotherapy for gastrointestinal cancer showed that prior weight loss was an independent prognostic factor, and patients with weight loss received less chemotherapy and developed more dose limiting toxicity. They concluded that there was a need to conduct nutritional intervention studies in these patients [Andreyev et al., 1998].

More recently, it has been shown that the presence of an ongoing systemic inflammatory response, as evidenced by an elevated C-reactive protein concentration, predicts the progressive nutritional decline of the patient with advanced gastrointestinal cancer [Lundholm et al., 1994;McMillan et al., 1999;O'Gorman et al., 1999].

Moreover, recent work has shown that the activity of the enzyme cytochrome P450 3A, which is involved in the biotransformation of more than half of all drugs currently available, is compromised in patients with an elevated C-reactive protein concentration [Rivory et al., 2002;Slaviero et al., 2003;Baker et al., 2004]. It may therefore be that there is a need to carry out studies to moderate the systemic inflammatory response rather than nutritional intervention in patients receiving chemotherapy.

Irrespective of the mechanisms involved, we believe that the presence or absence of a systemic inflammatory response should be evaluated as a possible influence on outcome in future trials of adjuvant chemotherapy in patients with colorectal cancer and should be used in the stratification of patients. This is however a small study and further larger studies are required to confirm these results.

In summary, the presence of a systemic inflammatory response appears to be an independent predictor of poor outcome in patients receiving adjuvant 5FU-based chemotherapy following potentially curative resection for colorectal cancer.

Table 7.1. Clinicopathological characteristics in patients undergoing potentially curative surgery with and without adjuvant 5FU chemotherapy for colorectal cancer.

		No adjuvant 5FU	Adjuvant 5FU	p-value
		172 (%)	50 (%)	
Age group	<65	40 (23)	26 (52)	
	65-74	58 (34)	18 (36)	
	≥75	74 (43)	6 (12)	<0.001
Sex	Male	88 (51)	33 (66)	
	Female	84 (49)	17 (34)	0.064
Site	Colon	100 (58)	28 (56)	
	Rectum	72 (42)	22 (44)	0.788
Dukes stage	A	23 (13)	0 (0)	
	B	96 (56)	9 (18)	
	C	53 (31)	41 (82)	<0.001
C-reactive protein	≤10mg/l	95 (55)	32 (64)	
	>10mg/l	77 (45)	18 (36)	0.270
Albumin	≥35g/l	132 (77)	45 (90)	
	<35g/l	20 (12)	0 (0)	0.010
Alive		126 (74)	35 (70)	
Dead	Cancer specific	23 (13)	9 (18)	
	Intercurrent	23 (13)	6 (12)	0.709

Table 7.2. Clinicopathological characteristics in patients undergoing potentially curative surgery and adjuvant 5FU chemotherapy for colorectal cancer (n= 222) and survival.

	No adjuvant chemotherapy (n= 172) HR (95% CI)	p-value	Adjuvant chemotherapy (n= 50) HR (95% CI)	p-value
Univariate analysis				
Age (<65/ 65-74/ ≥75)	2.33 (1.48-3.68)	<0.001	0.73 (0.31-1.71)	0.464
Sex (male/ female)	1.37 (0.77-2.46)	0.287	1.55 (0.55-4.36)	0.411
Site (colon/ rectum)	1.23 (0.69-2.21)	0.477	1.19 (0.43-3.29)	0.735
Dukes stage (A/ B/ C)	1.75 (1.06-2.89)	0.029	3.36 (0.44-25.85)	0.245
C-reactive protein (≤10, >10mg/l)	2.39 (1.32-4.34)	0.004	6.68 (2.05-21.72)	0.002
Albumin (≥35/ <35g/l)	1.42 (0.59-3.40)	0.433		
Multivariate analysis				
Age (<65/ 65-74/ ≥75)	1.87 (1.13-3.09)	0.015	1.21 (0.47-3.15)	0.693
Sex (male/ female)	1.08 (0.55-2.09)	0.828	0.92 (0.26-3.22)	0.894
Site (colon/ rectum)	1.57 (0.81-3.07)	0.185	1.15 (0.31-4.27)	0.834
Dukes stage (A/ B/ C)	1.39 (0.82-2.36)	0.219	2.56 (0.31-21.21)	0.384
C-reactive protein (≤10, >10mg/l)	2.10 (1.04-4.25)	0.039	5.57 (1.32-23.51)	0.019
Albumin (≥35/ <35g/l)	1.18 (0.48-2.88)	0.721		

8.0 DOES THE PRESENCE OF A PRE-OPERATIVE SYSTEMIC INFLAMMATORY RESPONSE PREDICT POORER SURVIVAL IN PATIENTS WITH TNM STAGE I/II COLON CANCER – A PILOT STUDY

8.1 Introduction

Numerous studies have shown that adjuvant chemotherapy following potentially curative surgery for colon cancer is of some benefit in those patients with node positive disease [Moertel, 1994;Moertel et al., 1995b]. However, the value of adjuvant chemotherapy in patients with node negative disease remains to be established [Moertel et al., 1995a;Benson, III et al., 2004;Chung and Kelsen, 2006].

More recently, it has been shown that the presence of an ongoing systemic inflammatory response, as evidenced by acute phase proteins such as elevated C-reactive protein and low albumin concentrations [Gabay and Kushner, 1999], is an important independent prognostic factor in patients with a variety of advanced cancers [McMillan et al., 2001b;Maltoni et al., 2005;Hauser et al., 2006]. Furthermore, it has been shown that the presence of an elevated C-reactive protein concentration, prior to and following potentially curative surgery, is associated with poorer overall and cancer specific survival in patients with colorectal cancer [McMillan et al., 1995;Nozoe et al., 1998;Nielsen et al., 2000;McMillan et al., 2003].

In light of such work, we have developed an inflammation based score based on C-reactive protein and albumin, the Glasgow Prognostic score (GPS), which has prognostic value, independent of clinical stage and performance status, in patients with

advanced cancer [Forrest et al., 2003;Forrest et al., 2005;Glen et al., 2006;Crumley et al., 2006b;Ramsey et al., 2007]. Recently, we have shown that the GPS has prognostic value in patients undergoing potentially curative surgery for colon and rectal cancer and in Dukes B stage disease [McMillan et al., 2007].

Recent work has highlighted the prognostic importance of accurate pathological assessment of tumour stage and vascular invasion [Morris et al., 2006] and the number of lymph nodes examined [Chen and Bilchik, 2006] in patients with TNM stage I/ II colon cancer. Therefore, the aim of the present study was to determine whether the GPS has prognostic value independent of pathological criteria and the number of lymph nodes examined in patients undergoing curative resection for node negative colon cancer.

8.2 Patients and Methods

Patients with histologically proven colon cancer who, on the basis of laparotomy findings and preoperative abdominal computed tomography, were considered to have undergone a potentially curative resection between December 1999 and November 2005 in a single surgical unit at Glasgow Royal Infirmary and in whom C-reactive protein and albumin was measured prior to surgery were included in the study. The extent of deprivation was defined using the Carstairs deprivation index, a measure derived from the 1991 census which divides the score into a seven-point index [Carstairs and Morris, 1991]. The tumours were staged using the conventional TNM classification [Greene Fl et al., 2002]. Patients who either had emergency presentation or who died within 30 days of surgery were excluded from the study. At this time no patient showed clinical evidence of infection or other inflammatory condition.

The study was approved by the Research Ethics Committee, Royal Infirmary, Glasgow.

Routine laboratory measurements of C-reactive protein and albumin at the time of diagnosis were carried out. The limit of detection of the C-reactive protein assay was <6mg/l. The coefficients of variation of these methods, over the range of measurements, were less than 5% as established by routine quality control.

The GPS was constructed as previously described [Forrest et al., 2003;Forrest et al., 2005]. Briefly, patients with both an elevated C-reactive protein (>10 mg/l) and hypoalbuminaemia (<35g/l) were allocated a score of 2. Patients in whom only one of

these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0.

Recently, this has been modified based on evidence that hypoalbuminaemia, in patients without an elevated C-reactive protein concentration, had no effect on cancer specific survival. Therefore, patients with an elevated C-reactive protein were assigned a modified GPS score (mGPS) of 1 or 2 depending on the absence or presence of hypoalbuminaemia [McMillan et al., 2007].

8.3 Statistics

Comparisons between groups of patients were carried out using contingency table analysis (X^2) as appropriate. Survival analysis of the group variables was performed using the Cox proportional hazard model. Deaths to the end of May 2007 were included in the analysis. Multivariate survival analysis was performed using a stepwise backward procedure to derive a final model of the variables that had a significant independent relationship with survival. To remove a variable from the model, the corresponding p-value had to be >0.05. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

8.4 Results

The baseline characteristics of the 89 patients who underwent elective potentially curative resection for TNM stage I/II colon cancer are shown in Table 8.1. The majority of patients were aged 65 years or more, were deprived, had T stage 3 or 4, had well or moderately differentiated tumours and had no evidence of vascular invasion. The median (range) number of nodes examined was 14 (3-52).

Forty four (49.4%) patients had an elevated mGPS (1 or 2) prior to surgery. Of the 11 patients with hypoalbuminaemia 10 (91%) also had an elevated C-reactive protein concentration. Ten (11%) patients received adjuvant 5FU- based chemotherapy.

The minimum follow-up was 18 months; the median follow-up of the survivors was 44 months; 16 patients died, 6 died of their cancer and 10 of intercurrent disease. On univariate analysis, age ($p<0.01$) and the mGPS ($p<0.05$) were associated with overall survival (Table 8.1). On multivariate analysis of all variables, only age ($p<0.05$) was independently associated with overall survival (Table 8.2).

On univariate analysis, there was a trend towards age being significant ($p<0.10$) and the mGPS ($p<0.05$) was significantly associated with cancer specific survival (Table 8.1). On multivariate analysis of all variables, there was a trend towards sex ($p<0.10$) and mGPS ($p<0.10$) being independently associated with cancer specific survival (Table 8.2).

The relationship between the mGPS and the clinicopathological characteristics of patients who underwent elective potentially curative resection for TNM stage I/II colon cancer are shown in Table 8.3. An increasing mGPS was associated with older age ($p<0.05$) and less adjuvant therapy ($p<0.05$).

8.5 Discussion

The results of the present study suggest that there is a trend between the presence of a systemic inflammatory response, as evidenced by an elevated mGPS and poorer cancer specific survival in patients undergoing potentially curative surgery for TNM stage I/II colon cancer. In contrast, neither tumour stage, vascular invasion or the number of lymph nodes examined appeared to be associated with cancer specific survival. Therefore, the present study provides some evidence that an inflammation based prognostic score, the mGPS, might be superior to recommended pathological criteria in predicting survival in patients with node negative colon cancer.

The results of the present pilot study are clearly preliminary, with relatively small numbers of patients and limited follow-up and therefore should be interpretated with caution. This relationship needs to be studied further in much larger numbers with longer follow-up to examine whether this trend does indeed show significance.

The use of adjuvant chemotherapy for medically fit patients with stage II colon cancer is currently not recommended except for those patients considered high risk. These include patients with emergency presentation (blood loss, obstruction or perforation), inadequately sampled nodes, T4 lesions, perforation, or poorly differentiated histology [Benson, III et al., 2004]. The results of the present study may suggest that an elevated GPS should be included in the criteria which define high risk patients with stage I/II colon cancer.

However, based on recent evidence it is not clear whether these patients will benefit from chemotherapy since patients with an elevated C-reactive protein concentration also had poorer survival following adjuvant 5-FU based chemotherapy (Chapter 7). Nevertheless, the mGPS, if validated in other centres, will improve the identification of high risk patients and may be useful in the stratification of patients with colorectal cancer entering trials for other adjuvant therapy regimens. Furthermore, future results of treatment in primary operable colorectal cancer should be reported, adjusted for the presence or absence of a systemic inflammatory response.

It was of interest that, in the present study, an elevated mGPS prior to surgery, was associated with older age and less adjuvant therapy but not associated with pathological criteria other than poor differentiation. Given that it is now recognised that the systemic inflammatory response is associated with progressive nutritional decline [Fearon et al., 1999;Kotler, 2000] and cardiovascular disease [Kritchevsky et al., 2005;Tsimikas et al., 2006] this raises the question of whether those patients with an elevated GPS prior to surgery had worse nutritional status or increased co-morbidity. Although we did not record nutritional status or co-morbidity in the present study it would be important to examine their relationship with the pre-operative systemic inflammatory response in future studies since it may shed light on whether a poorer health state results in the tumour behaving more aggressively, an important consideration in the administration of adjuvant chemotherapy.

In summary, an inflammation-based prognostic score (mGPS), which is simple to measure, routinely available and well standardised, may help predict cancer specific survival in patients with stage I/II colon cancer. This relationship needs to be studied

further in larger study to ascertain if the mGPS can be used as a independent prognostic factor in patients undergoing curative resection for colon cancer.

Table 8.1. Clinicopathological characteristics in patients undergoing potentially curative surgery for TNM stage I/ II colon cancer; Univariate survival analysis.

		Overall survival		Cancer specific survival	
	Patients (n= 89)	Hazard ratio (95%CI)	p-value	Hazard ratio (95%CI)	p-value
Age group (<65/ 65-74/ ≥75 yrs)	24/ 36/ 29	3.36 (1.46-7.73)	0.0043	3.80 (0.91-15.91)	0.0680
Sex (male/ female)	48/ 41	1.15 (0.43-3.07)	0.7776	0.23 (0.03-1.97)	0.1797
Deprivation (affluent/ intermediate/ deprived)	3/ 34/ 52	1.00 (0.73-1.38)	0.9840	0.89 (0.54-1.46)	0.6358
Tumour stage (T1/ T2/ T3/ T4)	4/ 13/ 58/ 14	1.35 (0.63-2.97)	0.4407	2.75 (0.70-10.84)	0.1484
Differentiation (well or moderate/ poor)	76/ 13	0.85 (0.19-3.76)	0.8336	2.80 (0.51-15.30)	0.2348
Vascular invasion (negative/ positive)	70/ 19	1.65 (0.53-5.18)	0.3900	2.30 (0.42-12.62)	0.3363
Nodes examined (1-7/ 8-14/ ≥15)	9/ 40/ 40	1.02 (0.65-1.59)	0.9310	0.77 (0.37-1.62)	0.4897
mGPS (0/ 1/ 2)	45/ 34/ 10	2.12 (1.05-4.25)	0.0350	3.11 (1.01-9.60)	0.0486
Adjuvant therapy (no/ yes)	79/ 10	0.04 (<0.01-22.1)	0.3172	0.04 (<0.01-1386)	0.5466

Table 8.2. Clinicopathological characteristics in patients undergoing potentially curative surgery for TNM stage I/ II colon cancer; Multivariate survival analysis.

		Overall survival		Cancer specific survival	
	Patients (n= 89)	Hazard ratio (95%CI)	p-value	Hazard ratio (95%CI)	p-value
Age group (<65/ 65-74/ ≥75 yrs)	24/ 36/ 29	3.11 (1.27-7.66)	0.0134	3.01 (0.69-13.24)	0.1443
Sex (male/ female)	48/ 41	0.86 (0.30-2.41)	0.7682	0.09 (0.01-1.10)	0.0598
Deprivation (affluent/ intermediate/ deprived)	3/ 34/ 52	0.93 (0.32-2.65)	0.8881	0.70 (0.09-5.70)	0.7390
Tumour stage (T1/ T2/ T3/ T4)	4/ 13/ 58/ 14	1.30 (0.55-3.10)	0.5506	6.24 (0.72-54.35)	0.0973
Differentiation (well or moderate/ poor)	76/ 13	0.33 (0.05-2.10)	0.2401	0.40 (0.02-7.19)	0.5368
Vascular invasion (negative/ positive)	70/ 19	2.90 (0.70-11.93)	0.1401	5.55 (0.52-59.24)	0.1557
Nodes examined (1-7/ 8-14/ ≥15)	9/ 40/ 40	0.96 (0.60-1.54)	0.8520	0.77 (0.29-2.01)	0.5907
mGPS (0/ 1/ 2)	45/ 34/ 10	1.65 (0.76-3.56)	0.2049	4.69 (0.90-24.37)	0.0663
Adjuvant therapy (no/ yes)	79/ 10	<0.001 (-)	0.9825	<0.001 (-)	0.9890

Table 8.3 Clinicopathological characteristics according to an inflammation based prognostic score (mGPS) in patients undergoing potentially curative surgery for TNM stage I/ II colon cancer

	mGPS 0 (n= 45)	mGPS 1 (n= 34)	mGPS 2 (n=10)	p-value
Age group (<65/ 65-74/ ≥75 yrs)	15/ 20/ 10	8/ 13/ 13	1/ 3/ 6	0.016
Sex (male/ female)	27/ 18	17/ 17	4/ 6	0.200
Deprivation (affluent/ intermediate/ deprived)	3/ 19/ 23	0/ 11/ 23	0/ 4/ 6	0.146
Tumour stage (T1/ T2/ T3/ T4)	4/ 8/ 26/ 7	0/ 4/ 23/ 7	0/ 1/ 9/ 0	0.239
Differentiation (well or moderate/ poor)	40/ 5	30/ 4	6/ 4	0.071
Vascular invasion (negative/ positive)	36/ 9	27/ 7	7/ 3	0.578
Nodes examined (<6/ 6-10/ 10-15/ >15)	6/ 22/ 17	3/ 13/ 8	0/ 5/ 5	0.172
Adjuvant therapy (no/ yes)	36/ 9	33/ 1	10/ 0	0.013

9.0 DISCUSSION

It has long been recognised that there is more to disease progression in cancer than the tumour characteristics alone. At the outset of this thesis there was an increasing body of evidence in a colorectal cancer that the inflammatory response, both local and systemic, has a role to play. Indeed, there were a number of studies which confirmed an independent relationship between an elevated C-reactive protein and poor survival in patients undergoing potentially curative resectional surgery for colorectal cancer [Nozoe et al., 1998;Nielsen et al., 2000;Canna et al., 2004;Miki et al., 2004]. In contrast two studies did not show independent prognostic value [Wigmore et al., 2001;Chung and Chang, 2003a].

As stated in chapter 2 the thesis had a number of aims.

1. To establish the prognostic value of the pre-operative compared with the post-operative systemic inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.
2. To examine the pre-operative inflammatory response in patients undergoing potentially curative surgery for colorectal cancer.
3. To examine the utility of the systemic inflammatory response as a guide to treatment in patient undergoing potentially curative surgery for colorectal cancer.

Chapter 3 examined the prognostic value of both the pre-operative and immediate post-operative systemic inflammatory response. Only the pre-operative C-reactive protein had prognostic value. These results would suggest that reducing the post-operative systemic inflammatory response by enhanced recovery and laparoscopic techniques will

be of little benefit in the long term survival of these patients. In contrast to such techniques little work has been carried out to evaluate the role of pre-operative modulation of the systemic inflammatory response in patients undergoing potentially curative surgery for colorectal cancer. This would be an important avenue of future research.

After showing that the pre-operative systemic inflammatory response is indeed prognostic in colorectal cancer the next aim was to try to examine the basis of this pre-operative systemic inflammatory response. Chapters 4, 5 and 6 each examine different aspects of the basis of such a relationship.

In chapter 4 the relationship between the systemic inflammatory response and tumour characteristics was examined in more detail. By looking specifically at various pathological characteristics of the tumour morphology including the presence of ulceration, degree of differentiation and maximal diameter it was shown that an elevated pre-operative C-reactive protein was associated with the maximal tumour diameter. These results apparently suggest that the tumour directly expresses factors which stimulate C-reactive protein production. However this study, in contrast to C-reactive protein, showed no association between survival and tumour diameter. Therefore, this would suggest that the direct relationship between C-reactive protein and tumour diameter may be due to a compromised immune response promoting tumour growth.

Chapter 5 examines the relationship between mode of presentation, systemic inflammatory response and survival. The study showed that emergency presentation was associated with a raised systemic inflammatory response, as evidence by an

elevated mGPS, and that emergency presentation was weakened as a predictor of survival when the systemic inflammatory response was included in the survival model. These results are consistent with the host derived systemic inflammatory response being important in determining survival in patients who present as an emergency.

Chapter 6 examined the relationship between C-reactive protein, interleukin-6 and interleukin-10 and lymphocyte subpopulations in patients with colorectal cancer. This would provide information on which aspect of the immune system was associated with an elevated C-reactive protein concentration. This study showed that, in patients undergoing curative resection for colorectal cancer, an elevated C-reactive protein concentration is primarily associated with increased circulating interleukin-6 concentrations. Furthermore, circulating lymphocytes subpopulations do not appear to be associated with an elevated C-reactive protein concentration.

Taking the three studies (chapter 4, 5 and 6) together we can conclude that a pre-operative systemic inflammatory response primarily reflects a host-, rather than a tumour-, derived response. Moreover interleukin-6 concentrations, but not interleukin-10, and lymphocyte subpopulations, are closely involved. This may suggest indirectly that macrophages are important in this host inflammatory response. However further work is required to examine the relationship between an elevated C-reactive protein and circulating macrophage numbers.

Another more clinical issue is that an elevated pre-operative C-reactive protein may be a marker for poor nutritional status and increased co-morbidities. Certainly, recent work has shown a link between C-reactive protein and various co-morbidities including

cardiac disease [Ridker, 2007]. Indeed, there has also been a recent study showing that patient physiology predicts overall and cancer specific survival independent of Dukes' stage in patients undergoing surgery for colorectal cancer [Jenkins et al., 2007]. Further work is required to examine the relationship between the systemic inflammatory response, co-morbid status and outcome in colorectal cancer.

The final aim of the thesis was to examine the utility of the systemic inflammatory response as a guide to treatment in colorectal cancer. This aim is covered in chapters 7 and 8.

Chapter 7 examines specifically those patients who received post-operative adjuvant chemotherapy. This study shows that the presence of a systemic inflammatory response appears to be an independent predictor of poor outcome in patients receiving adjuvant 5FU-based chemotherapy following potentially curative resection for colorectal cancer.

This is an interesting finding given that previous studies in this thesis and previous work have shown that the presence of an elevated pre-operative C-reactive protein is a poor prognostic factor. On the face of it this would suggest that this is a group that would benefit from further treatment but this study, albeit in small numbers, suggests the converse. The reason why these patients do worse with adjuvant chemotherapy is unclear but it may be that an elevated C-reactive protein is a marker for those patients who have compromised liver function [Brown et al., 2007] and therefore a poorer tolerance to chemotherapy.

Finally chapter 8 expands on this finding and looks specifically at those patients with node negative colon cancer. This is an interesting group because it is recognised that a proportion of these patients do badly with respect to recurrent disease and survival. Recent work has highlighted the prognostic importance of accurate pathological assessment of tumour stage and vascular invasion [Morris et al., 2006] and the number of lymph nodes examined [Chen and Bilchik, 2006] in identifying high risk patients with TNM stage I/ II colon cancer. These prognostic factors are now being used in decision making for adjuvant therapy.

We showed that there is a trend between an elevated systemic inflammatory response and outcome in these patients and a suggestion that it may be superior to the above established pathological factors. However this is a small study which does not reach significance in the multivariate analysis. It does suggest that the relationship needs to be examined further in a bigger study. Also the study does not manage to show significance for the various pathological factors other studies suggest which again might be a consequence of it being a small pilot study. If further work confirms these findings the systemic inflammatory response should also be used as part of the decision making process in patients with node-negative colon cancer.

Taken together these final two studies suggest that the systemic inflammatory response may be useful in helping to guide treatment especially in the adjuvant setting. Another important conclusion from the present thesis is that there may be a role for using a combination of chemotherapy and anti-inflammatory treatment in patients with node positive colorectal cancer. Alternatively in node-negative patients it may be that the

systemic inflammatory response should be routinely used to identify high risk patients who might need a more intensive follow-up.

Further Work

It would be important to confirm the value of an elevated pre-operative systemic inflammatory response should be confirmed in larger multi-centre studies and there are plans to examine this within the West of Scotland managed clinical network for colorectal cancer. The specific groups that need to be looked at in greater numbers and details are the node-negative patients and those patients receiving adjuvant chemotherapy.

Also it would be important to examine approaches to moderate the preoperative systemic inflammatory response. For example with non-steroidal anti-inflammatory agents or corticosteroids and to study their effect on long term survival.

10.0 REFERENCES

Aarnio M, Sankila R, Pukkala E, Salovaara R, Aaltonen LA, de la CA, Peltomaki P, Mecklin JP, Jarvinen HJ (1999) Cancer risk in mutation carriers of DNA-mismatch-repair genes. *International Journal of Cancer 81(2):214-8,*

Ali AA, McMillan DC, Matalka II, McNicol AM, McArdle CS (2004) Tumour T-lymphocyte subset infiltration and tumour recurrence following curative resection for colorectal cancer. *Eur J Surg Oncol* **30**: 292-295

Anderson JH, Hole D, McArdle CS (1992) Elective versus emergency surgery for patients with colorectal cancer. *British Journal of Surgery 79(7):706-9,*

Andreyev HJ, Norman AR, Oates J, Cunningham D (1998) Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer* **34**: 503-509

Arista MC, Callopoli A, De FL, Santini A, Schiratti M, Conti L, Di FF, Gandolfo GM (1994) Flow cytometric study of lymphocyte subsets in patients at different stages of colorectal carcinoma. *Dis Colon Rectum* **37**: S30-S34

Aronsen KF, Ekelund G, Kindmark CO, Laurell CB (1972) Sequential changes of plasma proteins after surgical trauma. *Scandinavian Journal of Clinical and Laboratory Investigation Supplement 124:127-36,*

Askling J, Dickman PW, Karlen P, Brostrom O, Lapidus A, Lofberg R, Ekbom A (2001) Family history as a risk factor for colorectal cancer in inflammatory bowel disease. *Gastroenterology* **120**: 1356-1362

Association of Coloproctology for Great Britain and Ireland. Association of Coloproctology of Great Britain and Ireland, Guidelines for the management of Colorectal cancer. 2001.
Ref Type: Generic

Baker SD, van Schaik RH, Rivory LP, Ten Tije AJ, Dinh K, Graveland WJ, Schenk PW, Charles KA, Clarke SJ, Carducci MA, McGuire WP, Dawkins F, Gelderblom H, Verweij J, Sparreboom A (2004) Factors affecting cytochrome P-450 3A activity in cancer patients. *Clin Cancer Res* **10**: 8341-8350

Balkwill F, Mantovani A (2001) Inflammation and cancer: back to Virchow? *Lancet* **357**: 539-545

Banerjee AK, Jehle EC, Shorthouse AJ, Buess G (1995) Local excision of rectal tumours. *British Journal of Surgery 82(9):1165-73,*

Barbaro B, Schulsinger A, Valentini V, Marano P, Rotman M (1999) The accuracy of transrectal ultrasound in predicting the pathological stage of low-lying rectal cancer after preoperative chemoradiation therapy. *Int J Radiat Oncol Biol Phys* **43**: 1043-1047

Bennett A, Tacca MD, Stamford IF, Zebro T (1977) Prostaglandins from tumours of human large bowel. *Br J Cancer* **35**: 881-884

Benson AB, III, Schrag D, Somerfield MR, Cohen AM, Figueredo AT, Flynn PJ, Krzyzanowska MK, Maroun J, McAllister P, Van Cutsem E, Brouwers M, Charette M, Haller DG (2004) American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer. *J Clin Oncol* **22**: 3408-3419

Berghella AM, Pellegrini P, Del BT, Maccarone D, Adorno D, Casciani CU (1996) Prognostic significance of immunological evaluation in colorectal cancer. *Cancer Biother Radiopharm* **11**: 355-361

Bergstrom A, Pisani P, Tenet V, Wolk A, Adami HO (2001) Overweight as an avoidable cause of cancer in Europe. *Int J Cancer* **91**: 421-430

Beynon J, Mortensen NJ, Foy DM, Channer JL, Virjee J, Goddard P (1986) Endorectal sonography: laboratory and clinical experience in Bristol. *International Journal of Colorectal Disease 1(4):212-5,*

Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, Clavel-Chapelon F, Kesse E, Nieters A, Boeing H, Tjonneland A, Overvad K, Martinez C, Dorronsoro M, Gonzalez CA, Key TJ, Trichopoulou A, Naska A, Vineis P, Tumino R, Krogh V, Bueno-de-Mesquita HB, Peeters PH, Berglund G, Hallmans G, Lund E, Skeie G, Kaaks R, Riboli E (2003) Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet* **361**: 1496-1501

Bisgaard ML, Fenger K, Bulow S, Niebuhr E, Mohr J (1994) Familial adenomatous polyposis (FAP): frequency, penetrance, and mutation rate. *Hum Mutat* **3**: 121-125

Blakeborough A, Sheridan MB, Chapman AH (1997) Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. *Clinical Radiology 52(2):142-8,*

Bostick RM, Potter JD, Kushi LH, Sellers TA, Steinmetz KA, McKenzie DR, Gapstur SM, Folsom AR (1994) Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes & Control 5(1):38-52,*

Braga M, Vignali A, Gianotti L, Zuliani W, Radaelli G, Gruarin P, Dellabona P, Di C, V (2002) Laparoscopic versus open colorectal surgery: a randomized trial on short-term outcome. *Ann Surg* **236**: 759-766

Bray F, Sankila R, Ferlay J, Parkin DM (2002) Estimates of cancer incidence and mortality in Europe in 1995. *European Journal of Cancer 38(1):99-166,*

Bromwich E, McMillan DC, Lamb GW, Vasey PA, Aitchison M (2004) The systemic inflammatory response, performance status and survival in patients undergoing alpha-interferon treatment for advanced renal cancer. *Br J Cancer* **91**: 1236-1238

Brown DJ, Milroy R, Preston T, McMillan DC (2007) The relationship between an inflammation-based prognostic score (Glasgow Prognostic Score) and changes in serum biochemical variables in patients with advanced lung and gastrointestinal cancer. *J Clin Pathol* **60**: 705-708

Buechter KJ, Boustany C, Caillouette R, Cohn I, Jr. (1988) Surgical management of the acutely obstructed colon. A review of 127 cases. *American Journal of Surgery 156(3 Pt 1):163-8,*

Burdy G, Panis Y, Alves A, Nemeth J, Lavergne-Slove A, Valleur P (2001) Identifying patients with T3-T4 node-negative colon cancer at high risk of recurrence. *Dis Colon Rectum* **44**: 1682-1688

Burkitt DP (1971) Epidemiology of cancer of the colon and rectum. *Cancer* **28**: 3-13

Cancer research UK. Cancer research UK 2004. 2004.
Ref Type: Internet Communication

Canna K, McArdle PA, McMillan DC, McNicol AM, Smith GW, McKee RF, McArdle CS (2005) The relationship between tumour T-lymphocyte infiltration, the systemic inflammatory response and survival in patients undergoing curative resection for colorectal cancer. *Br J Cancer* **92**: 651-654

Canna K, McMillan DC, McKee RF, McNicol AM, Horgan PG, McArdle CS (2004) Evaluation of a cumulative prognostic score based on the systemic inflammatory response in patients undergoing potentially curative surgery for colorectal cancer. *Br J Cancer* **90**: 1707-1709

Carstairs V, Morris R (1991) Deprivation and Health in Scotland. *Aberdeen University Press*

Cascinu S, Georgoulias V, Kerr D, Maughan T, Labianca R, Ychou M (2003) Colorectal cancer in the adjuvant setting: perspectives on treatment and the role of prognostic factors. *Ann Oncol* **14 Suppl 2**: ii25-ii29

Cengiz M, Akbulut S, Atahan IL, Grigsby PW (2001) Acute phase response during radiotherapy. *Int J Radiat Oncol Biol Phys* **49**: 1093-1096

Chan AT, Giovannucci EL, Meyerhardt JA, Schernhammer ES, Curhan GC, Fuchs CS (2005) Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer. *JAMA* **294**: 914-923

Chan AT, Ogino S, Fuchs CS (2007) Aspirin and the risk of colorectal cancer in relation to the expression of COX-2. *N Engl J Med* **356**: 2131-2142

Chapman MA, Buckley D, Henson DB, Armitage NC (1998) Preoperative carcinoembryonic antigen is related to tumour stage and long-term survival in colorectal cancer. *Br J Cancer* **78**: 1346-1349

Chen SL, Bilchik AJ (2006) More extensive nodal dissection improves survival for stages I to III of colon cancer: a population-based study. *Ann Surg* **244**: 602-610

Chung KY, Kelsen D (2006) Adjuvant Therapy for Stage II Colorectal Cancer: Who and with What? *Curr Treat Options Gastroenterol* **9**: 272-280

Chung YC, Chang YF (2003a) Serum C-reactive protein correlates with survival in colorectal cancer patients but is not an independent prognostic indicator. *Eur J Gastroenterol Hepatol* **15**: 369-373

Chung YC, Chang YF (2003b) Serum interleukin-6 levels reflect the disease status of colorectal cancer. *J Surg Oncol* **83**: 222-226

Clark JC, Collan Y, Eide TJ, Esteve J, Ewen S, Gibbs NM, Jensen OM, Koskela E, MacLennan R, Simpson JG (1985) Prevalence of polyps in an autopsy series from areas with varying incidence of large-bowel cancer. *International Journal of Cancer 36(2):179-86,*

Collett JA, Platell C, Fletcher DR, Aquilia S, Olynyk JK (1999) Distal colonic neoplasms predict proximal neoplasia in average-risk, asymptomatic subjects. *Journal of Gastroenterology & Hepatology 14(1):67-71,*

Cotton S, Sharp L, Little J (1996) The adenoma-carcinoma sequence and prospects for the prevention of colorectal neoplasia. *Crit Rev Oncog* **7**: 293-342

Crumley AB, McMillan DC, McKernan M, Going JJ, Shearer CJ, Stuart RC (2006a) An elevated C-reactive protein concentration, prior to surgery, predicts poor cancer-specific survival in patients undergoing resection for gastro-oesophageal cancer. *Br J Cancer* **94**: 1568-1571

Crumley AB, McMillan DC, McKernan M, McDonald AC, Stuart RC (2006b) Evaluation of an inflammation-based prognostic score in patients with inoperable gastro-oesophageal cancer. *Br J Cancer* **94**: 637-641

DerHagopian RP, Sugarbaker EV, Ketcham A (1978) Inflammatory oncotaxis. *JAMA* **240**: 374-375

Dinarello CA (1984) Interleukin-1 and the pathogenesis of the acute-phase response. *New England Journal of Medicine 311(22):1413-8,*

Du Clos TW (2000) Function of C-reactive protein. *Annals of Medicine 32(4):274-8,*

Du Clos TW, Mold C (2004) C-reactive protein: an activator of innate immunity and a modulator of adaptive immunity. *Immunol Res* **30**: 261-277

Dukes CE (1932) The classification of cancer of the rectum. *Journal of pathology* **35**: 323-332

Dukes CE, Bussey HJ (1958) The spread of rectal cancer and its effect on prognosis. *Br J Cancer* **12**: 309-320

Dunlop MG (1992) Screening for large bowel neoplasms in individuals with a family history of colorectal cancer. *British Journal of Surgery 79(6):488-94,*

Dunlop RJ, Campbell CW (2000) Cytokines and advanced cancer. *J Pain Symptom Manage* **20**: 214-232

Ekbom A, Adami HO, Helmick C, Zack M (1990a) Increased risk of large-bowel cancer in Crohn's disease with colonic involvement. *The Lancet* **336**: 357-359

Ekbom A, Helmick C, Zack M, Adami HO (1990b) Ulcerative colitis and colorectal cancer: A population-based study. *NEW ENGL J MED* **323**: 1228-1233

Erlinger TP, Platz EA, Rifai N, Helzlsouer KJ (2004) C-reactive protein and the risk of incident colorectal cancer. *JAMA* **291**: 585-590

Falconer JS, Fearon KC, Ross JA, Elton R, Wigmore SJ, Garden OJ, Carter DC (1995) Acute-phase protein response and survival duration of patients with pancreatic cancer. *Cancer 75(8):2077-82,*

Fearon ER, Vogelstein B (1990) A genetic model for colorectal tumorigenesis. *Cell 61(5):759-67,*

Fearon KC, Barber MD, Falconer JS, McMillan DC, Ross JA, Preston T (1999) Pancreatic cancer as a model: inflammatory mediators, acute-phase response, and cancer cachexia. *World J Surg* **23**: 584-588

Fearon KC, Falconer JS, Slater C, McMillan DC, Ross JA, Preston T (1998) Albumin synthesis rates are not decreased in hypoalbuminemic cachectic cancer patients with an ongoing acute-phase protein response.[see comment]. *Annals of Surgery 227(2):249-54,*

Fearon KC, Ljungqvist O, Von MM, Revhaug A, Dejong CH, Lassen K, Nygren J, Hausel J, Soop M, Andersen J, Kehlet H (2005) Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr* **24**: 466-477

Fenlon HM, Nunes DP, Schroy PC, Barish MA, Clarke PD, Ferrucci JT (1999) A Comparison of Virtual and Conventional Colonoscopy for the Detection of Colorectal Polyps. *N Engl J Med* **341**: 1496-1503

Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dagg K, Scott HR (2005) A prospective longitudinal study of performance status, an inflammation-based score (GPS) and survival in patients with inoperable non-small-cell lung cancer. *Br J Cancer* **92**: 1834-1836

Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ (2003) Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *British Journal of Cancer 89(6):1028-30,*

Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ (2004) Comparison of an inflammation-based prognostic score (GPS) with performance status (ECOG) in patients receiving platinum-based chemotherapy for inoperable non-small-cell lung cancer. *Br J Cancer* **90**: 1704-1706

Fuchs CS, Giovannucci EL, Colditz GA, Hunter DJ, Stampfer MJ, Rosner B, Speizer FE, Willett WC (1999) Dietary fiber and the risk of colorectal cancer and adenoma in women. *N Engl J Med* **340**: 169-176

Fujita T, Hara A, Yamazaki Y (1999) The value of acute-phase protein measurements after curative gastric cancer surgery. *Archives of Surgery 134(1):73-5,*

Gabay C, Kushner I (1999) Acute-phase proteins and other systemic responses to inflammation. *New England Journal of Medicine 340(6):448-54,*

Galizia G, Orditura M, Romano C, Lieto E, Castellano P, Pelosio L, Imperatore V, Catalano G, Pignatelli C, De VF (2002) Prognostic significance of circulating IL-10 and IL-6 serum levels in colon cancer patients undergoing surgery. *Clin Immunol* **102**: 169-178

Giardiello FM, Hamilton SR, Krush AJ, Piantadosi S, Hylind LM, Celano P, Booker SV, Robinson CR, Offerhaus GJ (1993) Treatment of colonic and rectal adenomas with sulindac in familial adenomatous polyposis. *N Engl J Med* **328**: 1313-1316

Giovannucci E (2001) An updated review of the epidemiological evidence that cigarette smoking increases risk of colorectal cancer. *Cancer Epidemiology, Biomarkers & Prevention 10(7):725-31,*

Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC (1995a) Physical activity, obesity, and risk for colon cancer and adenoma in men. *Annals of Internal Medicine 122(5):327-34,*

Giovannucci E, Egan KM, Hunter DJ, Stampfer MJ, Colditz GA, Willett WC, Speizer FE (1995b) Aspirin and the risk of colorectal cancer in women. *N Engl J Med* **333**: 609-614

Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC (1994) Aspirin use and the risk for colorectal cancer and adenoma in male health professionals. *Ann Intern Med* **121**: 241-246

Glen P, Jamieson NB, McMillan DC, Carter R, Imrie CW, McKay CJ (2006) Evaluation of an inflammation-based prognostic score in patients with inoperable pancreatic cancer. *Pancreatology* **6**: 450-453

Gold P, Freedman SO (1965) Specific carcinoembryonic antigens of the human digestive system. *J Exp Med* **122**: 467-481

Goransson J, Jonsson S, Lasson A (1996) Pre-operative plasma levels of C-reactive protein, albumin and various plasma protease inhibitors for the pre-operative assessment of operability and recurrence in cancer surgery. *Eur J Surg Oncol* **22**: 607-617

Graziano F, Cascinu S (2003) Prognostic molecular markers for planning adjuvant chemotherapy trials in Dukes' B colorectal cancer patients: how much evidence is enough? *Ann Oncol* **14**: 1026-1038

Greene Fl, Page DL, Fleming ID, Fritz A, Balch CM, Haller DG, Morrow M (2002) *TNM staging manual*. Springer-Verlag: New York, NY

Gunter MJ, Stolzenberg-Solomon R, Cross AJ, Leitzmann MF, Weinstein S, Wood RJ, Virtamo J, Taylor PR, Albanes D, Sinha R (2006) A prospective study of serum C-reactive protein and colorectal cancer risk in men. *Cancer Res* **66**: 2483-2487

Harrison LE, Guillem JG, Paty P, Cohen AM (1997) Preoperative carcinoembryonic antigen predicts outcomes in node-negative colon cancer patients: a multivariate analysis of 572 patients. *J Am Coll Surg* **185**: 55-59

Hauser CA, Stockler MR, Tattersall MH (2006) Prognostic factors in patients with recently diagnosed incurable cancer: a systematic review. *Support Care Cancer* **14**: 999-1011

Heald RJ, Ryall RD (1986) Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet 1(8496):1479-82,*

Herendeen JM, Lindley C (2003) Use of NSAIDs for the chemoprevention of colorectal cancer. *Ann Pharmacother* **37**: 1664-1674

Heys SD, Walker LG, Deehan DJ, Eremin OE (1998) Serum albumin: a prognostic indicator in patients with colorectal cancer. *J R Coll Surg Edinb* **43**: 163-168

Hodgson DC, Fuchs CS, Ayanian JZ (2001) Impact of patient and provider characteristics on the treatment and outcomes of colorectal cancer. *J Natl Cancer Inst* **93**: 501-515

Hole DJ, McArdle CS (2002) Impact of socioeconomic deprivation on outcome after surgery for colorectal cancer. *Br J Surg* **89**: 586-590

Ikeda Y, Koyanagi N, Mori M, Ezaki T, Toyomasu T, Minagawa S, Tateishi H, Sugimachi K (1996) Increased incidence of proximal colon cancer in the elderly. *Journal of Clinical Gastroenterology 23(2):105-8,*

IMPACT (1995) Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. International Multicentre Pooled Analysis of Colon Cancer Trials (IMPACT) investigators. *Lancet* **345**: 939-944

IMPACT (1999) Efficacy of adjuvant fluorouracil and folinic acid in B2 colon cancer. International Multicentre Pooled Analysis of B2 Colon Cancer Trials (IMPACT B2) Investigators. *J Clin Oncol* **17**: 1356-1363

ISD Online. ISD online. 2007.
Ref Type: Internet Communication

Jass JR, Do KA, Simms LA, Iino H, Wynter C, Pillay SP, Searle J, Radford-Smith G, Young J, Leggett B (1998) Morphology of sporadic colorectal cancer with DNA replication errors. *Gut 42(5):673-9,*

Jass JR, Love SB, Northover JM (1987) A new prognostic classification of rectal cancer. *Lancet* **1**: 1303-1306

Jass JR, Stewart SM (1992) Evolution of hereditary non-polyposis colorectal cancer. *Gut 33(6):783-6,*

Jedrychowski W, Steindorf K, Popiela T, Wahrendorf J, Tobiasz-Adamczyk B, Kulig J, Penar A (2002) Alcohol consumption and the risk of colorectal cancer at low levels of micronutrient intake. *Medical Science Monitor 8(5):CR357-63,*

Jee SH, Shen SC, Chiu HC, Tsai WL, Kuo ML (2001) Overexpression of interleukin-6 in human basal cell carcinoma cell lines increases anti-apoptotic activity and tumorigenic potency. *Oncogene* **20**: 198-208

Jenkins JT, O'Neill G, Morran CG (2007) The relationship between patient physiology and cancer-specific survival following curative resection of colorectal cancer. *Br J Cancer* **96**: 213-217

King J, Caplehorn JR, Ross WB, Morris DL (1997) High serum carcinoembryonic antigen concentration in patients with colorectal liver metastases is associated with poor cell-mediated immunity, which is predictive of survival. *Br J Surg* **84**: 1382-1385

Koc M, Taysi S, Sezen O, Bakan N (2003) Levels of some acute-phase proteins in the serum of patients with cancer during radiotherapy. *Biol Pharm Bull* **26**: 1494-1497

Kolb-Bachofen V (1991) A review on the biological properties of C-reactive protein. *Immunobiology* **183**: 133-145

Kotake K, Honjo S, Sugihara K, Kato T, Kodaira S, Takahashi T, Yasutomi M, Muto T, Koyama Y (2003) Changes in colorectal cancer during a 20-year period: an extended report from the multi-institutional registry of large bowel cancer, Japan. *Diseases of the Colon & Rectum 46(10 Suppl):S32-43,*

Kotler DP (2000) Cachexia. *Ann Intern Med* **133**: 622-634

Kritchevsky SB, Cesari M, Pahor M (2005) Inflammatory markers and cardiovascular health in older adults. *Cardiovasc Res* **66**: 265-275

Kudo T, Narisawa T, Abo S (1980) Antitumor activity of indomethacin on methylazoxymethanol-induced large bowel tumors in rats. *Gann* **71**: 260-264

Kune GA, Kune S, Watson LF (1988) Colorectal cancer risk, chronic illnesses, operations, and medications: case control results from the Melbourne Colorectal Cancer Study. *Cancer Res* **48**: 4399-4404

Kushner I (1982) The phenomenon of the acute phase response. *Annals of the New York Academy of Sciences 389:39-48,*

Labayle D, Fischer D, Vielh P, Drouhin F, Pariente A, Bories C, Duhamel O, Trousset M, Attali P (1991) Sulindac causes regression of rectal polyps in familial adenomatous polyposis. *Gastroenterology* **101**: 635-639

Lachin JM, Foulkes MA (1986) Evaluation of sample size and power for analyses of survival with allowance for nonuniform patient entry, losses to follow-up, noncompliance, and stratification. *Biometrics* **42**: 507-519

Lacy AM, Garcia-Valdecasas JC, Delgado S, Castells A, Taura P, Pique JM, Visa J (2002) Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet* **359**: 2224-2229

Longo WE, Virgo KS, Johnson FE, Oprian CA, Vernava AM, Wade TP, Phelan MA, Henderson WG, Daley J, Khuri SF (2000) Risk factors for morbidity and mortality after colectomy for colon cancer. *Dis Colon Rectum* **43**: 83-91

Longo WE, Virgo KS, Johnson FE, Wade TP, Vernava AM, Phelan MA, Henderson WG, Daley J, Khuri SF (1998) Outcome after proctectomy for rectal cancer in Department of Veterans Affairs Hospitals: a report from the National Surgical Quality Improvement Program. *Ann Surg* **228**: 64-70

Lundholm K, Gelin J, Hyltander A, Lonnroth C, Sandstrom R, Svaninger G, Korner U, Gulich M, Karrefors I, Norli B, . (1994) Anti-inflammatory treatment may prolong survival in undernourished patients with metastatic solid tumors. *Cancer Res* **54**: 5602-5606

Lynch HT, de la Chapelle A (1999) Genetic susceptibility to non-polyposis colorectal cancer. *J Med Genet* **36**: 801-818

Lynch HT, de la Chapelle A (2003) Hereditary colorectal cancer. *New England Journal of Medicine 348(10):919-32,*

Macdonald JS (1999) Carcinoembryonic antigen screening: pros and cons. *Semin Oncol* **26**: 556-560

MacFarlane JK, Ryall RD, Heald RJ (1993) Mesorectal excision for rectal cancer. *Lancet 341(8843):457-60,*

Maltoni M, Caraceni A, Brunelli C, Broeckaert B, Christakis N, Eychmueller S, Glare P, Nabal M, Vigano A, Larkin P, De CF, Hanks G, Kaasa S (2005) Prognostic factors in advanced cancer patients: evidence-based clinical recommendations--a study by the Steering Committee of the European Association for Palliative Care. *J Clin Oncol* **23**: 6240-6248

Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, Ederer F (1993) Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *New England Journal of Medicine 328(19):1365-71,*

Margarson MP, Soni N (1998) Serum albumin: touchstone or totem? *Anaesthesia* **53**: 789-803

McArdle CS, Hole D, Hansell D, Blumgart LH, Wood CB (1990) Prospective study of colorectal cancer in the west of Scotland: 10-year follow-up. *Br J Surg* **77**: 280-282

McArdle CS, Hole DJ (2002) Outcome following surgery for colorectal cancer: analysis by hospital after adjustment for case-mix and deprivation. *Br J Cancer* **86**: 331-335

McArdle CS, Hole DJ (2004) Emergency presentation of colorectal cancer is associated with poor 5-year survival. *Br J Surg* **91**: 605-609

McArdle CS, McMillan DC, Hole DJ (2006) The impact of blood loss, obstruction and perforation on survival in patients undergoing curative resection for colon cancer. *Br J Surg* **93**: 483-488

McCall JL, Black RB, Rich CA, Harvey JR, Baker RA, Watts JM, Toouli J (1994) The value of serum carcinoembryonic antigen in predicting recurrent disease following curative resection of colorectal cancer. *Dis Colon Rectum* **37**: 875-881

McCallion K, Mitchell RM, Wilson RH, Kee F, Watson RG, Collins JS, Gardiner KR (2001) Flexible sigmoidoscopy and the changing distribution of colorectal cancer: implications for screening. *Gut 48(4):522-5,*

McMillan DC, Canna K, McArdle CS (2003) Systemic inflammatory response predicts survival following curative resection of colorectal cancer. *Br J Surg* **90**: 215-219

McMillan DC, Crozier JE, Canna K, Angerson WJ, McArdle CS (2007) Evaluation of an inflammation-based prognostic score (GPS) in patients undergoing resection for colon and rectal cancer. *Int J Colorectal Dis*

McMillan DC, Elahi MM, Sattar N, Angerson WJ, Johnstone J, McArdle CS (2001a) Measurement of the systemic inflammatory response predicts cancer-specific and non-cancer survival in patients with cancer. *Nutr Cancer* **41**: 64-69

McMillan DC, Fyffe GD, Wotherspoon HA, Cooke TG, McArdle CS (1997) Prospective study of circulating T-lymphocyte subpopulations and disease progression in colorectal cancer. *Dis Colon Rectum* **40**: 1068-1071

McMillan DC, Watson WS, O'Gorman P, Preston T, Scott HR, McArdle CS (2001b) Albumin concentrations are primarily determined by the body cell mass and the systemic inflammatory response in cancer patients with weight loss. *Nutr Cancer* **39**: 210-213

McMillan DC, Wigmore SJ, Fearon KC, O'Gorman P, Wright CE, McArdle CS (1999) A prospective randomized study of megestrol acetate and ibuprofen in gastrointestinal cancer patients with weight loss. *Br J Cancer* **79**: 495-500

McMillan DC, Wotherspoon HA, Fearon KC, Sturgeon C, Cooke TG, McArdle CS (1995) A prospective study of tumor recurrence and the acute-phase response after apparently curative colorectal cancer surgery. *Am J Surg* **170**: 319-322

Meyenberger C, Huch Boni RA, Bertschinger P, Zala GF, Klotz HP, Krestin GP (1995) Endoscopic ultrasound and endorectal magnetic resonance imaging: a prospective, comparative study for preoperative staging and follow-up of rectal cancer. *Endoscopy* **27**: 469-479

Miki C, Konishi N, Ojima E, Hatada T, Inoue Y, Kusunoki M (2004) C-reactive protein as a prognostic variable that reflects uncontrolled up-regulation of the IL-1-IL-6 network system in colorectal carcinoma. *Dig Dis Sci* **49**: 970-976

Mocellin S, Marincola FM, Young HA (2005) Interleukin-10 and the immune response against cancer: a counterpoint. *J Leukoc Biol* **78**: 1043-1051

Modan B, Barell V, Lubin F, Modan M, Greenberg RA, Graham S (1975) Low-fiber intake as an etiologic factor in cancer of the colon. *J Natl Cancer Inst* **55**: 15-18

Moertel CG (1994) Chemotherapy for colorectal cancer. *N Engl J Med* **330**: 1136-1142

Moertel CG, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Tangen CM, Ungerleider JS, Emerson WA, Tormey DC, Glick JH, . (1995a) Intergroup study of fluorouracil plus levamisole as adjuvant therapy for stage II/Dukes' B2 colon cancer. *J Clin Oncol* **13**: 2936-2943

Moertel CG, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Tangen CM, Ungerleider JS, Emerson WA, Tormey DC, Glick JH, Veeder MH, Mailliard JA (1995b) Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. *Ann Intern Med* **122**: 321-326

Morris M, Platell C, de Boer B, McCaul K, Iacopetta B (2006) Population-based study of prognostic factors in stage II colonic cancer. *Br J Surg* **93**: 866-871

Muller AD, Sonnenberg A (1995) Prevention of colorectal cancer by flexible endoscopy and polypectomy. A case-control study of 32,702 veterans. *Annals of Internal Medicine 123(12):904-10,*

Muto T, Bussey HJ, Morson BC (1975) The evolution of cancer of the colon and rectum. *Cancer 36(6):2251-70,*

Mynster T, Christensen IJ, Moesgaard F, Nielsen HJ (2000) Effects of the combination of blood transfusion and postoperative infectious complications on prognosis after surgery for colorectal cancer. Danish RANX05 Colorectal Cancer Study Group. *Br J Surg* **87**: 1553-1562

Naito Y, Saito K, Shiiba K, Ohuchi A, Saigenji K, Nagura H, Ohtani H (1998) CD8+ T cells infiltrated within cancer cell nests as a prognostic factor in human colorectal cancer. *Cancer Res* **58**: 3491-3494

Ng CS, Whelan RL, Lacy AM, Yim AP (2005) Is minimal access surgery for cancer associated with immunologic benefits? *World J Surg* **29**: 975-981

Nielsen HJ, Christensen IJ, Sorensen S, Moesgaard F, Brunner N (2000) Preoperative plasma plasminogen activator inhibitor type-1 and serum C-reactive protein levels in patients with colorectal cancer. The RANX05 Colorectal Cancer Study Group. *Ann Surg Oncol* **7**: 617-623

Nielsen HJ, Hansen U, Christensen IJ, Reimert CM, Brunner N, Moesgaard F (1999) Independent prognostic value of eosinophil and mast cell infiltration in colorectal cancer tissue. *J Pathol* **189**: 487-495

NIH consensus conference (1990) NIH consensus conference. Adjuvant therapy for patients with colon and rectal cancer. *JAMA* **264**: 1444-1450

Nowacki MP, Szymendera JJ (1983) The strongest prognostic factors in colorectal carcinoma. Surgicopathologic stage of disease and postoperative fever. *Dis Colon Rectum* **26**: 263-268

Nozoe T, Matsumata T, Kitamura M, Sugimachi K (1998) Significance of preoperative elevation of serum C-reactive protein as an indicator for prognosis in colorectal cancer. *Am J Surg* **176**: 335-338

Nozoe T, Matsumata T, Sugimachi K (2000) Preoperative elevation of serum C-reactive protein is related to impaired immunity in patients with colorectal cancer. *Am J Clin Oncol* **23**: 263-266

O'Connell MJ, Mailliard JA, Kahn MJ, Macdonald JS, Haller DG, Mayer RJ, Wieand HS (1997) Controlled trial of fluorouracil and low-dose leucovorin given for 6 months as postoperative adjuvant therapy for colon cancer. *J Clin Oncol* **15**: 246-250

O'Gorman P, McMillan DC, McArdle CS (1999) Longitudinal study of weight, appetite, performance status, and inflammation in advanced gastrointestinal cancer. *Nutr Cancer* **35**: 127-129

O'Gorman P, McMillan DC, McArdle CS (2000) Prognostic factors in advanced gastrointestinal cancer patients with weight loss. *Nutr Cancer* **37**: 36-40

Ordemann J, Jacobi CA, Braumann C, Schwenk W, Volk HD, Muller JM (2002) Immunomodulatory changes in patients with colorectal cancer. *Int J Colorectal Dis* **17**: 37-41

Otani T, Iwasaki M, Sasazuki S, Inoue M, Tsugane S (2006) Plasma C-reactive protein and risk of colorectal cancer in a nested case-control study: Japan Public Health Center-based prospective study. *Cancer Epidemiol Biomarkers Prev* **15**: 690-695

Parkin DM (2001) Global cancer statistics in the year 2000. *Lancet Oncology 2(9):533-43,*

Parkin DM, Pisani P, Ferlay J (1999) Estimates of the worldwide incidence of 25 major cancers in 1990. *International Journal of Cancer 80(6):827-41,*

Pepys MB, Baltz ML (1983) Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *Advances in Immunology 34:141-212,*

Pepys MB, Hirschfield GM (2003) C-reactive protein: a critical update. *J Clin Invest* **111**: 1805-1812

Perlmutter DH, Dinarello CA, Punsal PI, Colten HR (1986) Cachectin/tumor necrosis factor regulates hepatic acute-phase gene expression. *Journal of Clinical Investigation 78(5):1349-54,*

Peters U, Sinha R, Chatterjee N, Subar AF, Ziegler RG, Kulldorff M, Bresalier R, Weissfeld JL, Flood A, Schatzkin A, Hayes RB (2003) Dietary fibre and colorectal adenoma in a colorectal cancer early detection programme. *Lancet* **361**: 1491-1495

Petersen VC, Baxter KJ, Love SB, Shepherd NA (2002) Identification of objective pathological prognostic determinants and models of prognosis in Dukes' B colon cancer. *Gut* **51**: 65-69

Phillips RK, Hittinger R, Fry JS, Fielding LP (1985) Malignant large bowel obstruction. *British Journal of Surgery 72(4):296-302,*

Pijl MEJ, Chaoui AS, Wahl RL, van Oostayen JA (2002) Radiology of colorectal cancer. *European Journal of Cancer* **38**: 887-898

Platz EA, Giovannucci E, Rimm EB, Rockett HR, Stampfer MJ, Colditz GA, Willett WC (1997) Dietary fiber and distal colorectal adenoma in men. *Cancer Epidemiol Biomarkers Prev* **6**: 661-670

Rae LC, Gibberd RW (2000) Survival of patients with colorectal cancer detected by a community screening program. *Medical Journal of Australia 172(1):13-5,*

Ramsey S, Lamb GW, Aitchison M, Graham J, McMillan DC (2007) Evaluation of an inflammation-based prognostic score in patients with metastatic renal cancer. *Cancer* **109**: 205-212

Ramsey S, Lamb GW, Aitchison M, McMillan DC (2006) The longitudinal relationship between circulating concentrations of C-reactive protein, interleukin-6 and interleukin-10 in patients undergoing resection for renal cancer. *Br J Cancer* **95**: 1076-1080

Ridker PM (2007) C-reactive protein and the prediction of cardiovascular events among those at intermediate risk: moving an inflammatory hypothesis toward consensus. *J Am Coll Cardiol* **49**: 2129-2138

Rivory LP, Slaviero KA, Clarke SJ (2002) Hepatic cytochrome P450 3A drug metabolism is reduced in cancer patients who have an acute-phase response. *Br J Cancer* **87**: 277-280

Ropponen KM, Eskelinen MJ, Lipponen PK, Alhava E, Kosma VM (1997) Prognostic value of tumour-infiltrating lymphocytes (TILs) in colorectal cancer. *J Pathol* **182**: 318-324

Rosenberg L, Palmer JR, Zauber AG, Warshauer ME, Stolley PD, Shapiro S (1991) A hypothesis: nonsteroidal anti-inflammatory drugs reduce the incidence of large-bowel cancer. *J Natl Cancer Inst* **83**: 355-358

Rozen P, Ron E, Fireman Z, Hallak A, Grossman A, Baratz M, Rattan J, Gilat T (1987) The relative value of fecal occult blood tests and flexible sigmoidoscopy in screening for large bowel neoplasia. *Cancer 60(10):2553-8,*

Salmon JS, Lockhart AC, Berlin J (2005) Anti-angiogenic treatment of gastrointestinal malignancies. *Cancer Invest* **23**: 712-726

Schrag D, Cramer LD, Bach PB, Begg CB (2001) Age and adjuvant chemotherapy use after surgery for stage III colon cancer. *J Natl Cancer Inst* **93**: 850-857

SCOTIA. (1995) Single-stage treatment for malignant left-sided colonic obstruction: a prospective randomized clinical trial comparing subtotal colectomy with segmental resection following intraoperative irrigation. The SCOTIA Study Group. Subtotal Colectomy versus On-table Irrigation and Anastomosis. *Br J Surg* **82**: 1622-1627

Scott HR, McMillan DC, Forrest LM, Brown DJ, McArdle CS, Milroy R (2002) The systemic inflammatory response, weight loss, performance status and survival in

patients with inoperable non-small cell lung cancer. *British Journal of Cancer 87(3):264-7,*

Scott NA, Jeacock J, Kingston RD (1995) Risk factors in patients presenting as an emergency with colorectal cancer. *British Journal of Surgery 82(3):321-3,*

Scottish Cancer Intelligence Unit (2000) *Trends in Cancer Survival 1971-1995*. Edinburgh

Slaviero KA, Clarke SJ, Rivory LP (2003) Inflammatory response: an unrecognised source of variability in the pharmacokinetics and pharmacodynamics of cancer chemotherapy. *Lancet Oncol* **4**: 224-232

Slevin ML (1996) Adjuvant treatment for colorectal cancer. *BMJ* **312**: 392-393

Smalley WE, DuBois RN (1997) Colorectal cancer and nonsteroidal anti-inflammatory drugs. *Adv Pharmacol* **39**: 1-20

Smyrk TC, Watson P, Kaul K, Lynch HT (2001) Tumor-infiltrating lymphocytes are a marker for microsatellite instability in colorectal carcinoma. *Cancer 91(12):2417-22,*

Steele RJ (2006) Fecal occult blood test screening in the United kingdom. *Am J Gastroenterol* **101**: 216-218

Stocchi L, Nelson H (2005) Minimally invasive surgery for colorectal carcinoma. *Ann Surg Oncol* **12**: 960-970

Thompson D, Milford-Ward A, Whicher JT (1992) The value of acute phase protein measurements in clinical practice. *Annals of Clinical Biochemistry 29 (Pt 2):123-31,*

Thun MJ, Namboodiri MM, Calle EE, Flanders WD, Heath CW, Jr. (1993) Aspirin use and risk of fatal cancer. *Cancer Res* **53**: 1322-1327

Thun MJ, Namboodiri MM, Heath CW, Jr. (1991) Aspirin use and reduced risk of fatal colon cancer. *N Engl J Med* **325**: 1593-1596

Towler B, Irwig L, Glasziou P, Kewenter J, Weller D, Silagy C (1998) A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, hemoccult. *BMJ 317(7158):559-65,*

Trikha M, Corringham R, Klein B, Rossi JF (2003a) Targeted anti-interleukin-6 monoclonal antibody therapy for cancer: a review of the rationale and clinical evidence. *Clin Cancer Res* **9**: 4653-4665

Trikha M, Corringham R, Klein B, Rossi JF (2003b) Targeted anti-interleukin-6 monoclonal antibody therapy for cancer: a review of the rationale and clinical evidence. *Clin Cancer Res* **9**: 4653-4665

Tsimikas S, Willerson JT, Ridker PM (2006) C-reactive protein and other emerging blood biomarkers to optimize risk stratification of vulnerable patients. *J Am Coll Cardiol* **47**: C19-C31

Vasen HF, Watson P, Mecklin JP, Lynch HT (1999) New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* **116**: 1453-1456

Vermeire S, Van AG, Rutgeerts P (2006) Laboratory markers in IBD: useful, magic, or unnecessary toys? *Gut* **55**: 426-431

Viiala CH, Zimmerman M, Cullen DJ, Hoffman NE (2003) Complication rates of colonoscopy in an Australian teaching hospital environment
5. *Intern Med J* **33**: 355-359

Vogelstein B, Fearon ER, Hamilton SR, Kern SE, Preisinger AC, Leppert M, Nakamura Y, White R, Smits AM, Bos JL (1988) Genetic alterations during colorectal-tumor development. *New England Journal of Medicine 319(9):525-32,*

Waddell WR, Ganser GF, Cerise EJ, Loughry RW (1989) Sulindac for polyposis of the colon. *Am J Surg* **157**: 175-179

Waddell WR, Loughry RW (1983) Sulindac for polyposis of the colon. *J Surg Oncol* **24**: 83-87

Wang WS, Lin JK, Chiou TJ, Liu JH, Fan FS, Yen CC, Lin TC, Jiang JK, Yang SH, Wang HS, Chen PM (2000) Preoperative carcinoembryonic antigen level as an independent prognostic factor in colorectal cancer: Taiwan experience. *Jpn J Clin Oncol* **30**: 12-16

Watson P, Lynch HT (1994) The tumor spectrum in HNPCC. *Anticancer Research 14(4B):1635-9,* -Aug

Werner J, Hartwig W, Uhl W, Muller C, Buchler MW (2003) Useful markers for predicting severity and monitoring progression of acute pancreatitis. *Pancreatology* **3**: 115-127

Whiteside TL (2003) 22. Immune responses to malignancies. *J Allergy Clin Immunol* **111**: S677-S686

Wigmore SJ, McMahon AJ, Sturgeon CM, Fearon KC (2001) Acute-phase protein response, survival and tumour recurrence in patients with colorectal cancer. *Br J Surg* **88**: 255-260

Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE (1990) Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *New England Journal of Medicine 323(24):1664-72,*

Xavier P, Belo L, Beires J, Rebelo I, Martinez-de-Oliveira J, Lunet N, Barros H (2006) Serum levels of VEGF and TNF-alpha and their association with C-reactive protein in patients with endometriosis. *Arch Gynecol Obstet* **273**: 227-231

Ytting H, Christensen IJ, Basse L, Lykke J, Thiel S, Jensenius JC, Nielsen HJ (2006) Influence of major surgery on the mannan-binding lectin pathway of innate immunity. *Clin Exp Immunol* **144**: 239-246

Appendix 1 – Database for chapter 3 - PRE- BUT NOT POST-OPERATIVE SYSTEMIC INFLAMMATORY RESPONSE CORRELATES WITH COLORECTAL CANCER SURVIVAL

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
1	65	1	1	04.03.1999	anterior resection	1	0
2	81	2	1	15.03.1999	Right hemicolectomy	0	0
3	41	0	0	16.03.1999	anterior resection	1	0
4	84	2	1	15.08.1999	anterior resection	1	0
5	70	1	0	05.10.1999	sigmoid colectomy	0	1
6	56	0	0	18.11.1999	Abdominoperineal excision of rectum	1	1
7	82	2	1	25.11.1999	Right hemicolectomy	0	0
8	72	1	0	16.12.1999	Right Hemicolectomy	0	1
9	45	0	1	08.03.2000	Right hemicolectomy	0	0
10	79	2	1	15.03.2000	Right hemicolectomy	0	0
11	60	0	0	06.04.2000	Anterior resection	1	1
12	63	0	0	25.07.2000	Right Hemicolectomy	0	1
13	89	2	1	08.09.2000	R hemicolectomy	0	0
14	72	1	0	28.09.2000	Anterior resection	1	0
15	70	1	0	27.10.2000	sigmoid colectomy	0	0
16	78	2	1	16.01.2001	Anterior resection	1	0
17	72	1	0	31.01.2001	R hemicolectomy	0	0
18	55	0	1	13.02.2001	Sigmoid colectomy	0	0
19	74	1	1	16.02.2001	Anterior resection	1	0
20	79	2	0	23.03.2001	Right Hemicolectomy	0	0
21	42	0	1	03.05.2001	Right Hemicolectomy	0	1
22	71	1	1	08.05.2001	sigmoid colectomy	0	0
23	68	1	0	19.07.2001	Right hemicolectomy	0	1
24	63	0	0	09.08.2001	Anterior resection	1	1
25	76	2	1	21.08.2001	Hartmann's procedure	0	0
26	73	1	1	21.08.2001	Sub-total colectomy + IRA	0	0
27	69	1	0	23.08.2001	Sub-total colectomy + IRA	0	0
28	75	2	1	06.09.2001	Right Hemicolectomy	0	0
29	72	1	1	07.09.2001	Right Hemicolectomy	0	0
30	32	0	0	18.09.2001	Anterior resection	1	1
31	54	0	0	18.09.2001	Sigmoid colectomy	0	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
32	77	2	0	20.09.2001	Anterior resection	1	1
33	77	2	0	21.09.2001	Anterior resection	1	0
34	58	0	0	26.09.2001	Proctectomy and coloanal anastomosis	1	1
35	82	2	1	27.09.2001	Sigmoid colectomy	0	0
36	80	2	1	02.10.2001	Right Hemicolectomy	0	0
37	73	1	0	05.10.2001	Proctectomy and coloanal anastomosis	1	0
38	80	2	1	09.10.2001	Sigmoid colectomy	0	0
39	32	0	0	12.10.2001	Right Hemicolectomy	0	1
40	61	0	1	15.10.2001	Sigmoid colectomy	0	0
41	79	2	0	16.10.2001	Right Hemicolectomy	0	0
42	46	0	0	25.10.2001	Sigmoid colectomy	0	1
43	83	2	0	30.10.2001	Right Hemicolectomy	0	0
44	80	2	0	06.11.2001	anterior resection	1	0
45	75	2	0	13.11.2001	anterior resection	1	0
46	70	1	0	15.11.2001	Anterior resection	1	0
47	59	0	0	20.11.2001	Anterior resection	1	1
48	82	2	1	22.11.2001	Right Hemicolectomy	0	0
49	81	2	1	28.11.2001	anterior Resection	1	0
50	60	0	0	12.12.2001	R hemicolectomy	0	0
51	69	1	0	30.12.2001	Hartmann's procedure	0	1
52	70	1	0	08.01.2002	Anterior resection	1	0
53	74	1	0	15.01.2002	anterior resection	1	1
54	77	2	0	18.01.2002	Anterior resection	1	0
55	78	2	1	20.01.2002	Hartmann's procedure	0	0
56	44	0	1	21.01.2002	sigmoid colectomy	0	0
57	89	2	1	30.01.2002	anterior resection	1	0
58	64	0	0	05.02.2002	anterior resection	1	1
59	81	2	1	28.02.2002	Anterior resection	1	0
60	65	1	1	08.03.2002	Proctectomy and coloanal anastomosis	1	0
61	74	1	0	20.03.2002	Right Hemicolectomy	0	0
62	63	0	0	04.04.2002	anterior resection	1	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
63	83	2	1	05.04.2002	Abdominoperineal excision of rectum	1	0
64	48	0	0	17.04.2002	anterior resection	1	1
65	50	0	1	24.04.2002	Right Hemicolectomy	0	1
66	61	0	1	26.04.2002	Proctectomy and coloanal anastomosis	1	0
67	84	2	0	02.05.2002	Right Hemicolectomy	0	1
68	50	0	1	07.05.2002	Right Hemicolectomy	0	1
69	64	0	1	08.05.2002	Hartmann's procedure	0	1
70	69	1	1	10.05.2002	Proctectomy and coloanal anastomosis	1	0
71	63	0	0	15.05.2002	anterior resection	1	0
72	76	2	1	17.05.2002	Right Hemicolectomy	0	0
73	75	2	0	28.05.2002	anterior resection	1	0
74	71	1	0	11.06.2002	sigmoid colectomy	0	0
75	63	0	0	13.06.2002	Sigmoid colectomy	0	1
76	69	1	1	20.06.2002	Right Hemicolectomy	0	0
77	68	1	0	20.06.2002	Right Hemicolectomy	0	0
78	76	2	0	20.06.2002	Right Hemicolectomy	0	0
79	79	2	0	26.06.2002	Right Hemicolectomy	0	0
80	73	1	0	06.07.2002	Sigmoid colectomy	0	0
81	80	2	1	10.07.2002	Right Hemicolectomy	0	0
82	67	1	1	11.07.2002	Proctectomy and coloanal anastomosis	1	1
83	59	0	1	12.08.2002	Proctectomy and coloanal anastomosis	1	0
84	77	2	1	13.08.2002	Anterior resection	1	1
85	50	0	0	20.08.2002	Proctectomy + ileoanal pouch	1	0
86	66	1	1	22.08.2002	Anterior resection	1	0
87	76	2	1	03.09.2002	Sigmoid colectomy	0	1
88	77	2	1	05.09.2002	Anterior resection	1	0
89	85	2	1	11.09.2002	Sigmoid colectomy	0	0
90	77	2	0	17.09.2002	Right Hemicolectomy	0	0
91	83	2	0	20.09.2002	Sigmoid colectomy	0	0
92	67	1	1	30.10.2002	anterior resection	1	0
93	79	2	0	01.11.2002	Proctectomy and coloanal anastomosis	1	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
94	68	1	1	05.11.2002	Right Hemicolectomy	0	0
95	75	2	1	12.11.2002	anterior resection	1	0
96	62	0	1	13.11.2002	Right Hemicolectomy	0	0
97	55	0	1	13.11.2002	Sigmoid colectomy	0	1
98	79	2	0	26.11.2002	sub-total colectomy + IRA	0	0
99	68	1	1	11.12.2002	Sigmoid colectomy	0	0
100	86	2	1	18.12.2002	Right Hemicolectomy	0	0
101	81	2	1	04.01.2003	Right Hemicolectomy	0	0
102	86	2	0	04.01.2003	Right Hemicolectomy	0	0
103	47	0	1	06.01.2003	anterior resection	1	0
104	53	0	0	08.01.2003	anterior resection	1	0
105	83	2	0	09.01.2003	Sigmoid colectomy	0	0
106	60	0	0	14.01.2003	Anterior resection	1	0
107	77	2	0	14.01.2003	anterior resection	1	0
108	74	1	0	23.01.2003	Sigmoid colectomy	0	0
109	83	2	1	29.01.2003	Abdominoperineal excision of rectum	1	0
110	56	0	0	30.01.2003	Sigmoid colectomy	0	1
111	69	1	1	06.03.2003	anterior resection	1	0
112	73	1	0	14.03.2003	sigmoid colectomy	0	0
113	63	0	0	19.03.2003	anterior resection	1	1
114	49	0	0	25.03.2003	Abdominoperineal excision of rectum	1	0
115	56	0	1	28.03.2003	Proctectomy and coloanal anastomosis	1	0
116	68	1	0	04.04.2003	Anterior resection	1	0
117	58	0	0	15.04.2003	anterior resection	1	0
118	64	0	0	21.04.2003	anterior resection	1	1
119	43	0	0	22.04.2003	Right hemicolectomy	0	0
120	79	2	0	23.04.2003	anterior resection	1	0
121	39	0	0	30.04.2003	Abdominoperineal excision of rectum	1	1
122	67	1	0	13.05.2003	Sigmoid colectomy	0	0
123	72	1	0	14.05.2003	Right Hemicolectomy	0	0
124	60	0	1	23.05.2003	Sigmoid colectomy	0	1

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
125	72	1	0	27.05.2003	Sigmoid colectomy	0	1
126	74	1	0	29.05.2003	Right Hemicolectomy	0	0
127	82	2	1	12.06.2003	Right Hemicolectomy	0	0
128	69	1	1	19.06.2003	anterior resection	1	0
129	83	2	1	04.07.2003	Right Hemicolectomy	0	0
130	76	2	1	31.07.2003	Right Hemicolectomy	0	0
131	64	0	1	01.08.2003	Anterior resection	1	0
132	38	0	1	05.08.2003	Right Hemicolectomy	0	1
133	56	0	1	07.08.2003	Anterior resection	1	1
134	76	2	1	15.08.2003	Abdominoperineal excision of rectum	1	0
135	87	2	1	15.08.2003	Right Hemicolectomy	0	0
136	74	1	0	20.08.2003	Subtotal colectomy	0	0
137	61	0	0	28.08.2003	Right hemicolectomy	0	1
138	83	2	1	29.08.2003	Right hemicolectomy	0	0
139	77	2	0	03.09.2003	Right Hemicolectomy	0	0
140	55	0	0	05.09.2003	Right Hemicolectomy	0	1
141	74	1	0	09.09.2003	Sigmoid colectomy	0	0
142	69	1	1	12.09.2003	Left hemicolectomy	0	0
143	75	2	0	18.09.2003	Sigmoid colectomy	0	1
144	77	2	0	19.09.2003	Anterior resection	1	1
145	75	2	1	03.10.2003	Sigmoid colectomy	0	0
146	72	1	1	03.10.2003	AP resection	1	0
147	65	1	0	09.10.2003	Anterior resection	1	1
148	65	1	0	10.10.2003	Sigmoid colectomy	0	0
149	74	1	0	16.10.2003	Right Hemicolectomy	0	0
150	41	0	0	17.10.2003	Anterior resection	1	0
151	48	0	0	21.10.2003	Anterior resection	1	0
152	54	0	0	23.10.2003	Anterior resection	1	0
153	84	2	0	24.10.2003	Right hemicolectomy	0	0
154	74	1	0	30.10.2003	Left hemicolectomy	0	0
155	71	1	0	12.11.2003	AP resection	1	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)
156	64	0	0	16.12.2003	Right Hemicolectomy	0	0
157	69	1	1	18.12.2003	Right Hemicolectomy	0	1
158	47	0	0	06.01.2004	Low anterior resection	1	1
159	70	1	0	08.01.2004	Anterior resection	1	0
160	69	1	0	08.01.2004	Sigmoid colectomy	0	0
161	64	0	0	09.01.2004	Proctectomy	0	0
162	73	1	1	09.01.2004	Right Hemicolectomy	0	1
163	68	1	1	24.02.2004	anterior resection	1	0
164	68	1	1	27.02.2004	Sigmoid colectomy	0	0
165	82	2	0	16.03.2004	Sigmoid colectomy	0	0
166	76	2	0	18.03.2004	right hemicolectomy	0	0
167	67	1	1	19.03.2004	right hemicolectomy	0	1
168	66	1	0	23.03.2004	anterior resection	1	1
169	69	1	1	25.03.2004	right hemicolectomy	0	0
170	77	2	1	25.03.2004	anterior resection	1	1
171	81	2	1	16.04.2004	anterior resection	1	0
172	59	0	1	20.04.2004	right hemicolectomy	0	0
173	75	2	1	23.04.2004	anterior resection	1	0
174	84	2	1	05.05.2004	right hemicolectomy	0	0
175	79	2	0	14.05.2004	right hemicolectomy	0	1
176	52	0	0	18.05.2004	anterior resection	1	1
177	81	2	0	08.06.2004	anterior resection	1	0
178	74	1	0	15.06.2004	anterior resection	1	0
179	72	1	1	15.06.2004	Left hemicolectomy	0	1
180	64	0	0	25.06.2004	anterior resection	1	0

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
1	25-Feb-02	1	36.3	3	1	0	2	well/mod	No
2	25-Aug-04	2	66.33	3	0	0	1	well/mod	No
3	20-Apr-06	0	86.4	2	2	0	2	well/mod	No
4	28-May-04	2	58.27	3	0	0	1	well/mod	Yes
5	20-Apr-06	0	79.63	3	2	0	2	well/mod	No
6	22-Mar-03	2	40.67	3	2	0	2	poorly	No
7	17-Jun-03	1	43.33	3	1	0	2	well/mod	No
8	20-Apr-06	0	77.23	3	0	0	1	well/mod	No
9	20-Apr-06	0	74.47	4	0	0	1	well/mod	No
10	12-Sep-01	2	18.2	3	0	0	1	well/mod	No
11	20-Apr-06	0	73.5	4	0	0	1	well/mod	No
12	18-Mar-02	1	20.03	4	1	0	2	well/mod	No
13	04-Jun-03	2	33.3	3	1	0	2	well/mod	No
14	20-Apr-06	0	67.67	2	1	0	2	well/mod	No
15	20-Apr-06	0	66.7	3	0	0	1	well/mod	No
16	20-Apr-06	0	64	4	0	0	1	well/mod	No
17	20-Apr-06	0	63.5	3	0	0	1	well/mod	No
18	20-Apr-06	0	63.07	3	0	0	1	well/mod	No
19	20-Apr-06	0	62.97	1	0	0	0	well/mod	No
20	20-Apr-06	0	61.8	3	0	0	1	well/mod	No
21	20-Apr-06	0	60.43	3	0	0	1	well/mod	No
22	20-Apr-06	0	60.27	3	0	0	1	well/mod	No
23	20-Apr-06	0	57.87	3	1	0	2	well/mod	No
24	20-Apr-06	0	57.17	2	1	0	2	well/mod	No
25	20-Apr-06	0	56.77	3	0	0	1	well/mod	No
26	20-Apr-06	0	56.77	3	0	0	1	poorly	No
27	20-Apr-06	0	56.7	3	0	0	1	well/mod	No
28	20-Apr-06	0	56.23	3	0	0	1	well/mod	No
29	20-Apr-06	0	56.2	3	1	0	2	well/mod	No
30	20-Apr-06	0	55.83	3	2	0	2	well/mod	Yes

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
31	20-Apr-06	0	55.83	1	0	0	0	moderately	no
32	20-Apr-06	0	55.77	3	1	0	2	well/mod	No
33	20-Apr-06	0	55.73	2	0	0	0	well/mod	No
34	18-Sep-03	2	24.07	3	1	0	2	moderately	No
35	09-Aug-04	2	34.9	3	0	0	1	well/mod	No
36	20-Apr-06	0	55.37	4	1	0	2	moderately	yes
37	20-Apr-06	0	55.27	2	2	0	2	well/mod	Yes
38	18-Jul-05	2	45.93	2	0	0	0	well/mod	No
39	20-Apr-06	0	55.03	3	0	0	1	well/mod	no
40	20-Apr-06	0	54.93	4	0	0	1	moderately	no
41	27-Apr-02	1	6.43	4	1	0	2	moderately	no
42	28-Dec-04	1	38.67	3	1	0	2	well/mod	Yes
43	20-Apr-06	0	54.43	3	0	0	1	well/mod	No
44	20-Apr-06	0	54.2	4	1	0	2	moderately	no
45	24-Jan-03	1	14.57	4	1	0	2	moderately	no
46	20-Apr-06	0	53.9	4	0	0	1	well/mod	No
47	19-Feb-03	2	15.2	3	0	0	1	well/mod	No
48	24-Dec-01	2	1.07	2	0	0	0	well	no
49	20-Apr-06	0	53.47	4	0	0	1	moderately	no
50	20-Apr-06	0	53	4	0	0	1	well/mod	No
51	28-Dec-03	1	24.27	4	2	0	2	poorly	No
52	06-Mar-06	2	50.6	3	0	0	1	well/mod	No
53	20-Apr-06	0	51.87	3	1	0	2	moderately	yes
54	12-Jun-03	2	17	2	1	0	2	well/mod	No
55	09-Feb-03	1	12.83	4	1	0	2	poorly	Yes
56	20-Apr-06	0	51.67	3	0	0	1	well/mod	no
57	20-Apr-06	0	51.37	2	0	0	0	well/mod	no
58	20-Apr-06	0	51.17	3	2	0	2	moderately	no
59	20-Apr-06	0	50.4	1	1	0	2	well/mod	No
60	20-Apr-06	0	50.13	2	2	0	2	poorly	No
61	24-Mar-03	1	12.3	4	2	0	2	well/mod	yes

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
62	05-Sep-04	1	29.5	3	1	0	2	well/mod	no
63	19-Jan-05	2	34	3	1	0	2	poorly	yes
64	20-Apr-06	0	48.8	3	1	0	2	well/mod	no
65	20-Apr-06	0	48.57	4	2	0	2	Moderately	yes
66	20-Apr-06	0	48.5	2	0	0	0	well/mod	No
67	23-May-03	1	12.87	3	1	0	2	poor	yes
68	21-Jun-03	1	13.67	3	1	0	2	well/mod	yes
69	20-Apr-06	0	48.1	4	1	0	2	well/mod	Yes
70	30-Sep-04	1	29.13	2	0	0	0	well/mod	No
71	18-Sep-04	2	28.57	3	0	0	1	well/mod	yes
72	16-Dec-03	1	19.27	4	1	0	2	well/mod	No
73	04-May-05	2	35.73	3	1	0	2	moderately	no
74	20-Apr-06	0	46.97	3	0	0	1	moderately	no
75	20-Apr-06	0	46.9	4	1	0	2	moderately	yes
76	20-Apr-06	0	46.67	3	0	0	1	poorly	No
77	15-Apr-04	2	22.17	3	0	0	1	Moderately	no
78	05-Sep-05	2	39.1	3	2	0	2	poorly	No
79	20-Apr-06	0	46.47	4	2	0	2	moderately	yes
80	20-Apr-06	0	46.13	2	0	0	0	moderately	no
81	05-Dec-05	1	41.47	4	1	0	2	well/mod	Yes
82	02-May-03	2	9.83	3	1	0	2	well/mod	Yes
83	20-Apr-06	0	44.9	3	0	0	1	well/mod	Yes
84	05-Dec-04	1	28.17	4	0	0	1	well/mod	Yes
85	20-Apr-06	0	44.63	2	0	0	0	well/mod	No
86	09-Nov-03	2	14.8	2	1	0	2	well/mod	Yes
87	20-Apr-06	0	44.17	2	1	0	2	well/mod	Yes
88	20-Apr-06	0	44.1	3	1	0	2	well/mod	Yes
89	20-Apr-06	0	43.9	4	0	0	1	moderately	no
90	13-Jun-05	1	33.33	4	0	0	1	poor	no
91	25-Feb-04	1	17.43	4	1	0	2	well/mod	yes
92	20-Apr-06	0	42.27	3	0	0	1	Moderately	No

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
93	23-Jul-04	2	21	3	0	0	1	well/mod	No
94	17-Mar-04	2	16.6	3	0	0	1	well/mod	No
95	04-Apr-04	2	16.97	3	0	0	1	moderately	no
96	20-Apr-06	0	41.8	3	0	0	1	moderately	no
97	20-Apr-06	0	41.8	3	0	0	1	Moderately	no
98	20-Apr-06	0	41.37	3	0	0	1	well/mod	No
99	03-Nov-05	2	35.27	4	0	0	1	moderately	no
100	20-Apr-06	0	40.63	3	0	0	1	well/mod	no
101	20-Apr-06	0	40.07	4	2	0	2	Moderately	yes
102	07-Oct-03	1	9.2	3	0	0	1	Moderately	No
103	20-Apr-06	0	40	2	0	0	0	Moderately	No
104	20-Apr-06	0	39.93	3	1	0	2	moderately	no
105	21-Feb-06	1	37.97	4	1	0	2	Moderately	no
106	20-Apr-06	0	39.73	3	0	0	1	Moderately	No
107	26-Nov-05	2	34.9	3	1	0	2	moderately	no
108	20-Apr-06	0	39.43	3	0	0	1	Moderately	yes
109	09-Jul-03	1	5.37	3	0	0	1	moderately	no
110	20-Apr-06	0	39.2	2	1	0	2	well/mod	no
111	20-Apr-06	0	38.03	3	0	0	1	Moderately	no
112	26-Mar-06	1	36.93	3	0	0	1	Moderately	No
113	25-Dec-03	2	9.37	3	0	0	1	Moderately	yes
114	20-Apr-06	0	37.4	3	0	0	1	Moderately	no
115	20-Apr-06	0	37.3	3	1	0	2	Moderately	No
116	20-Apr-06	0	37.07	3	0	0	1	Moderately	yes
117	23-May-05	2	25.63	3	1	0	2	poor	yes
118	24-Sep-05	1	29.57	3	1	0	2	moderately	no
119	20-Apr-06	0	36.47	2	0	0	0	moderately	no
120	20-Apr-06	0	36.43	3	0	0	1	moderately	no
121	30-Dec-05	1	32.5	3	1	0	2	moderately	yes
122	20-Apr-06	0	35.77	1	0	0	0	moderately	no
123	20-Oct-03	1	5.3	3	0	0	1	poor	yes

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
124	20-Apr-06	0	35.43	4	1	0	2	Moderately	No
125	20-Apr-06	0	35.3	4	0	0	1	poor	no
126	20-Apr-06	0	35.23	3	0	0	1	Moderately	No
127	20-Apr-06	0	34.77	3	0	0	1	poor	yes
128	20-Apr-06	0	34.53	3	1	0	2	moderately	yes
129	01-Jul-05	1	24.27	3	0	0	1	Moderately	No
130	20-Apr-06	0	33.13	2	0	0	0	moderately	no
131	20-Apr-06	0	33.1	2	0	0	0	well/mod	No
132	02-Mar-05	1	19.17	3	1	0	2	well/mod	Yes
133	20-Apr-06	0	32.9	2	1	0	2	well/mod	No
134	20-Apr-06	0	32.63	3	1	0	2	Well/mod	No
135	01-Jul-04	1	10.7	4	1	0	2	well/mod	Yes
136	20-Apr-06	0	32.47	3	0	0	1	Well/mod	No
137	20-Apr-06	0	32.2	3	0	0	1	well/mod	yes
138	20-Apr-06	0	32.17	2	0	0	0	well/mod	no
139	20-Apr-06	0	32	3	0	0	1	well/mod	No
140	20-Apr-06	0	31.93	3	1	0	2	poorly	No
141	20-Apr-06	0	31.8	4	1	0	2	well/mod	No
142	20-Apr-06	0	31.7	4	0	0	1	well/mod	No
143	20-Apr-06	0	31.5	3	1	0	2	well/mod	no
144	20-Apr-06	0	31.47	4	1	0	2	well/mod	Yes
145	20-Apr-06	0	31	4	1	0	2	well/mod	Yes
146	20-Apr-06	0	31	1	1	0	2	well/mod	No
147	20-Apr-06	0	30.8	3	0	0	1	well/mod	Yes
148	20-Apr-06	0	30.77	3	1	0	2	well/mod	Yes
149	20-Apr-06	0	30.57	2	0	0	0	well/mod	No
150	20-Apr-06	0	30.53	2	0	0	0	well/mod	No
151	20-Apr-06	0	30.4	3	0	0	1	well/mod	yes
152	20-Apr-06	0	30.33	1	0	0	0	well	No
153	20-Apr-06	0	30.3	3	0	0	1	poorly	Yes
154	20-Apr-06	0	30.1	3	1	0	2	moderately	No

Patient ID	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion
155	20-Apr-06	0	29.67	1	0	0	0	moderately	yes
156	20-Apr-06	0	28.53	3	0	0	1	moderately	No
157	20-Apr-06	0	28.47	4	1	0	2	moderately	Yes
158	20-Apr-06	0	27.83	3	1	0	2	moderately	Yes
159	15-Sep-05	2	20.53	4	0	0	1	moderately	Yes
160	20-Apr-06	0	27.77	4	0	0	1	moderately	No
161	20-Apr-06	0	27.73	3	0	0	1	moderately	Yes
162	20-Apr-06	0	27.73	3	1	0	2	moderately	No
163	21-May-04	1	2.9	4	2	0	2	poorly	Yes
164	20-Apr-06	0	26.1	2	0	0	0	moderately	No
165	20-Apr-06	0	25.5	3	0	0	1	moderately	No
166	20-Apr-06	0	25.43	4	0	0	1	moderately	Yes
167	21-Feb-05	1	11.3	4	2	0	2	poorly	Yes
168	20-Apr-06	0	25.27	3	1	0	2	moderately	Yes
169	20-Apr-06	0	25.2	3	0	0	1	moderately	Yes
170	20-Apr-06	0	25.2	4	1	0	2	moderately	Yes
171	20-Apr-06	0	24.47	3	0	0	1	moderately	Yes
172	20-Apr-06	0	24.33	3	0	0	1	undifferentiated	Yes
173	20-Apr-06	0	24.23	3	0	0	1	moderately	No
174	20-Apr-06	0	23.83	4	0	0	1	moderately	No
175	08-Mar-06	2	22.1	3	2	0	2	poorly	No
176	20-Apr-06	0	23.4	3	2	0	2	moderately	No
177	20-Apr-06	0	22.7	2	0	0	0	moderately	No
178	06-Sep-04	2	2.77	3	2	0	2	poorly	Yes
179	20-Apr-06	0	22.47	3	1	0	2	moderately	No
180	20-Apr-06	0	22.13	2	0	0	0	moderately	No

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
1	Clear	9	1	no	15	1	.	.
2	Clear	12	0	no	5	0	.	.
3	Clear	19	5	no	16	1	41	0
4	Clear	25	0	no	35	1	43	0
5	Clear	16	6	no	5	0	.	.
6	Clear	24	4	no	5	0	44	0
7	Clear	14	2	no	23	1	36	0
8	Clear	14	0	no	5	0	38	0
9	Clear	12	0	no	6	0	43	0
10	Clear	23	0	no	31	1	38	0
11	Clear	15	0	no	178	1	31	1
12	Clear	17	1	no	97	1	42	0
13	Clear	25	3	no	31	1	34	1
14	Clear	14	2	no	26	1	44	0
15	Clear	8	0	no	19	1	36	0
16	Clear	11	0	no	5	0	.	.
17	Clear	13	0	no	5	0	.	.
18	Clear	35	0	no	6	0	38	0
19	Clear	8	0	no	6	0	48	0
20	Clear	26	0	no	21	1	38	0
21	Clear	20	0	no	6	0	37	0
22	Clear	19	0	no	6	0	.	.
23	Clear	7	1	no	6	0	47	0
24	Clear	7	3	no	6	0	44	0
25	Clear	10	0	no	41	1	41	0
26	Clear	14	0	no	7	0	37	0
27	Clear	18	0	no	22	1	38	0
28	Clear	18	0	no	8	0	42	0
29	Clear	14	2	no	7	0	43	0
30	Clear	21	5	no	6	0	46	0

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
31	Clear	28	0	no	6	0	42	0
32	Clear	8	3	yes	6	0	42	0
33	Clear	13	0	no	7	0	43	0
34	Clear	14	1		6	0	42	0
35	Clear	21	0	no	33	1	39	0
36	Clear	8	3	no	29	1	42	0
37	Clear	12	6	no	6	0	45	0
38	Clear	15	0	no	12	1	40	0
39	Clear	26	0	no	24	1	43	0
40	Clear	10	0	no	71	1	32	1
41	Clear	14	2	no	5	0	41	0
42	Clear	18	2	no	9	0	47	0
43	Clear	7	0	no	6	0	44	0
44	Clear	17	1	no	6	0	38	0
45	Clear	7	1	no	48	1	37	0
46	Clear	11	0	no	6	0	40	0
47	Clear	26	0	no	34	1	43	0
48	Clear	10	0	no	46	1	32	1
49	Clear	10	0	no	8	0	43	0
50	Clear	17	0	no	15	1	38	0
51	Clear	19	6	no	26	1	38	0
52	Clear	12	0	no	6	0	44	0
53	Clear	16	1	no	6	0	42	0
54	Clear	11	1	no	6	0	50	0
55	Clear	9	1	no	20	1	45	0
56	Clear	18	0	no	6	0	42	0
57	Clear	22	0	no	41	1	38	0
58	Clear	17	4	no	6	0	42	0
59	Clear	13	2	no	11	1	42	0
60	Clear	19	5	no	6	0	46	0
61	Clear	20	9	no	58	1	34	1

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
62	Clear	17	1	no	14	1	44	0
63	Clear	15	3	no	6	0	.	.
64	Clear	20	2	no	5	0	47	0
65	Clear	24	7	yes	7	0	42	0
66	Clear	29	0	no	6	0	42	0
67	Clear	14	3		135	1	39	0
68	Clear	3	1	yes	28	1	40	0
69	Clear	8	1	no	56	1	37	0
70	Clear	6	0	no	20	1	41	0
71	Clear	11	0	no	5	0	44	0
72	Clear	19	2	no	6	0	38	0
73	Clear	18	3	no	5	0	36	0
74	Clear	10	0	no	6	0	42	0
75	Clear	11	2	no	9	0	42	0
76	Clear	19	0	no	12	1	41	0
77	Clear	15	0	no	9	0	41	0
78	Clear	10	9	no	31	1	40	0
79	Clear	22	4	no	19	1	36	0
80	Clear	7	0	no	20	1	38	0
81	Clear	10	2	no	5	0	42	0
82	Clear	14	2	no	22	1	41	0
83	Clear	12	0	no	6	0	52	0
84	Clear	24	0	no	26	1	41	0
85	Clear	16	0	no	6	0	43	0
86	Clear	10	2	yes	10	0	43	0
87	Clear	8	1	no	6	0	44	0
88	Clear	12	1	no	6	0	42	0
89	Clear	9	0	no	14	1	42	0
90	Clear	3	0	no	101	1	36	0
91	Clear	12	3	yes	6	0	35	0
92	Clear	15	0	no	5	0	38	0

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
93	Clear	15	0	no	26	1	41	0
94	Clear	7	0	no	7	0	44	0
95	Clear	12	0	no	19	1	47	0
96	Clear	26	0	no	17	1	36	0
97	Clear	15	0	no	5	0	47	0
98	Clear	20	0	no	41	1	40	0
99	Clear	16	0	no	8	0	44	0
100	Clear	16	0	no	27	1	42	0
101	Clear	10	3	yes	21	1	37	0
102	Clear	28	0	no	49	1	34	1
103	Clear	25	0	no	6	0	45	0
104	Clear	27	1	no	11	1	41	0
105	Clear	10	0	no	46	1	41	0
106	Clear	19	0	no	34	1	31	1
107	Clear	21	1	no	6	0	37	0
108	Clear	17	0	no	6	0	41	0
109	Clear	16	0	no	13	1	40	0
110	Clear	18	2	no	8	0	43	0
111	Clear	25	0	no	6	0	46	0
112	Clear	11	0	no	48	1	30	1
113	Clear	11	0	no	6	0	41	0
114	Clear	17	0	no	6	0	44	0
115	Clear	15	1	no	6	0	45	0
116	Clear	11	0	no	6	0	40	0
117	Clear	27	1	no	9	0	39	0
118	Clear	25	1	no	40	1	42	0
119	Clear	14	0	no	7	0	47	0
120	Clear	29	0	no	47	1	35	0
121	Clear	10	3	no	7	0	47	0
122	Clear	8	0	no	6	0	48	0
123	Clear	10	0	no	10	0	42	0

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
124	Clear	10	2	no	9	0	42	0
125	Clear	9	0	no	6	0	41	0
126	Clear	18	0	no	8	0	41	0
127	Clear	15	0	no	33	1	31	1
128	Clear	12	1	no	5	0	40	0
129	Clear	11	0	no	95	1	31	1
130	Clear	14	0	no	6	0	42	0
131	Clear	19	0	no	5	0	44	0
132	Clear	4	1	yes	38	1	42	0
133	Clear	19	3	no	11	1	42	0
134	Clear	11	2	no	5	0	42	0
135	Clear	12	1	no	94	1	32	1
136	Clear	13	0	no	5	0	39	0
137	Clear	10	0	no	10	0	43	0
138	Clear	8	0	no	6	0	34	1
139	Clear	14	0	no	7	0	39	0
140	Clear	8	1	yes	19	1	43	0
141	Clear	13	2	no	5	0	40	0
142	Clear	7	0	no	29	1	37	0
143	Clear	8	1	no	5	0	46	0
144	Clear	7	3	no	5	0	44	0
145	Clear	15	3	no	7	0	41	0
146	Clear	8	3	yes	5	0	41	0
147	Clear	15	0	no	7	0	39	0
148	Clear	12	1	no	5	0	43	0
149	Clear	11	0	no	12	1	38	0
150	Clear	7	0	no	5	0	42	0
151	Clear	19	0	no	5	0	45	0
152	Clear	9	0		8	0	45	0
153	Clear	9	0	no	40	1	40	0
154	Clear	16	1	no	21	1	43	0

Patient ID	Resection margins	Total nodes	Positive nodes	Apical node positive	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)
155	Clear	11	0	no	5	0	44	0
156	Clear	14	0	no	75	1	36	0
157	Clear	16	1	no	9	0	40	0
158	Clear	12	2	no	5	0	41	0
159	Clear	8	0	no	31	1	41	0
160	Clear	13	.	no	5	0	36	0
161	Clear	12	0	no	13	1	.	.
162	Clear	9	1	no	18	1	39	0
163	Clear	24	16	no	38	1	42	0
164	Clear	8	0	no	12	1	42	0
165	Clear	13	0	no	12	1	34	1
166	Clear	22	0	no	6	0	43	0
167	Clear	25	4	no	209	1	41	0
168	Clear	8	2	no	5	0	43	0
169	Clear	41	0	no	133	1	34	1
170	Clear	16	3	no	22	1	44	0
171	Clear	13	0	no	101	1	33	1
172	Clear	25	.	no	14	1	26	1
173	Clear	17	0	no	14	1	38	0
174	Clear	9	0	no	16	1	38	0
175	Clear	11	4	no	27	1	45	0
176	Clear	12	6	no	5	0	47	0
177	Clear	12	0	no	5	0	42	0
178	Clear	31	4	no	12	1	38	0
179	Clear	9	1	no	5	0	39	0
180	Clear	18	0	no	8	0	.	.

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
1	.	128	0	.	221
2	69	69	0	123	95
3	108	117	0	58	28
4	.	51	0	.	.
5	98	139	0	136	86
6	144	258	1	.	116
7	.	146	0	.	99
8	172	209	1	.	90
9	176	236	1	.	.
10	95	190	1	199	.
11	.	196	1	.	127
12	114	162	0	141	107
13	79	94	0	61	38
14	171	206	1	197	156
15	162	275	1	308	203
16	58	125	0	107	.
17	102	196	1	.	162
18	122	166	1	136	.
19	114	131	0	64	.
20	92	114	0	87	82
21	92	134	0	125	.
22	162	159	0	150	119
23	92	160	0	.	46
24	131	221	1	189	117
25	62	104	0	135	101
26	128	130	0	.	80
27	172	281	1	165	104
28	82	155	0	147	133
29	.	137	0	141	131
30	138	158	0	130	.

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
31	89	113	0	80	.
32	105	164	1	119	62
33	119	273	1	218	161
34	155	156	0	81	39
35	139	257	1	278	318
36	99	71	0	41	.
37	.	207	1	164	168
38	109	221	1	240	204
39	109	136	0	.	68
40	.	111	0	156	115
41	75	109	0	75	73
42	82	135	0	194	97
43	85	107	0	81	.
44	73	136	0	116	95
45	93	153	0	129	.
46	66	149	0	126	88
47	98	151	0	.	.
48	109	128	0	73	66
49	54	108	0	120	77
50	152	181	1	122	.
51	149	251	1	196	88
52	69	186	1	157	.
53	74	125	0	112	.
54	109	179	1	154	109
55	117	146	0	148	156
56	.	69	0	69	37
57	115	139	0	128	87
58	88	194	1	193	129
59	142	170	1	165	104
60	140	99	0	69	.
61	151	272	1	.	306

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
62	162	276	1	204	136
63	94	142	0	97	81
64	105	161	0	119	61
65	90	178	1	.	.
66	104	94	0	41	.
67	215	198	1	177	97
68	87	155	0	129	87
69	167	204	1	175	.
70	127	183	1	114	.
71	.	202	1	167	111
72	39	179	1	146	.
73	115	143	0	114	85
74	98	223	1	217	.
75	.	236	1	156	109
76	50	72	0	78	.
77	150	230	1	209	176
78	74	91	0	91	86
79	119	196	1	152	.
80	175	221	1	199	149
81	102	129	0	92	.
82	128	193	1	194	.
83	82	147	0	164	137
84	103	191	1	156	97
85	120	159	0	110	.
86	109	124	0	100	89
87	81	151	0	168	85
88	149	233	1	195	164
89	90	152	0	131	73
90	189	209	1	.	140
91	40	97	0	92	69
92	95	200	1	190	96

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
93	92	131	0	81	89
94	76	141	0	117	106
95	99	210	1	198	.
96	116	181	1	.	.
97	107	170	1	.	.
98	53	36	0	34	.
99	212	275	1	225	.
100	188	208	1	.	96
101	237	216	1	192	158
102	162	157	0	.	176
103	.	44	0	70	34
104	149	206	1	175	.
105	109	128	0	73	66
106	58	90	0	81	49
107	90	130	0	.	81
108	114	162	0	153	163
109	108	253	1	190	106
110	128	246	1	.	102
111	183	281	1	214	126
112	99	169	1	143	84
113	98	121	0	104	91
114	70	109	0	101	65
115	60	46	0	29	12
116	137	250	1	288	295
117	99	188	1	.	53
118	146	181	1	151	102
119	53	104	0	119	.
120	99	163	0	150	97
121	.	179	1	191	177
122	139	134	0	173	143
123	182	211	1	214	148

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
124	90	136	0	115	56
125	59	113	0	93	.
126	171	193	1	121	.
127	130	149	0	105	64
128	104	116	0	52	33
129	81	151	0	141	.
130	112	173	1	159	97
131	139	202	1	95	37
132	151	144	0	.	.
133	.	163	0	108	75
134	96	128	0	133	98
135	199	247	1	.	124
136	114	77	0	158	146
137	114	169	1	101	.
138	57	89	0	67	.
139	125	159	0	171	90
140	99	146	0	117	.
141	154	213	1	175	131
142	100	195	1	202	225
143	103	151	0	89	54
144	86	153	0	130	.
145	86	143	0	115	90
146	71	41	0	29	.
147	135	220	1	218	149
148	101	151	0	107	114
149	123	187	1	134	73
150	94	143	0	91	52
151	74	190	1	238	192
152	107	214	1	289	244
153	116	164	1	141	95
154	148	188	1	173	155

Patient ID	Day 1 CRP	Day 2 CRP	Day 2 CRP group	Day 3 CRP	Day 4 CRP
155	126	195	1	161	103
156	176	240	1	207	122
157	127	202	1	187	137
158	97	135	0	91	77
159	134	167	1	38	33
160	30	68	0	83	.
161	134	267	1	259	.
162	111	160	0	127	85
163	103	192	1	132	66
164	33	82	0	106	90
165	92	214	1	.	102
166	118	187	1	188	134
167	229	253	1	182	120
168	120	194	1	.	164
169	215	230	1	197	150
170	133	187	1	176	116
171	237	262	1	185	193
172	61	164	1	195	187
173	65	64	0	48	29
174	116	163	1	130	72
175	119	193	1	220	158
176	221	244	1	127	66
177	130	261	1	263	188
178	89	199	1	229	.
179	90	112	0	115	66
180	141	188	1	138	90

Appendix 2 – Database for chapter 4 - TUMOUR SIZE IS ASSOCIATED WITH THE SYSTEMIC INFLAMMATORY RESPONSE BUT NOT SURVIVAL IN PATIENTS WITH PRIMARY OPERABLE COLORECTAL CANCER

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
1	73	1	0	7	3	13/01/1999	R hemicolectomy
2	86	2	1	4	2	22/01/1999	sigmoid colectomy
3	74	1	0	7	3	10/02/1999	R hemicolectomy
4	63	0	1	6	3	17/02/1999	R hemicolectomy
5	73	1	1	7	3	25/02/1999	R hemicolectomy
6	65	1	1	7	3	04/03/1999	anterior resection
7	81	2	1	6	3	15/03/1999	Right hemicolectomy
8	41	0	0	7	3	16/03/1999	anterior resection
9	65	1	1	3	2	17/03/1999	sigmoid colectomy
10	77	2	1	6	3	08/05/1999	Sub-total colectomy + IRA
11	60	0	1	6	3	21/05/1999	L hemicolectomy
12	78	2	0	7	3	18/06/1999	L hemicolectomy
13	60	0	0	2	1	23/06/1999	anterior resection
14	73	1	0	7	3	29/06/1999	anterior resection
15	59	0	0	7	3	13/07/1999	R hemicolectomy
16	78	2	1	7	3	23/07/1999	L hemicolectomy
17	84	2	1	5	2	05/08/1999	R hemicolectomy
18	84	2	1	2	1	15/08/1999	anterior resection
19	66	1	1	7	3	18/08/1999	anterior resection
20	98	2	1	7	3	24/08/1999	anterior resection
21	87	2	0	1	1	08/09/1999	R hemicolectomy
22	78	2	0	4	2	15/09/1999	anterior resection
23	65	1	1	7	3	24/09/1999	R hemicolectomy
24	70	1	0	7	3	05/10/1999	sigmoid colectomy
25	60	0	1	4	2	21/10/1999	R hemicolectomy
26	72	1	0	3	2	22/10/1999	anterior resection
27	66	1	1	7	3	27/10/1999	anterior resection
28	56	0	0	6	3	18/11/1999	AP
29	82	2	1	4	2	25/11/1999	Right hemicolectomy
30	78	2	0	7	3	25/11/1999	R hemicolectomy
31	69	1	0	5	2	30/11/1999	sigmoid colectomy
32	72	1	0	7	3	08/12/1999	anterior resection
33	72	1	0	4	2	16/12/1999	Right Hemicolectomy
34	81	2	1	6	3	26/01/2000	R hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
35	66	1	0	4	2	03/03/2000	Anterior resection
36	45	0	1	7	3	08/03/2000	Right hemicolectomy
37	62	0	1	7	3	10/03/2000	Anterior resection
38	79	2	1	5	2	15/03/2000	Right hemicolectomy
39	60	0	0	3	2	06/04/2000	Anterior resection
40	72	1	1	7	3	19/05/2000	Anterior resection
41	67	1	0	5	2	21/07/2000	Anterior resection
42	63	0	0	3	2	25/07/2000	Right Hemicolectomy
43	89	2	1	7	3	08/09/2000	R hemicolectomy
44	85	2	1	7	3	08/09/2000	Anterior resection
45	72	1	0	6	3	28/09/2000	Anterior resection
46	70	1	0	7	3	27/10/2000	sigmoid colectomy
47	56	0	0	6	3	09/11/2000	Anterior resection
48	70	1	0	3	2	05/12/2000	anterior resection
49	64	0	0	7	3	14/12/2000	R hemicolectomy
50	78	2	1	5	2	16/01/2001	Anterior resection
51	64	0	0	6	3	30/01/2001	R hemicolectomy
52	72	1	0	6	3	31/01/2001	R hemicolectomy
53	55	0	1	6	3	13/02/2001	Sigmoid colectomy
54	74	1	1	6	3	16/02/2001	Anterior resection
55	83	2	0	2	1	09/03/2001	R hemicolectomy
56	55	0	0	.	4	13/03/2001	R hemicolectomy
57	79	2	0	6	3	23/03/2001	Right Hemicolectomy
58	42	0	1	4	2	03/05/2001	Right Hemicolectomy
59	60	0	1	5	2	08/05/2001	Proctectomy
60	71	1	1	4	2	08/05/2001	sigmoid colectomy
61	79	2	0	6	3	12/07/2001	R hemicolectomy
62	68	1	0	7	3	19/07/2001	Right hemicolectomy
63	63	0	0	3	2	09/08/2001	Anterior resection
64	76	2	1	3	2	21/08/2001	Hartmann's procedure
65	73	1	1	7	3	21/08/2001	Sub-total colectomy + IRA

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
66	69	1	0	4	2	23/08/2001	Sub-total colectomy + IRA
67	80	2	1	3	2	28/08/2001	Sigmoid colectomy
68	75	2	1	5	2	06/09/2001	Right Hemicolectomy
69	72	1	1	3	2	07/09/2001	Right Hemicolectomy
70	80	2	1	5	2	11/09/2001	Sigmoid colectomy
71	67	1	0	7	3	18/09/2001	anterior resection
72	32	0	0	7	3	18/09/2001	Anterior resection
73	54	0	0	4	2	18/09/2001	Sigmoid colectomy
74	77	2	0	7	3	20/09/2001	Anterior resection
75	77	2	0	3	2	21/09/2001	Anterior resection
76	58	0	0	.	4	26/09/2001	Proctectomy
77	82	2	1	4	2	27/09/2001	Sigmoid colectomy
78	80	2	1	6	3	02/10/2001	Right Hemicolectomy
79	73	1	0	6	3	05/10/2001	Proctectomy
80	80	2	1	6	3	09/10/2001	Sigmoid colectomy
81	32	0	0	7	3	12/10/2001	Right Hemicolectomy
82	61	0	1	6	3	15/10/2001	Sigmoid colectomy
83	79	2	0	4	2	16/10/2001	Right Hemicolectomy
84	46	0	0	3	2	25/10/2001	Sigmoid colectomy
85	83	2	0	6	3	30/10/2001	Right Hemicolectomy
86	80	2	0	7	3	06/11/2001	anterior resection
87	75	2	0	5	2	13/11/2001	anterior resection
88	70	1	0	6	3	15/11/2001	Anterior resection
89	59	0	0	7	3	20/11/2001	Anterior resection
90	82	2	1	7	3	22/11/2001	Right Hemicolectomy
91	81	2	1	7	3	28/11/2001	anterior Resection
92	60	0	0	4	2	12/12/2001	R hemicolectomy
93	69	1	0	4	2	30/12/2001	Hartmann's procedure
94	70	1	0	7	3	08/01/2002	Anterior resection
95	74	1	0	5	2	15/01/2002	anterior resection
96	77	2	0	5	2	18/01/2002	Anterior resection

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
97	78	2	1	4	2	20/01/2002	Hartmann's procedure
98	44	0	1	7	3	21/01/2002	sigmoid colectomy
99	89	2	1	6	3	30/01/2002	anterior resection
100	64	0	0	5	2	05/02/2002	anterior resection
101	81	2	1	4	2	28/02/2002	Anterior resection
102	67	1	0	3	2	02/03/2002	AP
103	65	1	1	1	1	08/03/2002	Proctectomy
104	74	1	0	6	3	20/03/2002	Right Hemicolectomy
105	63	0	0	3	2	04/04/2002	anterior resection
106	83	2	1	2	1	05/04/2002	AP
107	48	0	0	7	3	17/04/2002	anterior resection
108	50	0	1	3	2	24/04/2002	Right Hemicolectomy
109	61	0	1	4	2	26/04/2002	Proctectomy
110	84	2	0	7	3	02/05/2002	Right Hemicolectomy
111	50	0	1	6	3	07/05/2002	Right Hemicolectomy
112	64	0	1	4	2	08/05/2002	Hartmann's procedure
113	69	1	1	3	2	10/05/2002	Proctectomy
114	63	0	0	3	2	15/05/2002	anterior resection
115	76	2	1	6	3	17/05/2002	Right Hemicolectomy
116	75	2	0	7	3	28/05/2002	anterior resection
117	71	1	0	7	3	11/06/2002	sigmoid colectomy
118	63	0	0	7	3	13/06/2002	Sigmoid colectomy
119	68	1	0	7	3	20/06/2002	Right Hemicolectomy
120	69	1	1	7	3	20/06/2002	Right Hemicolectomy
121	76	2	0	3	2	20/06/2002	Right Hemicolectomy
122	79	2	0	5	2	26/06/2002	Right Hemicolectomy
123	73	1	0	7	3	06/07/2002	Sigmoid colectomy
124	80	2	1	6	3	10/07/2002	Right Hemicolectomy
125	67	1	1	7	3	11/07/2002	Proctectomy
126	59	0	1	3	2	12/08/2002	Proctectomy
127	77	2	1	4	2	13/08/2002	Anterior resection

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
128	90	2	1	7	3	14/08/2002	Sigmoid colectomy
129	50	0	0	4	2	20/08/2002	Proctectomy + ileoanal pouch
130	66	1	1	7	3	22/08/2002	Anterior resection
131	76	2	1	7	3	03/09/2002	Sigmoid colectomy
132	77	2	1	3	2	05/09/2002	Anterior resection
133	85	2	1	3	2	11/09/2002	Sigmoid colectomy
134	77	2	0	5	2	17/09/2002	Right Hemicolectomy
135	83	2	0	4	2	20/09/2002	Sigmoid colectomy
136	67	1	1	6	3	30/10/2002	anterior resection
137	79	2	0	6	3	01/11/2002	Proctectomy
138	68	1	1	4	2	05/11/2002	Right Hemicolectomy
139	75	2	1	6	3	12/11/2002	anterior resection
140	62	0	1	7	3	13/11/2002	Right Hemicolectomy
141	55	0	1	6	3	13/11/2002	Sigmoid colectomy
142	79	2	0	3	2	26/11/2002	sub-total colectomy + IRA
143	68	1	1	4	2	11/12/2002	Sigmoid colectomy
144	86	2	1	7	3	18/12/2002	Right Hemicolectomy
145	86	2	0	3	2	04/01/2003	Right Hemicolectomy
146	81	2	1	7	3	04/01/2003	Right Hemicolectomy
147	47	0	1	7	3	06/01/2003	anterior resection
148	53	0	0	7	3	08/01/2003	anterior resection
149	83	2	0	3	2	09/01/2003	Sigmoid colectomy
150	60	0	0	4	2	14/01/2003	Anterior resection
151	77	2	0	7	3	14/01/2003	anterior resection
152	74	1	0	7	3	23/01/2003	Sigmoid colectomy
153	83	2	1	5	2	29/01/2003	AP
154	56	0	0	6	3	30/01/2003	Sigmoid colectomy
155	76	2	1	6	3	14/02/2003	AP
156	69	1	1	7	3	06/03/2003	anterior resection
157	73	1	0	7	3	14/03/2003	sigmoid colectomy
158	63	0	0	7	3	19/03/2003	anterior resection

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
159	49	0	0	6	3	25/03/2003	AP
160	56	0	1	3	2	28/03/2003	Proctectomy
161	68	1	0	4	2	04/04/2003	Anterior resection
162	58	0	0	7	3	15/04/2003	anterior resection
163	64	0	0	7	3	21/04/2003	anterior resection
164	43	0	0	6	3	22/04/2003	Right hemicolectomy
165	79	2	0	7	3	23/04/2003	anterior resection
166	39	0	0	7	3	30/04/2003	AP
167	67	1	0	6	3	13/05/2003	Sigmoid colectomy
168	72	1	0	.	4	14/05/2003	Right Hemicolectomy
169	60	0	1	6	3	23/05/2003	Sigmoid colectomy
170	72	1	0	5	2	27/05/2003	Sigmoid colectomy
171	74	1	0	7	3	29/05/2003	Right Hemicolectomy
172	82	2	1	4	2	12/06/2003	Right Hemicolectomy
173	69	1	1	2	1	19/06/2003	anterior resection
174	83	2	1	6	3	04/07/2003	Right Hemicolectomy
175	76	2	1	7	3	31/07/2003	Right Hemicolectomy
176	64	0	1	3	2	01/08/2003	Anterior resection
177	38	0	1	7	3	05/08/2003	Right Hemicolectomy
178	61	0	1	4	2	07/08/2003	Right Hemicolectomy
179	56	0	1	7	3	07/08/2003	Anterior resection
180	87	2	1	3	2	15/08/2003	Right Hemicolectomy
181	76	2	1	3	2	15/08/2003	AP
182	74	1	0	3	2	20/08/2003	Subtotal colectomy
183	61	0	0	3	2	28/08/2003	Right hemicolectomy
184	83	2	1	7	3	29/08/2003	Right hemicolectomy
185	77	2	0	6	3	03/09/2003	Right Hemicolectomy
186	55	0	0	3	2	05/09/2003	Right Hemicolectomy
187	74	1	0	3	2	09/09/2003	Sigmoid colectomy
188	69	1	1	6	3	12/09/2003	Left hemicolectomy
189	75	2	0	4	2	18/09/2003	Sigmoid colectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
190	77	2	0	6	3	19/09/2003	Anterior resection
191	75	2	1	6	3	03/10/2003	Sigmoid colectomy
192	72	1	1	3	2	03/10/2003	AP
193	65	1	0	7	3	09/10/2003	Anterior resection
194	65	1	0	6	3	10/10/2003	Sigmoid colectomy
195	74	1	0	7	3	16/10/2003	Right Hemicolectomy
196	41	0	0	2	1	17/10/2003	Anterior resection
197	48	0	0	6	3	21/10/2003	Anterior resection
198	54	0	0	5	2	23/10/2003	Anterior resection
199	84	2	0	5	2	24/10/2003	Right hemicolectomy
200	74	1	0	7	3	30/10/2003	Left hemicolectomy
201	71	1	0	7	3	12/11/2003	AP
202	64	0	0	7	3	16/12/2003	Right Hemicolectomy
203	69	1	1	7	3	18/12/2003	Right Hemicolectomy
204	47	0	0	6	3	06/01/2004	Low anterior resection
205	70	1	0	3	2	08/01/2004	Anterior resection
206	69	1	0	4	2	08/01/2004	Sigmoid colectomy
207	73	1	1	6	3	09/01/2004	Right Hemicolectomy
208	79	2	0	4	2	23/01/2004	Sigmoid colectomy
209	70	1	0	6	3	06/02/2004	Sigmoid colectomy
210	67	1	1	5	2	24/02/2004	anterior resection
211	68	1	1	7	3	27/02/2004	Sigmoid colectomy
212	81	2	0	6	3	16/03/2004	Sigmoid colectomy
213	75	2	0	6	3	18/03/2004	right hemicolectomy
214	67	1	1	1	1	19/03/2004	right hemicolectomy
215	66	1	0	7	3	23/03/2004	anterior resection
216	69	1	1	7	3	25/03/2004	right hemicolectomy
217	77	2	1	4	2	25/03/2004	anterior resection
218	70	1	0	3	2	14/04/2004	anterior resection
219	80	2	1	7	3	16/04/2004	anterior resection
220	59	0	1	4	2	20/04/2004	right hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
221	75	2	1	5	2	23/04/2004	anterior resection
222	83	2	1	7	3	05/05/2004	right hemicolectomy
223	79	2	0	7	3	14/05/2004	right hemicolectomy
224	51	0	0	7	3	18/05/2004	anterior resection
225	80	2	0	3	2	08/06/2004	anterior resection
226	73	1	0	5	2	15/06/2004	anterior resection
227	72	1	1	4	2	15/06/2004	Left hemicolectomy

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
1	0	0	15-May-05	0	77.13	4	0	0	1
2	0	0	12-Mar-04	2	62.53	3	0	0	1
3	0	0	15-May-05	0	76.2	3	0	0	1
4	0	0	15-May-05	0	75.97	3	0	0	1
5	0	0	15-May-05	0	75.7	3	0	0	1
6	1	0	25-Feb-02	1	36.3	3	1	0	2
7	0	0	25-Aug-04	2	66.33	3	0	0	1
8	1	0	15-May-05	0	75.07	2	2	0	2
9	0	1	15-May-05	0	75.03	3	0	0	1
10	0	0	01-Dec-99	1	6.9	4	0	0	1
11	0	0	15-May-05	0	72.87	3	0	0	1
12	0	0	16-Aug-03	2	50.67	3	0	0	1
13	1	0	15-May-05	0	71.77	3	0	0	1
14	1	0	15-May-05	0	71.57	3	0	0	1
15	0	0	15-May-05	0	71.1	3	1	0	2
16	0	0	14-Oct-01	1	27.13	3	0	0	1
17	0	0	15-May-05	0	70.33	3	2	0	2
18	1	0	28-May-04	2	58.27	3	0	0	1
19	1	0	15-May-05	0	69.9	3	0	0	1
20	1	0	26-Oct-01	1	26.47	3	2	0	2
21	0	0	15-May-05	0	69.2	3	0	0	1
22	1	0	15-May-05	0	68.97	3	0	0	1
23	0	0	15-May-05	0	68.67	3	0	0	1
24	0	1	15-May-05	0	68.3	3	2	0	2
25	0	0	15-May-05	0	67.77	4	0	0	1
26	1	1	19-Feb-05	2	64.9	2	1	0	2
27	1	1	15-May-05	0	67.57	1	1	0	2
28	1	1	22-Mar-03	2	40.67	3	2	0	2
29	0	0	17-Jun-03	1	43.33	3	1	0	2
30	0	0	02-Jan-05	2	62.17	3	0	0	1

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
31	0	1	30-Oct-02	1	35.5	3	2	0	2
32	1	0	15-May-05	0	66.17	3	0	0	1
33	0	1	15-May-05	0	65.9	3	0	0	1
34	0	0	15-May-05	0	64.53	4	0	0	1
35	1	0	26-Aug-03	1	42.37	4	0	0	1
36	0	0	15-May-05	0	63.13	4	0	0	1
37	1	1	02-May-01	1	13.93	3	2	0	2
38	0	0	12-Sep-01	2	18.2	3	0	0	1
39	1	1	15-May-05	0	62.17	4	0	0	1
40	1	0	18-Mar-03	1	34.43	2	0	0	0
41	1	0	15-May-05	0	58.63	3	0	0	1
42	0	1	18-Mar-02	1	20.03	4	1	0	2
43	0	0	04-Jun-03	2	33.3	3	1	0	2
44	1	0	15-May-05	0	57	3	1	0	2
45	1	0	15-May-05	0	56.33	2	1	0	2
46	0	0	15-May-05	0	55.37	3	0	0	1
47	1	0	15-May-05	0	54.93	4	0	0	1
48	1	0	15-May-05	0	54.07	3	0	0	1
49	0	1	15-May-05	0	53.77	3	1	0	2
50	1	0	15-May-05	0	52.67	4	0	0	1
51	0	1	15-May-05	0	52.2	3	1	0	2
52	0	0	15-May-05	0	52.17	3	0	0	1
53	0	0	15-May-05	0	51.73	3	0	0	1
54	1	0	15-May-05	0	51.63	1	0	0	0
55	0	0	15-May-05	0	50.93	3	0	0	1
56	0	1	15-May-05	0	50.8	4	1	0	2
57	0	0	15-May-05	0	50.47	3	0	0	1
58	0	1	15-May-05	0	49.1	3	0	0	1
59	1	1	27-Feb-02	2	9.83	4	2	0	2
60	0	0	15-May-05	0	48.93	3	0	0	1
61	0	0	15-May-05	0	46.77	3	1	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
62	0	1	15-May-05	0	46.53	3	1	0	2
63	1	1	15-May-05	0	45.83	2	1	0	2
64	0	0	15-May-05	0	45.43	3	0	0	1
65	0	0	15-May-05	0	45.43	3	0	0	1
66	0	0	15-May-05	0	45.37	3	0	0	1
67	0	0	15-May-05	0	45.2	3	0	0	1
68	0	0	15-May-05	0	44.9	3	0	0	1
69	0	0	15-May-05	0	44.87	3	1	0	2
70	0	0	19-Sep-01	1	0.27	4	1	0	2
71	1	0	05-Oct-01	1	0.57	3	2	0	2
72	1	1	15-May-05	0	44.5	3	2	0	2
73	0	0	15-May-05	0	44.5	1	0	0	0
74	1	1	15-May-05	0	44.43	3	1	0	2
75	1	0	15-May-05	0	44.4	2	0	0	0
76	1	1	18-Sep-03	2	24.07	3	1	0	2
77	0	0	09-Aug-04	2	34.9	3	0	0	1
78	0	0	15-May-05	0	44.03	4	1	0	2
79	1	0	15-May-05	0	43.93	2	2	0	2
80	0	0	15-May-05	0	43.8	2	0	0	0
81	0	1	15-May-05	0	43.7	3	0	0	1
82	0	0	15-May-05	0	43.6	4	0	0	1
83	0	0	27-Apr-02	1	6.43	4	1	0	2
84	0	1	28-Dec-04	1	38.67	3	1	0	2
85	0	0	15-May-05	0	43.1	3	0	0	1
86	1	0	15-May-05	0	42.87	4	1	0	2
87	1	0	24-Jan-03	1	14.57	4	1	0	2
88	1	0	15-May-05	0	42.57	4	0	0	1
89	1	1	19-Feb-03	2	15.2	3	0	0	1
90	0	0	24-Dec-01	2	1.07	2	0	0	0
91	1	0	15-May-05	0	42.13	4	0	0	1
92	0	0	15-May-05	0	41.67	4	0	0	1
93	0	1	28-Dec-03	1	24.27	4	2	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
94	1	0	15-May-05	0	40.77	3	0	0	1
95	1	1	15-May-05	0	40.53	3	1	0	2
96	1	0	12-Jun-03	2	17	2	1	0	2
97	0	0	09-Feb-03	1	12.83	4	1	0	2
98	0	0	15-May-05	0	40.33	3	0	0	1
99	1	0	15-May-05	0	40.03	2	0	0	0
100	1	1	15-May-05	0	39.83	3	2	0	2
101	1	0	15-May-05	0	39.07	1	1	0	2
102	1	0	05-Mar-02	1	0.1	3	0	0	1
103	1	0	15-May-05	0	38.8	2	2	0	2
104	0	0	24-Mar-03	1	12.3	4	2	0	2
105	1	0	05-Sep-04	2	29.5	3	1	0	2
106	1	0	19-Jan-05	1	34	3	1	0	2
107	1	1	15-May-05	0	37.47	3	1	0	2
108	0	1	15-May-05	0	37.23	4	2	0	2
109	1	0	15-May-05	0	37.17	2	0	0	0
110	0	1	23-May-03	1	12.87	3	1	0	2
111	0	1	21-Jun-03	1	13.67	3	1	0	2
112	0	1	15-May-05	0	36.77	4	1	0	2
113	1	0	30-Sep-04	1	29.13	2	0	0	0
114	1	0	18-Sep-04	2	28.57	3	0	0	1
115	0	0	16-Dec-03	1	19.27	4	1	0	2
116	1	0	15-May-05	0	36.1	3	1	0	2
117	0	0	15-May-05	0	35.63	3	0	0	1
118	0	1	15-May-05	0	35.57	4	1	0	2
119	0	0	15-Apr-04	2	22.17	3	0	0	1
120	0	0	15-May-05	0	35.33	3	0	0	1
121	0	0	15-May-05	0	35.33	3	2	0	2
122	0	0	15-May-05	0	35.13	4	2	0	2
123	0	0	15-May-05	0	34.8	2	0	0	0
124	0	0	15-May-05	0	34.67	4	1	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
125	1	1	02-May-03	2	9.83	3	1	0	2
126	1	0	15-May-05	0	33.57	3	0	0	1
127	1	1	05-Dec-04	1	28.17	4	0	0	1
128	0	0	23-Aug-02	1	0.3	4	0	0	1
129	1	0	15-May-05	0	33.3	2	0	0	0
130	1	0	09-Nov-03	2	14.8	2	1	0	2
131	0	1	15-May-05	0	32.83	2	1	0	2
132	1	0	15-May-05	0	32.77	3	1	0	2
133	0	0	15-May-05	0	32.57	4	0	0	1
134	0	0	15-May-05	0	32.37	4	0	0	1
135	0	0	25-Feb-04	1	17.43	4	1	0	2
136	1	0	15-May-05	0	30.93	3	0	0	1
137	1	0	23-Jul-04	2	21	3	0	0	1
138	0	0	17-Mar-04	2	16.6	3	0	0	1
139	1	0	04-Apr-04	2	16.97	3	0	0	1
140	0	0	15-May-05	0	30.47	3	0	0	1
141	0	1	15-May-05	0	30.47	3	0	0	1
142	0	0	15-May-05	0	30.03	3	0	0	1
143	0	0	15-May-05	0	29.53	4	0	0	1
144	0	0	15-May-05	0	29.3	3	0	0	1
145	0	0	07-Oct-03	1	9.2	3	0	0	1
146	0	0	15-May-05	0	28.73	4	2	0	2
147	1	0	15-May-05	0	28.67	2	0	0	0
148	1	0	15-May-05	0	28.6	3	1	0	2
149	0	0	15-May-05	0	28.57	4	1	0	2
150	1	0	15-May-05	0	28.4	3	0	0	1
151	1	0	15-May-05	0	28.4	3	1	0	2
152	0	0	15-May-05	0	28.1	3	0	0	1
153	1	0	09-Jul-03	1	5.37	3	0	0	1
154	0	1	15-May-05	0	27.87	2	1	0	2
155	1	0	27-Feb-03	1	0.43	1	0	0	0

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
156	1	0	15-May-05	0	26.7	3	0	0	1
157	0	0	15-May-05	0	26.43	3	0	0	1
158	1	1	25-Dec-03	2	9.37	3	0	0	1
159	1	0	15-May-05	0	26.07	3	0	0	1
160	1	0	15-May-05	0	25.97	3	1	0	2
161	1	0	15-May-05	0	25.73	3	0	0	1
162	1	0	15-May-05	0	25.37	3	1	0	2
163	1	1	15-May-05	0	25.17	3	1	0	2
164	0	0	15-May-05	0	25.13	2	0	0	0
165	1	0	15-May-05	0	25.1	3	0	0	1
166	1	1	15-May-05	0	24.87	3	1	0	2
167	0	0	15-May-05	0	24.43	1	0	0	0
168	0	0	20-Oct-03	1	5.3	3	0	0	1
169	0	1	15-May-05	0	24.1	4	1	0	2
170	0	1	15-May-05	0	23.97	4	0	0	1
171	0	0	15-May-05	0	23.9	3	0	0	1
172	0	0	15-May-05	0	23.43	3	0	0	1
173	1	0	15-May-05	0	23.2	3	1	0	2
174	0	0	15-May-05	0	22.7	3	0	0	1
175	0	0	15-May-05	0	21.8	2	0	0	0
176	1	0	15-May-05	0	21.77	2	0	0	0
177	0	1	02-Mar-05	1	19.17	3	1	0	2
178	0	0	15-May-05	0	21.57	4	2	0	2
179	1	1	15-May-05	0	21.57	2	1	0	2
180	0	0	01-Jul-04	1	10.7	4	1	0	2
181	1	0	15-May-05	0	21.3	3	1	0	2
182	0	0	15-May-05	0	21.13	3	0	0	1
183	0	1	15-May-05	0	20.87	3	0	0	1
184	0	0	15-May-05	0	20.83	2	0	0	0
185	0	0	15-May-05	0	20.67	3	0	0	1
186	0	1	15-May-05	0	20.6	3	1	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
187	0	0	15-May-05	0	20.47	4	1	0	2
188	0	0	15-May-05	0	20.37	4	0	0	1
189	0	1	15-May-05	0	20.17	3	1	0	2
190	1	1	15-May-05	0	20.13	4	1	0	2
191	0	0	15-May-05	0	19.67	4	1	0	2
192	1	0	15-May-05	0	19.67	1	1	0	2
193	1	1	15-May-05	0	19.47	3	0	0	1
194	0	0	15-May-05	0	19.43	3	1	0	2
195	0	0	15-May-05	0	19.23	2	0	0	0
196	1	0	15-May-05	0	19.2	2	0	0	0
197	1	0	15-May-05	0	19.07	3	0	0	1
198	1	0	15-May-05	0	19	1	0	0	0
199	0	0	15-May-05	0	18.97	3	0	0	1
200	0	0	15-May-05	0	18.77	3	1	0	2
201	1	0	15-May-05	0	18.33	1	0	0	0
202	0	0	15-May-05	0	17.2	3	0	0	1
203	0	1	15-May-05	0	17.13	4	1	0	2
204	1	0	15-May-05	0	16.5	3	1	0	2
205	1	1	15-May-05	0	16.43	4	0	0	1
206	0	0	15-May-05	0	16.43	4	0	0	1
207	0	1	15-May-05	0	16.4	3	1	0	2
208	0	0	09-Feb-04	2	0.57	4	2	0	2
209	0	0	15-May-05	0	15.47	3	0	0	1
210	1	0	21-May-04	1	2.9	4	2	0	2
211	0	0	15-May-05	0	14.77	2	0	0	0
212	0	0	15-May-05	0	14.17	3	0	0	1
213	0	1	15-May-05	0	14.1	4	0	0	1
214	0	1	21-Feb-05	1	11.3	4	2	0	2
215	1	1	15-May-05	0	13.93	3	1	0	2
216	0	0	15-May-05	0	13.87	3	0	0	1
217	1	0	15-May-05	0	13.87	4	1	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
218	1	1	15-May-05	0	13.2	4	0	0	1
219	1	0	15-May-05	0	13.13	3	0	0	1
220	0	0	15-May-05	0	13	3	0	0	1
221	1	0	15-May-05	0	12.9	3	0	0	1
222	0	0	15-May-05	0	12.5	4	0	0	1
223	0	0	15-May-05	0	12.2	3	2	0	2
224	1	1	15-May-05	0	12.07	3	2	0	2
225	1	0	15-May-05	0	11.37	2	0	0	0
226	1	0	06-Sep-04	2	2.77	3	2	0	2
227	0	1	15-May-05	0	11.13	3	1	0	2

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
1	Poorly	no	clear	15	0	no	1	55	2	22	1
2	well/mod	no	clear	23	0	no	0	25	0	5	0
3	well/mod	no	clear	9	0	no	1	40	1	5	0
4	well/mod	no	clear	12	0	no	0	130	2	5	0
5	well/mod	yes	clear	9	0	no	1	85	2	5	0
6	well/mod	no	clear	9	1	no	0	35	0	15	1
7	well/mod	no	clear	12	0	no	0	29	0	5	0
8	well/mod	no	clear	19	5	no	0	40	1	16	1
9	well/mod	no	clear	10	0	no	1	17	0	8	0
10	well/mod	yes	clear	7	0	no	0	130	2	50	1
11	well/mod	no	clear	12	0	no	0	50	1	5	0
12	Poorly	no	clear	16	0	no	0	45	1	5	0
13	well/mod	no	clear	14	0	no	1	13	0	5	0
14	well/mod	no	clear	10	0	no	0	40	1	5	0
15	well/mod	yes	clear	19	1	no	1	40	1	9	0
16	well/mod	yes	clear	13	0	no	1	35	0	15	1
17	well/mod	no	clear	18	5	no	1	35	0	5	0
18	well/mod	yes	clear	25	0	no	0	55	2	35	1
19	well/mod	no	clear	26	0	no	0	40	1	5	0
20	well/mod	no	clear	10	6	yes	1	40	1	5	0
21	well/mod	no	clear	17	0	no	1	50	1	5	0
22	well/mod	no	clear	20	0	no	0	35	0	5	0
23	well/mod	no	clear	15	0	no	1	33	0	5	0
24	well/mod	no	clear	16	6	no	1	40	1	5	0
25	well/mod	no	clear	16	0	no	0	55	2	61	1
26	well/mod	no	clear	17	1	no	0	10	0	5	0
27	Poorly	no	clear	8	1	no	0	27	0	5	0
28	Poorly	no	clear	24	4	no	1	28	0	5	0

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
29	well/mod	no	clear	14	2	no	0	35	0	23	1
30	well/mod	no	clear	30	0	no	1	60	2	37	1
31	poorly	yes	clear	29	15	no	1	35	1	11	1
32	well/mod	no	clear	29	0	no	0	55	2	5	0
33	well/mod	no	clear	14	0	no	1	80	2	5	0
34	well/mod	no	clear	7	0	no	0	16	0	5	0
35	well/mod	yes	clear	21	.	no	1	25	0	5	0
36	well/mod	no	clear	12	0	no	0	50	1	6	0
37	well/mod	yes	clear	32	4	no	0	35	1	16	1
38	well/mod	no	clear	23	0	no	0	30	0	31	1
39	well/mod	no	clear	15	0	no	1	60	2	178	1
40	poorly	no	clear	.	.		0	36	1	6	0
41	well/mod	no	clear	26	0	no	0	55	2	35	1
42	well/mod	no	clear	17	1		1	70	2	97	1
43	well/mod	no	clear	25	3	no	1	80	2	31	1
44	well/mod	no	clear	10	1	no	1	45	1	7	0
45	well/mod	no	clear	.	.		0	50	1	26	1
46	well/mod	no	clear	8	0	no	0	30	0	19	1
47	well/mod	no	clear	20	0		0	55	2	77	1
48	well/mod	yes	clear	11	0	no	1	50	1	5	0
49	well/mod	no	clear	11	1	no	1	38	1	5	0
50	well/mod	no	clear	11	0	no	1	40	1	5	0
51	well/mod	no	clear	21	1	no	0	40	1	5	0
52	well/mod	no	clear	13	0	no	0	90	2	5	0
53	well/mod	no	clear	35	0	no	0	25	0	6	0
54	well/mod	no	clear	8	0	no	0	25	0	6	0
55	well/mod	no	clear	10	0	no	0	55	2	17	1
56	signet ring	no	clear	15	3	no	1	100	2	37	1
57	well/mod	no	clear	26	0	no	0	70	2	21	1

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
58	well/mod	no	clear	20	0	no	0	35	0	6	0
59	well/mod	yes	clear	12	5	no	0	40	1	120	1
60	well/mod	no	clear	19	0	no	0	45	1	6	0
61	well/mod	no	clear	20	2	no	0	110	2	92	1
62	well/mod	no	clear	7	1	no	0	30	0	6	0
63	well/mod	no	clear	7	3	no	1	43	1	6	0
64	well/mod	no	clear	10	0	no	0	80	2	41	1
65	poorly	no	clear	14	0	no	1	25	0	7	0
66	well/mod	no	clear	18	0	no	1	50	1	22	1
67	well/mod	no	clear	8	0	no	0	50	1	11	1
68	well/mod	no	clear	18	0	no	1	50	1	8	0
69	well/mod	no	clear	14	2	no	1	35	0	7	0
70	moderately	no	clear	6	1	no	0	15	0	6	0
71	moderately	no	clear	17	7	no	0	42	1	22	1
72	well/mod	yes	clear	21	5	no	0	48	1	6	0
73	moderately	no	clear	28	0	no	0	37	1	6	0
74	well/mod	no	clear	8	3	yes	0	50	1	6	0
75	well/mod	no	clear	13	0	no	0	30	0	7	0
76	moderately	no	clear	14	1		1	56	2	6	0
77	well/mod	no	clear	21	0	no	0	70	2	33	1
78	moderately	yes	clear	8	3	no	0	60	2	29	1
79	well/mod	yes	clear	12	6	no	0	45	1	6	0
80	well/mod	no	clear	15	0	no	0	28	0	12	1
81	well/mod	no	clear	26	0	no	1	80	2	24	1
82	moderately	no	clear	10	0	no	0	65	2	71	1
83	moderately	no	clear	14	2	no	0	30	0	5	0
84	well/mod	yes	clear	18	2	no	0	35	0	9	0
85	well/mod	no	clear	7	0	no	0	30	0	6	0
86	moderately	no	clear	17	1	no	0	45	1	6	0

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
87	moderately	no	clear	7	1	no	1	40	1	48	1
88	well/mod	no	clear	11	0	no	0	40	1	6	0
89	well/mod	no	clear	26	0	no	0	50	1	34	1
90	well	no	clear	10	0	no	1	80	2	46	1
91	moderately	no	clear	10	0	no	1	50	1	8	0
92	well/mod	no	clear	17	0	no	0	50	1	15	1
93	poorly	no	clear	19	6	no	0	50	1	26	1
94	well/mod	no	clear	12	0	no	0	60	2	6	0
95	moderately	yes	clear	16	1	no	0	50	1	6	0
96	well/mod	no	clear	11	1	no	0	30	0	6	0
97	poorly	yes	clear	9	1	no	0	30	0	20	1
98	well/mod	no	clear	18	0	no	0	55	2	6	0
99	well/mod	no	clear	22	0	no	0	40	1	41	1
100	moderately	no	clear	17	4	no	1	20	0	6	0
101	well/mod	no	clear	13	2	no	0	25	0	11	1
102	poor	no	clear	1	0	no	0	50	1	10	0
103	poorly	no	clear	19	5	no	1	38	1	6	0
104	well/mod	yes	clear	20	9	no	0	55	2	58	1
105	well/mod	no	clear	17	1	no	0	52	1	14	1
106	poorly	yes	clear	15	3	no	1	25	0	6	0
107	well/mod	no	clear	20	2	no	1	40	1	5	0
108	Moderately	yes	clear	24	7	yes	0	45	1	7	0
109	well/mod	no	clear	29	0	no	1	50	1	6	0
110	poor	yes	clear	14	3		0	60	2	135	1
111	well/mod	yes	clear	3	1	yes	0	35	0	28	1
112	well/mod	yes	clear	8	1	no	0	90	2	56	1
113	well/mod	no	clear	6	0	no	0	10	0	20	1
114	well/mod	yes	clear	11	0	no	0	35	0	5	0
115	well/mod	no	clear	19	2	no	0	30	0	6	0

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
116	moderately	no	clear	18	3	no	0	35	0	5	0
117	moderately	no	clear	10	0	no	0	35	0	6	0
118	moderately	yes	clear	11	2	no	1	30	0	9	0
119	Moderately	no	clear	15	0	no	0	55	2	9	0
120	poorly	no	clear	19	0	no	0	53	1	12	1
121	poorly	no	clear	10	9	no	0	57	2	31	1
122	moderately	yes	clear	22	4	no	0	55	2	19	1
123	moderately	no	clear	7	0	no	0	30	0	20	1
124	well/mod	yes	clear	10	2	no	0	30	0	5	0
125	well/mod	yes	clear	14	2	no	0	45	1	22	1
126	well/mod	yes	clear	12	0	no	1	35	0	6	0
127	well/mod	yes	clear	24	0	no	1	55	2	26	1
128	moderately	no	clear	9	9	no	0	80	2	26	1
129	well/mod	no	clear	16	0	no	1	40	1	6	0
130	well/mod	yes	clear	10	2	yes	0	25	0	10	0
131	well/mod	yes	clear	8	1	no	0	35	0	6	0
132	well/mod	yes	clear	12	1	no	0	60	2	6	0
133	moderately	no	clear	9	0	no	0	40	1	14	1
134	poor	no	clear	3	0	no	0	55	2	101	1
135	well/mod	yes	clear	12	3	yes	1	45	1	6	0
136	Moderately	no	clear	15	0	no	1	60	2	5	0
137	well/mod	no	clear	15	0	no	1	55	2	26	1
138	well/mod	no	clear	7	0	no	0	35	0	7	0
139	moderately	no	clear	12	0	no	0	60	2	19	1
140	moderately	no	clear	26	0	no	1	70	2	17	1
141	Moderately	no	clear	15	0	no	1	35	0	5	0
142	well/mod	no	clear	20	0	no	1	60	2	41	1
143	moderately	no	clear	16	0	no	0	50	1	8	0
144	well/mod	no	clear	16	0	no	0	55	2	27	1

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
145	Moderately	no	clear	28	0	no	1	75	2	49	1
146	Moderately	yes	clear	10	3	yes	1	60	2	21	1
147	Moderately	no	clear	25	0	no	1	55	1	6	0
148	moderately	no	clear	27	1	no	1	18	0	11	1
149	Moderately	yes	clear	13	2	no	0	40	1	19	1
150	Moderately	no	clear	19	0	no	0	87	2	34	1
151	moderately	no	clear	21	1	no	0	30	0	6	0
152	Moderately	yes	clear	17	0	no	0	35	0	6	0
153	moderately	no	clear	16	0	no	0	65	2	13	1
154	well/mod	no	clear	18	2	no	0	30	0	8	0
155	Moderately	no	clear	7	0	no	0	10	0	7	0
156	Moderately	no	clear	25	0	no	0	45	1	6	0
157	Moderately	no	clear	11	0	no	0	150	2	48	1
158	Moderately	yes	clear	11	0	no	0	35	0	6	0
159	Moderately	no	clear	17	0	no	0	60	2	6	0
160	Moderately	no	clear	15	1	no	0	40	1	6	0
161	Moderately	yes	clear	11	0	no	0	60	2	6	0
162	poor	yes	clear	27	1	no	0	60	2	9	0
163	moderately	no	clear	25	1	no	0	60	2	40	1
164	moderately	no	clear	14	0	no	1	30	0	7	0
165	moderately	no	clear	29	0	no	0	55	2	47	1
166	moderately	yes	clear	10	3	no	0	20	0	7	0
167	moderately	no	clear	8	0	no	0	35	0	6	0
168	poor	yes	clear	10	0	no	0	20	0	10	0
169	Moderately	no	clear	10	2	no	0	40	1	9	0
170	poor	no	clear	9	0	no	1	20	0	6	0
171	Moderately	no	clear	18	0	no	0	30	0	8	0
172	poor	yes	clear	15	0	no	0	50	1	33	1
173	moderately	yes	clear	12	1	no	0	22	0	5	0

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
174	Moderately	no	clear	11	0	no	0	90	2	95	1
175	moderately	no	clear	14	0	no	1	40	1	6	0
176	well/mod	no	clear	19	0	no	1	40	1	5	0
177	well/mod	yes	clear	4	1	yes	0	80	2	38	1
178	poorly	yes	clear	27	13	no	0	40	1	5	0
179	well/mod	no	clear	19	3	no	0	40	1	11	1
180	well/mod	yes	clear	12	1	no	0	80	2	94	1
181	Well/mod	no	clear	11	2	no	0	50	1	5	0
182	Well/mod	no	clear	13	0	no	0	30	0	5	0
183	well/mod	yes	clear	10	0	no	0	30	0	10	0
184	well/mod	no	clear	8	0	no	0	55	1	6	0
185	well/mod	no	clear	14	0	no	0	52	1	7	0
186	poorly	no	clear	8	1	yes	1	55	2	19	1
187	well/mod	no	clear	13	2	no	0	23	0	5	0
188	well/mod	no	clear	7	0	no	0	60	2	29	1
189	well/mod	no	clear	8	1	no	0	20	0	5	0
190	well/mod	yes	clear	7	3	no	0	50	1	5	0
191	well/mod	yes	clear	15	3	no	0	50	1	7	0
192	well/mod	no	clear	8	3	yes	0	35	0	5	0
193	well/mod	yes	clear	15	0	no	0	38	1	7	0
194	well/mod	yes	clear	12	1	no	0	50	1	5	0
195	well/mod	no	clear	11	0	no	0	65	2	12	1
196	well/mod	no	clear	7	0	no	0	25	0	5	0
197	well/mod	yes	clear	19	0	no	0	50	1	5	0
198	well	no	clear	9	0		0	30	0	8	0
199	poorly	yes	clear	9	0	no	0	90	2	40	1
200	moderately	no	clear	16	1	no	0	50	1	21	1
201	moderately	yes	clear	11	0	no	1	30	0	5	0
202	moderately	no	clear	14	0	no	0	85	2	75	1

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive	Ulceration (no=0 yes=1)	Tumour size (mm)	Tumour size Tertile	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)
203	moderately	yes	clear	16	1	no	0	24	0	9	0
204	moderately	yes	clear	12	2	no	0	30	0	5	0
205	moderately	yes	clear	8	0	no	0	70	2	31	1
206	moderately	no	clear	13	.	no	0	30	0	5	0
207	moderately	no	clear	9	1	no	0	60	2	18	1
208	moderately	no	clear	11	4	no	0	60	2	6	0
209	moderately	no	clear	28	0	no	0	80	2	27	1
210	poorly	yes	clear	24	16	no	0	65	2	38	1
211	moderately	no	clear	8	0	no	0	15	0	12	1
212	moderately	no	clear	13	0	no	0	60	2	12	1
213	moderately	yes	clear	22	0	no	0	50	1	6	0
214	poorly	yes	clear	25	4	no	0	95	2	209	1
215	moderately	yes	clear	8	2	no	0	80	2	5	0
216	moderately	yes	clear	41	0	no	0	90	2	133	1
217	moderately	yes	clear	16	3	no	0	40	1	22	1
218	moderately	no	clear	12	0	no	0	50	1	5	0
219	moderately	yes	clear	13	0	no	0	55	2	101	1
220	undifferentiated	yes	clear	25	.	no	0	60	2	14	1
221	moderately	no	clear	17	0	no	0	53	1	14	1
222	moderately	no	clear	9	0	no	0	40	1	16	1
223	poorly	no	clear	11	4	no	0	30	0	27	1
224	moderately	no	clear	12	6	no	1	20	0	5	0
225	moderately	no	clear	12	0	no	0	20	0	5	0
226	poorly	yes	clear	31	4	no	0	75	2	12	1
227	moderately	no	clear	9	1	no	0	100	2	5	0

Appendix 3 - Database for chapter 5 - THE RELATIONSHIP BETWEEN EMERGENCY PRESENTATION, THE SYSTEMIC INFLAMMATORY RESPONSE AND CANCER SPECIFIC SURVIVAL IN PATIENTS UNDERGOING POTENTIALLY CURATIVE SURGERY FOR COLORECTAL CANCER

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
1	41	0	0	7	3	16-Mar-99	anterior resection
2	56	0	0	6	3	18-Nov-99	AP
3	82	2	1	4	2	25-Nov-99	Right hemicolectomy
4	72	1	0	4	2	16-Dec-99	Right Hemicolectomy
5	45	0	1	7	3	08-Mar-00	Right hemicolectomy
6	79	2	1	5	2	15-Mar-00	Right hemicolectomy
7	60	0	0	3	2	06-Apr-00	Anterior resection
8	89	2	1	7	3	08-Sep-00	R hemicolectomy
9	72	1	0	6	3	28-Sep-00	Anterior resection
10	70	1	0	7	3	27-Oct-00	sigmoid colectomy
11	55	0	1	6	3	13-Feb-01	Sigmoid colectomy
12	74	1	1	6	3	16-Feb-01	Anterior resection
13	57	0	0	5	2	14-Mar-01	Hartmann's
14	79	2	0	6	3	23-Mar-01	Right Hemicolectomy
15	42	0	1	4	2	03-May-01	Right Hemicolectomy
16	68	1	0	7	3	19-Jul-01	Right hemicolectomy
17	63	0	0	3	2	09-Aug-01	Anterior resection
18	76	2	1	3	2	21-Aug-01	Hartmann's
19	73	1	1	7	3	21-Aug-01	Sub-total colectomy
20	69	1	0	4	2	23-Aug-01	Sub-total colectomy
21	75	2	1	5	2	06-Sep-01	Right Hemicolectomy
22	72	1	1	3	2	07-Sep-01	Right Hemicolectomy
23	32	0	0	7	3	18-Sep-01	Anterior resection
24	54	0	0	4	2	18-Sep-01	Sigmoid colectomy
25	77	2	0	7	3	20-Sep-01	Anterior resection
26	77	2	0	3	2	21-Sep-01	Anterior resection
27	58	0	0	5	2	26-Sep-01	Proctectomy
28	82	2	1	4	2	27-Sep-01	Sigmoid colectomy
29	80	2	1	6	3	02-Oct-01	Right Hemicolectomy
30	73	1	0	6	3	05-Oct-01	Proctectomy
31	80	2	1	6	3	09-Oct-01	Sigmoid colectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
32	32	0	0	7	3	12-Oct-01	Right Hemicolectomy
33	61	0	1	6	3	15-Oct-01	Sigmoid colectomy
34	79	2	0	4	2	16-Oct-01	Right Hemicolectomy
35	46	0	0	3	2	25-Oct-01	Sigmoid colectomy
36	83	2	0	6	3	30-Oct-01	Right Hemicolectomy
37	80	2	0	7	3	06-Nov-01	anterior resection
38	75	2	0	5	2	13-Nov-01	anterior resection
39	70	1	0	6	3	15-Nov-01	Anterior resection
40	59	0	0	7	3	20-Nov-01	Anterior resection
41	82	2	1	7	3	22-Nov-01	Right Hemicolectomy
42	81	2	1	7	3	28-Nov-01	anterior Resection
43	60	0	0	4	2	12-Dec-01	R hemicolectomy
44	52	0	0	7	3	19-Dec-01	Hartmann's
45	69	1	0	4	2	30-Dec-01	Hartmann's
46	70	1	0	7	3	08-Jan-02	Anterior resection
47	91	2	0	7	3	09-Jan-02	Right Hemicolectomy
48	74	1	0	5	2	15-Jan-02	anterior resection
49	77	2	0	5	2	18-Jan-02	Anterior resection
50	78	2	1	4	2	20-Jan-02	Hartmann's
51	44	0	1	7	3	21-Jan-02	sigmoid colectomy
52	89	2	1	6	3	30-Jan-02	anterior resection
53	64	0	0	5	2	05-Feb-02	anterior resection
54	81	2	0	7	3	19-Feb-02	Right Hemicolectomy
55	76	2	1	7	3	27-Feb-02	Sigmoid colectomy
56	81	2	1	4	2	28-Feb-02	Anterior resection
57	65	1	1	1	1	08-Mar-02	Proctectomy
58	58	0	0	6	3	13-Mar-02	sigmoid colectomy
59	74	1	0	6	3	20-Mar-02	Right Hemicolectomy
60	63	0	0	3	2	04-Apr-02	anterior resection
61	83	2	1	2	1	05-Apr-02	AP
62	76	2	1	6	3	16-Apr-02	Right Hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
63	48	0	0	7	3	17-Apr-02	anterior resection
64	50	0	1	3	2	24-Apr-02	Right Hemicolectomy
65	61	0	1	4	2	26-Apr-02	Proctectomy
66	65	1	0	6	3	02-May-02	Right Hemicolectomy
67	84	2	0	7	3	02-May-02	Right Hemicolectomy
68	50	0	1	6	3	07-May-02	Right Hemicolectomy
69	64	0	1	4	2	08-May-02	Hartmann's
70	69	1	1	3	2	10-May-02	Proctectomy
71	63	0	0	3	2	15-May-02	anterior resection
72	76	2	1	6	3	17-May-02	Right Hemicolectomy
73	75	2	0	7	3	28-May-02	anterior resection
74	54	0	1	4	2	29-May-02	Right Hemicolectomy
75	79	2	0	6	3	07-Jun-02	Sub-total colectomy
76	72	1	0	7	3	11-Jun-02	sigmoid colectomy
77	64	0	0	7	3	13-Jun-02	Sigmoid colectomy
78	69	1	1	7	3	20-Jun-02	Right Hemicolectomy
79	68	1	0	7	3	20-Jun-02	Right Hemicolectomy
80	76	2	0	3	2	20-Jun-02	Right Hemicolectomy
81	79	2	0	5	2	26-Jun-02	Right Hemicolectomy
82	73	1	0	7	3	06-Jul-02	Sigmoid colectomy
83	80	2	1	6	3	10-Jul-02	Right Hemicolectomy
84	67	1	1	7	3	11-Jul-02	Proctectomy
85	67	1	0	3	2	12-Jul-02	Right Hemicolectomy
86	66	1	1	5	2	18-Jul-02	AP
87	40	0	1	7	3	19-Jul-02	Proctectomy
88	67	1	1	3	2	25-Jul-02	Sigmoid colectomy
89	59	0	1	3	2	12-Aug-02	Proctectomy
90	77	2	1	4	2	13-Aug-02	Anterior resection
91	50	0	0	4	2	20-Aug-02	Proctectomy
92	66	1	1	7	3	22-Aug-02	Anterior resection
93	76	2	1	7	3	03-Sep-02	Sigmoid colectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
94	77	2	1	3	2	05-Sep-02	Anterior resection
95	85	2	1	3	2	11-Sep-02	Sigmoid colectomy
96	77	2	0	5	2	17-Sep-02	Right Hemicolectomy
97	83	2	0	4	2	20-Sep-02	Sigmoid colectomy
98	93	2	1	4	2	02-Oct-02	Sigmoid colectomy
99	67	1	0	4	2	15-Oct-02	Right Hemicolectomy
100	61	0	1	5	2	21-Oct-02	anterior resection
101	67	1	1	6	3	30-Oct-02	anterior resection
102	79	2	0	6	3	01-Nov-02	Proctectomy
103	68	1	1	4	2	05-Nov-02	Right Hemicolectomy
104	75	2	1	6	3	12-Nov-02	anterior resection
105	62	0	1	7	3	13-Nov-02	Right Hemicolectomy
106	55	0	1	6	3	13-Nov-02	Sigmoid colectomy
107	79	2	0	3	2	26-Nov-02	sub-total colectomy
108	68	1	1	4	2	11-Dec-02	Sigmoid colectomy
109	72	1	1	6	3	11-Dec-02	Subtotal colectomy
110	86	2	1	7	3	18-Dec-02	Right Hemicolectomy
111	81	2	0	7	3	30-Dec-02	Hartmann's
112	81	2	1	7	3	04-Jan-03	Right Hemicolectomy
113	86	2	0	3	2	04-Jan-03	Right Hemicolectomy
114	47	0	1	7	3	06-Jan-03	anterior resection
115	53	0	0	7	3	08-Jan-03	anterior resection
116	83	2	0	3	2	09-Jan-03	Sigmoid colectomy
117	62	0	0	7	3	13-Jan-03	Right Hemicolectomy
118	60	0	0	4	2	14-Jan-03	Anterior resection
119	77	2	0	7	3	14-Jan-03	anterior resection
120	57	0	0	1	1	17-Jan-03	AP
121	74	1	0	7	3	23-Jan-03	Sigmoid colectomy
122	83	2	1	5	2	29-Jan-03	AP
123	56	0	0	6	3	30-Jan-03	Sigmoid colectomy
124	69	1	1	7	3	06-Mar-03	anterior resection

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
125	73	1	0	7	3	14-Mar-03	sigmoid colectomy
126	70	1	0	6	3	14-Mar-03	Right Hemicolectomy
127	63	0	0	7	3	19-Mar-03	anterior resection
128	49	0	0	6	3	25-Mar-03	AP
129	56	0	1	3	2	28-Mar-03	Proctectomy
130	65	1	1	5	2	02-Apr-03	Sigmoid colectomy
131	68	1	0	4	2	04-Apr-03	Anterior resection
132	48	0	1	6	3	10-Apr-03	Right Hemicolectomy
133	58	0	0	7	3	15-Apr-03	anterior resection
134	64	0	0	7	3	21-Apr-03	anterior resection
135	43	0	0	6	3	22-Apr-03	Right hemicolectomy
136	79	2	0	7	3	23-Apr-03	anterior resection
137	39	0	0	7	3	30-Apr-03	AP
138	67	1	0	6	3	13-May-03	Sigmoid colectomy
139	72	1	0	4	2	14-May-03	Right Hemicolectomy
140	60	0	1	6	3	23-May-03	Sigmoid colectomy
141	72	1	0	5	2	27-May-03	Sigmoid colectomy
142	74	1	0	7	3	29-May-03	Right Hemicolectomy
143	67	1	1	3	2	06-Jun-03	AP
144	75	2	0	7	3	07-Jun-03	Right Hemicolectomy
145	82	2	1	4	2	12-Jun-03	Right Hemicolectomy
146	70	1	0	7	3	17-Jun-03	Right Hemicolectomy
147	69	1	1	2	1	19-Jun-03	anterior resection
148	72	1	1	7	3	03-Jul-03	Sigmoid colectomy
149	83	2	1	6	3	04-Jul-03	Right Hemicolectomy
150	63	0	1	4	2	30-Jul-03	Sigmoid colectomy
151	76	2	1	7	3	31-Jul-03	Right Hemicolectomy
152	64	0	1	3	2	01-Aug-03	Anterior resection
153	38	0	1	7	3	05-Aug-03	Right Hemicolectomy
154	76	2	0	7	3	06-Aug-03	Sigmoid colectomy
155	61	0	1	4	2	07-Aug-03	Right Hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
156	56	0	1	7	3	07-Aug-03	Anterior resection
157	58	0	0	7	3	07-Aug-03	Left Hemicolectomy
158	76	2	1	3	2	15-Aug-03	AP
159	87	2	1	3	2	15-Aug-03	Right Hemicolectomy
160	74	1	0	3	2	20-Aug-03	Subtotal colectomy
161	61	0	0	3	2	28-Aug-03	Right hemicolectomy
162	83	2	1	7	3	29-Aug-03	Right hemicolectomy
163	77	2	0	6	3	03-Sep-03	Right Hemicolectomy
164	55	0	0	3	2	05-Sep-03	Right Hemicolectomy
165	74	1	0	3	2	09-Sep-03	Sigmoid colectomy
166	69	1	1	6	3	12-Sep-03	Left hemicolectomy
167	75	2	0	4	2	18-Sep-03	Sigmoid colectomy
168	77	2	0	6	3	19-Sep-03	Anterior resection
169	75	2	1	6	3	03-Oct-03	Sigmoid colectomy
170	72	1	1	3	2	03-Oct-03	AP
171	41	0	1	4	2	06-Oct-03	Subtotal colectomy
172	65	1	0	7	3	09-Oct-03	Anterior resection
173	65	1	0	6	3	10-Oct-03	Sigmoid colectomy
174	74	1	0	7	3	16-Oct-03	Right Hemicolectomy
175	41	0	0	2	1	17-Oct-03	Anterior resection
176	48	0	0	6	3	21-Oct-03	Anterior resection
177	54	0	0	5	2	23-Oct-03	Anterior resection
178	84	2	0	5	2	24-Oct-03	Right hemicolectomy
179	74	1	0	7	3	30-Oct-03	Left hemicolectomy
180	78	2	1	7	3	04-Nov-03	Left hemicolectomy
181	44	0	1	6	3	11-Nov-03	Sigmoid colectomy
182	71	1	0	7	3	12-Nov-03	AP
183	61	0	0	3	2	10-Dec-03	Hartmanns
184	64	0	0	7	3	16-Dec-03	Right Hemicolectomy
185	69	1	1	7	3	18-Dec-03	Right Hemicolectomy
186	47	0	0	6	3	06-Jan-04	Low anterior

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
187	71	1	0	6	3	07-Jan-04	Right Hemicolectomy
188	70	1	0	3	2	08-Jan-04	Anterior resection
189	69	1	0	4	2	08-Jan-04	Sigmoid colectomy
190	64	0	0	7	3	09-Jan-04	Proctectomy
191	73	1	1	7	3	09-Jan-04	Right Hemicolectomy
192	21	0	0	5	2	14-Jan-04	Hartmanns
193	59	0	1	7	3	18-Jan-04	Hartmanns
194	70	1	0	6	3	06-Feb-04	Sigmoid colectomy
195	68	1	1	5	2	24-Feb-04	anterior resection
196	68	1	1	7	3	27-Feb-04	Sigmoid colectomy
197	82	2	0	6	3	16-Mar-04	Sigmoid colectomy
198	69	1	1	4	2	16-Mar-04	transverse colectomy
199	76	2	0	6	3	18-Mar-04	right hemicolectomy
200	67	1	1	1	1	19-Mar-04	right hemicolectomy
201	66	1	0	7	3	23-Mar-04	anterior resection
202	69	1	1	3	2	25-Mar-04	right hemicolectomy
203	77	2	1	4	2	25-Mar-04	anterior resection
204	72	1	1	7	3	06-Apr-04	right hemicolectomy
205	63	0	0	7	3	06-Apr-04	Sigmoid colectomy
206	70	1	0	3	2	14-Apr-04	anterior resection
207	81	2	1	6	3	16-Apr-04	anterior resection
208	59	0	1	4	2	20-Apr-04	right hemicolectomy
209	75	2	1	5	2	23-Apr-04	anterior resection
210	70	1	0	4	2	05-May-04	right hemicolectomy
211	84	2	1	7	3	05-May-04	right hemicolectomy
212	79	2	0	7	3	14-May-04	right hemicolectomy
213	52	0	0	7	3	18-May-04	anterior resection
214	81	2	0	3	2	08-Jun-04	anterior resection
215	74	1	0	5	2	15-Jun-04	anterior resection
216	72	1	1	4	2	15-Jun-04	Left hemicolectomy
217	64	0	0	6	3	25-Jun-04	anterior resection

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
218	75	2	1	6	3	13-Aug-04	AP
219	43	0	1	7	3	24-Aug-04	Sigmoid colectomy
220	57	0	0	4	2	27-Aug-04	Sigmoid colectomy
221	74	1	1	4	2	07-Sep-04	Sigmoid colectomy
222	73	1	1	4	2	14-Sep-04	AP
223	59	0	1	5	2	15-Sep-04	Sigmoid colectomy
224	74	1	1	4	2	17-Sep-04	Right hemicolectomy
225	77	2	0	6	3	28-Sep-04	Sigmoid colectomy
226	72	1	0	7	3	29-Sep-04	Hemicolectomy
227	72	1	1	6	3	02-Nov-04	Left hemicolectomy
228	68	1	0	5	2	02-Nov-04	Sigmoid colectomy
229	84	2	1	4	2	19-Nov-04	anterior resection
230	78	2	1	7	3	23-Nov-04	Anterior resection
231	46	0	1	3	2	02-Dec-04	Sigmoid colectomy
232	63	0	0	7	3	09-Dec-04	right hemicolectomy
233	78	2	0	5	2	15-Dec-04	anterior resection
234	79	2	0	6	3	21-Dec-04	anterior resection
235	74	1	1	6	3	21-Dec-04	right hemicolectomy
236	81	2	1	1	1	22-Dec-04	Hemicolectomy
237	50	0	0	2	1	31-Dec-04	Sigmoid colectomy
238	82	2	0	6	3	06-Jan-05	right hemicolectomy
239	77	2	1	4	2	07-Jan-05	right hemicolectomy
240	69	1	0	6	3	01-Feb-05	sub total colectomy
241	84	2	0	7	3	10-Feb-05	Sigmoid colectomy
242	70	1	0	5	2	11-Feb-05	right hemicolectomy
243	79	2	0	6	3	22-Feb-05	right hemicolectomy
244	84	2	1	6	3	22-Feb-05	right hemicolectomy
245	72	1	1	7	3	25-Feb-05	right hemicolectomy
246	74	1	1	3	2	11-Mar-05	anterior resection
247	76	2	1	6	3	15-Mar-05	right hemicolectomy
248	69	1	1	7	3	17-Mar-05	right hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
249	53	0	0	7	3	23-Mar-05	AP
250	79	2	0	5	2	29-Mar-05	anterior resection
251	81	2	0	7	3	14-Apr-05	right hemicolectomy
252	79	2	0	7	3	14-Apr-05	right hemi
253	61	0	0	3	2	15-Apr-05	sigmoid colectomy
254	50	0	0	6	3	22-Apr-05	right hemi
255	69	1	0	4	2	26-Apr-05	anterior resection
256	68	1	0	7	3	03-May-05	Anterior resection
257	66	1	0	6	3	12-May-05	Sigmoid colectomy
258	63	0	0	6	3	19-May-05	right hemicolectomy
259	50	0	1	7	3	19-May-05	anterior resection
260	70	1	1	7	3	19-May-05	Anterior resection
261	78	2	0	5	2	01-Jun-05	right hemi

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
1	1	0	01-Apr-07	0	93.87	2	2	0	3
2	1	1	22-Mar-03	2	40.67	3	2	0	3
3	0	0	17-Jun-03	1	43.33	3	1	0	3
4	0	1	01-Apr-07	0	84.7	3	0	0	2
5	0	0	01-Apr-07	0	81.93	4	0	0	2
6	0	0	12-Sep-01	2	18.2	3	0	0	2
7	1	1	01-Apr-07	0	80.97	4	0	0	2
8	0	0	04-Jun-03	2	33.3	3	1	0	3
9	1	0	01-Apr-07	0	75.13	2	1	0	3
10	0	0	01-Apr-07	0	74.17	3	0	0	2
11	0	0	01-Apr-07	0	70.53	3	0	0	2
12	1	0	01-Apr-07	0	70.43	1	0	0	1
13	0	0	21-Jun-06	1	64.17	3	0	0	2
14	0	0	01-Apr-07	0	69.27	3	0	0	2
15	0	1	01-Apr-07	0	67.9	3	0	0	2
16	0	1	01-Apr-07	0	65.33	3	1	0	3
17	1	1	01-Apr-07	0	64.63	2	1	0	3
18	0	0	01-Apr-07	0	64.23	3	0	0	2
19	0	0	01-Apr-07	0	64.23	3	0	0	2
20	0	0	01-Apr-07	0	64.17	3	0	0	2
21	0	0	01-Apr-07	0	63.7	3	0	0	2
22	0	0	01-Apr-07	0	63.67	3	1	0	3
23	1	1	01-Apr-07	0	63.3	3	2	0	3
24	0	0	01-Apr-07	0	63.3	1	0	0	1
25	1	1	01-Apr-07	0	63.23	3	1	0	3
26	1	0	01-Apr-07	0	63.2	2	0	0	1
27	1	1	18-Sep-03	2	24.07	3	1	0	3
28	0	0	09-Aug-04	2	34.9	3	0	0	2
29	0	0	01-Apr-07	0	62.83	4	1	0	3

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
30	1	0	01-Apr-07	0	62.73	2	2	0	3
31	0	0	18-Jul-05	2	45.93	2	0	0	1
32	0	1	01-Apr-07	0	62.5	3	0	0	2
33	0	0	01-Jun-06	3	56.33	4	0	0	2
34	0	0	27-Apr-02	1	6.43	4	1	0	3
35	0	1	28-Dec-04	1	38.67	3	1	0	3
36	0	0	01-Apr-07	0	61.9	3	0	0	2
37	1	0	01-Apr-07	0	61.67	4	1	0	3
38	1	0	24-Jan-03	1	14.57	4	1	0	3
39	1	0	01-Apr-07	0	61.37	4	0	0	2
40	1	1	19-Feb-03	2	15.2	3	0	0	2
41	0	0	24-Dec-01	2	1.07	2	0	0	1
42	1	0	01-Apr-07	0	60.93	4	0	0	2
43	0	0	01-Apr-07	0	60.47	4	0	0	2
44	0	1	22-Oct-04	1	34.6	4	0	0	2
45	0	1	28-Dec-03	1	24.27	4	2	0	3
46	1	0	06-Mar-06	2	50.6	3	0	0	2
47	0	0	27-Dec-03	1	23.9	3	0	0	2
48	1	1	01-Apr-07	0	59.33	3	1	0	3
49	1	0	12-Jun-03	2	17	2	1	0	3
50	0	0	09-Feb-03	1	12.83	4	1	0	3
51	0	0	01-Apr-07	0	59.13	3	0	0	2
52	1	0	01-Apr-07	0	58.83	2	0	0	1
53	1	1	01-Apr-07	0	58.63	3	2	0	3
54	0	0	10-Jun-02	1	3.7	4	1	0	3
55	0	0	01-Apr-07	0	57.9	4	1	0	3
56	1	0	01-Apr-07	0	57.87	1	1	0	3
57	1	0	01-Apr-07	0	57.6	2	2	0	3
58	0	1	29-Aug-05	1	42.17	3	1	0	3
59	0	0	24-Mar-03	1	12.3	4	2	0	3

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
60	1	0	05-Sep-04	1	29.5	3	1	0	3
61	1	0	19-Jan-05	2	34	3	1	0	3
62	0	0	04-Apr-06	1	48.3	3	0	0	2
63	1	1	01-Apr-07	0	56.27	3	1	0	3
64	0	1	01-Apr-07	0	56.03	4	2	0	3
65	1	0	01-Apr-07	0	55.97	2	0	0	1
66	0	1	01-Apr-07	0	55.77	4	0	0	2
67	0	1	23-May-03	1	12.87	3	1	0	3
68	0	1	21-Jun-03	1	13.67	3	1	0	3
69	0	1	01-Apr-07	0	55.57	4	1	0	3
70	1	0	30-Sep-04	1	29.13	2	0	0	1
71	1	0	18-Sep-04	2	28.57	3	0	0	2
72	0	0	16-Dec-03	1	19.27	4	1	0	3
73	1	0	04-May-05	2	35.73	3	1	0	3
74	0	0	01-Apr-07	0	54.87	3	0	0	2
75	0	0	17-Jul-04	1	25.7	3	0	0	2
76	0	0	01-Apr-07	0	54.43	3	0	0	2
77	0	1	01-Apr-07	0	54.37	4	1	0	3
78	0	0	01-Apr-07	0	54.13	3	0	0	2
79	0	0	15-Apr-04	2	22.17	3	0	0	2
80	0	0	05-Sep-05	2	39.1	3	2	0	3
81	0	0	01-Apr-07	0	53.93	4	2	0	3
82	0	0	01-Apr-07	0	53.6	2	0	0	1
83	0	0	05-Dec-05	1	41.47	4	1	0	3
84	1	1	02-May-03	2	9.83	3	1	0	3
85	0	0	01-Nov-02	1	3.73	3	2	0	3
86	1	0	01-Apr-07	0	53.2	1	0	0	1
87	1	0	01-Apr-07	0	53.17	2	0	0	1
88	0	1	01-Apr-07	0	52.97	3	1	0	3
89	1	0	01-Apr-07	0	52.37	3	0	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
90	1	1	05-Dec-04	1	28.17	4	0	0	2
91	1	0	01-Apr-07	0	52.1	2	0	0	1
92	1	0	09-Nov-03	2	14.8	2	1	0	3
93	0	1	01-Apr-07	0	51.63	2	1	0	3
94	1	0	01-Apr-07	0	51.57	3	1	0	3
95	0	0	01-Apr-07	0	51.37	4	0	0	2
96	0	0	13-Jun-05	1	33.33	4	0	0	2
97	0	0	25-Feb-04	1	17.43	4	1	0	3
98	0	0	01-Apr-07	0	50.67	4	0	0	2
99	0	1	01-Apr-07	0	50.23	3	1	0	3
100	1	1	01-Apr-07	0	50.03	1	1	0	3
101	1	0	01-Apr-07	0	49.73	3	0	0	2
102	1	0	23-Jul-04	2	21	3	0	0	2
103	0	0	17-Mar-04	2	16.6	3	0	0	2
104	1	0	04-Apr-04	2	16.97	3	0	0	2
105	0	0	01-Apr-07	0	49.27	3	0	0	2
106	0	1	01-Apr-07	0	49.27	3	0	0	2
107	0	0	01-Apr-07	0	48.83	3	0	0	2
108	0	0	03-Nov-05	2	35.27	4	0	0	2
109	0	0	27-Dec-05	1	37.07	4	1	0	3
110	0	0	01-Apr-07	0	48.1	3	0	0	2
111	0	0	01-Apr-07	0	47.7	3	0	0	2
112	0	0	01-Apr-07	0	47.53	4	2	0	3
113	0	0	07-Oct-03	1	9.2	3	0	0	2
114	1	0	01-Apr-07	0	47.47	2	0	0	1
115	1	0	01-Apr-07	0	47.4	3	1	0	3
116	0	0	21-Feb-06	1	37.97	4	1	0	3
117	0	0	01-Apr-07	0	47.23	4	0	0	2
118	1	0	01-Apr-07	0	47.2	3	0	0	2
119	1	0	26-Nov-05	2	34.9	3	1	0	3

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
120	1	1	01-Apr-07	0	47.1	2	0	0	1
121	0	0	01-Apr-07	0	46.9	3	0	0	2
122	1	0	09-Jul-03	1	5.37	3	0	0	2
123	0	1	01-Apr-07	0	46.67	2	1	0	3
124	1	0	01-Apr-07	0	45.5	3	0	0	2
125	0	0	26-Mar-06	1	36.93	3	0	0	2
126	0	0	27-Mar-05	1	24.8	4	0	0	2
127	1	1	25-Dec-03	2	9.37	3	0	0	2
128	1	0	01-Apr-07	0	44.87	3	0	0	2
129	1	0	01-Apr-07	0	44.77	3	1	0	3
130	0	1	12-May-04	1	13.53	4	1	0	3
131	1	0	01-Apr-07	0	44.53	3	0	0	2
132	0	1	01-Apr-07	0	44.33	4	0	0	2
133	1	0	23-May-05	2	25.63	3	1	0	3
134	1	1	24-Sep-05	1	29.57	3	1	0	3
135	0	0	01-Apr-07	0	43.93	2	0	0	1
136	1	0	01-Apr-07	0	43.9	3	0	0	2
137	1	1	30-Dec-05	1	32.5	3	1	0	3
138	0	0	01-Apr-07	0	43.23	1	0	0	1
139	0	0	20-Oct-03	1	5.3	3	0	0	2
140	0	1	01-Apr-07	0	42.9	4	1	0	3
141	0	1	01-Apr-07	0	42.77	4	0	0	2
142	0	0	01-Apr-07	0	42.7	3	0	0	2
143	1	0	01-Apr-07	0	42.43	4	0	0	2
144	0	0	01-Apr-07	0	42.4	4	0	0	2
145	0	0	01-Apr-07	0	42.23	3	0	0	2
146	0	0	01-May-06	1	34.97	3	0	0	2
147	1	0	01-Apr-07	0	42	3	1	0	3
148	0	1	01-Apr-07	0	41.53	3	0	0	2
149	0	0	01-Jul-05	1	24.27	3	0	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
150	0	1	01-Apr-07	0	40.63	3	1	0	3
151	0	0	01-Apr-07	0	40.6	2	0	0	1
152	1	0	01-Apr-07	0	40.57	2	0	0	1
153	0	1	02-Mar-05	1	19.17	3	1	0	3
154	0	1	28-Dec-03	1	4.8	4	2	0	3
155	0	0	01-Apr-07	0	40.37	4	2	0	3
156	1	1	01-Apr-07	0	40.37	2	1	0	3
157	0	1	01-Apr-07	0	40.37	3	1	0	3
158	1	0	10-Sep-06	2	37.4	3	1	0	3
159	0	0	01-Jul-04	1	10.7	4	1	0	3
160	0	0	01-Apr-07	0	39.93	3	0	0	2
161	0	1	01-Apr-07	0	39.67	3	0	0	2
162	0	0	01-Apr-07	0	39.63	2	0	0	1
163	0	0	01-Apr-07	0	39.47	3	0	0	2
164	0	1	01-Apr-07	0	39.4	3	1	0	3
165	0	0	28-Jun-06	3	34.1	4	1	0	3
166	0	0	01-Apr-07	0	39.17	4	0	0	2
167	0	1	01-Apr-07	0	38.97	3	1	0	3
168	1	1	01-Apr-07	0	38.93	4	1	0	3
169	0	0	01-Apr-07	0	38.47	4	1	0	3
170	1	0	01-Apr-07	0	38.47	1	1	0	3
171	0	1	01-Apr-07	0	38.37	3	1	0	3
172	1	1	01-Apr-07	0	38.27	3	0	0	2
173	0	0	01-Apr-07	0	38.23	3	1	0	3
174	0	0	01-Apr-07	0	38.03	2	0	0	1
175	1	0	01-Apr-07	0	38	2	0	0	1
176	1	0	01-Apr-07	0	37.87	3	0	0	2
177	1	0	01-Apr-07	0	37.8	1	0	0	1
178	0	0	01-Apr-07	0	37.77	3	0	0	2
179	0	0	01-Apr-07	0	37.57	3	1	0	3

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
180	0	0	01-Apr-07	0	37.4	3	2	0	3
181	0	0	01-Apr-07	0	37.17	4	1	0	3
182	1	0	01-Apr-07	0	37.13	1	0	0	1
183	0	1	01-Apr-07	0	36.2	3	2	0	3
184	0	0	01-Apr-07	0	36	3	0	0	2
185	0	1	01-Apr-07	0	35.93	4	1	0	3
186	1	1	01-Apr-07	0	35.3	3	1	0	3
187	0	1	01-Apr-07	0	35.27	4	2	0	3
188	1	1	15-Sep-05	2	20.53	4	0	0	2
189	0	0	01-Apr-07	0	35.23	4	0	0	2
190	0	0	01-Apr-07	0	35.2	3	0	0	2
191	0	1	01-Apr-07	0	35.2	3	1	0	3
192	0	1	17-Sep-06	1	32.57	4	2	0	3
193	0	0	01-Apr-07	0	34.9	3	0	0	2
194	0	0	01-Apr-07	0	34.27	3	0	0	2
195	1	0	21-May-04	1	2.9	4	2	0	3
196	0	0	01-Apr-07	0	33.57	2	0	0	1
197	0	0	01-Apr-07	0	32.97	3	0	0	2
198	0	0	03-Jul-04	1	3.63	4	2	0	3
199	0	0	16-May-06	1	26.3	4	0	0	2
200	0	1	21-Feb-05	1	11.3	4	2	0	3
201	1	1	01-Apr-07	0	32.73	3	1	0	3
202	0	0	01-Apr-07	0	32.67	3	0	0	2
203	1	0	01-Apr-07	0	32.67	4	1	0	3
204	0	1	25-Feb-06	1	23	4	1	0	3
205	0	1	01-Apr-07	0	32.27	2	1	0	3
206	1	1	01-Apr-07	0	32	4	0	0	2
207	1	0	01-Apr-07	0	31.93	3	0	0	2
208	0	0	01-Apr-07	0	31.8	3	0	0	2
209	1	0	01-Apr-07	0	31.7	3	0	0	2

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
210	0	0	01-Apr-07	0	31.3	3	0	0	2
211	0	0	01-Apr-07	0	31.3	4	0	0	2
212	0	0	08-Mar-06	2	22.1	3	2	0	3
213	1	1	01-Apr-07	0	30.87	3	2	0	3
214	1	0	01-Apr-07	0	30.17	2	0	0	1
215	1	0	06-Sep-04	2	2.77	3	2	0	3
216	0	1	01-Apr-07	0	29.93	3	1	0	3
217	1	0	01-Apr-07	0	29.6	2	0	0	1
218	1	0	15-Oct-06	1	26.43	4	1	0	3
219	0	1	01-Apr-07	0	27.6	4	0	0	2
220	0	0	01-Apr-07	0	27.5	2	0	0	1
221	0	0	01-Apr-07	0	27.13	4	0	0	2
222	1	0	01-Apr-07	0	26.9	1	0	0	1
223	1	0	01-Apr-07	0	26.87	3	0	0	2
224	0	0	01-Apr-07	0	26.8	3	0	0	2
225	0	0	01-Apr-07	0	26.43	3	0	0	2
226	0	0	01-Apr-07	0	26.4	4	2	0	3
227	0	0	01-Apr-07	0	25.27	3	0	0	2
228	0	0	01-Apr-07	0	25.27	3	1	0	3
229	1	0	01-Apr-07	0	24.7	2	0	0	1
230	1	1	01-Apr-07	0	24.57	4	1	0	3
231	0	0	01-Apr-07	0	24.27	3	0	0	2
232	0	0	01-Apr-07	0	24.03	3	0	0	2
233	1	0	01-Apr-07	0	23.83	3	0	0	2
234	1	0	14-Oct-06	1	22.07	3	0	0	2
235	0	0	01-Apr-07	0	23.63	3	0	0	2
236	0	0	01-Apr-07	0	23.6	2	0	0	1
237	0	1	01-Apr-07	0	23.3	3	0	0	2
238	0	0	01-Apr-07	0	23.1	3	0	0	2
239	0	0	01-Apr-07	0	23.07	2	0	0	1

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage
240	0	1	01-Apr-07	0	22.23	4	1	0	3
241	0	0	13-Mar-05	2	1.03	3	1	0	3
242	0	0	01-Apr-07	0	21.9	1	0	0	1
243	0	0	01-Apr-07	0	21.53	3	0	0	2
244	0	0	18-Jun-06	1	16.03	3	2	0	3
245	0	0	01-Apr-07	0	21.43	3	0	0	2
246	0	0	01-Apr-07	0	20.97	3	0	0	2
247	0	0	01-Apr-07	0	20.83	4	1	0	3
248	0	0	01-Apr-07	0	20.77	3	0	0	2
249	1	1	01-Apr-07	0	20.57	3	0	0	2
250	1	0	01-Apr-07	0	20.37	4	0	0	2
251	0	1	01-Apr-07	0	19.83	3	2	0	3
252	0	0	01-Apr-07	0	19.83	3	1	0	3
253	0	0	01-Apr-07	0	19.8	3	0	0	2
254	0	0	01-Apr-07	0	19.57	3	0	0	2
255	1	0	01-Apr-07	0	19.43	3	2	0	3
256	1	0	01-Apr-07	0	19.2	3	1	0	3
257	0	0	01-Apr-07	0	18.9	2	0	0	1
258	0	0	01-Apr-07	0	18.67	3	0	0	2
259	1	0	01-Apr-07	0	18.67	3	0	0	2
260	1	0	01-Apr-07	0	18.67	4	2	0	3
261	0	1	01-Apr-07	0	18.23	3	1	0	3

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
1	well/mod	No	clear	19	5	No
2	poorly	No	clear	24	4	No
3	well/mod	No	clear	14	2	No
4	well/mod	No	clear	14	0	No
5	well/mod	No	clear	12	0	No
6	well/mod	No	clear	23	0	No
7	well/mod	No	clear	15	0	No
8	well/mod	No	clear	25	3	No
9	well/mod	No	clear	12	2	No
10	well/mod	No	clear	8	0	No
11	well/mod	No	clear	35	0	No
12	well/mod	No	clear	8	0	No
13	well/mod	No	clear	24	0	No
14	well/mod	No	clear	26	0	No
15	well/mod	No	clear	20	0	No
16	well/mod	No	clear	7	1	No
17	well/mod	No	clear	7	3	No
18	well/mod	No	clear	10	0	No
19	poorly	No	clear	14	0	No
20	well/mod	No	clear	18	0	No
21	well/mod	No	clear	18	0	No
22	well/mod	No	clear	14	2	No
23	well/mod	Yes	clear	21	5	No
24	moderately	no	clear	28	0	No
25	well/mod	No	clear	8	3	Yes
26	well/mod	No	clear	13	0	No
27	moderately	No	clear	14	1	No
28	well/mod	No	clear	21	0	No
29	moderately	yes	clear	8	3	No
30	well/mod	Yes	clear	12	6	No

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
31	well/mod	No	clear	15	0	No
32	well/mod	no	clear	26	0	No
33	moderately	no	Clear	10	0	No
34	moderately	no	Clear	14	2	No
35	well/mod	Yes	Clear	18	2	No
36	well/mod	No	Clear	7	0	No
37	moderately	no	Clear	17	1	No
38	moderately	no	Clear	7	1	No
39	well/mod	No	Clear	11	0	No
40	well/mod	No	Clear	26	0	No
41	well	no	Clear	10	0	No
42	moderately	no	Clear	10	0	No
43	well/mod	No	Clear	17	0	No
44	well/mod	No	Clear	17	0	No
45	poorly	No	Clear	19	6	no
46	well/mod	No	Clear	12	0	no
47	poor	yes	Clear	17	0	no
48	moderately	yes	Clear	16	1	no
49	well/mod	No	Clear	11	1	no
50	poorly	Yes	Clear	9	1	no
51	well/mod	no	Clear	18	0	no
52	well/mod	no	Clear	22	0	no
53	moderately	no	Clear	17	4	no
54	well/mod	no	Clear	17	3	yes
55	well/mod	No	Clear	17	1	no
56	well/mod	No	Clear	13	2	no
57	poorly	No	Clear	19	5	no
58	well/mod	no	Clear	18	3	no
59	well/mod	yes	Clear	20	9	no
60	well/mod	no	Clear	17	1	no
61	poorly	yes	Clear	15	3	no

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
62	well/mod	yes	Clear	24	0	no
63	well/mod	no	Clear	20	2	no
64	Moderately	yes	Clear	24	7	yes
65	well/mod	No	Clear	29	0	no
66	well/mod	no	Clear	11	0	no
67	poor	yes	Clear	14	3	
68	well/mod	yes	Clear	3	1	yes
69	well/mod	Yes	Clear	8	1	no
70	well/mod	No	Clear	6	0	no
71	well/mod	yes	Clear	11	0	no
72	well/mod	No	Clear	19	2	no
73	moderately	no	Clear	18	3	no
74	poor	no	Clear	14	0	no
75	well/mod	No	Clear	13	0	no
76	moderately	no	Clear	10	0	no
77	moderately	yes	Clear	11	2	no
78	poorly	No	Clear	19	0	no
79	Moderately	no	Clear	15	0	no
80	poorly	No	Clear	10	9	no
81	moderately	yes	Clear	22	4	no
82	moderately	no	Clear	7	0	no
83	well/mod	Yes	Clear	10	2	no
84	well/mod	Yes	Clear	14	2	no
85	poorly	No	Clear	17	10	no
86	poorly	No	Clear	2	0	no
87	well/mod	No	Clear	12	0	no
88	Moderately	no	Clear	10	1	no
89	well/mod	Yes	Clear	12	0	no
90	well/mod	Yes	Clear	24	0	no
91	well/mod	No	Clear	16	0	no
92	well/mod	Yes	Clear	10	2	yes

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
93	well/mod	Yes	Clear	8	1	no
94	well/mod	Yes	Clear	12	1	no
95	moderately	no	Clear	9	0	no
96	poor	no	Clear	3	0	no
97	well/mod	yes	Clear	12	3	yes
98	well/mod	Yes	Clear	7	0	no
99	well/mod	No	Clear	36	2	no
100	moderately	no	Clear	12	1	no
101	Moderately	No	Clear	15	0	no
102	well/mod	No	Clear	15	0	no
103	well/mod	No	Clear	7	0	no
104	moderately	no	Clear	12	0	no
105	moderately	no	Clear	26	0	no
106	Moderately	no	Clear	15	0	no
107	well/mod	No	Clear	20	0	no
108	moderately	no	Clear	16	0	no
109	Moderately	no	Clear	13	1	no
110	well/mod	no	Clear	16	0	no
111	well/mod	No	Clear	14	0	no
112	Moderately	yes	Clear	10	3	yes
113	Moderately	No	Clear	28	0	no
114	Moderately	No	Clear	25	0	no
115	moderately	no	Clear	27	1	no
116	Moderately	Yes	Clear	13	2	no
117	moderately	no	Clear	22	0	no
118	Moderately	No	Clear	19	0	no
119	moderately	no	Clear	21	1	no
120	well/mod	No	Clear	12	0	no
121	Moderately	yes	Clear	17	0	no
122	moderately	no	Clear	16	0	no
123	well/mod	no	Clear	18	2	no

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
124	Moderately	no	Clear	25	0	no
125	Moderately	No	Clear	11	0	no
126	Moderately	no	Clear	15	0	no
127	Moderately	yes	Clear	11	0	no
128	Moderately	no	Clear	17	0	no
129	Moderately	No	Clear	15	1	no
130	moderately	yes	Clear	27	1	no
131	Moderately	yes	Clear	11	0	no
132	moderately	yes	Clear	29	0	no
133	poor	yes	Clear	27	1	no
134	moderately	no	Clear	25	1	no
135	moderately	no	Clear	14	0	no
136	moderately	no	Clear	29	0	no
137	moderately	yes	Clear	10	3	no
138	moderately	no	Clear	8	0	no
139	poor	yes	Clear	10	0	no
140	Moderately	No	Clear	10	2	no
141	poor	no	Clear	9	0	no
142	Moderately	No	Clear	18	0	no
143	well/mod	no	Clear	11	0	no
144	Moderately	no	Clear	17	0	no
145	poor	yes	Clear	15	0	no
146	moderately	no	Clear	17	0	no
147	moderately	yes	Clear	12	1	no
148	poorly	yes	Clear	13	0	no
149	Moderately	No	Clear	11	0	no
150	moderately	yes	Clear	10	2	no
151	moderately	no	Clear	14	0	no
152	well/mod	No	Clear	19	0	no
153	well/mod	Yes	Clear	4	1	yes
154	well/mod	No	Clear	9	9	yes

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
155	poorly	Yes	Clear	27	13	no
156	well/mod	No	Clear	19	3	no
157	well/mod	No	Clear	27	2	no
158	Well/mod	No	Clear	11	2	no
159	well/mod	Yes	Clear	12	1	no
160	Well/mod	No	Clear	13	0	no
161	well/mod	yes	Clear	10	0	no
162	well/mod	no	Clear	8	0	no
163	well/mod	No	Clear	14	0	no
164	poorly	No	Clear	8	1	yes
165	well/mod	No	Clear	13	2	no
166	well/mod	No	Clear	7	0	no
167	well/mod	no	Clear	8	1	no
168	well/mod	Yes	Clear	7	3	no
169	well/mod	Yes	Clear	15	3	no
170	well/mod	No	Clear	8	3	yes
171	well/mod	Yes	Clear	33	1	no
172	well/mod	Yes	Clear	15	0	no
173	well/mod	Yes	Clear	12	1	no
174	well/mod	No	Clear	11	0	no
175	well/mod	No	Clear	7	0	no
176	well/mod	yes	Clear	19	0	no
177	well	No	Clear	9	0	
178	poorly	Yes	Clear	9	0	no
179	moderately	No	Clear	16	1	no
180	moderately	No	Clear	14	5	yes
181	poorly	No	Clear	11	1	no
182	moderately	yes	Clear	11	0	no
183	moderately	No	Clear	9	4	no
184	moderately	No	Clear	14	0	no
185	moderately	Yes	Clear	16	1	no

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
186	moderately	Yes	Clear	12	2	no
187	moderately	Yes	Clear	12	4	no
188	moderately	Yes	Clear	8	0	no
189	moderately	No	Clear	13	.	no
190	moderately	Yes	Clear	12	0	no
191	moderately	No	Clear	9	1	no
192	moderately	yes	Clear	14	11	yes
193	moderately	Yes	Clear	8	0	no
194	moderately	No	Clear	28	0	no
195	poorly	Yes	Clear	24	16	no
196	moderately	No	Clear	8	0	no
197	moderately	No	Clear	13	0	no
198	poorly	yes	Clear	9	7	yes
199	moderately	Yes	Clear	22	0	no
200	poorly	Yes	Clear	25	4	no
201	moderately	Yes	Clear	8	2	no
202	moderately	Yes	Clear	41	0	no
203	moderately	Yes	Clear	16	3	no
204	poorly	Yes	Clear	10	3	no
205	moderately	No	Clear	24	1	no
206	moderately	No	Clear	12	0	no
207	moderately	Yes	Clear	13	0	no
208	undifferentiated	Yes	Clear	25	.	no
209	moderately	No	Clear	17	0	no
210	moderately	Yes	Clear	18	0	no
211	moderately	No	Clear	9	0	no
212	poorly	No	Clear	11	4	no
213	moderately	No	Clear	12	6	no
214	moderately	No	Clear	12	0	no
215	poorly	Yes	Clear	31	4	no
216	moderately	No	Clear	9	1	no

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
217	moderately	No	Clear	18	0	no
218	moderately	Yes	Clear	6	1	no
219	moderately	No	Clear	26	0	no
220	moderately	No	Clear	9	0	no
221	poorly	Yes	Clear	25	0	no
222	moderately	No	Clear	9	0	no
223	moderately	No	Clear	14	0	no
224	moderately	No	Clear	18	0	no
225	moderately	No	Clear	18	0	no
226	moderately	Yes	Clear	14	4	yes
227	moderately	Yes	Clear	32	0	no
228	moderately	Yes	Clear	16	2	no
229	moderately	No	Clear	4	0	no
230	moderately	Yes	Clear	18	1	no
231	moderately	No	Clear	13	0	no
232	moderately	No	Clear	14	0	no
233	moderately	Yes	Clear	20	0	no
234	moderately	no	Clear	8	0	no
235	moderately	No	Clear	12	0	no
236	poorly	No	Clear	5	0	no
237	moderately	yes	Clear	11	0	no
238	poorly	No	Clear	13	0	no
239	moderately	No	Clear	20	0	no
240	moderately	Yes	Clear	7	2	yes
241	moderately	No	Clear	22	2	no
242	moderately	No	Clear	4	0	no
243	moderately	No	Clear	3	0	no
244	moderately	Yes	Clear	17	5	no
245	moderately	No	Clear	21	0	no
246	moderately	No	Clear	10	0	no
247	moderately	yes	Clear	15	2	no

Patient ID	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
248	poorly	No	Clear	17	0	no
249	moderately	No	Clear	14	0	no
250	moderately	yes	Clear	13	0	no
251	moderately	yes	Clear	15	4	no
252	moderately	No	Clear	26	3	no
253	moderately	No	Clear	52	0	no
254	moderately	Yes	Clear	20	0	no
255	moderately	Yes	Clear	6	4	no
256	moderately	No	Clear	22	1	no
257	moderately	No	Clear	14	0	no
258	moderately	Yes	Clear	30	0	no
259	moderately	No	Clear	24	0	no
260	moderately	No	Clear	12	6	no
261	moderately	Yes	Clear	17	1	no

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
1	0	.	16	1	41	0	1
2	0	.	5	0	44	0	0
3	0	.	23	1	36	0	1
4	0	.	5	0	38	0	0
5	0	.	6	0	43	0	0
6	0	.	31	1	38	0	1
7	0	.	178	1	31	1	2
8	0	.	31	1	34	1	2
9	0	.	26	1	44	0	1
10	0	.	19	1	36	0	1
11	0	.	6	0	38	0	0
12	0	.	6	0	48	0	0
13	1	1	9	0	44	0	0
14	0	.	21	1	38	0	1
15	0	.	6	0	37	0	0
16	0	.	6	0	47	0	0
17	0	.	6	0	44	0	0
18	0	.	41	1	41	0	1
19	0	.	7	0	37	0	0
20	0	.	22	1	38	0	1
21	0	.	8	0	42	0	0
22	0	.	7	0	43	0	0
23	0	.	6	0	48	0	0
24	0	.	6	0	42	0	0
25	0	.	6	0	42	0	0
26	0	.	7	0	40	0	0
27	0	.	6	0	42	0	0
28	0	.	33	1	39	0	1
29	0	.	29	1	42	0	1

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
30	0	.	6	0	45	0	0
31	0	.	12	1	40	0	1
32	0	.	24	1	41	0	1
33	0	.	71	1	32	1	2
34	0	.	5	0	41	0	0
35	0	.	9	0	47	0	0
36	0	.	6	0	44	0	0
37	0	.	6	0	38	0	0
38	1	2	48	1	37	0	1
39	0	.	6	0	40	0	0
40	0	.	34	1	43	0	1
41	0	.	46	1	32	1	2
42	0	.	8	0	43	0	0
43	0	.	15	1	38	0	1
44	1	2	205	1	31	1	2
45	0	.	26	1	47	0	1
46	0	.	6	0	44	0	0
47	1	0	28	1	34	1	2
48	0	.	6	0	42	0	0
49	0	.	6	0	50	0	0
50	0	.	20	1	45	0	1
51	0	.	6	0	43	0	0
52	0	.	41	1	38	0	1
53	0	.	6	0	42	0	0
54	1	0	102	1	34	1	2
55	1	1	134	1	36	0	1
56	0	.	11	1	46	0	1
57	0	.	6	0	46	0	0
58	1	0	8	0	39	0	0
59	0	.	58	1	34	1	2

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
60	0	.	14	1	34	1	2
61	0	.	6	0	37	0	0
62	1	2	125	1	31	1	2
63	0	.	5	0	47	0	0
64	0	.	7	0	42	0	0
65	0	.	6	0	42	0	0
66	1	2	144	1	35	0	1
67	1	0	135	1	35	0	1
68	0	.	28	1	40	0	1
69	0	.	56	1	37	0	1
70	0	.	20	1	41	0	1
71	0	.	5	0	44	0	0
72	0	.	6	0	38	0	0
73	0	.	5	0	36	0	0
74	1	1	34	1	44	0	1
75	1	1	102	1	42	0	1
76	0	.	6	0	42	0	0
77	0	.	9	0	42	0	0
78	0	.	12	1	41	0	1
79	0	.	9	0	42	0	0
80	0	.	31	1	40	0	1
81	0	.	19	1	36	0	1
82	0	.	20	1	38	0	1
83	0	.	5	0	42	0	0
84	0	.	22	1	41	0	1
85	0	.	63	1	30	1	2
86	0	.	5	0	45	0	0
87	0	.	5	0	38	0	0
88	0	.	5	0	40	0	0
89	0	.	6	0	52	0	0

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
90	0	.	26	1	41	0	1
91	0	.	6	0	43	0	0
92	0	.	10	0	43	0	0
93	0	.	6	0	44	0	0
94	0	.	6	0	41	0	0
95	0	.	14	1	42	0	1
96	0	.	101	1	36	0	1
97	0	.	6	0	35	0	0
98	1	0	140	1	30	1	2
99	1	1	155	1	42	0	1
100	1	2	48	1	41	0	1
101	0	.	5	0	38	0	0
102	0	.	26	1	42	0	1
103	0	.	7	0	44	0	0
104	0	.	19	1	47	0	1
105	0	.	17	1	36	0	1
106	0	.	5	0	47	0	0
107	0	.	41	1	40	0	1
108	0	.	8	0	44	0	0
109	1	2	5	0	42	0	0
110	0	.	27	1	42	0	1
111	1	1	80	1	43	0	1
112	0	.	21	1	37	0	1
113	0	.	49	1	34	1	2
114	0	.	6	0	45	0	0
115	0	.	11	1	41	0	1
116	0	.	19	1	41	0	1
117	1	2	66	1	39	0	1
118	0	.	34	1	31	1	2
119	0	.	6	0	37	0	0

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
120	0	.	6	0	42	0	0
121	0	.	6	0	41	0	0
122	0	.	13	1	40	0	1
123	0	.	8	0	43	0	0
124	0	.	6	0	46	0	0
125	0	.	48	1	30	1	2
126	1	2	190	1	38	0	1
127	0	.	6	0	43	0	0
128	0	.	6	0	44	0	0
129	0	.	6	0	45	0	0
130	1	0	68	1	38	0	1
131	0	.	6	0	40	0	0
132	1	0	29	1	37	0	1
133	0	.	9	0	39	0	0
134	0	.	40	1	42	0	1
135	0	.	7	0	47	0	0
136	1	0	47	1	35	0	1
137	0	.	7	0	47	0	0
138	0	.	6	0	48	0	0
139	0	.	10	0	42	0	0
140	0	.	9	0	42	0	0
141	0	.	6	0	41	0	0
142	0	.	8	0	41	0	0
143	0	.	6	0	43	0	0
144	1	2	200	1	33	1	2
145	0	.	33	1	31	1	2
146	1	0	38	1	39	0	1
147	0	.	5	0	40	0	0
148	0	.	6	0	41	0	0
149	0	.	95	1	31	1	2

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
150	1	2	76	1	42	0	1
151	0	.	6	0	42	0	0
152	0	.	5	0	44	0	0
153	0	.	38	1	42	0	1
154	0	.	51	1	38	0	1
155	0	.	5	0	41	0	0
156	0	.	11	1	42	0	1
157	1	1	5	0	40	0	0
158	0	.	5	0	42	0	0
159	0	.	94	1	32	1	2
160	0	.	5	0	39	0	0
161	0	.	10	0	43	0	0
162	0	.	6	0	34	1	0
163	0	.	7	0	39	0	0
164	0	.	19	1	43	0	1
165	0	.	5	0	40	0	0
166	0	.	29	1	37	0	1
167	0	.	5	0	46	0	0
168	0	.	5	0	44	0	0
169	0	.	7	0	41	0	0
170	0	.	5	0	41	0	0
171	1	2	101	1	33	1	2
172	0	.	7	0	39	0	0
173	0	.	5	0	43	0	0
174	0	.	12	1	38	0	1
175	0	.	5	0	42	0	0
176	0	.	5	0	45	0	0
177	0	.	8	0	45	0	0
178	0	.	40	1	40	0	1
179	0	.	21	1	43	0	1

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
180	1	1	14	1	37	0	1
181	0	.	17	1	44	0	1
182	0	.	5	0	44	0	0
183	1	1	22	1	46	0	1
184	0	.	75	1	36	0	1
185	0	.	9	0	40	0	0
186	0	.	5	0	41	0	0
187	1	1	36	1	45	0	1
188	0	.	31	1	41	0	1
189	0	.	5	0	36	0	0
190	0	.	13	1	41	0	1
191	0	.	18	1	39	0	1
192	1	1	5	0	44	0	0
193	1	2	7	0	43	0	0
194	0	.	27	1	41	0	1
195	0	.	38	1	42	0	1
196	0	.	12	1	42	0	1
197	0	.	12	1	34	1	2
198	1	1	88	1	38	0	1
199	0	.	6	0	43	0	0
200	0	.	209	1	41	0	1
201	0	.	5	0	33	1	0
202	0	.	133	1	34	1	2
203	0	.	22	1	44	0	1
204	1	1	10	0	43	0	0
205	1	0	5	0	41	0	0
206	0	.	5	0	48	0	0
207	1	0	101	1	33	1	2
208	0	.	14	1	26	1	2
209	0	.	14	1	38	0	1

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
210	1	1	5	0	30	1	0
211	0	.	16	1	38	0	1
212	0	.	27	1	45	0	1
213	0	.	5	0	47	0	0
214	0	.	5	0	42	0	0
215	0	.	12	1	38	0	1
216	0	.	5	0	33	1	0
217	0	.	8	0	46	0	0
218	0	.	9	0	43	0	0
219	0	.	9	0	36	0	0
220	0	.	9	0	40	0	0
221	0	.	24	1	44	0	1
222	0	.	5	0	42	0	0
223	0	.	6	0	44	0	0
224	0	.	5	0	44	0	0
225	0	.	18	1	41	0	1
226	0	.	16	1	44	0	1
227	0	.	19	1	42	0	1
228	0	.	5	0	46	0	0
229	0	.	5	0	39	0	0
230	0	.	9	0	39	0	0
231	0	.	5	0	46	0	0
232	0	.	34	1	47	0	1
233	0	.	5	0	44	0	0
234	0	.	9	0	41	0	0
235	0	.	57	1	41	0	1
236	0	.	5	0	41	0	0
237	0	.	5	0	47	0	0
238	0	.	103	1	31	1	2
239	0	.	5	0	43	0	0

Patient ID	Presentation (elective=0, emergency=1)	Type of emergency (Bleed=0, obstruction=1, perforation=2)	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
240	1	1	5	0	38	0	0
241	0	.	5	0	39	0	0
242	0	.	5	0	43	0	0
243	0	.	5	0	40	0	0
244	0	.	14	1	34	1	2
245	0	.	15	1	41	0	1
246	0	.	5	0	41	0	0
247	0	.	17	1	38	0	1
248	0	.	16	1	29	1	2
249	0	.	9	0	43	0	0
250	0	.	5	0	40	0	0
251	0	.	19	1	44	0	1
252	0	.	6	0	38	0	0
253	0	.	19	1	36	0	1
254	0	.	6	0	42	0	0
255	0	.	10	0	47	0	0
256	0	.	7	0	46	0	0
257	0	.	5	0	43	0	0
258	0	.	11	1	40	0	1
259	0	.	41	1	35	0	1
260	0	.	7	0	45	0	0
261	0	.	12	1	39	0	1

Appendix 4 – Database for chapter 6 – THE RELATIONSHIP BETWEEN THE SYSTEMIC INFLAMMATORY RESPONSE (mGPS), INTERLEUKIN-6, INTERLEUKIN-10 AND LYMPHOCYTE SUBPOPULATIONS IN PATIENTS UNDERGOING POTENTIALLY CURATIVE RESECTION FOR COLORECTAL CANCER

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Date of followup
1	80	2	0	08.06.2004	anterior resection	1	01-Jun-07
2	72	1	1	15.06.2004	Left hemicolectomy	0	01-Jun-07
3	79	2	0	03.08.2004	right hemicolectomy	0	01-Jun-07
4	43	0	1	24.08.2004	Sigmoid colectomy	0	01-Jun-07
5	57	0	0	27.08.2004	Sigmoid colectomy	0	01-Jun-07
6	58	0	1	15.09.2004	Sigmoid colectomy	0	01-Jun-07
7	71	1	1	02.11.2004	Left hemicolectomy	0	01-Jun-07
8	83	2	1	19.11.2004	anterior resection	1	01-Jun-07
9	77	2	1	23.11.2004	Anterior resection	1	01-Jun-07
10	79	2	0	10.12.2004	Sigmoid colectomy	0	26-Dec-04
11	77	2	0	15.12.2004	anterior resection	1	01-Jun-07
12	79	2	0	22.02.2005	right hemicolectomy	0	01-Jun-07
13	84	2	1	22.02.2005	right hemicolectomy	0	18-Jun-06
14	71	1	1	25.02.2005	right hemicolectomy	0	01-Jun-07
15	74	1	0	25.02.2005	right hemicolectomy	0	01-Jun-07
16	75	2	1	15.03.2005	right hemicolectomy	0	01-Jun-07
17	68	1	1	17.03.2005	right hemicolectomy	0	01-Jun-07
18	50	0	0	22.04.2005	right hemi	0	01-Jun-07
19	69	1	0	26.04.2005	anterior resection	1	01-Jun-07
20	76	2	0	01.07.2005	anterior resection	1	05-Sep-05
21	91	2	1	01.07.2005	anterior resection	1	01-Jun-07
22	78	2	1	15.07.2005	Sigmoid colectomy	0	01-Jun-07
23	71	1	0	22.07.2005	Sigmoid colectomy	0	01-Jun-07
24	79	2	0	25.07.2005	Sigmoid colectomy	0	01-Jun-07
25	56	0	0	15.09.2005	Sigmoid colectomy	0	01-Jun-07
26	56	0	0	25.10.2005	anterior resection	1	01-Jun-07
27	65	1	1	25.10.2005	anterior resection	1	01-Jun-07
28	67	1	0	27.10.2005	right hemi	0	01-Jun-07
29	66	1	0	01.11.2005	right hemi	0	01-Jun-07
30	66	1	1	02.11.2005	anterior resection	1	01-Jun-07
31	67	1	1	22.11.2005	right hemi	0	11-Jun-06
32	50	0	0	12.12.2005	anterior resection	1	01-Jun-07

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Operation Date	Operation	Site (Rectum=1, colon=0)	Date of followup
33	53	0	1	21.02.2006	anterior resection	1	01-Jun-07
34	69	1	1	03.07.2006	Left hemicolectomy	0	01-Jun-07
35	50	0	0	06.07.2006	right hemi	0	01-Jun-07
36	66	1	1	21.07.2006	anterior resection	1	31-Jul-06
37	45	0	0	26.07.2006	AP resection	1	01-Jun-07
38	59	0	1	31.07.2006	right hemi	0	01-Jun-07
39	67	1	1	01.08.2006	right hemi	0	01-Jun-07
40	44	0	1	08.08.2006	Sigmoid colectomy	0	01-Jun-07
41	77	2	1	08.08.2006	anterior resection	1	01-Jun-07
42	83	2	1	08.08.2006	right hemi	0	01-Jun-07
43	85	2	0	14.08.2006	anterior resection	1	01-Jun-07
44	65	1	1	14.08.2006	Sigmoid colectomy	0	01-Jun-07
45	72	1	0	21.08.2006	right hemi	0	01-Jun-07
46	42	0	0	28.08.2006	AP resection	1	01-Jun-07
47	63	0	0	30.08.2006	Hartmanns	1	01-Jun-07
48	68	1	0	07.09.2006	anterior resection	0	01-Jun-07
49	76	2	1	28.09.2006	right hemi	0	01-Jun-07
50	62	0	0	04.10.2006	anterior resection	1	01-Jun-07
51	59	0	0	23.10.2006	anterior resection	1	27-Feb-07
52	58	0	0	24.10.2006	anterior resection	1	01-Jun-07
53	75	2	0	09.11.2006	AP resection	1	01-Jun-07

Patient ID	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion	Resection margins
1	0	36.27	2	0	0	1	moderately	No	clear
2	0	36.03	3	1	0	3	moderately	No	clear
3	0	34.4	3	1	0	3	moderately	Yes	clear
4	0	33.7	4	0	0	2	moderately	No	clear
5	0	33.6	2	0	0	1	moderately	No	clear
6	0	32.97	3	0	0	2	moderately	No	clear
7	0	31.37	3	0	0	2	moderately	Yes	clear
8	0	30.8	2	0	0	1	moderately	No	clear
9	0	30.67	4	1	0	3	moderately	Yes	clear
10	1	0.53	3	0	0	2	moderately	Yes	clear
11	0	29.93	3	0	0	2	moderately	Yes	clear
12	0	27.63	3	0	0	2	moderately	No	clear
13	1	16.03	3	2	0	3	moderately	Yes	clear
14	0	27.53	3	0	0	2	moderately	No	clear
15	0	27.53	3	0	0	2	moderately	Yes	clear
16	0	26.93	4	1	0	3	moderately	Yes	clear
17	0	26.87	3	0	0	2	Poorly	Yes	clear
18	0	25.67	3	0	0	2	moderately	Yes	clear
19	0	25.53	3	2	0	3	moderately	Yes	clear
20	2	2.2	1	0	0	1	moderately	No	clear
21	0	20.63	2	1	0	3	moderately	No	clear
22	0	22.87	3	1	0	3	moderately	Yes	clear
23	0	22.63	2	0	0	1	moderately	Yes	clear
24	0	22.53	1	0	0	1	moderately	No	clear
25	0	18.1	3	2	1	3	moderately	Yes	clear
26	0	19.47	3	0	0	2	moderately	No	clear
27	0	19.47	3	1	0	3	moderately	No	clear
28	0	19.4	4	0	0	2	Poorly	Yes	involved
29	0	19.23	3	0	0	2	moderately	No	clear
30	0	19.2	2	0	0	1	moderately	Yes	clear
31	2	6.7	4	0	0	2	moderately	Yes	involved
32	0	15.17	3	1	0	3	Poorly	Yes	involved

Patient ID	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M	Stage	Differentiation	Vascular invasion	Resection margins
33	0	12.8	3	0	0	2	moderately	Yes	clear
34	0	11.1	3	0	0	2	moderately	Yes	clear
35	0	8.3	4	2	0	3	moderately	Yes	clear
36	1	0.33	3	1	0	3	moderately	Yes	clear
37	0	7.63	3	0	0	2	moderately	No	clear
38	0	7.47	3	0	0	2	moderately	Yes	clear
39	0	7.43	4	1	0	3	moderately	Yes	clear
40	0	7.2	1	0	0	1	moderately	No	clear
41	0	7.2	2	0	0	1	moderately	No	clear
42	0	7.2	4	1	0	3	Poorly	No	clear
43	0	7	3	0	0	2	moderately	No	clear
44	0	7	4	1	0	3	moderately	Yes	clear
45	0	6.77	3	1	0	3	moderately	No	clear
46	0	6.53	3	2	0	3	moderately	Yes	clear
47	0	6.47	3	0	0	2	moderately	Yes	clear
48	0	6.2	3	0	0	2	moderately	Yes	clear
49	0	5.5	3	1	0	3	moderately	Yes	clear
50	0	5.3	3	0	0	2	moderately	Yes	clear
51	1	4.67	4	2	0	3	moderately	Yes	clear
52	0	4.63	3	0	0	2	moderately	yes	clear
53	0	4.1	3	0	0	2	Poorly	yes	positive

Patient ID	Total nodes	Positive nodes	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS	il6	il6cd
1	12	0	6	0	42	0	0	4.84	1
2	9	1	6	0	39	0	0	1.15	0
3	13	1	6	0	34	1	0	5.05	1
4	26	0	9	0	36	0	0	0.86	0
5	9	0	9	0	40	0	0	1.1	0
6	14	0	6	0	44	0	0	0.71	0
7	32	0	19	1	42	0	1	3.38	0
8	4	0	6	0	39	0	0	3.02	0
9	18	1	9	0	39	0	0	4.77	1
10	8	0	6	0	37	0	0	5.43	1
11	20	0	6	0	44	0	0	2.2	0
12	3	0	6	0	40	0	0	1.01	0
13	17	5	14	1	34	1	2	8.38	1
14	21	0	15	1	41	0	1	4.38	1
15	18	0	24	1	38	0	1	12.17	1
16	15	3	17	1	38	0	1	5.14	1
17	17	0	16	1	29	1	2	20.04	1
18	20	0	6	0	42	0	0	3.56	0
19	6	4	10	0	47	0	0	5.04	1
20	13	0	6	0	47	0	0	0.04	0
21	6	1	6	0	39	0	0	3.43	0
22	13	2	19	1	42	0	1	4.22	1
23	6	0	6	0	41	0	0	1.27	0
24	8	0	6	0	37	0	0	4.09	1
25	10	10	6	0	40	0	0	1.44	0
26	13	0	6	0	32	1	0	0.77	0
27	24	1	36	1	12	1	2	6.1	1
28	27	0	64	1	36	0	1	12.43	1
29	9	0	6	0	41	0	0	3.12	0
30	16	0	6	0	40	0	0	0.82	0
31	13	0	11	1	36	0	1	1.42	0
32	11	1	6	0	43	0	0	2.4	0

Patient ID	Total nodes	Positive nodes	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS	il6	il6cd
33	12	0	6	0	45	0	0	1	0
34	7	0	6	0	33	1	0	5.03	1
35	20	5	6	0	24	1	0	1.46	0
36	10	2	7	0	25	1	0	1.5	0
37	3	0	7	0	36	0	0	3.49	0
38	27	0	6	0	39	0	0	1.42	0
39	12	1	38	1	23	1	2	15.99	1
40	.	0	6	0	21	1	0	0.29	0
41	19	0	16	1	29	1	2	32.08	1
42	10	2	6	0	21	1	0	6.28	1
43	12	0	3	0	40	0	0	1.46	0
44	21	3	11	1	35	0	1	5.16	1
45	12	1	25	1	32	1	2	7.27	1
46	27	11	1	0	32	1	0	1.71	0
47	16	0	27	1	37	0	1	11.36	1
48	12	0	9	0	33	1	0	3.96	0
49	20	2	27	1	38	0	1	7.01	1
50	12	0	3	0	34	1	0	1.05	0
51	14	5	9	0	38	0	0	2.79	0
52	22	0	9	0	35	0	0	2.99	0
53	15	0	1	0	37	0	0	1.59	0

Patient ID	il10	il10cd	Wbc	lymphocyte count	T-Cell (CD3+)	T-Cell (CD3+)%	Helper t-Cell (CD3+CD4+)	Helper t-Cell (CD3+CD4+)%
1	7.56	0	8.4	2609	1826	70	979	37
2	7.6	0	8	1680	1197	71	839	51
3	.	.	6.6	1593	1327	83	567	38
4	9.68	0	9.7	3085	2340	76	1469	46
5	9.82	0	4.4	1040	554	53	461	42
6	7.06	0	5.9	1279	711	56	504	40
7	12.84	1	13.4	2734	2137	78	1726	65
8	8.88	0	8.3	869	572	66	478	57
9	8.89	0	6.6	917	523	57	336	35
10	7.12	0	4.9	1024	567	55	362	37
11	12.66	1	9.5	2739	1775	65	980	35
12	8.72	0	6.2	1430	1098	77	657	44
13	32.6	1	5.9	1267	996	79	480	38
14	12.9	1	4.7	1128	732	65	493	45
15	8.18	0	7.6	1777	1404	79	942	53
16	.	.	8.1	1419	1119	79	579	42
17	9.7	0	10.4	2235	1417	63	858	39
18	9.88	0	7.6	2367	1624	69	984	41
19	9.55	0	9.9	2688	1947	72	1021	38
20	27.16	1	9	1704	1218	72	775	43
21	11.9	1	15.5	5527	3344	60	1798	32
22	8.94	0	9.8	2381	1819	76	1099	44
23	8.78	0	7.5	1586	1065	67	893	56
24	10.02	1	5.2	1540	753	49	516	34
25	9.21	0	6.6	1903	1481	78	913	48
26	8.24	0	8.1	1046	712	68	414	40
27	12.87	1	8.5	2118	1272	60	582	28
28	16.57	1	16.1	2013	1761	87	877	44
29	9.31	0	8.2	2414	1819	75	1145	46
30	.	.	8.4	1604	1049	65	811	49
31	8.23	0	8.5	1945	1516	78	877	46
32	7.63	0	10.8	1947	1513	78	915	47

Patient ID	il10	il10cd	Wbc	lymphocyte count	T-Cell (CD3+)	T-Cell (CD3+)%	Helper t-Cell (CD3+CD4+)	Helper t-Cell (CD3+CD4+)%
33	7.43	0	6.6	1569	1154	74	679	46
34	9.03	0	8.1	3114	2588	83	1016	33
35	218.5	1	11.2	1825	1317	72	724	38
36	10.29	1	12.4	2532	1601	63	1268	49
37	8.95	0	10.7	647	387	60	287	43
38	12.11	1	7.4	1597	883	55	678	42
39	11.56	1	5.1	1848	1328	72	709	39
40	7	0	7	1625	1137	70	834	51
41	12.17	1	12	1837	1144	62	492	25
42	7.01	0	7.5	1955	1127	58	890	45
43	7.47	0	6.1	1345	681	51	281	21
44	11.16	1	6.3	1638	986	60	667	40
45	18.26	1	6.6	1704	1337	78	545	32
46	9.61	0	7.4	2053	1607	78	899	51
47	12.33	1	6.9	1182	1004	85	564	47
48	10.52	1	7	612	460	75	400	66
49	8.88	0	11.7	967	607	63	470	49
50	7.81	0	6.9	2092	1596	76	972	46
51	11.62	1	6.6	1132	739	65	582	52
52	8.08	0	8.4	2137	1504	70	1170	56
53	12.36	1	7.1	1081	744	69	471	44

Patient ID	Cytotoxic T-Cell (CD3+CD8+)%	B-Cell (CD19+)	B-Cell (CD19+)%
1	35	297	12
2	14	294	18
3	34	59	4
4	31	429	14
5	10	265	27
6	12	233	19
7	13	206	7
8	9	48	5
9	20	131	15
10	19	79	7
11	33	718	27
12	32	181	13
13	42	67	5
14	21	160	14
15	27	232	13
16	37	102	7
17	25	393	17
18	29	223	10
19	33	355	13
20	29	165	10
21	29	1486	27
22	30	270	12
23	9	346	22
24	15	449	29
25	29	209	11
26	28	118	11
27	32	182	9
28	42	157	8
29	30	149	6
30	18	183	12
31	33	207	10
32	29	179	9

Patient ID	Cytotoxic T-Cell (CD3+CD8+)%	B-Cell (CD19+)	B-Cell (CD19+)%
33	27	293	17
34	52	371	12
35	35	391	22
36	14	639	26
37	15	150	24
38	14	301	19
39	36	225	12
40	21	193	12
41	36	310	18
42	13	374	19
43	28	156	12
44	19	186	12
45	45	122	7
46	30	187	8
47	40	68	6
48	8	71	12
49	16	192	20
50	29	113	5
51	15	119	10
52	15	473	22
53	24	169	16

Appendix 5 – Database for chapter 7 - THE PRESENCE OF A SYSTEMIC INFLAMMATORY RESPONSE PREDICTS POORER SURVIVAL IN PATIENTS RECEIVING ADJUVANT 5-FU CHEMOTHERAPY FOLLOWING POTENTIALLY CURATIVE RESECTION FOR COLORECTAL CANCER.

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
1	72	1	0	7	3	12-Jan-99	0
2	73	1	0	7	3	13-Jan-99	0
3	86	2	1	4	2	22-Jan-99	0
4	74	1	0	7	3	10-Feb-99	0
5	63	0	1	6	3	17-Feb-99	0
6	73	1	1	7	3	25-Feb-99	0
7	65	1	1	7	3	04-Mar-99	1
8	81	2	1	6	3	15-Mar-99	0
9	41	0	0	7	3	16-Mar-99	1
10	65	1	1	3	2	17-Mar-99	0
11	77	2	1	6	3	08-May-99	0
12	60	0	1	6	3	21-May-99	0
13	78	2	0	7	3	18-Jun-99	0
14	60	0	0	2	1	23-Jun-99	1
15	73	1	0	7	3	29-Jun-99	1
16	59	0	0	7	3	13-Jul-99	0
17	78	2	1	7	3	23-Jul-99	0
18	84	2	1	5	2	05-Aug-99	0
19	84	2	1	2	1	15-Aug-99	1
20	66	1	1	7	3	18-Aug-99	1
21	98	2	1	7	3	24-Aug-99	1
22	87	2	0	1	1	08-Sep-99	0
23	78	2	0	4	2	15-Sep-99	1
24	65	1	1	7	3	24-Sep-99	0
25	70	1	0	7	3	05-Oct-99	0
26	60	0	1	4	2	21-Oct-99	0
27	72	1	0	3	2	22-Oct-99	1
28	66	1	1	7	3	27-Oct-99	1
29	56	0	0	6	3	18-Nov-99	1
30	78	2	0	7	3	25-Nov-99	0
31	82	2	1	4	2	25-Nov-99	0
32	69	1	0	5	2	30-Nov-99	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
33	72	1	0	7	3	08-Dec-99	1
34	72	1	0	4	2	16-Dec-99	0
35	81	2	1	6	3	26-Jan-00	0
36	66	1	0	4	2	03-Mar-00	1
37	45	0	1	7	3	08-Mar-00	0
38	62	0	1	7	3	10-Mar-00	1
39	79	2	1	5	2	15-Mar-00	0
40	60	0	0	3	2	06-Apr-00	1
41	72	1	1	7	3	19-May-00	1
42	67	1	0	5	2	21-Jul-00	1
43	63	0	0	3	2	25-Jul-00	0
44	89	2	1	7	3	08-Sep-00	0
45	85	2	1	7	3	08-Sep-00	1
46	72	1	0	6	3	28-Sep-00	1
47	70	1	0	7	3	27-Oct-00	0
48	56	0	0	6	3	09-Nov-00	1
49	70	1	0	3	2	05-Dec-00	1
50	64	0	0	7	3	14-Dec-00	0
51	78	2	1	5	2	16-Jan-01	1
52	64	0	0	6	3	30-Jan-01	0
53	72	1	0	6	3	31-Jan-01	0
54	55	0	1	6	3	13-Feb-01	0
55	74	1	1	6	3	16-Feb-01	1
56	83	2	0	2	1	09-Mar-01	0
57	55	0	0	.	.	13-Mar-01	0
58	79	2	0	6	3	23-Mar-01	0
59	42	0	1	4	2	03-May-01	0
60	71	1	1	4	2	08-May-01	0
61	60	0	1	5	2	08-May-01	1
62	79	2	0	6	3	12-Jul-01	0
63	68	1	0	7	3	19-Jul-01	0
64	63	0	0	3	2	09-Aug-01	1

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
65	76	2	1	3	2	21-Aug-01	0
66	73	1	1	7	3	21-Aug-01	0
67	69	1	0	4	2	23-Aug-01	0
68	80	2	1	3	2	28-Aug-01	0
69	75	2	1	5	2	06-Sep-01	0
70	72	1	1	3	2	07-Sep-01	0
71	32	0	0	7	3	18-Sep-01	1
72	54	0	0	4	2	18-Sep-01	0
73	77	2	0	7	3	20-Sep-01	1
74	77	2	0	3	2	21-Sep-01	1
75	58	0	0	.	.	26-Sep-01	1
76	82	2	1	4	2	27-Sep-01	0
77	80	2	1	6	3	02-Oct-01	0
78	73	1	0	6	3	05-Oct-01	1
79	80	2	1	6	3	09-Oct-01	0
80	32	0	0	7	3	12-Oct-01	0
81	61	0	1	6	3	15-Oct-01	0
82	79	2	0	4	2	16-Oct-01	0
83	46	0	0	3	2	25-Oct-01	0
84	83	2	0	6	3	30-Oct-01	0
85	80	2	0	7	3	06-Nov-01	1
86	75	2	0	5	2	13-Nov-01	1
87	70	1	0	6	3	15-Nov-01	1
88	59	0	0	7	3	20-Nov-01	1
89	82	2	1	7	3	22-Nov-01	0
90	81	2	1	7	3	28-Nov-01	1
91	60	0	0	4	2	12-Dec-01	0
92	69	1	0	4	2	30-Dec-01	0
93	70	1	0	7	3	08-Jan-02	1
94	74	1	0	5	2	15-Jan-02	1
95	77	2	0	5	2	18-Jan-02	1
96	78	2	1	4	2	20-Jan-02	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
97	44	0	1	7	3	21-Jan-02	0
98	89	2	1	6	3	30-Jan-02	1
99	64	0	0	5	2	05-Feb-02	1
100	81	2	1	4	2	28-Feb-02	1
101	65	1	1	1	1	08-Mar-02	1
102	74	1	0	6	3	20-Mar-02	0
103	63	0	0	3	2	04-Apr-02	1
104	83	2	1	2	1	05-Apr-02	1
105	48	0	0	7	3	17-Apr-02	1
106	50	0	1	3	2	24-Apr-02	0
107	61	0	1	4	2	26-Apr-02	1
108	84	2	0	7	3	02-May-02	0
109	50	0	1	6	3	07-May-02	0
110	64	0	1	4	2	08-May-02	0
111	69	1	1	3	2	10-May-02	1
112	63	0	0	3	2	15-May-02	1
113	76	2	1	6	3	17-May-02	0
114	75	2	0	7	3	28-May-02	1
115	71	1	0	7	3	11-Jun-02	0
116	63	0	0	7	3	13-Jun-02	0
117	69	1	1	7	3	20-Jun-02	0
118	68	1	0	7	3	20-Jun-02	0
119	76	2	0	3	2	20-Jun-02	0
120	79	2	0	5	2	26-Jun-02	0
121	73	1	0	7	3	06-Jul-02	0
122	80	2	1	6	3	10-Jul-02	0
123	67	1	1	7	3	11-Jul-02	1
124	59	0	1	3	2	12-Aug-02	1
125	77	2	1	4	2	13-Aug-02	1
126	50	0	0	4	2	20-Aug-02	1
127	66	1	1	7	3	22-Aug-02	1
128	76	2	1	7	3	03-Sep-02	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
129	77	2	1	3	2	05-Sep-02	1
130	85	2	1	3	2	11-Sep-02	0
131	77	2	0	5	2	17-Sep-02	0
132	83	2	0	4	2	20-Sep-02	0
133	67	1	1	6	3	30-Oct-02	1
134	79	2	0	6	3	01-Nov-02	1
135	68	1	1	4	2	05-Nov-02	0
136	75	2	1	6	3	12-Nov-02	1
137	62	0	1	7	3	13-Nov-02	0
138	55	0	1	6	3	13-Nov-02	0
139	79	2	0	3	2	26-Nov-02	0
140	68	1	1	4	2	11-Dec-02	0
141	86	2	1	7	3	18-Dec-02	0
142	81	2	1	7	3	04-Jan-03	0
143	86	2	0	3	2	04-Jan-03	0
144	47	0	1	7	3	06-Jan-03	1
145	53	0	0	7	3	08-Jan-03	1
146	83	2	0	3	2	09-Jan-03	0
147	60	0	0	4	2	14-Jan-03	1
148	77	2	0	7	3	14-Jan-03	1
149	74	1	0	7	3	23-Jan-03	0
150	83	2	1	5	2	29-Jan-03	1
151	56	0	0	6	3	30-Jan-03	0
152	69	1	1	7	3	06-Mar-03	1
153	73	1	0	7	3	14-Mar-03	0
154	63	0	0	7	3	19-Mar-03	1
155	49	0	0	6	3	25-Mar-03	1
156	56	0	1	3	2	28-Mar-03	1
157	68	1	0	4	2	04-Apr-03	1
158	58	0	0	7	3	15-Apr-03	1
159	64	0	0	7	3	21-Apr-03	1
160	43	0	0	6	3	22-Apr-03	0

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
161	79	2	0	7	3	23-Apr-03	1
162	39	0	0	7	3	30-Apr-03	1
163	67	1	0	6	3	13-May-03	0
164	72	1	0	.	.	14-May-03	0
165	60	0	1	6	3	23-May-03	0
166	72	1	0	5	2	27-May-03	0
167	74	1	0	7	3	29-May-03	0
168	82	2	1	4	2	12-Jun-03	0
169	69	1	1	2	1	19-Jun-03	1
170	83	2	1	6	3	04-Jul-03	0
171	76	2	1	7	3	31-Jul-03	0
172	64	0	1	3	2	01-Aug-03	1
173	38	0	1	7	3	05-Aug-03	0
174	61	0	1	4	2	07-Aug-03	0
175	56	0	1	7	3	07-Aug-03	1
176	76	2	1	3	2	15-Aug-03	1
177	87	2	1	3	2	15-Aug-03	0
178	74	1	0	3	2	20-Aug-03	0
179	61	0	0	3	2	28-Aug-03	0
180	83	2	1	7	3	29-Aug-03	0
181	77	2	0	6	3	03-Sep-03	0
182	55	0	0	3	2	05-Sep-03	0
183	74	1	0	3	2	09-Sep-03	0
184	69	1	1	6	3	12-Sep-03	0
185	75	2	0	4	2	18-Sep-03	0
186	77	2	0	6	3	19-Sep-03	1
187	75	2	1	6	3	03-Oct-03	0
188	72	1	1	3	2	03-Oct-03	1
189	65	1	0	7	3	09-Oct-03	1
190	65	1	0	6	3	10-Oct-03	0
191	74	1	0	7	3	16-Oct-03	0
192	41	0	0	2	1	17-Oct-03	1

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Site (Rectum=1, colon=0)
193	48	0	0	6	3	21-Oct-03	1
194	54	0	0	5	2	23-Oct-03	1
195	84	2	0	5	2	24-Oct-03	0
196	74	1	0	7	3	30-Oct-03	0
197	71	1	0	7	3	12-Nov-03	1
198	64	0	0	7	3	16-Dec-03	0
199	69	1	1	7	3	18-Dec-03	0
200	47	0	0	6	3	06-Jan-04	1
201	70	1	0	3	2	08-Jan-04	1
202	69	1	0	4	2	08-Jan-04	0
203	73	1	1	7	3	09-Jan-04	0
204	70	1	0	6	3	06-Feb-04	0
205	67	1	1	5	2	24-Feb-04	1
206	68	1	1	7	3	27-Feb-04	0
207	81	2	0	6	3	16-Mar-04	0
208	75	2	0	6	3	18-Mar-04	0
209	67	1	1	1	1	19-Mar-04	0
210	66	1	0	7	3	23-Mar-04	1
211	69	1	1	7	3	25-Mar-04	0
212	77	2	1	4	2	25-Mar-04	1
213	70	1	0	3	2	14-Apr-04	1
214	80	2	1	7	3	16-Apr-04	1
215	59	0	1	4	2	20-Apr-04	0
216	75	2	1	5	2	23-Apr-04	1
217	83	2	1	7	3	05-May-04	0
218	79	2	0	7	3	14-May-04	0
219	51	0	0	7	3	18-May-04	1
220	80	2	0	3	2	08-Jun-04	1
221	73	1	0	5	2	15-Jun-04	1
222	72	1	1	4	2	15-Jun-04	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
1	0	12-Sep-05	0	75.99	B	79	1	31	1
2	0	12-Sep-05	0	75.96	B	22	1	.	.
3	0	12-Mar-04	2	61.63	B	5	0	.	.
4	0	12-Sep-05	0	75.04	B	5	0	.	.
5	0	12-Sep-05	0	74.81	B	5	0	.	.
6	0	12-Sep-05	0	74.55	B	5	0	.	.
7	0	25-Feb-02	1	35.78	C	15	1	.	.
8	0	25-Aug-04	2	65.38	B	5	0	.	.
9	0	12-Sep-05	0	73.92	C	16	1	41	0
10	1	12-Sep-05	0	73.89	B	8	0	.	.
11	0	01-Dec-99	1	6.8	B	50	1	.	.
12	0	12-Sep-05	0	71.75	B	5	0	.	.
13	0	16-Aug-03	2	49.94	B	5	0	37	0
14	0	12-Sep-05	0	70.67	B	5	0	39	0
15	0	12-Sep-05	0	70.47	B	5	0	41	0
16	0	12-Sep-05	0	70.01	C	9	0	42	0
17	0	14-Oct-01	1	26.74	B	15	1	39	0
18	0	12-Sep-05	0	69.26	C	5	0	37	0
19	0	28-May-04	2	57.43	B	35	1	43	0
20	0	12-Sep-05	0	68.83	B	5	0	.	.
21	0	26-Oct-01	1	26.09	C	5	0	.	.
22	0	12-Sep-05	0	68.14	B	5	0	39	0
23	0	12-Sep-05	0	67.91	B	5	0	.	.
24	0	12-Sep-05	0	67.61	B	5	0	42	0
25	1	12-Sep-05	0	67.25	C	5	0	.	.
26	0	12-Sep-05	0	66.73	B	61	1	39	0
27	1	19-Feb-05	2	63.97	C	5	0	46	0
28	1	12-Sep-05	0	66.53	C	5	0	41	0
29	1	22-Mar-03	2	40.08	C	5	0	44	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
30	0	02-Jan-05	2	61.27	B	37	1	.	.
31	0	17-Jun-03	1	42.71	C	23	1	36	0
32	1	30-Oct-02	1	34.99	C	11	1	.	.
33	0	12-Sep-05	0	65.15	B	5	0	44	0
34	1	12-Sep-05	0	64.89	B	5	0	38	0
35	0	12-Sep-05	0	63.54	B	5	0	35	0
36	0	26-Aug-03	1	41.76	B	5	0	.	.
37	0	12-Sep-05	0	62.16	B	6	0	43	0
38	1	02-May-01	1	13.73	C	16	1	.	.
39	0	12-Sep-01	2	17.94	B	31	1	38	0
40	0	12-Sep-05	0	61.21	B	178	1	31	1
41	0	18-Mar-03	1	33.94	A	6	0	39	0
42	0	12-Sep-05	0	57.72	B	35	1	39	0
43	1	18-Mar-02	1	19.75	C	97	1	42	0
44	0	04-Jun-03	2	32.82	C	31	1	34	1
45	0	12-Sep-05	0	56.11	C	7	0	34	1
46	0	12-Sep-05	0	55.46	C	26	1	44	0
47	0	12-Sep-05	0	54.51	B	19	1	36	0
48	0	12-Sep-05	0	54.08	B	77	1	34	1
49	0	12-Sep-05	0	53.22	B	5	0	.	.
50	0	12-Sep-05	0	52.93	C	5	0	.	.
51	0	12-Sep-05	0	51.84	B	5	0	.	.
52	0	12-Sep-05	0	51.38	C	5	0	38	0
53	0	12-Sep-05	0	51.35	B	5	0	.	.
54	0	12-Sep-05	0	50.92	B	6	0	38	0
55	0	12-Sep-05	0	50.83	A	6	0	48	0
56	0	12-Sep-05	0	50.14	B	36	1	35	0
57	1	12-Sep-05	0	50	C	37	1	39	0
58	0	12-Sep-05	0	49.68	B	21	1	38	0
59	1	12-Sep-05	0	48.33	B	6	0	37	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
60	0	12-Sep-05	0	48.16	B	6	0	.	.
61	1	27-Feb-02	2	9.69	C	120	1	.	.
62	0	12-Sep-05	0	46.03	C	92	1	31	1
63	1	12-Sep-05	0	45.8	C	6	0	47	0
64	1	12-Sep-05	0	45.11	C	6	0	44	0
65	0	12-Sep-05	0	44.71	B	41	1	41	0
66	0	12-Sep-05	0	44.71	B	7	0	37	0
67	0	12-Sep-05	0	44.65	B	22	1	38	0
68	0	12-Sep-05	0	44.48	B	11	1	42	0
69	0	12-Sep-05	0	44.19	B	8	0	42	0
70	0	12-Sep-05	0	44.16	C	7	0	43	0
71	1	12-Sep-05	0	43.79	C	6	0	46	0
72	0	12-Sep-05	0	43.79	A	6	0	42	0
73	1	12-Sep-05	0	43.73	C	6	0	42	0
74	0	12-Sep-05	0	43.7	A	7	0	43	0
75	1	18-Sep-03	2	23.72	C	6	0	42	0
76	0	09-Aug-04	2	34.4	B	33	1	39	0
77	0	12-Sep-05	0	43.33	C	29	1	42	0
78	0	12-Sep-05	0	43.24	C	6	0	45	0
79	0	18-Jul-05	2	43.1	A	12	1	40	0
80	1	12-Sep-05	0	43.01	B	24	1	43	0
81	0	12-Sep-05	0	42.91	B	71	1	32	1
82	0	27-Apr-02	1	6.34	C	5	0	41	0
83	1	28-Dec-04	1	38.11	C	9	0	47	0
84	0	12-Sep-05	0	42.41	B	6	0	44	0
85	0	12-Sep-05	0	42.18	C	6	0	38	0
86	0	24-Jan-03	1	14.36	C	48	1	37	0
87	0	12-Sep-05	0	41.89	B	6	0	40	0
88	0	19-Feb-03	2	14.98	B	34	1	43	0
89	0	24-Dec-01	2	1.05	A	46	1	32	1

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
90	0	12-Sep-05	0	41.46	B	8	0	43	0
91	0	12-Sep-05	0	41	B	15	1	38	0
92	1	28-Dec-03	1	23.92	C	26	1	38	0
93	0	12-Sep-05	0	40.11	B	6	0	44	0
94	1	12-Sep-05	0	39.89	C	6	0	42	0
95	0	12-Jun-03	2	16.76	C	6	0	50	0
96	0	09-Feb-03	1	12.65	C	20	1	45	0
97	0	12-Sep-05	0	39.69	B	6	0	42	0
98	0	12-Sep-05	0	39.39	A	41	1	38	0
99	1	12-Sep-05	0	39.2	C	6	0	42	0
100	0	12-Sep-05	0	38.44	C	11	1	42	0
101	0	12-Sep-05	0	38.18	C	6	0	46	0
102	0	24-Mar-03	1	12.12	C	58	1	34	1
103	0	05-Sep-04	2	29.08	C	14	1	44	0
104	0	19-Jan-05	1	33.51	C	6	0	.	.
105	1	12-Sep-05	0	36.86	C	5	0	47	0
106	1	12-Sep-05	0	36.63	C	7	0	42	0
107	0	12-Sep-05	0	36.57	A	6	0	42	0
108	1	23-May-03	1	12.68	C	135	1	39	0
109	1	21-Jun-03	1	13.47	C	28	1	40	0
110	1	12-Sep-05	0	36.17	C	56	1	37	0
111	0	30-Sep-04	1	28.71	A	20	1	41	0
112	0	18-Sep-04	2	28.16	B	5	0	44	0
113	0	16-Dec-03	1	18.99	C	6	0	38	0
114	0	04-May-05	2	35.52	C	5	0	36	0
115	0	12-Sep-05	0	35.06	B	6	0	42	0
116	1	12-Sep-05	0	34.99	C	9	0	42	0
117	0	12-Sep-05	0	34.76	B	12	1	41	0
118	0	15-Apr-04	2	21.85	B	9	0	41	0
119	0	05-Sep-05	2	34.76	C	31	1	40	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
120	0	12-Sep-05	0	34.56	C	19	1	36	0
121	0	12-Sep-05	0	34.23	A	20	1	38	0
122	0	12-Sep-05	0	34.1	C	5	0	42	0
123	1	02-May-03	2	9.69	C	22	1	41	0
124	0	12-Sep-05	0	33.02	B	6	0	52	0
125	0	05-Dec-04	1	27.76	B	26	1	41	0
126	0	12-Sep-05	0	32.76	A	6	0	43	0
127	0	09-Nov-03	2	14.59	C	10	0	43	0
128	1	12-Sep-05	0	32.3	C	6	0	44	0
129	0	12-Sep-05	0	32.23	C	6	0	42	0
130	0	12-Sep-05	0	32.03	B	14	1	42	0
131	0	13-Jun-05	1	31.84	B	101	1	36	0
132	0	25-Feb-04	1	17.18	C	6	0	35	0
133	0	12-Sep-05	0	30.42	B	5	0	38	0
134	0	23-Jul-04	2	20.7	B	26	1	41	0
135	0	17-Mar-04	2	16.36	B	7	0	44	0
136	0	04-Apr-04	2	16.72	B	19	1	47	0
137	0	12-Sep-05	0	29.96	B	17	1	36	0
138	0	12-Sep-05	0	29.96	B	5	0	47	0
139	0	12-Sep-05	0	29.54	B	41	1	40	0
140	0	12-Sep-05	0	29.04	B	8	0	44	0
141	0	12-Sep-05	0	28.81	B	27	1	42	0
142	0	12-Sep-05	0	28.25	C	21	1	37	0
143	0	07-Oct-03	1	9.07	B	49	1	34	1
144	0	12-Sep-05	0	28.19	A	6	0	45	0
145	0	12-Sep-05	0	28.12	C	11	1	41	0
146	0	12-Sep-05	0	28.09	C	19	1	41	0
147	0	12-Sep-05	0	27.93	B	34	1	31	1
148	0	12-Sep-05	0	27.93	C	6	0	37	0
149	0	12-Sep-05	0	27.63	B	6	0	41	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
150	0	09-Jul-03	1	5.29	B	13	1	40	0
151	1	12-Sep-05	0	27.4	C	8	0	43	0
152	0	12-Sep-05	0	26.25	B	6	0	46	0
153	0	12-Sep-05	0	25.99	B	48	1	30	1
154	1	25-Dec-03	2	9.23	B	6	0	41	0
155	0	12-Sep-05	0	25.63	B	6	0	44	0
156	0	12-Sep-05	0	25.53	C	6	0	45	0
157	0	12-Sep-05	0	25.3	B	6	0	40	0
158	0	23-May-05	2	24.94	C	9	0	39	0
159	1	12-Sep-05	0	24.74	C	40	1	42	0
160	0	12-Sep-05	0	24.71	A	7	0	47	0
161	0	12-Sep-05	0	24.67	B	47	1	35	0
162	1	12-Sep-05	0	24.44	C	7	0	47	0
163	0	12-Sep-05	0	24.02	A	6	0	48	0
164	0	20-Oct-03	1	5.22	B	10	0	42	0
165	1	12-Sep-05	0	23.69	C	9	0	42	0
166	1	12-Sep-05	0	23.56	B	6	0	41	0
167	0	12-Sep-05	0	23.49	B	8	0	41	0
168	0	12-Sep-05	0	23.03	B	33	1	31	1
169	0	12-Sep-05	0	22.8	C	5	0	40	0
170	0	01-Jul-05	1	22.31	B	95	1	31	1
171	0	12-Sep-05	0	21.42	A	6	0	42	0
172	0	12-Sep-05	0	21.39	A	5	0	44	0
173	1	02-Mar-05	1	18.89	C	38	1	42	0
174	0	12-Sep-05	0	21.19	C	5	0	41	0
175	1	12-Sep-05	0	21.19	C	11	1	42	0
176	0	12-Sep-05	0	20.93	C	5	0	42	0
177	0	01-Jul-04	1	10.55	C	94	1	32	1
178	0	12-Sep-05	0	20.76	B	5	0	39	0
179	0	12-Sep-05	0	20.5	B	10	0	43	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
180	0	12-Sep-05	0	20.47	A	6	0	34	1
181	0	12-Sep-05	0	20.3	B	7	0	39	0
182	1	12-Sep-05	0	20.24	C	19	1	43	0
183	0	12-Sep-05	0	20.11	C	5	0	40	0
184	0	12-Sep-05	0	20.01	B	29	1	37	0
185	1	12-Sep-05	0	19.81	C	5	0	46	0
186	1	12-Sep-05	0	19.78	C	5	0	44	0
187	0	12-Sep-05	0	19.32	C	7	0	41	0
188	0	12-Sep-05	0	19.32	C	5	0	41	0
189	0	12-Sep-05	0	19.12	B	7	0	39	0
190	0	12-Sep-05	0	19.09	C	5	0	43	0
191	0	12-Sep-05	0	18.89	A	12	1	38	0
192	0	12-Sep-05	0	18.86	A	5	0	42	0
193	0	12-Sep-05	0	18.73	B	5	0	45	0
194	0	12-Sep-05	0	18.66	A	8	0	45	0
195	0	12-Sep-05	0	18.63	B	40	1	40	0
196	0	12-Sep-05	0	18.43	C	21	1	43	0
197	0	12-Sep-05	0	18	A	5	0	44	0
198	0	12-Sep-05	0	16.89	B	75	1	36	0
199	1	12-Sep-05	0	16.82	C	9	0	40	0
200	0	12-Sep-05	0	16.2	C	5	0	41	0
201	1	12-Sep-05	0	16.13	B	31	1	41	0
202	0	12-Sep-05	0	16.13	B	5	0	36	0
203	1	12-Sep-05	0	16.1	C	18	1	39	0
204	0	12-Sep-05	0	15.18	B	27	1	41	0
205	0	21-May-04	1	2.86	C	38	1	42	0
206	0	12-Sep-05	0	14.49	A	12	1	42	0
207	0	12-Sep-05	0	13.9	B	12	1	34	1
208	1	12-Sep-05	0	13.83	B	6	0	43	0
209	1	21-Feb-05	1	11.14	C	209	1	41	0

Patient ID	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	Dukes stage	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0=>35mg/l, 1=≤35mg/l)
210	1	12-Sep-05	0	13.67	C	5	0	43	0
211	0	12-Sep-05	0	13.6	B	133	1	34	1
212	0	12-Sep-05	0	13.6	C	22	1	44	0
213	1	12-Sep-05	0	12.94	B	5	0	48	0
214	0	12-Sep-05	0	12.88	B	101	1	33	1
215	0	12-Sep-05	0	12.75	B	14	1	26	1
216	0	12-Sep-05	0	12.65	B	14	1	38	0
217	0	12-Sep-05	0	12.25	B	16	1	38	0
218	0	12-Sep-05	0	11.96	C	27	1	45	0
219	1	12-Sep-05	0	11.83	C	5	0	47	0
220	0	12-Sep-05	0	11.14	A	5	0	42	0
221	0	06-Sep-04	2	2.73	C	12	1	38	0
222	1	12-Sep-05	0	10.91	C	5	0	39	0

Appendix 6 – Database for chapter 8 – DOES THE PRESENCE OF A PRE-OPERATIVE SYSTEMIC INFLAMMATORY RESPONSE PREDICT POORER SURVIVAL IN PATIENTS WITH TNM STAGE I/II COLON CANCER – A PILOT STUDY

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
1	72	1	0	4	2	16-Dec-99	Right Hemicolectomy
2	45	0	1	7	3	08-Mar-00	Right hemicolectomy
3	79	2	1	5	2	15-Mar-00	Right hemicolectomy
4	70	1	0	7	3	27-Oct-00	sigmoid colectomy
5	55	0	1	6	3	13-Feb-01	Sigmoid colectomy
6	79	2	0	6	3	23-Mar-01	Right Hemicolectomy
7	42	0	1	4	2	03-May-01	Right Hemicolectomy
8	76	2	1	3	2	21-Aug-01	Hartmann's procedure
9	73	1	1	7	3	21-Aug-01	Sub-total colectomy + IRA
10	69	1	0	4	2	23-Aug-01	Sub-total colectomy + IRA
11	75	2	1	5	2	06-Sep-01	Right Hemicolectomy
12	54	0	0	4	2	18-Sep-01	Sigmoid colectomy
13	82	2	1	4	2	27-Sep-01	Sigmoid colectomy
14	80	2	1	6	3	09-Oct-01	Sigmoid colectomy
15	32	0	0	7	3	12-Oct-01	Right Hemicolectomy
16	83	2	0	6	3	30-Oct-01	Right Hemicolectomy
17	82	2	1	7	3	22-Nov-01	Right Hemicolectomy
18	60	0	0	4	2	12-Dec-01	R hemicolectomy
19	44	0	1	7	3	21-Jan-02	sigmoid colectomy
20	71	1	0	7	3	11-Jun-02	sigmoid colectomy
21	69	1	1	7	3	20-Jun-02	Right Hemicolectomy
22	68	1	0	7	3	20-Jun-02	Right Hemicolectomy
23	73	1	0	7	3	06-Jul-02	Sigmoid colectomy
24	85	2	1	3	2	11-Sep-02	Sigmoid colectomy
25	77	2	0	5	2	17-Sep-02	Right Hemicolectomy
26	68	1	1	4	2	05-Nov-02	Right Hemicolectomy
27	62	0	1	7	3	13-Nov-02	Right Hemicolectomy
28	55	0	1	6	3	13-Nov-02	Sigmoid colectomy
29	79	2	0	3	2	26-Nov-02	sub-total colectomy + IRA
30	68	1	1	4	2	11-Dec-02	Sigmoid colectomy
31	86	2	1	7	3	18-Dec-02	Right Hemicolectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
32	86	2	0	3	2	04-Jan-03	Right Hemicolectomy
33	74	1	0	7	3	23-Jan-03	Sigmoid colectomy
34	73	1	0	7	3	14-Mar-03	sigmoid colectomy
35	43	0	0	6	3	22-Apr-03	Right hemicolectomy
36	67	1	0	6	3	13-May-03	Sigmoid colectomy
37	72	1	0	4	2	14-May-03	Right Hemicolectomy
38	72	1	0	5	2	27-May-03	Sigmoid colectomy
39	74	1	0	7	3	29-May-03	Right Hemicolectomy
40	82	2	1	4	2	12-Jun-03	Right Hemicolectomy
41	72	1	1	7	3	03-Jul-03	Sigmoid colectomy
42	83	2	1	6	3	04-Jul-03	Right Hemicolectomy
43	76	2	1	7	3	31-Jul-03	Right Hemicolectomy
44	74	1	0	3	2	20-Aug-03	Subtotal colectomy
45	61	0	0	3	2	28-Aug-03	Right hemicolectomy
46	83	2	1	7	3	29-Aug-03	Right hemicolectomy
47	77	2	0	6	3	03-Sep-03	Right Hemicolectomy
48	69	1	1	6	3	12-Sep-03	Left hemicolectomy
49	74	1	0	7	3	16-Oct-03	Right Hemicolectomy
50	84	2	0	5	2	24-Oct-03	Right hemicolectomy
51	64	0	0	7	3	16-Dec-03	Right Hemicolectomy
52	69	1	0	4	2	08-Jan-04	Sigmoid colectomy
53	64	0	0	7	3	09-Jan-04	Proctectomy
54	70	1	0	6	3	06-Feb-04	Sigmoid colectomy
55	68	1	1	7	3	27-Feb-04	Sigmoid colectomy
56	82	2	0	6	3	16-Mar-04	Sigmoid colectomy
57	76	2	0	6	3	18-Mar-04	right hemicolectomy
58	69	1	1	3	2	25-Mar-04	right hemicolectomy
59	59	0	1	4	2	20-Apr-04	right hemicolectomy
60	84	2	1	7	3	05-May-04	right hemicolectomy
61	43	0	1	7	3	24-Aug-04	Sigmoid colectomy
62	57	0	0	4	2	27-Aug-04	Sigmoid colectomy

Patient ID	Age (Years)	Age code (<65=0, 65-74=1, >75=2)	Sex (M=0 F=1)	Deprivation group	Deprivation group (1=1,2; 2=3-5;3=6,7)	Operation Date	Operation
63	74	1	1	4	2	07-Sep-04	Sigmoid colectomy
64	74	1	1	4	2	17-Sep-04	Right hemicolectomy
65	77	2	0	6	3	28-Sep-04	Sigmoid colectomy
66	72	1	1	6	3	02-Nov-04	Left hemicolectomy
67	46	0	1	3	2	02-Dec-04	Sigmoid colectomy
68	63	0	0	7	3	09-Dec-04	right hemicolectomy
69	74	1	1	6	3	21-Dec-04	right hemicolectomy
70	81	2	1	1	1	22-Dec-04	hemicolectomy
71	50	0	0	2	1	31-Dec-04	Sigmoid colectomy
72	82	2	0	6	3	06-Jan-05	right hemicolectomy
73	77	2	1	4	2	07-Jan-05	right hemicolectomy
74	70	1	0	5	2	11-Feb-05	right hemicolectomy
75	79	2	0	6	3	22-Feb-05	right hemicolectomy
76	72	1	1	7	3	25-Feb-05	right hemicolectomy
77	74	1	1	3	2	11-Mar-05	anterior resection
78	69	1	1	7	3	17-Mar-05	right hemicolectomy
79	61	0	0	3	2	15-Apr-05	sigmoid colectomy
80	50	0	0	6	3	22-Apr-05	right hemi
81	66	1	0	6	3	12-May-05	Sigmoid colectomy
82	63	0	0	6	3	19-May-05	right hemicolectomy
83	83	2	1	7	3	21-Jun-05	Sigmoid colectomy
84	71	1	0	2	1	22-Jul-05	Sigmoid colectomy
85	79	2	0	7	3	25-Jul-05	Sigmoid colectomy
86	64	0	0	6	3	07-Oct-05	R hemicolectomy
87	67	1	0	4	2	02-Nov-05	R hemicolectomy
88	68	1	1	6	3	04-Nov-05	L hemicolectomy
89	37	0	0	4	2	30-Nov-05	Panproctocolectomy

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M
1	0	1	01-Jun-07	0	90.8	3	0	0
2	0	0	01-Jun-07	0	88.03	4	0	0
3	0	0	12-Sep-01	2	18.2	3	0	0
4	0	0	01-Jun-07	0	80.27	3	0	0
5	0	0	01-Jun-07	0	76.63	3	0	0
6	0	0	01-Jun-07	0	75.37	3	0	0
7	0	1	01-Jun-07	0	74	3	0	0
8	0	0	01-Jun-07	0	70.33	3	0	0
9	0	0	01-Jun-07	0	70.33	3	0	0
10	0	0	01-Jun-07	0	70.27	3	0	0
11	0	0	01-Jun-07	0	69.8	3	0	0
12	0	0	01-Jun-07	0	69.4	1	0	0
13	0	0	09-Aug-04	2	34.9	3	0	0
14	0	0	18-Jul-05	2	45.93	2	0	0
15	0	1	01-Jun-07	0	68.6	3	0	0
16	0	0	01-Jun-07	0	68	3	0	0
17	0	0	24-Dec-01	2	1.07	2	0	0
18	0	0	01-Jun-07	0	66.57	4	0	0
19	0	0	01-Jun-07	0	65.23	3	0	0
20	0	0	01-Jun-07	0	60.53	3	0	0
21	0	0	01-Jun-07	0	60.23	3	0	0
22	0	0	15-Apr-04	2	22.17	3	0	0
23	0	0	01-Jun-07	0	59.7	2	0	0
24	0	0	01-Jun-07	0	57.47	4	0	0
25	0	0	13-Jun-05	1	33.33	4	0	0
26	0	0	17-Mar-04	2	16.6	3	0	0
27	0	0	01-Jun-07	0	55.37	3	0	0
28	0	1	01-Jun-07	0	55.37	3	0	0
29	0	0	01-Jun-07	0	54.93	3	0	0
30	0	0	03-Nov-05	2	35.27	4	0	0
31	0	0	01-Jun-07	0	54.2	3	0	0

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M
32	0	0	07-Oct-03	1	9.2	3	0	0
33	0	0	14-Apr-07	2	51.4	3	0	0
34	0	0	26-Mar-06	1	36.93	3	0	0
35	0	0	01-Jun-07	0	50.03	2	0	0
36	0	0	01-Jun-07	0	49.33	1	0	0
37	0	0	20-Oct-03	1	5.3	3	0	0
38	0	1	01-Jun-07	0	48.87	4	0	0
39	0	0	01-Jun-07	0	48.8	3	0	0
40	0	0	01-Jun-07	0	48.33	3	0	0
41	0	1	01-Jun-07	0	47.63	3	0	0
42	0	0	01-Jul-05	1	24.27	3	0	0
43	0	0	01-Jun-07	0	46.7	2	0	0
44	0	0	01-Jun-07	0	46.03	3	0	0
45	0	1	01-Jun-07	0	45.77	3	0	0
46	0	0	01-Jun-07	0	45.73	2	0	0
47	0	0	01-Jun-07	0	45.57	3	0	0
48	0	0	01-Jun-07	0	45.27	4	0	0
49	0	0	01-Jun-07	0	44.13	2	0	0
50	0	0	01-Jun-07	0	43.87	3	0	0
51	0	0	01-Jun-07	0	42.1	3	0	0
52	0	0	01-Jun-07	0	41.33	4	0	0
53	0	0	01-Jun-07	0	41.3	3	0	0
54	0	0	01-Jun-07	0	40.37	3	0	0
55	0	0	01-Jun-07	0	39.67	2	0	0
56	0	0	26-Mar-07	2	36.83	3	0	0
57	0	0	16-May-06	1	26.3	4	0	0
58	0	0	01-Jun-07	0	38.77	3	0	0
59	0	0	01-Jun-07	0	37.9	3	0	0
60	0	0	01-Jun-07	0	37.4	4	0	0
61	0	1	01-Jun-07	0	33.7	4	0	0
62	0	0	01-Jun-07	0	33.6	2	0	0

Patient ID	Site (Rectum=1, colon=0)	Adjuvant therapy (chemotherapy =1)	Date of followup	Cause of death (0=alive, 1=colorectal cancer, 2=non-cancer cause)	Survival (months)	T	N	M
63	0	0	01-Jun-07	0	33.23	4	0	0
64	0	0	01-Jun-07	0	32.9	3	0	0
65	0	0	01-Jun-07	0	32.53	3	0	0
66	0	0	01-Jun-07	0	31.37	3	0	0
67	0	0	01-Jun-07	0	30.37	3	0	0
68	0	0	01-Jun-07	0	30.13	3	0	0
69	0	0	01-Jun-07	0	29.73	3	0	0
70	0	0	01-Jun-07	0	29.7	2	0	0
71	0	1	01-Jun-07	0	29.4	3	0	0
72	0	0	01-Jun-07	0	29.2	3	0	0
73	0	0	01-Jun-07	0	29.17	2	0	0
74	0	0	01-Jun-07	0	28	1	0	0
75	0	0	01-Jun-07	0	27.63	3	0	0
76	0	0	01-Jun-07	0	27.53	3	0	0
77	0	0	01-Jun-07	0	27.07	3	0	0
78	0	0	01-Jun-07	0	26.87	3	0	0
79	0	0	01-Jun-07	0	25.9	3	0	0
80	0	0	01-Jun-07	0	25.67	3	0	0
81	0	0	01-Jun-07	0	25	2	0	0
82	0	0	01-Jun-07	0	24.77	3	0	0
83	0	0	03-Nov-05	2	4.5	3	0	0
84	0	0	01-Jun-07	0	22.63	2	0	0
85	0	0	01-Jun-07	0	22.53	1	0	0
86	0	0	01-Jun-07	0	20.07	3	0	0
87	0	0	01-Jun-07	0	19.2	3	0	0
88	0	0	01-Jun-07	0	19.13	4	0	0
89	0	1	01-Jun-07	0	18.27	4	0	0

Patient ID	Stage	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
1	2	well/mod	No	clear	14	0	no
2	3	well/mod	No	clear	12	0	no
3	2	well/mod	No	clear	23	0	no
4	2	well/mod	No	clear	8	0	no
5	2	well/mod	No	clear	35	0	no
6	2	well/mod	No	clear	26	0	no
7	2	well/mod	No	clear	20	0	no
8	2	well/mod	No	clear	10	0	no
9	2	poorly	No	clear	14	0	no
10	2	well/mod	No	clear	18	0	no
11	2	well/mod	No	clear	18	0	no
12	1	moderately	no	clear	28	0	no
13	2	well/mod	No	clear	21	0	no
14	1	well/mod	No	clear	15	0	no
15	2	well/mod	no	clear	26	0	no
16	2	well/mod	No	clear	7	0	no
17	1	well	no	clear	10	0	no
18	3	well/mod	No	clear	17	0	no
19	2	well/mod	no	clear	18	0	no
20	2	moderately	no	clear	10	0	no
21	2	poorly	No	clear	19	0	no
22	2	Moderately	no	clear	15	0	no
23	1	moderately	no	clear	7	0	no
24	3	moderately	no	clear	9	0	no
25	3	poor	no	clear	3	0	no
26	2	well/mod	No	clear	7	0	no
27	2	moderately	no	clear	26	0	no
28	2	Moderately	no	clear	15	0	no
29	2	well/mod	No	clear	20	0	no
30	3	moderately	no	clear	16	0	no
31	2	well/mod	no	clear	16	0	no

Patient ID	Stage	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
32	2	Moderately	No	clear	28	0	no
33	2	Moderately	yes	clear	17	0	no
34	2	Moderately	No	clear	11	0	no
35	1	moderately	no	clear	14	0	no
36	1	moderately	no	clear	8	0	no
37	2	poor	yes	clear	10	0	no
38	3	poor	no	clear	9	0	no
39	2	Moderately	No	clear	18	0	no
40	2	poor	yes	clear	15	0	no
41	2	poorly	yes	clear	13	0	no
42	2	Moderately	No	clear	11	0	no
43	1	moderately	no	clear	14	0	no
44	2	Well/mod	No	Clear	13	0	no
45	2	well/mod	yes	clear	10	0	no
46	1	well/mod	no	clear	8	0	no
47	2	well/mod	No	clear	14	0	no
48	3	well/mod	No	clear	7	0	no
49	1	well/mod	No	clear	11	0	no
50	2	poorly	Yes	clear	9	0	no
51	2	moderately	No	clear	14	0	no
52	3	moderately	No	clear	13	.	no
53	2	moderately	Yes	clear	12	0	no
54	2	moderately	No	clear	28	0	no
55	1	moderately	No	clear	8	0	no
56	2	moderately	No	clear	13	0	no
57	3	moderately	Yes	clear	22	0	no
58	2	moderately	Yes	clear	41	0	no
59	2	poorly	Yes	clear	25	.	no
60	3	moderately	No	clear	9	0	no
61	3	moderately	No	clear	26	0	no
62	1	moderately	No	clear	9	0	no

Patient ID	Stage	Differentiation	Vascular invasion	Resection margins	Total nodes	Positive nodes	Apical node positive
63	3	poorly	Yes	clear	25	0	no
64	2	moderately	No	clear	18	0	no
65	2	moderately	No	clear	18	0	no
66	2	moderately	Yes	clear	32	0	no
67	2	moderately	No	clear	13	0	no
68	2	moderately	No	clear	14	0	no
69	2	moderately	No	clear	12	0	no
70	1	poorly	No	clear	5	0	no
71	2	moderately	yes	clear	11	0	no
72	2	poorly	No	clear	13	0	no
73	1	moderately	No	clear	20	0	no
74	1	moderately	No	clear	4	0	no
75	2	moderately	No	clear	3	0	no
76	2	moderately	No	clear	21	0	no
77	2	moderately	No	clear	10	0	no
78	2	poorly	No	clear	17	0	no
79	2	moderately	No	clear	52	0	no
80	2	moderately	Yes	clear	20	0	no
81	1	moderately	No	clear	14	0	no
82	2	moderately	Yes	clear	30	0	no
83	2	moderately	Yes	clear	12	0	no
84	1	moderately	Yes	clear	6	0	no
85	1	moderately	No	clear	8	0	no
86	2	moderately	No	clear	18	0	no
87	2	moderately	No	clear	9	0	no
88	3	moderately	Yes	clear	8	0	no
89	3	moderately	Yes	clear	22	0	no

Patient ID	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
1	5	0	38	0	0
2	6	0	43	0	0
3	31	1	38	0	1
4	19	1	36	0	1
5	6	0	38	0	0
6	21	1	38	0	1
7	6	0	37	0	0
8	41	1	41	0	1
9	7	0	37	0	0
10	22	1	38	0	1
11	8	0	42	0	0
12	6	0	42	0	0
13	33	1	39	0	1
14	12	1	40	0	1
15	24	1	41	0	1
16	6	0	44	0	0
17	46	1	32	1	2
18	15	1	38	0	1
19	6	0	43	0	0
20	6	0	42	0	0
21	12	1	41	0	1
22	9	0	42	0	0
23	20	1	38	0	1
24	14	1	42	0	1
25	101	1	36	0	1
26	7	0	44	0	0
27	17	1	36	0	1
28	5	0	47	0	0
29	41	1	40	0	1
30	8	0	44	0	0
31	27	1	42	0	1

Patient ID	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
32	49	1	34	1	2
33	6	0	41	0	0
34	48	1	30	1	2
35	7	0	47	0	0
36	6	0	48	0	0
37	10	0	42	0	0
38	6	0	41	0	0
39	8	0	41	0	0
40	33	1	31	1	2
41	6	0	41	0	0
42	95	1	31	1	2
43	6	0	42	0	0
44	5	0	39	0	0
45	10	0	43	0	0
46	6	0	34	1	0
47	7	0	39	0	0
48	29	1	37	0	1
49	12	1	38	0	1
50	40	1	40	0	1
51	75	1	36	0	1
52	5	0	36	0	0
53	13	1	41	0	1
54	27	1	41	0	1
55	12	1	42	0	1
56	12	1	34	1	2
57	6	0	43	0	0
58	133	1	34	1	2
59	14	1	26	1	2
60	16	1	38	0	1
61	9	0	36	0	0
62	9	0	40	0	0

Patient ID	Preop CRP (mg/l)	CRP code (0=<10mg/l, 1= >10mg/l)	Preop albumin (mg/l)	Albumin code (0.35mg/l, 1=<35mg/l)	mGPS
63	24	1	44	0	1
64	5	0	44	0	0
65	18	1	41	0	1
66	19	1	42	0	1
67	5	0	46	0	0
68	34	1	47	0	1
69	57	1	41	0	1
70	5	0	41	0	0
71	5	0	47	0	0
72	103	1	31	1	2
73	5	0	43	0	0
74	5	0	43	0	0
75	5	0	40	0	0
76	15	1	41	0	1
77	5	0	41	0	0
78	16	1	29	1	2
79	19	1	36	0	1
80	6	0	42	0	0
81	5	0	43	0	0
82	11	1	40	0	1
83	48	1	44	0	1
84	6	0	41	0	0
85	6	0	37	0	0
86	6	0	40	0	0
87	6	0	41	0	0
88	11	1	43	0	1
89	6	0	40	0	0