CHRONIC PAIN FOLLOWING INGUINAL HERNIA REPAIR

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Abstract

Introduction

In the past five years chronic post herniorrhaphy pain has become the predominant post operative complication following the common procedure of inguinal hernia repair. However information regarding the precise aetiological factors of this chronic post surgical pain is lacking. To date no previous studies have assessed the long term outcome of patients who report chronic severe pain following inguinal hernia surgery. There are no studies assessing the presence of preoperative pain and the effect of surgical intervention on these pain scores. One factor thought to contribute to post herniorrhaphy chronic pain is the mesh type used by the surgeon. The characteristics of two different mesh types are evaluated with respect to postoperative chronic pain.

Aims

The aim of the first study was to assess the outcome of patients who report severe or very severe pain three months after groin hernia repair.

The aim of the second study was to quantify patients' pain from their inguinal hernia prior to surgery and to examine the effect of surgery on this pain.

The aim of the third study was to compare the composite partially absorbable and ultimately lighter weight (Vypro 11) mesh with an example of a conventional polyprolene mesh (Atrium) in a tension free repair of an inguinal hernia.

Methods

One hundred and twenty five patients were identified as experiencing severe chronic pain at 3 months post herniorrhaphy, from the prospective National Hernia database[1] of 5506 patients (97% of total) between 1 April 1998 and 31 march 1999. These 125 patients were assessed at 30 months post-surgery, with the use of the modified SF36 quality of life questionnaire.

For the second study, consecutive patients referred for elective inguinal hernia repair between January 1998 and October 2000 completed visual analogue pain scores (VAS) pre- and 1 year post-repair. These patients were Western Infirmary patients who were part of a larger multicenter clinical trial comparing local versus general anaesthesia [2] for inguinal hernia repair.

The third study examined patients who were involved in a multicenter trial comparing the incidence and severity of chronic pain following elective inguinal hernia repair, comparing the light weight or partially absorbable (PA) to the standard heavy weight or non-absorbable (NA) mesh.

Results

In the first study, of the 125 patients who experienced severe chronic pain at three months post repair, at 30 months post-surgery 25% had persistent, unchanged chronic pain 45% had a reduction in pain to mild or very mild, and 29% were pain-free. In the 25% of patients that had persistence of severe chronic pain, the symptoms had a significant effect on all daily activities and quality of life, for example in measurement of general enjoyment of life, those with mild pain scored 2.32 (1.5-3.13) compared to 7.14 (5.97 - 8.30) in those with persistent severe pain ($P<0.05$) .

In the second study 63% of patients completed VAS scores at follow-up. Prior to surgery the majority of patients had no pain or only mild pain at rest (80.5%) or on movement (58.8%). At 1 year follow-up the mean (SD) VAS score reduced by 2.9 (1.2) at rest, and reduced by 9.2 (1.8) on movement. However the majority of the beneficial effect was seen in those with moderate to high preoperative pain scores. Those with a preoperative VAS score >10 had a reduction of 22.8 (3.7) at rest, compared to a slight increase in pain (+1.8) in those with no pain pre-operatively ($P<0.05$). Similar effects were seen on movement (improvement of 32.2 (4.8) in those with preoperative pain score >10, and little change in pain, -0.3 (1.6), in those with no, or only mild, preoperative pain ($P<0.05$).

In the third study 162 patients received the PA mesh and 159 received the NA mesh. The PA mesh was not associated with less pain at 1 year postoperatively, compared to the NA mesh, with the proportion experiencing any pain being 39.5% in the PA group compared to 51.6% in the NA group ($P=0.033$). The proportion experiencing severe pain was similar, being 3% for the PA group and 4% for the NA group, and the recurrence rate was greater with the PA mesh compared to the NA mesh (4.9% versus 0.6%, $P=0.037$).

Conclusion

Of those with chronic severe pain at 3 months post inguinal hernia repair, the majority will have still have some pain at 30 months post operatively. The greatest benefit in terms of pain reduction in patients undergoing inguinal hernia repair is experienced by those with the more severe preoperative pain. From our data there is no clear overall benefit in using the PA mesh over the standard mesh, as whilst pain scores were slightly lower in the PA group, this was countered by a higher recurrence rate. Further attention

to the multiple factors that contribute to pain post-inguinal hernia repair is required, including the development of superior mesh technology.

Publications arising from the thesis

Published Abstract

B.Page, C.A.Courtney, K.Duffy, M.G.Serpell, P.J.O'Dwyer. Outcome of patients with severe chronic pain following repair of a groin hernia. *British Journal of Surgery* 2002 Vol. 89 Supplement 1 p4.

Published Paper

B.Page, C.Paterson, D.Young, P.J.O'Dwyer. Pain from a primary inguinal hernia and the effect of repair on pain. *British Journal of Surgery* 2002 Volume 89 (10) p1315-8

Published Book Chapter

B.Page and P.J.O'Dwyer Does the choice of prosthetic mesh type make a difference in post herniorrhaphy groin pain. *Book chapter in press in "Chronic Pain", Editors V.Schumpelick and R.Fitzgibbons, Publishers Springer 2009.*

Unpublished abstracts

Poster

B.Page and P.J.O'Dwyer. Pain from a primary inguinal hernia and the effect of repair on pain. May 2002 *West of Scotland Surgical Association*, poster presentation.

Oral Presentations

B.Page and P.J.O'Dwyer. Pain from a primary inguinal hernia and the effect of repair on pain. June 2002 *Amsterdam, European Hernia Society*.

B.Page and P.J.O'Dwyer. Outcome of patients with severe chronic pain post hernia repair. May 2002 Dublin, *Association of Surgeons of Great Britain and Ireland*.

List of symbols, abbreviations and nomenclature

Symbol	Definition
SF36	Short Form 36
VAS	Visual analogue scale
PA	Partially absorbable
NA	Non-absorbable
SD	Standard deviation
IASP	International Association for the Study of Pain
NHS	National Health Service
NMDA	N-Methyl-D-Aspartate
GP	General Practitioner
UK	United Kingdom
US	United States
RNA	Ribonucleic acid
PET	Positron emission tomography
MPQ	McGill pain questionnaire
MPI	Multidimensional pain inventory
BPI	Brief pain inventory
COPD	Chronic obstructive pulmonary disease
CABG	Coronary artery bypass grafting
BMI	Body mass index
PTPS	Post-thoracotomy pain syndrome
N	Newton
kPa	KiloPascal
RCT	Randomised controlled trial
EU	European Union
TEP	Totally extraperitoneal procedure
PVB	Para-vertebral block
GA	General anaesthetic
LA	Local anaesthetic
NSAID	Non-steroidal anti-inflammatory drug
SPS	Surgical Pain Scales

Statement of collaboration

Patients from study 1 (Outcome of patients with severe chronic pain following repair of a groin hernia. A population based study) came from a retrospective review of groin hernia repair in Scotland [1] and patients from study 2 (Pain from a primary inguinal hernia and the effect of repair on pain) were all patients recruited from one centre for part of a large multi-centred trial comparing local and general anaesthetic for groin hernia repair [2]. Data from study 1, (Outcome of patients with severe chronic pain following repair of a groin hernia: A population based study) and study 2 (Pain from a primary inguinal hernia and the effect of repair on pain) were taken from patient questionnaires, administered by Mr Phil Duffy, research assistant. The questionnaires used are long established and have previously been validated [3]. The data was interpreted by Mr Alec McConnachie and Mr David Young from the Department of Statistics at Glasgow University and myself.

Study 3 (Impact of absorbable or non absorbable mesh on chronic pain after inguinal hernia repair) was conceived and designed by the principle investigator, Professor O'Dwyer. It was a multicentre study supported by industry. I recruited, interviewed, examined and collected data for 100% of the patients at our centre (121 patients of the total 321 patients in the study). I constructed the database and collated all the data from this study. Statistical analysis was undertaken in collaboration with Ms Sue Bosie from the Department of Statistics at Oxford University.

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Chapter 1: Review of Literature

1.1. Introduction

Approximately 96% of all groin hernias are inguinal hernias, with the remaining 4% being femoral. Hernias are bilateral in 20% of cases. The most common abdominal wall hernia is an inguinal hernia with a male to female preponderance of 9 to 1. Femoral hernias are more common in women [4] .

Chronic pain is the most common and serious complication following inguinal hernia repair. In this thesis the role of chronic pain and its relationship to inguinal hernia repair is examined in three studies. In the first study the outcome of patients with chronic postoperative pain is assessed in a population based study. In the second study pain attributed to the hernia is quantified preoperatively and compared with pain and or discomfort at a time interval of one year post surgery. The third study, a randomised controlled trial, examines the effect of mesh type on postoperative pain. A review of the pathophysiology of pain and the factors that influence pain is given. This is followed by a review of the current literature on surgery and chronic pain. The significance of these results, their influence, and their impact on current thinking regarding hernia repair is debated. Finally the relevance of our results to future studies is explored.

1.2. Definition of pain; what is chronic pain?

The International Association for the Study of Pain (IASP) defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". This definition declares that pain, as well as having a physiological basis has a very real psychological or subjective component [5].

Transition between acute and chronic pain is defined by most authors in terms of time [5]. The two most commonly used chronological markers to denote chronic pain have been three and six months since the initiation of pain, however these distinctions are arbitrary. The IASP provides one of the most referenced definitions of chronic pain. Chronic pain is that which persists beyond the normal time frame for healing, usually taken to be 3 months. The IASP considers a further characteristic related to the "appropriateness" of the disorder. In acute pain there is an advantage to the individual, i.e. it allows rest and the inflammatory process of healing to occur. In chronic pain there is no biological value, i.e. there is no advantage to the individual in experiencing persistent pain. The Clinical Standards Advisory Board for the National Health Service (NHS) defines chronic pain "as that which persists beyond the expected time frame for healing or that which occurs in disease processes in which healing may never occur" [6]. The Practice Guidelines of the American Society of Anaesthesiologists for Chronic Pain Management considered chronic pain as a "persistent or episodic pain of a duration or intensity that adversely affects the function or well being of the patient, attributable to any non-malignant aetiology" [7]. Thus chronic pain may be as a result of the healing process gone awry. It may be persistent and unrelenting and conveys no benefit to the individual who experiences it. Sternbach has emphasized the differences between acute and chronic pain and argues that while acute pain is a symptom of disease, chronic pain itself is the disease [8].

It is not easy to classify pain. At best the classification is ambiguous and variable. As there is no consensus of agreement, there are a wide variety of classifications of pain. Pain can be classified based on anatomy, duration, aetiology, body system or severity. Portenoy categorised both acute and chronic pain as nociceptive, neuropathic or psychogenic [9]. Nociceptive pain is due to chronic activation of nociceptive afferent neurones and can be

somatic or visceral. In nococeptive pain and pain due to tissue inflammation, the sensory experience reflects the normal, adaptive functioning of the pain system [10]. Neuropathic pain is defined by the IASP as pain initiated or caused by a primary lesion or dysfunction in the nervous system [11]. It is due on the other hand to central reorganisation of sensory processing after injury to an afferent pathway. It may be sustained by mechanisms that involve disturbances in the peripheral nerve or nerve root, i.e. peripheral neuropathic pain, or the reorganisation of nociceptive information processing by the central nervous system, deafferentation syndrome [12]. Niv and Devor see neuropathic pain as a fundamental paradox, as injury to a sensory conduction pathway should decrease the signal transmitted not increase it [10]. They argue that it is important to remember that what we describe as conduction pathways are in fact protoplasmic extensions of living structures, neurones, and that these cells will respond actively to injury with changes in biological properties.

1.3. Pathophysiology of chronic pain

Possibly the most influential papers that contributed to the understanding of the neurophysiology of pain were published in the latter half of the twentieth century by Melzack and Wall [13, 14]. Their Gate Control theory of pain emphasized the central nervous system as an active system that filters, selects and modulates the inputs of the peripheral nervous system. It also emphasized the dorsal horns as dynamic activity stations where inhibition, excitation and modulation can occur.

The pathway for pain and temperature is known as the spinothalamic pathway. Nociceptors or pain receptors are non-encapsulated endings of peripheral nerves. Group α-delta fibres are thin and small and myelinated and carry the first sharp and well-localised impulse of pain. Neural impulses are transmitted rapidly at a rate of 40m/second. Group C fibres are larger,

coarser and unmyelinated and carry the second wave of diffuse pain slowly at < 2m/second. During inflammation, prolonged firing of C fibres causes increased production of glutamate that acts on n-methyl d-aspartate (NMDA) receptors leading to central sensitisation. NMDA antagonists can lead to decreased central sensitisation and thus the pain response can be modified [15]. Any noxious stimulus that excites a local inflammatory response results in an influx of tissue cytokines and mediators. This causes the release of substance p and bradykinin and the beginnings of the pain pathway are ignited.

The central processes of the primary afferents of spinal nerves constitute the dorsal roots, which break up into 12-15 rootlets that connect with the spinal cord. Larger axons go to the centre and medial part of the rootlets and to the centre part of the dorsal columns. The smaller myelinated fibres line up dorsolaterally and travel in the apex of the dorsal horns, dorsolateral pathway of Lissauer. Most primary afferent fibres terminate in the ipsilateral dorsal horn, but some course dorsal to the central canal and terminate in the contralateral horn. At this point interneurones within the substantia gelatinosa of the spinal cord can excite or inhibit the afferent impulse. Intraspinal opioids exert their primary effects on the substantia gelatinosa (lamina 11) of the spinal horn. Also exerting an influence on the dendrites of the substantsia gelatinosa are the axons of the raphe nuclei of the medulla, which travel in the reticulospinal tract. Thus descending pathways can influence the transmission in the ascending sensory tracts. Some axons of the substantial gelatinosa will also cross the midline in the ventral white commissural, these fibres continue upwards in the spinothalamic tract. They give off collateral branches that terminate in the medullar and pontine reticular formation and in the peraqueductal gray matter of the midbrain. The destination of the spinothalamic tract is the ventral posterior nucleus of the thalamus. Spinothalamic and medial lemniscus tracts terminate in the ventral posteriolateral division of the nucleus. The ventral posteriomedial

division receives the trigeminothalamic fibres. The axons of the ventral posterior nucleus of the thalamus cross the posterior limb of the internal capsule and the corona radiata to reach the somesthetic area in the parietal lobe [16]. Thus the human body is projected as a homunculus in the parietal lobe, with areas such as the fingers having a disproportionally large representation [17].

Melzack proposed a new extension on the gate control theory in the mid sixties (Figure 1.1.) [18]. In this paper he states that the selection and the modulation of the sensory input through the neospinothalamic projection system provides the neurological basis of the sensory discriminative dimension of pain. Activation of reticular and limbic structures underlies the powerful motivational drive and unpleasant affect that trigger the organism into action. Neocortical or higher central nervous system processes, such as the evaluation of the input in terms of past experience, exert control over activity in both the discriminative and motivational systems. Pain was thus thought now to be a multi dimensional experience. He summarises that the sensory-discriminative, motivational-affective and cognitive-evaluative components of pain all coexist and are produced by a complex matrix of interacting brain structures. Thus noxious stimuli i.e. touching a naked flame, usually stimulate the pathway of pain. Then a beneficial response i.e. removal of the hand from the naked flame takes place. This is a sequence of reflex pathways and also of pathways under the influence of higher cortical control (one can keep the hand in the naked flame if so desired). When the noxious stimulus is removed i.e. local tissue or nerve damage, even if it is not easily identified, pain may persist. The terminology used to describe chronic pain illustrates the abnormalities of these neural networks. There appears to be a faulty rewiring that occurs to change a positive protective, beneficial response into a negative, distressing one. This hints at a normal pathway gone awry but it does not explain the underlying faulty mechanisms. Definitions of

pain descriptors also hint at an underlying faulty mechanism. For example allodynia is pain due to a stimulus that does not normally cause pain. Hyperalgaesia is an increased response to a stimulus that is normally painful and dysaesthesia is an unpleasant abnormal sensation whether spontaneous or evoked. The concept of plasticity in excitatory or inhibitory transmitter systems is becoming better understood and changes induced in peripheral and central nervous systems can lead to chronic pain. Animal experiments on rats help to explain how acute pain becomes chronic, thus explaining plasticity [19], [20]. As the rat sciatic nerve is temporarily tied off the rat exhibits acute pain behaviour. However when the sciatic nerve is released and the rat is sacrificed some time later there are signs of chronic pain via microscopic evidence of neural changes in the dorsal horn, spinal cord and brain [21], [22]. Transmitter systems are different in the neonate and mature adult. That is, information is not transduced in the same manner from the moment of birth. There is plasticity or change and this is part of normal human development.

1.4. The economic burden of chronic pain

In 1998, a study commissioned by the Department of Health attempted to assess the incidence of back pain, a typical and common example of a chronic pain condition, in Great Britain. Fifteen percent of suffers said that they were in pain throughout the year and nearly 40% of suffers consulted their general practitioner (GP) for help. Ten percent visited a practitioner of complementary medicine. One third of those questioned, said that back pain had restricted their activities in the month prior to interview. Women and older people were more likely to report restriction of activity than men and younger people. Five percent of back pain suffers had taken time off work because of this pain. Thirteen percent of people who experienced back pain, and were unemployed, cited back pain as a reason as to why they were off work. Chronic back pain, they state was a feature of age, with 28% of those over the

age of 65 years reporting pain for the whole year compared to less than 5% of people aged 16-24 [23]. Back pain, as a major health problem in industrialised societies, was investigated by Maniadakis [24]. They report the results of a "cost-of -illness" study of the socio-economic costs of back pain in the UK. It estimated that the direct health care cost of back pain in 1998 to be £1632 million. Approximately 35% of this relates to services provided in the private sector and is thus most likely paid for by sufferers and their families. However they emphasise that the direct cost of back pain is insignificant compared to the cost of informal care and the production losses related to it, which total £10668 million [24]. A similar study in the United States (US) state that rheumatoid arthritis and low back pain have a great economic impact on society and that the costs of these are escalating problems. As populations increase in size and age, payment for medical care and indirect costs from loss of earnings will increase [25]. Murphy looked at annual low back pain claims over an eight-year period in the US and found that claims decreased by 34% over this period but that the trend was not monotonic [26]. However at the end of the eight-year period, in 1995 an estimated $8.8 billion was spent on low back pain claims and the rate of filing of low back pain claims was 1.8 per 100 workers [26]. In another study the average annual productivity losses per worker due to chronic backache were $1,230 for male workers, measured in 1996 dollars and $773 per female worker. These figures translate into aggregate annual productivity losses from chronic backache of approximately $28 billion in the US [27]. In 2003 Blyth, from the University of Sydney, preformed a population based telephone survey to assess the effects of chronic pain on work performance [28]. Employed subjects with chronic pain reported working with pain on an average of 84 days over a six-month period. Approximately 9% of subjects reported involvement in litigation. The factor they conclude most strongly related to pain-related disability was being involved in pain related litigation. Most workers can work effectively despite the presence of some pain, suggesting that complete absence of pain is not

essential for good treatment outcomes in workers with chronic pain. However being involved in litigation is associated with a substantial increase in the risk of pain related disability [28]. Nurses in long term care facilities had a period prevalence of back injuries nearly 1.5 times higher than all employees of long term care facilities and six times higher than all other occupations combined industry wide. Back injuries accounted for more than half of the indemnity and medical costs for all injuries occurred in nursing homes industry wide [29].

Chronic back pain is evidently associated with very significant financial burden both to the individual, to society, and to the economy of the nation.

1.5. The prevalence of chronic pain

It is estimated that chronic pain can affect up to 40% of the adult population [30]. This is much greater than the prevalence of cancer, with 2% of the population of the United Kingdom (UK) being alive, having received a diagnosis of cancer [31]. It is about the same as the prevalence of, diagnosed and undiagnosed diabetes, approximately 2.5 million adults. Therefore, chronic pain represents a major clinical problem. Although differences in the definition of chronic pain have been used in epidemiological studies, differentiating chronic pain on the basis of severity appears to identify important subgroups [32]. Chronic pain is commonplace within the community and its prevalence is widespread. In general it does not seem to exhibit a gender, racial, class or age bias.

Elliot et al undertook a study to quantify and describe the prevalence and distribution of chronic pain in the community [33]. They found that 50% of their respondents self reported chronic pain and this is equivalent to 46.5% of the general population. Back pain and arthritis were the most common complaints and accounted for a 1/3 of all complaints. They

concluded that chronic pain is a major problem in the community [33]. In a four-year follow up study these same authors described the pattern and predictors of change in chronic pain over time. They concluded that the overall prevalence of chronic pain increased from 45.5% at baseline to 53.8% at follow up. At the end of follow up 79% of those who had pain initially still had it four years later. The average annual incidence was 8.3% and the average annual recovery rate was 5.4 [34]. In their telephone study of 1037 households Bowsher et al found the prevalence of chronic pain sufferers to be at 7% [35]. Geographical variations were noted, with the proportion of pain suffers in the south of England being half of that in the north. The mean age of chronic pain sufferers was forty-four. Roughly 51% were over the age of fifty-four. Arthritis / rheumatism was the most common complaint, with the back and the lower limb being the most common locations affected [36]. Crook et al in their random survey of 500 households, found that the prevalence rate of persistent pain was almost twice that of temporary pain [37]. More women than men reported temporary than persistent pain. Again the back and lower extremities followed by the head and face, were the most frequently identified sites of pain [37]. The prevalence of chronic pain in non-westernised populations is unclear. In their study Ng et al, show that the prevalence of chronic pain in Hong Kong adults is approximately 10.8% [38]. The female gender and age greater than 60 years were two risk factors identified for developing chronic pain. Work and daily life are significantly affected and there is considerable demand on the health care system. Despite the ethnic difference, the prevalence, pattern and demographic differences of chronic pain in Hong Kong were ultimately very similar to those seen in Western countries [38].

On the 27th of February 2002, the Scottish Parliament debated the plight of chronic pain patients. The motion stated, “chronic pain was regarded as the most neglected health issue in Scotland”. The Clinical Standards Advisory Group cited a figure of 7% of the population as

suffering from chronic pain [39]. This was thought to amount to between 350,000 and 500,000 patients in Scotland. The Pain Research Institute in Liverpool was also quoted, citing "overall 1 in 14 of all adults have chronic pain rising to 1 in 7 as people get older". Petition PE 374 called for the Scottish Parliament "to act urgently to investigate and redress the under funding of chronic pain management Services, to debate the matter in Parliament and to urge the Minister for Health and Community Care and Health Boards to move chronic pain up the health agenda".

Despite claiming to understand the position of chronic pain suffers, the Scottish Parliament stated that there were no immediate plans to conduct an audit of facilities and budgets for chronic pain relief in the NHS [39]. Recently in Ireland, where chronic pain is stated to effect 13% of the population, it has been declared that a national strategy is needed to reduce cost, standardise teaching and to increase pain clinic resources to maximise patient care [40].

It is very difficult to accurately quantify the number of people in the general population that have chronic pain of one type or the other [10]. Pain is stated to be the chief complaint in 40% of primary care visits and persistent chronic pain is reported in 20% [41]. Open-ended questions tend to generate large numbers of responses from people, 50% answering in the affirmative [33]. Using the IASP definition, estimates of the prevalence of chronic pain are at 35% [42]. Surveys that more closely define intensity and duration yield prevalence figures of around 20% [43].

Ospina reviewed recent epidemiological studies on chronic pain [42]. It was argued that the variation in the prevalence of chronic pain can be attributed to the population sampled, the method used to collect the data and the definition of chronic pain used [42]. From the analysis

of these studies the author felt that the frequency of chronic pain increased with age, was higher among women and that there was an association between social status and specific pain types. The weighted mean prevalence of chronic pain was 35.5% ranging from 11.5% to 55.2%. They also noted that the method of data collection was an associated variable and contributed to the variations in prevalence.

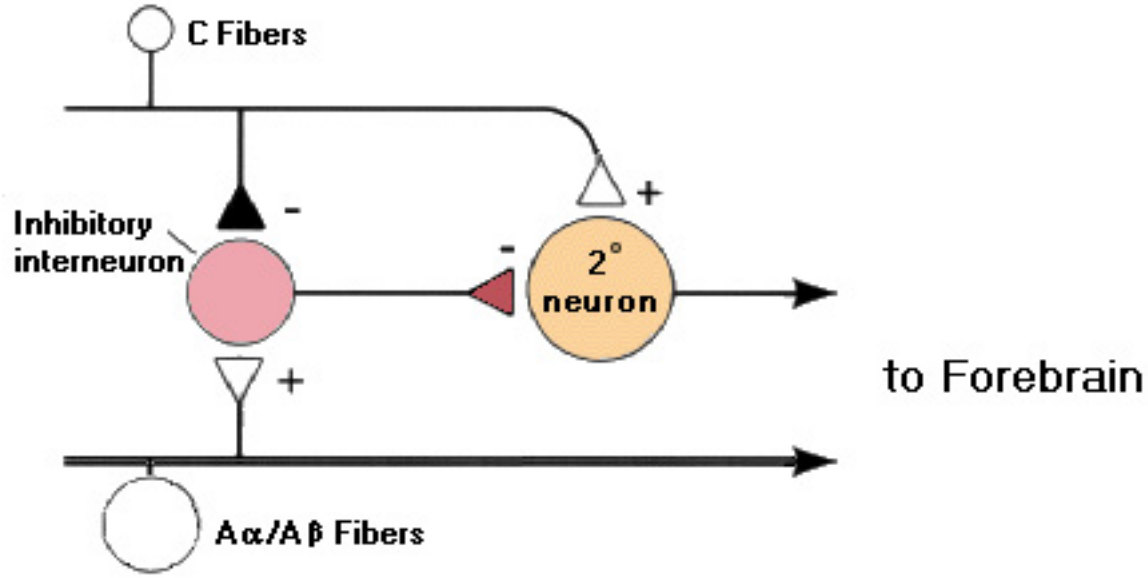

Figure 1.1. Melzack's gate theory of pain [44].

1.6. Race and ethnic influences on chronic pain

Progression to a chronic pattern of pain is more closely dependent on demographic, psychosocial and on occupational factors than on the medical characteristics of the pain itself [45]. Edwards et al show that there is an ethnic difference in terms of both clinical and experimental pain [46]. They argue that the African-American population are more sensitive to noxious stimuli and therefore experience relatively greater clinical pain [46]. In another study by the same authors, where responses to experimental thermal pain were evaluated in the African-American and White populations, the former group reported higher rates of unpleasantness than the latter group at similar temperatures [47]. Group differences in terms of noxious stimuli were unchanged even when adjustment for psychological factors were made. They tentatively conclude that whites and African-Americans differ primarily in affective rather than sensory processing of noxious stimuli. Thus there may be fundamentally different physiological processes that contribute to explain the fact that racial differences exist in chronic pain [1]. Racial differences in chronic pain are noted both in terms of healthcare provided and perception of chronic pain. Five commonly reported chronic pain conditions; back, head, face/jaw, chest and abdomen were examined in the context of race. Racial differences were not found for chronic pain of the back, head, chest and abdomen. However significant racial differences were found regarding facial pain and symptoms related to temporomandibular disorders above and beyond socio-economic status. Not only did Caucasians, compared to African-Americans report facial and jaw symptoms more frequently, but they were also reported to have an earlier onset [48]. In a cross sectional study of chronic moderate to severe knee and/or hip pain in just fewer than 600 adult males, (44% African-American and 56% White), the severity of symptoms was compared with the extent of skeletal damage as ascertained by radiographs. The authors conclude that in this sample of

male veterans, African-Americans and Whites perceived the same degree of pain and functional disabilities at any given radiographic severity of osteoarthritis. Differences in the perception of symptoms, they argue cannot be therefore used to explain the observed ethnic disparity in utilisation of joint replacement. However, what exactly does explain this difference is unclear [49]. Chronic pain, as perceived by six different ethnic groups, was examined in approximately 400 patients attending a multidisciplinary chronic pain centre. It seems that variation in pain intensity may be affected by differences in attitudes, beliefs and emotional and psychological states associated with the different ethnic groups. These authors concluded that while pain intensity variation was not significantly associated with diagnosis, present medication types or types of past treatment or surgeries for chronic pain, it is likely that attitudes and emotions influence reported perceptions of pain intensity [50]. In a cross sectional study of seven cultural groups in Canada, considerable differences in the groups were found in the reporting of pain, emotional function and cognitive function [51]. The variation in the scores across the cultural groups could not be explained in terms of socio-economic status [51]. In a review of the current literature Green et al suggest that African-Americans with chronic pain report more pain severity and disability due to pain than non-hispanic Whites [52]. It is not clear, they say, whether these findings reflect under-treatment, over-reporting, differences in pain sensitivity or some combination of the above. They conclude that consistent with the Institute of Medicine's report on health care disparities, racial and ethnic disparities in pain perception, assessment and treatment were found at all stages when assessed, and for all pain types assessed including chronic pain. The literature they state, suggests that the sources of pain disparities among racial and ethnic minorities are complex, involving patient (e.g. patient/health care provider communication, attitudes), health care provider (e.g. decision making), and health care system factors (e.g. access to pain

medication) [52]. There is also data to suggest that chronic pain is relatively under-treated in racially and ethnically diverse populations [53].

Therefore, whilst there is strong evidence that there are consistent and substantial differences in the experience of chronic pain between different racial and ethnic groups, there remains no clear explanation for these differences. An awareness of these racial and ethnic factors can be important considerations when interpreting and managing chronic pain.

1.7. Age and sex influences on chronic pain

Animal experiments as well as observations in humans have shown that gonadal hormones influence somatosensory perception and pain sensitivity. These effects are exerted in part at least by the binding of oestrogen to oestrogen - receptors located in the superficial layers of the dorsal horn. Here, neurones containing oestrogen receptors contain m-ribonucleotide acid (RNA) for the endogenous opioid enkephalin, and administration of oestrogen has been shown to increase enkephalin transcription in the spinal cord [54]. Craft et al found that opioid agonist analgesics act preferentially at mu receptors and are more potent in male rodents than in females, however the reverse effect is found in the human population. The possible mechanisms underlying these sex differences, however may deal with the pharmokinetics of the drugs or in their pharmodynamics [55]. It has also been shown that reproductive age women have greater mu opioid receptor binding potential than men in numerous cortical and subcortical areas on PET scans, and this may account for their greater response to opioids [56]. A recent study published this year in the Southern Medical Journal, evaluated whether there was a sex difference in the analgesic response to the prototypical mu receptor agonist, morphine sulphate, compared with the prototypical kappa agonist, butorphanol, in the emergency department [57]. Patients attending the emergency room with moderate to severe

traumatic pain of injury were randomised to receive morphine or butorphanol. Both groups were similar in terms of demographics. At 60 minutes, women had significantly lower visual analogue pain scores (VAS) scores with butorphanol than with morphine. Therefore the authors suggest that kappa receptor agonists should be chosen preferentially for female patients with acute traumatic pain [57]. Bush et al analysed symptom presentation, sensitivity to pain, personality and illness behaviour in two samples of patients suffering from chronic orofacial pain [58]. The results showed few gender differences based on ratings of chronic or experimental pain, pain-related illness behaviour or personality. The higher ratio of women versus men with temporomandibular disorders seeking care is consistent, they say with greater health awareness or interest in symptoms by women than by men [58]. It is well established that women report more severe pain, more frequent pain and pain of longer duration than men. What is unclear is why they do so. Arguments varying from differing social rules for expression of pain to fundamental differing biological principles in the processing of pain have been put forward. In contrast to the previous paper, Dao et al, hypothesise that the higher prevalence of chronic orofacial pain in women is a result of sex differences in generic pain mechanisms and of as yet unidentified factors unique to the craniofacial system [59]. There is also animal evidence to support this gender disparity [60]. Fillingim in his study found that females are at greater risk of developing several chronic pain disorders and that women exhibit greater sensitivity to noxious stimuli in the laboratory compared with men [61]. Psychosocial factors, such as sex role beliefs, pain coping strategies, mood, and pain related expectancies are all thought to contribute to this effect [61]. Using imaging techniques gender differences of the brain were recently demonstrated in neurophysiological response and pain perception to heating of the skin. Thus gender differences in the biological processing of pain, in the perception of pain and in the action of certain analgesics exists [62]. Chronic stable angina pain has detrimental effects on quality of

life, particularly in women. Although these authors found that men and women have similarities in terms of pain characteristics, but women report more physical limitations and a more intensity of pain than do men for similar extent of disease [63]. Challenging the accepted evidence that women merely complain more when in pain, is a paper by Hunt et al [64]. This looked at whether women or men were more likely to have consulted their general practitioner in the past year when experiencing five common chronic conditions. They found that women were no more likely than men to consult their GP for common chronic conditions, nor were they more likely to consult at any given level of severity [64].

It is well known that pain, both temporary and chronic increases with age. Population based studies estimate that 25-50% of community dwelling older adults report chronic pain problems [65, 66]. In nursing home residents 45-80% of people experience chronic pain. This increase is thought to be due to the fact that a large number of the aged population here are female [67]. However in a review of the literature on chronic pain and the elderly population, it was found that although there were considerably more female than male subjects in the studies reviewed, it was still difficult to determine whether older women's experiences with chronic pain are unique and require special attention from health care providers or whether the causes, treatments, and consequences of chronic pain should be considered universal to the older population as a whole [12]. A recent review of epidemiological studies show that the peak or plateau in the prevalence of pain is at age 65 [30]. There is a decline in reported pain in the old i.e. 75-84 years. The reasons underlying this are unclear, but factors ranging from the methodology of the studies reviewed to the impact of age – associated memory impairment and dementia have been postulated [68]. When site of pain is looked at with respect to age it is seen that head, abdominal and chest pain frequency is reduced among older people, whereas musculo-skeletal joint pain increases slowly at least to 80 years of age [69]. There is some

limited evidence to support age related changes in the physiological functioning of the peripheral and central nervous system. A reduction in the density of myelinated and unmyelinated nerve fibres has been noted in the older adults [70]. Nerve conduction studies indicate prolonged latencies in peripheral sensory nerves in apparently healthy older adults [71].

1.8. Psychology and its influence on chronic pain

Depression or anxiety is diagnosed in 58% of patients with chronic pain [72]. Coexisting psychological distress predicts the development of a more relentless chronic pain problem [73], [74]. Chronic pain has an important adverse effect on quality of life of the individual and on their spouses. There are several difficulties that researchers face when attempting to study the effects of chronic pain and its disability on the sexual well being of patients in this group. For example analgesics and other prescribed medication for chronic pain may interfere with sexual function, also sexual difficulties may predate the onset of chronic pain. In a UK study of 327 patients with chronic pain, the authors noted that 73% of those that responded had pain related difficulty with sexual activity. There were few differences noted between men and women and only weak relations emerged between specific problems and mood and disability [75]. Fillingham et al indicate that the behaviour of the spouse has a strong impact on the pain and disability expressed by chronic pain patients [61]. These authors note that " female patients may need to display greater pain related disability to elicit supportive responses from their husbands, while the wives of male patients require less pain related disability to provide increased support" [61]. This interpretation is aided by the earlier finding that the wives of male pain patients are more strongly affected by their husband's pain and disability than the husbands of female patients [76]. The effects of pain and depression on quality of sleep reported by suffers of chronic pain was investigated by a study conducted by the department of anaesthetics and psychiatry in Pennsylvania. They found that those patients who were more

physically active and had chronic pain of a shorter duration reported higher overall quality of sleep. Daytime sleepiness was associated with younger age and depressed mood. They conclude that their data suggests that physical functioning, duration of pain and age may be more important than pain intensity and depressed mood in contributing to overall quality of sleep [77]. Depression is commonly reported among chronic pain patients. However it is largely unclear whether depression in this group of patients is as a function of pain, disability or gender. In this study of 63 patients, male and female depressed and non-depressed chronic pain patients largely did not differ in terms of demographic and medical history data but sex differences were found in patterns of the relationships of depression, activity and pain. For women depression was largely related to pain reported, whereas for men depression was more strongly related to impairment of activity [78]. Chronic pain adversely impacts on mood as opposed to a negative mood being a predisposing factor in the development of chronic pain [79]. Psychological and social factors have an important role to play in the adjustment towards chronic pain. In a multiple-regressional analysis, Jensen et al showed that psychosocial predictors made a statistically significant contribution to the concurrent prediction of average phantom limb pain. Pain interference and depression at initial assessment of the amputees was significant in predicting adjustment of patients to chronic pain at a 5 month follow-up [80]. This paper argues the importance of considering bio psychosocial factors in chronic pain patients [80]. Behavioural treatment of chronic pain has usually been along the lines of coping. Recently a study by McCracken et al aimed to compare a coping approach to pain with a different behavioural approach referred to as acceptance of chronic pain [81]. Results showed that coping variables were relatively weakly related to acceptance of pain and relatively unreliably related to pain adjustment variables. On the other hand acceptance of chronic pain was associated with less pain, disability, pain related anxiety, depression and better work status [81].

Individuals suffering from chronically painful conditions show elevated rates of suicidal ideation and suicide attempts. Fisher et al emphasise that when individuals with chronic pain report suicidal intent, it is imperative that measures preventing self-harm be implemented immediately and that patients' depression be treated aggressively [82].

Therefore, we have defined pain and chronic pain. We have reviewed the pathophysiology of pain in neuroanatomical terms. We have seen that chronic pain is present in all communities throughout the world. We know that there are subtle influences for example, age, sex, psychology and social factors that influence ones perception and determine the extent of chronic pain. Chronic pain, in general has an effect on the health of the nation as a whole and on the economy in particular. The question then becomes how is all this relevant to the specific surgical procedures of hernia repair. How can we modify the above influences on chronic pain and so avoid it? The answer is not clear. This is because what affects a certain individual and results in chronic pain is largely unknown and certainly multi-factorial.

It is often assumed that workers who are in the process of litigation exaggerate their pain for financial gain. However there is a growing body of evidence that people who receive workers compensation are no different from those who do not [83].

1.9. How to measure pain

Pain is a subjective experience and as such it is difficult to precisely quantify it in an objective manner. Pain intensity like other sensations and perceptions displays considerable variability both across patients and within a patient across time [84]. Thus a logical approach and the use of validated tools are necessary to assess and quantify pain. Several different

tools have been constructed to achieve this aim. The importance of pain quantification lies in its role as an assessment tool and research tool. The advantages and disadvantages of the tools used most frequently to measure pain were reviewed comprehensively by Ong in 2004 [84].

Pain therefore has an intensity that can be directly measured and it also has an effect on psychology and functional ability [85]. Assessment and measurement of psychological distress and functional impairment is thus an indirect assessment and measurement of pain.

The McGill Pain Questionnaire (MPQ) (Figure 1.2.) consists primarily of three major classes of word descriptors sensory, affective and evaluative that are used by patients to specify subjective pain experience [86]. The questionnaire was designed to provide quantitative measures of clinical pain that can be treated statistically [86]. It is sufficiently sensitive to detect differences among the various methods to relieve pain. The MPQ can be used in both clinical and laboratory settings and this means that similarities and differences in pain types can be clarified [87]. It can also be used as a reliable index of the overall affective status of pain patients [88]. It was one of the first pain assessment tools, however as it has been found to be detailed and time consuming a shortened version is available [44]. An early study which illustrated that the MPQ is useful in the assessment of the reactive component of pain also suggested that further research into the autonomic indices as physiological correlates of the reactive aspect of pain [89] was indicated. The intensity rating of the individual words in the MPQ has been shown by Towery and Fernandez [90] to correlate very highly with those reported by Melzack and Torgerson [91]. The words used in the MPQ are efficient and unambiguous in the clinical assessment of pain.

The psychological assessment of chronic pain is often accomplished using questionnaires such as the West-Haven-Yale Multidimensional Pain Inventory (MPI or BPI or BPQ) (Figure 1.3.), which is constructed to capture the multidimensionality of chronic pain. The MPI theoretically originates from behavioural and cognitive behavioural theories of pain [92]. The MPI meets standards of reliability and convergent validity and is thought to be an improvement over current psychometric devices [93]. The advantage of the MPI is that it has been shown to be accurate and reproducible across various cultures and therefore is suitable for cross cultural and international research [94] . The MPI was developed in order to fill a widely recognized void in the assessment of clinical pain [95]. It is a clear and short questionnaire with a strong psychological component. It examines the impact of pain on patients' lives, the responses of others to the patients' communications of pain and how chronic pain impacts on activities of daily living. It has been compared with the SF36 in noncancerous patients and found to give similar results [96]. As well as being found to be reliable and valid [97], it has also been found to be sensitive to changes in chronic pain conditions [96].

Simpler measures to assess and quantify pain include visual analogue pain scales (VAS) (Figure 1.4.), numeric rating scales and verbal rating scales. The VAS measures pain on a 100mm scale. Pain is marked along this line from 0 to 100. When data from over 11 randomised controlled studies was analysed it was found that 30 or less equated to mild pain, 31 to 54 equated to moderate pain and that greater than 55 was equivalent to severe pain. When pain was scored as 55 or more, that is severe pain, it was noted that this usually corresponded to functional interference [98]. At the time of constructing these studies for this thesis there was no precise definition as to the significance of mild, moderate and severe pain. Subsequently Chow et al [99] examined how patients with bone metastases categorized their

pain using two commonly employed scales. Patients rated their pain on a visual analogue pain scale of 0 -10 (0 = no pain, 10 = worse pain possible) and a categorized scale of none, mild, moderate and severe. Based on patient evaluated symptoms, 60% of patients describing mild pain gave it a numerical rating of 3 or 4, 63% of those who described pain as moderate scored it as a 5, 6 or 7, and 80% who categorized it as severe gave it a numerical value of 8, 9 or 10. They concluded that pain was mild if given a numerical value of 1-4, moderate if scored between 5-7 and severe if > or = 8 [99]. Again what point on the VAS indicates or reflects moderate pain was investigated by Collins et al [100]. In their study, 85% of patients reporting moderate pain scored over 30mm on a corresponding VAS with a mean of 49mm. Those patients who described severe pain scored a mean of 75mm with more than 85% scoring over 54mm. They found no difference between men and women. They concluded that if a patient records a baseline VAS in excess of 30mm then the equivalent in terms of the four point verbal categorical scale is at least moderate pain.

The Faces Pain Scale (Figure 1.5.) is a communication tool. It is a schematic drawing of happy and sad faces in a linear fashion that depicts the intensity of children's pain. It has been validated in studies to show that it has the properties of a scale [101]. Overall the Faces Pain Scale incorporates conventions used by children, has achieved strong agreement in the rank ordering of pain, has indications that the intervals are close to equal and is treated by children as a scale. It is a reliable index of self reported pain with time.

The Numeric rating scale rates pain from 0, no pain to 10, severe pain. Its use in clinical research is however controversial [102]. Verbal rating scales allow the individual to rate pain verbally from none to mild to moderate to severe.

Deloach [103] compared changes in VAS scores compared to verbal assessment of changes in pain in the acute postoperative period. He concluded that the single VAS score in the immediate postoperative period should be considered to be imprecise to a degree of 20mm. In general the VAS is an appropriate tool for the assessment of postoperative acute and chronic pain as it corresponds well to an 11 point verbal scale but they stress that any individual measurement may actually vary by 20mm in either direction. Gallagher [104] using paired data comparing clinically significant changes in pain versus changes in VAS measurements, showed that a difference of 13mm on a VAS represents an average minimal change in acute pain that is clinically significant. Kelly [105] asked the question does clinically significant changes in VAS vary with sex, age and cause of pain and found that it does not. Kelly [106] in 2001 determined that the minimal clinically significant difference in VAS pain scores that can be detected does not vary according to severity of pain. This means that if you improve a little or a lot, or deteriorate a little or a lot, the VAS will pick this up. McCarthy [107] constructed four visual analogue scales, referred to as the Surgical Pain Scales (SPS) to assess sensory and affective components of postoperative pain. The SPS can be used therefore, to compare pain measures between groups at a single point in time or to track change for individual patients over time or after operations [107].

Pain is known to alter the electrogalvanic properties of the skin. In a small study, postoperative patients were assessed for pain severity using the numeric rating scale and non-fluctuating skin conductance by blinded observers. Skin conductance has a predictive sensitivity of 89% and specificity of 74% and it has been therefore suggested that it may prove a useful tool for postoperative pain assessment [108].

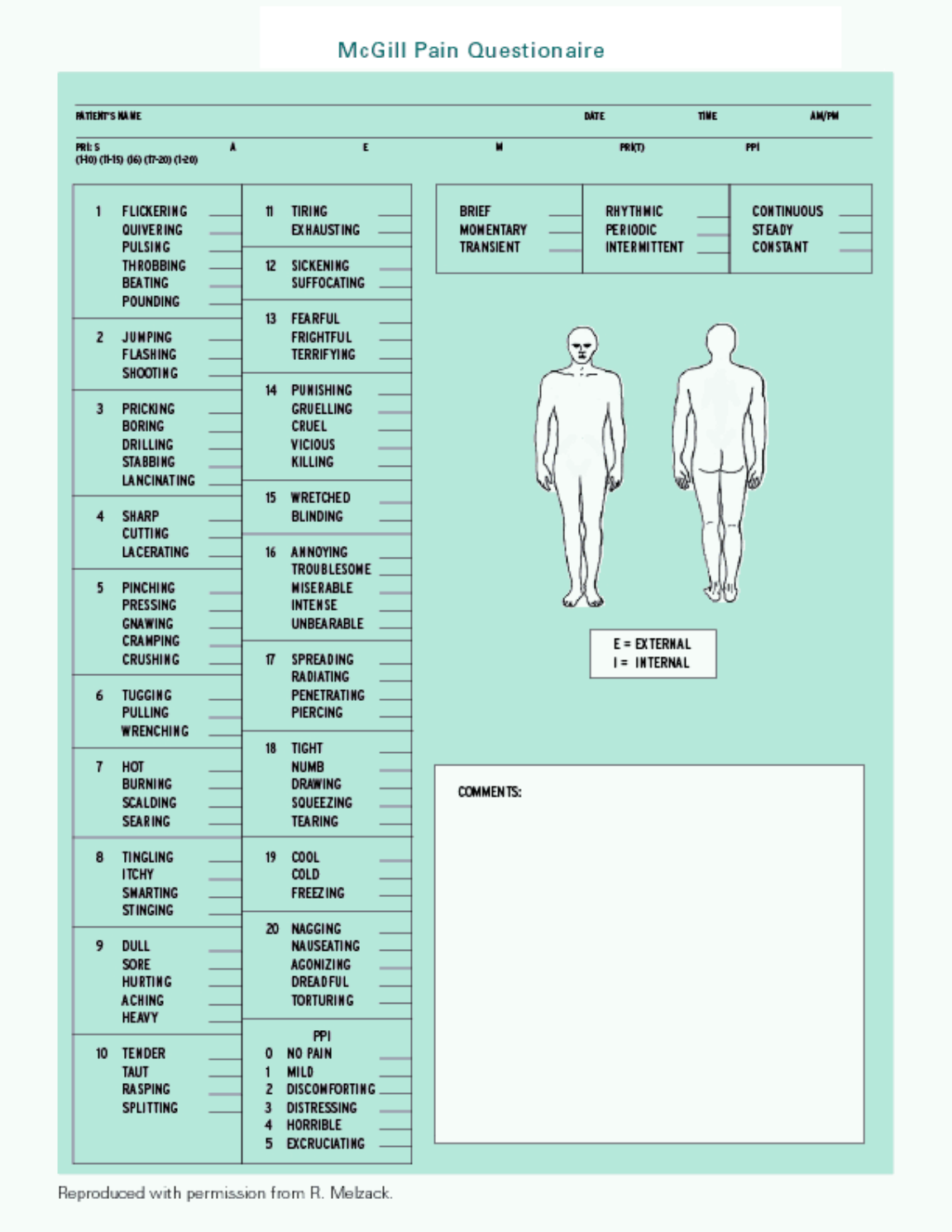

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Figure 1.2. McGill pain questionnaire [86].

Brief Pain Inventory (Short Form)

Study ID# _____ Hospital # _____

Do not write above this line.

Date: _____

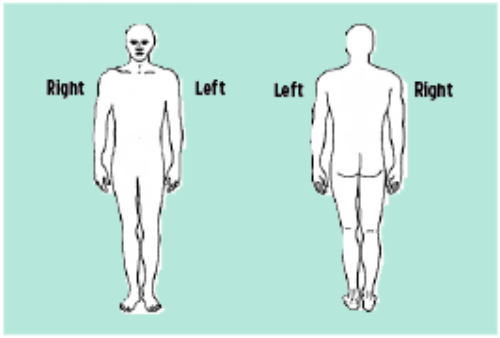
Time: _____

Name: _____
Last First Middle Initial

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

1. yes 2. no

2) On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3) Please rate your pain by circling the one number that best describes your pain at its **WORST** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its **LEAST** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on the **AVERAGE**.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

6) Please rate your pain by circling the one number that tell how much pain you have **RIGHT NOW**.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

_____

8) In the past 24 hours, how much **RELIEF** have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
No Relief — Complete Relief

9) Circle the one number that describes how, during the past 24 hours, **PAIN HAS INTERFERED** with your:

A. General Activity:

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

C. Walking Ability

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

D. Normal work (Includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

E. Relation with other people

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

G. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

Figure 1.3. Multidimensional (West-Haven-Yale) pain inventory or brief pain inventory [97].

No pain Worst pain imaginable

0 100

Figure 1.4. Visual analogue pain scale.

Figure 1.5. Faces pain scale.

The Short Form 36 was developed in 1988 and the standard form was brought out in 1990. It is a multipurpose short form survey of functional health and well being. It is a generic measurement as opposed to one that targets specific age, disease or treatment group. It is a useful in surveys of general and specific populations in differentiating health benefits produced by a wide variety of treatments. There have been several peer reviewed articles about the SF36 in terms of its history, development, reliability and validity [109]. Over the past decade it has been modified and improved. It is the most widely evaluated quality of life patient assessment form that is available. Diseases most frequently studied using the SF36 include depression, cancer, COPD, back pain and arthritis. It has been translated into many different languages. It has been constructed to satisfy minimum psychometric requirements for group comparisons. It came about as an amalgamation of inventory used in the seventies and the eighties [110]. It is available in both standard four week and the acute one week recall versions. The latter is more sensitive to recent changes in health status. The physical and mental health variances detected have been shown to be reliable in the US population, and among populations in Sweden [111] and in the UK [112]. The reliability of the 8 scales and two summary measures has been estimated using both internal consistency and test retest methods. It is reliable and can be replicated over different patient groups and different socioeconomic backgrounds. Studies of validity generally support the intended meaning of high and low SF 36 forms as documented by Ware et al [113]. It has been shown to be valid in content and in comparison to more in depth questionnaires or measurements [114].

Because it is short, the SF36 can be reproduced in a questionnaire with ample room for more precise general and specific measures and studies have been done which illustrate the advantage of supplementing the SF36. Other assessment questionnaires are 5-10 times longer and convey greater respondent burden, ie the advantage of the SF36 is that it is short, brief

and comprehensive. Experience from over 400 randomised controlled trials has shown that SF36 is a useful tool for evaluating benefits of alternative treatment methods [114].

1.10. Chronic pain in relation to surgery

Chronic pain can be an unexpected adverse outcome following surgical procedures. Alternatively surgical intervention can be used to treat the chronic pain of disease, benign or malignant. In a recent study the results of surgery for chronic pancreatitis of varying aetiology were evaluated. One of the postoperative outcome measures was degree of pain control. The authors suggest that surgical resection should be preformed when required by the anatomical conditions as it is associated with good long term pain control, 71.4% achieved complete pain control at an average follow-up of 6 years [115]. There are a wide number of surgical treatments available for the chronic pain of pancreatitis with no single surgical technique being superior to the other [116]. In a study, which looked at the outcome of women following hysterectomy for non-malignant conditions, 18% of the population underwent surgery for chronic pelvic pain. The authors report that hysterectomy resulted in marked improvement in a range of symptoms including pelvic pain, urinary symptoms, fatigue, psychological symptoms and sexual function [117]. In a consensus statement for the management of chronic pelvic pain associated with endometriosis, these authors conclude that there is some evidence that adjuvant presacral neurectomy adds benefit for midline pain but that hysterectomy alone has undocumented value in the surgical management of women with chronic pelvic pain related to endometriosis [118]. Chronic pain is also well recognised as occurring as part of the malignant process. It has been shown that cancer patients report higher values of physical interference than non cancerous chronic pain patients with the same level of pain intensity [119]. The operation of anterolateral open cordotomy for intractable pain

of malignancy was evaluated over a ten-year period. The effect of this procedure on the patient group was evaluated over three years or until death. The results show that 95% of survivors had an effective relief from pain at discharge and that this fell to 73% at 6 months and to 55% at one year follow up [120]. The first study to quantitatively compare chronic post surgical pain using similar methodologies in heterogeneous populations was reported in 2004 [121]. This study found that the prevalence and characteristics of chronic pain was remarkably similar across different operative groups. The surgical procedures evaluated were mastectomy, inguinal hernia repair and cardiac surgery with or without saphenous vein grafting. This was a retrospective study that compared chronic postoperative pain in patients operated upon over a ten-year period. The prevalence of chronic pain after inguinal hernia repair in this study was 30% and was found to be sensory-discriminative in quality [121].

Chronic pain as an unexpected consequence of common surgical procedures was reviewed recently [122]. This article detailed the incidence of chronic pain following cholecystectomy, thoracotomy, mastectomy, and limb amputation. The incidence of phantom limb pain is thought to vary from 30-81%. Stump pain is also common with an overall incidence of 60% [123]. Following breast surgery, pain can be experienced in the chest wall, breast or scar (11-57%), as phantom breast pain (13-24%) or as arm /shoulder pain (12-51%). The post thoracotomy pain syndrome is thought to have an incidence of approximately 50% [124]. Chronic abdominal pain following gallbladder surgery is common and ranges from 3-56%. The frequency and the intensity of chronic pain, as well as the related factors, were assessed in a cohort of breast cancer patients in a recent retrospective study. Patients who had completed their treatment at least 6 months previously and deemed free from cancer were studied. Although almost half of the early stage breast cancer patients experienced post treatment chronic pain they rated the intensity of their pain as mild to moderate. Younger age

and receiving radiotherapy were factors that contributed to developing chronic pain. Chronic pain did not however interfere, seriously with life function[125]. Recently chronic postoperative pain has been analyzed following cardiac surgery, specifically coronary artery bypass grafting (CABG). The cumulative prevalence of post cardiac surgery chronic pain was 39.3%. The prevalence of chronic pain decreased with age, 55% in those patients less than 60 years and 34% in those less than 70 years. Patients with preoperative angina and those with a body mass index (BMI) > 25 were more likely to report pain as were those who had lower quality of life scores [126]. Chronic pain following Caesarean section has also been investigated [127]. The average follow up period was 10.2 months. These authors state that while most pain resolves, in 5.9% of women chronic post Caesarean pain is a significant problem. These patients were more likely to have undergone general rather than spinal anaesthesia [127]. Perkins recently described a model, which details the origins of chronic pain (Table 1.1) [122].

Preoperative factors	Intraoperative factors	Postoperative factors
Pain (moderate to severe) lasting >/= 1 month	Surgical approach and risk of nerve damage	Acute pain (moderate to severe)
Repeat surgery		Radiation therapy to area
Psychological vulnerability		Neurotoxic chemotherapy
Workers' compensation		Depression
		Psychological vulnerability
		Neuroticism
		Anxiety

Table 1.1. Predictive factors for chronic pain as per Perkins [122].

They argue that it is by understanding the aetiology of chronic pain in a particular individual; we are then better placed to manage and/or treat it effectively. So far treatment modalities are educative guesswork. There are no true reproducible animal models available. Animal studies at best infer cause. Perkins reviewed post thoracotomy chronic pain syndrome, post mastectomy chronic pain and post herniotomy chronic pain in terms of three stages, preoperative, intraoperative and postoperative [122]. Physiological and psychological factors come into play pre and post operatively. Post-thoracotomy pain syndrome (PTPS) is at its most severe 12 months following surgery [128] . It is in the order of 40% at 12 months. Anterior or muscle sparing thoracotomy is least painful but there is no difference in chronic pain reported when the video assisted thorascopic approach is compared to open posteriolateral thoracotomy. Preoperative state, anxiety or depression traits were not related to long-term pain. However acute postoperative pain was a predictor of long-term pain. Loss of intercostal nerve function was also related to long-term pain. This supports the theory that local anaesthetic infiltration of the thoracotomy wound, intra and immediate postoperative thoracic epidural are associated with a decrease in long-term postoperative pain [129, 130]. Chronic pain does decrease with time i.e. from one to twelve months [131]. Following breast surgery postoperative pain includes chest wall, breast or scar pain, phantom breast pain and ipsilateral arm and /or shoulder pain. The incidence of chronic pain at 12 months in one or more of the above sites is in the order of 50%. Preoperative breast pain is a predictor of postoperative chronic pain, i.e., phantom breast pain but not other types. Preoperative anxiety and depression are more common in those with chronic pain but this is not statistically significant. Breast conserving surgery is more likely to be associated with chronic pain as is mastectomy with implantation. High acute postoperative pain scores are associated with long-term pain. Chronic breast pain decreases with time i.e., after 12 months whereas chronic arm pain may not.

1.11. Chronic pain and inguinal hernia repair

Inguinal hernia surgery has advanced considerably over the past two decades. Despite this, the average general surgeon is still uncertain as how best to manage patients with an inguinal hernia both pre and post operatively. Over the years inguinal hernia repair has evolved from sutured to mesh repair. Mesh repair brings with it the advantage of low recurrence rate (< 5%) and is the most common method of repair [1]. There is less postoperative pain following mesh rather than sutured repair of an inguinal hernia [132]. One of the perceived disadvantages of this type of repair appears to be an increase in the reporting of post-operative pain and discomfort [133], [134-136]. Chronic postoperative inguinal hernia pain can be severe and debilitating. It has a negative effect on the individual in terms of lifestyle and work. This may also have a negative effect on the economy when one considers the number of repairs performed. Inguinal hernia repair has an annual procedural rate of 2,800 per million people in the United States alone. Approximately 70,000 hernias are performed in the UK in a given year [137]. Given the frequency of post herniorrhaphy pain, it is not entirely clear whether the surgeon should be repairing inguinal hernias in all patients [138] . Are patients best served by repairing all hernias even in those patients with little or no discomfort from their hernia [139]? If we decide on repair, when and how best should it be done?

More recently in 1987, Ralph Ger first described laparoscopic hernia repair and since then there have been numerous modifications and advances on his original technique [140]. Does laparoscopic inguinal hernia repair per se reduce chronic postoperative pain? If mesh repair is associated with chronic pain does reducing the size, shape or composition of the mesh alter this association in any way? How, when and with what type of mesh should we be repairing an inguinal hernia, in order to minimise or avoid post-operative chronic pain?

In 1999 Callesen et al published a prospective consecutive case series study that examined the incidence of chronic postoperative pain at one-year post elective day case local anaesthetic hernia repair. Pain was scored at rest, on coughing and at mobilisation as none, mild, moderate and severe at one year and compared with data collected at one and four weeks post repair. Just fewer than 20% of patients reported some degree of pain at one year. The incidence of moderate to severe pain was higher after repair of a recurrent hernia. Those patients who complained of persistent pain at one year were more likely to have high pain scores at one week and four weeks post surgery. Thus they concluded that the intensity of early postoperative pain is a good predictor of long term chronic pain [141]. Another study in 1999 compared long-term outcome following local anaesthetic open mesh repair with the size of the hernia as found at operation. In total 220 hernias were repaired and the average follow-up was 15 months. Most patients (approximately 90%) were able to do sports and perform usual activities of daily living including driving within 4 weeks of surgery. Chronic unpleasant postoperative sequelae were classed as mild or moderate pain, local hypoaesthesia, and weather dependent changes in sensitivity and hyperaesthesia. This study found that those patients most likely to complain of moderate pain at one-year follow-up were those that had a small intra-operative hernia. The authors did not find a relation between pain of any sort and age and sex of the patient. They conclude that patients with small intra-operative hernias are not necessarily well served by surgery [142]. The Cooperative hernia study assessed postoperative pain in a prospective trial as part of a larger study looking at the recurrence rate and other morbidity of the Bassini, McVay and Shouldice repair. Just over three hundred patients were randomised to one of the repairs. At two years 50% of patients had some degree of pain and 10% had moderate to severe pain. They concluded that the predictors of long term post operative pain include, absence of visible bulge preoperatively, numbness in the immediate postoperative period and the need for the patient to spend 4

weeks or more off work postoperatively [143]. One year after inguinal hernia repair, pain is common at 28.7% and is associated with functional impairment in more than half of those with pain [144] . In 2003, Poobalan et al reviewed all studies to date on chronic pain post inguinal hernia repair [145]. In their own follow up study they identified a cumulative prevalence of chronic pain of 30% at 3 years post surgery. One third of this 30% reported moderate to unbearable pain. The definition of chronic pain used by these authors was that used by the IASP. As stated by these authors standardization of definition, length of follow up and quantification of chronic pain is lacking. Direct comparisons between studies to tease out causative factors are therefore difficult if not impossible. This is illustrated in the study by Amid et al [146]. The descriptor of chronic pain that they used was neuralgia and among other reasons is an explanation for their low chronic pain result [146]. Pain during sexual activity and subsequent sexual dysfunction represent a clinically significant problem in about 3% of younger male patients with previous inguinal herniorrhaphy [147]. Intraoperative nerve damage and disposition to other chronic pain conditions are the most likely pathogenic factors. Chronic pain post inguinal hernia repair ranges from 0 – 63% and is usually broadly classified into three categories mild, moderate and severe. Severity may be determined by extent of interference with social, daily and work related activities, number of painkillers used and attendance at chronic pain clinics. Perkins looked at post herniorrhaphy pain in the context of their chronic pain model and estimated that it may be as high as 50% at one year [122]. They believe that the presence and extent of preoperative pain may influence the degree of postoperative pain. Some authors would argue that it is not imperative to repair all hernias as soon as they are detected. In the context of postoperative chronic pain there is a defined point where the surgeon must intervene, quantifying this point however is not clear. Repair of recurrent hernia and type of mesh used may be related to long-term chronic postoperative

pain. The results of chronic pain studies in response to detailed questionnaires are summarised in Table 1.2.

Author	Year	Surgery	Sample Size	Time to Follow-up	Response Rate	Chronic Pain Incidence
Cunningham[143]	1996	Sutured	818	12 months 24 months	36%	63% 54%
Callesen[141]	1999	Mesh	466	12 months	93%	19%
Schmitz[142]	1999	Mesh	186	15 months	75%	36%
MRC group[3]	1999	Laparoscopic and open	928	12 months	91%	29% 37%
Poobalan[136]	2001	Mesh and sutured	351	36 months	65%	30%
Bay-Neilson[144]	2001	Mesh and sutured	3265	12 months 48 months	80%	29% 18%

Table 1.2. Results from chronic pain studies that used detailed questionnaires.

1.12. Preoperative factors that may contribute to post herniorrhaphy chronic pain

Chronic groin pain, as well as being a consequence of inguinal hernia repair, may also be as a result of a previously undiagnosed hernia. A small bulge in the posterior wall of the inguinal canal may not be large enough to be clinically detected but may account for chronic groin pain. Surgical mesh repair of this small direct hernia has been reported to alleviate in 87% and improve in the remainder of cases, previously unexplained chronic groin pain [148]. This study had fit sportsmen as its population base. In another similar study surgical exploration and repair of a previously undiagnosed inguinal hernia should be undertaken in sportspeople unable to compete due to chronic groin pain. That is, when all other explanations of chronic groin pain are exhausted, a clinically silent groin hernia may be the explanation for chronic groin pain [149]. The majority of patients that present with an uncomplicated hernia report a protruding mass and /or pain or discomfort in the groin [150]. As many as 66% report pain at the time of initial presentation and this increases to 90% in those patients that have their hernia for 10 years or more [151]. What degree of preoperative pain needed to make repair worthwhile is not clear. For the patient to believe that the surgical experience has been worthwhile, the reduction in preoperative symptoms has to be greater than the risk of severe postoperative chronic pain and more than chronic pain per se. Arguments supporting repair are based on alleviating symptoms and avoiding the risk of an acute hernia accident, the latter being often estimated at between 4 and 6% [152]. However because large population based studies detailing the natural course of an untreated hernia are scarce, this commonly held assumption that the life time risk of strangulation is between 4 and 6% is more likely one of speculation than fact. In the study by Hair et al the incidence of bowel resection was 0.3% , indicating that the risk of strangulation is approximately 1 in 300 [151].

1.13. Anatomy and physiology of the inguinal canal

A thorough knowledge of the anatomy and function of the preperitoneal space and groin region is required by any surgeon with an interest in the surgical management of groin hernias. The position and variability of nerve structures should be understood, irrespective of whether the surgeon is approaching the hernia from the anterior (open mesh repair as described by Lichtenstein [153]) or posterior route (laparoscopic transabdominal [154] or preperitoneal procedure [155]).

The nerves encountered using the anterior approach are the ilioinguinal and iliohypogastric nerves as well as the genital branch of the genitofemoral nerve. The ilioinguinal is usually smaller than the iliohypogastric and may be absent. These two nerves arise from the first lumbar nerve and are both mixed sensory nerves. The ilioinguinal nerve passes through the inguinal canal, under cover of the external oblique and becomes superficial at the external ring. It innervates the skin of the scrotum and the medial upper thigh. Damage to the ilioinguinal nerve in the inguinal canal causes sensory loss as the motor fibres have already been given off to the conjoint tendon. The iliohypogastric nerve emerges through the external oblique aponeursosis to innervate the supra pubic skin. It may be damaged when the superior aspect of the mesh is stapled or sutured underneath the upper leaf of the external oblique.

The nerves of most importance to the laparoscopic surgeon are the genitofemoral nerve, the lateral cutaneous nerve of the thigh, and the femoral nerve. The genitofemoral nerve comes from the first and second lumbar nerves and completes the innervations of the groin region. It passes obliquely through the substance of the psoas major muscle and emerges from this crossing deep to the peritoneum and the ureter. It splits behind the deep inguinal ring into the genital and femoral branches. The genital branch lies on the floor of the inguinal canal behind

the spermatic cord and supplies the cremasteric muscle via its motor branches and the scrotal skin via its sensory branches. The femoral branch contributes to the sensation of the anterior thigh. The lateral cutaneous nerve of the thigh crosses the iliacus muscle after emerging from the lateral border of the psoas muscle. It passes beneath the iliopubic tract just medial to the anterior superior iliac spine and innervates the skin on the anterior and lateral surface of the thigh. The femoral nerve is the largest of the three nerves and lies deep to the iliopsoas fascia. It can be seen emerging between the psoas and iliacus muscles, passing beneath the iliopubic tract and innervating the muscles of the anterior compartment of the thigh and the skin of the anterior aspect of the lower thigh and leg [156].

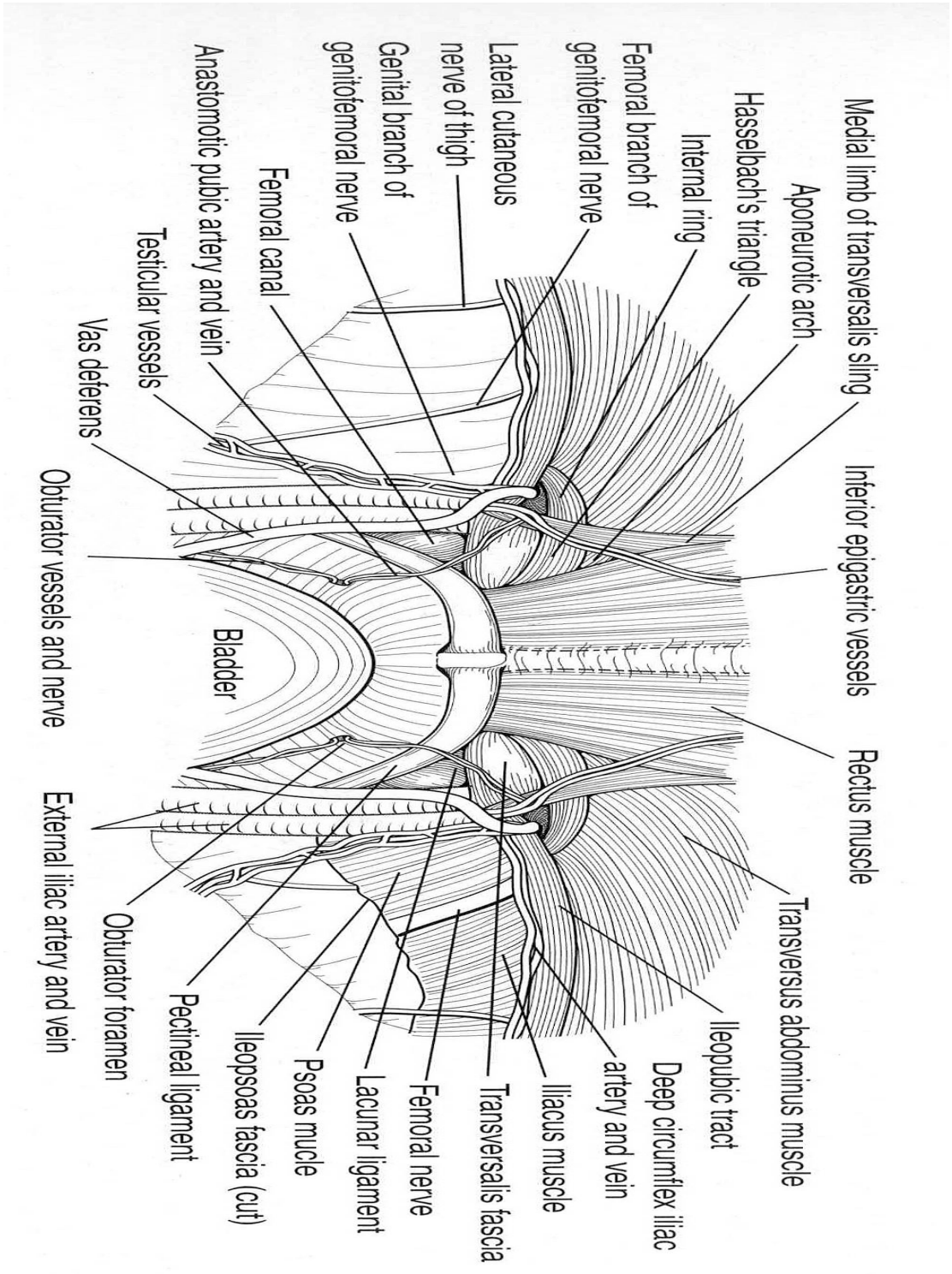


Figure 1.6. The pre-peritoneal pelvic anatomy with the iliopsoas fascia partially excised to expose the femoral nerve on the right side.

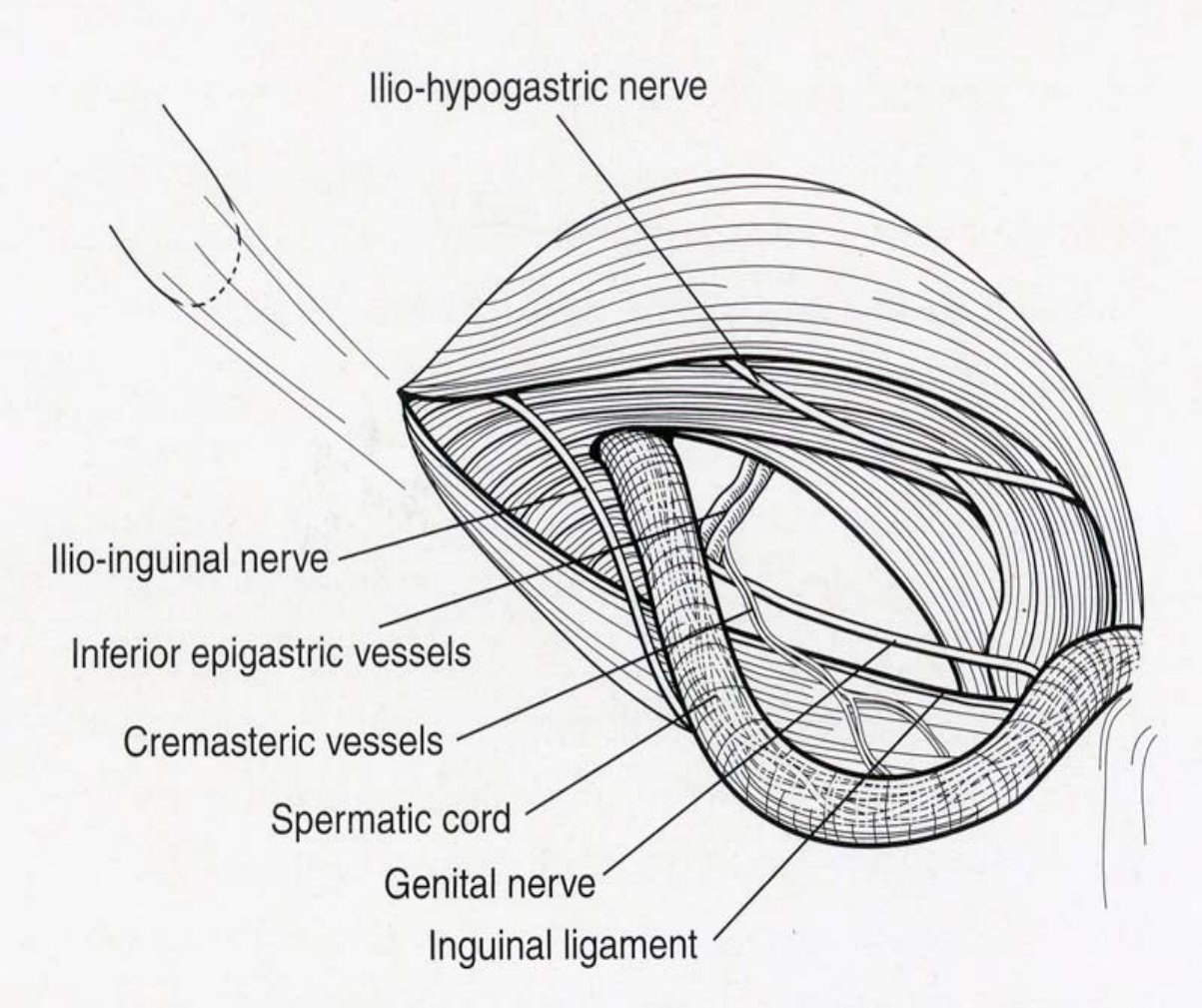


Figure 1.7. Position of the nerves from the anterior approach in the right inguinal canal.

1.14. Intraoperative factors that may contribute to post herniorrhaphy chronic pain

Chronic pain can be neuropathic or nociceptive in origin. Neuropathic pain is believed to be as result of nerve damage and is usually described as electric, sharp and shooting pain. Nociceptive pain on the other hand is as a result of tissue damage and is described as aching, heavy and dragging [86]. There are three nerves of anatomical and physiological importance in the groin area that may contribute to chronic post inguinal herniorraphy pain of neuropathic origin. These are the ilioinguinal, iliohypogastric nerves and the genital branch of the genitofemoral nerve.

Ducic et al believe that severe and chronic postoperative testicular pain after inguinal surgery can be treated by a designed approach that identifies the genital branch of the genitofemoral nerve in the proximal inguinal canal, resects it proximal to the previous operative field and subsequently places it behind the peritoneum [157]. From cadaveric anatomical studies that highlighted the variability in the course of this nerve as it exited the external ring, they showed that proximal ligation of this nerve provides relief of chronic scrotal pain. Despite this being a small study, all four patients had relief of subjective symptoms and evidence of objective improvement with reduction in level and frequency of pain postoperatively. Al-Dabbagh et al reviewed the anatomical variations in the course of the ilioinguinal and iliohypogastric nerves in 110 hernia repairs [158]. They found that the course of both nerves was consistent with that found in anatomical textbooks in just fewer than 50% of cases. This difference in the variation of the nerve along its pathway may leave it susceptible to injury at operation. However these differences in the course of the nerves can be readily appreciated and should be easily identified by the surgeon.

Since the early 1980's peripheral nerve entrapment syndrome following common surgical procedures to the lower abdominal wall have been recognised. Ilioinguinal or iliohypogastric nerve entrapment is typically diagnosed as a burning pain near the incision that radiates to the area supplied by the nerve with associated impaired sensory perception. Resolution occurs, albeit temporarily, when the two nerves are infiltrated with local anaesthetic as they leave the internal oblique. Surgical repair of the scar and resection of the nerve was advocated as the method of treatment for this condition [159]. It is important to note that this early study involved very small numbers and that at least 25% of their patients had persistent chronic pain following the proposed treatment. In 1996 Bower et al reported that severe chronic postoperative inguinal hernia neuralgia was rare [160]. They suggested that in the small number of patients in whom non operative methods of treatment were refractory, the involved nerve should be mapped out prior to its surgical high ligation and division [160]. Understanding the typical nerve anatomy and variation, is fundamental in treating this rare but debilitating postoperative complication. A larger series of just under 500 patients, this time confining the surgical procedure to the sutured Shouldice repair of an inguinal hernia, states that inguinal entrapment syndrome can be reduced to below 2% if the genital branch of the genitofemoral nerve is deliberately dissected free or cut cleanly [161]. The early postoperative complication rate or the recurrence rate is not affected [161]. Again, identifying the nerve and ligating it is advocated as a solution for severe chronic neuralgic pain which these authors state is uncommon but debilitating following hernia repair [160]. Dittrick et al reviewed 90 patients who underwent Lichtenstein inguinal hernia repair over a seven year period [162]. The two surgeons who performed the operations differed in the fact that one preformed ilioinguinal neurectomy on a routine basis. Neuralgia and paraesthesia were assessed through telephone and personal patient interviews at 1 month, 6 months, 1 year and 3 years post surgery. There was no data recording preoperative symptoms or no data on potential confounding conditions

e.g., stroke, diabetes etc. They concluded that the incidence of postoperative neuralgia was significantly lower in the neurectomy group versus the nerve preservation group at 1 month and 1 year but there was no significant difference in postoperative neuralgia at 3 years, though they did admit that numbers followed up at 3 years were small. At the same time the incidence of postoperative paraesthesia was not significantly higher in the neurectomy group versus the nerve preservation group at 1 month, 1 or 3 years. Those that reported postoperative paraesthesia in the neurectomy group at one month and six months had lower mean scores on the visual analogue scale than those in the nerve preservation group. These authors argue that routine division of the ilioinguinal nerve is a reasonable option during inguinal hernia repair [162]. The drawback of this study was that it was retrospective and that small numbers of patients were used. Recently a double blind randomised controlled study was published in the Archives of Surgery from Italy [163]. In four centres, 813 patients were randomised to inguinal hernia repair with either preservation or elective transection of the ilioinguinal nerve. The primary outcome was chronic pain at one year. At one year pain was absent in 76% of those with nerve preservation and in 73% of those with nerve transection. The majority of patients that reported pain had mild to moderate pain. However at 1 and 6 months postoperatively loss of pain and touch sensation were significantly greater in the group with the iliioinguinal nerve transected. Touch sensation remained decreased in the group with nerve transection even at one year follow up [163]. The problem with nerve studies is that in the main they evaluate the lack of function of one nerve only whereas there are three nerves involved in the sensory innervations of the groin.

In a second Italian study the identification and preservation of all three nerves during open mesh repair was associated with a reduction in chronic incapacitating groin pain and in the majority of these patients with chronic pain at six months the pain was resolved with

conservative or medical management at 1 year [164]. Madura et al state that the incidence of post herniorrhaphy neuropathies is not well known but is estimated to be in the region of 0 to 30% [165]. They argue that the most successful treatment is surgical resection of the nerve with good pain relief. Complete pain relief was seen in 72% of patients in their study and 10% reported a marked decrease in their symptoms. The only difference between patients who had complete relief and those who had partial relief of their symptoms was previous repair of a recurrent hernia. This seems to be the only available indirect evidence of chronic pain post repair of a recurrent inguinal hernia. To date there are no available studies that look at the incidence of post herniorrhaphy pain in patients who have had recurrent hernias repaired. One would assume that there is a higher incidence of chronic pain in these patients as tissue and nerve damage is twice as likely second time round. As an indirect result of our first study we found that patients who had a recurrent hernia repaired were no more likely to report pain at three months post surgery than those who had a primary hernia repaired.

Therefore one can argue that chronic postoperative pain is partly explained by nerve damage at initial surgery. When any of the nerves are not recognised and as a result traumatised, chronic postoperative pain can ensue. However it would appear that the situation is not clear. While cleanly dividing the nerves does not exacerbate postoperative pain it does play a role in disturbed sensory changes after repair. On the other hand clean nerve division can also be a solution for severe chronic neuropathic pain. It has been postulated that when these nerves are caught or trapped in permanent stitches or tacks or bound up in the mesh during the various methods of repair it is then that postoperative chronic neuropathic pain may result.

1.15. Characteristics of mesh types

Successful treatment of abdominal wall hernias and the prevention of recurrence is largely due to the insertion of a mesh. Meshes are synthetic alloplastic materials and are thought to work by mechanical sealing or by induction of a strong scar plate. Irrespective of which way the groin hernia is approached, meshes are necessary and indeed paramount to ensuring the low recurrence rates of less than 4% [166]. The incorporation of a large amount of biomaterial can lead to seroma development, wound contracture and reduction in abdominal wall mobility. Meshes show migration and erosion of bladder and bowel with the formation of fistulas and bowel obstruction. It has been postulated that the very structure of the mesh and its inflammatory characteristic may contribute to post herniorrhaphy discomfort and pain. The host reaction is influenced by the mesh type used, particularly the amount of mesh used and the pore size. The optimum amount of material and pore size needed to adequately treat the hernia and avoid recurrence is unclear. Textile analysis of the various mesh types available show variations in weight, structure, stiffness and strength. There is an asymmetry to meshes in that different strain properties are seen in the horizontal and vertical direction. The basic mesh type is composed of polyprolene monofilament and this has a high bending stiffness. Increasing the size of the pores [167] and replacing part of the polyprolene multifilament with polyglactin results in a lighter partially absorbable mesh. Vipro 11 mesh has equal parts of absorbable polyglactin and non-absorbable polyprolene thread and an additional violet polyglactin and polyprolene thread placed rhombically over the mesh. After absorption of the polyglactin component the polyprolene mesh remains. It is this which has been optimally designed to cope with the physiological stresses of the abdominal wall. The main purpose of implantable meshes is their tensile strength. This can be defined by the modified Law of La Place, which states that F = P x d / 4, where F = force (in Newtons, N) per cm^2, P = intra abdominal pressure (in kiloPascals, kPA) and d = diameter (cm) [168].

Assuming an intra abdominal pressure of 20 kPa, the calculated tensile strength is a maximum of 16 N/cm^2 [169]. This corresponds to the measured strength of tearing sutures out of tissues and exceeds the forces applied for suture repair of hernias. The tensile strength of Vipro 11 after 90 days, that is, when the polyglactin component is absorbed is 19.6 N/cm^2 (standard deviation 6.9) [170]. This suggests that the minimal tensile strength required may actually be less than 16 N/cm^2. The differing textile properties of a non-absorbable standard mesh (Atrium) and a partially absorbable mesh (Vipro11) are compared in Table 1.3.

	ATRIUM (NA) mesh	**VYPRO 11 (PA) mesh**
material	polyprolene	polyprolene polyglactin
Type of filament	monofilament	multifilament
Weight (g/m^2)	90.2	54.6
Pore size (um)	800	5000
Maximum tensile strength(N/5cm)		
vertical	245	387
horizontal	616	63
Subsequent tearing force(N)		
vertical	3.7	1.1
horizontal	4.1	1.2
Forces tearing out the seam(N)		
vertical	58.8	29.6
horizontal	56.2	29.0

Table 1.3. Textile properties of mesh materials.

The asymmetrical tensile strength property of meshes has been studied by Junge et al [170]. These authors found that when the mesh is fixed at opposite ends there is a difference in elongation and strength in both directions between partially absorbable and non-absorbable meshes.

Another important property difference between these two mesh types is the suture pull out force. That is the force the sutures exert on the mesh filament in a particular direction. The sutures require to be less than or equal to the innate strength of the mesh so they are not pulled out. Much less effort or strength is needed to distort the partially absorbable mesh than is required for the non-absorbable polyprolene one. From in vitro experiments, Junge et al demonstrated that to prevent the sutures from being pulled out it is imperative that they are sutured 1 cm from the edge of the mesh [170] .

1.16. Laparoscopic hernia repair and chronic pain

In the year 2001/2 95.9% of patients in the UK had their primary hernia repaired at open surgery, only 4.1% of patients with a hernia had a laparoscopic repair [137]. The first report of a hernia repaired laparoscopically was in 1982 by Ralph Ger [171]. Since then many surgeons have contributed to modifications and improvements on the original technical description but only 5% of surgeons have adopted this technique into routine surgical practice [172]. Laparoscopic hernia repair can be done either transabdominally or extraperitoneally, using either general or regional anaesthesia. The advantage of laparoscopic inguinal hernia surgery lies in the fact that the whole of the inguinal floor on both sides is exposed and as a result direct, indirect, contralateral and femoral hernias can be detected and repaired. It also has the advantages of laparoscopic surgery in general, in terms of recovery period and incision length. The last decade has witnessed enthusiastic investigation comparing laparoscopic

versus open inguinal surgery repair. Approximately four meta-analyses, two systematic reviews, nearly 70 randomised controlled trials (RCT) and numerous retrospective reviews have been published [172]. The problem with many of the RCTs is poor quality. Many are not well designed and have been found to be underpowered [172]. Patients recruited to both open and laparoscopic repair groups were not necessarily homogeneous. End points that are easily measured i.e.; hernia recurrence, length of operation, are usually reported accurately but more subjective endpoints i.e.; postoperative pain, type of pain and return to normal activities are not usually reported in a standard quantified manner except in a few circumstances [172]. The European Union (EU) hernia trialists' collaboration has organised the most extensive meta-analysis to date and continues to accrue data to constantly refine its conclusions. In the Group's 2000 review, recurrence rates for open and laparoscopic repairs were not significantly different. In 2002, the Groups' opinion was that return to normal activity is faster after laparoscopic repair and that persistent pain is less [173]. In a five year follow up study laparoscopic hernia repair is shown to be associated with less long-term numbness and probably less pain in the groin than open mesh repair [174]. Kumar et al found that chronic pain or discomfort was reported by 30% of patients after groin hernia repair and was significantly more common after open mesh repair than after laparoscopic total extra peritoneal repair (TEP) repair [175]. It restricted physical or sporting activities in 18% of patients and specifically more so after open mesh repair [175] .

Postoperative neuralgia following laparoscopic repair was examined by Fitzgibbons et al, and they found that leg pain decreased significantly from 7% to 1.8% after the surgeon preformed 30 cases [176]. Chronic pain and neuralgia occurs with an incidence of 0.5% and 4.6% respectively depending on the laparoscopic method used and as the surgeon becomes more familiar with the normal anatomy and its variants this incidence decreases [172] .

1.17. Postoperative factors that may influence post herniorrhaphy chronic pain

Adequate analgesia in the postoperative period is a priority in enabling the post-surgical patient to cope with the tissue damage of surgery. Irrespective of whether the hernia is repaired under local, regional or general anaesthesia, the patient will not be deemed fit for discharge until the pain of surgery is controlled with appropriate analgesia. Inguinal hernias have been repaired under general, regional or local anaesthesia.

It is well established, for example that open inguinal hernia repair can be conducted under local anaesthesia, regardless of comorbidity and with minimal morbidity [177]. Paravertebral blocks (PVB) have recently been used as the sole anaesthetic technique and randomised against general anaesthetic (GA) fast tracking for inguinal hernia repair. Patients who had their hernia repaired using PVB were discharged sooner, ambulated earlier, had less postoperative adverse events including acute postoperative pain than those in the GA group [178]. Patients' general fitness for anaesthesia and preference are important in determining what type of anaesthesia is ultimately chosen. Despite this and despite the fact that local or regional anaesthesia is safe, cost effective and shown to decrease postoperative pain in inguinal hernia [179] repair, the majority of anaesthetists choose GA to facilitate this surgical procedure [180]. In a randomised controlled trial comparing post operative pain following inguinal hernia repair under general or local anaesthesia (LA), the only difference noted between the two groups was a reduction in pain scores noted at six hours in the LA group. All patients underwent psychometric testing and pain score assessments at 6, 24 hrs, 3 months and one-year post repair. Regional anaesthesia is also an option but appears to be used exclusively only by hernia specialists [181]. It is thought that acute post inguinal hernia surgery pain, that is pain in the first few days and weeks following surgery can influence the

development of long term chronic pain. Therefore adequate and effective immediate postoperative pain control not only determines timing of discharge but may also contribute to a reduction in chronic pain. It has been suggested that treatment designed to prevent pain in advance of surgical trauma may be more effective than simply instituting analgesic therapy in response to the pain after surgery [182]. The benefit of local anaesthetic field block before hernia surgery has been investigated by Tverskoy et al [183]. They reported that constant pain and incident pain were less severe for 48 hours after surgery in patients who received a preoperative field block with bupivicaine compared with patients who received no local anaesthetic at all. Inguinal field block is superior to local anaesthetic skin infiltration in terms of less pain postoperative pain until day 7, increased patient satisfaction, faster mobilisation and lower analgesic consumption [184] Analgesia in advance of the pain stimulus prevents central sensitisation and neuronal hyperexcitability i.e., "wind-up". Central sensitisation is thought to be dependent on painful stimuli acting on NMDA receptors located within the central neuraxis [185]. Pre-emptive treatment with local anaesthetics, anti-inflammatories or NMDA inhibitors have all been proposed as methods of inhibiting transmission of noxious stimuli thereby preventing stimulation of NMDA receptors and central sensitisation [182, 185]. Thus the idea is to dampen the pain pathway before it even starts. Pre-emptive treatment using a single agent is often not sufficient enough to demonstrate a significant clinical difference [186]. Pre-emptive therapies may have more success when used in combination than when used alone [187]. Pavlin and co-workers combined preoperative use of a non-steroidal anti-inflammatory drug (NSAID), an NMDA inhibitor and an LA field block was compared with a standard LA field block in terms of pain reduction post inguinal hernia repair. Despite small numbers, this study did show that trimodal therapy with a NSAID, NMDA inhibitor and LA field block prior to inguinal hernia repair led to a reduction in pain scores and analgesic consumption in the first 24 hours after surgery. The authors did admit that it was

unclear whether it was a true pre-emptive effect or an additive effect of various analgesics that was demonstrated [188].

1.18 Current treatment options for those with post herniorrhaphy pain.

Although health care providers are becoming better educated about the science of pain management [204], it is clear from some authors that there is an educational void when it comes to caring for those patients with chronic pain of any aetiology [205].

In the majority of cases patients who have post herniorrhaphy pain are not troubled by it. When assessed by questionnaire, only a half of those with severe pain seek medical assistance. Fewer still are referred back to their operating surgeon, while only a small group see a pain specialist. In a small number of cases chronic severe pain will persist post repair. For these people quality and function of life is affected. We have found that with time the pain disappears in 30%, becomes mild in 45% and continues to be severe in the remainder.

The management of patients with severe pain is largely based on empirical management of other chronic pain conditions. The treatments available fall into the following groups, physical (acupuncture), drugs (analgesia, tricyclics), nerve blocks and psychological support. Dependence on long term analgesics is common. Patients should be referred to pain clinics for further management.

In some cases the removal of the mesh may be necessary, but this is usually only undertaken when all other methods are exhausted. The role of surgery in patients with chronic pain is contraversial, some report excellent results with neurectomy with or without mesh removal. Mesh removal is usually confined to those with severe adverse psychological response to

their mesh. In a recent retrospective study the incidence of chronic pain and recurrence was examined at 44 months in patients who had to have the mesh removed for chronic groin sepsis and infection. These authors found 14 out 2139 patients over an eight year period that required removal of the mesh for infection. At the time of follow up, none had chronic pain and two had evidence of asymptomatic hernia recurrence [206].

The essence of inflammatory or nociceptive pain is that it is ultimately protective. The human body has adaptive mechanisms for fighting infection and repairing damaged tissue. This occurs at a local level and also at a more complex tertiary level where there is an inter play between the physiological reactions of fight and flight. The body can eliminate the cause of inflammatory or nociceptive pain by using built in local mechanisms, for example diffuse noxious inhibitory controls, distraction or the endogenous opiate systems. The body however has little control or ability to recover from neural injury. It is poorly adapted to restore optimal functioning after injury or disease, which cause major damage to the nervous system Neuropathic pain seems to persist indefinitely. It is difficult to treat or modify, as our understanding of it is relatively poor. We can describe it in analogous terms but this merely simplifies it.

Two families of systemically administrated drugs, anticonvulsants and tricyclic antidepressants, have statistical success in the treatment of neuropathic chronic pain. They do not however provide complete relief. Oral formulations bring about a 50% reduction in pain intensity in only about half of clinical trial subjects. Intra-venous administration of local anaesthetic agents works better but not in reality this is not practical [207]. These medications have side effects including significant sedation, somnolence and nausea. The use of opiates which pharmacologically engage intrinsic pain inhibitory circuits are no longer relevant in the

treatment of chronic neuropathic pain[208]. A possible explanation for this is that nerve injury induces down regulation of mu-opiate receptors in primary sensory neurones in the central spinal terminals and their postsynaptic spinal targets [209]. As a result opiates become less effective. Neurolysis is invasive and as a result carries significant risks. It does work but transiently. It is not unknown for the pain to return more severely than it was initially. The process of neuromodulation, that is, of implantable devices, overcomes the transient success of neurolysis. However these devices are expensive and the procedure is still an invasive one. Topical agents offer moderate relief from superficial skin tenderness i.e., pain of nociception. They unfortunately do not offer relief for the ongoing evoked deep pain. Ilioinguinal neuropathy can be detected using nerve conduction studies and has been reported in a case study [210] to be successfully treated albeit temporarily by local anaesthetic blocks and permanently by complete transection of the ilioinguinal nerve..

Chapter 2: AIMS

From a previous retrospective study documenting groin hernia repair in Scotland over a one year period [1], patients were questioned about the presence and severity of pain at three months post hernia repair. This is the period beyond which normal tissue healing is expected to have occurred. The aim of the first study was to assess the outcome of patients who complained of severe or very severe pain at three months following groin hernia repair. The main outcome measures included the number of patients with persistent pain and the effect of pain on daily activities and quality of life. Secondary outcome measures included the presence of other chronic pain conditions.

No previous studies have attempted to quantify pain from a primary inguinal hernia. The aim of the second study was to quantify patients' pain from a primary inguinal hernia at rest and on moving and to assess the effect of hernia repair on this pain. The patients were those who attended one hospital as part of a seperate multicenter trial [2].

The aim of the third randomized controlled study was to compare outcome in terms of pain using a partially absorbable or light weight mesh and a non-absorbable or heavy weight mesh. The primary endpoint of the study was the incidence of chronic pain of any severity at the site of hernia repair at 12 months.

Chapter 3: Outcome of patients with severe chronic pain following repair of a groin hernia.

3.1. Introduction

Severe chronic pain is the most serious long-term complication that can occur after repair of a groin hernia. In the past it has been thought to occur rarely, but more recently prospective and population based studies indicate that up to 6% of patients may have moderate to severe pain one year following this surgery [141]. Overall approximately 1/3 of patients will report some form of pain at one year after the operation [144].

Given that groin hernia repair is a common procedure with an annual rate of repair of 100-150 per 100,000 of the population, in a country the size of the UK, over 5000 new patients may suffer moderate to severe chronic pain each year. This has obvious cost implications for the Health service and the economy as a whole. Many of these patients delay returning to work and normal activities. In some cases they may not even be able to resume previous employment [189].

In this first study we report the outcome of patients who had severe or very severe pain three months after groin hernia repair. This is the period beyond which normal healing is assumed to have occurred and fulfils the definition of chronic pain as stated by the International Association for the Study of Pain.

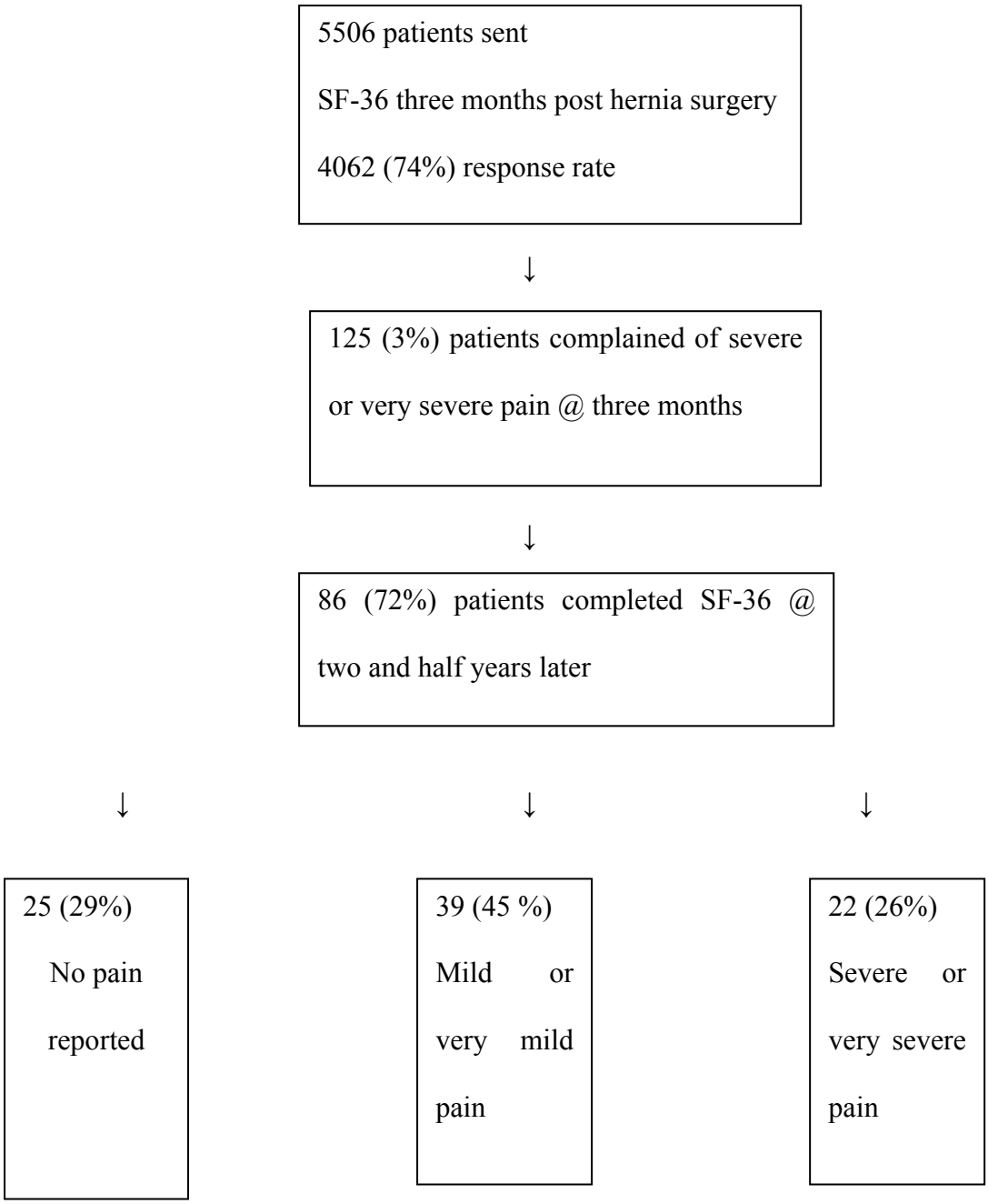
3.2. Patients and Methods

Ethical approval was obtained from the Institutional Ethics Committee of the Western Infirmary, Glasgow. Between April 1998 and March 1999 data was gathered on patients who underwent groin hernia repair in Scotland [1]. At a minimum of three months after surgery all

patients were sent a modified SF-36 questionnaire (appendix 1). This questionnaire evaluated their outcome and satisfaction with the surgical procedure. All patients were asked if they had pain in their groin at the site of the hernia repair at any point in the past week. In addition men were asked if they had pain in their testes on the same side. Those that had pain were asked to grade it as very mild, mild, severe or very severe. Patients were also asked about numbness around the groin and in the thigh on the side of the hernia operation.

Patients who reported severe or very severe pain were sent a further questionnaire (appendix 2) in April 2001. In addition to the modified SF-36 they were asked about the character of their pain and were asked to complete a Wisconsin Brief Pain questionnaire [97]
(Table 3.1. Flow diagram). The latter is designed to assess the effect of pain on general activity, mood walking ability, normal work, personal relations, sleep and enjoyment of life. Patients score 0 if pain does not interfere with the previous activities to a maximum of 10 if it completely interferes. The words used to characterise the patient's pain were based on previous studies [190] that set out to validate verbal responses for neuropathic (related to nerve damage) and nociceptive (related to tissue damage) pain.
Also patients were asked if they suffered from other chronic pain conditions such as chronic backache, headache, irritable bowel syndrome or any other chronic condition associated with pain.

Table 3.1. Flow diagram of patients for Study 1.



3.3. Statistical analysis

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) for Windows, version 9.01 (SPSS Chicago, Illinois, USA). A chi squared or Fisher's exact test was used to examine any association between different variables and whether the pain was very mild, mild, severe or very severe. A T-Test was used to examine the effect of chronic pain on daily activities and quality of life. Data are presented where appropriate with 95% confidence intervals.

3.4. Results

Information was gathered on 5,506 patients who had a groin hernia repair in Scotland in 1998. Of these 4,062 (74%) returned the modified SF-36 questionnaire. 1,733 (42.6%) still had very mild or mild pain while 125 (3%) had severe or very severe pain at the site of their hernia repair. Patients with severe or very severe pain were significantly ($p < 0.001$) younger, that is 54 versus 60 years of age and more likely to be female (odds ratio 1.73, 95% CI 1.07-2.81) when compared with the total population that had a hernia. There was no association between hernia type, primary or recurrent, operation type, mesh or non mesh, grade of operator and whether the operation was performed as a day case or not and incidence of severe or very severe pain following operation.

In April 2001, a median of 30 months (range 24 to 36 months) after groin hernia repair 86 (72%), of the 120 patients (5 had either died or could not be contacted at the original address)

with severe or very severe pain replied to the second questionnaire (Table 3.4.1.). Twenty-five (29%) recorded no pain at the site of their hernia while 39 (45%) described the pain as very mild or mild. Twenty- two (26%) still had severe or very severe pain. Of the 61 patients with pain, 39 (64%) had groin pain, 1 (2%) had testicular pain while 21 (34%) had both groin and testicular pain. Seventeen patients (28%) described the pain as continuous while thirty-six (59%) felt that the pain was brought on by activity. Twenty-six (43%) had returned to their general practitioner with pain while eighteen (29%) had returned to their surgeon. Five (8%) had further surgery while 9 (15%) had attended a pain clinic. Unfortunately the outcome of these latter 14 patients is not clear. Patients with severe or very severe pain were significantly more likely to seek further treatment when compared with those experiencing mild or very mild pain post repair, 19 of 22 versus 10 of 39 (p=0.0001).

3.4.1. Effects on daily activities and quality of life

The presence of chronic pain interfered significantly with all of the activities measured irrespective of the degree of severity of the pain (p=0.0001). Not surprisingly this effect was more marked in the severe/very severe group (Table 3.4.2).

3.4.2. Character of pain and numbness

The most common descriptor of pain used in this study was aching (45%) followed by throbbing (28.3%) and stabbing (23.3%). Patients with very mild or mild pain were more likely to describe their pain using a single term that indicated that the character of their pain was either neuropathic or nociceptive. In contrast patients with severe or very severe pain were more likely to use multiple descriptors to describe their pain. This would tend to suggest that the cause of severe chronic pain is both neuropathic and nociceptive in origin (Table 3.4.3). Numbness was present in significantly more patients in the severe or very severe

group 18 of 22 versus 18 of 38 (p=0.001) (Table 3.4.4). In addition the numbness was more extensive in these patients and was likely to involve both groin and thigh.

3.4.3. Other chronic pain conditions

Patients in the severe / very severe group were significantly more likely to suffer from other chronic pain conditions when compared with the very mild/mild pain group (20 of 22, versus 23 of 37, p=0.016). The most common illness was chronic back pain in both groups while significant numbers also had suffered from headache and irritable bowel (Table 3.4.5). Other conditions causing chronic pain in these patients included pain from scars elsewhere in the body and peptic ulcer disease.

Patient demographics	
Age* [median (IQR)]	54 years (40-66)
Male	74 (86%)
Female	12 (14%)
Hernia type	
Primary	73 (84.8%)
Recurrent	13 (15.0%)
Bilateral	7 (8.1%)
Inguinal	83 (96.5%)
Femoral	3 (3.5%)
Operation type	
Open mesh	77 (89.5%)
Open non mesh	8 (9.3%)
Laparoscopic	1 (1.2%)
Principle surgeon	
SHO	16 (18.6%)
Registrar	27 (34.0%)
Staff Grade	8 (9.3%)
Associate Specialist	2 (2.3%)
Consultant	33 (36.4%)

Table 3.4.1. Details of patients, hernia and operation type and grade of surgeon performing the operation who completed the second questionnaire.

*Values are median (interquartile range); other values in parentheses are percentages.

	Mild (38*)	Severe (22)
General activity	2.29 (1.61 - 2.97)	6.55 (5.54 -7.55)
Mood	1.78 (1.14 - 2.43)	6.45 (4.94 - 7.97)
Walking	2.34 (1.55 - 3.13)	6.05 (4.80 - 7.29)
Work	2.59 (1.73 - 3.45)	6.45 (5.26 - 7.65)
Relationships	1.42 (0.69-2.15)	5.05 (3.40 - 6.70)
Sleep	1.32 (0.76 - 1.92)	6.41 (5.33 - 7.49)
General enjoyment of life	2.32 (1.5 - 3.13)	7.14 (5.97 - 8.30)

Table 3.4.2 Effect on daily activities and quality of life values, given as mean (95% confidence interval). * One patient did not complete this section.

	Mild (38*)		Severe (22)		P value
Neuropathic					
Aching	15	(39.5%)	12	(54.5%)	NS
Burning	3	(7.8%)	4	(18.2%)	NS
Cutting	0	(0%)	2	(9.1%)	NS
Electric shock	0	(0%)	0	(0%)	NS
Itching	1	(2.6%)	1	(4.5%)	NS
Prickling	3	(7.8%)	1	(4.5%)	NS
Shooting	7	(18.4%)	4	(18.2%)	NS
Stabbing	7	(18.4%)	7	(31.8%)	NS
Tingling	3	(7.8%)	2	(9.2%)	NS
Nociceptive					
Drilling	0	(0%)	0	(0%)	NS
Gnawing	5	(13.2%)	5	(22.7%)	NS
Pounding	1	(2.6%)	1	(4.5%)	NS
Pulling	3	(7.8%)	11	(50.0%)	0.001
Sickening	2	(5.3%)	4	(18.2%)	NS
Tender	5	(13.2%)	8	(36.4%)	0.027
Throbbing	5	(13.2%)	12	(54.4%)	0.001
3 or more words	6	(15.8%)	13	(59.1%)	0.001

Table 3.4.3 Descriptors of pain. * One patient did not complete this section.

	Mild (38*)	Severe (22)	All patients (60)
Groin	12 (31.5%)	5 (22.7%)	17 (28.3%)
Thigh	1 (2.6%)	0 (0%)	1 (1.6%)
Both	5 (13.1%)	13 (59%)	18 (30 %)

Table 3.4.4 Numbness ($p < 0.001$). * One patient did not complete this section.

	Mild (37*)	Severe (22)	All patients (59)
Backache	17 (45.7%)	17 (77.3%)	34 (57.6%)
Headache	7 (18.9%)	6 (27.3%)	13 (22.0%)
Irritable Bowel	4 (10.8%)	7 (31.8%)	11 (18.6%)
Other	5 (13.5%)	3 (13.6%)	5 (8.5%)

Table 3.4.5 Other chronic illnesses ($p=0.016$). * Two patients did not complete this section.

Chapter 4: Pain from a primary inguinal hernia and the effect of repair on pain.

4.1. Introduction

Recent evidence indicates that up to one third of patients undergoing hernia repair have a painless hernia that has little or no effect on work or leisure activities [151]. However following operation it is now apparent that 3-6% of patients will have severe pain and as many as 30% will have mild pain at one year after hernia repair [141].

The aim of this study was to quantify patients' pain from an inguinal hernia at rest and on moving and to assess the effect of hernia repair on pain.

4.2. Patients and Methods

All patients undergoing elective repair for a primary inguinal hernia who were admitted to the care of one surgical unit, (Western General Infirmary, Glasgow) between January 1998 and October 2000 were entered into the study. Ethical approval was obtained from the Institutional Ethics Committee of the Western Infirmary, Glasgow. Patients were asked to complete a linear analogue pain score of the degree of pain caused by the hernia at rest and on movement. Pain scores were recorded on a 100-mm line, where 0 represented no pain and 100 the most severe pain, by a single observer 24hr before operation (appendix 3). The surgical procedure performed for a groin hernia was a standard Lichtenstein open mesh repair. At one-year post repair pain scores were again recorded and all patients were clinically examined for evidence of a recurrence at this time. Arbitrarily a score of less than 10 was graded as mild pain, a score of 10-50 as moderate pain and a score of more than 50 as severe pain.

4.3. Statistical analysis

Differences between groups were analysed using the Student's t-test. Where there was sufficient doubt about the validity of parametric assumptions (assessed graphically), a Wilcox on or Mann-Whitney U test was preformed.

4.4. Results

A total of 323 patients with a primary inguinal hernia underwent an open tension free mesh repair during the study period. Characteristics of the patient group are shown in Table 4.4.1. The majority of patients had no pain from their hernia, or only mild pain, at rest (80.5%) or on moving (58.8%). Only 1.5% experienced severe pain at rest and 10.2% had severe pain on movement prior to repair (Table 4.4.2).

Patients older than 50 were significantly more likely to have pain associated with the hernia on movement, than their younger counterparts ($p<0.01$). Surprisingly there was no association between hernia type, direct or indirect, or patient occupation and the presence of pain at the hernia site. Although women were more likely to have pain at rest and on moving, this effect was not significant and is likely to reflect the small number of women (17) in the study (Table 4.4.3).

At 1 year after operation 204 patients (63.2 %) returned for clinical review and completed pain scores from the hernia repair site at rest and on movement (Table 4.4.4). This is the complete response rate despite several attempts at contacting patients both via GP, by phone and by letter. The low repeat response rate is thought to be explained by the fact that the questionnaires were labour and time intensive as they were part of a much larger and different study. The time taken to complete the questionnaire was approximately an hour. It is

also well known that low response rates are frequently seen when patients in clinical trials are seen by a variety of doctors [191]. Only 24.5% of patients had no pain at rest and only 21.6% of patients had no pain on moving. Overall the group showed a significant reduction in pain scores at rest ($p=0.019$) and on moving ($p<0.001$) compared with preoperative levels. This was due mainly to the large effect observed in patients with high preoperative values (Table 4.4.5). In contrast, patients who had no pain at rest before operation had significant pain scores at rest at 1 year ($p<0.001$). No patient had recurrence of the hernia or other chronic complication at the one-year follow up visit.

		Number of patients (n = 323)
Age	> 50 years	201 (62.2%)
	< 50 years	122 (37.8%)
Sex	Male	306 (94.7%)
	Female	17 (5.3%)
Site	Right	170 (52.6%)
	Left	127 (39.3%)
	Bilateral	26 (8.0%)
Type	Direct	176 (54.5%)
	Indirect	147 (45.5%)
Occupation	Moderate manual	57 (17.6%)
	Heavy manual	53 (16.4%)
	Sedentary	72 (22.3%)
	Retired	141(43.7%)

Table 4.4.1. Patient characteristics. Values in parentheses are percentages.

	At rest	On moving
No pain (0)	86 (26.6%)	53 (16.4%)
Mild (< 10)	174 (53.9%)	137 (42.4%)
Moderate (10-50)	58 (18.0%)	100 (31.0%)
Severe (> 50)	5 (1.5%)	33 (10.2%)

Table 4.4.2. Severity of pain in 323 patients. Data given is, number of patients (% of total).

		At rest mean (S.D)	On moving mean (S.D)
Age	> 50 years	7.5 (11.9)	18.5 (23.8)
	< 50 years	6.7 (13.0)	14.4 (19.6)
Sex	Male	6.8 (12.2)	16.2 (21.9)
	Female	12.0 (14.6)	28.7 (29.2)
Site	Right	6.7 (12.4)	18.2 (23.4)
	Left	7.9 (13.1)	15.1 (20.3)
	Bilateral	5.1 (7.5)	16.5 (26.1)
Type	Direct	7.4 (12.8)	16.4 (22.5)
	Indirect	6.7 (11.8)	17.3 (22.5)
Occupation	Moderate manual	9.0 (14.7)	17.4 (20.4)
	Heavy manual	5.9 (13.7)	16.0 (19.8)
	Sedentary	5.8 (9.6)	18.1 (25.1)
	Retired	7.7 (12.5)	16.7 (23.0)

Table 4.4.3. Pain scores in relation to patient characteristics. Values are mean (s.d).

	At rest	On moving
No pain (0)	50 (24.5%)	44 (21.6%)
Mild (< 10)	128 (62.7%)	114 (55.9%)
Moderate (10-50)	22 (10.8%)	41 (20.1%)
Severe (> 50)	4 (2.0%)	5 (2.5%)

Table 4.4.4. Severity of pain 1 year after hernia repair in 204 patients. Data given is number of patients (% of total).

	Number of patients	**At rest**	**On moving**
All patients	204	-2.9 (1.2)*	-9.2 (1.8)*
Preoperative score at rest			
0	40	1.8 (0.3)*	-0.3 (1.6)
>10	37	-22.8 (3.7)*	-32.2 (4.8)*

Table 4.4.5. Effect of operation on postoperative pain score. Values are mean (s.e.m.).

*P < 0.01 versus baseline value (t- test).

Chapter 5: Impact of light or heavyweight mesh on chronic pain after inguinal hernia repair.

5.1. Introduction

Severe chronic pain is one of the most serious long-term problems that can occur following inguinal hernia repair. Population based studies and randomised clinical trials indicate that around 30% of patients have some form of pain, while 3% have severe pain at one year following hernia repair [144], [192]. The reason for such pain is not clear. There may be intraoperative factors that contribute to this pain, such as nerve and/ or tissue injury and the use of the biomaterials. In the latter context a recent study has indicated that the type of material, rigid versus smooth may affect postoperative pain and recovery after laparoscopic inguinal hernia repair [193]. There is also some evidence from trials of abdominal wall closure that absorbable suture materials cause less chronic pain when compared with non-absorbable ones [194], [195].

The aim of this study was to compare a partially absorbable, lightweight mesh with a non-absorbable, heavyweight mesh within the context of a randomised clinical trial. The primary endpoint of the study was the degree of chronic pain of any severity at the site of hernia repair in both groups at 12 months.

5.2. Patients and Methods

Ethical approval was obtained in 5 surgical units to randomise patients with an inguinal hernia to repair with a light or heavy weight mesh, using the Lichtenstein technique. Computer generated random numbers with block sizes to ensure balanced recruitment within each centre, achieved randomisation. Patients were 18 years or older and were excluded if the hernia was strangulated or irreducible or if they had previously undergone open tension free mesh repair on the same side. The study was observer and patient blinded i.e. the member of

staff conducting the postoperative assessment and the patients were unaware of the treatment allocation.

5.3. Mesh types

The lightweight or partially absorbable (PA) mesh (Figure 5.1.) used in this study was constructed of multifilament of polyprolene with additional absorbable polyglactin (Vypro 11, Ethicon). The mesh had a pore size of 4mm and weighs 82g/m at implantation and 32g/m after absorption of the polyglactin component, which usually takes 56-70 days. The heavyweight or non absorbable (NA) mesh (Figure 5.2.) used in the study had a pore size of 1mm and weighs 85g/m (Atrium).

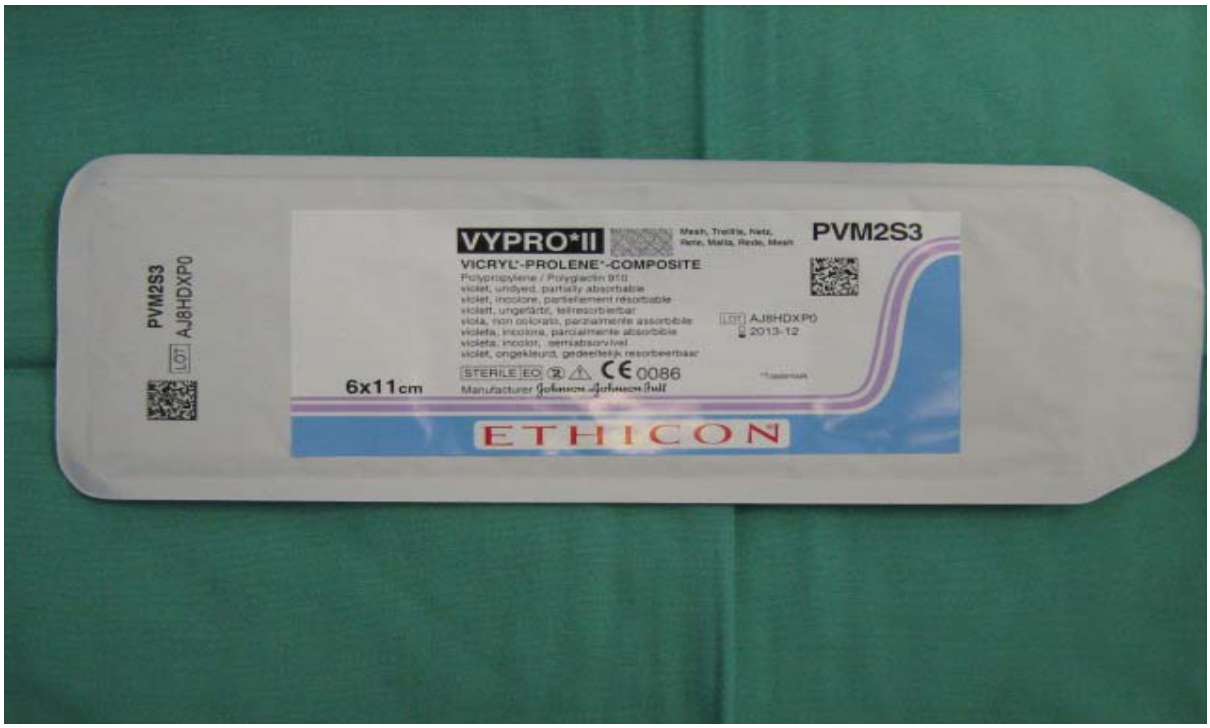


Figure 5.1. (PA) Light weight (Vypro 11)

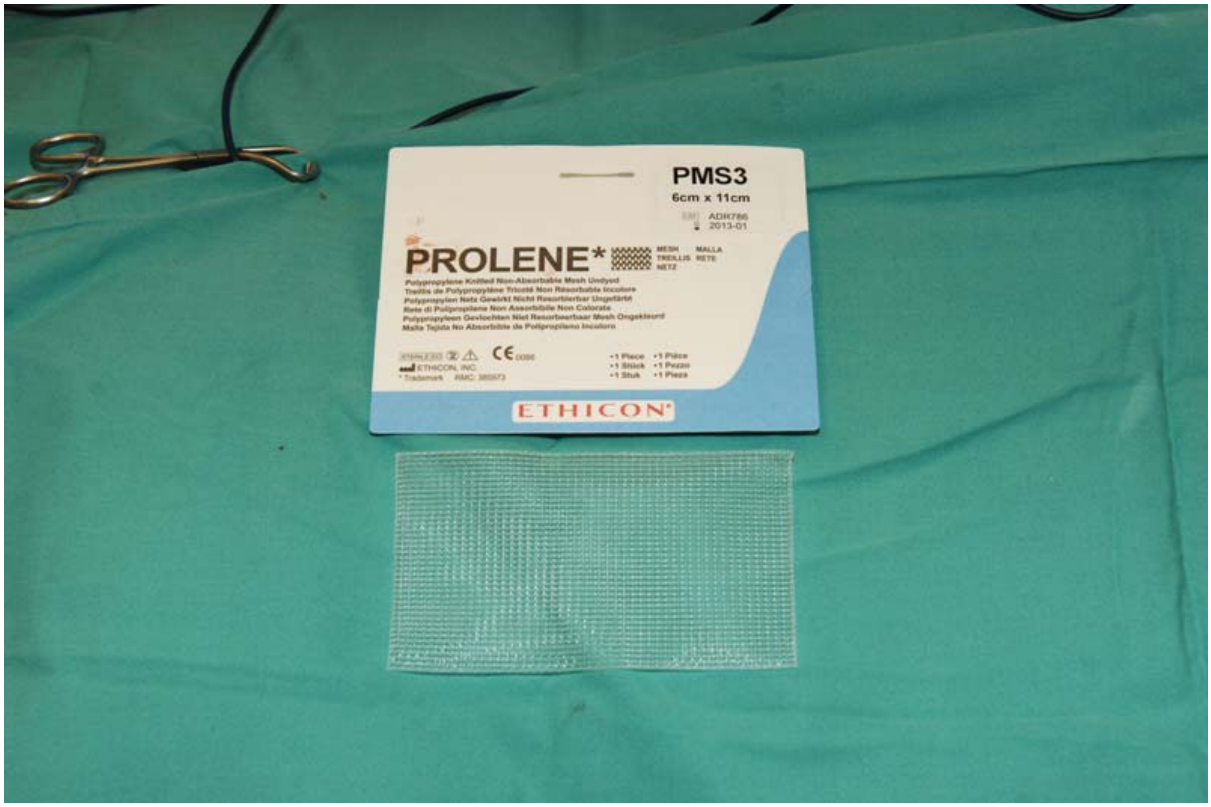


Figure 5.2. (NA) Prolene (Atrium) mesh

Preoperatively all patients had visual analogue pain scores (VAS) measured at rest and on moving and all patients completed a SF-36 questionnaire (appendix 4). At operation patients underwent a standard open tension free mesh repair (Lichtenstein technique) with a detailed record of hernia type and size, whether the nerves were identified and preserved or divided, and any adverse operative event that may have occurred. All postoperative complications were recorded and patients were telephoned with set questions at 10, 20 and 30 days postoperatively to assess wound related infection and/or any other wound problems. Those that reported a wound infection or haematoma were recalled and examined clinically. Hospital stay and time to return to work and normal activities were also recorded for all patients. Patients were sent a VAS pain scale at 1, 3 and 12 months and a modified SF-36 questionnaire. The modifications included questions on pain of any severity at the site of hernia repair (none, very mild, mild severe or very severe). Patients were also asked if the pain was present all of the time, some of the time, a little of the time or none of the time. In addition they all underwent a detailed clinical examination at 12 months looking for any evidence of chronic wound problems, testicular atrophy or development of a recurrent or contra-lateral hernia. Patients were also asked about any pain or numbness at the site of their hernia repair. If they answered in the affirmative a record of the site and distribution of both was mapped out on a diagram.

5.4. Statistical analysis

The study needed to enrol 300 patients as this was the sample size calculated to ensure an 80% power to detect a benefit to PA mesh of 15% for primary efficacy (incidence of chronic pain at 12 months: NA mesh 35%; PA mesh 20%) at 5% significance using a two-sided test. Data have been summarised using both the number and percentage in each category, or by using the mean and standard deviation when data are normally distributed, or by using the

median and inter-quartile range when data are not normally distributed. An intent-to-treat analysis has been performed, i.e., all subjects regardless of their compliance with the protocol, were included in the analysis. For efficacy analyses, patients with missing data for an assessment have been analysed using the last valid observation carried forward.

All statistical tests were interpreted at the 5% significance level (two-tailed) and 95% confidence intervals have been presented. For primary efficacy these are one-tailed, for all other parameters they are two-tailed. No adjustments for multiple testing have been performed.

5.5. Results

333 patients consented to participate in the study. Two patients were not randomised as they had a femoral hernia and 1 patient withdrew consent prior to surgery. Therefore 330 patients were randomised to surgical repair with either PA or NA mesh. Following randomisation 9 patients either withdrew consent or failed to complete their post-operative assessment. This left 162 patients in the PA group and 159 patients in the NA group. The patients in both groups were similar with respect to all pre and intra-operative parameters measured (Tables 5.5.1 and 5.5.2.). All patients had a primary hernia apart from 6 in the PA and 2 in the NA group. All these had previously undergone a sutured, non-mesh repair. The ilioinguinal nerve was identified in over 90% of patients while the genital branch of the genitofemoral nerve and the iliohypogastric nerves were identified in less than 50% of patients. Postoperative complications were similar in both groups with 6 wound infections in the PA group (3.7%) and 10 (6.3%) in the NA group.

The percentage of patients with pain, as assessed by visual analogue scores at 1 and 3 months

postoperatively, did not demonstrate any difference between the groups (Table 5.5.3. and 5.5.4). Return to normal activities was similar in both groups, taking around 10 days to return to social activities and 3 weeks to return to paid employment (Table 5.5.5.).

5.5.1. Pain at 12 months post hernia repair

Significantly fewer patients in the PA group, 39.5% versus 51.6% in the NA group, experienced pain of any severity at 12 months (difference – 12.1%; 95% CI –23%, to –1%; p=0.033). The primary end point was analysed by carrying the last observation forward and recording pain for those with a missing response as agreed per protocol in both groups. This diluted the treatment effect which otherwise was 45 (33.3%) of 135 in the PA group compared to 64 (51.2%) of 125 in the NA group (p=0.004). Analysis adjusting for divided nerves did not alter the treatment effect. Interestingly the increase in pain in the NA group was not associated with any effect on physical function. The reason for this is likely to be related to the fact that most patients in both groups had mild or very mild pain. Only 3% of patients in the PA group experienced severe or very severe pain at 12 months compared to 4% in the NA group. Testicular pain was also reported more frequently in the NA group (22.1% versus 16.3%). The descriptor of pain most commonly used for all patients was aching (64%). In patients with pain, social activity was affected in 13%, work in 22% and sexual activity in 33%. Numbness around the groin was reported in 34% of patients and thigh numbness was reported in 13.5% of patients at 12 months. This however only affected quality of life in 4.5% of patients.

5.5.2. Clinical outcome at 12 months

142 patients in both groups were examined clinically at 12 months, 3 patients died from neoplastic disease while 34 were lost to follow up. These clinical examination findings are

illustrated in Table 5.5.6. In the intent to treat population, hernia recurrence was observed more often in the PA group, 8 out of 162 (4.9%) versus 1 of 159 (0.6%), p=0.037. This was evident following repair of both direct (5) and indirect (3) hernias. Recurrence did not appear to be related to the size of the defect as measured at operation. Most of the recurrences in the PA group (5) were associated with one particular centre. The median time to recurrence was 261.5 days with a range of 163 to 339 days.

	PA group n=162	**NA group** n =159
Age in years	55.7 (16.4)	57.3 (15.8)
Male	156 (96%)	154 (97%)
BMI	25.5 (3.4)	25.7 (3.0)
Site of hernia		
Right	80 (49.4%)	86 (54.1%)
Left	82 (50.6%)	73 (45.9%)
Type of defect		
Direct		
Indirect	64 (39.5%)	51 (32.1%)
Combined	77 (47.5%)	78 (49.1%)
	21 (13.0%)	30 (18.9%)
Size of defect		
<1.5cm		
1.5 – 3 cm	27 (16.7%)	24 (15.1%)
>3cm	74 (45.7%)	68 (42.8%)
	61 (37.7%)	65 (40.9%)

Table 5.5.1. Patient and hernia characteristics (Values are mean (s.d.))

	PA group n=162	**NA group** n=159
Type of anaesthesia		
General	90 (55.6%)	94 (59.1%)
Local	64 (39.5%)	62 (39.0%)
Epidural	0	0
Spinal	8 (4.9%)	3 (1.9%)
Operation time (minutes)	42.50 (17.2*)	42.86 (16.6*)
Incision length (centimetres)	7.44 (1.9*)	7.42 (1.5*)
Identified nerves		
Ilioinguinal	145 (89.5%)	146 (91.8%)
Genital	74 (45.7%)	77 (48.4%)
Iliohypogastric	68 (42.0%)	67 (42.8%)
Divided Nerves		
Ilioinguinal	32 (19.8%)	32 (20.1%)
Genital	13 (8.0%)	16 (10.1%)
Iliohypogastric	10 (6.2%)	11 (6.9%)

Table 5.5.2. Anaesthetic and operative details, * values are mean (s.d).

	PA group n=162	**NA group** n=159	Difference (95% CI) p-value (Fishers exact test)
Pain @ 1 month Yes No	 133 (82.1%) 29 (17.9%)	 130 (81.8%) 29 (18.2%)	 0.3% (-8% to 9%) P = 1.0
Pain @ 3 months Yes No	 92 (56.8%) 70 (43.2%)	 90 (56.6%) 69 (43.4%)	 0.2% (-11% to 11%) P = 1.0

Table 5.5.3. Pain at 1 and 3 months.

VAS pain score	**PA group** (n =162) Mean (SD)	**NA group** (n = 159) Mean (SD)	**P- value ***
At rest			
Pre-operative	10.10 (17.10)	10.27 (16.36)	
1 month	8.34 (12.03)	9.67 (16.86)	0.4
3 months	5.19 (11.44)	6.63 (16.74)	0.9
When moving			
Pre -operative	17.13 (22.36)	17.92 (21.56)	
1 month	13.37 (16.68)	14.75 (20.47)	0.9
3 months	8.15 (15.07)	8.69 (17.31)	0.9

Table 5.5.4. Visual Analogue Pain Scores (VAS) at 1 and 3 months. The statistical test used was the Mann-Whitney U *.

	PA group	**NA group**	P-value (Log-rank test)
Paid work	21 (14-42) n=82	26 (10-49) n=77	0.4
Looking after house	10 (5-24) n=161	10 (4-21) n=154	0.6
Social Life	10 (5-21) n=161	14 (7-24) n=154	0.6
Sex	28 (14-365) n=161	28 (14-365) n=154	0.6
Hobbies	20 (10-40) n=161	14 (7-31) n=154	0.3

Table 5.5.5. Return to normal activities (days). Values given are medians (inter-quartile range).

	PA group (n=162)	**NA group** (n=159)	P –value (Fisher's exact test)
*Recurrence	8 (5.6%)	1(0.7%)	0.037
Contralateral hernia	2 (1.4%)	4 (2.8%)	0.684
Testicular atrophy	2 (1.4%)	0 (0%)	0.246
Wound sinus	0 (0%)	0 (0%)	-

Table 5.5.6. Clinical outcome at 12 months. * Analysis performed with respect to numbers who completed postoperative assessment.

Chapter 6: Discussion

Summary of findings of the three trials.

6.1.1. Trial 1

Chronic pain persists in most patients who report severe or very severe pain at three months after hernia repair and has a significant effect on patients' daily activities and quality of life. Of those with chronic severe pain at 3 months, 71% did not report severe or very severe pain at 2 ½ years follow up. Only 26% had severe or very severe pain, 45% claimed mild or very mild pain and 29% had no pain at all at 2 ½ years follow up. Most patients therefore, will report a reduction in severity of pain with time.

A secondary conclusion is that persistent pain is an indication of other chronic severe pain conditions.

6.1.2. Trial 2

The main conclusion from the second trial is that most people with preoperative pain attributable to their inguinal hernia will have a reduction in this pain following surgical repair. Some patients with little or no pain from their hernia are made worse by surgery.

6.1.3. Trial 3

This study explores the concept that reducing the amount of mesh left in situ after inguinal hernia repair does not reduce long term pain. Partially absorbable meshes need to be handled differently to non absorbable meshes.

Significance of findings

In the first study we found that severe or very severe pain was reported in 3% of patients at 3 months after groin hernia repair in Scotland. At an average follow up of two and half years later 25% still reported severe or very severe pain. This had profound effects on daily activities and quality of life. Only 29% of the group reported no pain while in 45% the pain had become mild or very mild. Almost half of these patients had sought treatment for their pain by visiting their GP, surgeon or pain clinic.

This is the second study that has examined chronic pain after hernia repair on a nationwide basis. In the initial Danish study looking at 1,652 patients operated on for a groin hernia over a two month period, 28.7% reported pain at one year after surgery [144]. Although 11% reported the pain to affect leisure activities only 4.5% sought or received medical treatment while 3% reported the pain to be moderate or severe [144]. In the Medical Research Council randomised trial of laparoscopic versus open groin hernia repair, 28.7% of laparoscopic and 36.7% of open patients had groin pain at one year [3]. The respective figures for severe or very severe pain were 3.8 and 2.2 %. In a subset of 379 patients operated on under the care of one surgeon from the same study and followed clinically for a median of five years, 6 (1.6%) required referral to a pain clinic for management of severe or very severe pain. In 3 of these patients the pain resolved while 2 still had mild pain and 1 died from bronchogenic cancer.

This is the first population-based study to determine what happens to patients reporting severe or very severe pain after repair of a groin hernia over a period of time. As with a previous study, the indications are that post repair pain resolves or becomes mild or very mild in the majority of patients. However, around 25% continue to have severe or very severe

pain. This is similar to that reported in a retrospective study where 30% of those with pain at three months after operation reported moderate or unbearable pain at a median follow-up of 43 months [136].

The aetiology of chronic groin pain post hernia repair is related in part to nerve injury. This is supported by the high frequency of sensory symptoms and numbness in these patients. However other factors including the role of tissue injury need to be considered. The character and distribution pattern of pain suffered by these patients is similar to that observed in athletes in groin injury where the source of pain is thought to be muscular or ligamentous injury. A third factor that needs to be considered includes the role of non-absorbable material be it sutures or mesh. While there have been no comparative studies in hernia repair, use of absorbable suture materials have consistently been shown to cause less chronic pain after abdominal wall closure when compared with non absorbable materials. The individual perception of pain is also important. Patients who develop chronic pain post inguinal hernia repair are more likely to have complained of pain preoperatively from their hernia when compared to those who have no postoperative pain. In addition our study indicates that they are more likely to suffer other chronic pain conditions when compared with the normal population. In population-based studies 27-39% of patients surveyed indicated they had back pain in the last week or month, the respective figures for patients with very mild or mild pain and severe or very severe pain in this study are 45.7% and 77.3%. An alternative explanation for the high incidence of back pain in those patients with severe pain following groin hernia repair is that this group of people may be related to placing excessive strain on their back muscles in an effort to protect their groin. Further studies on the interrelationship between chronic pain conditions in general and the psychological profile of these patients are required. The current study may underestimate the frequency of severe or very severe pain following

hernia repair in that some patients may develop this problem after the first questionnaire was sent out. However in a study by Callesen *et al* moderate or severe pain at four weeks was a significant predictor of the same type of pain at one year [141]. Therefore better or more effective postoperative pain control in the acute period following surgical repair is necessary to reduce risk of long term severe chronic pain. Despite this around one half of the patients that had moderate or severe pain at one year had none or mild pain at four weeks following surgery in their study. In a similar study where we followed 379 patients for a median of five years after groin hernia repair, 25% of patients that had chronic pain developed their pain after the one year follow up period. Most, however we found were concerned that their repair had broken down and when reassured that this was not the case their symptoms resolved. Over 2/3 of patients that complain of severe or very severe chronic pain at three months after groin hernia repair still have pain two – three years later. While the mechanism of this pain is unclear counselling patients on its probability before surgery is important. Early referral to an established pain clinic should be considered for those who develop this debilitating problem.

The second study demonstrates that most primary inguinal hernias repaired electively are painless or cause the patient only mild pain. The decision to classify mild pain as a score of less than 10 in this study was arbitrary and is lower than that suggested by some workers [17]. The findings that almost 60% of patients indicated that the hernia was painless or caused mild pain only on movement, while 80% had no pain or mild pain at rest are, therefore conservative. This remains so even if acute inguinal hernias causing severe pain are included, as they account for only 5% of all inguinal hernias treated in the region [1]. At one year follow up, patients who had no pain at rest from the hernia before the operation reported significant pain scores from the hernia repair site. Although these scores were low the finding goes some way to explaining the relatively low level of satisfaction reported by some patients following

hernia repair [3]. When asked about change in day-to-day life 1 year after hernia repair in one study, almost 30% of patients reported no change while 5% were slightly or much worse after surgery [3]. A further 12% reported that hernia repair made day-to-day life only slightly better, and 55% were much better. The presence of pain in patients who were asymptomatic from the hernia in the first place is worrying and leads one to question whether these patients should have had a hernia repair in the first instance. It may therefore be suggested that some patients, typically those that have no symptoms attributable to their hernia are made worse by surgery. The most common reason for recommending patients for repair is the risk of strangulation or incarceration. However it is known that the probability of the latter occurring is rare and is observed in only one in every 300-400 patients [151]. The cumulative risk of strangulation of an inguinal hernia at three months is 2.8% increasing to 4.5% after 2 years [152]. Moreover patients who develop an acute hernia accident may not be aware that they have a hernia and if so have sufficient co-morbidities that they are turned down for elective repair [196]. There was no association in this study between hernia type, direct or indirect or the patients' occupation sedentary or manual labour, and pain at the hernia site. Conventionally it has been thought that indirect hernias are more likely to be symptomatic and that a hernia in someone who does heavy manual labour may be an inconvenience. Indeed one may be persuaded that this patient group may be more likely to register high pain scores on moving. We did not find this to be the case. Indeed the trend in this study was for these patients to have the lowest pain scores at rest and on moving. Results from this study indicate that hernia repair has less effect than might be expected on the mild pain caused by the hernia. Pain scores at rest and moving were reduced to only about half the level before operation. Furthermore it is disappointing that there was not a significant increase in the number of patients who recorded no pain at rest or on movement at one year after the operation.

The major effect of hernia repair as seen in this study appears to be to convert those with

moderate or severe pain on moving to mild pain on moving. One of the drawbacks of this present study is that other quality of life issues such as the effect of a hernia on social or sexual activity has not been examined here. In a previous study [151], however we have shown that leisure activities were affected in only 29% of patients with an inguinal hernia, while only 13% had to take time off work because of the hernia. Further studies are needed in this area to look at these factors in more detail, particularly in those patients who report little or no symptoms from their inguinal hernia.

This study demonstrated that those patients that had most in the way of symptoms from their hernia, i.e. moderate to severe pain on moving and at rest, were most helped by surgery, i.e. their symptoms were improved. In contrast it is clear that some patients are made worse by surgery, i.e. those with little or no symptoms. Therefore further studies are necessary to precisely define the population group with an inguinal hernia that will most benefit from surgery with the least risk of postoperative pain [138], [139].

The final study shows that there is no difference in pain scores at rest and on movement between patients randomised to a (PA) partially absorbable or (NA) non absorbable mesh. There was also no difference in severe pain between these two groups. It is likely that the small differences in all types of pain reported in favour of the PA group reflected differences in mild and very mild pain in this study. This finding is in keeping with other studies where patients were less likely to feel a foreign body in their groin after inguinal hernia repair with Vypro mesh [197] . This study compared a composite lightweight mesh (Vypro) developed for incisional hernia repair, with a heavy weight polyprolene 100-110g/m mesh in inguinal hernia patients. Patients in the Vypro group had less pain on exercise and were less likely to report the feeling of a foreign body at 6 months. This study included bilateral hernias where a

different type of mesh was placed on either side and the primary outcome measure was the feeling of a foreign body at six months. One previous study has compared a rigid and smooth heavy weight polypropylene mesh following laparoscopic inguinal hernia repair in a randomised clinical trial [193]. In that study patients had less pain and better physical function during the early recovery period with the smooth mesh. The study was however underpowered with only 20 patients in each group. In addition pain scores were high and return to work and normal activities was longer than one might expect after laparoscopic hernia repair.

Severe chronic pain is a serious long-term problem that occurs after inguinal hernia repair. It has a significant negative impact on quality of life and ability to work. These effects are associated with significant healthcare costs and can persist for several years. Experimental studies indicate that the addition of polyglactin filaments to a lighter weight polypropylene mesh reduces the inflammatory reaction and formation of fibrous tissue. In addition it causes less restriction of abdominal wall movement when compared with heavy weight meshes. These findings are not consistent with the clinical results of the current study in that the patients with the lightweight mesh do not have significantly less pain at 12 months. Based on the law of La Place and maximal intra-abdominal pressures, Klinge and colleagues have calculated that a mesh with a tensile strength of 16N cm is sufficiently strong to use in repair of abdominal wall hernias [198]. This is thought to represent the physiological strength of the human abdominal wall and is significantly lower than that of most meshes. Experimental studies with the composite polyglactin and polypropylene as used in the current study show that the tensile strength at the suture fascia mesh interface is in fact in excess of 16N.

One of the disappointing results of this study was a significant increase in recurrence rates in the partially absorbable group. Subsequent investigation revealed that the reason for this was that the suture pull out force in the knitted direction of the mesh was low. This may have

caused or contributed to the high recurrence rate in the partially absorbable group. The manufacturers had stressed that suture bites of least 1cm were required with their product. Surgeons used to taking smaller bites of mesh as is routine with conventional polypropylene mesh, underestimated the consequence of inadequate fixation with Vypro 11. This may explain why most of the recurrences, 5 of 8, were observed in one particular centre. Surgeons in this centre admitted that they did not adhere to taking suture bites of at least 1cm with the PA product.

The PA mesh used in this study was among the first of its type to be investigated in a randomised clinical trial. The perceived advantage of leaving about one third of the amount of polypropylene in situ after the polyglactin component is absorbed has been exploited in other products which maintain the tensile strength of the absorbable component for a longer period (e.g. Ultrapro [199]). These products may perform better than Vypro 11 but require to be evaluated in a similar fashion. The manufacture of meshes with less polypropylene and larger pore size, 3-4mm, should also be evaluated in randomised clinical trials. The in-vitro performance of these products may not be matched by what happens in patients. New products such as polyvinylidenfluoride which have a similar weight to conventional polypropylene meshes but a larger pore size also require further careful evaluation in long term follow up studies [200]. Biological products which are thought to help stimulate ingrowth of normal human blood vessels and collagen have also had limited testing in inguinal hernia repair [201] .

One of the drawbacks of the many new products is the increased costs. Some of these products are several times more expensive than conventional polypropylene meshes. It follows therefore that a dramatic improvement in quality of life to the patients with similar or reduced recurrence rates would be required to justify their routine use in inguinal hernia

repair. While this seems unlikely, cost to the health service of a product would reduce if proven advantages resulted in increased use.

This study does not supports the concept that reducing the amount of mesh left in-situ after inguinal hernia repair reduces long-term pain. The increase in hernia recurrence in the PA mesh group warrants further research. This can be explained as a technical error, i.e. not seen if appropriate suture bites of the mesh are taken rather than a specific defect inherent in the mesh itself. We have found that the Vypro mesh must be handled differently to the standard prolene mesh. For optimum results it must be sutured with a 1cm flap to the ilioinguinal ligament and it cannot be placed on the stretch.

These results are similar to a study by Bringman et al [202]. These authors' randomised six hundred men to open Lichtenstein repair with a prolene or a Vypro 11 mesh in several different centres. Pain, recurrence and quality of life were assessed at one year post surgery. They found no statistical difference in each of the previous parameters. They concluded that the results of Lichtenstein's operation with either prolene or Vypro 11 mesh did not seem to differ significantly. Their results at three years were a little different. They found that use of the light weight mesh had improved some aspects of pain and discomfort at three years post repair [203].

This study demonstrates no clinical advantage for the use of a partially absorbable mesh in inguinal hernia repair. The significant reduction in mild discomfort observed warrants further investigation with different products in larger multi centred controlled clinical trials.

Further research

The conclusions of the previous trials raise further points for discussion and future research. In order to reduce the incidence of post herniorrhaphy pain, future research needs to address the patient with an inguinal hernia at several stages.

In order to quantify how much postoperative pain is truly related to post surgical changes, it is important to be aware of the incidence of groin pain per se, in the general population. What extent of pain experienced postoperatively by our patients is truly related to the hernia repair and what amount is indigenous or related to other factors? for example, osteoarthritis of the hip, prostate pathology. The significance of these other pathologies in contributing to postoperative pain is not widely known. These other causes of groin pain are known to increase in prevalence in the aged male population and need to be excluded. Symptoms attributable to a groin hernia by the patient may not actually be related to the groin lump and therefore it is these symptoms that will continue post repair, resulting in pain.

In a recent study by Franneby et al [211] long term postoperative pain was assessed. They found a baseline level of pain in the contralateral groin, but the level of pain was significantly higher in the operated groin. The contralateral groin was used as a control and it is important to note that it was not pain free. The baseline level of pain in the non operated non hernia side served as a reference point. Future studies should include assessment of baseline levels of pain not only in the preoperative groin but also in the contralateral side.

Studies that try to quantify a subjective emotion have faults and one of these is that the tools used to accrue information are too precise. What is the clinical significance of 5mm of pain difference on the visual analogue scale? We assume that if a difference is statistically detectable then it is clinically significant. This may not be the case. The scales we employ to detect change may be too powerful. That is they detect differences where none actually exist clinically.

Another concern of the pain scales is their reproducibility. Do scoring systems have the same numerical outcome when repeated several times over the same day by the same individual? These tools account for patient personality. That is, those with a propensity to exaggerate or remain stoical will continue to do so irrespective of how often the test is performed. These tests may not, however allow for intention tremors and other features of the elderly population that make precision tasks more difficult. This may or may not explain why older people complain of less postoperative pain. It is not clear why younger people, who are more inclined to be in work, be independent or self employed complain of more pain than their elder counterparts.

In those that have pain more precise psychological information is needed, for example, features of depression. Preoperative assessment of psychological state or traits can help in the understanding of the subjective postoperative emotion of pain.

The expectations of patients attending a surgical outpatient clinic with an inguinal hernia need to be better understood. Is reassurance of the benign nature of the lump all that patients wish or do they expect a surgical solution from the outset? Is it that those on the waiting list become more symptomatic the longer they wait? And if so, is this a reflection of the underlying pathology of the hernia or is it because their initial expectations of surgery are not

being met? When patients are placed on the waiting list for surgical repair the degree and type of pain should be assessed over time waiting for repair.

The fact that many men have minimal if any symptoms attributable to their hernia led Fitzgibbons et al [138] to design a multicentred, randomised controlled trial to determine if watchful waiting was an acceptable alternative to surgical intervention in patients with minimal or no symptoms from their hernia. Over 750 patients were enrolled to either standard Lichtenstein tension free open mesh repair or to watchful waiting for a period of 2 years. The end points at two years were symptoms including pain. They concluded that watchful waiting was an acceptable alternative for patients with minimally symptomatic hernias [212]. Delaying surgery until symptoms increase is safe as acute accidents occur rarely, they conclude. However in a similar study by O'Dwyer et al [139] surgery was compared with wait and see policy in asymptomatic hernia patients. In 160 patients, aged 55 years or older the authors were surprised at the high number of patients crossing over from watchful waiting to surgical intervention because of an increase in symptoms. Postoperative pain and symptoms were no different in either group at 12 months post surgery. They concluded that repair of an asymptomatic hernia does not affect the long term incidence of chronic pain and may be beneficial in improving overall general health. Clearly there is a point that varies with each individual that decides benefit of surgical intervention in terms of reduction in symptoms with little or no postoperative pain.

Most of our studies are relatively short term. It would be worthwhile to follow patients for longer in order to see what happens to those initially reporting chronic severe pain. If they are followed long enough will postoperative pain eventually disappear? What happens to those patients with chronic postoperative pain that are referred to the pain clinic? The average general surgeon looses track of their patients once they are referred to the chronic pain

speciality. Chronic pain specialists have a better understanding and knowledge of the longterm outcome of these patients. Hernia specialists should liaise closely with chronic pain specialists in order to fully appreciate the longterm outcome of these patients.

APPENDIX 1

QUESTIONNAIRE (MODIFICATION OF SF36)

1. During the last week how much of the time have you had pain in your groin (the site of the hernia operation)

All of the time

Most of the time

Some of the time

A little of the time

None of the time

2. How bad has the pain in your groin (the site of the hernia operation) been in the past week?

No pain

Very mild

Mild

Severe

Very severe

3. Have you experienced any numbness in your groin (the site of your hernia operation) in the last week?

Not at all

Slightly

Moderately

Quite a bit

Extremely

4. Have you experienced any numbness down your thigh on the side of your hernia operation in the last week?

Not at all

Slightly

Moderately

Quite a bit

Extremely

5. Have you experienced any pain in your testis on the side of your hernia operation in the last week?

All of the time

Most of the time

Some of the time

A little of the time

None of the time

6. Is the pain you experience

Intermittent

Continuous

Present at rest

Brought on by activity

APPENDIX 2

QUESTIONNAIRE (BPI) AND ABOVE

1. Please tick the box number that best describes how, during the past 24 hours **PAIN** has interfered with your;

Does not ***Completely***

Interfere ***Interferes***

A.General Activity

0	1	2	3	4	5	6	7	8	9	10

B. Mood

0	1	2	3	4	5	6	7	8	9	10

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10

D. Normal Work (including work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10

F. Sleep

0	1	2	3	4	5	6	7	8	9	10

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10

2. What words best describe your pain?

Aching	Prickling
Burning	Pulling
Cutting	Shooting
Drilling	Sickening
Electric	Stabbing
Gnawing	Tender
Itching	Throbbing
Pounding	Tingling

3. Have you been to the GP with your pain? Yes No

Have you been to your surgeon with the pain? Yes No

Have you been to a pain clinic with your pain? Yes No

Have you had another operation on your hernia? Yes No

4. Are you taking any medication for pain relief?

If Yes, please specify name dosage

5. Do you or have you suffered from other chronic problems, such as

Backache yes no

Headache yes no

Irritable Bowel yes no

Other (please specify) yes no

APPENDIX 3

(VISUAL ANALOGUE PAIN SCALES)

1. Please put a vertical (straight up and down) line through the scale from 0 to 100 corresponding to how much pain you have from your groin (the site of the hernia operation) **TODAY.**

The scale goes from 0 (no pain) to 100 (worst pain imaginable).

On the scale below please mark the amount of pain you have at **REST** today

0 …….100

No pain *Worst pain imaginable*

2. On the scale below, please mark the amount of pain you have on **MOVING** today.

0……100

No pain *Worst pain Imaginable*

APPENDIX 4

STUDY FLOW CHART

	IN-PATIENT VISIT 1	TELEPHONE ASSESSMENT DAYS 10, 20 AND 30	POSTAL ASSESSMENT 1, 3 AND 12 MONTHS	CLINIC VISIT 2 @ 12 MONTHS
Inclusion/exclusion	X			
Demographics	X			
Medical history	X			
Prior/concomitant medication	X			X
Patient consent	X			
SF-36 and modified hernia questions	X**		X	
Visual analogue scale	X		X	
Intra-operative details/Surgery OT form	X			
Mesh handling questionnaire*	X			

Adverse events	X	X	X	X
Wound assessment telephone questionnaire		X		
End of study form	X	X	X	X
Annual follow-up form				X

*Only to be carried out on the first 10 patients per study group per surgeon.

X** At this time-point **ONLY** questions 1-10 of the SF36 should be given pre-operatively.

SF36 PRE-OPERATIVE QUESTIONNAIRE

GENERAL HEALTH (please circle)

1. In general would you say your health is

Excellent (1) Very Good (2) Good(3) Fair(4) Poor(5)

2. Compared to one year ago, how would you rate your health in general now?

Much Better (1) Somewhat Better (2) About the Same (3) Somewhat Worse (4) Much Worse (5)

HEALTH AND DAILY ACTIVITIES (please circle)

3. Does your health limit you in any of these activities of a typical day?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities (running, lifting heavy objects)	1	2	3
Moderate activities (hovering, golf)	1	2	3
Lifting groceries	1	2	3
Climbing several flights of stairs	1	2	3
Climbing one flight of stairs	1	2	3
Bending, kneeling or	1	2	3

stooping			
Walking more than a mile	1	2	3
Walking half a mile	1	2	3
Walking a 100 yards	1	2	3
Bathing or dressing	1	2	3

4. During the past four weeks, have you had any of the following problems with your work or other daily activities as a **result of your physical health**?

1. Cut down on the time you spend on work or other activities Yes (1) No (2)
2. Accomplished less than you would have liked? Yes (1) No (2)
3. Were limited in the kind of work or other activities? Yes (1) No (2)
4. Had difficulty performing the work or other activities? Yes (1) No (2)

5. During the past four weeks have you had any of the following problems with your work or other regular daily activities as a **result of any emotional problems**?

1. Cut down on the amount of time you spend on work or other activities Yes (1) No(2)
2. Accomplished less than you would have liked Yes(1) No (2)
3. Did not do work or other activities as carefully as usual Yes (1) No(2)

6. During the **past four weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with families, friends or neighbours? **(please circle)**

Not at all (1) Slightly (2) Moderately (3) Quite a bit (4) Extremely (5)

7. How much bodily pain have you had over the **past four weeks**? **(please circle)**

None (1) Very mild (2) Mild (3) Moderate (4) Severe (5) Very severe (6)

8. During the **past four weeks** how much did pain interfere with your normal work? **(please circle)**

Not at all (1) A little bit (2) Moderately (3) Quite a bit(4) Extremely(5)

9. The following questions are about how you feel and how things have been with you **during the last month,** please **circle the number** that best describes how you have been feeling.

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	1	2	3	4	5	6

Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and low?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6
Has your health limited your social activities?	1	2	3	4	5	6

HEALTH IN GENERAL

10. Please choose the answer that best describes how **true** or **false** each of the following statements is for you

1. I seem to get ill more easily than other people

   Definitely true (1) Mostly true (2) Not sure (3) Mostly false (4) Definitely false (5)

2. I am as healthy as anyone I know

   Definitely true (1) Mostly true (2) Not sure (3) Mostly false (4) Definitely false (5)

3. I expect my health to get worse

   Definitely true (1) Mostly true (2) Not sure (3) Mostly false (4) Definitely false (5)

4. My health is excellent

   Definitely true (1) Mostly true (2) Not sure (3) Mostly false (4) Definitely false (5)

VISUAL ANALOGUE SCALE (VAS)

Please put a vertical (straight up and down) line through the scale from 0-100 corresponding to how much pain you have from your hernia **TODAY**. The scale goes from 0 (no pain) to 100 (worst pain imaginable).

1. On the scale please mark the amount of pain you have at **REST** today

0 100

---

2. On the scale below please mark the amount of **ON MOVING** today pain you have

0 100

VISIT 1

INCLUSION CRITERIA

1. Primary or recurrent uncomplicated inguinal hernia yes no
2. Unilateral hernia yes no
3. Elective surgery only yes no
4. Male and female patients yes no
5. Patients able to comply with follow-up yes no
6. Patients willing to give signed consent yes no

Informed consent has been signed and dated on .....

EXCLUSION CRITERIA

1. Patients in other investigational drug/medical device studies yes no
2. Patients with strangulated, irreducible inguinal hernia yes no
3. Patients with a previous hernia mesh repair yes no
4. Patients under the age of 18 years yes no

If the answer to any of these questions is ***yes*** the patient is **not** eligible for the study.

DEMOGRAPHIC DATA

1. Date of birth ……
2. Gender male female
3. Height ……..m
4. Weight ……Kg

EMPLOYMENT STATUS

1. Full-time
2. Part-time
3. Self-employed
4. Retired
5. Not employed

OCCUPATIONAL TYPE: DEFINE LEVEL OF WORK

1. Largely sedentary work
2. Predominantly sedentary
3. Active work
4. Essentially always on feet
5. Very labour intensive
6. Not working/retired

HOME ACTIVITIES/HOBBIES

Activity type: define level of activity during a normal day

1. Largely sedentary (Sit down > 75%)
2. Fairly sedentary (Sit down 50-75%)
3. Moderately active (Sit down 25-50%)
4. Very active (Sit down 10-25%)
5. Always on feet (Sit down <10%)

RISK FACTORS

Please review the patient's medical history and record the presence of any risk factors as noted below.

1. Diabetes mellitus
2. Chronic obstructive airways disease
3. Renal insufficiency
4. Malnutrition (serum albumen <30g/l)
5. Corticosteroid therapy

MEDICAL HISTORY

Please review the patient's medical history and record details of any co-existent disease. Enter the system code from the list below and provide details in the *specific illness/disease* section.

1. Endocrine
2. Skin
3. CNS
4. Respiratory
5. Genito-urinary
6. Gastro-intestinal
7. Cardiovascular
8. Musculoskeletal
9. Other (please specify below)

SYSTEM (code from options above)	SPECIFIC ILLNESSES/DISEASE

VISIT 1 AND 2.

PRIOR AND CONCOMITANT MEDICATION.

This list should be added to as the patient progresses through the study.

Any medication not on the list should be added in the free space at the bottom.

Medication	Yes
Temazepam	
Omnopon	
Atropine	
Hyoscine	
Scopolamine	
Omnoscop	
Morphine	
Propofol	
Suxamethonium	
Atracurium	
Pancuronium	
Thiopentone	
Fentanyl	
Nitrous Oxide	
Halothane	
Enflurane	
Lignocaine	

Medication	Yes
Cephalosporin	
Penicillin	
Gentamicin	
Codeine	
Paracetamol	
Cocodamol	
Codydramol	
Dihydrocodeine	
Temgesic	
Metoclopramide	
Prochlorperazine	
Cyclizine	
Domperidone	
Lactulose	
Fybogel	
Senna	
Coproxamol	

Bupivicaine			Diclofenac	
Diuretics			Ibuprofen	
Ranitidine			Aspirin	

SURGERY

POST-OPERATIVE DETAILS

1. Has there been any untoward bleeding?
2. Has there been urinary retention requiring catheterisation?
3. Is there evidence of seroma formation?
4. Has there been an immediate recurrence of hernia?
5. Other

Ensure that the Surgery (OT) form has been completed

Ensure that intra-operative mesh evaluation form has been completed (if appropriate)

TO BE COMPLETED ON DAY OF DISCHARGE

Date of Admission .....

Date of Surgery .....

Date of Discharge .....

UNSCHEDULED INTERIM VISIT

WOUND INFECTION

Each unscheduled interim visit for wound infection only should be documented here

FIRST UNSCHEDULED INTERIM APPOINTMENT

Date of 1st post-discharge clinic attendance .....

Is the wound clinically infected? Yes No

If Yes, please complete an adverse event form

SECOND UNSCHEDULED INTERIM APPOINTMENT

Date of 2nd post-discharge clinic attendance .....

Is the wound clinically infected? Yes No

If Yes, please complete an adverse event form

THIRD UNSCHEDULED INTERIM APPOINTMENT

Date of 3rd post-discharge clinic attendance .....

Is the wound clinically infected? Yes No

If Yes, please complete an adverse event form

AT FINAL (12 MONTH) VISIT

There were no clinical wound infections for this patient Yes No

.

ADVERSE EVENTS FORM

Adverse event	Onset date	Intensity 1.Mild 2.Moderate 3.Severe	Serious 1.Yes 2. No	Action taken 1.None 2.Medical 3.Surgical	Outcome 1.Resolved with treatment 2.Resolved spontaneously 3.Ongoing at study end 4.Death	Stop date	Relationship of event to device 1. Probable 2. Possible 3. Unlikely 4. Not related
1.							
2.							
3.							
4.							

Comments

VISIT 2 12 MONTHS (OR EARLIER WITHDRAWL)

EVENTS OVER LAST 12 MONTHS RELATED TO HERNIA REPAIR

1. Surgery for recurrence Yes No
2. Any surgery related to hernia repair? Yes No

SYMPTOMS RELATED TO HERNIA REPAIR

1. PAIN Yes No

*If **no** complete the visual analogue scale form*

*If **yes** please mark distribution on diagram*

If yes, is the pain .....Intermittent Yes No

Continuous Yes No

Present at rest Yes No

Brought on by activity Yes No

What word best describes the pain?

Aching Shooting

Throbbing Electric

Gnawing Tingling

Burning Itching

Stabbing

Does the pain affect any of the following,

1. Work or daily activities Yes No
2. Social activities Yes No
3. Is the patient sexually active? Yes No

4. If Yes, does the pain affect sexual activity Yes No

Mark the amount of pain ***at rest*** on the visual analogue pain scale

Mark the amount of pain ***on movement*** on the visual analogue pain scale

2. NUMBNESS Yes No

If ***yes*** mark distribution on diagram

Does this affect you in any way? Yes No

If ***yes*** please expand

FINDINGS ON EXAMINATION

1. Recurrence Yes No
2. New contra-lateral hernia Yes No
3. Testicular atrophy Yes No
4. Wound sinus Yes No
5. Allodynia Yes No

DIAGRAM TO ILLUSTRATE DISTRIBUTION OF PAIN

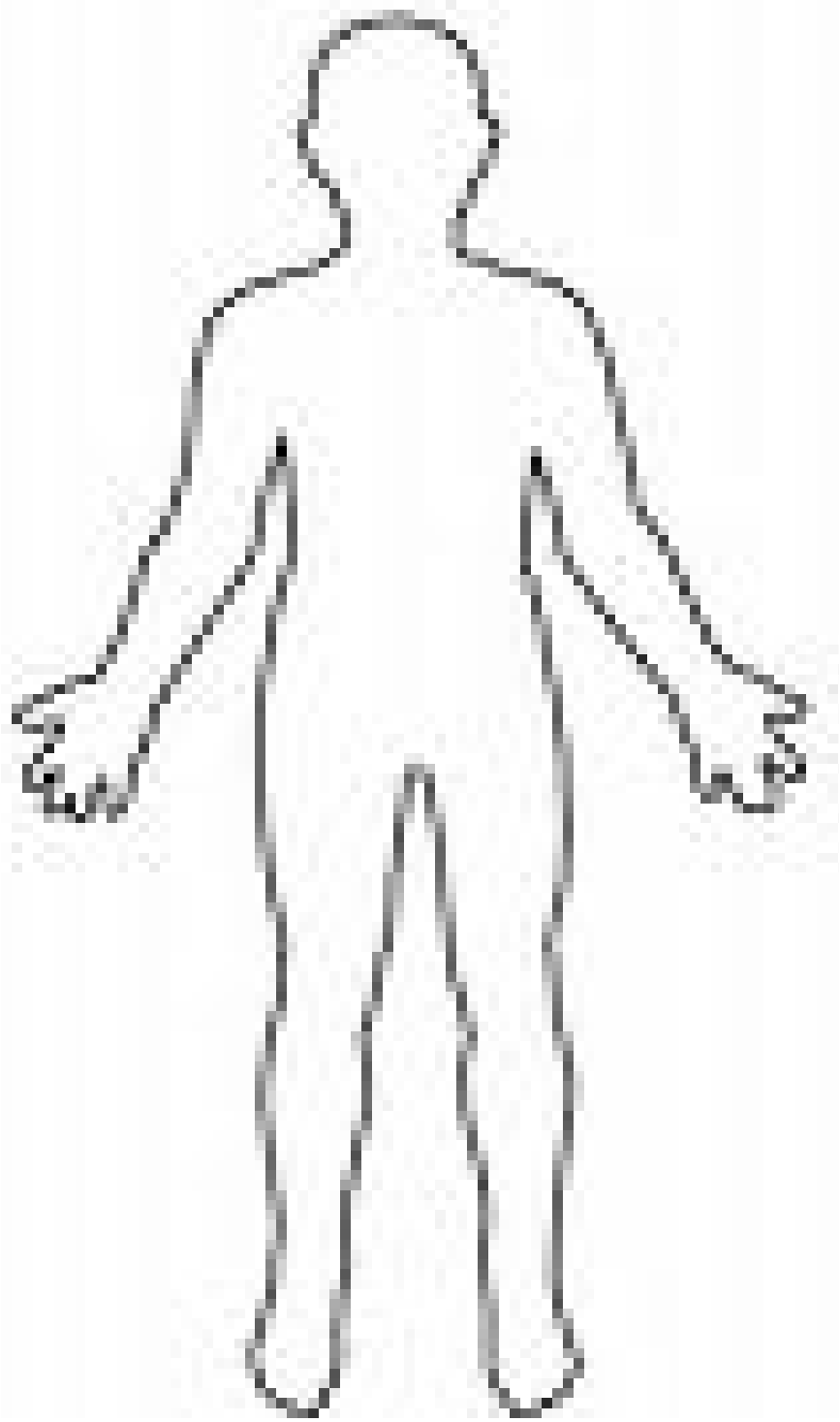
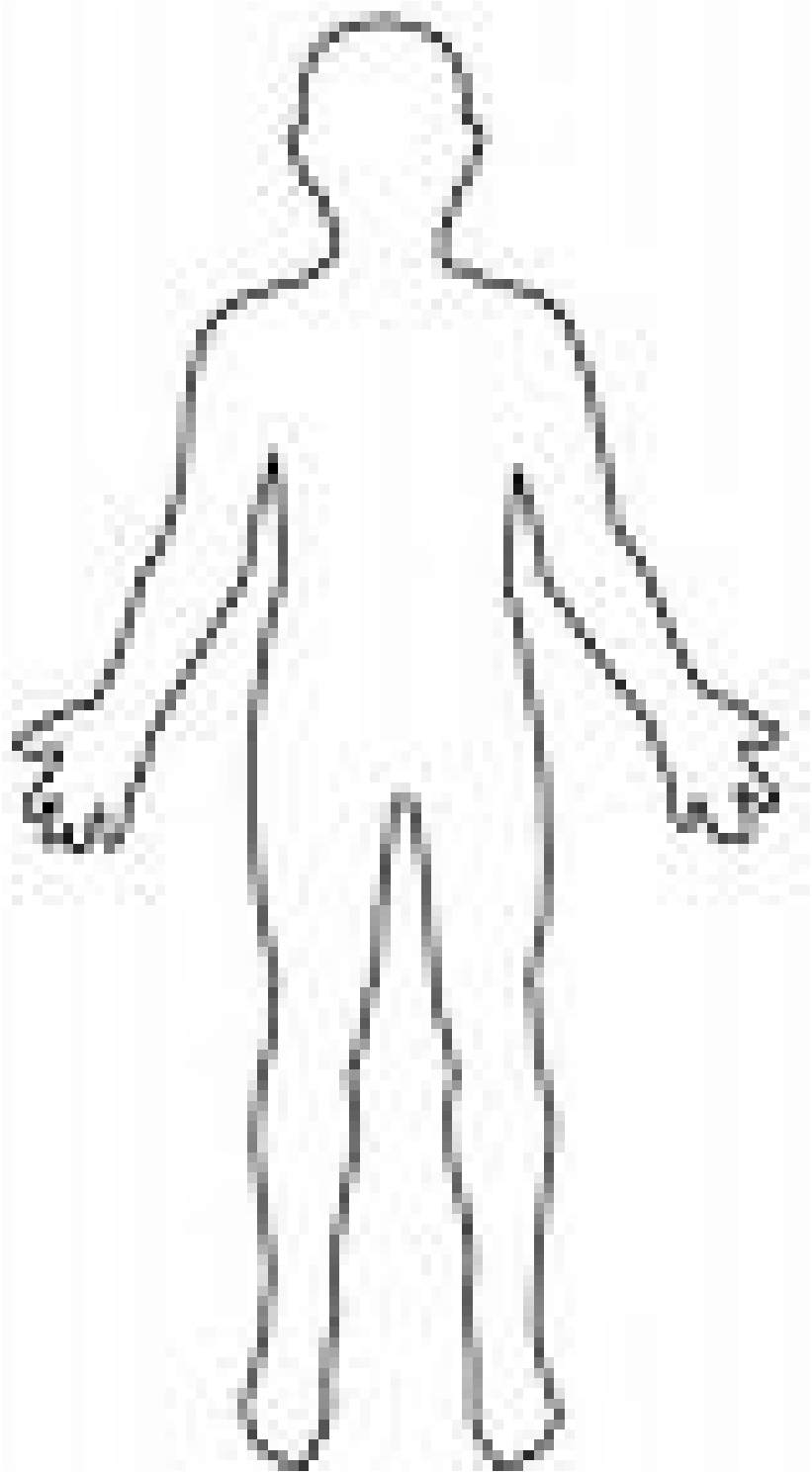


DIAGRAM TO ILLUSTRATE DISTRIBUTION OF NUMBNESS



VYPRO 11 for inguinal hernia repair

Patient consent form

Have you read and understood the patient information leaflet and what will be required of you if you take part? Yes No

Have you had an opportunity to ask questions and discuss this study?
Yes No

Have received satisfactory answers to your questions?
Yes No

Do you understand that your participation in the study is voluntary and that you may withdraw from the study: Yes No

-at any time

- without having to give a reason for withdrawing

- without affecting your future medical care

Do you agree to allow authorised trial personnel to check trial data against your medical records for accuracy, on the understanding that any personal information will be treated in the strictest confidence? Yes No

Do you agree to take part in this study? Yes No

Who explained this study to you?

Dr/Miss/Mr…….

Patient's signature…….. Date…….

Please print name…….

Investigator's Signature……..
*The patient **MUST** sign **AND** date this form **PERSONALLY.***

VYPRO™ II for Inguinal Hernia Repair

Information Form for Patient's Medical Records

This patient has agreed to participate in the above trial and written informed consent was obtained prior to surgery. In order to ensure the timely recording of data this form should be placed in the front of the patient's medical notes. It is intended as an aide memoire for participating centres and will not be returned to the sponsor.

Patient Surname _____

Patient First Name: _____

Patient Hospital No: _____

Patient Trial No: | | | | | | |

Date of Surgery: | | | | | | | | |

Investigator Name: _____

This patient will attend an out-patient clinic at approximately 12 months after the date of surgery. In the interim period between discharge and 12 months it would be appreciated if any wound infections, hospital admissions or unexpected adverse events were reported to the Investigator as soon as possible

Thank you.

West Glasgow Hospitals

WESTERN INFIRMARY
DUMBARTON ROAD
GLASGOW G11 6NT

TEL: 0141 211 2425
FAX: 0141 211 2861

Protocol CT-VYP II-001-00

A Study of Two Meshes (VYPRO™II and Atrium™) for Inguinal Hernia Repair

INFORMATION FOR FAMILY DOCTOR

Patient Surname..... Patient Hospital No.....

First Name ..... Trial ID No | | | | | |

Date of Birth .....

Dear Doctor

Your patient, while an in-patient for surgical treatment of an inguinal hernia, consented to take part in the above study (see attached Patient Information Leaflet) and was randomised to one of two treatment groups:

1. Repair using VYPRO™II Mesh
2. Repair using Atrium™ Mesh

He/she has been investigated and admitted for surgery in the usual manner. We will arrange any post-operative follow-up clinics, which will not involve you in extra work.

Your patient has been asked to contact the Investigator if he/she develops a wound infection post-operatively. If, however, you are in contact with the patient during the first post-operative year and the patient reports any adverse events (including infection) to you which may or may not be related to their inguinal hernia surgery I would greatly appreciate you reporting this to me (contact details below).

I have enclosed a copy of the Patient Information Leaflet that outlines the study. If you have any queries regarding the study please contact:

Name: .....

Position: .....

Address: .....

.....

.....

Notification of Patient Randomisation

Please complete this form for each patient randomised then fax immediately to the number below:

FAX Number: +44 (0) 131 442 5648

After faxing, please place this form in the plastic pocket provided in the Study File

TRIAL ID CT – VYP II – 001 – 00 (VYPRO™ II for Inguinal Hernia)

PATIENT ID [ ][ ] [ ][ ][ ]

Centre No Patient No (from Randomisation Envelope)

DATE OF SURGERY [ ][ ] [ ][ ] [ ][ ]

Day Month Year

Signature of Sender: _____

UK sites only: please ensure that the Patient Contact Details have also been faxed to the Glasgow centre co-ordinating the Telephone Questionnaires

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