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REVIEW ARTICLE

Management of persistent postsurgical inguinal pain

Mads U. Werner

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Abstract
Purpose Severe persistent pain is a major postsurgical complication affecting 2–4 % of patients following inguinal hernia repair and may cause critical physical and socioeconomic disability. This review introduces relevant criteria and analyses the current evidence base underlying recommended management strategies.
Results Development of persistent postsurgical pain (PPP) following inguinal hernia repair cannot automatically be considered to follow a simple trajectory from acute to chronic pain. Surgical management comprising neurectomy with or without meshectomy was described in 25 studies. Local anesthetic blocks, pharmacological management, and treatment with sensory stimulation methods were presented in seven studies. In spite of shortcomings, the data on surgical management demonstrate that neurectomy with or without mesh removal may provide long-lasting analgesic effects in most patients with severe PPP following inguinal hernia repair. The evidence base for other management methods is still fragile, although promising results appear in the neuromodulation studies.
Conclusions There is a need for improved study designs and, launching of large multicenter collaborative studies supplying the necessary long-term data for recommendation of future management strategies.

Keywords Analgesics · Inguinal hernia repair · Local anesthetic nerve block · Neuromodulation · Persistent postsurgical pain · Surgical techniques

M. U. Werner (✉)
Multidisciplinary Pain Center, Neuroscience Center, Rigshospitalet, Copenhagen University Hospitals, Blegdamsvej 9, 2100 Copenhagen, Denmark
e-mail: mads.u.werner@gmail.com

Introduction

One of the most conspicuous and serious outcomes after inguinal hernia repair is persistent pain. The development of severe persistent postsurgical pain (PPP) after this procedure is seen in 2–4 % [1] affecting an estimated number of 3,000 to 6,000[1] individuals each year in Germany. An overwhelming number of publications are available reflecting the interest in this topic [2], but at least to the author, navigation in the field may require quite an effort. The present article is not an attempt to perform a systematic review, but rather to present a comprehensive overview of the topic.

Defining persistent postsurgical pain

The criteria for PPP are important tools for anchoring and tailoring research strategies and as adjuncts in evaluation of research papers. The first definition containing operational criteria was proposed by Macrae and Davies in 1999 [3] and further expanded 2001 [4]. Additional minor improvements were presented in 2010 [5] and 2012 [6], mainly in respect of the duration of PPP postsurgery and of PPP induced by surgical implants. Recently, upgraded criteria for PPP have been suggested [2, 7], as presented in Table 1. Some of these criteria are particularly important for a relevant discussion of PPP following inguinal hernia repair [1] and a detailed discussion follows below.

The *first* criterion (Table 1) denotes a temporal and causal relationship with the surgical procedure that in many cases are very obvious, but pain and discomfort are not at all infrequent findings presurgery [8]. In these circumstances and in order to qualify as PPP, it has been suggested that a significant increase

[1] 2,000 inguinal hernia repairs per year per million inhabitants; population in Germany, 80 million.

Table 1 Suggested updated criteria for persistent postsurgical pain [7]

1. The pain develops after a surgical procedure or increases in intensity after the surgical procedure.
2. The pain should be of at least three to six months' duration and significantly affect the health-related quality of life (HR-QoL).
3. The pain is either a continuation of acute post-surgery pain or develops after an asymptomatic period.
4. The pain is either localised to the surgical field, projected to the innervation territory of a nerve situated in the surgical field, or referred to a dermatome (following surgery in deep somatic or visceral tissues).
5. Other causes of the pain should be excluded, e.g. infection or continuing malignancy in cancer surgery.

in pain intensity is required, preferably accompanied by a change in distribution or character of the pain [7].

The *second* criterion states the pain should be of at least 3 or probably better 6 months' duration after surgery to allow some of the mesh-related inflammatory responses to subside [2]. The pain should significantly affect the activities of daily living including health-related quality of life (HR-QoL). Pain during sexual activity due to either dysejaculation or mechanical action on the genital region or the groin, is a significant source of deterioration of HR-QoL [9, 10].

The *third* criterion questions the development of PPP in terms of an automatic trajectory from acute to chronic pain [1, 7]. Obviously, one of the most consistent predictive factors of PPP is high-intensity, acute postsurgical pain indicating a close correlation between acute and persistent pain [6]. One of the first comprehensive nationwide questionnaire studies (n= 1,170) 1 year after open inguinal hernia repair, demonstrated that 17 % experienced physical constraints during work or leisure activities, probably as a consequence of chronic groin pain [11]. In addition, 20–32 % experienced groin pain during dynamic testing conditions, e.g., standing up, climbing stairs, sitting, or getting up from a chair. These restrictions in physical functioning are in agreement with results from a number of inguinal hernia repair studies [12–14]. In a follow-up study 6 years after the inguinal hernia repair, in the same patients from the nationwide questionnaire study [11], 75 % had less pain, while only 25 % had the same pain intensity level or higher [15]. The PPP-related impact on ADL-functions decreased from 17 % at the 1-year follow-up to 6 % at the 6-year follow-up and thus it is reasonable to assume that there is a time effect, i.e., the longer the time from the primary injury the lower the pain intensity and impact on ADL-functions. But, very interestingly the data indicated that only 15 % of the patients with pain/impaired ADL-functions belonged to the same category of pain intensity (none, light, moderate, severe) both at the 1- and 6-year follow-up. In other words, of the 30 % (n=59/174) experiencing moderate to severe intensity pain at the 1-year follow-up, only 16 % (n=10/59) of these experienced the same intensity of pain at the 6-year follow-up. At the 6-year follow-up, 10 % (n=18/174) experienced moderate to severe intensity pain. Obviously, the limited number of patients with pain and functional impairment at the 6-year follow-up precludes a firm statistical conclusion, but it would seem that a change in phenotype may occur with time. A recent, very interesting study with 6-month and 5-year follow-ups in 645 inguinal hernia repair patients substantiates these findings, however with a more detailed methodology [16]. In this study, 33 patients reported chronic pain at 6 months but no pain after 5 years. Chronic pain was recorded in 16 patients after both the 6-month and 5-year follow-up. In 36 patients, chronic pain was recorded after 5 years but *not* after 6 months. These data indicate that more than two-thirds of the PPP patients after inguinal hernia repair develop chronic pain with a *delayed* onset! Thus, development of PPP cannot automatically be considered to follow a direct trajectory from acute to chronic pain. Several explanations may be speculated upon. *First*, nerve damage sometimes is associated with a late onset of neuropathic pain symptoms. Indeed, neuropathic pain components are considered a major contributor to PPP, particularly following inguinal hernia repair [1, 17, 18]. *Second*, partial dehiscence or dislocation of the inguinal mesh may lead to PPP after a pain-free postsurgical period. Some authors, however, do not consider this true PPP since it may rather reflect a mechanical complication following surgery [6, 7]. However, if the postsurgical examination, usually performed within 3 months of surgery, does not indicate any need for surgical re-exploration, and if the pain persists, the most reasonable alternative would be to term the condition PPP, bearing in mind that this does not exclude the future possibility of corrective surgery [1, 7]. *Third*, in surgical procedures, nonspecific and beneficial short-lived effects may be prominent [19] and the immediate period postsurgery has, in this respect, been called the "honeymoon period" [7, 20]. *Fourth*, although quite speculative, reinstatement of nocifensive behavior has been observed in rodents following a deep tissue injury. Several weeks after complete recovery of the injury, administration of naltrexone, an inverse μ-opioid receptor agonist, leads to re-instatement of tactile hypersensitivity and pain-behavior [21, 22]: a phenomenon called demasking of latent sensitisation. During the resolution of the injury, endogenous receptor activity successively enhances pain inhibitory signaling. This upregulated, tonic activation of endogenous opioid receptors seems responsible for counterbalancing the latent sensitisation, persisting beyond the resolution of the injury. Administration of naltrexone leads to blockade of the endogenous opioid system and demasking of latent sensitisation: a putative mechanism for development of persistent pain. Translational research in humans has hitherto been negative [23], but recently an analogous mechanism has been uncovered in man, albeit only with use of very high doses of naloxone (Pereira et al. submitted 2014).

The *fourth* criterion indicates that the pain in PPP patients is commonly located to an area at or near the surgical field, but location may depend on the surgical approach, i.e., open or

endoscopical [24]. Sensory abnormalities in the surgical areas have been demonstrated, across a number of different surgical procedures [25–27]. Interestingly, *all* subjects following inguinal hernia repair, both pain-patients and pain-free controls, demonstrate increased tactile and thermal thresholds on the surgical side compared to the nonsurgical side, indicating development of a neuropathy in all subjects postsurgery [13, 26, 28]. Detailed sensory analyses in addition reveal augmented *hyposensitivity* to tactile and thermal stimuli, and augmented *hypersensitivity* to noxious mechanical stimuli in PPP inguinal hernia repair patients compared to nonpain operated controls [26, 28]. The hyposensitivity to thermal stimuli in the skin may represent a neuropathic pain component, while the hypersensitivity to noxious mechanical stimuli, generated from deeper somatic tissues, may indicate an inflammatory pain component [7]. These pathophysiological considerations are very much in agreement with clinical classifications of PPP following inguinal hernia repair [2, 29–31]. The distribution of the "classical" neuropathic pain, related to nerve discontinuity, partial deafferentiation, or entrapment, may reach beyond the surgical field, as demonstrated in laparoscopic inguinal hernia repair surgery, not infrequently leading to diagnostic ambiguities [1, 7, 24, 32].

Surgical management

A comprehensive review of 25 studies [29, 31, 33–55] in the surgical management of PPP following inguinal hernia repair is presented in Table 2 (n=1,365). The primary surgical procedure associated with PPP was an open approach in 93 % (n=1,268) and a laparoscopic approach in 7 % (n=97) of the cases. Seven studies included examination and investigation of the patient by a multidisciplinary team, pain management center, or a pain specialist [29, 34, 39, 43, 46, 51, 55] prior to the exploratory surgery. Thirteen studies [31, 34, 36, 38, 41, 42, 44–47, 49, 50, 55] reported the use of peripheral nerve blocks or paravertebral blocks before surgery. In three studies [38, 41, 46], the success of diagnostic blocks was a prerequisite for neurectomy, vis-á-vis three studies [42, 44, 47] where failure of diagnostic or therapeutic blocks was confirmed in all patients prior to surgery! Among the two, the positive block studies, one interesting study [46] used a comprehensive presurgery workup with imaging techniques (CT, MRT, and ultrasound scans), placebo-controlled blocks, and evaluation of blocks during resting and dynamic conditions, while one study [41] used EMG-measurements of the pyramidalis muscle in order to confirm specific involvement of the ilioinguinal nerve.

In the exploratory surgery, an open approach was used in 20 studies [29, 31, 33–41, 43, 45, 47–53] (Table 2), a laparoscopic approach in two studies [46, 55], and a combined approach in three studies [42, 44, 54]. All studies included resection of the genitofemoral (GFN; main trunk or genital branch), iliohypogastric (IHN), ilioinguinal (IIN), or lateral femoral cutaneous (LFCN) nerves, and, comprised open selective/tailored neurectomies [31, 33–42, 44, 45, 47–50, 52–54], open triple neurectomies [29, 39, 43], open extended triple neurectomies [51], endoscopic retroperitoneal neurectomy [46], or laparoscopic retroperitoneal triple neurectomies [55]. Mesh removal was performed in 11 studies, either complete [31, 36, 40, 42, 44, 47, 48, 52–54] or partial [50, 54]. A new mesh was implanted in five studies [31, 42, 44, 47, 52]. The postsurgery follow-up duration was not reported in three studies [33, 34, 38] but in the remaining 22 studies the weighted mean (SD) follow-up[2] was 51 weeks (3 weeks) with a range of 4 to 486 weeks [49, 51].

The follow-up methods were clinical visits, phone-questionnaires, and mail-questionnaires in 20 studies [29, 31, 35–37, 39, 40, 43–55], while five studies [33, 34, 38, 41, 42] did not provide any information on this issue. Thirteen studies [29, 33–36, 38–44, 51] did not present quantitative data on the pain outcomes. In the remaining 12 studies [31, 37, 45–50, 52–55], the outcomes assessed were pain scores [29, 33–36, 38–44, 51], pain-related impairment of functional performance [37, 46, 48, 53], pain during sexual activity [48, 50, 53], quality of life [45], and analgesic requirement [46]. Figure 1 illustrates the improvement in pain outcome for each study indicated as ratios (number of patients with improved scores divided by the total number of patients). The weighted mean ratios for improvement in pain[3] were 0.90 for the 14 neurectomy studies and 0.81 for the 11 combined neurectomy and meshectomy studies.

Eight studies [29, 31, 33, 35, 38, 43, 51, 54] did not supply information regarding early surgical complications, while 17 studies [34, 36, 37, 39–42, 44–50, 52, 53, 55] reported a small number of wound infections (n=6), hematomas (n=6), orchidectomy due to impingement in scar tissue (n=2), seroma (n=1) wound dehiscence (n=2), pulmonary thromboembolism (n=1), deep venous thrombosis (n=1), urinary tract infection (n=1), and a perforation of the posterior diaphragm following an endoscopic procedure, requiring chest-drainage (n=1).

In regard to late surgical complications, in the six studies [36, 40, 48, 50, 53, 54] performing meshectomy without mesh-replacement, two studies [48, 53] reported recurrence of inguinal hernias in 2/21 and 4/54 cases, respectively. Out of five studies [31, 42, 44, 47, 52] performing meshectomy and mesh-replacement, two studies [47, 52] reported recurrences in 1/43 and in 7/67 of the cases. In addition, ischemic orchitis

[2] Calculated in study$_i$ as: follow-up weeks$_i$ x (number of patients$_i$/total number of patients). Values for each study are summed up giving a weighted mean value.

[3] Calculated in study$_i$ as: pain relief ratio$_i$ x (number of patients$_i$/total number of patients). Ratios for each study are summed up giving a weighted mean ratio.

Table 2 Studies including more than 10 patients on surgical management of persistent postsurgical pain following inguinal hernia repair (n=1,365)

First author [ref] (year)	N	Primary surgery	Re-surgery	Neurectomy	Mesh removal	New mesh	Main results	Follow-up (range)	Follow-up method (RR%)
Starling JR [33] (1987)	26[a]	Open	Open	GFN, IHN or IIN	N/A	N/A	Pain-free (GFN) 10/13	NR	NR
Starling JR [34] (1989)	31[a]	Open	Open	GFN, IHN or IIN	N/A	N/A	Considerable/complete pain relief (GNF) 12/17 Complete pain relief (IIN/IHN) 17/19	NR	NR
Bower S [35] (1996)	15	Open	Open	GFN, LFCN, IHN or IIN	No	No	Improved 9/12	66 months	CV (no data)
Heise CP [36] (1998)	20	Open 17 Lap.scop. 3	Open	Selective (IIN or IHN)	Yes	No	Improved 12/20	16 months (SD: 3 months)	Phone/CV/CR (no data)
Lee CH [37] (2000)	11[a]	Open 8 Lap.scop. 3	Open	GFN, LFCN, IHN or IIN	NR	NR	Excellent 41/60 Good 13/60 Poor 6/60 (pain relief/# groins)	10 months (6–18 months)	CR/phone (pain score +functional score)
Deysine M [38] (2002)	22[a]	Open nonmesh 28 mesh 19 mesh/plug 2	Open	IIN	No	No	Pain-elimination 22/22	NR	NR
Amid PK [39] (2002)	49[c]	Open	Open	TNE	No	No	Pain-free 39/49 Improved 8/49 Not improved 2/49	1 month	CV (no data)
Amid PK [29] (2004)	225[c]	Open 219 Lap.scop. 6	Open	TNE	No	No	Pain-free 180/225 Improved 34/225 No improvement 11/225	1 month	CV+phone 6 months (no data)
Madura JA [40] (2005)	100[d]	Open 87 Lap.scop. 13	Open	Selective (GFN, IIN or IHN)	Yes	No	Pain-free 72/100 Partial/no relief 28/100	1 month	CV (no data)
Kim DH [41] (2005)	16[e]	Open	Open	IIN or IIN+IHN	NR	NR	Pain relief (IIN) 21/23 Pain relief (IIN+IHN) 9/10	12–46 months	Phone/CR (no data)
Rosen MJ [42] (2006)	12[c]	Open	Comb.	IIN 2 IIN+IHN 9	Yes	Yes	Improved 12/12	6 weeks (min)	CV (no data)
Amid PK [43] (2007)	415[c]	Open: nonmesh 212 mesh 195 lap.scop. 8	Open	TNE	No	No	Pain-free 85 % Improved 15 % No improvement 1 %	1 month 100 % 6 months>90 %	CV+phone 6 months (no data)
Keller JE [44] (2008)	21[c]	Open: nonmesh 2 mesh/plug 14 lap.scop. 6	Comb.	IIN 2 IIN+IHN 9 TNE 7	Yes	Yes	Pain-free 15/21 Improved 5/21 Pain recurrence 1/21	6 weeks (min)	CV (no data)
Ducic I [45] (2008)	18[a]	NR	Open	IIN[e] 4 IIN+IHN 1 IIN+GFN 6 IIN+IHN+LFCN 1 IIN+IHN+GFN 5 IIN+GF+LFCN 2	No	No	Improvement in pain and QoL[f] 16/19	24 months	CV (pain score +QoL data)
Giger U [46] (2009)	33[a]	Open: nonmesh 20 mesh 9 lap.scop. 4	Lap.scop.	ERN: GFN 19 GFN+IIN 20	No	No	Improvement in pain, functional performance +occup. disability[g] 27/39	12 months	CV (pain score+medication +functional performance +occup. disability)
Vuilleumier H [47] (2009)	43	Open 31 Lap.scop. 12	Open	IIN 35 IHN 11	Yes	Yes	Pain-free 41/43 Improved 2/43	6 months 100 % 12 months 91 %	CV (pain score)
Aasvang EK [48] (2009)	21[c]	Open: mesh 17 plug 4	Open	IHN 9 IIN 16	Yes	No	Improved PRI-ADL 13/21 Unchanged PRI-ADL 5/21 Worsened PRI-ADL 3/21	6 months	CV+QST (3 months) Q (pain score+functional performance+sexual function)
Zacest AC [49] (2010)	18[a]	NR	Open	IIN[h] 25 GFN 2	No	No	Pain-free[h] 5/19 Improved 7/19	35 months (3–108 months)	Phone-Q 73 % (pain score)

Table 2 (continued)

First author [ref] (year)	*N*	Primary surgery	Re-surgery	Neurectomy	Mesh removal	New mesh	Main results	Follow-up (range)	Follow-up method (RR%)
							Unchanged 3/19 Worsened 3/19		
Loos MJ [50] (2010)	54	Open[i]: mesh 36 nonmesh 24 lap.scop. 10	Open	Tailored: IIN 44 GFN 25 IHN 9	Part. 19/54	No	Pain-free (+/almost) 25/49 Improved 12/49 Unchanged 4/49 Worsened 8/49	18 months	CV Q 91 % (pain score+dysejaculation /−orgasm)
Amid PK [51] (2011)	16	Open Lap.scop.	Open	Extend. TNE	Part. (meshomas)	Part. (meshomas)	Improved 14/16 No improvement 2/16	4–6 weeks	CV (no data)
Koopmann M [52] (2011)	67	Open 54 Lap.scop. 13	Open	Selective (GFN, IHN, IIN)[i]	Yes	Yes[j]	AHD: improved 29/35 AWM: improved 23/32	AHD: 32 months AWM: 80 months	Phone-Q[k] 56 % (pain score+satisfaction)
Bischoff JM [53] (2013)	54[c,l]	Open: mesh 46 plug-based 8	Open	Selective: IIN 37 IHN 19 GFN 10	Yes	No	Improved 16/25 Unchanged 6/25 Worsened 3/25	36 months	CV 3 months Qs[m] 89 % (pain score+functional performance+ sexual function)
Campanelli G [31] (2013)	46	Open	Open[n]	TNE 44/46 IHN 2/46	Yes 40/46	Yes 42/46	Pain-free 40/46 No improvement 6/46	12 months (12–66 months)	CV 100 % (pain score)
Valvekens E [54] (2013)	12[a,o]	Open 2 Lap.scop. 10	Comb.[n]	NE 4/12	Yes 5/12 Part. 1/12	No	Improved 4/12 Unchanged 7/12 Worsened 1/12	32 months (11–118 months)	Q (pain ratios+DN4)
Chen DC [55] (2013)	20	Open 10 Lap.scop. 10	Lap.scop	LS-TNE 20/20	No[p]	No	Improved 20/20	22 weeks (16–40 weeks)	CV (pain score)

AHD acellular human dermis repair, *AWM* anatomical repair without mesh, *Comb.* open+laparoscopic approach, *CR* chart review, *CV* clinical visit, *DN4* Douleur Neuropathique 4 Questionnaire, *Extend. TNE* TNE+resection of retroperitoneal GFN trunk, *ERN* endoscopic retroperitoneal neurectomy, *GFN* genitofemoral nerve (genital branch), *IHN* iliohypogastric nerve, *IH-patients* inguinal hernia repair patients, *IIN* ilioinguinal nerve, *Lap.scop* laparoscopic, *LFCN* lateral femoral cutaneous nerve, *LS-TNE* laparoscopic retroperitoneal triple neurectomy, *N/A* not applicable, *NE* unspecified neurectomy, *NI* no information, *NR* not reported, *PRI-ADL* pain-related impairment of everyday activity, *Q* questionnaire, *QoL* quality of life, *QST* quantitative sensory testing, *RR%* response rate %, *TNE* triple neurectomy

[a] includes noninguinal hernia surgery (the number indicates inguinal hernia patients)

[b] includes eight patients with successful therapeutic nerve blocks

[c] likely sequentially reported cumulated data

[d] mostly inguinal hernia repair patients (conflicting information on exact number)

[e] total 33 patients

[f] one noninguinal hernia surgery patient included

[g] six noninguinal hernia surgery patients included

[h] up to eight noninguinal hernia surgery patients included

[i] including recurrent inguinal hernia surgery

[j] with AHD from 2002 to 2007 (total study duration 1997 to 2007)

[k] total 119 patients

[l] 21 patients previously reported [48]

[m] 25 out of 28 available

[n] combined anterior and posterior (preperitoneal) approach

[o] total number includes three noninguinal hernia surgery patients

[p] two patients with residual meshoma pain, subsequently had the mesh removed

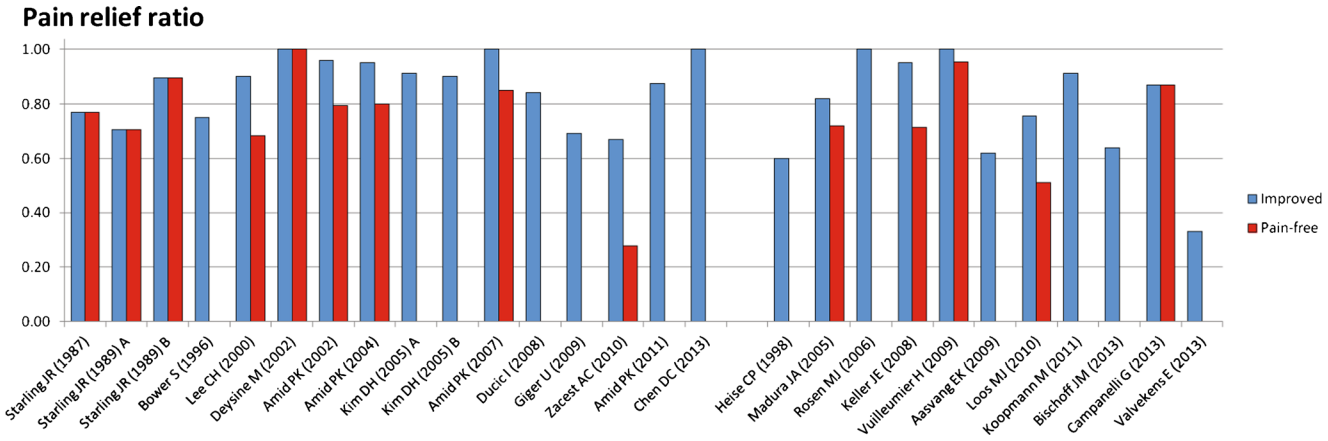

Fig. 1 Pain outcomes indicated as pain relief ratios (number of patients with improved pain (*blue*) or pain-free (*red*) divided by the total number of patients for each study). *Left side* indicates the 14 neurectomy studies and the *right side* the 11 combined neurectomy and meshectomy studies. For information about the number of patients in each study the reader is referred to Table 2

leading to testicular atrophy was described in five studies [36, 48–50, 53], in 1/20, 2/21, 1/18, 1/54 and 2/54 cases, respectively. Transient or permanent sensory dysfunction in the innervation areas of the resected nerves (n=6) were reported by three studies [37, 42, 55].

In order to evaluate these compiled data properly, it is necessary to consider a number of confounding factors inherent to individual studies. *First*, three studies reported likely, and four studies reported de facto, sequentially cumulated data, and thus duplicate data on 274 patients [29, 39, 43] and 33 patients [42, 44, 48, 53], respectively, are included in the present review. *Second*, pain intensity outcomes were heterogeneously and often rather inadequately reported. *Third*, effects on pain-related impairment of functional performance, recommended in chronic pain studies [56, 57], were only reported in 4/25 studies in spite of availability of several validated inguinal hernia repair specific questionnaires [58–60]. *Fourth*, although the weighted mean follow-up time (1 year) seems reasonable, the follow-up time was not reported in three studies, was 4 to 6 weeks in four studies and was a minimum of 6 weeks in two studies: making it very difficult to evaluate the therapeutic effects of the surgical intervention, particularly in regard to the neurectomy procedure. Nerve transection is known be associated with delayed onset of neuropathic pain symptoms [18, 61], from months to years, suggesting that extended follow-up times are prudent measures in neurectomy studies. *Fifth*, only one study [54] reported the use of a neuropathic pain questionnaire, generally recommended in pain research [62, 63]. *Sixth*, only one study [48] consistently used neurological examination techniques, i.e., quantitative sensory testing and sensory mapping, in order to delineate changes in nociceptive function before and after the exploratory surgery. In this study, meshectomy and selective neurectomy (in case of macroscopic nerve injury) were performed. Statistical significant increases in pressure algometry and thermal thresholds after surgery were demonstrated postsurgery.

Consequently, and in spite of these shortcomings, the data on surgical management clearly demonstrate that neurectomy with or without mesh removal may provide long-lasting analgesic effects in most patients with severe PPP following inguinal hernia repair. However, the study designs and the surgical techniques applied seem too heterogeneous to allow firm clinical recommendations. Evidently, there is a need for improved study designs and implementation of large multicenter collaborative studies supplying consistent long-term data [2].

Local anesthetic blocks

As previously mentioned, thirteen studies [31, 34, 36, 38, 41, 42, 44–47, 49, 50, 55] reported the use of diagnostic blocks presurgery. Only one study [46] reported use of a placebo-controlled design, a requirement necessary for valid assessment of the local anesthetic blocking effect [63–65], since a placebo-response is a prominent finding in block studies [66, 67]. The use of ultrasound-guided regional anesthesia has increased in the last decade and enables direct visualization of peripheral nerves, facilitating the success rate of the blocks [66]. Techniques for ultrasound-guided IHN, IIN, GFN, and paravertebral blocks [68–70] have been described in adults. Interestingly, recent data indicate that IHN and IIN *cannot* be selectively blocked by use of ultrasound guidance [71], a finding important for proper interpretation of presurgery blocks.

Only three publications, two clinical studies [66, 72], and a trial report [73] are available on the effect of local anesthetic blocks in PPP following inguinal hernia repair. One questionnaire-based, uncontrolled clinical study (n=43; response rate 38/43) [72], using either a nerve stimulator-based (n=17) or an ultrasound-guided technique (n=21), evaluated the long-term effect of IIN blocks. All patients

fulfilled the Douleur Neuropathique 4 Questionnaire (DN4)-criteria for neuropathic pain [62, 63] prior to treatment. The blocks used a mixture of bupivacaine and triamcinolon, and the median number of blocks performed was 2 (range: 1–7). The median follow-up duration was 21 months (range: 3–68 months). The outcomes reported were that 12/38 patients no longer reported moderate to severe pain and 21/38 patients no longer fulfilled the DN4-criteria for neuropathic pain.

The second clinical study [66] utilized a randomized, double-blind, placebo-controlled, crossover design in patients with severe PPP after inguinal hernia repair (n=12), including a control group of healthy volunteers (n=12). Ultrasound-guided blocks of the IIH and IIN were performed with lidocaine or normal saline. The study outcomes were analgesic efficacy, evaluated during resting and dynamic conditions, and, sensory effects assessed by sensory mapping and quantitative sensory testing (QST). One of 12 pain patients was a lidocaine responder, six patients were nonresponders, and five patients were placebo responders. No consistent QST changes were observed in patients after the lidocaine block. However, in 10 of 12 controls significant changes in sensory mapping or QST developed in the groin after the lidocaine block.

As a result, there is no scientific evidence of any short-term or long-term analgesic efficacy of local anesthetic blocks in PPP following inguinal hernia repair. However, the potential for local anesthetic blocks in predicting surgical outcome should be considered, particularly in excision of painful neuromas [74], e.g., if a diagnostic nerve block is ineffective in relieving pain, patients will most likely *not* benefit from surgical treatment.

Pharmacological management

In regard to systemically acting analgesics, only one study is available [75]. In this randomized, placebo-controlled, double-blinded study, a single dose of gabapentin 1,200 mg was administered immediately before an open inguinal hernia repair procedure (n=60). The aim of the study was to examine preventive effects of gabapentin on postsurgical acute and chronic pain. At the 6-month follow-up, the pain scores (numerical rating scale 0–10) were significantly lower in the gabapentin group compared to the placebo group, i.e., 1.9 (SD 1.4) and 1.0 (0.7), respectively. However, the pain scores are hardly of any clinical significance and are below the significance limits of PPP.

In regard to topically administered analgesics, two studies are available, one published [76] and one submitted (Bischoff et al. 2014), in patients with severe PPP following inguinal hernia repair. In a randomized, double-blind, placebo-controlled, crossover study [76] (n=21), lidocaine patch (5 %) and placebo patch treatments were administered in periods of 14 days separated by a 14-day washout. The main outcomes were summed pain intensity scores (at rest, during movement, and pressure evoked) assessed before treatments and on the last 3 days of each treatment period. There was no statistical significant difference in summed pain intensity differences between the patch treatments indicating a lack of analgesic effect of the lidocaine (5 %) patch. However, the lidocaine patch compared to the placebo patch was associated with a significant increase in pressure pain threshold at the surgery site. The most likely interpretation is that the increase represents a surrogate measure of analgesia difficult to translate into a proper clinical context.

In the submitted study (Bischoff et al. 2014) (n=42), in patients with severe PPP following inguinal hernia repair, the analgesic efficacy of a capsaicin 8 % patch was examined using a randomized, double-blind, placebo-controlled, parallel design. Summed pain intensity scores (at rest, during movement, and during pressure) were evaluated under standardized conditions at baseline and at 1, 2, and 3 months after application of the capsaicin patch (n=22) or the placebo patch (n=20). The maximum differences in summed pain intensity scores (comparing the capsaicin and placebo treatments) were observed at 1-month control after patch application, but the reduction in pain scores was not statistically significant (P=0.046; the assigned significance level of the study was 0.01).

Thus, the evidence base for analgesic efficacy of pharmacological therapies in PPP following inguinal hernia repair is very frail, clearly emphasizing the need for future procedure-specific randomized trials. Current recommendations depend heavily on extrapolating evidence from studies of diabetic polyneuropathy, postherpetic neuralgia, HIV-related painful neuropathy, and trigeminal neuralgia, conditions remote from PPP [77].

Sensory stimulation methods

Several different techniques of neuromodulation have been used in severe PPP following inguinal hernia repair. Pulsed radiofrequency (PRF) is an invasive pain treatment technique that employs electromagnetic energy deposited in or near nerve tissue [78, 79]. An insulated needle with an active tip is inserted at the vertebral level or at the peripheral level. Paraesthesias are then elicited in the painful area, by electrical stimulation as an indication of adequate positioning of the needle tip. The voltage applied to the treatment needle is rapidly raised and lowered, with voltages typically alternating between 0 and 40 V with a frequency of 300–500 kHz. The temperature is held below 42 °C avoiding structural damage to the nerve tissue. The moderate heating of the nerve tissue is believed to temporarily block the nerve conduction. Conventional continuous radiofrequency (CRF) produces temperatures at the tip of the treatment needle of 45–80 °C leading to irreversible thermo-coagulation of nerve structures,

and has proven considerably more efficacious than PRF in various chronic pain states [78].

A recent review [79] concluded that the evidence base of PRF and CRF in PPP following inguinal hernia repair is fairly limited. Since then, two retrospective uncontrolled studies [80, 81] have been published, most likely with overlapping patient cohorts. The studies used CRF guided by CT-fluoroscopy utilizing three neurolytic 90 s cycles at 70 °C, 80 °C, and 90 °C targeted at IHN and IIN, at the level of the anterior superior iliac spine. The first study [80] comprised patients (n=42) with refractory chronic inguinal neuralgias including patients following inguinal hernia repair (n=25). Using a nonrandomized design, patients either received local anesthetic blocks (ropivacaine/cortivazol; n=28) or CRF (n=16). Both groups at the 1-month control had significantly reduced pain scores (visual analog scores [VAS] 0–10) compared to base line: in the block group from 7.5 to 4.8 and in the CRF group from 7.7 to 1.4. However, the duration of pain relief in the CRF group, in 15/16 patients, lasted longer (12 months) than in the block group. In the second study (n=12; 7 patients following inguinal hernia repair) [81] with an identical set-up and test-paradigm for the CRF procedure as in the previous study, the pain scores at 1-month control decreased with 6.2 VAS-units. The mean duration of pain relief was 12 months (range 3–36 months) and the authors concluded that the study showed excellent long-term pain reduction following CRF in patients with refractory inguinal pain.

Peripheral nerve stimulation utilizing a transperitoneal laparoscopic approach with selective implantation of quadripolar electrodes at the GFN (anterior surface psoas major muscle) or, IHN, IIN, and FCLN (anterior surface quadratus lumborum muscle) has recently been presented [82]. In a very detailed study including 23 consecutive patients with intractable PPP following groin surgery, with a follow-up of 29 months (range 6–68 months) after the implantation, the pain scores in 19 patients were reduced from 8.1 VAS-units (6–10 VAS-units) to 3.1 VAS-units (0–5 VAS-units).

Although preliminary reports with neuromodulation techniques are enthusiastic and promising, the evidence is still of low quality, and the strength of recommendation is weak to moderate [79]. The scientific rigor is generally not considered adequate and study designs should be improved in regard to control-groups, randomization, blinding procedures, and adequate sampling sizes. *But* a statistical idiomatic expression should be remembered: absence of evidence is not evidence of absence [83].

Conclusion

Reviewing the available treatment modalities in severe persistent postsurgical pain following inguinal hernia repair, exploratory surgical procedures have produced consistently satisfactory results in the majority of patients. In the reviewed studies, most patients suffered from intractable pain prior to surgery, indicating that miscellaneous other interventional and noninterventional specialties had failed. However, limited and variable information on the preoperative demographics, and, differences in surgical techniques, the follow-up times and the outcome assessments hinder recommendations for the optimal surgical procedure. As previously mentioned, there seems to be a dire need for homogeneous high quality randomized long-term studies, preferably in a collaboration between surgeons and pain-specialists carried out at several surgical centers.

It has been stated that "….different types of neurectomy with or without mesh removal should be regarded as the last treatment option…" [2], indicating that surgery on the peripheral nervous system during certain conditions may lead to untoward outcomes [74, 84, 85]. Identification of evidence-based alternatives to surgery therefore, has a high priority.

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