

Chronic Pain as an Outcome of Surgery

A Review of Predictive Factors

Frederick M. Perkins, M.D.,* Henrik Kehlet, M.D., Ph.D.†

ONE potential adverse outcome from surgery is chronic pain. Analysis of predictive and pathologic factors is important to develop rational strategies to prevent this problem. Additionally, the natural history of patients with and without persistent pain after surgery provides an opportunity to improve the understanding of the physiology and psychology of chronic pain.

Ideally, studies of chronic postoperative pain should include (1) sufficient preoperative data (assessment of pain, physiologic and psychologic risk factors for chronic pain); (2) detailed descriptions of the operative approaches used (location and length of incisions, handling of nerves and muscles); (3) the intensity and character of acute postoperative pain and its management; and (4) follow-up at intervals to 1 yr or more. In addition, there would be information about postoperative interventions that may influence pain, such as radiation therapy or chemotherapy. At long-term follow-up visits, patient function, physical signs, and symptoms would be evaluated using a standardized algorithm, including quantitative and descriptive pain assessments. We found no studies that contain all of these data.

For this review, we specifically sought population data that reflect the incidence of chronic postoperative pain or predictors (medical, physiologic, and psychologic) of chronic pain. We selected five groups of surgeries (limb amputations, breast surgery, gallbladder surgery, lung surgery, and inguinal hernia surgery). These surgeries were selected because the incidence of pain is known to be high, thus improving the probability of detecting predictive factors. They also represent a range of major surgical procedures.

Methods

We performed a computerized search of the medical literature using the OVID search engine (OVID Technol-

ogies, Wolters Kluwer, Amsterdam, The Netherlands). The search was performed on the entire database in January 1999 and covered 1966 through most of 1998. Additional articles published during the review process have also been included. Terms were used in their "exploded" format. The term "pain" was combined with the other appropriate term (e.g., "cholecystectomy"); also the text words associated with the pain syndromes were searched, resulting in more than 1,700 citations. Letters to the editor were not reviewed. Additionally, articles known to the authors but not found in the search were used. If the article contained data about persistent pain (12 weeks or more after surgery), it was considered for inclusion in this review. To calculate the incidence of pain, we used the number of individuals responding at the time the chronic pain data was gathered, and only used data from articles in which the methods section indicated that there was systematic collection of long-term pain information from patients. Studies of fewer than 50 patients were excluded in the incidence data analysis for breast surgery, gallbladder surgery, and lung surgery. Studies of fewer than 100 patients were excluded from the data analysis for inguinal hernia surgery. Amputation studies of 25 subjects or more were included because of the higher incidence of chronic pain.

Results

Limb Amputation

Pain Incidence. The reported incidence of phantom limb pain varies from 30 to 81% (table 1). Finch *et al.*¹ reported pain in 30% of 57 long-term survivors of amputation for vascular insufficiency. Fisher and Hanspal² described 93 consecutive amputees referred to a prosthetic rehabilitation clinic; therefore, selection bias may be a factor. The remainder of the studies (table 1) report an incidence of phantom limb pain of more than 50%. Sherman *et al.*³ noted at least a 78% incidence of phantom limb pain, and perhaps as high as 85%; however, their questionnaire response rate was not high (55%). Stump pain was noted in 66% of patients with phantom pain and in half of those without phantom pain; therefore, the overall stump pain incidence exceeds 60%. Warran *et al.*⁴ reported a 62% incidence of phantom limb pain and 63% for stump pain. Similar to Sherman *et al.*, 66% of patients with phantom limb pain also have stump pain.

* Associate Professor, Department of Anesthesiology, University of Rochester; † Professor, Department of Surgical Gastroenterology, University of Copenhagen and Hvidovre University Hospital.

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Address reprint requests to Dr. Perkins: Anesthesia, VAMC & ROC # 112, White River Junction, Vermont 05009. Address electronic mail to: fred.perkins@med.va.gov. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

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Table 1. Amputation

Reference	Size	Stump Pain Incidence	Phantom Pain Incidence (%)	Preoperative Pain Incidence	Preoperative Physiologic Data	Acute Pain Data
Finch, 1980 ¹	57	18%§	30§	—	—	—
Sherman, 1984 ³	2,694	—	78††	—	—	—
Jensen, 1985 ¹⁶	51	—	65*	98%	—	—
	(34)	—	59‡	98%	—	—
Pohjolainen, 1991 ⁹⁸	124	5%†	53†	—	—	—
Krane, 1995 ⁷	24	—	83	+	—	—
Nikolajsen, 1997 ¹⁰	16‡‡	—	81*	22%	—	+
	20§§	—	55*	97%	—	+
Wartan, 1997 ⁴	526	57%**	55**	—	—	—
Fisher, 1998 ²	93	—	31#	—	—	—
Nikolajsen, 1998 ⁹⁹	14‡‡	—	79*	+	+	+
	17§§	—	59*	+	+	+

* Pain at 6 months. † Pain at 1 yr. ‡ Pain at 2 yr. § Mean follow-up at 2.5 yr. || Mean follow-up at 16 months. # Mean follow-up at 10 yr. ** Median follow-up at 50 yr. †† Mean follow-up at 26 yr after amputation for those with pain. ‡‡ Preoperative and postoperative epidural analgesia. §§ Preoperative systemic opioid analgesia. |||| Number of patients who survived 2 yr of initial 59.

Acute pain data = extent of acute pain measured and reported; preoperative physiologic data = pain sensitivity data reported; preoperative psychologic data = psychologic testing data reported (no data reported for studies on this table); — = no data presented; + = data presented.

Preoperative Factors: Smith and Thompson⁵ reported that pain was more common after amputation for cancer than for trauma, but this study was a chart review (phantom pain noted in medical record), and there were only eight amputations for trauma. No large studies systematically evaluate the incidence of phantom limb pain after trauma, vascular disease, and cancer-related surgeries. The presence of intense preoperative pain in the extremity increases the probability of phantom limb pain (from 33 to 72% at 3 months).^{6,7} Some early reports^{8,9} indicated that the incidence of phantom limb pain decreased with prolonged (72 h) preoperative epidural pain control, followed by postoperative epidural pain control. Both studies were small (23 and 24 patients, respectively at 6 months follow-up), and neither was properly randomized. In a subsequent randomized controlled study,¹⁰ this observation was not confirmed, but preoperative pain control was limited to 18 h, and the extent and intensity of perioperative blockade was not sufficient to control pain without supplemental systemic opioids.

Intraoperative Factors. The effect of anesthesia (epidural, spinal, or general) alone has not been studied. Surgical handling of the major nerves is rarely mentioned, so we cannot assess the effect of nerve ligation or clipping *versus* section alone.

Postoperative Factors. Administration of chemotherapy increases the incidence of phantom limb pain.⁵ Stump pain at 1 week is significantly associated with phantom pain at 1 week,⁶ and long-term stump pain predicts long-term phantom limb pain.³ There is also a correlation between nonpainful phantom sensations and phantom pain.⁴ Control of acute postoperative pain with nerve sheath infusion of local anesthetic decreased the

incidence of phantom limb pain in one series of 11 patients,¹¹ but a subsequent randomized controlled trial (n = 14 at long term follow-up)¹² failed to confirm this finding. Both of these studies are small, and the negative study¹² does not have the statistical power to conclude that there is no significant effect. There has also been a negative retrospective report of this technique (n = 21).¹³ As mentioned previously, data regarding epidural analgesia⁸⁻¹⁰ as a method to decrease the incidence of phantom limb pain conflict.

Apparent Etiology. Most authorities believe that phantom limb sensation and phantom limb pain are central phenomena and explain them using the neuromatrix theory expounded by Melzack.^{14,15} That is, there is a matrix in the central nervous system for the perception of a body part, and this matrix exists even when the body part does not. Sherman *et al.*³ emphasized that multiple etiologies may lead to phantom limb pain, based on the inconsistency of therapeutic responses.

Progression. The incidence of phantom limb pain decreases during the first year after amputation, as does the frequency of painful episodes^{7,16}; however, about half the individuals with long-term phantom pain report no decrease in the intensity of this pain.³

Section Summary. Phantom limb pain is common after extremity amputation, and documented predictors of this pain include preamputation pain and persistent stump pain (acute and chronic). No conclusive studies have evaluated the effect of acute or subacute stump pain control on long-term stump pain or on long-term phantom limb pain. Also no psychologic studies have evaluated patients before amputation for predictors of chronic pain.

Thoracotomy

Pain Incidence. Long-term pain after thoracotomy, the postthoracotomy pain syndrome (PTPS), may have an incidence of more than 50%.^{17,18} Six studies met our inclusion-exclusion criteria (table 2), assessing 878 patients, of whom 417 (47%) had PTPS.

Preoperative Factors. Katz *et al.*² could not predict PTPS from preoperative psychologic testing (state or trait anxiety, depression inventory) or preoperative pain sensitivity as determined by pressure algometry. This study (n = 23) was the extension of a previous acute pain study; it therefore lacks statistical power and may be subject to selection bias. Perttunen *et al.*¹⁹ noted the presence of preoperative pain in 17% of their patients but did not analyze it as an independent risk factor.

Intraoperative Factors. Several recent case series report that video-assisted thoracoscopic lung surgery (VATS) is associated with a low incidence of PTPS. Walker *et al.*²⁰ reported only 1 case of 83 (1.2%), and Mouroux *et al.*²¹ noted a 3% incidence of PTPS, but neither group reports systematically looking for PTPS. In a large retrospective survey, Landreneau *et al.*²² (table 2) noted a lower incidence of pain in patients who had VATS compared with those who underwent lateral thoracotomy (30 *vs.* 44%); however, pain medication requirements did not differ. The difference in pain incidence was statistically significant only during the first year after surgery. In a small (n = 30), nonrandomized prospective study, Furrer *et al.*²³ found a 36% incidence of PTPS in patients undergoing VATS wedge resection, and a 33% incidence of PTPS in a matched group of patients undergoing lobectomy by a classic posterolateral thoracotomy. However, the results are confounded because the thoracotomy group received thoracic epi-

dural analgesia with local anesthetic and opioid, whereas the thoracoscopic group received intravenous patient-controlled opioids. Nomori *et al.*²⁴ retrospectively and Benedetti *et al.*²⁵ prospectively (case series) reported a decreased severity of chronic pain after anterolateral thoracotomy when compared with classic posterolateral thoracotomy (mean visual analog scale [VAS] score, 6 of 100 *vs.* 21 of 100). Both studies were small (24 and 42 patients), and chronic postoperative pain was not a primary outcome parameter. In descriptions of the surgical technique for posterolateral thoracotomy, details about whether a rib was resected or about how the intercostal nerves were handled were missing from most reports.

A recent report by Obata *et al.*²⁶ (table 2) found a significant effect of intraoperative plus postoperative epidural analgesia when compared with just postoperative epidural analgesia (decreasing the incidence of pain at 6 months from 67% to 33%). This is a prospective, randomized, single-blind study.

Postoperative Factors. The intensity of acute postoperative pain is a statistically significant predictor^{18,27} of PTPS (36 *vs.* 56% PTPS for minor *vs.* moderate to severe acute pain). As mentioned previously herein, the combination of intraoperative plus postoperative epidural analgesia with local anesthetic was associated with a decreased incidence of pain at 6 months. An attempt at preemptive analgesia²⁸ had not improved analgesia on long-term follow-up.¹⁸ Another small study found that the type of postoperative analgesia affected the incidence of pain at 12 weeks (less pain with epidural analgesia or intercostal nerve cryoablation), but data of only 33 subjects divided among four treatment regimens were reported.²⁹ Benedetti *et al.*^{25,30} showed that inter-

Table 2. Thoracotomy

Reference	Size	Surgical Approach	Chronic Pain Incidence	Preoperative Pain Incidence	Acute Pain Data
Dajczman, 1992 ¹⁰⁰	56	PL-thor	54%‡	—	—
Kalso, 1992 ²⁷	134	—	44%§	—	+
Landreneau, 1994 ²²	142	VATS	30%*	—	—
	36	VATS	22%†	—	—
	97	PL-thor	44%*	—	—
	68	PL-thor	29%†	—	—
Bertrand, 1996 ¹⁷	146	VATS	63%	—	—
	87	PL-thor	61%#	—	—
Perttunen, 1999 ¹⁹	62	—	61%**	+	+
Obata, 1999 ²⁶	28	PL-thor	33%††	—	+
	30	PL-thor	67%‡‡	—	+

See table 1 legend for further information (no information reported for studies in this table regarding preoperative physiologic data or psychologic data).

* Follow-up at 3–12 months. † Follow-up at 13–31 months. ‡ Median follow-up at 20 months. § Median follow-up at 30 months. || Mean follow-up at 25 months.

Mean follow-up at 33 months. ** Follow-up at 12 months. †† Follow-up at 6 months, intra- and postoperative epidural analgesia. ‡‡ Follow-up at 6 months, postoperative epidural analgesia.

PL-thor = posterolateral thoracotomy; VATS = video-assisted thoracic surgery (thoracoscopic).

Table 3. Breast Surgery

Reference	Size	Surgical Approach	Chronic Symptoms	Breast or Chest Pain	Phantom Breast Pain	Arm or Shoulder Pain	Preoperative Pain Incidence	Preoperative Physiologic Data	Preoperative Psychologic Data	Acute Pain Data
Staps, 1985 ⁴⁵	89	Mastect	—	—	24%*	—	—	—	—	—
Chiverton, 1987 ¹⁰¹	32	Lumpect	66%	25%‡	—	19%‡	—	—	—	—
	65	Mastect	68%	11%‡	—	26%‡	—	—	—	—
Krøner, 1989 ³⁶	110	Mastect	—	23%	13%	—	16%	—	—	—
Bratschi, 1990 ⁴⁹	101	Mastect	—	—	—	12%*	—	—	—	—
Skov, 1990 ⁵⁰	110	Mastect	—	23%	—	—	+	—	—	—
Krøner, 1992 ⁵¹	69	Mastect	—	31%**	17%**	—	+	—	—	—
Keramopoulos, 1993 ⁴³	72	Partmastect	—	—	—	14%‡	—	—	—	—
	32	Mastect	—	—	—	22%‡	—	—	—	—
Maunsell, 1993 ⁴²	201	+	79%	—	—	25%§	—	—	—	—
Krøner, 1994 ⁵²	68	Mastect	—	31%**	17%**	—	+	—	—	—
Stevens, 1995 ¹⁰²	95	+	—	35%†	—	—	—	—	—	—
Husted, 1995 ³⁵	163	Mastect	79%	45%††	—	45%††	—	—	—	—
	35	Lumpect	82%	57%††	—	51%††	—	—	—	—
Tasmuth, 1995 ³⁹	283	Mastect	—	36%#	—	34%#	—	—	—	+
	184	Lumpect	—	47%#	—	42%#	—	—	—	+
Wallace, 1996 ⁴⁰	103	Mastect	—	31%††	—	—	—	—	—	—
	78	M + R	—	49%††	—	—	—	—	—	—
	52	Augmentation	—	36%††	—	—	—	—	—	—
	49	Reduction	—	22%††	—	—	—	—	—	—
Tasmuth, 1996 ³⁷	93	+	—	—	—	17%	+	—	+	+
Tasmuth, 1996 ³⁸	53	Mastect	83%	17%	23%	13%	+	+	+	+
	40	Lumpect	82%	33%	—	23%	+	+	+	+
Tasmuth, 1997 ⁴⁴	509	+	—	37%§§	—	33%§§	—	—	—	+

See table 1 legend for further information.

* Intercostal-brachial neuralgia. † Cancer related pain, follow-up time not stated. ‡ Follow-up at greater than 3 months after surgery. § Follow-up at 18 months.

|| Follow-up at 12 months. # Median follow-up at 30 months. ** Follow-up at 6 yr. †† Follow-up at 2–6 yr. ‡‡ Follow-up at 3–5 yr. §§ Follow-up at 10–58 months.

||| Mean follow-up at 5.25 yr.

Lumpect = lumpectomy/partial resection of breast; M + R = mastectomy with reconstruction; mastect = mastectomy.

costal nerve dysfunction (loss of the superficial abdominal reflex) is associated with more acute, subacute, and chronic (3 months) pain. Of 23 patients with intact reflexes on postoperative day 1, none had pain at 2 to 3 months, whereas 50% of individuals with persistent loss of the reflex still had pain at this time.

Apparent Etiology. The etiology of PTPS may depend on nerve damage because it is more severe after chest wall resection,^{31–33} and the loss of superficial abdominal reflexes is associated with an increased probability of PTPS.^{25,30} Another contributing factor is recurrence of tumor.³¹

Progression. For thoracoscopic surgeries and posterolateral thoracotomy, Landreneau *et al.*²² noted a 30% decrease in the incidence in pain reported by patients more than 12 months after surgery compared with those 3–12 months after surgery. The prospective study by Perttunen *et al.*¹⁹ noted the incidence of pain at 3, 6, and 12 months to be decreasing (80, 75, and 61%, respectively). Of patients with long-term pain after thoracotomy, up to half describe their pain as moderate or severe,¹⁸ and 66% are prescribed analgesics for the pain.²⁷

Section Summary. Postthoracotomy pain syndrome is common. The predictors of this syndrome (when

tumor recurrence is excluded) include the extent of acute postoperative pain and intercostal nerve dysfunction (which may link more acute pain and persistent pain). One prospective, randomized controlled study²⁸ found that the combination of intraoperative plus postoperative thoracic epidural analgesia decreases the incidence of PTPS at 6 months.

Breast Surgery

Incidence. Table 3 summarizes various studies of pain after breast surgery. Women who undergo breast surgery experience chest wall, breast, or scar pain (range, 11–57%), phantom breast pain (13–24%), and arm and shoulder pain (12–51%). The incidence of pain in one or more of these sites is close to 50% 1 yr after breast surgery for cancer. The postmastectomy pain syndrome (PMPS) has recently been reviewed,³⁴ with some disagreement about which pains to include in this syndrome. Husted *et al.*³⁵ documented that, of 163 women who had undergone mastectomy with axillary node dissection, 45% reported cicatrix pain, 45% reported arm, neck, or shoulder pain, and only 21% were symptom free (symptoms included pain, paresthesia, lymphedema, and

impaired shoulder function) 1–5 yr after surgery. Moderate to severe pain was reported by 16 patients (10%).

Preoperative Factors. Krøner *et al.*³⁶ reported a significant relation between preoperative breast pain and postoperative phantom breast pain in a prospective study of 120 patients. In contrast, Tasmuth *et al.*,^{37,38} in a prospective study of 93 patients, did not find the presence of preoperative pain to be a predictive factor, but only 9 patients had pain before surgery. Preoperative depression and anxiety were more common in patients in whom chronic pain developed when compared with those in whom chronic pain did not develop, although statistical significance was not achieved.³⁷

Intraoperative Factors. The type of surgery may affect the incidence of pain. Tasmuth *et al.*³⁹ found that chronic pain was more common after breast conserving surgery than after radical surgery in their large retrospective study, but did not confirm this in smaller prospective studies.^{37,38} Wallace *et al.*,⁴⁰ in their questionnaire survey of women who had undergone breast surgery, found that mastectomy combined with implantation of a breast prosthesis yielded a higher incidence of pain (53%) than did mastectomy alone (31%). Abdullah *et al.*⁴¹ reported sensory deficits in the distribution of the intercostobrachial nerve at 3 months after axillary node dissection in 61% of women in whom the nerve was preserved and in 80% of women in whom it was divided. Maunsell *et al.*⁴² found that axillary dissection increased the likelihood of arm problems and greater levels of psychologic distress. Kerampoulos *et al.*⁴³ also found the extent of axillary dissection correlated with the incidence of arm pain and symptoms.

Postoperative Factors. Tasmuth *et al.*⁴⁴ performed a multivariate analysis of factors that predisposed the patient to chronic pain after breast cancer surgery. The extent of acute postoperative pain and the number of doses of postoperative analgesics were the best predictors of persistent pain in both the breast area and the ipsilateral arm. Additionally, adjuvant postoperative radiation therapy was a risk factor for chronic pain in both the breast area and the arm.⁴⁴ Kerampoulos *et al.*⁴³ found that immediate axillary radiation therapy increased the incidence of arm pain and symptoms. Neither Staps *et al.*⁴⁵ nor Krøner *et al.*³⁶ found a relation between phantom breast sensations and radiation therapy, but their studies were smaller and only sought a particular subgroup of symptoms.

Apparent Etiology. Much of the pain after breast surgery has been attributed to nerve damage, whether from surgery or radiation.^{39,46,47} Courtiss and Goldwyn⁴⁸ demonstrated that nipple and areola sensation decreased (intercostal nerve dysfunction) in the long-term in 15% of 249 women undergoing augmentation mammoplasty and 65% of 138 women undergoing reduction mammoplasty, but pain data were not reported. Sensation was

altered in the distribution of the intercostobrachial nerve in 48–84% of women undergoing axillary dissection. In turn, in 25–50% of women with these sensory alterations intercostobrachial neuralgia developed.^{41,49} Psychologic distress was associated with a higher incidence of arm pain and arm symptoms⁴²; and both were more common after breast surgery with axillary node dissection. The relations among distress, pain, and preoperative psychologic characteristics have not been elucidated among women undergoing breast surgery.

Progression. The natural history of pain during the first year after surgery has not been well-characterized. In one study, the incidence of pain in the breast area decreased from 35 to 23% from 3 weeks to 1 yr after surgery, whereas the incidence of hyperesthesia decreased from 38 to 13%.⁵⁰ In another study, the incidence of arm pain decreased insignificantly from 3 to 15 months after surgery (55 to 51%, respectively).⁴² The incidence of phantom breast pain is constant from 3 weeks to 6 yr.^{51,52}

Section Summary. Chronic pain is common after breast surgery, and the major predictive factors are the extent of acute postoperative pain, the presence of pain before surgery, the type of surgery, intercostobrachial nerve damage, adjuvant radiation therapy, and possibly preoperative anxiety or depression.

Gallbladder Surgery

Incidence. Chronic abdominal pain after cholecystectomy is common (range, 3–56%; table 4), but less frequent than the preoperative incidence of pain (83–100%). The postcholecystectomy syndrome (PCS) has a number of components in addition to abdominal pain, and may not have a single underlying etiology.⁵³ “Pathogenic” factors include postoperative somatic incisional pain; pain caused by postoperative sphincter of Oddi dysfunction; pain caused by a preoperatively undiagnosed disease other than gallbladder stone; pain caused by a bile duct stone; and other preoperative factors that predispose the patient to an unfavorable outcome.⁵⁴

Preoperative Factors. Psychologic vulnerability is a predictor of long-term pain and symptoms after cholecystectomy,^{54–56} whereas other risk factors include female gender⁵⁷ and long-standing symptoms before surgery.⁵⁸ A history of classic gallbladder attack symptoms is associated with reduced risk of chronic pain and symptoms.^{59–61}

Intraoperative Factors. The surgical approach appears to make no significant difference in overall complaints. Nicholl *et al.*,⁶² in a randomized controlled trial (n = 163), noted that patients randomized to lithotripsy had more complications related to biliary “colic,” whereas patients randomized to open cholecystectomy had more complaints of scar pain and diarrhea; they did

not report pain incidence data. There appears to be no difference in chronic abdominal pain when laparoscopic cholecystectomy is compared with open cholecystectomy.⁶³ Gui *et al.*⁶¹ reported a 30% incidence of nonspecific abdominal pain more than 1 yr after cholecystectomy, but this incidence did not include 16 patients (17.4%) with wound pain. Stiff *et al.*⁶⁴ noted significantly more right upper quadrant pain after open cholecystectomy than after laparoscopic surgery and hypothesized that there was more intercostal nerve damage from the open procedures.

Postoperative Factors. Borly *et al.*,⁵⁶ in a prospective study of 100 patients who underwent cholecystectomy, noted that pain at 6 weeks was a strong predictor of persistent pain and other symptoms at 1 yr (written communication, L. Borly and H. Kehley, 1999). We found no studies that evaluated acute postoperative pain as a predictor of chronic pain.

Apparent Etiology. There are multiple etiologies of the PCS, including sphincter of Oddi dysfunction, bile duct stones, ulcer, colonic dysfunction, and scar pain. The relative importance of each factor has not been evaluated.

Progression. Despite the frequency of persistent symptoms after cholecystectomy, patient satisfaction after the procedure is high, with authors documenting satisfaction rates that exceed 90%.⁶⁵⁻⁶⁷ This may relate to patient expectations⁶⁸ because most patients with abdominal pain and gallstones believe that they will worsen without surgery and that their lives will improve after surgery.

Section Summary. Chronic symptoms are common after cholecystectomy, as is chronic abdominal pain. Predictive factors include psychologic vulnerability, long-standing preoperative symptoms (including pain), and pain at 6 weeks after surgery. Prospective studies of the postcholecystectomy syndrome have not separated scar pain and neuropathic pain from other causes of chronic visceral pain and symptoms.

Inguinal Hernia Surgery

Incidence. A number of studies have evaluated chronic pain after groin surgery, with the reported incidence of chronic pain varying from 0 to 37% (table 5). The overall incidence from these studies is 11.5% (616 of 5,357). Chronic pain was a primary outcome parameter

Table 4. Gallbladder Surgery

Reference	Size	Surgical Approach	Chronic Symptoms	Chronic Abdominal Pain	Preoperative Pain Incidence	Preoperative Physiologic Data	Preoperative Psychologic Data	Acute Pain Data
Bates, 1991 ⁵⁸	278	Open	+	34%	100%	—	—	—
Jørgensen, 1991 ⁵⁴	115	Open	—	22%#	100%	—	+	—
Peters, 1991 ¹⁰³	52	Lap	—	17%**	—	—	—	—
Qureshi, 1993 ¹⁰⁴	100	Lap	39%	12%	95%	—	—	—
Velpen, 1993 ⁶³	56	Open	+	48%§	+	—	—	—
	68	Lap	+	54%§	+	—	—	—
Wilson, 1993 ⁶⁷	100	Lap	+	6.0%	+	—	—	—
	167	Open	+	6.6%##	+	—	—	—
Stiff, 1994 ⁶⁴	205	Lap	30%‡,***	3%*,***	95%	—	—	—
	155	Open	37%‡,†††	10%*,†††	92%	—	—	—
Ure, 1995 ⁸⁶	468	Lap	56%§§	26%‡,§§	83%	—	—	—
McMahon, 1995 ⁶⁵	115	Mini	60%	47%	+	—	—	+
	118	Lap	57%	54%	+	—	—	+
Fenster, 1995 ⁵⁹	154	Lap	+	18%‡‡	100%	—	—	—
	44	Lap-acal	+	39%††	100%	—	—	—
Luman, 1996 ¹⁰⁵	97	Lap	+	13%‡	+	—	+	—
de Pourvoirville, 1997 ¹⁰⁶	72	Lap	—	56%‡‡	—	—	—	+
	24	Open	—	23%‡‡	—	—	—	+
Gui, 1998 ⁶¹	92	+	+	30%***	100%	+	—	—
Jess, 1998 ⁵⁵	94	Lap	—	18%	+	+	+	—
Middelfart, 1998 ⁵⁷	519	Open	+	37%‡‡‡	—	—	—	—
Borly, 1999 ⁵⁶	80	—	38%	26%	—	+	+	—

See table 1 legend for further information.

* Right upper quadrant pain. † Noncolicky pain. ‡ Indigestion. § Follow-up at 6–30 months. || Abdominal pain at 12 months. # Abdominal pain at 6–12 months. ** Follow-up at more than 3 months. †† Follow-up at 15–79 months. ‡‡ Follow-up at 3 months. §§ Median follow-up at 19 months. ||| Median follow-up at 14 months. ## Median follow-up at 28 months. *** Mean follow-up at 32 months. ††† Mean follow-up at 15 months. ‡‡‡ 5–10 yr follow-up.

Lap = laparoscopic cholecystectomy; lap-acal = laparoscopic cholecystectomy for acalculous gallbladder; mini = small incision open cholecystectomy; open = open cholecystectomy.

in only four studies,⁶⁹⁻⁷² and these studies report a variable incidence.

Preoperative Factors. In a prospective study of 500 surgeries, surgery for a recurrent hernia had a higher incidence of moderate to severe pain at 12 months than did surgery for a primary repair.⁷⁰ Patients receiving care under workers' compensation for work-related injury have a higher pain incidence at 6 months than those who are being cared for by commercial insurance (5 of 22 *vs.* 1 of 22)⁷³; additionally, they have had pain for a longer period of time before surgery.

Intraoperative Factors. The data are inconclusive about whether the surgical approach alters the incidence of chronic pain. Liem *et al.*,⁷⁴ in a prospective randomized controlled study that evaluated recurrence rates, found a lower incidence of chronic pain (2%) after a laparoscopic repair when compared with an open nonmesh repair (14%). The Medical Research Council study⁷² also found a significantly lower incidence of pain at 12 months after a laparoscopic repair (28%) compared with an open repair (37%). Dirksen *et al.*⁷⁵ found no difference in the incidence of chronic pain in their prospective randomized controlled study that compared an open repair (14%) to a laparoscopic repair (20%). Likewise, Gillion and Fagniez⁷¹ found no difference in the incidence of pain in their case series, with both open and laparoscopic repairs having approximately a 14% incidence of chronic pain. Two of the studies^{71,75} noted that

complications, including pain, were more common early in their experience with laparoscopic hernia repair.

In a prospective multicenter study, Hay *et al.*⁷⁶ did not find statistically significant differences in chronic pain after open repairs (Bassini, Cooper ligament, or Shouldice). Likewise, in a prospective analysis of 500 surgeries, Callesen *et al.*,⁷⁰ found no significant differences in chronic pain between mesh and nonmesh open repairs in primary hernia surgery. Whether the experience of the surgeon or the degree of specialization is a factor in chronic pain or recurrence has been debated.⁷⁷ The incidence of chronic pain in case series data from hernia centers is low,^{78,79} whereas reports with higher incidences of chronic pain typically come from teaching institutions.^{72,74,75,80} There are no controlled, prospective studies of this factor.

Postoperative Factors. The extent of pain at 1 and 4 weeks after surgery is a predictive factor⁷⁰ for pain at 1 yr. Neither length of convalescence nor type of employment affects the incidence of chronic pain.⁷⁰

Apparent Etiology. The demonstrated relation between postoperative sensory dysfunction and chronic pain⁷¹ supports the interpretation that nerve damage is a pathologic factor. Most authors assume the pain is usually of neuropathic origin,⁸¹⁻⁸³ although Wantz⁸⁴ also mentions the possibility of the repair being too tight.

Progression. Callesen *et al.*⁷⁰ noted the incidence of moderate to severe pain decreased from 11% at 4 weeks

Table 5. Hernia Surgery

Study Reference	Size	Surgical Approach	Chronic Pain Incidence	Preoperative Pain Incidence	Preoperative Physiologic Data	Preoperative Psychologic Data	Acute Pain Data
Hay, 1995 ⁷⁶	418	Bassini	6.0%*	—	—	—	—
	407	Cooper	3.7%*	—	—	—	—
	818	Should	4.6%*	—	—	—	—
Cunningham, 1996 ⁶⁹	276	Open	12%§	—	—	—	+
Zieren, 1996 ¹⁰⁷	80	Lichten	2.5%†	—	—	—	+
	80	Should	5.0%†	—	—	—	+
	80	Lap	3.8%†	—	—	—	+
Liem, 1997 ⁷⁴	507	Open	14%	83%	+	—	+
	487	Lap	2%	85%	+	—	+
Dirksen, 1998 ⁷⁵	87	Bassini	14%§	—	—	—	+
	86	Lap	20%§	—	—	—	+
Rutkow, 1998 ⁷⁸	383	Plug ^z	0%§	—	—	—	—
Wellwood, 1998 ⁸⁰	176	Lichten	23%‡	—	+	+	—
	182	Lap	15%‡	—	+	+	—
Callesen, 1999 ⁷⁰	419	Open	6.0%§	—	—	—	+
Gillion, 1999 ⁷¹	351	Open	15%#	—	—	—	—
	139	Lap	14%#	—	—	—	—
MRC, 1999 ⁷²	394	Open	37%§	—	—	—	+
	362	Lap	29%	—	—	—	+

See table 1 legend for further information.

* Exertional pain at 6 months. † Groin, leg, or testicular pain lasting more than 2 months. ‡ Pain at 3 months. § Pain at 1 yr. || Median follow-up at 607 days.

Median follow-up at 38 months. ** Recurrent hernia repairs.

Bassini = Bassini repair; Cooper = Cooper ligament repair; Lap-PP = laparoscopic transabdominal preperitoneal repair; Lichten = Lichtenstein repair; Plug = plug and patch technique described by authors; Should = Shouldice repair.

to 6% at 1 yr. Moderate to severe pain at 1 and 4 weeks was the strongest predictor of pain at 1 yr.

Section Summary. Chronic pain after groin hernia surgery is not rare, but it appears to be less common than chronic pain after the surgeries previously cited. Because hernia surgery is common, a large number of individuals are affected by chronic pain. Nerve dysfunction has been shown to be a factor, as has the intensity of early postoperative pain. The role of acute pain therapy on the incidence of chronic pain is unknown.

Discussion

Although patient satisfaction with surgical results is reported to be high,⁶⁵⁻⁶⁷ the studies reported herein show that chronic pain is common after these surgeries, and this has been confirmed in a recent review.⁸⁵ Chronic pain is costly to society in terms of suffering and disability. For humanitarian and economic reasons, the problem of chronic pain after surgery should be addressed. It is also clear there is significant variability in the incidence of chronic pain among these surgical procedures (11.5–47% for inguinal hernia and thoracic surgery). We believe that our review has been thorough, but despite the use of broad search criteria, our electronic search did not detect all articles known to the authors that relate to the development or incidence of chronic pain after the selected surgeries. Reasons for this include publication in journals not included in the Index Medicus at the time of publication (*e.g.*, Kanner *et al.*³¹ and Gillion and Fagniez⁷¹) or “pain” not being identified as a key word or used in the title or abstract (*e.g.*, Hay *et al.*⁷⁶). As a result, we are not certain that we identified all articles that contain data relevant to this review.

We identified a number of risk factors for prolonged pain after surgery and divide these factors into three categories: (1) preoperative factors, (2) intraoperative factors, and (3) postoperative factors (table 6). Preoperative pain is a predictor of chronic pain for postamputation pain,¹⁶ phantom breast pain,³⁶ and noncolicky abdominal pain and symptoms after cholecystectomy.^{56,58,86} For each of these surgeries, the characteristic

of the preoperative pain that predicted chronic pain tended to be continuous pain of 1 month or more in duration. Psychologic vulnerability is a risk factor for persistent pain after cholecystectomy⁵⁴⁻⁵⁶ but has not been evaluated in the other surgeries reviewed herein. It has also been found to predict outcome after lumbar spine surgery.⁸⁷

Nerve damage is an intraoperative factor that contributes to chronic postoperative pain. Patients undergoing anterior thoracotomy are less likely to have intercostal nerve dysfunction and less likely to have PTPS.^{24,25} After breast surgery, intercostobrachial neuralgia is associated with damage of that nerve, and attempts to preserve the nerve are associated with a lower incidence of pain.⁴¹ However, nerve damage *per se* does not necessarily cause pain because the incidence of decreased sensation was 2–4 times higher than the incidence of pain in the distribution of the intercostobrachial nerve after axillary node dissection.^{41,49} Likewise, Benedetti *et al.*^{25,30} found chronic pain in only 50% of individuals with intercostal nerve dysfunction after thoracotomy. Nevertheless, nerve dysfunction appears to be associated with chronic pain.³⁰

The most striking predictive postoperative factor is the severity of acute postoperative pain after breast surgery,⁴⁴ thoracic surgery,^{18,27} and hernia repair.⁷⁰ Postoperative adjuvant radiation therapy increases the risk of chronic pain after breast surgery,⁴⁴ and neurotoxic chemotherapy increases the risk of phantom limb pain.⁵

Whether acute pain causes chronic pain has been debated.⁸⁸⁻⁹² Dworkin⁸⁸ proposed a model that incorporates psychosocial and pathophysiologic factors and the severity of acute pain as factors in the development of chronic pain. Using his model, we believe that ongoing nociceptive input from peripheral nerve injury increases acute pain and maintains early (3–12 months) chronic pain. Basbaum⁹³ recently reviewed changes in the nervous system associated with acute pain, with the conclusion that “persistent pain should be considered a disease state of the nervous system, not merely a symptom of some other disease conditions.” If persistent pain after surgery results from sensitization, prevention may be possible if sensitization can be blocked. Obata *et al.*²⁶ achieved

Table 6. Predictive Factors for Chronic Pain

Preoperative Factors	Intraoperative Factors	Postoperative Factors
Pain, moderate to severe, lasting more than 1 month Repeat surgery Psychologic vulnerability Workers' compensation	Surgical approach with risk of nerve damage	Pain (acute, moderate to severe) Radiation therapy to area Neurotoxic chemotherapy Depression Psychologic vulnerability Neuroticism Anxiety

this in thoracotomy patients with intraoperative plus postoperative epidural analgesia, but other clinical studies of preemptive analgesia are far from consistent.⁹⁴⁻⁹⁶

Psychosocial factors are also predictors of chronic pain. Of the surgical procedures we reviewed, the only reproducible psychologic predictor has been "psychologic vulnerability." The questionnaire for psychologic vulnerability measures a personality disorder that correlates with neuroticism.⁵⁵ Neither depression nor anxiety are preoperative predictors of chronic pain after surgery.^{18,37} Gatchel *et al.*⁹⁷ noted similar findings when trying to predict chronic back pain in acute back pain patients. They concluded that psychopathology (*e.g.*, depression) is not associated with an increased risk of development of chronic low back pain, but personality disorders may reflect psychosocial vulnerabilities or deficits in coping skills that are antecedents to chronic pain. The hypothesis of Gatchel *et al.*⁹⁷ is consistent with the psychologic vulnerability observations in PCS.

In conclusion, chronic pain is common after amputation, inguinal hernia surgery, breast surgery, gallbladder surgery, and lung surgery, and this is also confirmed in another recent review.⁸⁵ For each of these surgeries, data may be interpreted as showing chronic neuropathic pain as one etiology. Intensity of acute postoperative pain is a predictor of chronic pain. Future studies should characterize the factors of importance in the transition from acute to chronic pain. Such knowledge may result in designing more effective and more rational early interventions. We hypothesize that, in some patients, the type of nerve injury may explain both the increase in acute pain and the chronic pain, but the extent of pain will be modified by other factors, particularly psychologic and physiologic factors that heighten pain sensitivity.

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