

Risk and Prevention of Persistent Neuropathic Post-Surgical and Post-Trauma Pain

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Persistent Post-trauma Pain

- 18.7% of patients in pain clinics have pain related to trauma (Crombie et al, 1998)
- Pain present 5-7 years after pelvic fracture or major extremity injury (Castillo et al, 2006; Mkandawire et al, 2002)
- PTSD (Bryant et al, 1999; Duckworth, Iezzi, 2006) and depression (Castillo et al, 2006; Von Korff et al, 2005) common

Persistent Post-trauma Pain (Rivara et al, 2008)

- Multicenter (69) prospective cohort study of 3047 patients 12 months after major traumatic injury
- 62.7% reported pain related to injury
- 59.3% of these had multiple pain sites (mean 2.2); average severity 4.5 (1 site) and 8.5 (6 sites)
- Unaffected by sex; more common in younger than older individuals

Persistent Post-surgical Pain

(Wildgaard et al, 2009)

- Incidence is highly variable and comparisons difficult because there is no consensus on when and what to report:
 - Intensity of a certain level is reached
 - Pain requires regular analgesia
 - Pain beyond a certain period of time

Persistent Post-surgical Pain

- Criteria established (Macrae, 2008):
 - Pain developed after surgery
 - Pain is of at least 2 months duration
 - Other causes have been excluded
- Pain that lasts for 3 to 6 months after surgery (Kehlet et al, 2006)
- Hard to prevent and treat and often is associated with disability and poor quality of life (Katz, Cohen, 2004)

Epidemiology

(Kehlet et al, 2006; Macrae, 2008; Visser, 2006)

- ~ 20% of patients in pain clinics
- Incidence varies with surgical procedure

<u>Surgery</u>	<u>Incidence</u>	<u>Severe disability</u>
Amputation	30-85%	5-10%
Thoracotomy	5-67%	10%
Inguinal hernia	10-63%	2-4%
Breast surgery	11-57%	5-10%
CABG	30-50%	5-10%
C-section	10-12%	4%

Predictors (Risk Factors)

(Perkins & Kehlet, 2000; Visser, 2006)

- #1: Surgeries with significant nerve or tissue injury, e.g., thoracotomy, cardiac, amputation, inguinal hernia, breast, limb
 - Lower incidence with minimally invasive thoracoscopy than lateral thoracotomy (Landreneau, 1994); however, this is influenced by the degree of intercostal nerve injury (Wildgaard et al, 2009)
- Females more than males (Caumo et al, 2002; Gotoda et al, 2001; Katz et al, 2005)

Other Predictors

- Moderate-to-severe pre and/or early postop pain (Brandsborg et al, 2007; 2009; Franneby et al, 2006; Gerbershagen et al, 2009; Hanley et al, 2007; Jensen et al, 1985; Nikolajsen et al, 1997; Poobalan et al, 2001)
- Greater early postop analgesic needs (Taillefer et al, 2006; Tasmuth et al, 1997)

Other Predictors

- Higher BMI (Bruce et al, 2003; Massaron et al, 2007, 2008; Smith et al, 1999)
- Higher incidence of postop complications (Franneby et al, 2006)
- Reoperation (Poobalan et al, 2001)
- Genetic factors; predisposed conditions (Macrae, 2008; Wildgaard et al, 2009)?

Preop Responses as Predictors

- Response to preop experimental pain stimuli (Granot et al, 2003; Werner et al, 2004) and to ice water test (Bisgaard et al, 2001) predicted severity of early but not late postop pain.
- Preop catastrophizing score correlated with severity of early but not late postop pain (Bisgaard et al, 2005).

Predictors: Amputation

- Preoperative pain in extremity (Hanley et al, 2007; Krane, Heller, 1995)
- Presence of acute and/or chronic stump pain (Nikolajsen et al, 1997)
- High early postop pain intensity (Hanley et al, 2007)
- Psychosocial factors (Hanley et al, 2004; Lame et al, 2005; Sperber et al, 2008)
- Neurotoxic chemotherapy (Smith, Thompson, 1995)

Predictors: Thoracotomy

- Extent of intercostal nerve dysfunction (Benedeti et al, 1997;1998; Wildgaard et al, 2009)
- Extent of acute postop pain and analgesia
 - Higher if EA started postop (Obata, 1999)
 - Higher if high postop pain intensity after EA discontinued (Gottschalk, Ochroch, 2008)
 - Higher with IV PCA than with preop thoracic EA (Senturk et al, 2002)

Risk Factors: Breast Surgery

- Axillary lymph node dissection (Abdullah et al, 1998; Husted et al, 1995; Legeby et al, 2002)
- Immediate axillary radiation (Keramopoulos et al, 1993)
- Preop pain (Kroner et al, 1989)
- Extent of postop pain and number of analgesic doses (Tasmuth et al, 1997)
- Possibly preop anxiety and depression (Tasmuth et al, 1996)

Predictors: Inguinal Hernia

- Preop pain (Poobalan et al, 2001)
- Intensity of continued postop pain at 1 and 4 weeks (Callesen et al, 1999)
- Recurrent repair (Callesen et al, 1999)
- Use of heavy-weight mesh for repair (Massaron et al, 2007, 2008)
- Risk higher in younger than older adults (Aasvang, Kehlet, 2005; Massaron et al, 2007, 2008; Pooblan et al, 2003)

Etiology

(Kehlet et al, 2006; Macrae, 2008)

- Major nerves “trespass” the surgical field of most surgical procedures; damage to these nerves is a prerequisite for the establishment of persistent pain.
- After surgery/trauma: Nociceptive, inflammatory, and neuropathic pain processes persist in absence of peripheral stimuli.

Neuroplasticity

- Neuronal reorganization (re-mapping) and new connections between neurons
- No simple continuum from acute (reversible, inflammatory) to persistent (changes in hardware) pain
 - Peripheral sensitization leads to reduced threshold and increased excitability
 - Central sensitization amplifies signals; constitutes abnormal perceptual response to normal sensory input and spreads sensitivity beyond peripheral injury site

Punctuate Mechanical Hyperalgesia (Brennan, Kehlet, 2005)

- Area of the body that encompasses uninjured tissue surrounding the site of tissue injury (incision, trauma)
- Thought to represent a measurement of central sensitization and so, plasticity
- Not typically measured in the clinical setting but may be more in the future

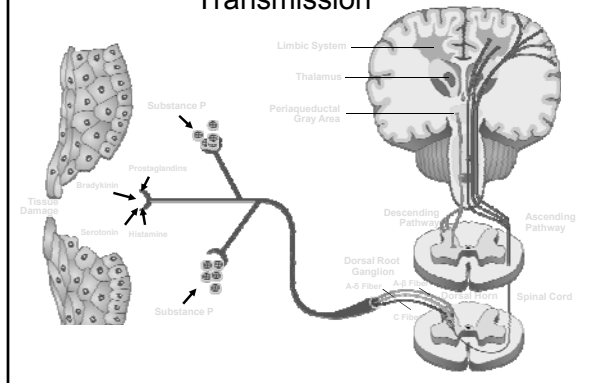
Pathophysiology Identified in Patient Subsets

- Inguinal mesh hernia repair, mastectomy: Continuous inflammatory response (Jung et al, 2003; Mikkelsen et al, 2004)
- Thoracotomy: Extensive nerve damage → sensory threshold changes and somatosensory evoked responses to electrical stimulation correlate with pain intensity (Benedeti et al, 1998)

Phantom Pain

- Neuromatrix Theory (Melzack, 1990): Matrix in the CNS for the perception of a body part; exists even when the body part does not
- Remapping (fooling the brain): Intact limb mirror therapy (Hanling et al, 2010); virtual limb therapy (Gaggioli et al, 2010)
- Inconsistency in therapeutic response indicates multiple etiologies (Kehlet, Perkins, 2000; Sherman et al, 1984)

Nociception: "Normal" Pain Transmission



Etiology: Research Needed

(Kehlet et al, 2006; Mikkelsen et al, 2004)

- Factors other than nerve damage are likely involved in most syndromes.
- Many questions unanswered:
 - Why such variation in pain descriptions?
 - Why such inconsistency in response to treatment?
 - How do comorbidities affect syndromes?

Prevention

(Kehlet et al, 2006; Macrae, 2001; 2008)

- Surgical technique: Minimally invasive whenever possible; careful dissection
- Suppression of pain at time of surgery or trauma is not enough
- Preventive and aggressive multimodal analgesia; more research needed
 - Adequate afferent blockade
 - NSAIDs and opioids for inflammatory pain
 - Ketamine, local anesthetics, anticonvulsants

Key: Multimodal Analgesia

(Kehlet et al, 2006)

- Combinations of drugs that attack more than one pain mechanism
- Some drugs add analgesia
- Some drugs work synergistically
- Added benefit: Lower doses of each drug → fewer adverse effects

Multimodal Approach

(Fassoulaki et al, 2005)

- RCT (N = 50): Breast cancer surgery
- Placebo or oral gabapentin, EMLA to surgical area, and ropivacaine in wound
- Pain at 3 months: 44% v. 82% (placebo)
- Pain at 6 months: 30% v. 57% (placebo)
- Methodology/conclusions criticized: Did not control for other factors, e.g., chemo or radiation therapy (Kehlet, 2006).

Three Methods Compared

(Senturk et al, 2002)

- RCT (N = 69): Thoracotomy
- Groups: Pre, intra, postop thoracic EA (1); just postop TEA (2); IV PCA (3)
- Far superior early pain relief with group 1
- Incidence of pain at 6 mo: Group 3: 78% group 2: 63%; group 1: 45%
- Highest pain severity in group 3, but no affect on daily life in any of the groups

Preventive EA

(Katz, Cohen, 2004; Katz et al, 2003)

- RCT (N = 131): Major GYN surgery
- Pre and post incision EA reduced postop morphine consumption and hyperalgesia
- Surveyed at 3 wks: Reduced pain/disability
- Surveyed at 6 months: No reduction
- May have failed to address all underlying mechanisms that initiate persistent pain

IV Ketamine and EA

(Lavand'homme et al, 2005)

- RCT (N = 85): Colon resection for neoplasm
- Combinations of IV ketamine plus IV or EA local anesthetic, clonidine, and opioid administered intraop or postop
- PMH almost completely eliminated by each preventive intervention
- 1-year residual pain: IV only (28%); EA postop only (11%); EA intra and EA and IV postop (0%)

Further Research Needed

- Spinal anesthesia
 - Survey (N =1299): 32% post hysterectomy pain; lower risk with spinal than intra or postop EA (Brandsborg et al, 2007)
- Continuous peripheral nerve block (De Cosmo et al, 2009)
- Best methods for prevention of both post-surgical and post-trauma pain

Clinical Presentation

(Kehlet et al, 2006)

- Key warning sign: Pain that persists beyond expected healing period
- Poor response to initial (traditional) treatments
- Wide range of sensory-discriminative descriptors: Aching, cramping, sharp, shooting, stabbing, tender, numb and other dyesthesias

Clinical Presentation

(Massaron et al, 2008)

- SF McGill Pain Questionnaire (N = 1311) post inguinal hernia
- 18.1% had chronic pain; severe and interfered with normal activities in 2.1%
- Descriptors:
 - 71.3% = nociceptive; 8.9% neuropathic; 19.8% nociceptive + neuropathic
 - “Tender” and “aching” most common

Treatment

(Kehlet et al, 2006; Macrae, 2001; 2008)

- Early referral to a pain specialist with access to multiple disciplines for evaluation and treatment of both pain and co-morbidities
- Avoid pigeon-holing: Treatment does not depend on type of surgery or trauma.
- Target the progression of mechanisms, not just the disturbances they produce.

Treatment

(Kehlet et al, 2006; Macrae, 2001; 2008)

- Use multimodal approach to attack multiple underlying mechanisms:
 - NSAIDs and opioids for those with persistent inflammatory pain
 - Ketamine, local anesthetics, anticonvulsants, and antidepressants for neuropathic pain
- Often multiple drug trials required

The Good News

- Persistent post-surgical and post-trauma pain have become a focus of increasing interest among clinicians and researchers (Kehlet et al)
- Several studies currently underway to identify mechanisms and best methods for prevention and treatment
- For many, pain gradually decreases over months to years

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References and Suggested Reading

Aasvang E, Kehlet H. (2005). Chronic postoperative pain: The case of inguinal herniorrhaphy. *Br J Anaesth* 95:69-76.

Abdullah TI, Iddon J, Barr I, et al. (1998). Prospective randomized controlled trial of preservation of the intercostalbrachial nerve during axillary node clearance for breast cancer. *Br J Surg* 85:1443-1445.

Bach S, Noreng MF, Tjellden NU. (1988). Phantom limb pain in amputees during the first 12 months following limb amputation after preoperative lumbar epidural blockade. *Pain* 33:297-301.

Benedetti F, Amanzio M, Casadio C, et al. (1997). Postoperative pain and superficial abdominal reflexes after posterolateral thoracotomy. *Ann Thorac Surg* 64:207-210.

Benedetti F, Vighetti S, Ricco C, et al. (1998). Neurophysiologic assessment of nerve impairment in posterolateral muscle-sparing thoracotomy. *J Thorac Cardiovasc Surg* 115:841-847.

Bisgaard T, Klarskov B, Rosenberg J, et al. (2001). Characteristics and prediction of early pain after laparoscopic cholecystectomy. *Pain* 90:261-269.

Bisgaard T, Rosenberg J, Kehlet H. (2005). From acute to chronic pain after laparoscopic cholecystectomy: A prospective follow-up analysis. *Scand J Gastroenterol* 40:1358-1364.

Brandsborg B, Dueholm M, Nikolajsen L, et al. (2009). A prospective study of risk factors for pain persisting 4 months after hysterectomy. *Clin J Pain* 25(4):263-268.

Brandsborg B, Nikolajsen L, Hansen CT, et al. (2007). Risk factors for chronic pain after hysterectomy: A nationwide questionnaire and database study. *Anesthesiology* 106(5):1003-1012.

Brandsborg B, Nikolajsen L, Kehlet H, et al. (2008). Chronic pain after hysterectomy. *Acta Anaesthesiol Scand* 52(3):327-331.

- Brennan TJ, Kehlet H. (2005). Preventive analgesia to reduce wound hyperalgesia and persistent postsurgical pain (Editorial Views). *Anesthesiology* 103:681-683.
- Bruce J, Drury N, Poobalan AS, et al. (2003). The prevalence of chronic chest and leg pain following cardiac surgery: A historical cohort study. *Pain* 104:265-273.
- Bruce J, Poobalan AS, Smith WC, et al. (2004). Quantitative assessment of chronic postsurgical pain using the McGill Pain Questionnaire. *Clin J Pain* 20(2):70-75.
- Bryant RA, Marosszeky JE, Crooks J, et al. (1999). Interaction of post-traumatic stress disorder and chronic pain following traumatic brain injury. *J Head Trauma Rehabil* 14(6):588-594.
- Callesen T, Bech K, Kehlet H. (1999). Chronic pain after inguinal hernia repair—a prospective study after 500 operations. *Br J Surg* 86:1528-1531.
- Carpenter JS, Sloan P, Andrykowski MA, et al. (1999). Risk factors for pain after mastectomy/lumpectomy. *Cancer Pract* 7:66-70.
- Castillo RC, MacKenzie EA, Wegner ST, et al. (2006). Prevalence of chronic pain seven years following limb threatening lower extremity trauma. *Pain* 124(3):321-329.
- Caumo W, Schmidt AP, Schneider CN, et al. (2002). Preoperative predictors of moderate to intense acute postoperative pain in patients undergoing abdominal surgery. *Acta Anaesthesiol Scand* 56:1265-1271.
- Crombie IK, Davies HT, Macrae WA. (1998). Cut and thrust: Antecedent surgery and trauma among patients attending a chronic pain clinic. *Pain* 76(1-2):167-171.
- De Cosmo G, Aceto P, Gualtieri E, et al. (2009). Analgesia in thoracic surgery: Review. *Minerva Anesthesiol* 75(6):393-400.
- Duckworth MP, Iezzi T. (2005). Chronic pain and posttraumatic stress symptoms in litigating motor vehicle accident victims. *Clin J Pain* 21(3):251-261.
- Fassoulaki A, Triga A, Melemeni A, et al. (2005). Multimodal analgesia with gabapentin and local anesthetics prevents acute and chronic pain after breast surgery for cancer. *Anesth Analg* 101:1427-1432.
- Franneby U, Sandblom G, Nordin P, et al. (2006). Risk factors for long-term pain after hernia surgery. *Ann Surg* 244(2):212-219.
- Gaggioli A, Amoresano A, Gruppioni E, et al. (2010). A myoelectric-controlled virtual hand for the assessment and treatment of phantom limb pain in trans-radial upper extremity amputees: A research proposal. *Stud Health Technol Inform* 154:220-222.

- Gerbershagen HJ, Ozgur E, Dagtekin O, et al. (2009). Preoperative pain as a risk factor for chronic post-surgical pain – six month follow-up after radical prostatectomy. *Eur J Pain* 13(10):1054-1061.
- Gotoda Y, Kambara N, Sakai T, et al. (2001). The morbidity, time course and predictive factors for persistent post thoracotomy pain. *Eur J Pain* 5:89-96.
- Gottschalk A, Ochroch EA. (2008). Clinical and demographic characteristics of patients with chronic pain after major thoracotomy. *Clin J Pain* 24(8):708-716.
- Granot M, Lowenstein L, Yarnitsky D, et al. (2003). Postcesarean section pain prediction by preoperative experimental pain assessment. *Anesthesiology* 98:1422-1426.
- Granot M, Feber SG. (2005). The role of catastrophizing and anxiety in the prediction of postoperative pain intensity: A prospective study. *Clin J Pain* 21:439-445.
- Hanley MA, Jensen MP, Ehde DM, et al. (2004). Psychosocial predictors of long-term adjustment to lower-limb amputation and phantom limb pain. *Disabil Rehabil* 26:882-893.
- Hanley MA, Jensen MP, Smith DG, et al. (2007). Pre-amputation pain and acute pain predict chronic pain after lower extremity amputation. *J Pain* 8(2):102-109.
- Hanling SR, Wallace SC, Hollenbeck KJ, et al. (2010). Pre-amputation mirror therapy may prevent development of phantom limb pain: A case series. *Anesth Analg* 10:611-614.
- Ho SC, Royse CF, Royse AG, et al. (2002). Persistent pain after cardiac surgery: An audit of high thoracic epidural and primary opioid analgesia therapies. *Anesth Analg* 95:820-823.
- Husted H, Lauridsen MC, Torsleff K, et al. (1995). Late symptoms among patients surgically treated for breast cancer. A questionnaire in the county of Southern Jutland. *Ugeskrift for Laeger* 157:6868-6872.
- Jensen TS, Krebs B, Nielsen J, et al. (1985). Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain* 21:267-278.
- Jung BF, Ahrendt GM, Oaklander AL, et al. (2003). Neuropathic pain following breast cancer surgery: Proposed classification and research update. *Pain* 104:1-13.
- Kalliomaki ML, Meyerson J, Gunnarsson U, et al. (2008). Long-term pain after inguinal hernia repair in a population-based cohort; risk factors and interference with daily activities. *Eur J Pain* 12:2214-225.

Katz J, Cohen L. (2004). Preventive analgesia is associated with reduced pain disability 3 weeks but not 6 months after major gynecologic surgery by laparotomy. *Anesthesiology* 101:169-174.

Katz J, Cohen L, Schmid R, et al. (2003). Postoperative morphine use and hyperalgesia are reduced by preoperative but not intraoperative epidural analgesia. *Anesthesiology* 98:1449-1460.

Katz J, Poleschuck EL, Andrus CI, et al. (2005). Risk factors for acute pain and its persistence following breast cancer surgery. *Pain* 119:16-25.

Kehlet H. (2006). Perioperative analgesia to prevent chronic postmastectomy pain. (Letter to Editor) *Anesth Analg* 103(2):494. Response to letter: 103(2):495.

Kehlet H, Jensen TS, Woolf C. (2006). Persistent postsurgical pain: Risk factors and prevention. *Lancet* 367:1618-1625.

Keramopoulos A, Tsionou C, Minaretzis D, et al. (1993). Arm morbidity following treatment of breast cancer with total axillary dissection: A multivariate approach. *Oncology* 50:445-449.

King KM, Parry M, Southern D, et al. (2008). Women's recovery from sternotomy-extension (WREST-E) study: Examining long-term pain and discomfort following sternotomy and their predictors. *Heart* 94(4):493-497.

Krane EJ, Heller LB. (1995). The prevalence of phantom limb sensation and pain in pediatric amputees. *J Pain Symptom Manage* 10:21-29.

Kroner K, Krebs B, Stov J, et al. (1989). Immediate and long-term phantom breast syndrome after mastectomy: Incidence, clinical characteristics and relationship to pre-mastectomy breast pain. *Pain* 36:327-334.

Lame IE, Peters ML, Vlaeyen JW, et al. (2005). Quality of life in chronic pain is more associated with beliefs about pain, than with pain intensity. *Eur J Pain* 9:15-24.

Landreneau RJ, Mack MJ, Haelrigg SR, et al. (1994). Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg* 107:1079-186.

Lavand'homme P. (2010). Chronic pain after vaginal and cesarean delivery: A reality questioning our daily practice of obstetric anesthesia. (Editorial). *Int J Obstet Anesth* 19(1):1-2.

Lavand'homme P, De Kock M, Waterloos H. (2005). Intraoperative epidural analgesia combined with ketamine provides effective preventive analgesia in patients undergoing major digestive surgery. *Anesthesiology* 103:813-820.

Legeby M, Segerdahl M, Sandelin K, et al. (2002). Immediate reconstruction in breast cancer surgery requires intensive post-operative pain treatment but the effects of axillary dissection may be more predictive of chronic pain. *Breast* 11:156-162.

Macrae WA. (2001). Chronic pain after surgery. *Br J Anaesth* 87(1):88-98.

Macrae WA. (2008). Chronic post-surgical pain: 10 years on. *Br J Anaesth* 101(1):77-86.

Massaron S, Bona S, Fumagalli U, et al. (2007). Analysis of post-surgical pain after inguinal hernia repair: A prospective study of 1,440 operations. *Hernia* 11(6):517-525.

Massaron S, Bona S, Fumagalli U, et al. (2008). Long-term sequelae after 1,311 primary inguinal hernia repairs. *Hernia* 12(1):57-63.

Melzack R. (1990). Phantom limbs and the concept of a neuromatrix. *Trends Neurosci* 13:88-92.

Mikkelsen T, Werner MU, Lassen B, et al. (2004). Pain and sensory dysfunction 6 to 12 months after inguinal herniotomy. *Anesth Analg* 99:146-151.

Mkandawire NC, Boot DA, Braithwaite IJ, et al. (2002). Musculoskeletal recovery 5 years after severe injury: Long-term problems are common. *Injury* 33(2):111-115.

Nikolajsen I, Ilkjaer S, Kroner K, et al. (1997). The influence of preamputation pain on postamputation stump and phantom pain. *Pain* 72:393-405.

Obata H, Saito S, Fujita N, et al. (1999). Epidural block with mepivacaine before surgery reduces long-term post-thoracotomy pain. *Can J Anaesth* 46:1127-1132.

Pasero C, Polomano R, Portenoy RK, et al. (2011). Adjuvant analgesics. In *Pain Assessment and Pharmacologic Management*. St. Louis, Mosby/Elsevier.

Perkins FM, Kehlet H. (2000). Chronic pain as an outcome of surgery. *Anesthesiology* 93:1123-1133.

Poobalan AS, Bruce J, King PM, et al. (2001). Chronic pain and quality of life following open inguinal hernia repair. *Pain* 88:1122-1126.

Poobalan AS, Bruce J, Smith WC, et al. (2003). A review of chronic pain after inguinal herniorrhaphy *Clin J Pain* 19:48-54.

Ramesh, Shukla NK, Bhatnagar S. (2009). Phantom breast syndrome. *Indian J Palliat Care* 15(2):103-107.

- Rivara FP, MacKenzie EJ, Jurkovich GJ, et al. (2008). Prevalence of pain in patients 1 year after major trauma. *Arch Surg* 143(3):282-287.
- Senturk M, Ozcan PE, Talu GK, et al. (2002). The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg* 94:11-15.
- Sherman RA, Sherman CJ, Parker L. (1984). Chronic phantom and stump pain among American veterans: Results of a survey. *Pain* 18:83-95.
- Smith J, Thompson JM. (1995). Phantom limb pain and chemotherapy in pediatric amputees. *Mayo Clinic Proc* 70:357-364.
- Smith WC, Bourne D, Squair J, et al. (1999). A retrospective cohort study of post mastectomy pain syndrome. *Pain* 83:91-95.
- Sperber AD, Morris CB, Greemberg L, et al. (2008). Development of abdominal pain and IBS following gynecological surgery. *Gastroenterology* 134:75-84.
- Taillefer MC, Carrier M, Belisle S, et al. (2006). Prevalence, characteristics, and predictors of chronic nonanginal postoperative pain after a cardiac operation: A cross-sectional study. *J Thor Cardiovasc Surg* 131:1274-1280.
- Tasmuth T, Estlanderb AM, Kalso E. (1996). Effect of present pain and mood on the memory of past postoperative pain in women treated surgically for breast cancer. *Pain* 68:343-347.
- Tasmuth T, Kataja M, Blomqvist C, et al. (1997). Treatment-related factors predisposing to chronic pain in patients with breast cancer—a multivariate approach. *Acta Oncol* 36:625-630.
- Visser EJ. (2006). Chronic post-surgical pain: Epidemiology and clinical implications for acute pain management. *Acute Pain* 8:73-81.
- Von Korff M, Crane P, Lane M, et al. (2005). Chronic spinal pain and physical-mental comorbidity in the United States: Results from the national comorbidity survey replication. *Pain* 113(3):331-339.
- Wartan SW, Hamann W, Wedley JR, et al. (1997). Phantom pain and sensation among British veteran amputees. *Br J Anaesth* 78:652-659.
- Werner MU, Duun P, Kehlet H. (2004). Prediction of postoperative pain by preoperative nociceptive responses to heat stimulation. *Anesthesiology* 100:115-119.
- Wildgaard K, Ravn J, Kehlet H. (2009). Chronic post-thoracotomy pain: A critical review of pathogenic mechanisms and strategies for prevention. *Eur J Cardiothorac Surg* 36(1):171-181.