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REVIEW

Risk Factors for Acute Postsurgical Pain: A Narrative Review

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Abstract: Acute postsurgical pain (APSP) has received growing attention as a surgical outcome. When poorly controlled, APSP can affect short- and long-term outcomes in patients. Despite the steady increase in awareness about postoperative pain and standardization of pain prevention and treatment strategies, moderate-to-severe APSP is frequently reported in clinical practice. This is possibly because pain varies widely among individuals and is influenced by distinct factors, such as demographic, perioperative, psychological, and genetic factors. This review investigates the risk factors for APSP, including gender, age, obesity, smoking history, preoperative pain history, pain sensitivity, preoperative anxiety, depression, pain catastrophizing, expected postoperative pain, surgical fear, and genetic polymorphisms. By identifying patients having an increased risk of moderate-to-severe APSP at an early stage, clinicians can more effectively manage individualized analgesic treatment protocols with a combination of pharmacological and non-pharmacological interventions. This would alleviate the transition from APSP to chronic pain and reduce the severity of APSP-induced chronic physical disability and social psychological distress.

Keywords: acute postoperative pain, acute postsurgical pain, risk factors, predictors

Introduction

Pain is a complex, unpleasant sensory and emotional experience that occurs following actual or potential tissue damage.[1] Because of the increase in the aging population and advancements in medical technology, more than 312.9 million surgical procedures are performed annually worldwide.[2] According to epidemiological studies, postoperative pain remains under-treated,[3–5] thereby adversely affecting cardiovascular, respiratory, and immune system functions and delaying postoperative recovery.[6]

Postoperative pain is acute in nature and occurs immediately after surgery and usually lasts for 3–7 days.[7] According to a United States national survey, approximately 80% surgical patients experienced acute postsurgical pain (APSP), of which 86% reported moderate, severe, or extreme pain.[8] When poorly controlled, APSP can prolong hospital stay, increase opioid use, and contribute to health care costs.[9,10] Additionally, APSP is correlated with poor prognosis including postoperative delirium, cardiovascular events, thromboembolism, pulmonary complications, and chronic pain syndrome.[11–15] Although the interest in APSP is growing in the recent decades, effective pain management is a clinical challenge.[8,16] Identifying patients with high APSP-related risk factors on the basis of individual differences in patients' social, psychological, and genetic factors is essential for the early prevention and individualized treatment of APSP.

APSP-related risk factors vary according to the surgery type. Ip et al[17] were the first to systematically review APSP predictors. They found that preoperative pain, anxiety, age, and surgery type were the four most significant predictors of APSP. Sobol-Kwapinska et al[18] reviewed APSP-related psychological factors and noted the probable association between APSP and anxiety, pain catastrophizing, expectation of pain, and depression. On conducting a systematic review of literature on pain sensitivity for predicting APSP, Werner et al[19] observed that the predictive strength of pain sensitivity is

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considerably higher than that of demographics and psychologic factors. Through a systematic review and meta-analysis, Yang et al[20] explored preoperative predictors of poorly controlled APSP. However, they could not identify the predictive role of some factors, such as pain sensitivity and genetic polymorphisms.

By conducting an extensive literature review, we here provide a comprehensive overview of APSP-related risk factors in terms of demographic, perioperative, psychological, and genetic factors. Identification of these risk factors will allow early prevention and active intervention in high-risk patients for reducing short- and long-term postoperative complications and accelerating postoperative recovery.

Methods

We here conducted a literature search of the electronic databases of PUBMED, Embase, Web of Science, and Cochrane Library between January 1990 and December 2023 to identify APSP-related risk factors. Search strategy is presented in Supplementary Table 1. Only studies involving adult patients, which were published in English were included in the study. The study selection process for the narrative review is shown in Figure 1. A systematic literature search identified 20,829 potentially relevant studies. After eliminating duplicates and excluding all ineligible studies, 64 studies were included. Furthermore, six crucial studies retrieved through manual search were also included. Ultimately, 70 studies were included in the narrative review. Important information of the studies is described in Supplementary Table 2. Table 1 lists some references about APSP-related risk factors.

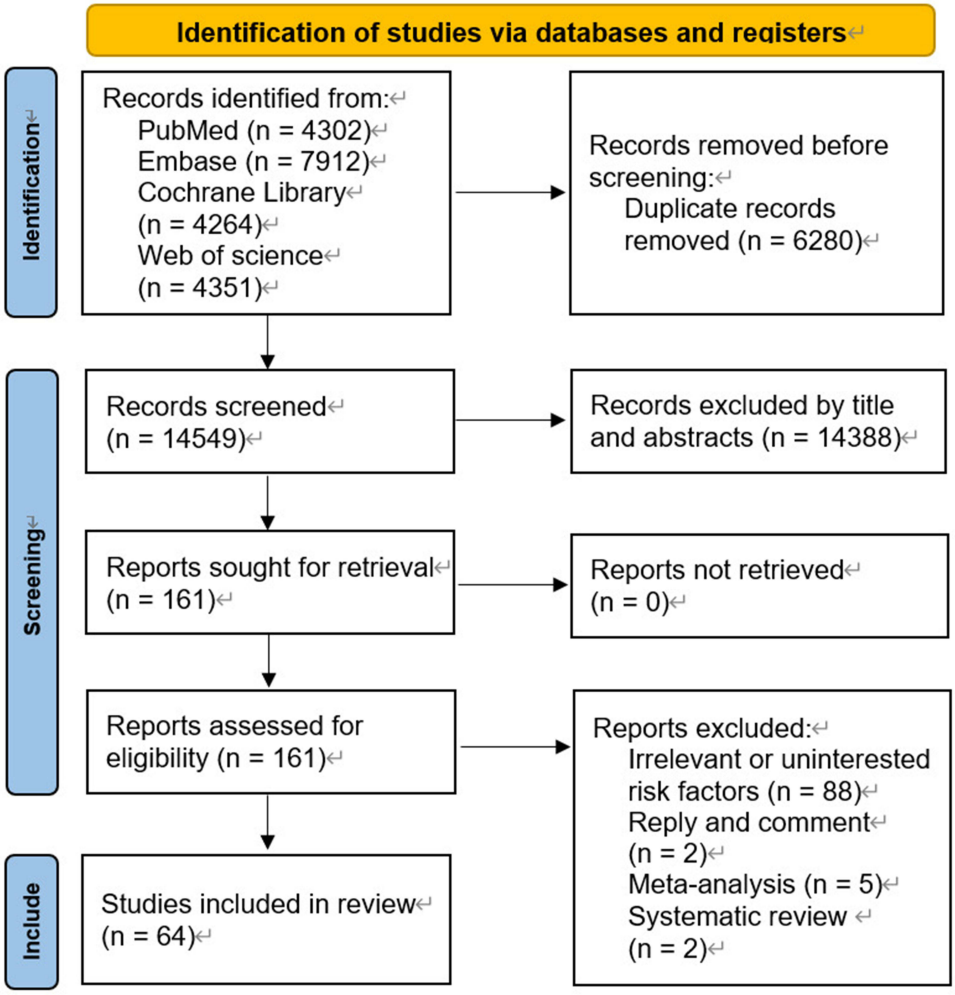

Figure 1 Flowchart of study selection.

Table 1 Risk Factors for Acute Postsurgical Pain

	Variables	References with Predictive Power	References Without Predictive Power
Demographic characteristics	Age	21–37	38–42
	Gender	30,44–51	24,26,40,42,52
	Obesity	29,30,38,45,49,54–56	22,35,39,42,57–60
	Smoking	29,51,62,63	30,38,64–68
Perioperative factors	Preoperative pain history	23,26,27,29–32,37,51,59,68–71	None
	Pain sensitivity	22,45,52,72–77	64,68
	Types of surgery	27,51,79–81	25
	Surgical approaches	22,38,56,62,63,69,72	None
	Analgesic consumption	21,42,66,87	None
Psychological factors	Anxiety	22,23,35,59,67–69,88–92	42,64,76,94
	Depression	31,38,59,23	39,42,60,87,95
	Pain catastrophizing	34,39,46,60,67,68,75,76,94,96,97	26,45,52
	Expected pain	25,64,67,76,96	None
	Surgical fear	25,26,96	32,76
Genetic factors	μ-opioid receptors gene	102,103	87,104,105
	Catechol-O-methyl transferase	None	87,105

Demographic Characteristics

Age

Pain sensitivity varies with age. Three prospective cohort studies, one retrospective cohort study, and one cross-section study have reported that being a categorical variable, younger age is an independent predictor of moderate-to-severe APSP.[21–25] Furthermore, two cross-section studies, one prospective cohort study, and one retrospective cohort study have revealed that as a continuous variable, younger age can predict moderate-to-severe APSP.[26–29] Liu et al[30] reported that the incidence of moderate-to-severe postoperative pain at rest decreased by 4% for per year increase in age, but that of pain with activity showed no decrease. The incidence of postoperative moderate-to-severe resting pain decreased by 20% for per 5-year increase in age, but that of movement pain exhibited no decrease.[31]

Five prospective cohort studies have demonstrated that age, as a continuous variable, is negatively associated with APSP intensity.[32–36] Moreover, Gerbershagen et al[37] reported that the continuous variable age predicted not only APSP intensity but also severe pain.

However, some studies have reported results inconsistent with these findings. Two prospective cohort studies and two retrospective cohort studies have revealed that age, being a continuous variable, is not an independent risk factor for moderate-to-severe APSP after the confounding factors are controlled.[38–41] Strutz et al[42] reported that the continuous variable age was not significantly related to APSP intensity after the perioperative opioid dose was controlled. Significant heterogeneity may be observed because of the variable age and other strong confounding factors. Age as a categorical variable seems to be more predictive for moderate-to-severe APSP.

Gender

As observed through most clinically relevant pain models, women are more sensitive to pain and suffer from more severe postoperative pain than men.[43] Two prospective cohort studies have reported that female gender is a significant risk factor for APSP intensity in patients surgically treated for thumb base osteoarthritis and those undergoing primary knee arthroplasty, respectively.[44,45] In patients who had undergone one-level instrumented lumbar fusion surgery, female gender predicted APSP intensity at rest, but not during activity.[46]

A cross-section study reported that female gender predicted moderate-to-severe APSP at rest as well as pain with activity after total hip and knee replacement.[30] The female gender was an independent predictor of moderate-to-severe APSP only in

patients who had received no regional anesthesia perioperatively.[47] A secondary analysis of three randomized controlled trials demonstrated that women exhibited considerably higher levels of moderate-to-severe APSP than men after arthroscopic surgery (RR 1.47, 95% CI 1.23–1.74).[48] Furthermore, a retrospective cohort study, a prospective cohort study, and a secondary analysis have unveiled that female gender is a significant risk factor for severe APSP.[49–51]

However, two prospective cohort studies and one cross-section study have demonstrated that female gender is not significantly related to APSP intensity.[26,42,52] Moreover, two retrospective cohort studies have reported that female gender fails to independently predict moderate-or-severe acute pain after orthopedic surgery.[24,40] A major problem of gender research data heterogeneity and study complexity.

Obesity

The effect of obesity on pain remains controversial.[53] Saloom et al[54] reported that obesity independently predicted the mean pain level at each time point during the first week after fixed-appliance orthodontic placement (β 4.42, 95% CI 0.79–8.05, $P = 0.018$). In a retrospective study, obese patients with a body mass index (BMI) of ≥30 kg/m^2 required a higher narcotic dose for controlling early pain after total joint arthroplasty.[55] Two prospective cohort studies and one cross-sectional study have shown that BMI can independently predict acute pain intensity or severity after knee arthroplasty.[30,45,49] Moreover, BMI was reported to be a significant risk factor for moderate-to-severe acute pain after open radical gastrectomy,[56] thoracoscopic surgery,[29] and breast cancer surgery.[38]

One retrospective study and one cross-section study have noted the correlation between BMI and APSP. These studies reported that BMI is not significantly correlated with APSP intensity following total hip arthroplasty and anterior cervical discectomy and fusion.[57,58] According to five prospective cohort studies, BMI fails to independently predict APSP intensity and severity after confounding factors, such as preoperative chronic pain, anxiety, and pain catastrophizing, are controlled for.[22,35,39,59,60] Furthermore, on evaluating the relation between obstructive sleep apnea and APSP, Strutz et al[42] found that obstructive sleep apnea was unlikely to be a strong risk factor for APSP severity. The results were possibly inconsistent because of the differences in vital confounding factors such as preoperative chronic pain and psychological factors.

Smoking

The underlying effects of smoking in APSP development are complex and not completely understood yet.[61] In a retrospective study, smoking history increased the incidence of moderate-to-severe pain at 24 and 48 h postoperatively by 86 and 53%, respectively.[29] One prospective cohort study and one secondary analysis have revealed that current smoking can significantly predict moderate-to-severe APSP.[51,62] Moreover, Chowdhury et al reported that current smoking significantly predicted APSP intensity after endoscopic sinus surgery.[63]

A few studies have not revealed the predictive effect of current smoking or smoking history on APSP. Former and current smoking did not exhibit a significant correlation with moderate-to-severe pain during the first 3 days after video-assisted thoracoscopic surgery. The only predictor was the preoperative average intensity of expected postoperative pain.[64] Similarly, Chiang et al[65] found that former and current smoking could not independently predict APSP intensity after the adjustment for age, a variable. Furthermore, two prospective cohort studies and one cross-section study have demonstrated that current smoking does not significantly predict moderate-to-severe APSP after the confounding factors preoperative stress, BMI, or age are controlled for.[30,38,66] Two prospective cohort studies have shown that current smoking fails to predict APSP intensity, but some psychological factors can.[67,68] Given the heterogeneity of studies, the predictive effect of smoking on APSP remains inconsistent. In addition, the predictive effect of the dose of smoking on APSP also needs to be investigated.

Perioperative Factors

Preoperative Pain History

Chronic pain patients generally have lower preoperative pain thresholds and higher postoperative pain intensity. As the effect is in the same direction in all studies, preoperative pain is likely to strongly predict APSP. Two prospective cohort

studies, one cross-section study, and one retrospective study have reported that preoperative chronic pain history independently predicts moderate-or-severe APSP.[27,29,69,70] According to Raza et al,[71] the independent predictor of APSP intensity after breast cancer surgery was preexisting chronic pain in the breast (β 1.00, 95% CI 0.58–1.44), not elsewhere (β 0.08, 95% CI −0.23 to 0.39). However, past surgery-related pain and -unrelated pain both are related to APSP intensity after general, thoracic, and gynecological surgeries.[32]

Two cross-section studies and one prospective cohort study have found that preoperative chronic pain intensity predicts APSP intensity and severity.[26,30,68] In 30 surgical groups,[37] preoperative chronic pain intensity was significantly related to higher postoperative pain intensity and severe pain. Furthermore, three prospective studies have shown that preoperative moderate-to-severe pain is an independent risk factor for moderate-to-severe APSP.[23,31,59] According to the results of a secondary analysis of the perioperative quality improvement program dataset, preoperative moderate and severe pain was significantly related to severe acute pain after major surgery.[51]

Finally, a qualitative systematic review including 48 studies with 23,037 patients also confirmed the role of preoperative pain as an independent predictor of APSP.[17]

Pain Sensitivity

Pain sensitivity assessment mainly includes quantitative sensory testing (QST) and pain sensitivity questionnaire (PSQ). In QST, pain hypersensitivity can be quantitatively measured based on the responses of the subject, and the measurements are possibly correlated with postoperative pain. Eight studies were included in this QST. Three studies have unveiled that the mechanical temporal summation of pain (TSP) significantly predicts moderate-to-severe pain after breast surgery and acute pain intensity after knee arthroplasty or thoracotomy.[45,52,72] In two studies, the preoperative finger pressure pain threshold (PPT) and vaginal PPT were found to be related to acute pain intensity after anorectal surgery and hysterectomy, respectively.[73,74] A weaker conditioning pain modulation (CPM), which was calculated as [(PPT at baseline) – (PPT during the conditioning stimulus)]/(PPT at baseline) × 100 (%), was linked to more acute pain following orthognathic surgery.[75] The CPM, which was quantified as test stimulus rating during the conditioning stimulus-test stimulus rating before the conditioning stimulus, independently predicted maximum pain intensity after breast surgery in patients without pre-existing chronic pain.[76] PSQ are an alternative to QST for inferring central sensitization. According to a prospective cohort study, the PSQ is an independent risk factor for at least moderate pain after breast cancer surgery.[22] Similarly, Ruscheweyh et al[76] reported that the PSQ was an independent risk factor for maximum pain intensity following breast surgery. The PSQ also predicted pain in patients with pre-existing chronic pain. Pan et al[77] reported the preoperative thermal pain threshold to heat stimuli in the back as a predictor of resting and evoked pain 24 h after undergoing cesarean section.

However, according to Lunn et al,[68] preoperative short (5 seconds) and long (7 minutes) heat stimuli on the thigh 16 cm above the upper patellar border are not independent clinically relevant predictors of acute pain after total knee arthroplasty. Moreover, the suprathreshold cold stimulus on the forearm did not predict moderate-to-severe acute pain following video-assisted thoracoscopic surgery.[64] Results obtained for the different QST tools, postoperative pain assessment, and type of surgery are inconsistent. Usually, central QST variables, such as TSP and CPM, are likely reliable predictors of APSP in patients after elective surgery.[78] Future high-quality studies should focus on combining different QST tools and considering pain-related psychosocial factors for the establishment of the clinical significance of QST.

Types of Surgery and Surgical Approaches

Tissue and nerve injury generally cause postoperative pain. This pain varies by the types of surgery and surgical approaches used. Patients who undergo major surgery experience more severe APSP.[51] On examining the pain pattern in 10,008 ambulatory surgical patients, Chung et al[79] found that patients who underwent urological, general, or orthopedic surgery were at least 17 times more likely to develop severe pain than those who underwent ophthalmic surgery. Meanwhile, neurological, gynecological, or plastic surgery is at least 9 times more likely to develop severe pain than ophthalmic surgery. Similarly, some types of surgery, such as orthopedic and abdominal surgeries, are independent predictors of severe postoperative pain compared with ophthalmic surgery.[80] Caesarean section and some invasive

laparoscopic procedures such as laparoscopic ectopic pregnancy surgery exhibited significant correlations with a higher acute pain risk compared with other gynecological surgeries.[27,81] Furthermore, a qualitative systematic review revealed that abdominal, orthopedic, and thoracic surgeries exhibited a positive relationship with APSP. In fact, surgery type is among the independent predictors of APSP.[17] However, surgery type was not significantly related to APSP after day-case surgery, possibly because tissue injury for minor and intermediate day-case surgeries is not severe.[25]

Axillary lymph node dissection (ALND) is a standard initial approach for breast cancer patients. ALND potentially damages the sympathetic nerve and is correlated with APSP. Prospective and retrospective cohort studies have revealed that ALND is among the independent predictors of moderate-to-severe acute pain following breast cancer surgery.[22,38,72] Additionally, this surgical approach exhibited an independent association with APSP among other surgery types, such as inguinal hernia repair,[62] cesarean section,[69] open radical gastrectomy,[56] and endoscopic sinus surgery.[63] Postoperative pain is generally accepted to be more severe in patients undergoing major surgeries or surgeries with more extensive nerve damage.

Analgesic Consumption

At present, randomized controlled trials have focused on the efficacy for decreasing pain intensity and analgesic consumption. Observational studies investigating the association between analgesic consumption and APSP are scant. Opioid requirements vary widely among patients, and pharmacokinetics and pharmacodynamics may influence these requirements. In addition, age,[82,83] obesity,[84] pain sensitivity,[85] and genetic heritability[86] have been found to be strongly correlated with postoperative analgesic consumption, which is generally significantly related to APSP.[21]

In a prospective cohort study investigating predictors of APSP in 109 patients following total knee arthroplasty, the mean opioid consumption over 5 days postoperatively was positively correlated to the mean resting pain intensity over 5 days postoperatively ($\beta = 0.0053$, $P < 0.001$).[87] Postoperative morphine consumption by patients controlled analgesia (mg/kg) and predicted moderate-to-severe APSP (OR 1.02, 95% CI 1.01–1.04). Furthermore, the perioperative opioid dose exhibited significant association with maximum postoperative pain at days 1–3 after non-neurosurgical inpatient operation (β 0.123, 95% CI 0.081–-0.166).[42]

Psychological Factors

Anxiety

Preoperative anxiety is always considered a significant predictor of APSP, especially in gynecological, obstetric, and gastrointestinal surgeries.[17] Twelve prospective cohort studies have confirmed that preoperative anxiety is strongly associated with APSP. Of these, seven studies have shown that preoperative anxiety independently predicted APSP intensity during different postoperative periods.[35,59,67,68,88–90] Five studies have demonstrated that preoperative anxiety independently predicted moderate-to-severe acute pain after cesarean section or breast cancer surgery.[22,23,69,91,92] According to a systematic review, preoperative anxiety independently predicted APSP following breast cancer surgery.[93]

Inconsistently, one cross-sectional study revealed that preoperative anxiety is not a significant risk factor for APSP intensity after cardiac surgery, but pain catastrophizing is. Pain catastrophizing was found to fully mediate the relationship between anxiety and APSP intensity.[94] Moreover, a retrospective cohort study and three prospective cohort studies have reported that preoperative anxiety has no significant relationship with APSP when confounding factors such as pain catastrophizing, expected postoperative pain, and perioperative opioid dose are controlled for.[39,42,64,76] Heterogeneity was observed among studies, especially regarding strong psychological confounding factors and perioperative opioid.

Depression

Psychological distress, such as depression and a negative effect, may influence APSP. According to a retrospective cohort study, preoperative depression independently predicts moderate-to-severe acute pain following mastectomy.[38] Two prospective cohort studies have unveiled that preoperative depression is a significant risk factor for moderate-to-severe acute pain after radical prostatectomy, total knee replacement, and abdominal surgery.[23,59] Preoperative depression

independently predicted moderate-to-severe resting pain (OR 2.87, 95% CI 1.04–7.97) following total knee replacement, but not movement pain (OR 2.70, 95% CI 0.83–8.79) on postoperative day 2.[31]

On the other hand, some studies have found no independent correlation between preoperative depression and APSP intensity after the adjustment for strong confounding factors.[42,60] In knee replacement surgery, preoperative anxiety, but not depression independently predicted the mean postoperative pain intensity.[87] Furthermore, no significant correlation was observed between preoperative depression and APSP intensity after breast cancer surgery.[39,95] Overall, preoperative depression seemed to be significantly correlated with APSP severity, but not APSP intensity.

Pain Catastrophizing

Cognitive and psychological factors play a critical role in postoperative pain progression. Pain catastrophizing is an exaggerated and negative cognitive–affective response observed during actual or perceived painful stimulation and is correlated with APSP. Pain catastrophizing has been found to be strongly associated with APSP intensity.[34,39,46,60,67,75,94] Furthermore, Ruscheweyh et al[76] reported that pain catastrophizing independently predicted maximum pain intensity in patients with pre-existing chronic pain who underwent breast surgery. Two prospective cohort studies have revealed that pain catastrophizing independently predict moderate-to-severe acute pain.[68,96] According to Pinto et al,[97] pain catastrophizing is a significant risk factor for moderate-to-severe pain (OR 3.37, 95% CI 1.63–6.95) and acute pain intensity at 48 h after hysterectomy ($\beta = 0.245$, $P < 0.01$).

Furthermore, two prospective cohort studies have explored the predictive role of pain catastrophizing in pain intensity when confounding factors such as TSP were controlled for. They found that pain catastrophizing failed to predict APSP intensity.[45,52] Additionally, in a cross-sectional study, pain catastrophizing exhibited no significant association with APSP severity following orthopedic surgery.[26] The heterogeneity for pain catastrophizing studies was due to confounding factors such as TSP and other psychological factors. On the whole, some reviews highlighted that pain catastrophizing is the psychological factor most strongly correlated with APSP.[18,98]

Expected Pain

The effect of expected pain on the subjective pain experience has been well established. Psychological expectation is a central mechanism of placebo analgesia.[99] In prospective cohort studies, expected postoperative pain (VAS > 40 mm) increased the incidence of moderate-to-severe pain on day 0–4 after ambulatory surgery[25] and on day 1–4 after elective surgery.[96] Bayman et al[64] evaluated the relationship between expected pain and APSP in patients who underwent thoracoscopic surgery. They noted that the average expected pain was the only predictor of moderate-to-severe mean pain intensity over the 3-day postoperative period (OR 1.12, 95% CI 1.02–1.23).

Similarly, expected postoperative pain (VAS > 40 mm) exhibited a significant correlation with maximum pain intensity on day 1 after breast surgery.[76] However, Minic et al[67] reported that only expected postoperative pain predicted pain intensity in the "immediate early" period (1–8 h) after open nephrectomy. This independent association diminished in the "early" period (12–24 h) and "late early" period (48–72 h). Expected postoperative pain is a simple and effective tool for predicting APSP and is recommended for routine use before surgery.

Surgical Fear

Surgical fear is an easily identifiable emotional state prior to surgery. It includes fear of short-term consequences (eg, anesthesia, pain, and side effects) and long-term consequences (eg, surgical recovery). The German version of the surgical fear questionnaire is a clear predictor of APSP.[26]

In fact, preoperative surgical fear was found to be an independent risk factor for APSP in 1490 patients undergoing different elective ambulatory surgeries.[96] In day-case surgery, Gramke et al[25] reported that the fear of short-term consequences significantly predicted moderate-to-severe pain (defined by VAS > 40 mm) on postoperative days 0–2, but the fear of long-term consequences did not. Additionally, Ruscheweyh et al[76] evaluated psychological predictors of APSP after breast surgery. According to their findings, preoperative surgical fear did not independently predict maximum pain intensity in patients with or without pre-existing chronic pain. Wang et al[32] also reported that surgical fear was not

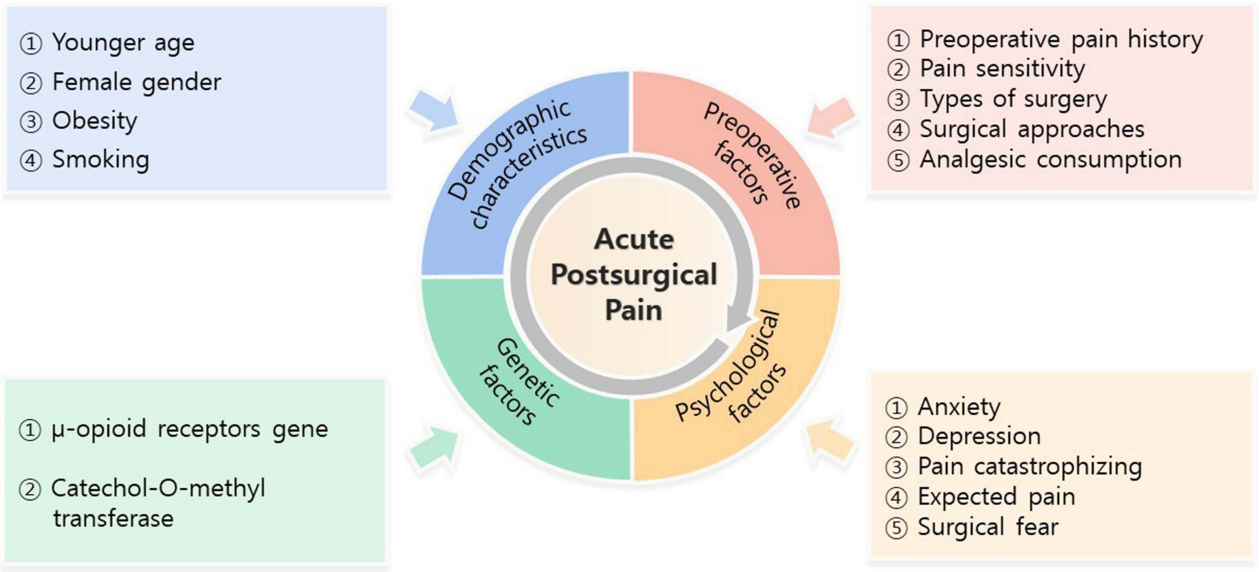

Figure 2 Risk factors for acute postsurgical pain.

associated with acute pain intensity after gynecologic and thoracic surgeries. Given the heterogeneity of studies, the predictive effect of surgical fear on APSP remains fluctuating.

Genetic Factors

According to accumulated evidence, genetic polymorphisms may influence pain perception. Individual differences in pain sensitivity have been explained based on catechol-O-methyl transferase (COMT) activity and genetic polymorphism of the opioid receptor mu 1 (OPRM1) gene.[100] On examining the correlation between the A118G single nucleotide polymorphism (SNP) of OPRM1 and pain sensitivity in healthy adults, a study found that this rare allele could predict higher pressure pain thresholds.[101] Sia et al[102] investigated the correlation between the OPRM1 gene SNP and opioids used for APSP following abdominal hysterectomy. They found that patients with OPRM1 118GG carriers had higher pain scores than those with the 118GA and 118AA genotypes. Additionally, on evaluating DNA methylation at the OPRM1 promoter, a prospective cohort study exhibited that methylation at CpG sites 4, 17, and 18 was associated with spine fusion-induced acute pain.[103]

However, in their genome-wide association study, Kim et al[104] examined the relationship between candidate SNPs and APSP after oral surgery. The results revealed that the candidate SNP (rs17122021) was correlated with maximum postoperative pain, and rs6693882 was related to the time of onset of postoperative pain. But these genetic associations did not sustain after adjustments were made for multiple comparisons. Moreover, Thomazeau et al[87] investigated genetic risk factors for acute pain following knee arthroplasty. They exhibited that a COMT SNP did not predict the mean resting pain over a 5-day postoperative period ($\beta = 0.0865$, $P = 0.265$). In another prospective cohort, OPRM1 and COMT SNPs were not correlated with APSP intensity after third molar removal.[105] This inconsistency in results was possibly caused by the difference in the predictive gene allele for different surgeries.

Conclusion

Managing APSP remains a considerable challenge. Individual variations in postoperative pain are prominent in terms of the impact of different risk factors for APSP. For example, younger age, female gender, preoperative pain, pain sensitivity, analgesic consumption, preoperative anxiety, pain catastrophizing, and expected pain exhibit significant association with APSP (Figure 2). Early identification of predictors in patients at a high APSP risk will promote the development of more effective interventions.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161(9):1976–1982. doi:10.1097/j.pain.0000000000001939
2. Weiser TG, Haynes AB, Molina G, et al. Size and distribution of the global volume of surgery in 2012. *Bull World Health Organ*. 2016;94. doi:10.2471/BLT.15.159293
3. Benhamou D, Berti M, Brodner G, et al. Postoperative Analgesic THerapy Observational Survey (PATHOS): a practice pattern study in 7 central/Southern European countries. *Pain*. 2008;136:134–141.
4. Fletcher D, Fermanian C, Mardaye A, Aegerter P. A patient-based national survey on postoperative pain management in France reveals significant achievements and persistent challenges. *Pain*. 2008;137:441–451. doi:10.1016/j.pain.2008.02.026
5. Sommer M, de Rijke JM, van Kleef M, et al. The prevalence of postoperative pain in a sample of 1490 surgical inpatients. *Euro J Anaesthesiol*. 2008;25:267–274.
6. Rawal N. Current issues in postoperative pain management. *Euro J Anaesthesiol*. 2016;33:160–171. doi:10.1097/EJA.0000000000000366
7. Sun E, Dexter F, Macario A. Can an acute pain service be cost-effective? *Anesthesia Analg*. 2010;111:841–844. doi:10.1213/ANE.0b013e3181f33533
8. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesthesia Analg*. 2003;97:1.
9. Sriwatanakul K, Weis OF, Alloza JL, Kelvie W, Weintraub M, Lasagna L. Analysis of narcotic analgesic usage in the treatment of postoperative pain. *JAMA*. 1983;250:926–929.
10. Peters CL, Shirley B, Erickson J. The effect of a new multimodal perioperative anesthetic regimen on postoperative pain, side effects, rehabilitation, and length of hospital stay after total joint arthroplasty. *J Arthroplas*. 2006;21(6):132–138. doi:10.1016/j.arth.2006.04.017
11. Vaurio LE, Sands LP, Wang Y, Mullen EA, Leung JM. Postoperative delirium: the importance of pain and pain management. *Anesthesia Analg*. 2006;102(4):1267–1273. doi:10.1213/01.ane.0000199156.59226.af
12. Beattie WS, Buckley DN, Forrest JB. Epidural morphine reduces the risk of postoperative myocardial ischaemia in patients with cardiac risk factors. *Canad J Anaesthes J Canad D anesthesie*. 1993;40:532–541.
13. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesthesia Analg*. 1998;86:598–612.
14. Lynch EP, Lazor MA, Gellis JE, Orav J, Goldman L, Marcantonio ER. The impact of postoperative pain on the development of postoperative delirium. *Anesthesia Analg*. 1998;86:781–785.
15. Gärtner R, Jensen M-B, Nielsen J, Ewertz M, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery. *JAMA*. 2009;302:1985–1992. doi:10.1001/jama.2009.1568
16. Price TJ, Basbaum AI, Bresnahan J, et al. Transition to chronic pain: opportunities for novel therapeutics. *Nat Rev Neurosci*. 2018;19:383–384. doi:10.1038/s41583-018-0012-5
17. Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology*. 2009;111:657–677. doi:10.1097/ALN.0b013e3181aae87a
18. Sobol-Kwapinska M, Bąbel P, Plotek W, Stelcer B. Psychological correlates of acute postsurgical pain: a systematic review and meta-analysis. *Eur J Pain*. 2016;20:1573–1586. doi:10.1002/ejp.886
19. Werner MU, Mjöbo HN, Nielsen PR, Rudin A. Prediction of postoperative pain: a systematic review of predictive experimental pain studies. *Anesthesiology*. 2010;112:1494–1502. doi:10.1097/ALN.0b013e3181dcd5a0
20. Yang MMH, Hartley RL, Leung AA, et al. Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ open*. 2019;9:e025091. doi:10.1136/bmjopen-2018-025091
21. Cachemaille M, Grass F, Fournier N, et al. Pain intensity in the first 96 hours after abdominal surgery: a prospective cohort study. *Pain Med*. 2020;21:803–813. doi:10.1093/pm/pnz156
22. Rehberg B, Mathivon S, Combescure C, Mercier Y, Savoldelli GL. Prediction of acute postoperative pain following breast cancer surgery using the pain sensitivity questionnaire: a cohort study. *Clin J Pain*. 2017;33:57–66. doi:10.1097/ajp.0000000000000380
23. Caumo W, Schmidt AP, Schneider CN, et al. Preoperative predictors of moderate to intense acute postoperative pain in patients undergoing abdominal surgery. *Acta Anaesthesiol Scand*. 2002;46:1265–1271. doi:10.1034/j.1399-6576.2002.461015.x
24. Davoudi A, Sajdeya R, Ison R, et al. Fairness in the prediction of acute postoperative pain using machine learning models. *Front Digit Health*. 2022;4:970281. doi:10.3389/fdgth.2022.970281
25. Gramke HF, de Rijke JM, van Kleef M, et al. Predictive factors of postoperative pain after day-case surgery. *Clin J Pain*. 2009;25:455–460. doi:10.1097/AJP.0b013e31819a6e34
26. Riecke J, Zerth SF, Schubert AK, et al. Risk factors and protective factors of acute postoperative pain: an observational study at a German university hospital with cross-sectional and longitudinal inpatient data. *BMJ Open*. 2023;13:e069977. doi:10.1136/bmjopen-2022-069977

27. Cruz JJ, Kather A, Nicolaus K, et al. Acute postoperative pain in 23 procedures of gynaecological surgery analysed in a prospective open registry study on risk factors and consequences for the patient. *Sci Rep*. 2021;11:22148. doi:10.1038/s41598-021-01597-5
28. Schnabel A, Yahiaoui-Doktor M, Meissner W, Zahn PK, Pogatzki-Zahn EM. Predicting poor postoperative acute pain outcome in adults: an international, multicentre database analysis of risk factors in 50,005 patients. *Pain Rep*. 2020;5:e831. doi:10.1097/PR9.0000000000000831
29. Sun K, Liu D, Chen J, et al. Moderate-severe postoperative pain in patients undergoing video-assisted thoracoscopic surgery: a retrospective study. *Sci Rep*. 2020;10:795. doi:10.1038/s41598-020-57620-8
30. Liu SS, Buvanendran A, Rathmell JP, et al. Predictors for moderate to severe acute postoperative pain after total Hip and knee replacement. *Int Orthop*. 2012;36:2261–2267. doi:10.1007/s00264-012-1623-5
31. Rakel BA, Blodgett NP, Zimmerman BM, et al. Predictors of postoperative movement and resting pain following total knee replacement. *Pain*. 2012;153:2192–2203. doi:10.1016/j.pain.2012.06.021
32. Wang Y, Liu Z, Chen S, et al. Pre-surgery beliefs about pain and surgery as predictors of acute and chronic post-surgical pain: a prospective cohort study. *Int J Surg*. 2018;52:50–55. doi:10.1016/j.ijsu.2018.02.032
33. Cuff DJ, O'Brien KC, Pupello DR, Santoni BG. Evaluation of factors affecting acute postoperative pain levels after arthroscopic rotator cuff repair. *Arthroscopy*. 2016;32:1231–1236. doi:10.1016/j.arthro.2015.12.021
34. Roth ML, Tripp DA, Harrison MH, Sullivan M, Carson P. Demographic and psychosocial predictors of acute perioperative pain for total knee arthroplasty. *Pain Res Manag*. 2007;12:185–194. doi:10.1155/2007/394960
35. Pinto PR, Vieira A, Pereira D, Almeida A. Predictors of acute postsurgical pain after inguinal hernioplasty. *J Pain*. 2017;18:947–955. doi:10.1016/j.jpain.2017.03.003
36. Jacobsen PB, Butler RW. Relation of cognitive coping and catastrophizing to acute pain and analgesic use following breast cancer surgery. *J Behav Med*. 1996;19:17–29. doi:10.1007/bf01858172
37. Gerbershagen HJ, Pogatzki-Zahn E, Aduckathil S, et al. Procedure-specific risk factor analysis for the development of severe postoperative pain. *Anesthesiology*. 2014;120:1237–1245. doi:10.1097/ALN.0000000000000108
38. Pak LM, Pawloski KR, Sevilimedu V, et al. How much pain will I have after surgery? A preoperative nomogram to predict acute pain following mastectomy. *Ann Surg Oncol*. 2022;29:6706–6713. doi:10.1245/s10434-022-11976-5
39. Habib AS, Kertai MD, Cooter M, Greenup RA, Hwang S. Risk factors for severe acute pain and persistent pain after surgery for breast cancer: a prospective observational study. *Reg Anesth Pain Med*. 2019;44:192–199. doi:10.1136/rapm-2018-000040
40. Shi G, Liu G, Gao Q, et al. A random forest algorithm-based prediction model for moderate to severe acute postoperative pain after orthopedic surgery under general anesthesia. *BMC Anesthesiol*. 2023;23:361. doi:10.1186/s12871-023-02328-1
41. Wu H, Ding T, Yan S, Huang Z, Zhang H. Risk factors for moderate-to-severe postoperative pain after percutaneous nephrolithotomy: a retrospective cohort study. *Sci Rep*. 2022;12:8366. doi:10.1038/s41598-022-12623-5
42. Strutz PK, Kronzer V, Tzeng W, et al. The relationship between obstructive sleep apnoea and postoperative delirium and pain: an observational study of a surgical cohort. *Anaesthesia*. 2019;74:1542–1550. doi:10.1111/anae.14855
43. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, and pain: a review of recent clinical and experimental findings. *J Pain*. 2009;10:447–485. doi:10.1016/j.jpain.2008.12.001
44. Wouters RM, Porsius JT, van der Oest MJW, et al. Psychological characteristics, female sex, and opioid use predict acute postoperative pain in patients surgically treated for thumb base osteoarthritis: a cohort study. *Plast Reconstr Surg*. 2020;146:1307–1316. doi:10.1097/prs.0000000000007337
45. Abrecht CR, Cornelius M, Wu A, et al. Prediction of pain and opioid utilization in the perioperative period in patients undergoing primary knee arthroplasty psychophysical and psychosocial factors. *Pain Med*. 2019;20:161–171. doi:10.1093/pm/pny020
46. Papaioannou M, Skapinakis P, Damigos D, Mavreas V, Broumas G, Palgimesi A. The role of catastrophizing in the prediction of postoperative pain. *Pain Med*. 2009;10:1452–1459. doi:10.1111/j.1526-4637.2009.00730.x
47. Persson AKM, Åkeson J. Prediction of acute postoperative pain from assessment of pain associated with venous cannulation. *Pain Pract*. 2019;19:158–167. doi:10.1111/papr.12729
48. Rosseland LA, Stubhaug A. Gender is a confounding factor in pain trials: women report more pain than men after arthroscopic surgery. *Pain*. 2004;112:248–253. doi:10.1016/j.pain.2004.08.028
49. Lwt L, Suh J, Chen JY, et al. Early postoperative pain after total knee arthroplasty is associated with subsequent poorer functional outcomes and lower satisfaction. *J Arthroplasty*. 2021;36:2466–2472. doi:10.1016/j.arth.2021.02.044
50. Edgley C, Hogg M, De Silva A, Braat S, Bucknill A, Leslie K. Severe acute pain and persistent post-surgical pain in orthopaedic trauma patients: a cohort study. *Br J Anaesth*. 2019;123:350–359. doi:10.1016/j.bja.2019.05.030
51. Armstrong RA, Fayaz A, Manning GLP, Moonesinghe SR, Oliver CM. Predicting severe pain after major surgery: a secondary analysis of the Peri-operative Quality Improvement Programme (PQIP) dataset. *Anaesthesia*. 2023;78:840–852. doi:10.1111/anae.15984
52. Weissman-Fogel I, Granovsky Y, Crispel Y, et al. Enhanced presurgical pain temporal summation response predicts post-thoracotomy pain intensity during the acute postoperative phase. *J Pain*. 2009;10:628–636. doi:10.1016/j.jpain.2008.12.009
53. Guneli E, Gumustekin M, Ates M. Possible involvement of ghrelin on pain threshold in obesity. *Med Hypotheses*. 2010;74:452–454. doi:10.1016/j.mehy.2009.10.006
54. Saloom HF, Papageorgiou SN, Carpenter GH, Cobourne MT. The effect of obesity on orofacial pain during early orthodontic treatment with fixed appliances: a prospective cohort study. *Euro J Orthodo*. 2018;40:343–349. doi:10.1093/ejo/cjx064
55. Campbell AL, Yu S, Karia R, Iorio R, Stuchin SA. The effects of body mass index on pain control with liposomal bupivacaine in hip and knee arthroplasty. *J Arthroplas*. 2018;33:1033–1039. doi:10.1016/j.arth.2017.10.048
56. Xie H, Wei J, Ma Z, Ge W. Predictive factors for acute postoperative pain after open radical gastrectomy for gastric cancer. *Front Public Health*. 2022;10:907222. doi:10.3389/fpubh.2022.907222
57. Motaghedi R, Bae JJ, Memtsoudis SG, et al. Association of obesity with inflammation and pain after total Hip arthroplasty. *Clin Orthopaedics Related Res*. 2014;472:1442–1448. doi:10.1007/s11999-013-3282-2
58. Narain AS, Hijji FY, Haws BE, et al. Impact of body mass index on surgical outcomes, narcotics consumption, and hospital costs following anterior cervical discectomy and fusion. *J Neurosurg Spine*. 2018;28:160–166. doi:10.3171/2017.6.SPINE17288

59. Gerbershagen HJ, Dagtekin O, Gaertner J, et al. Preoperative chronic pain in radical prostatectomy patients: preliminary evidence for enhanced susceptibility to surgically induced pain. *Eur J Anaesthesiol*. 2010;27:448–454. doi:10.1097/EJA.0b013e3283349d9a
60. Wang Y, Liu Z, Chen S, et al. Identifying at-risk subgroups for acute postsurgical pain: a classification tree analysis. *Pain Med*. 2018;19:2283–2295. doi:10.1093/pm/pnx339
61. Shi Y, Weingarten TN, Mantilla CB, Hooten WM, Warner DO. Smoking and pain: pathophysiology and clinical implications. *Anesthesiology*. 2010;113:977–992. doi:10.1097/ALN.0b013e3181ebdaf9
62. Kubiliute E, Venskutonis D, Parseliunas A, Margelis E, Kiudelis M. Risk factors predicting acute postoperative pain immediately after minimally invasive inguinal hernia repair. *Wideochir Inne Tech Maloinwazyjne*. 2023;18:475–480. doi:10.5114/wiitm.2023.128037
63. Chowdhury NI, Turner JH, Dorminy C, Wu J, Chandra RK. Preoperative quality-of-life measures predict acute postoperative pain in endoscopic sinus surgery. *Laryngoscope*. 2019;129:1274–1279. doi:10.1002/lary.27763
64. Bayman EO, Parekh KR, Keech J, Larson N, Vander Weg M, Brennan TJ. Preoperative patient expectations of postoperative pain are associated with moderate to severe acute pain after VATS. *Pain Med*. 2019;20:543–554. doi:10.1093/pm/pny096
65. Chiang H-L, Chia -Y-Y, Lin H-S, Chen C-H. The implications of tobacco smoking on acute postoperative pain: a prospective observational study. *Pain Res Manag*. 2016;2016:9432493. doi:10.1155/2016/9432493
66. Caumo W, Nazare Furtado da Cunha M, Camey S, Maris de Jezus Castro S, Torres ILS, Cadore Stefani L. Development, psychometric evaluation and validation of a brief measure of emotional preoperative stress (B-MEPS) to predict moderate to intense postoperative acute pain. *Br J Anaesth*. 2016;117:642–649.
67. Mimic A, Bantel C, Jovicic J, et al. Psychological factors as predictors of early postoperative pain after open nephrectomy. *J Pain Res*. 2018;11:955–966. doi:10.2147/JPR.S152282
68. Lunn TH, Gaarn-Larsen L, Kehlet H. Prediction of postoperative pain by preoperative pain response to heat stimulation in total knee arthroplasty. *Pain*. 2013;154:1878–1885. doi:10.1016/j.pain.2013.06.008
69. Bekele Z, Ayana M, Haile M, Tesfaye A, Tasew A. Incidence and predictors of postoperative severe acute pain within 24 hours after cesarean section performed under spinal anesthesia at public hospitals in West Shoa, Ethiopia, 2022 prospective cohort study. *Ann Med Surg*. 2023;85:4239–4247. doi:10.1097/ms9.0000000000001031
70. García-López J, Polanco-García M, Montes A. Factors associated with the risk of developing moderate to severe acute postoperative pain after primary total knee arthroplasty: results from the PAIN OUT registry. *J Arthroplasty*. 2021;36:1966–1973. doi:10.1016/j.arth.2021.02.005
71. Raza MM, Zaslansky R, Gordon DB, et al. Chronic breast pain prior to breast cancer surgery is associated with worse acute postoperative pain outcomes. *J Clin Med*. 2021;10. doi:10.3390/jcm10091887
72. Schreiber KL, Zinboonyahgoon N, Xu X, et al. Preoperative psychosocial and psychophysical phenotypes as predictors of acute pain outcomes after breast surgery. *J Pain*. 2019;20:540–556. doi:10.1016/j.jpain.2018.11.004
73. Luedi MM, Schober P, Hammoud B, Andereggen L, Hoenemann C, Doll D. Preoperative pressure pain threshold is associated with postoperative pain in short-stay anorectal surgery: a prospective observational study. *Anesth Analg*. 2021;132:656–662. doi:10.1213/ane.0000000000005072
74. Brandsborg B, Dueholm M, Kehlet H, Jensen TS, Nikolajsen L. Mechanosensitivity before and after hysterectomy: a prospective study on the prediction of acute and chronic postoperative pain. *Br J Anaesth*. 2011;107:940–947. doi:10.1093/bja/aer264
75. Takashima K, Oono Y, Takagi S, Wang K, Arendt-Nielsen L, Kohase H. Acute postoperative pain after orthognathic surgery can be predicted by the preoperative evaluation of conditioned pain modulation and pain catastrophizing. *Pain Rep*. 2022;7:e989. doi:10.1097/pr9.0000000000000989
76. Ruscheweyh R, Viehoff A, Tio J, Pogatzki-Zahn EM. Psychophysical and psychological predictors of acute pain after breast surgery differ in patients with and without pre-existing chronic pain. *Pain*. 2017;158:1030–1038. doi:10.1097/j.pain.0000000000000873
77. Pan PH, Coghill R, Houle TT, et al. Multifactorial preoperative predictors for postcesarean section pain and analgesic requirement. *Anesthesiology*. 2006;104:417–425.
78. Braun M, Bello C, Riva T, et al. Quantitative sensory testing to predict postoperative pain. *Curr Pain Headache Rep*. 2021;25:3. doi:10.1007/s11916-020-00920-5
79. Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery. *Anesthesia Analg*. 1997;85:808–816.
80. Kalkman CJ, Visser K, Moen J, Bonsel GJ, Grobbee DE, Moons KGM. Preoperative prediction of severe postoperative pain. *Pain*. 2003;105:415–423.
81. Joo J, Moon HK, Moon YE. Identification of predictors for acute postoperative pain after gynecological laparoscopy (STROBE-compliant article). *Medicine*. 2019;98:e17621. doi:10.1097/md.0000000000017621
82. Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251. doi:10.1136/bmj.g1251
83. Dagenais-Beaulé V, Tourigny J-F, Papillon-Ferland L. Opioid use and pain control in the elderly after elective or urgent orthopaedic surgery: a retrospective cohort study. *Clin. Drug Invest.* 2019;39:301–308. doi:10.1007/s40261-018-00744-7
84. Cohen B, Tanios MA, Koyuncu O, et al. Association between higher BMI and postoperative pain and opioid consumption in pediatric inpatients - A retrospective cohort study. *J Clin Anesth*. 2020;62:109729. doi:10.1016/j.jclinane.2020.109729
85. Ahmad S, De Oliveira GS, Bialek JM, McCarthy RJ. Thermal quantitative sensory testing to predict postoperative pain outcomes following gynecologic surgery. *Pain Med*. 2014;15:857–864. doi:10.1111/pme.12374
86. Ren Z-Y, Xu X-Q, Bao Y-P, et al. The impact of genetic variation on sensitivity to opioid analgesics in patients with postoperative pain: a systematic review and meta-analysis. *Pain Physician*. 2015;18:131–152.
87. Thomazeau J, Rouquette A, Martinez V, et al. Acute pain Factors predictive of post-operative pain and opioid requirement in multimodal analgesia following knee replacement. *Eur J Pain*. 2016;20:822–832. doi:10.1002/ejp.808
88. Scheel J, Sittl R, Griessinger N, et al. Psychological predictors of acute postoperative pain after hysterectomy for benign causes. *Clin J Pain*. 2017;33:595–603. doi:10.1097/ajp.0000000000000442
89. Raichle KA, Osborne TL, Jensen MP, Ehde DM, Smith DG, Robinson LR. Preoperative state anxiety, acute postoperative pain, and analgesic use in persons undergoing lower limb amputation. *Clin J Pain*. 2015;31:699–706. doi:10.1097/ajp.0000000000000150
90. Pud D, Amit A. Anxiety as a predictor of pain magnitude following termination of first-trimester pregnancy. *Pain Med*. 2005;6:143–148.

91. Borges NC, Pereira LV, de Moura LA, Silva TC, Pedroso CF. Predictors for moderate to severe acute postoperative pain after cesarean section. *Pain Res Manag*. 2016;2016:5783817. doi:10.1155/2016/5783817
92. Katz J, Poleshuck EL, Andrus CH, et al. Risk factors for acute pain and its persistence following breast cancer surgery. *Pain*. 2005;119:16–25. doi:10.1016/j.pain.2005.09.008
93. McCowat M, Fleming L, Vibholm J, Dixon D. The psychological predictors of acute and chronic pain in women following breast cancer surgery: a systematic review. *Clin J Pain*. 2019;35:261–271. doi:10.1097/ajp.0000000000000672
94. Tai AL, Hsieh HF, Chou PL, Chen HM, Liu Y. The influence of preoperative anxiety, optimism, and pain catastrophizing on acute postoperative pain in patients undergoing cardiac surgery: a cross-sectional study. *J Cardiovasc Nurs*. 2021;36:454–460. doi:10.1097/jcn.0000000000000687
95. Baudic S, Jayr C, Albi-Feldzer A, et al. Effect of alexithymia and emotional repression on postsurgical pain in women with breast cancer: a prospective longitudinal 12-month study. *J Pain*. 2016;17. doi:10.1016/j.jpain.2015.10.001
96. Sommer M, de Rijke JM, van Kleef M, et al. Predictors of acute postoperative pain after elective surgery. *Clin J Pain*. 2010;26:87–94. doi:10.1097/AJP.0b013e3181b43d68
97. Pinto PR, McIntyre T, Almeida A, Araújo-Soares V. The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy. *Pain*. 2012;153:218–226. doi:10.1016/j.pain.2011.10.020
98. Khan RS, Ahmed K, Blakeway E, et al. Catastrophizing: a predictive factor for postoperative pain. *Am J Surg*. 2011;201:122–131. doi:10.1016/j.amjsurg.2010.02.007
99. Hanssen MM, Vancleef LMG, Vlaeyen JWS, Peters ML. More optimism, less pain! The influence of generalized and pain-specific expectations on experienced cold-pressor pain. *J Behav Med*. 2014;37:47–58. doi:10.1007/s10865-012-9463-8
100. Edwards RR. Genetic predictors of acute and chronic pain. *Curr Rheumatol Rep*. 2006;8(6):411–417. doi:10.1007/s11926-006-0034-2
101. Fillingim RB, Kaplan L, Staud R, et al. The A118G single nucleotide polymorphism of the μ-opioid receptor gene (OPRM1) is associated with pressure pain sensitivity in humans. *J Pain*. 2005;6(3):159–167. doi:10.1016/j.jpain.2004.11.008
102. Sia AT, Lim Y, Lim ECP, et al. Influence of mu-opioid receptor variant on morphine use and self-rated pain following abdominal hysterectomy. *J Pain*. 2013;14(10):1045–1052. doi:10.1016/j.jpain.2013.03.008
103. Chidambaran V, Zhang X, Martin LJ, et al. DNA methylation at the mu-1 opioid receptor gene (OPRM1) promoter predicts preoperative, acute, and chronic postsurgical pain after spine fusion. *Pharmgenomics Pers Med*. 2017;10:157–168. doi:10.2147/pgpm.S132691
104. Kim H, Ramsay E, Lee H, Wahl S, Dionne RA. Genome-wide association study of acute post-surgical pain in humans. *Pharmacogenomics*. 2009;10(2):171–179. doi:10.2217/14622416.10.2.171
105. Weckwerth GM, Dionísio TJ, Costa YM, et al. Multifocal analysis of acute pain after third molar removal. *Front Pharmacol*. 2021;12:643874. doi:10.3389/fphar.2021.643874