Individualized multidisciplinary analgesia to prevent persistent postsurgical pain

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Purpose of review
Persistent postsurgical pain as outcome of surgery has reached more attention in the past years. In the first place because of related disability, long-term use of (opioid)analgesics and impact on the quality of life of individual patients. In addition, the individual and societal socio-economic burden of PPSP is high and increasing in the light of increasing numbers of surgery world-wide.

Recent findings
Actual studies identified risk factors for persistent postsurgical pain in relevant patient populations. Astonishingly, most of predicting factors seem unrelated to surgery.

Summary
Future perioperative practice will have to focus on identifying patients at risk for PPSP before surgery and develop/offer suitable individually tailored preventive interventions.

Keywords
persistent postsurgical pain, prediction, risk factor

INTRODUCTION

Worldwide, the number of surgical procedures increases every year [1]. Due to the improved treatment methods and aging of the general population, we are facing an increasing number of patients with persistent postsurgical pain (PPSP) as outcome of surgery, long-term use of (opioid)analgesics and related reduction of the quality of life. The prevalence of PPSP varies between 5 and 85% depending on the type of surgery [2]. The wide variation in the incidence of PPSP already suggest that data quality and methodology is a matter of concern. However, recognition of the problem has led to the International Association for the study of pain (IASP) definition of PPSP as 'pain developing or increasing in intensity after a surgical procedure or a tissue injury and persisting beyond the healing process, that is, at least 3 months thereafter. The pain is either localized to the surgical field and/or area of injury, projected to the innervation territory of a nerve situated in this area, or referred to a dermatome. Other causes of pain need to be excluded' [3]. Consequently PPSP has been added to the ICD-11 [4].

In the past 20 years, a number of risk factors for the development and severity of PPSP have been identified: age, preexisting chronic pain complaints unrelated to surgery, gender and type as well as technique of surgery. However, the extent of surgical trauma does not seem to be the most important factor for the development of PPSP as Stessel *et al.* [5] demonstrated that also in ambulatory surgery, the incidence of severe pain with the risk of conversion into a chronic pain syndrome is significant.

In this topical review, we are discussing promising approaches for perioperative (preventive) pain management strategies of two groups of patients with a high possibility to develop chronic treatment-related pain complaints. First, PPSP following breast cancer surgery as an example for patients undergoing complex treatments as the cause of PPSP and second: PPSP following arthroplasty as an example for patients with preexisting chronic pain complaints in the surgical area. In particular, we will

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KEY POINTS

- PPSP is an adverse outcome of about 30% of surgical interventions.
- The risk for PPSP is influenced by individual factors unrelated to the extent of surgery.
- Early identification of patients at risk for long-term pain complaints, related invalidity and (opioid)analgesic use form the bases of individually tailored prevention strategies.

discuss new developments in the field of patient-related factors with special attention for psychological factors contributing to the perception of acute postoperative pain and the development of PPSP. It becomes more and more clear that these factors do play an important role in the chronification of acute postoperative pain and the continuous use of (opioid)analgesics [6–8,9▪] (Fig. 1).

BREAST CANCER-RELATED PERSISTENT POSTSURGICAL PAIN

The patient population of women undergoing breast cancer surgery is a group, which deserves special attention, as a relatively high proportion (15–65%) of patients develop a chronic complex pain syndrome also referred to as persistent pain after breast cancer treatment (PPBCT) or upper quadrant pain [10–12]. PPBCT is a complex pain syndrome with neuropathic [13] and myofascial [14] components together with features of central sensitization. The severity of PPBCT has significant impact on the quality of life and psychosocial functioning of breast cancer survivors [15,16▪]. Once chronic PPBCT is difficult to treat, requiring a multidisciplinary approach [17].

Research of the past 20 years has identified breast cancer treatment related and individual risk factors. Patients undergoing more intense treatment including chemotherapy and radiation therapy and axillary lymph-node dissection have a higher risk to retain PPBCT [18–22]. On the individual level, younger age, high BMI, preoperative pain in the breast area and presence of other chronic pain complaints, more intense acute postoperative pain and psychological distress are correlated with a higher prevalence of PPBCT. Positive affect, social support [23], behavioral coping style seem to be protective whereas negative affect, higher depression scores and maladaptive coping strategies are associated with increased pain-related disability and prolonged postoperative use of opioids [24▪▪]. Psychological factors likely interfere with the nociceptive system. Increased pain sensitivity [25–27] and impaired endogenous pain inhibitory mechanisms [20–23,24▪▪,25–28] seem to predict more of the variance of (acute) postoperative pain than breast-cancer treatment-related factors. This hypothesis seems to be confirmed by a recent prospective longitudinal observational cohort study by the group of Schreiber *et al.* [29▪▪]. In 259 women undergoing different kinds of breast cancer surgery, they identified younger age, higher BMI, preexisting surgical area pain, baseline sleep disturbance, less education, greater pain catastrophizing, negative affect, increased somatization as predictors for PPPBCT at 12 months. In this study, axillary dissection and chemotherapy emerged as the only treatment-

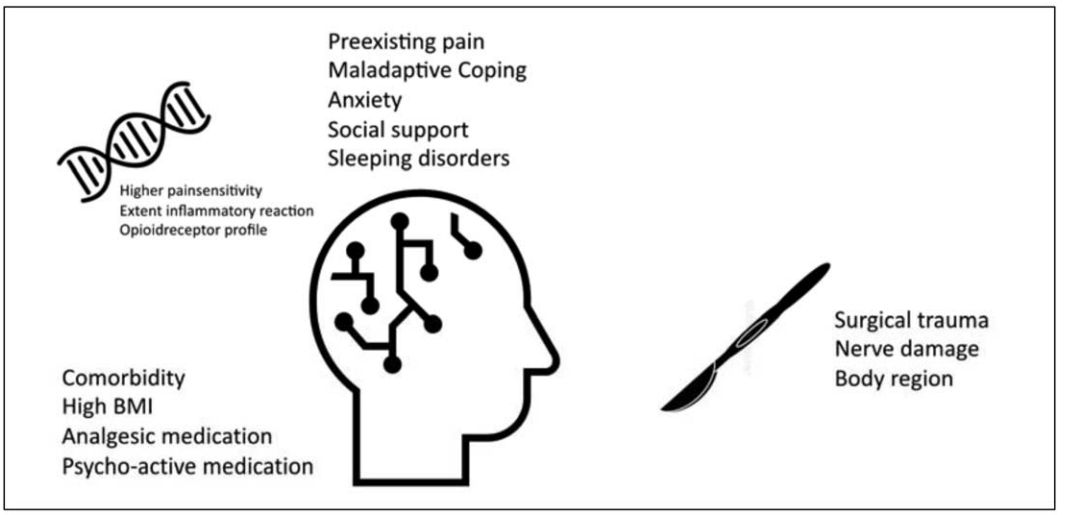

FIGURE 1. Assessable risk factors for the development of persistent postsurgical pain.

related predictors of pain. Sensory disturbance was predicted by higher preoperative temporal summation of pain [29▪▪].

Higher sensitivity of the nociceptive system or deficient pain-defence mechanisms are influenced by genetic and epigenetic variations of cytokine metabolism [30–31] and catecholamine metabolism [32] as well as by the expression of opioid-receptor subtypes [33]. All of which have been shown to interfere with PPBCT.

Quite a few studies have investigated the effect of intensified perioperative analgesia to prevent PPBCT by presumed reduction of nociceptive sensitization through reducing acute postoperative pain. So far, neither (preventive) medication [34–39] nor regional anaesthesia techniques [40–44] have been shown to consistently reduce the prevalence of PPBCT [45–46] despite successfully reducing acute postoperative pain. Interestingly regional anesthesia seems more effective in reducing the severity and duration of acute postoperative pain after breast cancer surgery in patients scoring higher for pain catastrophizing before surgery [47] again emphasizing the importance of psychological factors for pain processing.

OSTEOARTHRITIS-RELATED PERSISTENT POSTSURGICAL PAIN SYNDROME

Pain is the most devastating symptom of osteoarthritis, and guidelines for hip and knee osteoarthritis recommend nonpharmacological and pharmacological treatment options. In case of insufficient pain relief with conservative treatment, joint replacement (total knee replacement, TKA or total hip replacement, THA) is still recommended. The prevalence of PPSP after TKA is 10–34 and 7–23% after hip replacement [48–49]. Fourteen percent of TKA patients report signs of neuropathic pain 1 and 5 years after surgery. Neuropathic pain is accompanied by higher levels of disability after TKA [50] and paralleled by higher pain intensities and higher scores for pain catastrophizing and depression [51].

In 160 patients scheduled for THA, 24.5% reported symptoms of neuropathic pain before THA. That proportion decreased to 5.5% 2 months after THA. Preoperative signs of neuropathic pain were correlated with neuropathic symptoms postoperatively. Interestingly there was NO correlation between neuropathic pain and the radiographic severity of arthrosis [52].

In a carefully designed trial, Rice *et al.* [53] identified preoperative pain intensity, expected pain, trait anxiety, and temporal summation to predict moderate to severe long-term pain in 300 patients undergoing primary unilateral TKA. Patients were also genotyped for the OPRM1 (rs1799971) polymorphism (SNP) and for the COMT (rs4680) SNP in this study but an association with PPSP could not be shown in this study. Preoperative neuropathic pain-like symptoms predicted PPSP 6 months after TKA [54] and were accompanied by signs of central sensitization (facilitated temporal summation of pain and reduced pressure pain thresholds) distant to the knee. Lewis *et al.* [55] found preoperative pain, other chronic pain sites, catastrophizing, depression, mental health and the number of comorbidities to predict PPSP after TKA.

A high proportion of the patients undergoing THA or TKA use analgesic drugs preoperatively [56▪▪]. Recently, the group of Rajamäki *et al.* investigated 13 000 patients undergoing THA and TKA in a retrospective, observational study with regards to prescription and use of analgesics and risk factors for postoperative analgesic consumption. The authors found an increase of the prescriptions of analgesics before surgery, peaking immediately after surgery. THA patients used more NSAIDs and mild opioids than TKA patients, so in general all forms of knee surgery seems to have a higher incidence of PPSP as compared with hip surgery. In the first year after surgery, analgesic use decreased to 23% (THR) and 30% (TKP), respectively. A considerable proportion of patients continued to use analgesics during the 2-year follow-up, and thus possibly suffers from PPSP [56▪▪]. In the same population, Rajamäki *et al.* [57] found patients with a history of antidepressant or benzodiazepine use to receive more postoperative prescriptions of analgesics and opioids compared with patients without this history. Preoperative analgesic, benzodiazepine and antidepressant prescriptions, obesity, higher age and the number of comorbidities predicted analgesic prescriptions 1 year after surgery [58]. Register-based studies also have limitations. The pharmacological dispensing data do not inform whether the drug was redeemed because of pain in the operated joint or whether the patient has taken the drug or not [58].

CONCLUSION

The development of PPSP is largely independent from surgery-specific risk factors. Altogether patients with a nociceptive system prone to sensitization and accompanied by character traits of negative affect and maladaptive coping are at increased risk to develop longer lasting and more intense postoperative pain and related long-term opioid use. Future perioperative medicine will have to focus on a more tailored early-onset perioperative pain management strategy based on comprehensive preoperative psycho-physical screening. The identification of patients

at risk for long-term pain complaints, related invalidity and (opioid)analgesic use and will allow resource direction to effective prevention strategies, such as preoperative life-style optimalization psychological coaching, perioperative regional anesthesia, early-onset adapted physiotherapy.

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Conflicts of interest

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