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A survey of postoperative pain treatments and unmet needs

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More than 300 million patients undergo surgery worldwide each year. Pain associated with these procedures is associated with short- and long-term negative sequelae for patients, healthcare providers, and healthcare systems. The following chapter is a review of the reality of postoperative pain management in everyday clinical routine based on survey- and registry-derived data with a focus on care in adults. Between 30% and up to 80% of patients report moderate to severe pain in the days after surgery. Structures, processes, and outcomes vary widely between hospitals and indicate gaps between evidence-based findings and practice. Pain assessment is not effectively implemented in many hospitals and should consider cultural differences. Few data exist on the situation of pain management in low- and middle-income countries, indicating lack of resources and available medication in many of these areas. Certain types of surgery as well as demographic and clinical factors are associated with increased risk of severe postoperative pain.

Introduction

Worldwide, approximately 312 million surgical procedures were performed in 2012 [1], with an estimated increase of 4–5% every year. Surgery can reduce the risk of death and improve the quality of life of millions worldwide; yet, it is also associated with potential harm, which frequently includes pain, once

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patients awake from the procedure [2]. The pain can persist for days, weeks, or months. It is difficult to make a global evaluation about the epidemiology of postoperative pain as the figures vary depending on the methods used; however, the incidence of "moderate to severe" equivalent to "unacceptable" postoperative pain, on the first postoperative day, is reported by approximately 30% and up to 80% of patients [3], and this prevalence has remained consistently high during the past four decades [4].

Identifying and implementing effective and safe perioperative pain management is an important challenge for clinicians and researchers in view of the negative consequences of poor pain management, which can result in patient suffering, diminished quality of life [5], and increased risk of surgical complications developing in the immediate postoperative period and of chronic pain developing in the months after surgery [6]. Barriers to optimal perioperative pain management include a variety of factors. *Patient*-related factors include reluctance to report pain, reluctance to take medications, and fear of addiction. Those related to *care providers* include distrust of subjective pain assessments, knowledge gaps about available evidence, and fear of lawsuits. *Health system* factors include low priority attributed to this topic in many countries and opioid policies that may have a widespread effect on practices worldwide [7].

The aims of this chapter are to review contemporary treatment methods and practices of perioperative pain, to point out to areas of unmet needs and propose areas for future research. The findings in this chapter are based on publications derived from survey- and registry-based data with a focus on the treatment of adult patients.

Surveys and registries

Both surveys and patient registries use observational study methods. Whereas there are no clear definitions for surveys in the medical field, a "patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure and that serves one or more predetermined scientific, clinical, or policy purposes." Registries can serve many purposes, and this includes to the following: (1) to describe the natural history of the disease, (2) to determine clinical effectiveness or cost-effectiveness of healthcare products and services, (3) to measure or monitor safety and harm and/or to measure quality of care [8–10]. Advances in computer technology and the Internet in recent decades make it possible to share information between hospitals nationally and internationally, thereby advancing from unicenter databases to multicenter databases or registries.

In contrast to findings from randomized controlled trials (RCTs) and their associated meta-analysis, survey- and registry-derived information reflects management and outcomes from the clinical routine for reasons such that they generally do not use strict inclusion and exclusion criteria, e.g., excluding patients who are elderly or burdened with comorbidities. Yet, findings from RCTs, registries, and surveys provide complimentary sets of information, allowing clinicians to judge the characteristics of the population in question, what may be achievable, and what is actually achieved in clinical practice [8,11].

A specific strength of registries and surveys is their ability to survey the degree to which evidence-based structures and processes have been implemented in clinical routine and whether desired outcomes are achieved. Consequently, registry and survey findings have the potential to define the "gaps" between evidence and practice [12].

The American Institute of Medicine in its 2011 report on pain has called for greater development of use of patient outcomes registries that can support point of care treatment decision making as well as for the aggregation of large numbers of patients to enable the assessment of the safety and effectiveness of therapies [13]. Few registries focus on pain. CHOIR in the US (https://choir.stanford.edu/) and ePPOC in Australia and New Zealand (https://ahsri.uow.edu.au/eppoc/index.html) address chronic pain. Even fewer registries address acute, postoperative pain. These include the international PAIN OUT network (http://pain-out.med.uni-jena.de/) as well as QUIPS (www.quips-projekt.de) and the Network for Regional Anesthesia (https://www.ak-regionalanaesthesie.dgai.de/nra.html) in Germany.

Evaluating quality of care

The Structure-Process-Outcome model developed by Donabedian is a useful framework for measuring different elements of quality of care [14]. *Structures* are defined as the physical and organizational properties of the setting in which care is provided, e.g., availability of institutionalized policies and procedures or staff trained in pain management. *Processes* refers to what is done for patients, e.g., whether pain was assessed or whether patients received analgesics. *Outcomes* relate to what is accomplished for patients, e.g., pain severity or pain interference; short- and long-term side effects or complications. These dimensions can be measured from different perspectives, e.g., those of healthcare providers, payers, or patients. As pain is an individual and subjective experience, modulated by physiological, psychological, and environmental factors such as previous events, culture, prognosis, coping strategies, fear, and anxiety, most measures evaluating pain from the patients' perspective are based on self-report. Thus, patient-reported outcomes (PROs) are of particular relevance in any type of study in this field. However, there is no broad consensus as to which outcomes are most relevant. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) group on the research design of clinical trials in acute pain recommends that patients evaluate different domains including pain intensity and relief, interference of pain with activities and affect, and adverse events [15]. A currently running European project, funded by the Innovative Medicines Initiative (IMI) and includes many stakeholders, aims to align which PROs should be used in evaluating care in both acute postoperative and chronic pain conditions. This should allow to standardize follow-up of treatments in clinical practice and clinical trials and reduce bias in the reporting of results (www.imi-paincare.eu) [16].

Surveys and registries on postoperative pain management tend to obtain data on structures and clinical practice by questionnaires sent to Health-Care Providers (HCPs) or by reviewing medical records. Patient-reported or physiological outcomes are obtained less frequently, and outcome measures differ substantially between surveys. Only very few surveys used standardized measurements to obtain data in different countries or even continents. Therefore, it is often difficult to carry out valid comparisons between the different studies.

Perioperative pain clinical practice guidelines

Clinical practice guidelines aim to promote evidence-based, effective, and safe management of perioperative pain and invasive procedures. They are often published by national and international professional societies. These guidelines can then be adapted for use at the level of local hospitals or wards. The following structural and process elements tend to be recommended uniformly across the majority of guidelines [17,18]:

- Establishing Acute Pain Services (APS), i.e., teams specializing in the management of pain.
- Providing educational programs that foster understanding of the complex biological and psychosocial aspects to pain and the multimodal approach to treatment. Teaching should include all medical specialties including surgery, medicine, physical and occupational therapy, and nursing.
- Providing patients and families with information about perioperative pain and management, which is age, culture, language, and health literacy appropriate.
- Involving patients and families in treatment decisions.
- Carrying out systematic and standardized assessment of pain and side effects.
- Using “multimodal” procedure-specific, pain management approaches, i.e., using a variety of analgesic medications and techniques, including local and/or regional analgesia techniques, combined with nonpharmacological interventions.

The majority of these recommendations are not new and have been published for more than 20 years [19,20]. However, implementation of these recommendations seems to be far from optimal in most countries where data are available [4]. Gaps between evidence and practice are found in many fields of medicine. It is estimated that one-third of patients do not benefit from evidence-based treatments, a quarter of patients receive care that is not needed or is potentially harmful, and up to three-quarters of patients and more than half of physicians report not having the information they need for decision making [21].

The failure of implementation of guidelines may also be related to the approach of developing and presentation of the guidelines [22,23]. Most recommendations are derived from evidence that is pooled from several surgical procedures and is not presented in the format that could be included in a procedure-specific enhanced recovery pathway.

Thus, although further research might be called for, consideration should also be directed on how to better implement and disseminate the wealth of existing knowledge to providers, policy makers, patients, and families [24]. In the following paragraphs, we evaluate the degree that evidence-based recommendations for structures, processes, and outcomes are adhered to, relying largely on survey data.

Quality of perioperative pain management: the status quo

Clinical practice: structures

The concept of a formal APS was introduced by Ready in 1988 as an anesthesiology-based postoperative pain management service. This would be a team who would supervise and administer pain relief and would be responsible for teaching and training about postoperative pain management. Guidelines for the management of postoperative pain were then published in Australia, the UK, the USA in Germany, and other countries, by anesthesia and/or pain societies. They recommended the establishment of institutional multidisciplinary APS. Consequently, APS were set up in many countries [25].

In 1999, Stamer et al. surveyed hospitals in Germany about the existence of APS [26]. Of 446 responses, 36% operated some type of APS. The authors compared this finding with data from other countries where this number ranged from less than 5%–75%. However, the definition of an APS varied widely, from dedicated teams with clearly described tasks to one person “on call.” Stamer et al. therefore proposed the following minimal quality criteria for an APS: 1. assigning personnel to postoperative pain management; 2. organizing patients' care at night and on weekends; 3. availability of written protocols for postoperative pain management; 4. regular assessment and documentation of pain scores. At the time when the study was carried out, only half of German APS complied with these criteria. Yet, epidural analgesia and patient controlled analgesia (PCA) techniques were more often available in wards with APS fulfilling the quality criteria. In light of surveys describing differences in the definitions of APS and the services they provided, Rawal also outlined basic tenets for an APS in 2002. The core goals were similar to the ones outlined by Stamer.

In 2008, the PATHOS study (Postoperative Analgesic THerapy Observational Survey) was conducted in 7 European countries (Austria, Belgium, France, Germany, Portugal, Spain, and Switzerland) [27]. Surgeons and anesthesiologists were surveyed regarding clinical practices in postoperative pain. On average, an APS was reported to be established in 37% of respondents' institutions, ranging from 21% in Portugal to 73% in Switzerland. However, there was considerable variability in how these APS were run.

The German survey was repeated in 2012 [28]. The number of APS had increased considerably from one-third to 81% of respondents' hospitals. However, only 45% fulfilled the minimum quality criteria for the availability of an APS. Similar findings are described for APS in the UK in a survey carried out between 2014 and 2016 [29], in that the services provided by throughout the UK are highly variable and the majority do not meet core UK standards [12]. The authors point that this situation exists despite there being clear descriptions of requirements for staffing and functions of an APS in the UK.

Interestingly, by 2015, based on self-disclosure, the majority of hospitals in the Netherlands operated an APS, providing not only daily rounds but also education to staff and patients [30]. It is possible that the move to set up the APS was brought about by the Dutch Hospital Patient Safety Program (DHPSP) [30].

In Denmark, surveys conducted for a decade (2000–2009) indicate that the number of APS decreased with a concurrent increase in hospitals adopting Accelerated Post-Operative Rehabilitation Programs for select abdominal, gynecology, and orthopedic procedures [31]. The character of staff taking part in postoperative pain management changed so that fewer anesthesiologists were involved but a higher number of surgeons and ward nurses. Analgesia techniques changed from using intravenous and epidural PCA to peripheral nerve blocks and high-volume local infiltration analgesia during anesthesia and surgery, resulting in less involvement of APS staff. On the wards, nursing care protocols and physician standing orders are being used by the vast majority of hospitals taking part in the Danish survey. Unfortunately, the methodology used by the authors did not allow for evaluating PROs and comparing them over time.

APS have traditionally focused on providing analgesic management during the preoperative and immediate postoperative phases. New models of analgesic teams are emerging with the aim of offering strategies and protocols to improve continuity of care beyond the immediate postoperative phase and to be proactive about preventing the development of chronic postsurgical pain (CPSP) [32]. Two examples of such new models are the Transitional Pain Service (TPS), launched in 2014 at the Toronto General Hospital [33], and the Acute Pain Service Out-patient Clinic (APS-OP) developed by staff at Helsinki University Hospital [17]. Both services aim to identify patients at risk of developing CPSP at an early stage in their care and offer coordinated and comprehensive care by multidisciplinary teams. The TPS aims to transition patients back to their primary care providers within 6 weeks to 6 months after discharge from hospital after surgery. Patients had a median of 3 visits (range 1–14) to the APS-OP, with opioids being tapered off for the majority of patients. Twenty-two percent of patients were later referred to the Multidisciplinary Pain Clinic.

Clinical practice: processes and outcomes

Survey and registry data show large variation in processes and outcomes across wards and hospitals, with a large proportion of patients reporting high pain intensities, inadequate reduction of pain-related interference, and/or high proportion of side effects.

In the PATHOS study, a third of the 1550 responding HCPs from 746 hospitals, reported that in their institution, staff did not receive on-site training about postoperative pain management and that pain was not routinely assessed [27]. Only half of the patients were offered information on postoperative pain management. In 75% of the institutions surveyed, the treatment provided was not based on written protocols. Although large differences between countries were observed, deficits in pain management practices were observed in all countries. Overall, analgesic management was better organized in anesthesia-centered care. Outcomes data were not obtained in this survey.

Ten years later, the situation had only partially changed: A large survey carried out in 138 German hospitals evaluated process and outcome data from more than 21,000 patients undergoing four commonly carried out surgeries, namely, cholecystectomy, herniotomy, hip, and knee joint replacement [34]. Variation in outcomes seemed to result preliminary from differences between institutions. Patients in the ten “worst” hospitals reported a pain intensity of 6.3 ± 2.2, compared with that of 3.6 ± 2.1 in the ten “best” hospitals (11-point NRS; mean ± standard deviation) (see Fig. 1). Interhospital reporting of pain-related functional restriction ranged between 27% and 95%. This large variation was independent of operation type. Interestingly, hospital size or type of ownership (communal, private, and federal) had practically no effect on outcome variability.

The parameter with the greatest influence on outcome quality was the hospitals' level of care. After adjusting for confounders, patients in university hospitals reported high pain intensity and pain-related functional restriction more frequently and were more often dissatisfied with pain treatment than those cared for in district hospitals. This study also found a large variability in processes. In district hospitals, pain was assessed more often and a higher proportion of patients felt informed about the various options for pain therapy than that in university hospitals. Receipt of information on pain treatment was a relatively strong predictor of satisfaction. In contrast, the association between routine documentation of pain and patient-reported outcome quality was less pronounced.

It is possible that district hospitals differ from university hospitals in some features of “culture of the organization.” Culture of an organization is defined as the set of shared assumptions, values, and beliefs that govern how people behave in an organization. Organizational culture in hospitals includes 5 domains: (1) learning environment, (2) psychological safety, (3) commitment to the organization, (4) senior management support, and (5) time for improvement efforts [35]. A positive “organizational culture” is increasingly understood as fundamental for achieving high performance in healthcare settings [35,36].

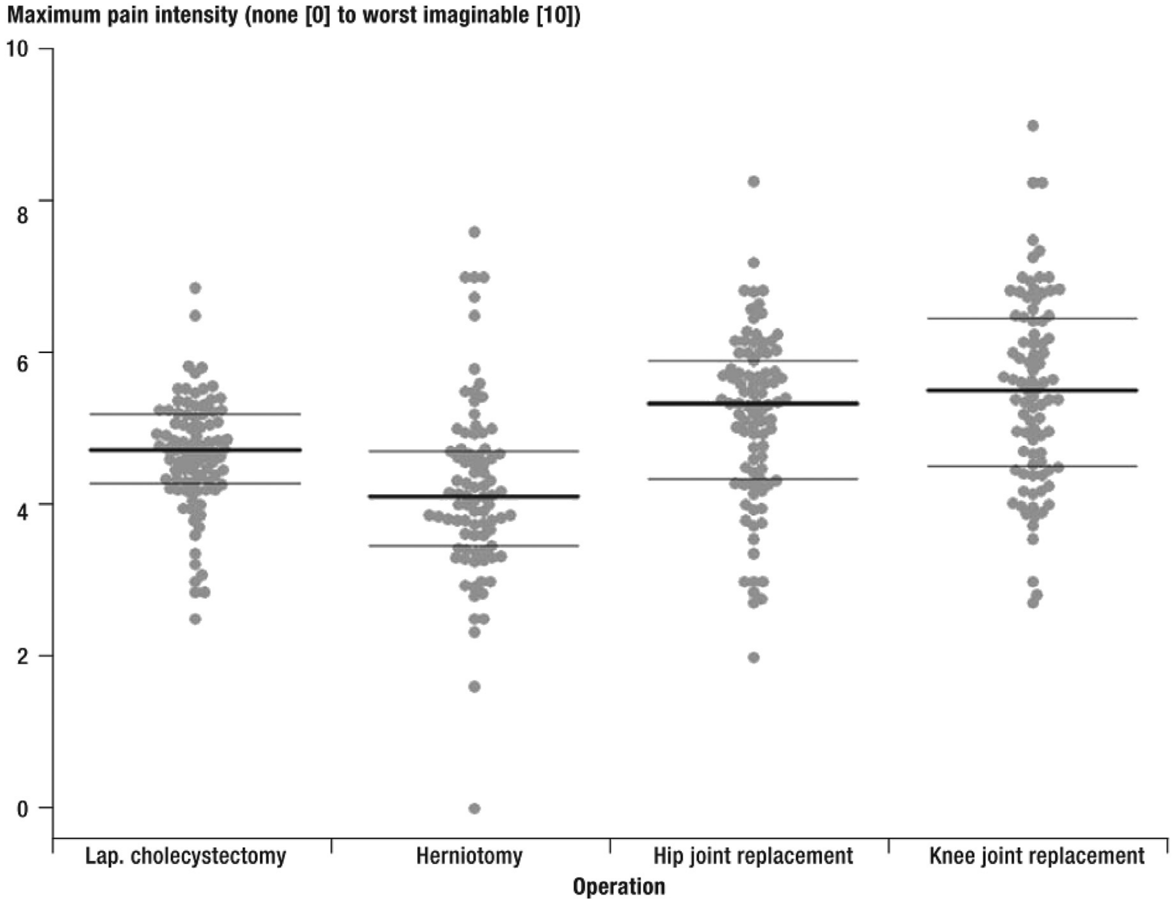

Fig. 1. Distribution of mean responses for maximum pain intensity per hospital for four operations analyzed in 103 hospitals with at least 20 data sets. The horizontal lines represent quartiles 1 to 3. Lap., laparoscopic [34].

In a study on 2500 patients aged 4–85 years from 52 German hospitals after tonsillectomy, there was substantial variability in maximal pain among hospitals even after adjusting for age, gender, and other covariables [37].

A study of 3895 patients in 16 Dutch hospitals revealed low compliance with pain assessment in postoperative patients even after implementation of a national safety program, which included quality indicators for pain assessment in postoperative patients. Interestingly, as in Germany, compliance was highest in district hospitals as compared to that in tertiary teaching and academic hospitals [38].

Another approach for evaluating the quality of postoperative pain management and PROs was used by Maier et al. [39]. They surveyed 2252 surgical and 999 nonsurgical inpatients in 25 hospitals to evaluate the quality of their pain management by using school grades. Fifty-five percent of the surgical and 57% of the nonsurgical patients judged their pain as unacceptable. In the nonsurgical group, 39% of the patients were given no pain treatment at all, although they were in pain. The corresponding number in surgical patients was 15%.

Findings in other Western countries are similar in terms of poor PROs. In a study evaluating 2922 general surgery and orthopedic patients on the first day after surgery in 13 tertiary care Spanish hospitals, pain was assessed in 83% of patients, and 63.3% patients regarded they were informed about their pain management options. However, perceived participation in decision making about pain treatment was very low (4.8%). Mean worst pain scores were 5.6 (NRS 0–10) and a mean of 39.4% of patients reported being in severe pain [40].

Fletcher et al. carried out a national survey on postoperative pain management in a representative sample of 76 surgical centers in France, interviewing 1900 adult patients on the first postoperative day, extracting detailed information about management from patients' medical records [41]. Sixty-nine percent of patients were able to recollect that they received information about their pain treatment options. Pain was evaluated in a high proportion of patients (94%); however, the evaluation tools were not standardized. In terms of intensity, the proportion of patients who reported severe pain (≥7/10) was 4.2% at rest and 27% during movement, and 51% reported this as the worst pain since surgery. A quarter of patients reported experiencing side effects, of which nausea and vomiting were the most common. Morphine was administered more often by subcutaneous injection than by intravenous PCA. Paracetamol was the most commonly administered nonopioid analgesic. Regional analgesia was under used. Twenty-five percent of patients did not have a treatment protocol in their medical file. The authors report that these findings indicate improvement in outcomes and management compared to earlier surveys in France and to international surveys. They attribute the improvements to the high proportion of patients whose pain was assessed by nurses and the importance of teaching ward nurses about postoperative pain management. Recommended areas for improvement included better means for providing patients with information about their treatment options, using pain as a criterion for discharge from the recovery room and improved treatment protocols.

A study of 550 patients, in seven Polish hospitals, indicated that 4 h after surgery, approximately 60% of patients reported being in moderate or severe pain [42].

Cross-country outcome evaluations

Only very few surveys or registries have compared outcomes between different countries. On the basis of data from the PAIN OUT project, Zaslansky et al. compared PROs in 6347 patients from 11 hospitals in Europe and Israel [43,44]. Variability in PROs and processes is evident here too. The median of worst pain in general surgery differed from 4 (0–10 NRS) in the best to 7 (0–10 NRS) in hospitals with the poorest outcomes. Practices also varied widely: routine pain assessment, as documented in the medical records, ranged from 0.3 to 99% in different hospitals. The proportion of patients reporting they received information about treatment ranged from 27% to 85%. The proportion of patients reporting worst pain scores of ≥6 and receiving an opioid, ranged from 44% to 93% across the different hospitals. Use of regional anaesthesia for patients undergoing knee arthroplasty, ranged between 2% to 80% across the different hospitals.

Interestingly, differences in processes were only slightly associated with differences in outcomes. Providing information about pain treatment options had almost no clinically relevant effect on pain intensity, but patients who received information about their pain treatment options were more satisfied. Likewise, routine pain assessment was only modestly associated with less pain intensity and anxiety and higher levels of satisfaction. Surprisingly, patients with at least one routine pain assessment reported more side effects.

Positive association between the recommended process – supported by high-quality evidence – and outcomes in the clinical routine was demonstrated in a study evaluating the association between administering epidural analgesia and PROs in 646 matched-pair cases following abdominal surgery. Regional analgesia compared to general anesthesia was associated with significantly better PROs on the first postoperative day. For example, pain intensity, functional interference, and side effects were improved [45]. However, fewer patients with epidural analgesia got out of bed on the first postoperative day, indicating that staff was unable to exploit these improved PROs to facilitate early rehabilitation.

Overall, the findings from the national and international studies demonstrate considerable variation in both processes and outcomes between hospitals. Approximately half of the patients report moderate to severe pain after surgery. The scant information on nonsurgical patients indicates that the quality of pain management is even worse in this population. Findings such as those from the survey in France show improvement in some of the variables evaluated. Data from two countries suggest that quality of care and PROs in university hospitals are poorer than those in district hospitals. The relationship between processes and outcomes was modest in any type of hospital.

Assessment – single measures vs. trajectories

As stated in the previous section, the reasons for the limited impact of routine pain assessment on outcomes are not well understood. One reason could be the low validity of pain measurement in individual patients. Under routine clinical conditions, single measures are imprecise and may not provide information that is clinically useful for determining treatment. Resolution over time is a key feature of postoperative pain, and the rate of pain resolution is a potentially important clinical outcome. Plotting pain scores of an individual patient over time reveals a trend of pain resolution, or a "trajectory." This could inform clinicians about the pain intensity at a particular time and also about its rate of change. Since Chapman et al. introduced the trajectory concept in 2011, it has been used to characterize pain in the sub-acute postoperative period and to better understand risk factors for developing CPSP [46]. Chapman et al. examined pain trajectories during the first 6 postoperative days in a survey of 502 patients after a variety of surgical procedures and found that the trajectories across the cohort displayed 3 distinct groupings. In the majority of patients, i.e., 63%, the slope was negative; in 25%, it was stable; and in 12%, it increased over time. Similar results were obtained in a sample of adults undergoing cardiac surgery [47]. These findings indicate that patterns of individual differences exist in pain responses over time and that clinicians can identify these differences as they emerge and treat patients accordingly. According to Chapman et al., the slope of the trajectory, rather than the isolated daily scores, should be the target of pain management [28].

Booth et al. used trajectory methodology to evaluate women's pain scores during the first two months after cesarean delivery [48]. They hypothesized that lack of such knowledge limits the clinical ability to rationally prescribe medications and to identify patients who may need frequent follow-up visits or interventions after surgery. The authors found 6 clusters of pain responses. Predictors of cluster membership included severity of acute pain, perceived stress, surgical factors, and smoking status.

Althaus et al. created trajectories from patients after a variety of surgeries, and Okamoto et al. evaluated women after surgery for breast cancer [49,50]. Both studies found that successful pain resolution appeared to be a better predictor of pain intensity six months after surgery than the initial pain readings, immediately after surgery. Li et al. evaluated trajectories of opioid use in adolescents undergoing surgery to correct for idiopathic scoliosis [51]. The authors found five opioid consumption trajectories during the in-hospital period – high-opioid consumers and low-opioid consumers, showing different pain responses. Opioid consumption behavior was not associated with pain, the functional activity of the use of pain medications 6 months after surgery. The authors suggest that their results support previous studies indicating that opioid consumption in the acute postoperative period is dynamic and evolves with time. Furthermore, they concluded that consumption of analgesics in the acute postoperative period did not influence functional outcome after surgery.

The drawback of this methodology is that collecting and analyzing trajectory data are challenging and demanding on staff and patients. It is, thus, not currently practical as a tool for determining day-to-day treatment. Developing methods for electronic data collection and automated analysis could be a way forward.

Assessment – is intensity the optimal metric?

There are a number of reasons that in the field of chronic pain, pain intensity is no longer considered a meaningful or primary outcome [52]. First, reduced pain intensity is not closely associated with improved quality of life, function, or satisfaction. Second, use of unimodal intensity scales such as Numerical Pain Scale suggests a linear relationship between lower pain scores and improved quality, leading to misconceptions such as “pain-free hospitals.” Some argue that focusing on low pain intensity scores may have contributed in some way to the opioid crisis in the USA [53]. However, others argue that the problem is not with the unimodal tool but in the way it is implemented [54]. Restoration of function is broadly consented as the ultimate goal of chronic pain treatment [55]. However, discussion of meaningful goals of management for acute pain lags far behind. Pain intensity is still the most frequently reported primary outcome and a mandatory variable for drug approval studies. Yet, experts have recently called to pay attention to functional improvement when evaluating acute pain [56,57]. The European project IMI PainCare, among others, is working toward a consensus on functional outcome measures in postoperative pain conditions (www.imi-paincare.eu).

Outcomes – satisfaction

Satisfaction of patients with pain treatment has been studied in many surveys. Patients typically rate their satisfaction as high, even if they report high pain intensity. Instead, variables related to communication and the quality of the caregiver–patient relationship are consistently important predicators of satisfaction [58,59]. In a large survey on 16,868 patients from 42 centers in 11 countries, three PRO items showed strong associations and explained 35% of the variability present in the satisfaction variable: more pain relief received, higher allowed participation in pain treatment decisions, and no desire to have received more pain treatment [60]. Effects were highly consistent across centers and countries. Interestingly, the relation between the extent of “allowed participation in treatment decisions” and satisfaction was curved rather than linear. Satisfaction was lowest when patients reported low scores for allowed participation (3/10) and highest when they perceived they were considerably involved (7/10 and 10/10; 11-item NRS with 0 = not at all and 10 = very much). Across all centers, patients with very low allowed participation (0/10) reported higher satisfaction than patients with some allowed participation. These patients may not have been interested in being involved in decision processes or may have not considered participation as an option.

Although there is longstanding and ongoing debate if satisfaction should be a legitimate outcome variable in pain management [58] and in other areas of medicine, it is an important variable for patients' decision for treatment options and choice of HCPs. Therefore, its relation to pain-related processes and PROs is important for understanding patients' preferences and wishes. Moreover, the gap between effectiveness of medications in RCTs and its often poor effectiveness in the clinical routine might – at least partly – be explained by co-variables such as amount of support and interaction between HCPs and patients. Although thousands of RCTs have studied often smallest variations in pharmacological techniques, the body of evidence addressing how to meet patients' expectations to achieve satisfying levels of communication and participation in health-care processes is small [60,61].

Postoperative pain management worldwide

Cultural differences in evaluating pain

Although the proportion of patients reporting moderate or severe pain is similar in the countries where this has been evaluated and ranges approximately 50%, there are some exceptions. In a study of

1002 Chinese patients after thoracic and abdominal surgery, only 15% reported pain of NRS ≥ 4 [62]. In contrast, in an international sample of 14,000 orthopedic patients, American patients reported considerably higher worst pain, higher proportion of side effects, and a higher proportion of patients who wished for more pain treatment than patients from 14 countries in Europe, SE Asia, and Israel, even after adjusting for risk factors and patient mix [63]. However, other PROs such as time in severe pain and perceived pain-related interference with function did not differ between the two populations (Fig. 2). One major difference between the cohorts was that American patients' pain was assessed more frequently than the international group (99% vs. 77%), possibly leading to a nocebo effect and have rendered the American patients more aware of their pain and less able to use coping mechanisms. However, it is not clear why this would affect “worst pain” more than other PROs evaluating severity.

Interestingly, in US patients, not only was pain assessed more often, but also continuous regional analgesia techniques (38% vs. 16%) and opioids on the ward were administered more frequently in these patients (98% vs. 71%) than in non-US patients. In the US, 29% of patients received opioids before admission for orthopedic surgery compared with 9% outside the USA, suggesting that opioid-induced hyperalgesia might partly explain these differences. However, findings in the subgroup of opioid-naïve patients were comparable to the main study. The authors discuss whether the differences in some but not all PROs are related to culture, patient expectation, or ethnicity. As there is limited agreement regarding terminology and appropriate methods for defining ethnicity and culture, this question is difficult to answer and might require other methods of research such as qualitative interviews.

Although only very few surveys assessed PROs across several countries using standardized data collection tools, findings from this study suggest that apart from differences in pain management practices, differences in the understanding of at least some PROs exist between populations. When comparing the Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R) between Icelandic, Australian, US, and Danish patients, a high degree of between-group similarity was found in item-factor loadings of variables coded as “pain experience” but not for “pain management” [64,65]. However, it is not clear which factors have a role in the observed findings, whether they are cultural, psycho-social, or political; related to patient beliefs, social acceptability of pain, and pain treatments; expectations triggered by the healthcare systems; or, perhaps, semantic.

Perioperative pain management in low- and middle-income countries and unmet needs

Eighty-five percent of the world's population live in low- and middle-income countries (LMICs), of which Brazil, Russia, India, and China are the four largest middle-income countries, accounting for approximately 40% of the world's total population. By comparison, the USA comprises 4.3% of the world's population and Germany 1%. However, the majority of information about any facet of preoperative pain management is largely based on studies from the US and Western European countries. There is scant information about questions such as the scale and prevalence of postoperative pain, chronic pain after surgery, and perioperative pain management practices in LMIC, and of the published studies few are well designed, using valid measures [66,67]. With advances in medical care, the burden of disease in these countries has shifted from communicable diseases such as HIV to noncommunicable diseases such as cardiovascular disease, cancer, trauma, and other disease states associated with chronic pain, including low back pain. Many noncommunicable diseases require surgical intervention for diagnosis, treatment, or palliation. Consequently, the number of surgical procedures is projected to increase during the coming years [1,66]. This increase in surgical procedures will inevitably lead to challenges in the management of postoperative and chronic pain due to lack of personnel and personnel trained in perioperative pain management, lack of access to analgesics and adjuvant analgesics, lack of treatment protocols, and inadequate government policies [68].

In view of the considerable variability terms of culture and ethnicity, health services provided, education levels, and living standards, it is questionable whether findings from high-resource countries can be extrapolated to LMIC. Studies, to name a very few, evaluating the prevalence of postoperative pain have been carried out in Ethiopia [69], Ghana [70], and China [71] and reviewed in detail [72].

Eshete et al. carried out a qualitative, multicenter study to explore barriers and facilitators for providing quality pain management in Ethiopia [73]. The authors interviewed patients, healthcare

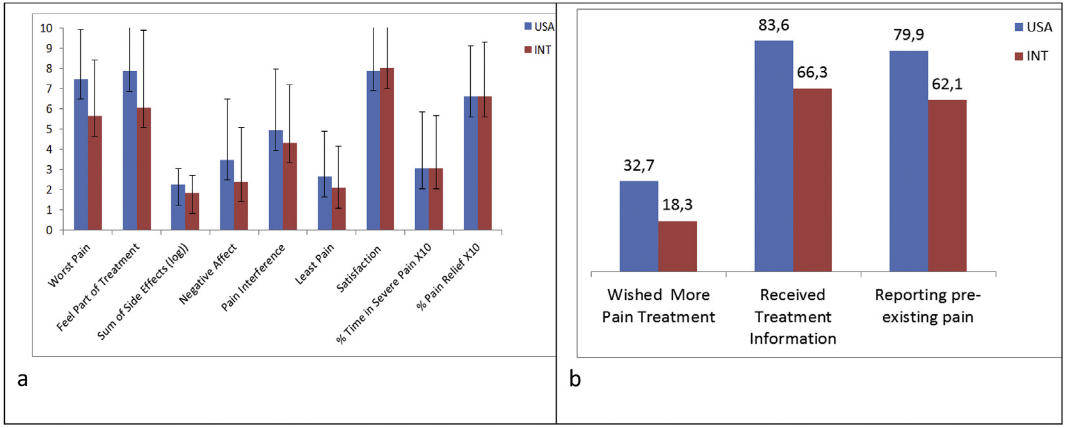

Fig. 2. Differences in PROs between the US and international patients are presented in Figure 2, a and b. Reports for “worst pain”, “receipt of treatment information”, and sum of the adverse effects were significantly higher in the USA compared to the international (INT) patients. The difference qualified as a medium effect size. The proportion of patients reporting persisting pain for at least 3 months, extent of “participation in decisions about treatment,” and “wishing for more pain treatment” were also significantly higher in the USA patients but the effect size was smaller. Differences for the rest of the PROs were not clinically significant. The findings are presented in two panels depending on the units of measurement. Data, expressed as mean and standard deviation, is shown in ‘a’ and proportions are shown in ‘b’. Two PROs scaled in percentage units were multiplied by 10 to make them visually comparable to the other PROs, evaluated using an 11-point NRS (modified from [63]).

providers, and hospital officials, and they suggest that the perspectives of these three stakeholders should be addressed in the bid to improve pain management services to surgical patients. Patients reported that HCP's lack of empathy was vital for undertreatment of pain. HCPs attributed this to patients' reluctance of taking analgesics. They also reported the lack of knowledge regarding methods for assessing pain and of treatment protocols. Hospital officials related lack of education about pain among all providers as a key barrier to providing good care. Lack of medications was cited as another barrier.

Lack of access to analgesics

In 2011, four countries – the USA, Canada, the UK, and Australia – used 89% of global opioids, whereas, low- and middle-income countries together accounted for 7% of global use [74]. It is difficult to provide effective treatment of moderate to severe pain when opioids are unavailable or are underused and when there is a climate of opioid phobia, i.e., prejudice and misinformation about the appropriate medical use of opioids, among providers and patients [75,76]. Access to opioids is controlled by international agencies that have an adopted law enforcement approach that makes it difficult for countries to obtain sufficient opioids to treat severe acute and cancer pain in their populations [77].

Risk factors for increased postoperative pain

As discussed above, variability in perioperative pain-related outcomes is often difficult to explain and not clearly attributable to treatment processes. However, for some populations, there are clear hints for being at risk of experiencing greater levels of pain, functional interference, and/or side effects after surgery.

Type of surgery

It is a common belief that the intensity of pain is primarily related to the extent of the surgical trauma. However, a survey of 2250 surgical patients found the highest pain intensity score after some surgeries with small or medium tissue lesion as appendectomies, coronary artery interventions, hip surgery, and tonsillectomies [39]. These findings were confirmed and extended in a study by Gerbershagen et al. who used registry data to compare movement-related pain and worst pain intensity on POD 1 in 50,000 patients who underwent 179 different types of surgical procedures [78]. Patients undergoing obstetric and orthopedic procedures reported the highest pain intensities (see Figure 3).

When evaluating 179 individual surgical procedures, 15 of the most painful 20 surgeries were orthopedic, mainly surgery of the spine and the extremities. Pain intensity after cesarean section scored also in the top 20, with a mean worst pain intensity of 6.1 and an interquartile range of 4.5–8 (NRS 0–10). However, high levels of pain were reported as well after many “minor” surgical procedures including appendectomy, cholecystectomy, hemorrhoidectomy, and tonsillectomy. Open and laparoscopic appendectomy ranked 19 and 47, respectively, and tonsillectomy, an operation with very limited surgical trauma, ranked 24 with a mean worst pain of 5.9. In contrast, patients after open left hemicolectomy reported a mean worst pain of 4.8, after open lung resection of 4.5 and after radical laparoscopic prostatectomy of 3.6 and therefore were “ranked” as 109, 118, and 141 of the 179 procedures. As the severity of pain reported in this survey is the result of both pain induced by the surgical procedure and management provided, these data point to severe deficits in perioperative pain management. It is widely accepted that pain after large abdominal and orthopedic interventions can be effectively reduced by comprehensive pain management techniques and that patients are visited routinely by specialized pain care teams. Survey data suggest that these practices are implemented in clinical routine in many hospitals. However, patients undergoing “minor” surgeries such as appendectomies and tonsillectomies are rarely seen by pain specialists, and the low morphine equivalents given during POD 1 (tonsillectomy: 7 mg) clearly indicate that pain intensity and associated treatment are underestimated by care givers. Moreover, some of these “minor” but painful procedures belong to the most commonly carried out surgical procedures worldwide. Nevertheless, research on

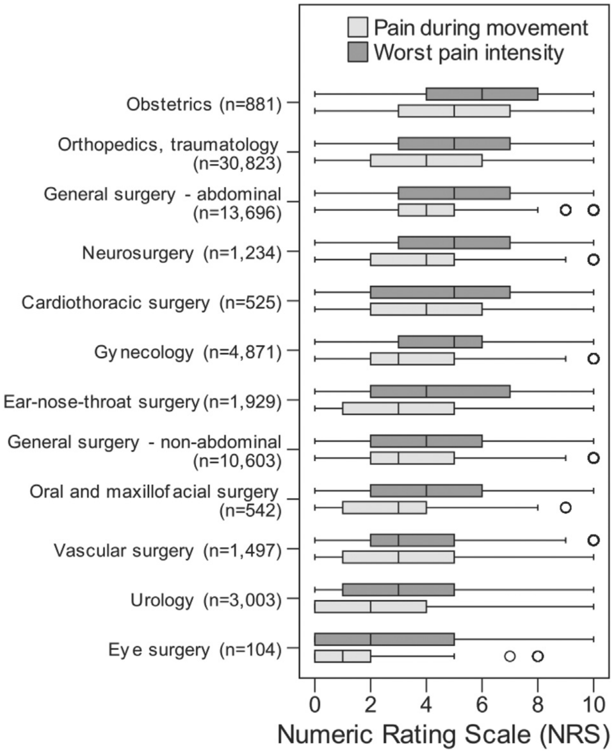

Fig. 3. Comparison of pain intensities between surgical specialties. Worst pain and pain during movement since surgery were assessed on the first postoperative day [78].

perioperative pain management often focuses on major surgeries, resulting in lack of recommendations in guidelines and clinical practice papers for some of the “minor” operations. PROSPECT, is an easy-to-use web-based tool that provides clinicians with evidence-based recommendations for 12 surgical procedures; however, appendectomies and tonsillectomies are not yet addressed.

Cesarean section (C section)

Survey data also indicate deficits in pain management after C section. Compared with hysterectomies, pain intensity and interference with pain were much higher in a study comparing 811 women after C section with 2406 patients after hysterectomies [79]. Women after C section received significantly less opioids; two thirds did not receive an opioid on the ward. However, the wish for more analgesics was higher in patients who underwent C section, and the few patients who were provided with intravenous PCA devices requested approximately 30 mg morphine equivalents in the first 24 h. These findings indicate that women after C section suffer from considerable pain and are willing to accept analgesic treatment.

Perioperative factors

A large meta-analysis including more than 53,000 patients from 33 publications studied the impact of preoperative factors in postoperative pain-related outcomes [80]. Nine variables reached statistical significance: younger age, female sex, smoking, history of depressive and anxiety symptoms, sleep difficulties, higher body mass index, presence of preoperative pain, and use of preoperative analgesia.

The strongest negative prognostic factors were a history of sleeping difficulties and depression, which were associated with approximately twofold higher odds of poor postoperative pain control.

A single analysis of survey data from more than 22,000 patients, using the same standardized data collection process in all patients, quantified the impact of gender, age, and preoperative pain on PROs after 30 different surgical procedures [81]. Analysis of pooled surgical groups indicated that postoperative pain intensity increased by 0.14 points for each higher score on the preoperative chronic pain scale. Females reported 0.29 points higher pain intensity. Pain decreased by 0.28 points on the numeric rating scale (0–10) per decade age increase. This relation was almost linear over all decades in patients over 18 years of age.

Only very few studies have included both children as well as adults in the same survey. Pain intensity after tonsillectomy seems to peak with an age of 18 and decline in older and younger patients [37].

Although survey data suggests that male gender and older age is associated with reports of lower pain scores, it is unclear whether this means that these groups require less- or different pain treatment or alternatively, that younger females require more pain treatment. For example, it is discussed that reporting of lower pain intensity by older patients may be attributed to elderly people offering answers that are socially desired, misconception of assessment tools, or little knowledge of pain management possibilities [82].

Summary

In the past decades, knowledge obtained by survey- and registry-derived data has provided many new insights about the multidimensional nature of pain and into perioperative pain management practices. However, offering quality pain management to patients, cared for in the clinical routine, remains a challenge. There remain gaps between outcomes obtained in RCTs as opposed to the clinical routine. Questions remain such as how to set up effective specialized pain services in many different settings, worldwide. Which domains and which tools should be used to assess pain and its consequences, and are there differences between countries and cultures? What is “good quality” in perioperative pain management from the perspectives of different stakeholders? The scope of perioperative pain management and study needs to be broadened to healthcare providers, patients, and their families in LMICs. Strategies should also be directed on how to better implement and disseminate the wealth of existing knowledge to patients, providers, and policy makers. The ultimate goal is to provide patients and their families with effective and safe care of pain related to surgery, leading to enhanced recovery after surgery and minimal short- and long-term disabilities.

Practice points

- Guidelines unanimously recommend providing patients whose pain is inadequately controlled access to pain specialists. Additionally, to employ specialized staff (e.g., APS) and protocols when treating patients with continuous blocks and other forms of specialized pain management.
- However, these structures and protocols are not widely implemented. This might be due to lack of consensus as to the definition of structures and responsibilities of the APS, lack of resources, low priority given to these structures, unavailability of locally adapted treatment protocols, and lack of data demonstrating cost-effectiveness of this service.
- Most experts recommend the following minimum requirements of teams providing specialized pain management: specialized staff; availability of the service around the clock; availability of algorithms for management of pain and complications; standardized assessment of pain and side effects; training and education of nonspecialized staff, and regular quality assurance/audits.
- Standard evidence-based pain management practices such as routine pain assessment or providing adequate information to patients about their pain treatment options are not implemented comprehensively.

- However, even if implemented, the association between evidence-based processes and outcomes, in clinical routine, is generally poor.
- Restoration of function is the ultimate goal of pain treatment
- Pain intensity – and its reduction – is a required but is not a sufficient single parameter for measuring quality of pain treatment.
- Factors associated with communication, participation in decision making, and experience of care are major predictors of satisfaction with pain treatment.
- Intercultural differences in the understanding of pain-related questionnaires might exist.
- Findings from populations in "Western" countries, which represent the majority of clinical trials, should be translated to other regions in the world with great care.
- Whereas, in some Western countries, opioids seem to be used uncritically, resulting in misuse and addiction, the majority of patients worldwide – specifically in LMIC – have very limited access to opioids.
- The magnitude of the surgical trauma does not always parallel postoperative pain intensity. Other factors such as type of tissue damage (e.g., bone vs. soft tissue), lesions of neural structures, and inflammation might increase the severity of pain.
- Pain after some "minor" surgeries is clearly underestimated and undertreated.
- Clinical pathways should pay special attention to these surgeries, including provision of local anesthesia whenever possible, multimodal analgesia, administration of nonopioid analgesics at regular intervals, and close monitoring.

Research agenda

Research gaps should address the following questions:

- Evaluate the groups of patients and types of surgery that benefit most from specialized pain services.
- Evaluate the structural element(s) in the specialized teams associated with improved outcomes.
- Evaluate the quality of care provided to patients treated in Accelerated Postoperative Rehabilitation Programs, as alternative structures to APS.
- Future studies should address the reasons for the considerable variation and barriers for implementing evidence-based practices.
- The gap between efficacy of some of these processes in RCTs, on the one hand, and lack of effectiveness in clinical routine, on the other hand, urgently deserve further study.
- There is a need to employ study designs that mirror the clinical reality as opposed to conventional RCTs
- What content and format of information about pain management do patients and their families wish to receive? How does this vary in different countries?
- There is an urgent need for an international discussion, research, and consensus among the different stakeholders involved in the management of patients undergoing surgery, including patients and their families, as to meaningful goals and outcome criteria for perioperative pain management.
- Consensus on areas and measures of functional improvement should be aimed for.
- Further research is called for in evaluating the impact of communication between patients and care providers and the extent of patient participation in decision making on quality of care.
- This should be evaluated in different patient populations and countries.
- Future research should address potential differences in the understanding of PROs between populations, considering cultural, societal, and semantic variables.
- There is a need for epidemiological studies evaluating the scale and prevalence of postoperative pain, of chronic pain after surgery and treatment practices, including opioids and nonopioid medications in LMIC.

- Devise national education programs for physicians, nurses, allied professionals, and students of these professions, which will promote the safe and effective use of medications including opioids for the management of perioperative pain in LMIC. Include patients and their families and policymakers.
- Investigate means of creating safe and effective treatment guidelines in countries where access to analgesics is limited.
- Pain research should focus on improving pain management after these commonly carried out surgeries.

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