New Advances in Acute Postoperative Pain Management

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Abstract
Purpose of Review Postoperative pain remains one of the most common challenges following inpatient and outpatient surgeries. With our advances in modern medicine, pain following surgical procedures still remains a challenge, though significant accomplishments have been made over the past few decades. This article highlights some of the promising new advances and approaches in postoperative pain management.

Recent Findings Over the last decade, Enhanced Recovery after Surgery (ERAS) pathways and protocols are becoming the benchmark standards for enhancing postoperative recovery. Multimodal analgesia (MMA) is an essential component of such care. Further, in the wake of serious and persistent concern on the opioid epidemic in the USA, there has been a recent renewal of interest in non-opioid alternatives or adjuncts in controlling postoperative pain, often in the context of MMA. Intravenous (IV) acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), magnesium, ketamine, dexmedetomidine, liposomal bupivacaine, and newer neuraxial and peripheral regional techniques as well as patient-controlled modalities are gaining importance. Gabapentinoids have become popular but recent meta-analytic reviews have cast doubt on their routine use in perioperative settings. Among opioids, sublingual sufentanil, IV oxycodone, and iontophoretic transdermal fentanyl hold promise. Acupuncture and transcutaneous electrical nerve stimulation may be useful as adjuncts in MMA packages. Genetic testing, derivatives of herbal preparations, and an extended role of acute pain services may emerge as potential areas of importance in the future. There are, however, critical gaps in good quality evidence in many of the practice guideline recommendations.

Summary In the era of opioid epidemic, several lines of evidence have emerged to support non-opioid-based drugs and approaches along with a few newer opioid formulations for postoperative pain management, although more research is needed to find the right balance of efficacy and safety.

Keywords Pain · Postoperative · Advances · ERAS · Management

Introduction
Postoperative pain remains one of the most common complaints following inpatient and outpatient surgeries. With our advances in modern medicine, pain following surgical procedures still remains a challenge, though significant accomplishments have been made over the past few decades. After inpatient surgery up to 66% of patients experience moderate to severe pain at discharge, with 59% experiencing this same scale of pain 2 weeks later in orthopedic, general, neurosurgical, and gynecological
Traditionally, opioids have been the mainstay of postoperative pain management but the opioid epidemic and advances in multimodal and Enhanced Recovery After Surgery (ERAS) protocols have moved towards adjuvant modalities for treating postoperative pain.

Opioids do have their important place in postoperative pain management, but are limited by adverse effects and other consequences when used as the sole agent for postoperative pain management. Current ERAS protocols are directed at “minimal use” or “opioid sparing” techniques for administration. In a large meta-analysis, reviewers compared patient-controlled intravenous analgesia (PCA) vs. conventional opioid regimens and routes including intramuscular, non-PCA intravenous, and subcutaneous administration of opioids [5]. Across a wide range of surgeries, patients using PCAs had lower visual pain scores and greater overall satisfaction with care with no differences in hospital length of stay or adverse events. When administering opioids, PCA is an effective and safe way to administer narcotics in the right patient population.

On the other side, undertreated pain is a problem. Poor postoperative pain management leads to prolonged hospitalization, delayed wound healing, poor patient satisfaction, increase in health care costs, and psychological consequences among other repercussions [6]. One severe complication, chronic postsurgical pain, is linked to preoperative pain, opioid use, and importantly the intensity of postoperative pain [7]. Thus, effective modalities for pain management are needed beyond opioid prescriptions.

We had highlighted some advances in this area in an article published in 2010 [8]. Since then, a few recent reviews have provided further updates on this topic [6, 9–11, 12••, 13]. This article highlights some of the promising new advances and approaches in postoperative pain management. We reviewed relevant articles from the standard databases (PubMed, Google, Google Scholar), focusing particularly over the last 5–7 years, combining search words such as “postoperative,” “postsurgical,” “pain,” “analgesia,” “control,” “management,” “acute,” “recent,” “advances,” “multimodal,” “review,” “systematic,” and “meta-analysis,” using appropriate filters and further cross-linked searches with narrower relevant search terms with individual agents, strategies, or approaches (e.g., dexmedetomidine, perineural, acupuncture, acute pain service). Because of the very large number of hits (e.g., PubMed search for review articles on postoperative pain management in human subjects in English language over the last 5 years alone yielded 995 citations!), we had to be necessarily selective and narrative in our approach. We have not focused on recent advances in molecular pain mechanisms in this article because that would have made it unmanageably complex and lengthy, and because other recent reviews are available [12••, 14]; rather, we intend this review to be clinician-oriented, marking some of the recent trends and directions in postoperative pain management.

The review is organized under the following heads and sub-heads:

**The Era of ERAS**

- ERAS-Like Protocols as a Mainstay of Therapeutic Regimens
- Multimodal Analgesia as Essential Component of ERAS Protocols

**Non-Opioid Agents as Alternatives/Adjuncts to Opioids**

- IV Ketamine
- Acetaminophen IV or PO
- IV NSAIDs
- Magnesium
- Alpha 2 Agonists
- Gabapentinoids
- Intravenous Lidocaine

**Opioids in New Formulations for Postoperative Pain**

- Sublingual Sufentanil
- IV Oxycodone
- Fentanyl ITS
- Others

**Newer Molecules/Techniques for Postoperative Pain Control**

- Liposomal Bupivacaine
- Aerosolized Intraperitoneal Local Anesthetic
- Neuraxial/Epidural Use
- TAP Blocks

**Other Aspects of Postoperative Pain Care**

- Patient-Centered Care
- Acupuncture and Transcutaneous Electrical Nerve Stimulation

**Future Prospects**

- Genetic Aspects of Postoperative Pain Control
- Experimental Studies Using Herbal Extracts on Animal Models
- Acute Pain Service: Time to Embrace More?

**Conclusion**

- What Has Been Achieved?
- What Needs to be Achieved: Research Gaps

**The Era of Eras**

**ERAS-Like Protocols as a Mainstay of Therapeutic Regimens [15, 16••, 17, 18]**

ERAS, the popularized acronym for Enhanced Recovery after Surgery, is a perioperative care plan designed to substantially improve patient outcomes [19]. Originally developed for
elective colon resection in 2001, a meta-analysis in 2013 showed ERAS protocols reduced length of stay by 2.5 days and significantly reduced complication rates 30–50% [20]. The functional goal of ERAS is to interconnect the services provided, return key functions to homeostasis (bowel, bladder, ambulation, inflammation), and interject evidence-based modalities into an effective protocol as the patient traverses the perioperative period.

Why is ERAS so effective? It is thought that the reduction of metabolic stress leads to less catabolism and perioperative insulin resistance, both of which are well known to lead to poor surgical outcomes. Fluid balance is essential. Excessive fluid delays return of bowel functions and increases surgical complications. Avoidance of bowel preparation leads to less dehydration and hypotension on anesthesia induction, thereby decreasing the need for excessive fluid administration [19, 21]. Adhering to these simple tenants proves paramount in decreasing the need for excessive fluid administration [19, 21].

The functional goal of ERAS is to interconnect the services provided, return key functions to homeostasis (bowel, bladder, ambulation, inflammation), and interject evidence-based modalities into an effective protocol as the patient traverses the perioperative period.

Multimodal Analgesia as Essential Component of ERAS Protocols

In this era of well-known opioid epidemic in North America, there have been repeated calls for utilizing opioid-sparing approaches in the perioperative setting. This is best conceptualized in the context of multimodal analgesia (MMA), also called balanced analgesia, an approach that targets different pain receptors and pathways with a combination of different drugs and routes so as to achieve synergistic analgesic effect with less adverse effects. This is now seen as an essential component of ERAS [13, 22±, 23, 24±, 25].

MMA has preoperative, intraoperative, and postoperative components. A recent review of 15 MMA protocols mostly across USA and one in New Zealand for colorectal surgery identified several similarities among such programs such as use of acetaminophen, NSAIDs, gabapentinoids, and judicious use of opioids. Use of lidocaine, ketamine, magnesium, and dexamethasone were noted in some protocols. The widest variation was noted in the use of types, routes, doses, and patient control of opioids [25]. Another recent review focused on MMA in ERAS protocols across surgeries on different organ systems either as systemic or regional approaches [22±]. A few head-to-head comparisons of multimodal analgesia vs. traditional agents are also available now [26, 27]. Taken together, it may be said that in the era of ERAS, MMA has now established itself as the gold standard of perioperative analgesic care.

Non-OPIOID Agents as Alternatives/Adjuncts to Opioids

As mentioned above, in the wake of serious and persistent concern on the opioid epidemic in the USA, there has been a recent renewal of interest in non-opioid alternatives or adjuncts in controlling postoperative pain, often in the context of MMA [24, 28±].

IV Ketamine [27]

Ketamine, a non-competitive NMDA receptor antagonist commonly used for acute pain management in the perioperative setting, may have renewed interest. Ketamine is thought to be effective by decreasing pro-inflammatory cytokine formation such as TNF-α and IL-6 [29]. It is well known that the use of ketamine in opioid-dependent patient prevents opioid-induced hyperalgesia, which lowers the pain threshold and can be seen clinically with alldynia, or apparent opioid tolerance despite higher opioid doses [30]. These two unique factors make could make ketamine a particularly attractive adjuvant to ERAS protocols, especially in opioid-dependent patients.

Oral ketamine may be on the horizon as a postoperative pain management tool but its safety and utility have yet to be determined [31]. There is concern for the low bioavailability of the oral formulation making the other formulations more attractive in the initial perioperative period.

A recent randomized controlled study demonstrated that intraoperative ketamine reduces immediate postoperative opioid consumption after spinal fusion surgery in chronic pain patients with opioid dependency [32]. If replicated, this could provide an important option for postoperative pain management in this difficult-to-treat group of patients [33].

IV Acetaminophen [34±]

As mentioned above, acetaminophen is the commonest ingredient in the 15 MMA protocols [25]. This is also supported by several recent meta-analyses [35, 36]. Liang [36] meta-analyzed four studies on IV acetaminophen and came to same conclusion. A recent Cochrane meta-analysis on 75 studies of IV paracetamol (acetaminophen or its pro-drug propacetamol) found high-quality evidence that 36% of participants receiving IV paracetamol or propacetamol experienced at least 50% pain relief over 4 h compared with 16% of those receiving placebo (number needed to treat to benefit = 5) [37±]. However, the effect decreased after 6 h. Further, at higher doses or in hepatically compromised patients, liver damage remains a concern.
Dexmedetomidine [41] has been extensively studied. A number of meta-analyses are now available, including one recent meta-analysis of 32 studies of perineural dexmedetomidine in brachial plexus block, which found that it improves block onset and quality and enhances pain relief significantly [42]. Another meta-analysis of 14 studies specifically in pediatric surgeries also found it to be useful, without significant side effects, at a dose of \( \geq 0.5 \, \mu g/kg \) [43]. An earlier meta-analysis found both clonidine and dexmedetodine to have opioid-sparing properties, but dexmedetomidine was better [44].

**Gabapentinoids [45]**

Similarly, there has been extensive research on gabapentin and pregabalin in mitigating postoperative pain and reducing opioid consumption, with a number of meta-analyses, almost all of which indicate their efficacy [46, 47].

However, a recent meta-analysis of 97 studies with improved methodology has sounded a word of caution by balancing the modest opioid-sparing effect of pregabalin (about 6 mg morphine equivalent over 24 h) against the nearly three times raised risk of serious adverse events [48•]. A similar meta-analytic study on gabapentin by the same authors on 132 trials came to similar conclusion [49•]. Based on these two meta-analyses, the authors conclude that routine use of gabapentinoids for postoperative pain treatment cannot be recommended. Another recent meta-analysis showed that perioperative pregabalin does not prevent development of chronic postsurgical pain [50]. Thus, further research is needed to identify the specific groups of patients where it might be clinically meaningful.

**Magnesium [38]**

The second most common intracellular ion, paramount in neurotransmission, and importantly antagonist of NMDA receptors, magnesium has been largely studied for postoperative pain management. According to a 2013 meta-analysis of randomized control trials [35], magnesium has been shown to be effective for early (0–4 h) pain with rest and late (24 h) pain with rest and movement when compared to controls. The authors additionally found decreased perioperative opioid consumption (10.52 mg, 99% CI = 13.50 to −7.54). There is some suggestion that magnesium may play a role in postoperative headache, nausea, vomiting, dizziness, or cardiovascular side effects, but studies have not shown this to be consistent. It does, however, decrease the incidence of postoperative shivering. Concerns around magnesium revolve around the aforementioned postoperative bradycardia, hypotension, nausea and/or vomiting, and shivering.

**Alpha 2 Agonists**

Dexmedetomidine [41] has been extensively studied. A number of meta-analyses are now available, including one recent meta-analysis of 32 studies of perineural dexmedetomidine in brachial plexus block, which found that it improves block onset and quality and enhances pain relief significantly [42]. Another meta-analysis of 14 studies specifically in pediatric

**Intravenous Lidocaine [51]**

A recent systematic review with trial sequential analysis of 45 trials did find some effect of IV lidocaine on reducing postoperative pain and opioid consumption, along with decreasing hospital stay and better recovery in patients undergoing abdominal surgeries; however, the evidence was limited in quality [52].

Other less-studied drugs or those with mixed results include ondansetron [36], tizanidine [53], clonidine, amantadine, duloxetine, tricyclic anti-depressants, esmolol, and caffeine [28•]. More studies are needed for these drugs.

**Opioids in New Formulations for Postoperative Pain**

Even in this era of heightened sensitivity to the opioid epidemic crisis, opioids do retain their important place in acute postoperative pain management, especially in conditions with severe postoperative pain. The focus in the recent years has been shifting to safer use of opioids for a shorter period of time.

**Sublingual Sufentanil [54, 55, 56•, 57•]**

Currently, sublingual sufentanil is approved in the EU for management of acute postoperative pain. Sufentanil is a pure \( \mu \)-opioid receptor agonist within the CNS. It is...
roughly 7000 times more potent than morphine with onset times similar to fentanyl with a half-life of 6.5 h [57•]. The sublingual formulation bypasses the intestinal and hepatic first-pass metabolism leading to a higher bioavailability than its oral counterpart [58]. Current studies use a patient-controlled dispensary system similar to PCA pumps, allowing for 15-μg tablets to be dispensed every 20 min with recommended treatment up to 72 h postoperatively. Head-to-head trials with morphine PCA have shown that the advantages of sublingual sufentanil are faster onset of analgesia, ease of use, and greater overall provider and patient satisfaction [57•].

Potential drawbacks include the lack of investigative evidence in patients with hepatic and renal impairment. Authors recommend proceeding with caution in these patient populations. Safety concerns are similar to those of other PCA devices including nausea, vomiting, pruritus, and respiratory depression [59–61]. Additionally, cost-effective administration could prove to be difficult and may be a future barrier to its use in the USA.

**IV Oxycodone [62]**

Oxycodone is a selective μ-opioid receptor agonist with potential kappa-opioid receptor agonism with its first use dating back to 1917. When compared with IV morphine, IV oxycodone patients required roughly 40% less demand doses with PCA and had lower visual pain scores in laparoscopic hysterectomies [63]. Other studies have shown oxycodone to be particularly effective in visceral and somatic pain in abdominal surgeries, and may be an adjuvant in patients unable or unwilling to receive epidurals for labor pain relief [64, 65]. With recent approval of IV oxycodone in Korea, there have been a few PCA head-to-head trials with other opioids including alfentanil, sufentanil, with mixed results [33, 66].

Adverse effects are similar to other opioids including nausea, vomiting, constipation, and respiratory depression [62]. In addition, approval in the USA will be needed for this medication with sources stating the potential for abuse holding up its passing by FDA [62]. This makes the intravenous formulation of oxycodone unlikely to become part of the armament given the collective move away from opioids and towards other methods of postoperative analgesia. Regardless, further studies and widespread use are needed to determine if IV oxycodone is indeed useful.

**Other Opioids**

**Fentanyl ITS Preparation**

An iontophoretic transdermal system (ITS) formulation of fentanyl has been available since earlier studies showed it to be comparable to PCA morphine. A recent study, co-authored by employees of the pharmaceutical company that markets the product, recently published an open-label RCT to show that fentanyl ITS was better than IV PCA morphine to promote early mobilization following surgery [67].

**Correct/Incorrect Use of Remifentanil [68]**

Remifentanil, a potent opioid, has been associated with opioid-induced hyperalgesia. A recent meta-analysis of 27 studies concluded that “high intraoperative doses of remifentanil may slightly increase pain intensity at rest during the first postoperative 24 h, and moderately increase morphine use after surgery with no increase in morphine-related side effects” [69]. Another study conducted after this meta-analysis found that remifentanil-based anesthesia is associated with worse pain-related outcomes such as higher worst pain and lower satisfaction in patients undergoing thyroidectomy despite receiving more frequent intraoperative analgesic administration [41]. Thus, one has to be cautious while using remifentanil intraoperatively especially in high doses.

**Newer Molecules/Regional Techniques for Postoperative Pain Control**

**Liposomal Bupivacaine [70•, 71, 72]**

With the trend towards increased utilization of peripheral nerve blocks, leading towards decreased length of stay, decreased opioid use, and overall inclusion in several ERAS protocols, liposomal bupivacaine is a new player on the traditional scene. DepoFoam, distributed by Pacira Pharmaceuticals in San Diego, CA, encapsulates bupivacaine in multivesicular liposomes [73]. Multiple lipid layers surround bupivacaine thus allowing for liposomal bupivacaine diffuse up to 72 h after a single injection.

Epidural use of bupivacaine also demonstrated enhanced motor blockade, prolong decrease of sensation to pinprick, and cold sensitivity [74]. The epidural injection was well tolerated in this study group.

A common concern among anesthesiologist use of bupivacaine is the recognized association between bupivacaine and cardiotoxicity. According to a single-center, randomized, double-blinded study, liposomal bupivacaine did not increase the QTc above 500 in healthy individuals [75]. Other studies found no difference or changes in baseline QRS and QTc length when compared with controls [76]. Although some concern exists for poor wound healing, studies found that there was no significant difference in clinician satisfaction wound healing, wound status, and scarring [77]. There were no significant local reactions to liposomal bupivacaine in
terms of erythema, pain, or swelling at injection site when compared with bupivacaine hydrochloride [73].

The downside to this medication is the current limited insight into liposomal bupivacaine’s use in peripheral nerve block due its lack of literature. Large multicenter trials are needed to determine the safety and efficacy in peripheral nerve blockade.

**Aerosolized Intraperitoneal Local Anesthetic**

Though the concept is attractive, one recent study did not find any significant difference [78]. More studies will be needed.

**Neuraxial/Epidural Use [79]**

Epidural analgesia is well established. A recent Cochrane review of 15 trials further supported the role of epidural analgesia compared to systemic opioid-based analgesia for abdominal aortic surgery; in that, it provided better pain management, reduced myocardial infarction, time to tracheal extubation, postoperative respiratory failure, gastrointestinal bleeding, and intensive care unit length of stay [57•].

**TAP Blocks [80•]**

Although specific for abdominal surgeries, transversus abdominis plane (TAP) block has the potential to replace its predecessor and gold standard, epidural analgesia. This is in part due to the absence of hemodynamic instability, early mobilization, and no required urinary catheter system. The TAP block deposits regional anesthesia in the transverse abdominis fascial plane under ultrasound guidance targeting superficial pain generated by T6-L1 nerve roots [81]. This approach has shown to decrease postoperative opioid consumption in the first 24 h (random effect model $MD = -25.46$ [95% CI $-32.22$ to $-18.69$], $P < 0.00001$), correlating with the duration time depending on local anesthetic formulations injected [82].

TAP blocks have shown advantages in postoperative visual pain scores over other competing methods including ilioinguinal/iliohypogastric nerve block, local infiltration by surgeon, placebo, and showed no advantage over intrathecal morphine and epidural anesthesia [80•]. The risks of the TAP block include inadequate placement, time required for placement, inadvertent bowel infiltration, and direct nerve injury.

**Other Aspects of Postoperative Pain Care**

### Patient-Centered Care [9, 83, 84]

The psyche should not be underestimated in its participation in postoperative pain management as it plays a significant role. According to guidelines put out by American Pain Society, ASRA, and the ASA, the first step to a successful regimen is to define a patient-centered individually tailored pain management plan with the patient [16••]. This includes plans, goals, treatment options, and postoperative pain expectations. So often this step is missed in the initial encounter with patient before the procedure has started and as physicians we are playing catch up with expectations instead of being on the forefront. Improving communication from provider to patients is essential. As with most other aspects of medicine, involving the patient in shared decision-making leads to greater satisfaction with rates as high as 94% of patients who wish to be involved in decision making [85].

Another tenant is to identify patients at significant risk for postoperative pain, a recommendation which is endorsed by the major pain societies [16••]. They recommend a physician who specializes in acute pain management for patients with inadequately controlled postoperative pain be available for immediate consultation. This is significant particularly in patients with a history of substance use disorder or other addiction as their pain may be undertreated or overtreated by physicians with bias or inexperience. Acute pain relief should not be withheld from this patient population as poorly treated pain is a trigger for relapse, never mind the ethical concerns surrounding this issue [86].

### Acupuncture and Transcutaneous Electrical Nerve Stimulation [87, 88, 89]

Although certainly not “new” developments, the evidence base for these two non-pharmacological therapies as adjunct to traditional treatments for postoperative pain management has been somewhat weak and controversial. A narrative review claimed that acupuncture not only is useful for postoperative analgesia but also its benefits extend to reduction of anesthesia-related complications and organ protection [90]. A few recent systematic reviews have helped to clarify the picture to some extent. Wu conducted a meta-analysis of 13 studies and concluded that conventional acupuncture and transcutaneous electric acupoint stimulation (TEAS), but not electroacupuncture, resulted in lower postoperative pain on the first postoperative day, while only TEAS reduced opioid consumption [90]. Another recent review (the Acupuncture Evidence Project) found acupuncture to be an effective adjunct for postoperative pain management [91]. Xiang too reached similar conclusion [92]. Similarly, a recent detailed systematic review found moderate evidence of effectiveness of transcutaneous electrical nerve stimulation (TENS) in perioperative settings for reducing pain and opioid consumption [93]. These modalities may find a useful place as a part of a package for multimodal analgesia.
Future Prospects

Genetic Aspects of Postoperative Pain Control

Genetic polymorphisms are known to affect pain sensitivity and analgesic response and tolerance, which may be mediated by pharmacokinetic or pharmacodynamic mechanisms [94]. Some of the genes and genetic systems involved are the cytochrome P450, opioid receptors, sodium channels, neurotransmitter metabolizing enzymes, and blood-brain transporters, among others. Some of these have been implicated in postoperative pain as well [92]. However, actual data are either sparse or conflicting. A few recent studies have shown preliminary evidence of specific polymorphisms of the mu-opioid receptor (MOR) gene, catechol-o-methyl transferase (COMT), and voltage-gated sodium channel being associated with postoperative pain and analgesic response [95]. A recent review has found some but inconsistent evidence of the role of MOR and COMT genotypes predicting labor analgesia outcomes [96]. However, this is an area that, although promising, is fraught with many methodological as well as ethical issues at present [97•].

Experimental Studies Using Herbal Extracts on Animal Models

In the recent years, a number of studies have looked at the role of extracts of herbal sources with anti-nociceptive effects in animal models of postincisional pain. Although part of complementary and alternative medicine (CAM) rather than mainstream medicine, research has tried to combine traditional knowledge with modern scientific methods in this area. Thus, studies have shown analgesic effects in postoperative (mostly postincisional) rat models of extracts of Devil’s claw [90], sinomenine [98], and the gelsemium alkaloid kuomine [99]. Another study showed that vitexin, a C-glycosylated flavone present in several medicinal herbs, may exert behaviorally specific anti-nociception against postoperative pain mediated through opioid receptors and GABAA receptors, suggesting that vitexin may be useful for the control of postoperative pain [98]. Some of these studies may also help to further elucidate postoperative pain mechanisms as well. However, a cautious approach needs to be taken because these herbal extracts may have their side effects and drug interactions as well. A systematic review is currently underway in this promising area [100].

Acute Pain Service: Time to Embrace More?

Acute Pain Service (APS) is regarded as an important organizational requisite for systematic postoperative pain management. However, there are many barriers to an effective implementation of such programs. It has recently been proposed to expand the mandate and scope of APS to a Perioperative Pain Service (PPS) [101•]. Such “Role expansion of the APS into the preoperative and postdischarge phases, so as to embrace the entire perioperative episode, can provide patients at risk for postoperative pain with comprehensive and continuous perioperative pain management. This new proactive PPS model attempts to provide patient-centered, value-based health care and may improve health outcomes and produce cost savings for at-risk populations” [101•]. This model envisages a comprehensive care package of patients starting from the preoperative phase, through the intraoperative phase to the acute postoperative phase and extending into the postdischarge phase. This is an exciting proposal which potentially holds a lot of promise for the future; however, it remains to be seen how it pans out in the real world.

Conclusion

What Has Been Achieved?

Over the last decade, ERAS pathways and protocols are becoming the benchmark standards for enhancing postoperative recovery. Multimodal analgesia is an essential component of such care. In the era of opioid epidemic, several lines of evidence have emerged to support non-opioid-based drugs and approaches, although more research is needed to find the right balance of efficacy and safety.

What Needs to Be Achieved: Research Gaps [7, 102••]

The American Pain Society commissioned an evidence-based guideline released in 2014. Despite a large body of evidence, strong recommendations were made but left many areas of acute postoperative pain with low quality or insufficient evidence [102••]. While there is convincing evidence for the use of multimodal analgesia, there are numerous combinations which have yet to be vigorously studied on which combination is optimal. Mostly centered around effectiveness of modalities, this group came up with 31 key questions for review. They asked the same three questions of multiple phases of perioperative care. (1) How effective are the various methods on postoperative pain? (2) What harms are associated with these interventions? (3) How does effectiveness or harm perioperative analgesia change with specific surgeries and subgroups of patients?

While we do know that perioperative education is helpful in postoperative pain, which methods are more effective than others and which populations benefit the most? When transitioning from inpatient to outpatient care, there was no study found methods from transitioning patients from inpatient to outpatient. What are the appropriate doses and methods for transitioning patients off opioids? Which patients should follow with primary care or a pain specialist? One of...
the safety concerns brought up was the optimal timing and frequency of pain monitoring. Should we monitor patients every hour, half hour? Which patients need intensive monitoring? Which patients need less?

The group stated that there was insufficient evidence to recommend or discourage, massage therapy, cold therapy, or acupuncture to multimodal pain regimens. While significant studies have been done including randomized control trials on acupuncture, the results are mixed, and the evidence was of low quality. The comparison between peripheral and neuraxial analgesia is still yet to be backed by convincing evidence. Most of the studies on peripheral nerve techniques were in comparison to systemic opioids rather than intrathecal morphine. Other aspects of regional technique needing further review include optimal techniques in comparison to one regional method against another, injectants, adjuvants, and prevention of rare adverse events.

On a larger public health scale, which models of care coordination are most effective? Which organizational structure produces the safest and optimal outcomes for postoperative pain control in their health care system delivery? Although it is recommended to utilize an acute pain service with patients at high risk for severe or uncontrolled postoperative pain, which of these patient populations actually benefit from an acute pain service compared to a service without one?

In conclusion, there have been several advances in acute postoperative pain management over the last decade, some older issues have been settled and others questioned, with a call for expanding the scope of acute pain services from a postoperative post hoc service to a pre-planned perioperative service, and newer vistas coming up. At the same time, however, some previous knowledge has been questioned and newer questions asked that merit further research over the coming years.

Compliance with Ethical Standards

Conflict of Interest Sukanya Mitra, Daniel Carlyle, Gopal Kodumudi, Vijay Kodumudi, and Nalini Vadivelu declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance.


23. Wardhan R, Chelly J. Recent advances in acute pain management: understanding the mechanisms of acute pain, the prescription of opioids, and the role of multimodal pain therapy. F1000Res. 2017;6:2605.


A recent addition to the acupuncture literature for postoperative pain management.


