Acute Post-Surgical Pain Management: A Critical Appraisal of Current Practice

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The Acute Pain Summit 2005 was convened to critically examine the perceptions of physicians about current methods used to control postoperative pain and to compare those perceptions with the available scientific evidence. Clinicians with expertise in treatment of postsurgical pain were asked to evaluate 10 practice-based statements. The statements were written to reflect areas within the field of acute-pain management, where significant questions remain regarding everyday practice. Each statement made a specific claim about the usefulness of a specific therapy (eg, PCA or epidural analgesia) or the use of pain-control modalities in specific patient populations (eg, epidural analgesia after colon resection). Members of the American Society of Regional Anesthesia and Pain Medicine (ASRA) were asked, via a Web-based survey, to rate their degree of agreement with each of the 10 statements; 22.8% (n = 632) of members responded. In preparation for the pain summit, a panel member independently conducted a literature search and summarized the available evidence relevant to each statement. Summit participants convened in December 2005. The assigned panel member presented the available evidence, and workshop participants then assigned a category for the level of evidence and recommendation for each statement. All participants then voted about each statement by use of the same accept/reject scale used earlier by ASRA members. This manuscript details those opinions and presents a critical analysis of the existing evidence supporting new and emerging techniques used to control postsurgical pain. *Reg Anesth Pain Med 2006;31:1-42.*

Key Words: Acute postoperative pain, Patient-controlled analgesia, Regional analgesia, Epidural analgesia.

Fear of uncontrolled postsurgical pain is among the primary concerns of many patients about to undergo surgery. During the past 2 decades, new technologies to aid postoperative-pain control have gained widespread use, and formal acute-pain services have evolved in many institutions.[1] The use of microprocessor-driven, patient-controlled analgesia (PCA) devices has become routine, and the extension of epidural analgesia beyond the operating room to control pain in the postoperative period is now common. At the same time, our understanding of the pharmacology and clinical usefulness of spinal opioids has rapidly improved.[2] In more recent years, we have seen the emergence of continuous peripheral-nerve blocks as a promising new approach for improving pain control after a number of specific surgical procedures.[3] As these new technologies have achieved more common use, public awareness of pain management and expectations about pain treatment have risen. The medical community has worked toward a more uniform approach to assessment and treatment of pain through the preparation and dissemination of practice guidelines.[4]

As experts in perioperative medicine, we are called upon to make sense of these new technologies and guide the implementation of safe and effective practices in our own institutions for control of postsurgical pain. The Acute Pain Summit 2005 was convened to critically examine the perceptions

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of physicians in our field about current methods used to control postoperative pain and to compare those perceptions with the available scientific evidence. This manuscript details those opinions and presents a critical analysis of the existing evidence that supports new and emerging techniques used to control postsurgical pain.

Methods

A group of clinicians, chosen for their knowledge, expertise, and track records for meaningful research and publication in the field of perioperative pain control, was assembled via the Acute Pain Summit 2005 to evaluate 10 practice-based statements. This summit was supported by an unrestricted educational grant from the PriCara division of Ortho-McNeil, Inc. and executed by Consensus Medical Communications in collaboration with the American Society of Regional Anesthesia and Pain Medicine (ASRA). The statements were written by the leaders of the summit (Drs. Rathmell, Sinatra, and Wu) to reflect areas within the field of acute-pain management where significant questions remain regarding everyday practice when choices were made among various pain-control techniques. The statements are admittedly arbitrary and were chosen with the guidance of summit participants, but each statement makes a specific claim about the usefulness of various delivery methods (eg, PCA or epidural analgesia) or the use of pain-control modalities in specific patient populations (eg, epidural analgesia and return of bowel function after colon resection).

Members of ASRA, the majority of whom are closely involved with treating perioperative pain in their regular clinical practices, were then polled by use of the same 10 practice statements. An electronic survey was circulated to all members with working e-mail addresses. They were then directed to a Web site where they rated their degree of agreement or disagreement with each of the 10 statements (Appendix A). Overall, the response rate to the survey was 22.8%, with a total of 632 respondents.

Each of the 10 statements was assigned by the summit leaders (Drs. Rathmell, Sinatra, and Wu) to a specific participant, who independently carried out a detailed literature search and summarized the available evidence relevant to the statement. Each participant was responsible for independently conducting a detailed literature search regarding their assigned statement and summarizing the available scientific evidence. All authors queried the National Library of Medicine's MEDLINE database, the American College of Physicians Journal Club, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews in late November 2005. The specific literature search terms each participant used to gather the evidence are described in detail for each statement. All Acute Pain Summit 2005 participants convened December 2-4, 2005 in Fort Lauderdale, Florida and were assigned to 1 of 2 workshops that pertained to delivery methods or patient populations. Each panel member presented the available evidence regarding their statement to the workshop participants, and a detailed discussion of the evidence ensued. After that discussion, workshop participants were asked to assign a category for the level of evidence that supported or refuted the statement and assign a final category to the evidence (Table 1). After hearing a summary of the evidence, all summit participants then voted on their level of acceptance or rejection by use of the same scale employed earlier by ASRA members in the electronic survey (Table 1); the participants' opinions were compared with the ASRA poll for each statement in the sections that follow.

Statement 1

Use of intravenous (IV) PCA leads to improved patient outcomes when compared with nurse-administered parenteral opioids.

Rationale and Definition of Statement

The common perception is that use of IV PCA for the delivery of opioid analgesics produces improved outcomes when compared with nurse-administered parenteral opioids. IV-PCA devices have been in use for more than 25 years and have become widely accepted as the preferred means for delivering opioid analgesics for postoperative analgesia, as well as other acute-pain conditions. These devices allow the patient to self-administer an opioid analgesic on an as-needed basis within the parameters set by the ordering physician. In most settings, the readily available drug afforded by the PCA device has the potential to allow safe individualization of opioid analgesic dosing, improve pain control, and increase patient satisfaction.

Literature Search

Specific text words used in the literature search were "patient controlled analgesia and outcome" (348 articles), "nurse controlled analgesia and outcome" (21 articles), "nurse controlled analgesia and patient controlled analgesia" (16 articles), "nurse controlled analgesia" (22 articles), "patient controlled analgesia" (2816 articles), "patient controlled analgesia and meta-analysis" (17 articles), and "nurse

Table 1. Workshop Grading of Level of Evidence and Subgroup Support for Each Statement

Category	Level of evidence*
Ia	Evidence obtained from meta-analysis, including at least 1 large, randomized, controlled trial
Ib	Evidence obtained from meta-analysis, including at least 1 small, randomized, controlled trial or well-designed, large, randomized, controlled trial alone
II	Evidence obtained from well-designed cohort or case-controlled studies
III	Evidence obtained from case series, case reports, or flawed clinical trials
IV	Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees
V	Insufficient evidence to form an opinion
	Level of Subgroup support for statement
A	Good evidence to support the statement
B	Fair evidence to support the statement
C	Poor evidence to support the statement, but recommendations may be made on other grounds
D	Fair evidence to reject the statement
E	Good evidence to reject the statement

Summit panel (group at large) voting	Individual level of support
1	Accept recommendation completely
2	Accept recommendation with some reservations
3	Accept recommendation with major reservations
4	Reject recommendation with reservations
5	Reject recommendation completely

*Definitions for level of evidence were modified from those proposed by the Oxford Center for Evidence Based Medicine and available at http://www.cebm.net/levels_of_evidence.asp. The Acute Pain Summit 2005 participants modified the existing levels by dividing Level 1 evidence into 1a and 1b, as the group consensus was that a meta-analysis that contained at least 1 large, randomized, controlled trial was stronger than a single large, randomized trial alone or a meta-analysis composed only of a group of small trials.

controlled analgesia and meta-analysis" (0 articles). The reference lists of the meta-analyses were also reviewed for relevant articles. After careful review of the resulting articles, a total of 11 articles (9 randomized controlled trials and 2 meta-analyses) were felt to represent the wide variety of patients and surgical procedures studied and have the most direct relevance to the statement.

Evidence

Pettersson et al[5] examined the efficacy and amount of opioid delivered with PCA *v* nurse-controlled analgesia (NCA) after extubation in 48 patients after coronary artery bypass surgery (CABG).[5] The authors found that visual analog scores (VAS) did not differ on the day of surgery. On postoperative day 1, VAS scores were higher in the NCA group (VAS 3-4/10 *v* 2/10 in the PCA group, $P < .01$). The PCA group used more opioid analgesic than did the NCA group ($P < .01$). Additional oral analgesics were required in 50% of the NCA group *v* none in the PCA group. The side effects were equal in both groups. They concluded that PCA resulted in better pain treatment and increased use of opioids without an increase in side effects compared with NCA.

Boldt et al[6] assessed the degree of sedation, satisfaction, and pain for the first 3 postoperative days in 60 cardiac surgery patients with a comparison between standard therapy (intermittent bolus doses on demand or as determined by the staff nurse) and a PCA regimen. In addition, they examined vital capacity (VC) and forced expiratory volume in 1 second (FEV_1), cortisol, and troponin levels. Postoperative pain scores were significantly lower, and more opioid was used throughout the observation period in the PCA group. The VC and FEV_1 were significantly lower in the standard group than in the PCA group. Cortisol, troponin, and side effects were similar in both groups. The authors concluded that PCA improved pain relief and increased patient satisfaction after cardiac surgery when compared with standard nurse-based pain therapy.

Murphy et al[7] compared PCA to nurse-titrated, continuous IV opioid infusions in 200 patients undergoing major thoracic or abdominal surgery. The patients were examined for pain, level of sedation, nausea, presence of adverse effects, and cumulative opioid dose over 24 hours. They found no significant differences in the quality of analgesia, frequency, and severity of adverse effects or the cumulative dose of opioid. The authors concluded that nurse-controlled infusions are as effective as PCA and may be used as an alternative to PCA when it is unavailable or unsuitable.

Myles et al[8] compared PCA and a nurse-titrated continuous infusion of morphine in 72 patients after cardiac surgery. They examined pain and nausea scores 5, 20, 32, and 44 hours after surgery and serum cortisol levels 24 and 48 hours after surgery; they found no differences in pain or nausea scores, serum cortisol, morphine consumption, time to extubation, or discharge from the intensive care unit (ICU) between the 2 groups. A significant association was seen between pain and serum cortisol at 48 hours. The authors concluded that no benefit was obtained from routine PCA use in cardiac surgical patients. The differences in staffing time required with each technique were not evaluated in this study.

Gust et al[9] examined the effect of PCA on pulmonary complications in 120 patients for 72 hours after CABG. They examined 3 groups; PCA, PCA and non-

steroidal anti-inflammatory drugs (NSAIDS), and traditional NCA. They found that chest radiographic atelectasis and VAS scores were similar on the first and second days. On the third day, atelectasis scores were better in the PCA and PCA with NSAID groups, and VAS scores were higher in the NCA group. The authors concluded that PCA significantly decreases postoperative pulmonary atelectasis compared with NCA and produces a higher quality of analgesia.

Weldon et al[10] examined the uses of PCA, PCA with concurrent basal infusion, and NCA for 72 hours in 54 pediatric patients (ages 5 to 20 years) undergoing elective scoliosis surgery. The authors found no differences between the PCA and the PCA plus basal infusion groups with respect to morphine use, pain relief, side effects, or patient satisfaction. They found that nurses consistently underestimated their patients' pain and that children in the NCA group received less morphine per kilogram than those who self-administered their medication. The authors concluded that NCA is an acceptable alternative in the ICU setting for patients incapable of self-administering pain medication.

Forst et al[11] examined pain therapy after total-hip or knee arthroplasty in 42 patients who received either PCA or conventional demanded pain therapy. The authors found no significant differences in pain scores or side effects. The PCA group used twice as much opioid ($P < .001$). Patient satisfaction with the therapy was good in both groups but was significantly better in the PCA group ($P < .01$). The authors concluded that even when patients feel satisfied by the administered pain therapy, the majority are objectively treated below their individual subjective pain threshold.

Nitschke et al[12] examined whether PCA would achieve better pain control with fewer adverse effects than intramuscular (IM) analgesia in 92 patients undergoing major colon resection. They compared PCA morphine with IM morphine or IM ketorolac. Only 2 patients had adverse effects and they were receiving PCA morphine. More patients receiving IM ketorolac required alternative analgesia (32% IM ketorolac *v* 16% IM morphine and 0% PCA). The ketorolac group had a significantly shorter duration of ileus ($P < .01$), significantly lower pain scores ($P < .04$), and less postoperative confusion ($P < .03$) than the morphine groups. The ketorolac group had a significantly shorter duration of stay than either morphine group ($P < .01$), with no significant difference between the morphine groups. The patients preferred PCA to the other analgesic methods. The authors concluded that although ketorolac appears to provide a better postoperative course than either IM or PCA morphine, 18% of ketorolac patients required additional analgesia, with a strong preference for PCA.

Wheatley et al[13] examined hypoxemia and pain relief for 24 hours after upper abdominal surgery in 44 patients who received either IM or PCA analgesia with morphine. They found that 9 of 19 in the PCA group rated their pain control excellent *v* 2 of 20 in the IM group ($P < .05$). No significant difference was seen in the incidence of hypoxemia. Severe hypoxemia (SpO_2 <85% for more than 6 minutes) was seen in 3 IM patients and in 1 PCA patient. The authors concluded that PCA is not associated with an increased risk of severe hypoxemia compared with IM analgesia and that severe hypoxemia can occur in upper abdominal surgery patients with poor pain relief. However this study was too small to draw meaningful conclusions regarding the risk of hypoxemia.

Ballantyne et al[14] performed a meta-analysis that examined the initial randomized control trials (RCTs) in patients who received postoperative PCA. The meta-analysis included 15 RCTs with a total of 787 adult patients aged 16 to 65 years who were undergoing various operative procedures and who received either PCA or conventional analgesia for postoperative pain control. The authors extracted data on analgesic efficacy, analgesic use, patient satisfaction, length of hospital stay, and side effects. The meta-analysis found greater analgesic efficacy when PCA was used. A nonsignificant trend toward reduced analgesic use in PCA patients was observed. On the basis of an analysis of 3 studies that examined patient satisfaction with PCA *v* conventional analgesia, a mean difference of 42% occurred in the probability of satisfaction with PCA *v* conventional analgesia. A nonsignificant trend toward shortening length of stay with PCA use was seen. The authors concluded that patients obtain better pain relief with PCA, compared with those who use conventional analgesia, without an increase in side effects, and they strongly prefer PCA over conventional analgesia.

Walder et al[15] subsequently performed a meta-analysis that examined the efficacy and safety of PCA for acute postoperative pain. Included in their meta-analysis were 32 RCTs, with a total of 2,072 patients who received morphine (22), piritramide (3), nalbuphine (1), and tramadol (1). Three morphine trials and 1 meperidine trial demonstrated patient preference for PCA (89.7% *v* 65.8%). The combined data on pain intensity and relief and the need for rescue analgesics from morphine (8 trials), meperidine (1 trial), piritramide (1 trial), and nalbuphine (1 trial) all were in favor of PCA. In 2 morphine trials, pulmonary complications were less frequent in those who received PCA. The trials

demonstrated equivalence for cumulative opioid consumption, pain scores, duration of hospital stay, and opioid-related adverse events. The authors concluded that PCA with opioids, compared with conventional opioid administration, improves analgesia and decreases the risk of pulmonary complications; patients also prefer PCA over traditional NCA.

Grading of Evidence

On the basis of the evidence in these 9 RCTs and the 2 meta-analyses, the members of this workshop agreed that the nature of evidence available regarding this statement was Category Ia (evidence obtained from meta-analysis, including at least 1 large, randomized, controlled trial) (Table 1).

Level of Support for Statement

On the basis of the available evidence, 4 out of the 5 workshop participants agreed that their level of support was Category C (poor evidence to support the statement, but recommendations may be made on other grounds) and 1 participant voted for Category D (fair evidence to reject the statement) (Table 1). Workshop participants struggled with the term "improved patient outcomes," but agreed to define this term as any outcome that is seen as beneficial to the patient in the postoperative period. Across the majority of randomized trials and both meta-analyses, IV PCA improves postoperative pain relief and overall patient satisfaction with pain control after surgery. The effectiveness of IV PCA in improving other postoperative outcomes is variable.

In the group at large, 18% (2 of 11) of the summit participants voted "1" (accept completely), 45% (5 of 11) voted "2" (accept with some reservations), 18% (2 of 11) voted "3" (accept with major reservations), 18% (2 of 11) voted "4" (reject with reservations), and none voted "5" (reject completely) (Table 1). This result was compared with the vote of the ASRA membership survey of 57% for "1," 34% for "2," 4% for "3," 4% for "4," and 1% for "5" (Fig 1).

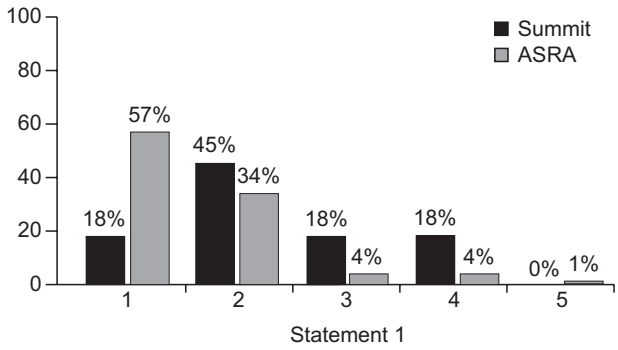

Fig 1. Voting comparison for Statement 1 (Use of IV PCA leads to improved patient outcomes when compared with nurse-administered parenteral opioids). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

On the basis of the available evidence, the most consistent difference relates to patient satisfaction and preference for PCA *v* NCA. This outcome may reflect satisfaction regarding the ability to maintain a degree of control during hospitalization, especially over something as individual as pain control. The value of self-determination is reflected in the wide variability of total opioid use by individuals undergoing the same surgical procedure. This variable cannot be predicted in advance in most cases and may cause some patients to be undertreated if a one-size-fits-all approach is used to order postoperative analgesics. The use of PCA does not appear to lead to improvement in other outcomes. However, the potential benefits outlined in some small studies include improved pulmonary function, provision for a wide variability in opioid dose, and reduced hospital stay.

The absence of clearly defined and widely accepted measures of patient outcomes limits comparisons between studies and makes accumulation of sufficient patient numbers to draw clear conclusions a challenge. The absence of improvements in areas such as side effects may reflect the drug itself and not the delivery system. The strong support for PCA is evident in the survey of the ASRA membership, and this support likely reflects the routine use of PCA for postoperative analgesia. It may also reflect the widespread acceptance of PCA as the standard of care. Given the relative equivalence of the 2 methods and the strong patient preference for IV PCA, the currently held opinion that favors PCA seems quite reasonable. Other issues regarding the inherent safety of PCA devices need to be resolved for the future but are not widely reported in the medical literature. Data regarding these problems are available in the Manufacturer and User Facility Device Experience (MAUDE) database, which outlines numerous adverse events related to PCA devices (see *Discussion* in Statement 5). These complications include overdose, drug switches, inaccurate drug delivery, and others. Improved devices capable of recognizing the drug, its concentration, and common dosing, in addition to improved delivery accu-

racy, may reduce device-related and human-related errors but may not make significant changes in most routine outcomes.

Future Directions

Future directions suggested by the workshop participants reflect weaknesses of the currently available data to support the widely held perception that PCA improves postoperative outcomes. Appropriately constructed studies that more closely reflect current practice with much larger numbers are required to provide a better picture of current PCA use and whether or not it truly improves outcomes as compared with NCA. In addition, use of validated patient-oriented (eg, patient satisfaction, quality of life, quality of recovery) and functional outcomes should be incorporated into these studies. Although large RCTs are ideal, larger population-based studies capable of identifying trends, complications, and outcomes are also needed. Such large observational studies would be ideal for characterizing the frequency and severity of PCA device–related problems. Current studies are too small to identify these outcomes with any accuracy, as their total numbers are small, even within the confines of a meta-analysis. As a result, many descriptions of unusual complications are based on case reports, small case series, or self-reported data to federal device registries that provide a numerator but no denominator.

Statement 2

Use of continuous peripheral analgesic techniques leads to improved patient outcomes.

Rationale and Definition of Statement

The use of continuous perineural analgesia is increasing in popularity for both hospitalized and ambulatory patients. These peripheral techniques offer the ability to provide effective focal analgesia and reduce the need for systemic opioid analgesics and are considered to have less risk of bleeding complications in anticoagulated patients.[3] However, performance of these techniques requires skill and a formal infrastructure for postoperative management and may increase anesthesia-related time. Thus, solid evidence of analgesic efficacy, reduced side effects, and, ideally, functional and long-term benefit would support making the required investment to routinely employ these techniques. For the purposes of this analysis, we were interested in prospective RCTs that compare continuous perineural analgesia to systemic opioids for postoperative analgesia. Thus, either sham perineural catheters, catheters infused with placebo, or no placebo were considered acceptable control groups. Specific outcomes extracted included postoperative pain, side effects (nausea/vomiting, sedation, pruritus, motor/sensory block), opioid use, and patient satisfaction compared with opioid analgesia.

Literature Search

A literature search for RCTs that compare continuous peripheral-nerve block with opioids for the management of postoperative pain yielded 788 articles by use of the terms "pain, postoperative" (13,752 articles) combined with "nerve block" (7,399 articles). The limitation of those results to only RCTs of humans and all adults (older than 18 years of age) yielded 236 articles. No language limitations were used. Each article's abstract was reviewed to determine if it included the use of continuous peripheral-nerve catheters for postoperative pain in one of the randomized groups and opioids (either oral or parenteral) in the other randomized group. This search identified 37 articles for further full-text review to determine if our analysis-inclusion criteria were met. A hand-search of the author's (Dr. Liu's) files and references from the original search results yielded an additional 7 articles for full-text review. Inclusion criteria were a clearly defined anesthetic technique (combined general anesthesia [GA]/regional, GA, peripheral-nerve block); randomized trial; adult patient population (older than 18 years of age); continuous peripheral-nerve block (or analgesia) used postoperatively (intrapleural catheters were deemed not to be classified as a peripheral-nerve catheter); and opioids administered for postoperative analgesia in groups who did not receive peripheral-nerve block. Exclusion criteria were no measurement of pain score that could be converted to VAS or no comparison of opioid to continuous peripheral-nerve block.

Evidence

Nineteen articles, related to studies that enrolled a total of 603 patients, were ultimately included in the meta-analysis.[3] Included articles came primarily from hospitals in Europe (58%) and North America (38%). More studies involved lower-extremity surgery (60%) than upper-extremity surgery (40%), and femoral nerve/lumbar plexus was the most common catheter location for analgesia (51%), followed by interscalene (35%). Randomized clinical trials that compared perineural catheters with opioids were very limited for other locations (13%).

Studies in the analysis included 11 with data obtained by intention to treat (all enrolled patients were included in the data analysis, with no treat-

ment failures), but only adequately functioning catheters were included in the remaining 8 studies. A total of 13 patients were withdrawn from the catheter group after randomization, and 7 were excluded from the opioid group in these 8 studies. Ten additional patients were withdrawn before randomization. Overall, 10 catheter-placement failures and 11 catheter dislodgements occurred; 2 patients in the catheter groups were excluded for other reasons, and a total of 5 patients in the opioid groups were withdrawn because of nausea and 2 were withdrawn for failure to complete surveys.

When all studies and observations were combined, the analysis revealed that perineural analgesia provided better postoperative analgesia compared with opioids ($P < .001$). This effect was seen for all time periods measured for both mean VAS (1.4 *v* 3, global mean) and maximum VAS (3 *v* 5.4) at 24 ($P < .001$), 48 ($P < .001$), and 72 (mean VAS only) ($P < .001$) hours postoperatively. When analyzed by catheter location, perineural analgesia provided superior analgesia to opioids ($P < .05$) for all locations and time periods.

No major complications were reported in any of the 19 studies. Twelve of the 19 studies (63%) reported at least one minor complication; sedation occurred most frequently overall. Motor block was the adverse effect most attributed to peripheral-nerve block (31% *v* 15%, $P < .001$), whereas nausea/vomiting (49% *v* 21%), sedation (52% *v* 27%), and pruritus (27% *v* 10%) all occurred more commonly with opioid analgesia ($P < .001$). Number needed to harm was calculated for nausea/vomiting, sedation, and pruritus with 4, 4, and 6 patients who received perineural analgesia expected to result in 1 fewer patient with nausea/vomiting, sedation, and pruritus, respectively, compared with opioid analgesia.

Four trials measured patient satisfaction on a VAS and demonstrated a higher composite mean VAS satisfaction for catheters 9.6 (n = 93) (95% CI 9.5-9.7) compared with opioids 7.1 (n = 90) (95% CI 6.9-7.2). Total opioid consumption for both groups for the duration of catheter use was calculated for 12 of the 19 studies. Seven studies either failed to document total opioid consumption for both groups or did not provide the data in a manner that could be converted for direct comparison. Total opioid consumption over 48 hours was significantly less ($P < .001$) with the use of perineural analgesia (20.8 mg morphine [n =165 patients; 95% CI 18.5-23.1]) compared with opioid analgesia (54.1 mg morphine [n = 174 patients; 95% CI 50.8-57.4]).

Grading of Evidence

On the basis of the evidence in these 19 RCTs, all members of this workshop agreed that the level of evidence available regarding this statement was Ia (evidence obtained from meta-analysis, including at least 1 large, randomized, controlled trial [Table 1]).

Level of Support for Statement

On the basis of the available evidence, the workshop members voted that their level of support was Category A (good evidence to support the statement) (Table 1). In the group at large, 73% (8 of 11) of the summit participants voted "1" (accept completely), and 27% (3 of 11) voted "2" (accept with some reservations) (Table 1). Reservations included the level of skill and clinical infrastructure required to achieve similar positive efficacy with perineural catheters, unknown incidences of serious complications, and the overall heterogeneity of the RCTs in the meta-analysis. This level of support was similar to results from the ASRA survey, but the ASRA survey reported a greater incidence (43%) of "2" (accept with some reservations) (Fig 2). This support may reflect a greater "real world" concern of previously mentioned reservations of level of required skill, clinical-management infrastructure, and potential complications.

Discussion

On the basis of our meta-analysis, continuous peripheral-analgesic techniques provide superior analgesia, reduce opioid consumption, and reduce opioid-related side effects (nausea/vomiting, seda-

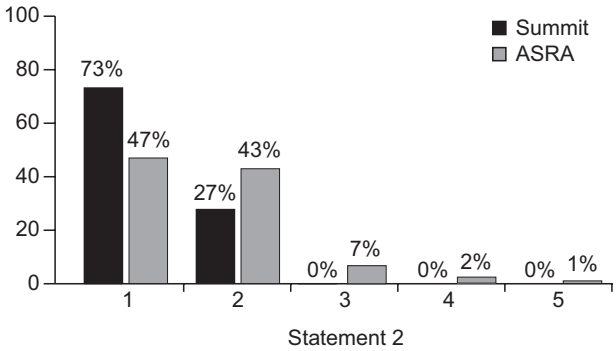

Fig 2. Voting comparison for Statement 2 (Use of continuous peripheral analgesic techniques leads to improved patient outcomes). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

tion, pruritus). However, several unresolved issues remain concerning the technique. Current subject numbers are insufficient to truly gauge the safety of techniques. General applicability of techniques is uncertain because of the required level of technical skill and infrastructure to manage these catheters, especially for outpatients. Current RCTs are relatively small and heterogeneous; thus, little can be concluded regarding optimal techniques, especially for individual surgical procedures. Finally, insufficient evidence is available to determine the ability of continuous peripheral-analgesic techniques to affect venue for recovery (inpatient *v* outpatient), duration of hospital stay, long-term functional outcome, or major morbidity. One small study examined the ability of continuous sciatic analgesia to allow conversion of inpatient foot surgery to outpatient surgery.[16] Although more patients in the perineural analgesia group were able to go home, the difference was not statistically significant. Two RCTs that examined total-knee replacement have noted shorter hospital stays with continuous femoral analgesia *v* IV PCA,[17,18] but both study protocols included inpatient physical rehabilitation and hospital stays that were quite long (16-45 days) compared with current data from the United States Hip and Knee Registry (4-day average hospital stay).[19] These same studies reported faster initial recovery of joint flexion with femoral-nerve analgesia, but no differences were noted by 3 months. Finally, no RCT has addressed effects on major morbidity or mortality.

Future Directions

An examination of the included studies for methodology found no consistency in analgesic regimen for either the opioid or peripheral-nerve catheter group. The opioid group included a variety of opioids, routes of administration (oral, parenteral), and frequency of administration, whereas the catheter group included different local anesthetics (bupivacaine and ropivacaine), concentrations (ranging from 0.125% to 0.5%), infusion rates and boluses, and catheter locations. Both groups also commonly had supplemental analgesics administered, including various NSAIDs. Further studies to determine the ideal local anesthetic, concentration, infusion rate, bolus dose, and additives for each catheter site and surgical location are still needed to determine the optimal use of continuous peripheral-nerve block. Large prospective surveys are needed to accurately determine the risk of complications with these techniques. Large RCTs are needed to evaluate potential effects on venue for recovery (inpatient *v* outpatient), duration of hospital stay, long-term functional outcome, and major morbidity.

Statement 3

The use of multimodal analgesia improves postoperative pain control and reduces analgesia-related adverse effects.

Rationale and Definition of Statement

The common perception is that combining two or more analgesic agents, an approach termed multimodal analgesia, may provide at least additive, if not synergistic, analgesia.[20] Another perception is that combining analgesic modalities with different mechanisms of action may reduce the use of individual analgesic agents and, thereby, decrease the incidence of side effects associated with each agent, particularly with the opioid analgesics.

The broad term "multimodal analgesia" is used to describe any combination of two or more analgesic modalities. Numerous permutations of analgesic agents and techniques are possible (some of which may not be routinely used in clinical practice on a global basis), which makes a meaningful comprehensive assessment particularly difficult. The available evidence for most multimodal regimens is scant; thus, to allow for a meaningful analysis, the statement focused on the examination of analgesic efficacy and side-effect profiles of the combination of nonspecific NSAIDs, cyclooxygenase-2 (COX-2) inhibitors, or acetaminophen in conjunction with IV PCA. The definition of "multimodal analgesia" in this case did not refer to the multimodal approach to patient convalescence, which also incorporates nonpharmacologic approaches. Our focused definition of "multimodal" examined whether the addition of these commonly used adjuvant agents would provide superior analgesia, while decreasing the incidence of opioid-related side effects and adverse events.

Literature Search

The literature search was conducted by use of the specific text words "nonsteroidal anti-inflammatory agents" or "NSAID," which yielded a total of 130,606 articles, and "acetaminophen," which yielded a total of 10,783 articles. These two searches were combined with the "OR" function for a total of 138,559 articles. This search was combined with "postoperative pain" (17,797) articles by use of the "AND" function and limited further by use of the English language and meta-analysis functions to yield a total of 26 articles, each of which was examined for relevance to the statement. The reference lists of these articles were also examined.

Evidence

A total of 5 articles were ultimately included in the analyses. Twenty-one of 26 articles were rejected because they did not examine postoperative pain, used only single-dose regimens, or evaluated pediatric patients. The first meta-analysis, which examined 22 randomized, controlled trials (2,307 subjects), attempted to assess the effect of NSAIDs on morphine-related adverse events.[21] The included studies compared the addition of an NSAID *v* placebo to standard IV PCA morphine for pain management after a range of operative procedures. The authors' analyses demonstrated that NSAIDs decreased the relative risk (RR) *v* placebo of postoperative nausea and vomiting (PONV) by 30% (RR = 0.70; 95% CI = 0.59-0.84) and of sedation by 29% (RR = 0.71; 95% CI = 0.54-0.95). NSAIDs did not reduce the risk of developing pruritus, urinary retention, or respiratory depression. Effects on pain were not assessed.

The second meta-analysis, which included 7 randomized, controlled trials (491 subjects), examined the effect of acetaminophen on morphine-related adverse events.[22] The studies compared the addition of acetaminophen *v* placebo to standard IV PCA morphine for pain control after major surgery. The authors' analyses suggested that use of acetaminophen decreased morphine use by approximately 20% (9 mg) over the first 24 hours after surgery (95% CI = −15 to −3 mg). The addition of acetaminophen did not reduce the risk of any opioid-related side effects. Although the effect of acetaminophen on postoperative pain was not quantitatively analyzed as a single-pooled estimate, the authors noted that only 2 of 6 studies found that use of acetaminophen improved pain scores when compared with placebo.

The most recent meta-analysis examined whether multimodal analgesia combined with a variety of agents provided any advantage when added to IV PCA morphine.[23] Included in their meta-analysis were 10 randomized controlled trials that examined the addition of acetaminophen, 14 that examined addition of the COX-2 inhibitors, and 33 that assessed the addition of an NSAID to standard IV PCA morphine for pain control after surgery. As in the previous reports, the comparison was between the additions of an analgesic agent (acetaminophen, COX-2 inhibitors, or NSAIDs) *v* placebo. The results suggested all of the analgesic agents studied provided an opioid-sparing effect; however, this decrease in opioid consumption did not consistently result in a decrease in opioid-related side effects or adverse events. Use of NSAIDs was associated with a significant decrease in the relative risks of PONV and sedation, similar to those seen in the previous meta-analysis.[21,23] However, use of acetaminophen or COX-2 inhibitors did not significantly decrease the risk of opioid-related adverse events compared with placebo. NSAIDs (multiple dose and infusion only), but not acetaminophen or single-dose NSAIDs, were associated with a statistically significant decrease in pain scores, but whether this decrease was clinically meaningful was not clear. The analgesic efficacy of COX-2 inhibitors was not assessed in this meta-analysis.

Finally, 2 systematic reviews were conducted of the analgesic efficacy of a COX-2 inhibitor compared with placebo in addition to a standard opioid analgesic regimen for postoperative pain control.[24,25] One systematic review examined the effect of preoperative COX-2 inhibitors on postoperative outcomes in 22 randomized trials (2,246 subjects).[24] Compared with placebo, preoperative administration of a COX-2 inhibitor reduced postoperative pain and analgesic consumption in 15 of 20 trials; however, no significant differences were seen between placebo and COX-2 inhibitors in the overall relative risk of PONV or incidence of PONV in 13 of 17 trials. The other systematic review was a meta-analysis of 9 trials (1,738 subjects) that examined patients' global evaluation of analgesia after IV parecoxib for postoperative pain.[25] Compared with placebo, subjects who received parecoxib, particularly the 40-mg dose, had a significantly superior analgesic outcome (ie, they more frequently rated their pain control as "good" or "excellent"), but here again, COX-2 inhibitors did not significantly decrease the risk of opioid-related adverse events compared with placebo.

Grading of Evidence

On the basis of the evidence in these 4 meta-analyses and 1 systematic review, all members of this workshop agreed that the level of the evidence available regarding this statement was Category Ia (evidence obtained from meta-analysis, including at least 1 large randomized, controlled clinical trial [Table 1]).

Level of Support for Statement

On the basis of the available evidence, discernable differences exist in analgesic and side-effect profiles for different agents. Thus, the level of support for this statement was assessed separately for postoperative pain control and reduction of analgesia-related adverse (opioid-related) effects by individual classes of agents (acetaminophen *v* COX-2 inhibitors *v* nonspecific NSAIDs). All of the mem-

bers of this workshop agreed on the level of support for each statement as follows.

With regard to the first part of the statement (*the use of multimodal analgesia [NSAID-based] improves postoperative pain control*), all members of this workshop agreed that the level of support was Category A (good evidence to support the statement) only for nonspecific NSAIDs (multidose or infusion) and COX-2 inhibitors. However, when acetaminophen and single-dose NSAIDs were considered, all members of this workshop agreed the level of support was Category E (good evidence to reject the statement) (Table 1).

With regard to the second part of the statement (*the use of multimodal analgesia [NSAID-based] reduces analgesia-related adverse [opioid-related] effects*), all members of this workshop agreed that the level of support was Category E (good evidence to reject the statement) for acetaminophen and COX-2 inhibitors only. For nonspecific NSAIDs, all members of this workshop agreed that the level of support was Category B (fair evidence to support the statement) (Table 1).

When voting on support of this statement, 73% (8 of 11) of the summit participants voted "2" (accept with some reservations) and 27% (3 of 11) voted "3" (accept with major reservations); none voted for "1" (accept completely), "4" (reject with reservations), or "5" (reject completely) (Table 1). This result was compared with the vote of the ASRA membership of 73% for "1," 23% for "2," 3% for "3," 0% for "4," and 1% for "5" (Fig 3).

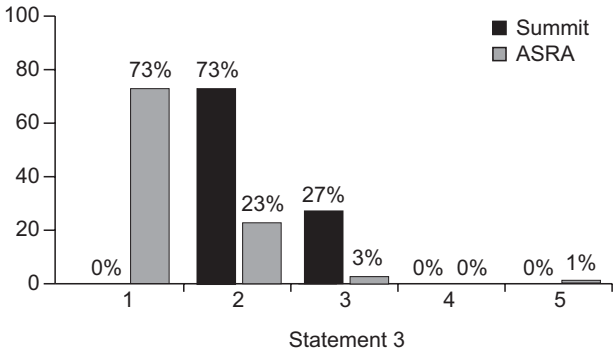

Fig 3. Voting comparison for Statement 3 (Use of multimodal analgesia improves postoperative pain control and reduces analgesia-related adverse effects). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

On the basis of the available evidence, it appears that multimodal analgesia (use of NSAIDs, COX-2 inhibitors, or acetaminophen in combination with IV PCA) does result in an opioid-sparing effect. However, this decrease in opioid consumption does not consistently translate into a decrease in opioid-related adverse events or side effects. The use of acetaminophen and COX-2 inhibitors does not appear to decrease the relative risk of opioid-related side effects (eg, PONV, sedation, pruritus, urinary retention) or adverse events (respiratory depression). Use of nonspecific NSAIDs does appear to decrease the relative risk of some opioid-related side effects (ie, PONV, sedation) but not others (ie, pruritus, urinary retention, respiratory depression). With regard to postoperative analgesia, addition of NSAIDs (multiple dose or infusion), but not acetaminophen or single-dose NSAIDs, produces a statistically significant decrease in postoperative-pain scores. Two systematic reviews seem to indicate that the addition of COX-2 inhibitors also provides superior postoperative analgesia; however, no quantitative analysis of the extent of this benefit was done.

This statement, like many of the statements included in the summit, is broad and can be interpreted in different ways. The interpretation of this statement depends on the particular definition assigned to specific words (eg, "multimodal" and "adverse effect") in the statement. Because available evidence was limited regarding other forms of multimodal analgesia, this analysis was limited to the combination of an NSAID, acetaminophen, or a COX-2 inhibitor with an opioid regimen for pain control after surgery. Indeed, ASRA members voted strongly in support of the statement, and this support likely reflects a strong bias toward the clinical impression that a multimodal analgesia regimen that includes regional anesthesia can improve clinical outcomes. In addition, the methodology used in some of the randomized controlled trials examined does not accurately reflect conditions in actual clinical practice (ie, they lack external validity). For instance, addition of a single-dose of NSAID did not provide superior analgesia compared to placebo; however, NSAIDs would more likely be used in multiple doses (which do provide superior analgesia *v* placebo) in the typical clinical setting.[23] Whether statistically significant reduction in weighted pain scores (approximately −1 on a scale of 0 to 10) for multiple doses or continuous infusion of NSAIDs would be clinically meaningful is also unclear.[23]

Finally, the intent of the statement was to address the effect of NSAIDs, COX-2 inhibitors, and acetaminophen on opioid-related side effects; however,

we did not discuss the possible increased relative risks of these treatments (severe bleeding: number needed to harm [NNH] = 59; renal failure in cardiac patients for COX-2 inhibitors: NNH = 73; and other serious adverse events [including death, myocardial infarction, sternal wound infection, and cardiac failure] for COX-2 inhibitors: NNH = 11).[23]

Future Directions

Future directions suggested by workshop participants reflect some of the limitations already discussed. The studies used to assess this statement may be considered "bimodal" therapy (IV PCA + one adjuvant). Appropriately constructed studies are needed to evaluate a more comprehensive multimodal approach (eg, combinations of regional-analgesic techniques, other adjuvant agents, and opioid analgesics). Future studies should be designed to reflect actual clinical practice (eg, use of a multiple rather than a single-dose NSAID regimen). Use of validated patient-oriented (eg, patient satisfaction, quality of life, quality of recovery) and functional outcomes should also be incorporated into these trials. Future trials should assess outcomes in not only the short term (days) but also a longer time frame (weeks to months).

Statement 4

Technology-related problems limit the safety and effectiveness of IV and epidural PCA.

Rationale and Definition of Statement

PCA was introduced as a method of closing the loop between patients in pain and their sources of analgesia. This technique allowed patients to deliver small, intermittent doses of opioids to provide analgesia and minimize the risks of sedation and respiratory depression. PCA devices come with intrinsic safety features, such as lockout intervals during which additional doses of medication cannot be delivered and 1-hour or 4-hour maximum allowable doses. Another factor critical to the safety of PCA is that the button should only be pressed by the patient, to avoid repeated dose administration if sedation ensues. PCA has improved pain control and patient satisfaction, but has this new technology introduced additional risks for patients?

Postoperative epidural analgesia was initially limited to the use of preservative-free epidural opioids given as a single bolus dose. Epidural infusions of different analgesic combinations have been given in the epidural space to provide prolonged analgesia, with reduced need for bolus injections. An infusion device is required to provide continuous epidural analgesia, and this feature is often combined with a patient-control function similar to IV PCA. Thus, a similar question arises concerning continuous epidural analgesia: Do the limitations of the technology add new risks for the pain patient?

PCA, via both IV and epidural routes, has involved the introduction of sophisticated technology into widespread use in a variety of settings. In this section, we assess whether the technological limits of current therapy reduce the safety or effectiveness of these techniques.

Literature Search

The specific text words used to carry out the literature search were "patient controlled analgesia," and they yielded a total of 2,863 articles, which when combined with "medication errors" yielded 30 articles. The combination of "patient controlled analgesia" and "technological failure" yielded 16 articles. No meta-analyses looked at technological failures; the majority of articles examined were case reports. Some of these references were not in traditional peer-reviewed journals but rather in reports from drug-safety monitoring groups. These references were identified from the reference lists of cited articles or by summit participants, and these databases are described along with the evidence below.

Evidence

MEDMARX is USP's (United States Pharmacopeia, Rockville, MD) interactive, anonymous, Internet-accessible system that allows self-reporting of medication errors and adverse drug reactions (available at https://www.medmarx.com/, accessed February 15, 2006). The most common errors involving PCA pumps as reported by MEDMARX were improper dose/quantity (38.9%), unauthorized/wrong drug (18.4%), and dose omission (17.6%). Opioids were the drugs most likely to be associated with medical injury. Forty-five percent of these opioid-related adverse events were attributed to misuse or malfunction of infusion devices.

MEDMARX uses the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Error Outcome Category Index (Table 2).[26] The average overall rate for errors of the types in categories E through I submitted to MEDMARX has been approximately 2%. However, when PCA pumps were involved, the chance for error leading to patient harm increases to 7% (a 3.5-fold increase).[27]

A recent observational study detailed 56 adverse events associated with use of PCA reported over a 1-year period in a tertiary referral hospital. Program-

ming errors accounted for 71% of PCA adverse events.[28] The majority (75%) of these errors resulted in overmedication, and 25% resulted in inadequate analgesia caused by undermedication. Another prospective observational study in a tertiary referral center demonstrated that in just over 2 years IV PCA was used in 3,758 patients and 14 critical events occurred (1:946 patients or 1:2,280 patient days).[29] They divided the problems into four categories: programming errors, machine tampering, doses administered by others, and poor clinical judgment by the prescribing physician (Table 3). Fifty percent of these adverse events were caused by programming errors, with one of the eight resulting in a serious consequence. A retrospective analysis of adverse events in a major teaching hospital in New Zealand found that 3 of 14 potentially life-threatening complications were caused by programming errors.[30]

The United States Food and Drug Administration (FDA) Center for Devices and Radiological Health maintains an Internet-based, self-report database; the Medical Device Reporting (MDR) database contains over 600,000 reports entered between 1984 and 1993. The MAUDE database contains reports from facilities, distributors, and manufacturers from as early as 1991 (available at http://www.fda.gov/cdrh/mdr/index.html, accessed February 15, 2006). The Safe Medical Devices Act of 1990 requires user facilities to report device-related deaths to the FDA and the device manufacturer and to report device-related serious injuries to the manufacturer or to the FDA if the manufacturer is not known. Analysis of the MDR database found programming errors that resulted in patients receiving 5-fold to 10-fold higher amounts of PCA medication than was intended. These errors resulted in 5 to 8 deaths, depending on the method used for counting total number of events (whether 3 of the same deaths were reported by 2 different individuals is unclear from the database). Utilizing this data, the author postulated that because only 1.2% to 7.7% of adverse events are usually reported, these 5 to 8 deaths out of the 22 million users of this PCA pump before March 2001 represent a death rate of 1 in 33,000 to 300,000.[31]

Table 2. NCC MERP Error Outcome Category Index

Category	Description
A	Circumstances or events that have the capacity to cause error
B	An error occurred but the error did not reach the patient
C	An error occurred that reached the patient but did not cause patient harm
D	An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm
E	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
F	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization
G	An error occurred that may have contributed to or resulted in permanent patient harm
H	An error occurred that required intervention necessary to sustain life
I	An error occurred that may have contributed to or resulted in the patient's death

Table 3. Categories of Critical Events That Occurred with IV PCA in an Observational Study

Programming errors
Machine tampering
Doses administered by others
Poor clinical judgment by the prescribing physician

A review of the MAUDE database demonstrated that malfunction of the PCA device may cause patient harm.[32] During the 2-year period January 2001 to December 2003, 2,108 problems related to PCA pumps were reported. Seventy-nine percent of these events were caused by device-related problems; 61% were confirmed by the manufacturer. A host of other reports have appeared in the literature relating malfunctioning of the PCA devices and resultant delivery of excessive amounts of opioid (free flow of opioid caused by cracked syringes or poorly designed pumps and delivery systems).[33] Many of the currently available PCA pumps do not default to zero when programming delays occur. If a delay in entering a numeric value is detected or if the pump is turned off during programming, several commonly used PCA pumps default back to the value that was last entered rather than to zero.[34] Experts have recommended the PCA pump should default to "000," which would require the active selection of a value. Errors in PCA programming are also influenced by the pump design. Many available pumps incorporate software that is not intuitive or is often repetitive, tedious, and sometimes illogical.[35] In a recent prospective review of IV infusions on a single day in a tertiary referral center in 2003, 66.9% of 426 medication infusions had 1 or more errors.[36] Thirty-seven of these errors out of 389 deviations were rate related (9%) and 3 were caused by programming errors. The severity ratings of these errors required that 29 have increased monitoring and determined that 4 were likely to cause temporary harm, 1 was likely to result in increased hospitalization, and 3 could have produced permanent harm.

Unauthorized/wrong drug. Several case reports and advisories are about one of the safety fea-

tures of the PCA device being circumvented when the button is pushed by others. Family members and health professionals have administered doses for patients, by proxy, hoping to keep them comfortable. Ashburn et al[29] and Sidebotham et al[30] documented that 3 out of 14 PCA-related adverse events were caused by family members pushing the button while the patient slept. A report from the Joint Commission for Accreditation of Healthcare Organizations (JCAHO) indicated that 15 of 460 PCA-related errors were caused by unauthorized people pushing the PCA button; 12 of 15 cases were attributed to family members, 2 to a nurse, and 1 to a pharmacist.[37]

Another type of error occurs because the opioids used in the PCA pumps have similar packaging with similar names: morphine and hydromorphone. These opioids, which often are not easy to differentiate from one another, are also available in higher concentrations, a potential source of error. For example, many devices allow entry in either mL or mg; if morphine at a concentration of 1 mg/mL is mistakenly replaced with hydromorphone 1 mg/mL and the pump is programmed to deliver a 1 mL dose, the result is a 5-fold overdose because of the potency differences of the drugs.[38]

Grading of Evidence

On the basis of the evidence in these case reports and epidemiologic surveys, all members of this workshop agreed that the level of evidence available regarding this statement was Category III (evidence obtained from case series, case reports, or flawed clinical trials) (Table 1).

Level of Support for Statement

Because of the paucity of data on technological issues and the similarity between pumps used to deliver IV PCA and epidural infusions, the same data were used to address the safety and effectiveness of both routes of delivery. On the basis of the available evidence, the workshop participants voted their level of support was Category B (fair evidence to support the statement) (Table 1). In the group at large, 27% (3 of 11) of the summit participants voted "1" (to accept the statement completely), 55% (6 of 11) voted "2" (to accept the statement with some reservations), and 18% (2 of 11) voted "4" (to reject the statement with reservations); none voted for "3" (accept with major reservations) or "5" (reject completely) (Table 1). This result was compared with the vote of the ASRA membership of 13% for "1," 34% for "2," 10% for "3," 32% for "4," and 11% for "5" (Fig 4).

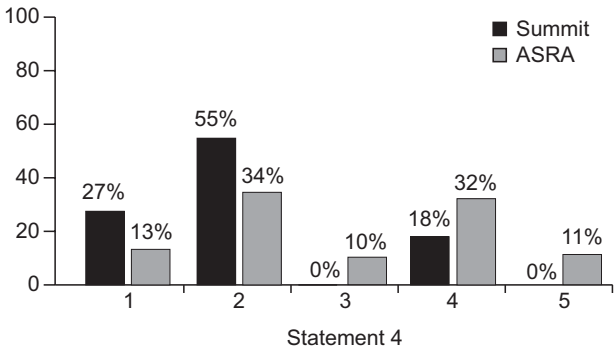

Fig 4. Voting comparison for Statement 4 (Technology-related problems limit the safety and effectiveness of IV and epidural PCA). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

Although currently used pain technology has improved patient satisfaction, the limited evidence indicates that the technology has been far from infallible. The majority of the members attending the summit recognized the limitations and safety concerns associated with our current technology; the most prominent concern is programming errors associated with infusion devices. The views of ASRA members who participated in the survey differed from those of the faculty at the summit, but the majority did accept that technology is problematic.

Future Directions

Many of the technological limitations to the use of PCA and epidural analgesia can be addressed by modifying existing technology. Redesigning the software of commercially available PCA pumps can reduce the number of human programming errors.[35] Smart pumps with preprogrammed hard and soft limits on the amount of analgesic that can be infused may reduce programming errors. However, a prospective review of infusion pumps only identified a small percentage of errors that would be reduced by employing this technology.[36] Another potential way to reduce programming errors would be to equip the PCA devices with bar-code readers that would prevent entry of the wrong drug or concentration; a number of devices that incorporate bar-code technology are now available. Other options include a patient-activated fentanyl transdermal system, a disposable, self-contained PCA device that has been demonstrated in controlled trials as

equivalent to standard IV PCA with morphine that eliminates the potential for human programming errors.

Statement 5

New and emerging therapies offer advantages over existing analgesic options for treating postoperative pain.

Rationale and Definition of Statement

Current data suggest that patients are likely to experience significant pain after surgery. Although recent pain initiatives and pain guidelines exist, statistics on pain after surgery have remained largely unchanged.[39] Under ideal conditions, available technologies may provide reasonable control of postoperative pain. However, these technologies have a number of problems that limit results. Invasive technologies that have indwelling catheters and external pumps are perceived to be cumbersome and labor intensive. Such pumps are also implicated in medication errors that lead to patient harm.[40] Additionally, mechanical delivery systems have an inherent failure rate related not only to the pump but also to the catheter and tubing. Consequently, patients may experience analgesic "gaps" or periods of unrelieved pain.[41]

New and emerging technologies may offer advantages over older technologies by reducing failure rate, improving safety, and eliminating analgesic gaps. Newer technologies may facilitate patient mobility, be compatible with anticoagulation protocols, and reduce burdens on health-care providers.

Two technologies meet the criteria of new and emerging techniques. Fentanyl HCl Patient Activated Transdermal Analgesia (PATS) (IONSYSTM; Ortho-McNeil, Raritan, NJ) is an iontophoretic needle-free, active-drug delivery system. Extended Release Epidural Morphine (DepoDur; Endo Pharmaceuticals, Chadds Ford, PA) is a liposomal morphine preparation for epidural administration that was recently approved by the FDA. Both technologies may address unmet needs associated with existing approaches to the treatment of postoperative pain.

Literature Search

Literature review included all published papers found on the MEDLINE database for the respective technologies. Because both technologies are new, available literature is rather limited and related to studies from the drug-approval process. Results of 6 well-designed RCTs are published—3 for each technology at this time.

Fentanyl HCl PATS

Fentanyl HCl PATS is a small, needle-free, self-contained delivery system about the size of a credit card that delivers small charged molecules by iontophoresis. The system is preprogrammed to deliver fentanyl (40 μg) over 10 minutes upon patient demand, up to 80 doses a day. The system deactivates after 24 hours of use, or 80 doses. The fentanyl HCL PATS was granted marketing authorization by the European Commission in January 2006; approval by the FDA is pending.

To date, 3 pivotal trials have been published, including an open-label comparison with a standard morphine IV-PCA protocol and 2 double-blind, placebo-controlled trials. These trials were intended to demonstrate safety and efficacy, not superiority to standard therapy.

Fentanyl HCl was compared with a standard morphine IV-PCA protocol in an open-label randomized study of 320 patients.[42] Patients reported similar global assessments of treatment success between the groups. Withdrawal because of inadequate pain control and last pain score were similar between the groups. The adverse-event profile was also similar between the groups and reflected typical opioid-related side effects.

Two additional studies compared fentanyl HCl PATS to an identical placebo system.[43,44] Both studies demonstrated superiority over placebo. Additionally, these trials also demonstrate a side-effect profile typical of opioids, with both fentanyl HCl PATS and morphine via IV PCA.

None of the trials published thus far were intended to examine potential benefits over standard therapy. Several studies presented as abstracts explore some of these issues. A resource-utilization study of IV PCA of 540 patients identified an average of 39 nursing interventions per patient, which suggests that standard IV PCA is complex and labor intensive.[45] Another abstract identified problems associated with IV-PCA pumps found in the MAUDE database.[32] Although these data showed 79.1% to be device-related, 6.5% were identified to be user errors, which suggests that operator error is a significant source of IV PCA–related problems. In a recent abstract that compared "ease of care" as rated by patients, nurses, and physical therapists with fentanyl HCl PATS *v* morphine IV PCA, Phillips[46] suggests that less-invasive technology may be preferable.

Extended-Release Epidural Morphine

Extended-release epidural morphine (EREM) exploits a lysosomal carrier (DepoFoam; SkyePharma, San Diego, CA), which consists of naturally occur-

ring lipids, that provides an extended period of drug release without the need for an indwelling epidural catheter. Three randomized, double-blind trials explore the safety and efficacy of EREM compared with placebo plus IV-PCA fentanyl or with standard epidural morphine in several surgical models.

EREM was compared with a placebo saline epidural with IV-PCA fentanyl in a hip arthroplasty study.[47] Patients who received placebo demonstrated a consistent need for supplemental fentanyl, whereas patients who received EREM had a significantly reduced need for rescue within 48 hours. Additionally, patients who received EREM demonstrated better control of pain during the 0 to 24-hour period after surgery. Adverse events were consistent with those expected with the use of any opioid analgesic. Up to 4% of patients required an opioid antagonist across all trials.[48] However, these trials were dose-finding studies, with some doses in excess of the approved doses. Also, the trials utilize opioid monotherapy, not opioid-sparing multimodal therapy, as practiced by most clinicians. Hence, these numbers may represent something of a "worst-case scenario" for respiratory depression. At recommended doses, all incidents of respiratory depression occurred by 16 hours. EREM was compared with standard epidural morphine for lower abdominal surgery.[49] Patients who received EREM demonstrated a reduction in supplemental fentanyl requirements over 48 hours. In a caesarean-delivery study, EREM was compared with standard epidural morphine.[50] Patients who received EREM demonstrated reduced need for analgesic supplement, better pain scores, and better functional ability over 48 hours.

Grading of Evidence

On the basis of these studies, members of this workshop agreed that the level of evidence available to support this statement was Category Ib (evidence from at least one well-designed, randomized, controlled trial) for both new technologies presented (Table 1).

Level of Support for Statement

On the basis of the available evidence, the level of support for this statement was assessed separately for each new technology. The results of 3 multicenter trials are published for each.

For both technologies, workshop members rated the level of support for this statement as Category C (poor evidence to support the statement but recommendations may be made on other grounds) (Table 1) but recognized that these trials were not designed to address the statement as written.

When the group at large voted on the support of this statement for fentanyl HCl PATS, none of the summit participants voted "1" (accept completely), 27% (3 of 11) voted "2" (accept with some reservations), 64% (7 of 11) voted "3" (accept with major reservations), 9% (1 of 11) voted "4" (reject with reservations), and none voted "5" (reject completely) (Table 1). This result was compared with the ASRA membership of 4% for "1," 29% for "2," 23% for "3," 14% for "4," and 6 % for "5" (Fig 5A). Of the ASRA participants, 24% had not heard of this technology.

When voting on the support of this statement for epidural extended-release liposomal morphine, none of the summit participants voted "1" (accept completely), 9% (1 of 11) voted "2" (accept with some reservations), 73% (8 of 11) voted "3" (accept with major reservations), 18% (2 of 11) voted "4" (reject with reservations), and none voted "5" (reject completely) (Table 1). This result was compared with the ASRA membership of 5% for "1," 35% for "2,"

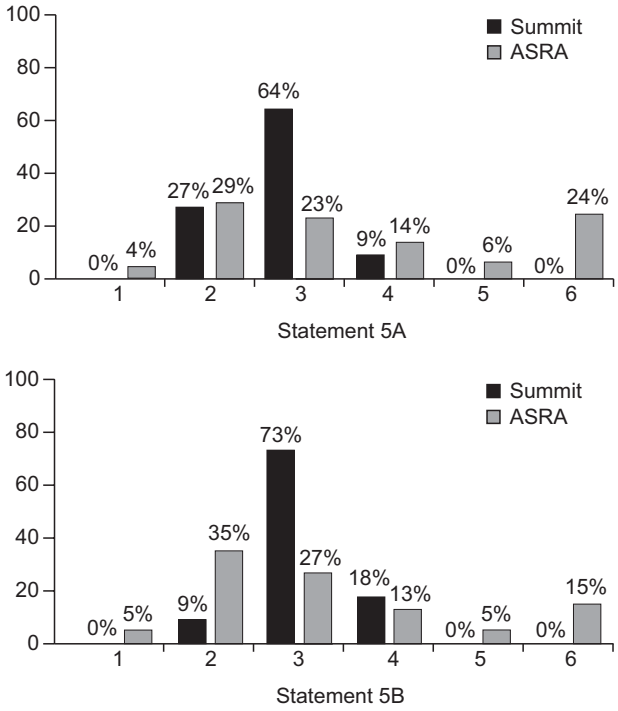

Fig 5. Voting comparison for Statement 5 (New and emerging therapies offer advantages over existing analgesic options for treating postoperative pain). (A) Iontopheretic transdermal fentanyl therapy. (B) Extended-release morphine therapy. Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

27% for "3," 13% for "4," and 5% for "5" (Fig 5B). Surprisingly, 15% of the ASRA participants had not heard of this already-approved technology.

Discussion

On the basis of the available evidence, the statement that new and emerging therapies offer advantages over existing therapies is not well supported. However, the purpose of these studies was not to demonstrate superiority, but rather to show safety and efficacy compared with standard therapy or placebo. This study is typical of studies designed for the drug-approval process. After approval, further studies are needed to evaluate potential advantages in a clinical setting.

Studies with fentanyl HCl PATS demonstrated analgesia with a preprogrammed system and without the need for an intravenous delivery of drug. Likewise, studies with EREM successfully demonstrate 48 hours of analgesic effect with a single dose, with a significant reduction in the need for supplemental analgesics during the first 48 hours after surgery.

Future Directions

Carefully designed future studies will be needed to explore and confirm these observations. Workshop participants recognized the limitations of the initial trials that are part of the drug-approval process. These studies are not intended to address advantages over existing therapy in most cases, but to establish the safety and efficacy of a novel technology. Hence, the level of support for the statement is not unexpected at this point or predictive of actual clinical advantage. Future studies should be designed to reflect actual clinical practice and evaluate complex comparisons to existing therapies. Also, validated instruments to address questions such as ease of use and burden of care must be used or created.

Statement 6

The creation and dissemination of acute-pain guidelines has improved postoperative-pain management.

Rationale and Definition of Statement

Clinical-practice guidelines (CPGs) are systematically developed statements meant to assist practitioners and their patients in making decisions about appropriate health care for specific clinical conditions. Originally designed as a tool to control costs of Medicaid and Medicare programs, CPGs are now commonly viewed as a means to introduce evidence into practice and make positive contributions to the quality and outcomes of care. Definitive reviews of CPGs in other areas of health care have demonstrated improvement in the quality of clinical decisions.[51-53] However, little is known about the impact of CPGs, specifically the American Society of Anesthesiologists (ASA) "Practice Guidelines for Acute Pain Management in the Perioperative Setting,"[4] on practice behaviors and patient outcomes. Developed in 1994 and updated in 2004, the ASA CPG currently serves as the most relevant guideline for individuals who manage perioperative pain.

Literature Search

Since the 1980s, CPGs have proliferated to number more than 1,000 documents approved through the National Guideline Clearinghouse (NGC).[54] A search of the NGC Web site (www.guideline.gov) by use of the words "acute pain management" generated 433 relevant guidelines, including the ASA acute-pain management CPG. A search for outcome studies of the ASA acute-pain guidelines by combining the text words "practice guideline" (PG) or "clinical guidelines" (CG), "pain," and "effectiveness" resulted in 26 abstracts, none of which addressed the ASA guidelines. A combination of only "practice guidelines" and "evaluation studies" identified 162 relevant abstracts that were further examined for relevance to the statement. Additionally, key citations were reviewed from a recent literature search performed and previously described for a revision of the American Pain Society quality-improvement recommendations.[55]

Evidence

We reviewed only investigations specific to pain-management CPGs and rigorous systematic reviews of guideline-evaluation studies. However, 1 study was included to allow a better understanding of the phenomenology of CPGs.[56] A total of 5 clinical studies and 2 systematic reviews on the effectiveness and efficiency of guideline dissemination and evaluation were included in our final analysis. The first clinical study reviewed is a prospective RCT of 26 medical oncologists in outpatient-clinic settings.[57] The primary objective was to compare a guideline-based cancer-pain algorithm to standard practice. Implementation of an algorithm-based cancer-pain management guideline that standardized analgesic drug choice and side-effect management demonstrated that guideline implementation could enhance pain outcomes. Patients randomized to the pain-algorithm group achieved a significant

reduction in usual pain intensity, when compared with standard practice ($P < .02$).

The second clinical study was the only reference found specific to acute postoperative-pain management. The outcomes of the national Post-Operative Pain Management Quality Improvement Project were described.[58] The intervention consisted of written resource materials, including the ASA acute-pain guidelines, accompanied by support services that included an e-mail listserve, a resource Web page, and assistance from project staff via telephone. Data regarding critical structures, processes (practice patterns), and patient outcomes were collected from 56 hospitals at baseline and at follow-up 12 to 18 months after implementation. Results revealed a significant increase in the presence of structural elements that are critical to improvement of pain management from baseline (45%) to follow-up (72%). Improvements in practice were significant, including documented use of pain-rating scales, decreased use of IM opioids, and increased use of nonpharmacologic strategies. Patient outcome data were collected, including pain intensity, pain interference with life activities, and overall satisfaction with pain management.[59] Patient-survey data revealed no change in these pain outcomes. The study was limited by voluntary reporting of data, emphasis of the project on changes in structure as opposed to treatment practices, and the short time frame from implementation to follow-up.

The third clinical study, a randomized controlled trial, examined implementation of the Dutch Low Back Pain Guideline for general practitioners and found small changes in patient management.[60] General practitioners in the intervention group (n = 21) received the Dutch pain guideline, a clinical practice workshop, scientific articles on low-back pain management, the guideline for occupational physicians, a tool for patient education, and a tool for reaching agreement on low-back care with physical therapists. The control group (n = 20) received no intervention. Guideline implementation resulted in fewer inappropriate follow-up referrals to physical therapy. However, no differences were noted in patient education, initial referral to physical therapy, or prescription of pain medicine.

The fourth and fifth clinical studies examined organizational predictors to CPG implementation success. Although not specific to pain management, both articles provide important context to understanding barriers to guideline development, dissemination, and evaluation. One study utilized qualitative open-ended interviews with 45 key physician, nursing, quality management, and administrative participants from 8 hospitals in the United States to identify factors that influence the success of efforts to increase beta-blocker use after acute myocardial infarction.[56] The interviews revealed 6 factors that can be used to classify efforts to adopt guideline recommendations. Four characteristics were found only in hospitals where practice improvement was seen and included shared goals for improvement, substantial administrative support, strong physician leadership that advocated change, and use of credible feedback data (Table 4). The other study examined adherence to 3 screening CPGs (depression, tobacco use, and alcohol use) and included 114 acute-care facilities and use of 3 large databases from the American Hospital Association and Veterans Administration.[61] Specific organizational factors were important: mission, capacity, professionalism, and patient-population characteristics were highly significant predictors that confirmed the importance of organizational context for guideline adherence (Table 5).

The 2 review articles included in our analysis provided further evidence of the complexity of examining outcomes of CPGs. A Cochrane review examined the effects of CPGs on nursing, midwifery, and allied health and found insufficient evidence to draw conclusions.[62] Eighteen studies that involved more than 467 health-care professionals were included in the review. Most used inadequate study methods. The authors suggest that knowledge of barriers and incentives to change drawn from observational studies, as well as available theories and models of the change process, should be utilized when implementing CPGs.[63] In the second systematic review analyzed, Grimshaw et al.[64] used MEDLINE, Healthstar, Cochrane Controlled Trial Register, EMBASE, SIGLE, and the specialized register of the Cochrane Effective Practice and Organisation of Care (EPOC) group to examine 235 studies that reported 309 comparisons of CPG-implementation strategies. Most interventions, including educational outreach, reminder systems, audit and feedback, use of local opinion leaders, and computerized information systems, were shown to be effective under some circumstances; however, none were effective under all circumstances. The observed effects both within and across implementation interventions were shown to be variable and at best relatively weak (mean 10%, range −1 to +34%).

Table 4. Factors Seen in Hospitals That Successfully Implemented Clinical-Practice Guidelines

Shared goals for improvement
Substantial administrative support
Strong physician leadership advocating change
Use of credible feedback data

Table 5. Hospital Organizational Characteristics That Influence CPG Adherence in a Large Multiinstitutional Sample That Involved Multiple Provider Practices

Mission	Council of Teaching Hospitals members *v* nonmembers; hospitals with approved residency training programs *v* those without
Capacity	Total beds set up and staffed, nonemergency outpatient visits, physician FTEs per 1,000 outpatient visits, organizational resources (created as a ratio of staff to patients by dividing FTEs by the average daily census), and inpatient occupancy
Professionalism	Proportion of all FTEs represented by registered nurses (RNs)
Patient population	Average number of conditions, race, age, and length of stay

Grading of Evidence

On the basis of the evidence of these 2 randomized trials, 1 qualitative study, 2 descriptive studies, and 2 systematic reviews, all members of this subsection of the workshop agreed that the level of evidence available regarding this statement was Category Ib (evidence obtained from at least 1 well-designed randomized, controlled trial) (Table 1).

Level of Support for Statement

Level of workshop support was Category C (poor evidence to support the statement, but recommendations may be made on other grounds) (Table 1). When the group at large voted on support of this statement, 55% (6 of 11) of the summit participants rejected the statement with reservations ("4"). None of the participants completely agreed ("1") or disagreed ("5") with the statement. Nine percent (1 of 11) accepted the statement with some reservation ("2"), and 36% (4 of 11) accepted with major reservation ("3") (Table 1). This result was compared with the vote of the ASRA membership of 37% for "1," 42% for "2," 11% for "3," 8% for "4," and 2% for "5" (Fig 6).

Discussion

Many believe that the creation and dissemination of evidence-based guidelines would lead to improvements in the quality and outcomes of care. Unfortunately, a paucity of evidence is available for acute-pain management guidelines and conclusions are difficult to draw from studies of guidelines in other areas of health care. To assume that simply making a CPG available through passive dissemination will result in its application by practitioners is naive.

Caution is advised because unintended negative outcomes can result from a misinterpretation of guideline recommendations or from inappropriate decisions made in the care of individuals with complex comorbidities whose care falls under overlapping and potentially conflicting guidelines.[65] For example, in 2001, JCAHO released pain assessment and management standards. Although the JCAHO standards are not CPGs, they directly reiterate recommendations of institutional responsibility provided in available evidence-based CPGs developed by groups such as the American Pain Society (APS) and the Agency for Healthcare Research and Quality (formerly the Agency for Healthcare Policy and Research). "Make Pain Visible" became a central theme in many settings, leading to the genesis of the now familiar "Pain As a Fifth Vital Sign" campaign. In response, many institutions implemented treatment policies guided by patient pain-intensity ratings indexed with a numerical scale. The Institute for Safe Medication Practices (ISMP) soon took notice that overaggressive pain management appeared to be linked to an alarming increase in oversedation and fatal respiratory-depression events.[66] In one setting alone, the incidence of opioid oversedation adverse-drug reactions per 100,000 inpatient hospital days increased from 11.0 before use of a numerical pain-treatment algorithm to 24.5 after implementation ($P < .001$).[67] In response to this confusion, and to support what was stated earlier (that the "fifth vital sign" slogan was never intended to mandate treatment of pain intensity as a fifth vital sign), that implementation model has been removed from all standards manuals.[68] The American Medical Association Council on Scientific

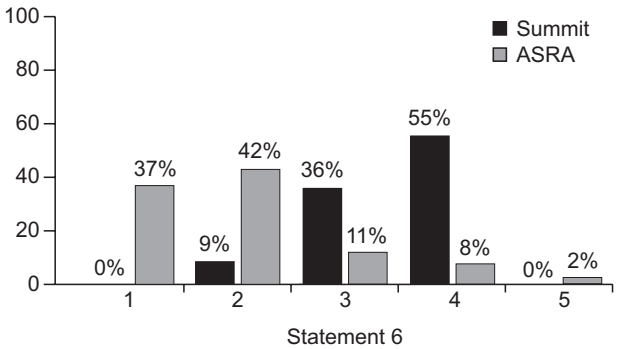

Fig 6. Voting comparison for Statement 6 (Creation and dissemination of acute-pain guidelines has improved postoperative-pain management). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Affairs (CSA) concluded that much of physicians' concerns regarding the JCAHO pain-management standards reflect a misunderstanding of the actual requirements of the standards.[69]

Confusion has persisted about the requirement of the JCAHO to specify PRN-range opioid orders for acute pain in institutional policies.[70] Statements on the JCAHO Web site implied that organizations could no longer use PRN-range orders for analgesic medications without specific implementation protocols. Again, institutions felt pressured to develop rigid, unsafe policies or protocols that would specify opioid doses on the basis of numeric pain-intensity ratings. The JCAHO has since clarified that their intent is not to dictate prescribing, but rather to assure patient safety. Range orders should be written in a way to assure that the physician who ordered the medication and the nurse who administers it has the same understanding of how the patient will be treated. The original intent of a CPG is to assist clinical decision making. An important lesson learned is that this original intent can be misconstrued during translation to practice and create a risk of diminished safety and quality of care.

Future Directions

Guideline implementation is a complex phenomenon and likely to be most successful when multifaceted interventions are used to introduce and implement the guideline, and strategies are based on an assessment of potential barriers. Rather than a specific type or number of intervention strategies, barriers and incentives to change in practice should be identified, categorized, and used to tailor interventions to facilitate desired changes.

When guidelines are promulgated, they should include an implementation and evaluation plan, developed by the implementer, that includes both qualitative and quantitative data. Evaluation studies should not be limited to expensive, sophisticated clinical trials. Measuring outcomes from any kind of practice guideline is in its infancy and much work is needed.

Statement 7

Poorly controlled postoperative pain leads to an increased likelihood of chronic pain.

Rationale and Definition of Statement

Over the past decade, a number of papers have concluded that more severe postoperative pain is a risk factor for the development of chronic pain after surgery.[71] This prospect raises the question of whether interventions that decrease acute postoperative pain can also decrease the incidence of chronic postoperative pain.

As discussed in a recent review,[71] we have defined acute postoperative pain as pain at the surgical site or sites during the 2 weeks immediately after the surgical procedure. Chronic postoperative pain is pain at the surgical site or sights longer than 3 months after the surgical procedure, and time zero is the most recent surgical procedure at the site of interest.[71] Pain must have been measured in the cohort in a consistent manner and the data must have been gathered systematically. Interventions to decrease acute postoperative pain, including the use of local anesthetics administered as regional or epidural anesthetics, or the use of adjuvant analgesics—such as anticonvulsants (eg, gabapentin), antidepressants (eg, venlafaxine), or NMDA inhibitors—to decrease acute pain or modify the incidence of chronic pain were examined. Because the surgical approach has a significant effect on acute pain, it was also examined. In most cases, the control population received opioids and NSAIDs for pain control; in some cases, the amount of opioid consumed was used as a surrogate measure for the acute-pain response to the operative procedure.

Literature Search

For the database search, the term "pain, postoperative" (8,121 articles) was combined with the text word "chronic pain" (4,728 articles) and they yielded 188 citations. These results were then limited to "English language" and "meta-analysis" and yielded 2 citations, neither of which were appropriate to the search by hand. The 188 articles were then limited to "English language" and "review" and yielded 44 citations whose abstracts were reviewed, and of which 15 had some pertinence to the literature search. The terms "hernia, inguinal" or "hernia" or text word "hernia" (10,442 articles), or the term "mastectomy" or word "mastectomy" (6,592 articles), or the term "thoracotomy" or word "thoracotomy" (5,958 articles) were combined (22,791 articles). The results were then combined with the 188 pain citations above and yielded 64 citations, which when limited to "English language" and "clinical trial," yielded 15 citations. Those abstracts were reviewed, and 14 were determined to have some pertinence. The full texts of the 29 citations identified by the database screen were read. Articles previously identified in a detailed literature search were also used.[71]

Evidence

A meta-analysis of the subject of acute-pain intensity and subsequent chronic pain does not exist.

A thorough review of the relation between acute-pain intensity and the development of chronic pain was done, and the authors conclude that increased acute-pain intensity is a predictor of chronic pain in conditions such as postherpetic neuralgia and low-back pain.[72] Whether generalizations can be made to all chronic pain after surgery is not clear. For this analysis, 3 specific surgical repairs were examined.

Chronic pain after inguinal hernia repair was of interest because of the high frequency of this surgery, with estimates of 500,000 to 700,000 operations a year in North America. Even if a small percentage of these patients were to develop chronic pain, a large number of people in the population would be affected. For inguinal hernia repair, 2 recent reviews are available, and both identify high levels of postoperative pain as a risk factor for chronic pain.[73,74] As noted in 1 review, the frequency of chronic pain varied from 0% to 53%, but only 6 studies had chronic pain as a specified endpoint, and in those studies, chronic pain was found in 15% to 53% of patients.[73] They concluded that approximately 10% of patients appear to have moderate to severe chronic pain after inguinal hernia repair. In addition to the intensity of acute postoperative pain, other predictive factors for chronic pain include: preoperative pain, female gender, surgery for a recurrent hernia, and open surgery (Table 6). A recent meta-analysis that compared laparoscopic hernia repair to open hernia repair found evidence that laparoscopic repair was associated with less acute and chronic pain.[75] Open-mesh hernia repair may also have less acute and chronic pain.[76]

After mastectomy, with or without axillary dissection, an estimated 30% or more of women experience some chronic surgery-related pain at 12 months.[71] A recent review concluded that the most frequent type of postmastectomy pain is neuropathic pain.[77] The intensity of acute pain is a predictor of chronic pain, as is the amount of opioid consumed in the period after surgery.[71,77] Additional risk factors for chronic pain include immediate adjuvant radiation therapy and surgery type.[71] Less invasive surgical approaches, such as sentinel-node biopsy, are associated with less acute and chronic pain. Sentinel-node biopsy is also associated with less intercostobrachial nerve dysfunction.[78] A number of recent studies have looked at the use of paravertebral local-anesthetic blocks or thoracic epidural local-anesthetic analgesia to reduce acute postoperative pain.[79-82] Long-term follow-up studies have not yet been published, but the prolonged decrease in pain after a preoperative paravertebral block may well be associated with less chronic pain.

Table 6. Predictive Factors for Chronic Pain after Surgery

Predictors of chronic pain after hernia surgery
Intensity of acute postoperative pain
Preoperative pain
Female gender
Surgery for recurrent hernia
Open surgery
Predictors of chronic pain after mastectomy
Intensity of acute postoperative pain
Amount of opioid consumed in the period after surgery
Immediate adjuvant radiation therapy
Axillary dissection (when compared with sentinel node biopsy)

After thoracotomy, the prevalence of chronic pain approaches 50% at 12 months.[71,83] More intense acute pain predicts chronic pain. Three studies document that use of continuous thoracic-epidural analgesia in the perioperative period is associated with a decreased prevalence of pain at 6 months.[84-86] Two of these studies compared preincisional epidural local anesthetics to postincisional dosing; both studies found less acute postoperative pain and less chronic pain with preincisional dosing. Continuous thoracic paravertebral block has been reported to achieve superior or equivalent postoperative analgesia when compared with epidural analgesia, but long-term follow-up studies on chronic-pain prevalence have not been published.[87,88] Thoracoscopic surgery appears to be associated with less acute and chronic pain.[71,89]

The use of adjuvant analgesics (eg, antiarrhythmics, anticonvulsants, antidepressants, and NMDA receptor blockers) to decrease acute pain and prevent chronic pain has not been well studied. Fassoulaki et al.[90] noted that either gabapentin or mexiletine decreased acute postoperative analgesic use after mastectomy, and burning pain at 3 months was decreased. Venlafaxine did not significantly alter either postoperative pain at rest or analgesic consumption after mastectomy, but pain with movement was decreased; at 6 months, the prevalence of pain was significantly less in the venlafaxine group.[91] Definitive studies on the use of perioperative NMDA blockers such as ketamine or dextromethorphan are lacking.

Grading of Evidence

On the basis of studies, members of this workshop agreed that the level of evidence available to support this statement was Category II (evidence obtained from well-designed cohort or case-controlled studies) (Table 1). Appropriately blinded randomized, controlled studies are lacking.

Level of Support for Statement

The workshop level of support was Category A (good evidence to support the statement) (Table 1). The literature supports the observation that more intense acute pain is a risk factor for chronic pain. Less-invasive surgical approaches, such as laparoscopic hernia repair, sentinel-node biopsy, and thoracoscopic chest surgery, appear to be associated with less acute and chronic pain. Use of local anesthetics via the epidural route is associated with a lower frequency of chronic pain after thoracotomy and with less acute pain. This approach is most effective if the epidural is dosed before skin incision and then analgesia is continued. Paravertebral block with local anesthetics has documented prolonged postoperative analgesia after breast surgery or thoracotomy, but long-term follow-up studies have not been published.

When the group at large voted on support of this statement, 82% (9 of 11) of the summit participants voted "2" (accept with some reservations); one vote was for "1" (accept completely), and one vote was for "3" (accept with major reservations); no votes were for "4" (reject with reservations) or "5" (reject completely) (Table 1). The ASRA membership voted 36% for "1," 37% for "2," 14% for "3," 10% for "4," and 3% for "5" (Fig 7).

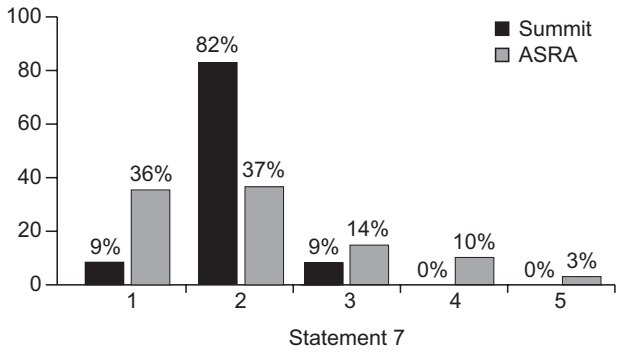

Fig 7. Voting comparison for Statement 7 (Poorly controlled postoperative pain leads to an increased likelihood of chronic pain). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

Chronic pain after surgery is a significant problem. Many patients report that pain interferes with daily activities after hernia surgery.[92,93] Functional impairment is also common after mastectomy and thoracotomy.[71] More intense acute postoperative pain, indicated by either higher pain scores or more opioid use or both, is a predictor of chronic pain. Interventions that decrease postoperative pain and opioid use, such as minimally invasive surgical procedures or effective local-anesthetic block, are associated with less chronic pain. Perioperative use of adjuvant analgesics may also decrease acute and chronic pain.

The statement "Poorly controlled postoperative pain leads to an increased likelihood of chronic pain" is broad, and it does not address why some patients have more acute pain than others. As worded, the statement also implies a causative link between poorly controlled postoperative pain and chronic pain, rather than an association between the two. Yet, the literature supports the observation that more intense acute pain is a risk factor, not a causative factor, for chronic pain. Indeed, those who experience more severe pain after surgery may well go on to develop chronic pain regardless of our best efforts to control their pain. For any individual patient, the appropriate perioperative pain management will depend on a number of factors other than the proposed surgery. Factors not addressed in this focused statement include management of preexisting pain at the operative site, patients with chronic pain at other sites, and psychosocial risk factors and their management. Also, individual differences in pain sensitivity do exist, which makes broad statements questionable as to the "best" management of a population of patients undergoing a specific surgical procedure.[94]

Future Directions

Future directions discussed by the summit participants reflect the problems of trying to prevent an adverse outcome that not everyone will experience. For the individuals who will not experience significant acute pain and are at low risk for chronic pain, adding medications and interventions offers little benefit and probably some risk. Can these low-risk individuals be identified prospectively? For individuals at high risk, which interventions will provide the most benefit? Prospective studies are needed to address numerous questions in this area.

Statement 8

Use of continuous postoperative epidural analgesia leads to improved patient outcomes when compared with parenteral opioids in patients with preexisting cardiovascular and pulmonary disease.

Rationale and Definition of Statement

During the 1980s, the use of epidural analgesia became a favored option for pain control after sur-

gery. Epidural analgesia had been used to provide analgesia for labor and childbirth, utilizing high-dose local anesthetics, and rendering the mothers either totally or partially paralyzed below the waist. It also had been used occasionally to provide postoperative analgesia, particularly after thoracic surgery, even though patients who received this treatment would not be able to ambulate and would need to remain in bed for the duration of the analgesic treatment. These practices changed after endogenous opioids and endogenous opioid receptors were identified in the 1970s, and experimentation began on the administration of opioids directly into the intrathecal or epidural space. The addition of an opioid to the epidural infusate was then found to produce excellent analgesia—subsequently named *selective spinal analgesia* because of the ability of spinally delivered opioids to bind selectively to spinal-cord receptors. The local anesthetic was then either not needed, or, as was subsequently found, could be used in combination with the opioid to provide additional analgesia, but at markedly lower doses than had been used previously. Epidural analgesia for postoperative pain immediately became popularized, and, at least anecdotally, patients were observed to do better—get out of bed sooner, cough without bracing, regain an appetite sooner, and generally appear less prostrate than they had under old treatment regimes. The question remained, however, whether this observed improvement could be substantiated with real data that confirmed an improvement in surgical outcome, and whether the improvement was attributable to superior pain relief alone, rather than to factors such as opioid sparing or sympathectomy. These questions have formed the basis of countless studies undertaken and published since the 1980s that attempted to clarify whether epidural analgesia improves surgical outcome.[95] The question is often focused on patients at risk, as is the present statement, because these patients are most likely to benefit from careful analgesic intervention.

The statement, as worded, produced some difficulty for the workshop members. First, "preexisting cardiovascular and pulmonary disease" is not defined as such in the literature and can only be assumed. The assumption was made either from the measure of general health status used in the trials (typically, ASA grading) or from the surgery itself (eg, cardiovascular disease is assumed to exist in patients undergoing vascular or cardiac surgery). Second, "improved patient outcomes" can be interpreted in many ways. Mortality and life-threatening morbidity have been the outcomes of interest for many investigators and reviewers, but the panel decided that for the present assessment and scoring, "outcomes" would encompass any outcome that might be beneficial to patients, including outcomes generally considered as minor morbidities, such as pain, bowel mobility, and ambulatory capacity.

Literature Search

The literature search was conducted with the subject headings "pain, postoperative" and "analgesia, epidural" and yielded 15,265 and 6,208 articles, respectively. Combining these terms with "OR" yielded 1,621 articles. Eight articles were identified when the search was limited to English language and meta-analysis, and 11 were identified when the search was limited to English language and multicenter study. Upon further review of the 19 meta-analyses and multicenter studies identified by the November 2005 search, only 4 meta-analyses and 1 multicenter study had been correctly identified. By use of hand searches and cross references from this and previous literature reviews, an additional 3 published meta-analyses and 4 published multicenter or large studies (>50 patients) were identified. A total of 6 meta-analyses and 5 large or multicenter studies were identified. All 6 of the meta-analyses[96-101] and 3 of the large studies that were RCTs[102-104] were considered for this review. Two multicenter studies were removed from consideration because of a lack of randomization. These studies also did not specify that their patients were "at risk," so it could not be assumed.[105,106]

Evidence

In 1987, Yeager et al.[107] published a small, randomized study that assessed surgical outcome in high-risk patients who received or did not receive epidural anesthesia and analgesia. Fifty-three patients were included in this study, and the results strongly favored the epidural treatment (reduction in mortality, $P = .04$, overall postoperative complication rate, $P = .002$, incidence of cardiovascular failure, $P = .007$ and incidence of major infectious complications, $P = .02$). Although the anesthesia community embraced these findings as validation for epidural analgesia and its ability to improve surgical outcome, several groups felt that anesthesia practice should not be driven by the results of such a small trial. Some set about conducting large, multicenter studies attempting to reproduce the findings of Yeager et al,[107] specifically in high-risk patients undergoing major procedures. Park et al[102] published their results of a 1,021-patient multicenter randomized trial in 2001. In contrast to Yeager et al,[107] these authors found no significant differences in mortality or rates of major (life-threatening) complica-

tions, except in the subset of patients undergoing abdominal aortic aneurysm (AAA) surgery. In AAA patients, the overall incidence of death and major complications was significantly lower in the epidural group (22% *v* 37%, $P < .01$), attributable to lower rates of respiratory failure ($P < .01$), new onset stroke ($P = .03$), new myocardial infarction ($P = .05$), and overall cardiovascular complications ($P = .03$). In 2002, Rigg et al[103] published results of an Australian multicenter randomized study that comprised 915 patients. They found no significant differences in mortality or major morbidity, except for a lower incidence of respiratory failure in the epidural group ($P < .02$). A later reanalysis of the Australian data, in which respiratory depression from the assessment of respiratory failure was removed, found no difference in respiratory failure overall but did find a small difference in the duration of postoperative ventilation ($P = .048$).[104] On the strength of these large RCTs, a claim that epidural anesthesia and analgesia reduces mortality can no longer be made (expect possibly in the case of AAA surgery), although the large RCTs do support an improvement in some potentially disastrous outcomes, most notably pulmonary outcomes.

Meta-analyses have tended to be more targeted than these large randomized trials. A 1998 meta-analysis by Ballantyne et al.[108] that specifically assessed pulmonary outcomes in relation to a number of analgesic interventions found that epidural analgesia with local anesthetic produced lower rates of hypoxia ($P = .047$), pulmonary infection (RR 0.36, $P < .001$), and pulmonary complications overall (RR 0.58, $P < .001$). A 2001 meta-analysis by Beattie et al.[98] that specifically assessed cardiac outcome, found a reduced incidence of myocardial infarction in patients who received epidural analgesia ($P = .049$). More recently, Liu et al.,[96] in a meta-analysis of trials that assessed epidural analgesia in patients undergoing coronary artery bypass grafting (CABG), found no differences in mortality or myocardial infarction but did find differences in rates of cardiac arrhythmias (odds ratio 0.52, $P = .03$), time to extubation (weighted mean difference −4.5 h, $P = .0005$), and pulmonary complications overall (odds ratio 0.41, $P < .00001$). Apart from these specific findings related to cardiac and pulmonary outcomes, the meta-analyses agree with the large RCTs in finding no differences in mortality or major morbidity attributable to perioperative epidural anesthesia and analgesia.[98,99,109] Superior analgesic efficacy, on the other hand, is overwhelmingly supported.[97,99-101,110]

Grading of Evidence

On the basis of the quantity of high-level evidence available to make the assessments regarding the present statement (7 meta-analyses and 3 large RCTs), the workshop unanimously agreed that the level of evidence was Category Ia (evidence obtained from meta-analysis, including at least 1 large randomized, controlled trial) (Table 1).

Level of Support for Statement

The consensus of the workshop, before considering of the evidence and before the vote, was that "improved patient outcome" should apply to all outcomes, regardless of whether the outcomes were likely to result in serious (life-threatening) morbidity or mortality. Accordingly, on the basis of the evidence that supported a beneficial effect of epidural anesthesia and analgesia in terms of some measures of cardiac and pulmonary function, and that overwhelmingly supported superior analgesic efficacy, the workshop level of support was unanimously agreed to be Category A (good evidence to support the statement) (Table 1). However, the workshop members also considered the strong evidence of no effect on major morbidity or mortality and agreed that had the statement specified improvement in major morbidity or mortality, their level of support would change to Category E (good evidence to reject the statement) (Table 1). Further, because the evidence on cardiac outcome supported an effect only on myocardial infarction and arrhythmias, with no improvement in cardiac failure or cardiac death, the level of support for overall cardiac morbidity, as distinct from general morbidity, would change to a Category D (fair evidence to reject the statement).

The workshop participants accepted that the existence of cardiovascular and pulmonary disease (as explicitly delineated in the statement) could only be presumed, either from a stated high risk by use of a broad measure of anesthesia or surgical risk (eg, ASA status),[102-104,107] or from the surgical procedure (cardiac,[96] intraabdominal,[101] or hip and knee replacement[99]). Several of the meta-analyses did not specify either high-risk surgery or high-risk patients,[97,98,108] and those that specifically selected high-risk patients (likely, but not necessarily, with cardiovascular or pulmonary disease), were predominantly the large RCTs. The fact that these patients were in a known high-risk category adds weight to the finding that major morbidity and mortality is not improved by epidural analgesia and anesthesia in the stated population.

In the group at large, 45% (5 of 11) of the summit participants voted "2" (accept with some reser-

vation), 27% (3 of 11) voted "1" (accept completely), and 27% (3 of 11) voted "3" (accept with major reservations). None of the summit participants voted to reject the statement ("4" or "5") (Table 1). The ASRA membership voted 43% for "1" and 45% for "2"; therefore, 88% voted to accept the statement either completely or with some reservations. Seven percent had major reservations about accepting the statement, and 5% rejected the statement (4% with reservation and 1% completely) (Fig 8).

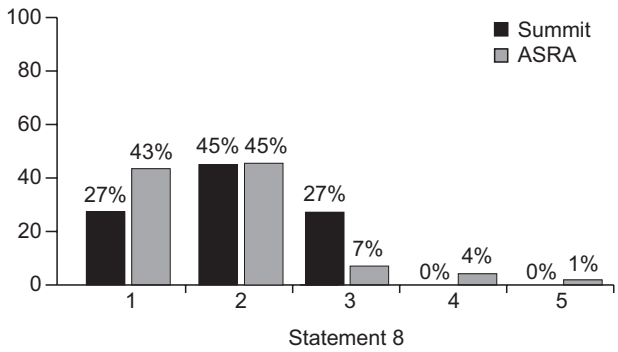

Fig 8. Voting comparison for Statement 8 (Use of continuous postoperative epidural analgesia leads to improved patient outcomes when compared with parenteral opioids in patients with preexisting cardiovascular and pulmonary disease). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

The statement concerns an area of pain practice that has been intensely studied in an effort to address the issue of whether perioperative epidural anesthesia and analgesia improve surgical outcome. For this reason, the evidence was rated at the highest level (Category Ia) (Table 1). Less clarity exists, however, on the assessment of level of support for this statement. The exact meaning of "improved patient outcome" was the first area of uncertainty. The panel decided to interpret this wording broadly, and, by use of a broad interpretation, voted unanimously for Category A (good evidence to support the statement). However, neither the summit participants nor the ASRA membership had the opportunity to arrive at a consensus on the meaning of "improved patient outcome," which probably explains the uncertainty in their voting. Only 27% of the summit participants and 43% of the ASRA membership accepted the statement without reservation, despite the strong level of evidence.

The second area of uncertainty is the specification that patients had "preexisting cardiovascular and pulmonary disease." As stated above, trials have not been conducted specifically in patients with cardiovascular and pulmonary disease, so the existence of these conditions can only be assumed from the stated high risk of the patients or the surgical procedures. As discussed under "Level of Support for Statement," the fact that the large RCTs provide strong evidence that perioperative epidural anesthesia and analgesia do not improve serious surgical morbidity or mortality in a population that is known to be at risk cannot be ignored. Because of the vagueness of the statement, the statement could as easily be judged strongly supported as strongly rejected on the basis solely of clarification of the statement (ie, all outcomes *v* specific outcomes; all patients *v* only patients with cardiovascular or pulmonary disease).

Future Directions

The summit participants discussed the need to refocus future trials on identifying rare but catastrophic outcomes of epidural catheterization, especially epidural hematoma, which seems increasingly prevalent, at least anecdotally. Pain relief aside, the most important benefits of neuraxial block are thought to be related to the sympathectomy (a local-anesthetic effect), which, in turn, improves blood flow and reduces coagulation, thrombosis, and thromboembolism. Yet modern thromboprophylaxis has surpassed neuraxial block in its capacity to protect against thromboembolism, and in addition, increases the risk of epidural bleeding and hematoma with subsequent spinal-cord or nerve-root compression. Thus, one major benefit is lost, and a significant risk factor is added. Also, as the present review shows, improvement in serious morbidity and mortality is no longer supported, even though epidural anesthesia and analgesia is seen to provide certain circumscribed benefits, including good analgesic efficacy. The present review helps provide a perspective on the state of the evidence that supports continuous postoperative epidural analgesia. Well-designed observational studies could be used to quantify rare but catastrophic outcomes, particularly those related to spinal-cord injury. Such studies could also be used to reassess rates of serious morbidity and mortality related to epidural analgesia, where differences may not be identified other than by very large (observational) studies. This work would contribute considerably to

the quest for well-founded risk:benefit analysis of an intervention for which the primary benefit is pain relief.

Statement 9

Opioid-sparing analgesic regimens result in an earlier return of bowel function after major abdominal surgery.

Rationale and Definition of Statement

Postoperative ileus, usually defined as a transient impairment in bowel motility for more than 3 days after surgery, is common after major abdominal surgery.[111] Ileus may be associated with nausea, vomiting, and stomach cramps and lead to significant abdominal discomfort, which contributes to delayed oral intake, immobilization, prolonged hospital stay, and increased medical expenditures.[112] The pathogenesis of postoperative ileus is multifactorial and includes activation of inhibitory reflexes, release of inflammatory mediators, and the presence of opioids (endogenous and exogenous).[112] Because opioids produce a dose-dependent inhibition of gastrointestinal motility,[113] opioid-sparing analgesic techniques can reasonably be assumed to result in an earlier return of bowel function.

The average duration of postoperative ileus after major abdominal surgery ranges from 0 to 24 hours in the small intestine, 24 to 48 hours in the stomach, and 48 to 72 hours in the colon.[111] The duration of ileus is related to the anatomic location of surgery and occurs after both intraperitoneal and extraperitoneal abdominal surgeries. Colonic surgery is associated with significant postoperative pain and the longest duration of postoperative ileus.[114] Because of the significant variability in the extent of surgical trauma, and the incidence of ileus after "major abdominal surgery," we chose to examine the evidence of opioid-sparing analgesic techniques on postoperative ileus after only colonic surgery.

Literature Search

The literature search was conducted by use of specific text words as follows. "Opioid" and "opioid sparing" were used and combined with the term "OR" (search 1: 93,949 articles). "Colectomy" and "colon" were used to search the database and combined with the term "OR" (n = 11,258). This search was combined with search 1 with the term "and" (n = 10). All final searches were limited by "human" and "clinical trials." After selection of the initial articles, the reference lists of all of the analyzed articles were checked for any additional studies.

Evidence

Few RCTs have examined the effect of opioid-sparing analgesic techniques on the incidence of postoperative ileus. A total of 7 articles were incorporated in our final analyses, which included 1 meta-analysis.[12,110,115-119] Opioid-sparing techniques were aimed at reducing the total doses of either parenteral or epidural opioid analgesics. Chen et al[115] examined the effect of adding ketorolac to intravenous morphine PCA on bowel function after colorectal surgery. This prospective, randomized, double-blind study was designed and adequately powered ($\alpha = 0.05$ and $\beta = 0.8$) to test the primary endpoint that the opioid-sparing effect of ketorolac in PCA morphine can shorten the duration of postoperative ileus by at least 1 day. A total of 79 consecutive patients undergoing elective colorectal resection were randomly allocated into 2 groups who received IV PCA morphine (1 mg/mL) or IV PCA morphine (1 mg/mL) plus ketorolac (1.2 mg/mL). The PCA was programmed to deliver a bolus of 2 mL with a 10-minute lockout interval without a continuous infusion for all patients. The PCA bolus dose was adjusted according to the patient's pain intensity at the time of each daily visit. Patients who received ketorolac demonstrated a 29% reduction in total morphine use for the duration of this study (approximately 6 days) and reported comparable pain scores. The time to first flatus as well as the time to first oral intake was not different between the 2 groups. The time [median (range)] to first bowel movement was significantly ($P < .05$) earlier in the ketorolac group, 1.5 (0.7 to 1.9) days *v* 1.7 (1.0 to 2.8) days in the morphine group. The authors concluded that the addition of ketorolac to PCA morphine has a "limited benefit in shortening the duration of bowel immobility" after colorectal surgery.

Albert and Talbott[116] evaluated the effects of PCA *v* IM morphine on the duration of postoperative ileus after colon surgery. This prospective, randomized, open-label study evaluated patients who received either PCA morphine (n = 32) or IM morphine (n = 30) for 72 hours after colon surgery. Patients assigned to PCA were administered 1 mg of morphine every 10 minutes, which was titrated up or down according to the patients' reported pain scores. Patients in the IM-morphine group were administered 5 to 12 mg of morphine every 3 to 4 hours on an as-needed basis. The specific postoperative day of ileus resolution, as assessed by passage of flatus or stool, as well as the total dose of morphine for the 3-day period, were recorded. This study revealed a significantly ($P < .05$) lower use of morphine [mean (range)] in the PCA group, 69.6 (3

to 133) mg *v* 92.2 (35 to 204) mg in the IM group. Patients in both groups reported similar pain scores. Despite this 25% reduction in 72-hour morphine use, the duration of ileus was not significantly different between the 2 groups. However, a power analysis was not performed for this clinical investigation, which makes the determination of whether these results are clinically meaningful difficult.

In a prospective RCT, Nitschke et al.[12] compared the effect of 3 analgesic regimens for 5 days in patients undergoing colon resection: PCA morphine (n = 31), IM morphine (n = 31), and IM ketorolac (n = 28). IM medications were administered on the basis of "pain scores and nurse's assessment," and PCA morphine doses were determined "individually for each patient" on the basis of weight and age. A basal-rate infusion was utilized for the first 2 postoperative days. Patients were assessed for resolution of postoperative ileus as determined by passage of first flatus. Unlike the previous study,[116] this study revealed significantly (P =.02) lower use of morphine (mean ± SE) in the IM-morphine group (105.9 ± 12.1 mg) compared with the PCA-morphine group (147.4 ± 11.0 mg). Despite this 28% reduction in 5-day morphine use, the duration of ileus was not significantly different between the 2 morphine groups. Similar to the study by Albert and Talbott,[116] the authors failed to perform a power analysis for this clinical investigation, which makes interpretation of the significance of these results difficult. Overall, patients assigned to the ketorolac group passed flatus 1 day earlier than in either of the 2 morphine groups (P = .006). Although ketorolac appears to be more advantageous, 43% declined participation in this study and requested PCA, 18% of patients assigned to ketorolac required additional analgesia, and 32% in the ketorolac group broke protocol and required alternative analgesia.

Several other interventions for postoperative analgesia have been examined after colon surgery. Results from a prospective RCT suggest that mechanical massage of the abdominal wall by use of an intermittent negative-pressure device for the first 7 postoperative days can reduce pain, analgesic use, and the duration of postoperative ileus.[117] The use of guided imagery with audiotapes for the first 6 postoperative days also reduced pain, opioid use, and duration of postoperative ileus.[118]

In addition to parenteral opioid-sparing techniques, other investigators have examined the effect of reducing epidural opioids on the duration of postoperative ileus after colon surgery. A systematic review of RCTs of epidural analgesia for abdominal surgery has concluded that the use of thoracic epidural block with local anesthetics decreases the duration of postoperative ileus compared with the systemic administration of opioid analgesics.[110] A meta-analysis of 5 studies with 261 patients revealed that epidural local anesthetics alone reduced postoperative ileus by 54 hours when compared with systemic opioid administration.[110] Although the addition of an opioid to an epidural local anesthetic may improve analgesic efficacy, the duration of postoperative ileus may be prolonged compared with epidural local anesthesia alone. A meta-analysis of RCTs revealed a 21-hour reduction in postoperative ileus when epidural local anesthetics were compared with epidural opioids and a 16-hour reduction when compared with epidural local anesthetic and opioid infusions.[110] The duration of ileus was similar with administration of epidural opioids compared with systemic opioids.[110]

Only 1 RCT has evaluated whether a reduction in epidural local anesthetic/opioid consumption can reduce the incidence of ileus. This prospective, double-blind, RCT evaluated the efficacy of administering dextromethorphan with thoracic epidural anesthesia and analgesia on bowel function after colonic surgery.[119] Epidural catheters were placed at the T6-12 interspaces, and a test dose of 1% lidocaine was used to confirm the location of the catheter. On arrival to the postanesthesia care unit, all patients were given a patient-controlled epidural analgesia (PCEA) pump and received an initial dose of 10 mL of PCEA solution that contained 0.2% ropivacaine and 0.1 mg/mL. These investigators concluded that the combination of preincisional dextromethorphan, intraoperative thoracic epidural anesthesia, and postoperative PCEA enhanced analgesia and facilitated earlier return of bowel function. Patients administered dextromethorphan required significantly ($P < .0001$) smaller amounts of PCEA (47.1 ± 4.4 mL) to achieve a similar level of analgesia during the first 72 hours compared with 87.9 ± 12.1 mL in the group not given dextromethorphan. This 46% reduction in epidural local anesthetic/opioid use resulted in a significantly ($P < .0001$) shorter time to first passage of flatus (40.8 ± 7.8 hours) compared with the general anesthesia group (66.5 ± 7.8 hours). No other studies to date have examined the effect of administering nonopioid analgesics in combination with epidural analgesics on the duration of ileus after colon surgery.

Grading of Evidence

On the basis of the evidence in these 7 articles,[12,110,115-119] all members of this workshop agreed the level of evidence regarding this statement was Category Ib (evidence obtained from at least 1 well-designed large, randomized, controlled trial) (Table 1).

Level of Support for Statement

On the basis of the available evidence, the overall level of support for this statement was Category C (poor evidence to support the statement, but recommendations may be made on other grounds) (Table 1). However, differences in opinion existed on the level of support for the statement within the subsection of the workshop, with 3 members voting Category C and 2 members voting Category E (good evidence to reject the statement).

In the group at large, 10% (1 of 11) of the summit participants voted "2" (accept with some reservations), 36% (4 of 11) voted "3" (accept with major reservations), 36% (4 of 11) voted "4" (reject with reservations), 18% (2 of 11) voted "5" (reject completely), and none voted "1" (accept completely) (Table 1). In comparison, the ASRA membership voted 50% for "1," 40% for "2," 7% for "3," 3% for "4," and 0% for "5" (Fig 9).

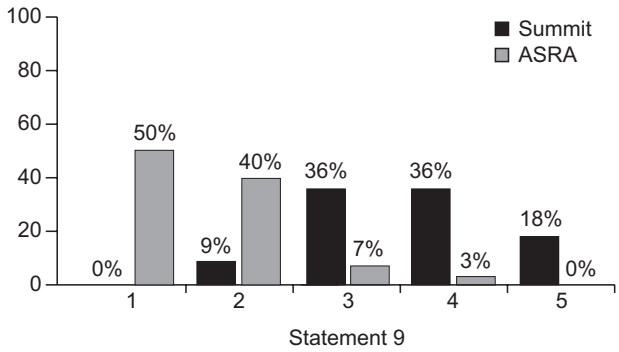

Fig 9. Voting comparison for Statement 9 (Opioid-sparing analgesic regimens result in an earlier return of bowel function after major abdominal surgery). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

On the basis of the limited data available, opioid-sparing analgesic regimens appear not to result in an earlier return of bowel function after colonic surgery. This outcome may result from the fact that postoperative ileus is influenced by multiple factors in addition to opioids, including the extent of surgical trauma, severity of postoperative pain, excessive hydration, immobilization, use of nasogastric tubes, and lack of enteral feeding.[111] Therefore, analgesic strategies designed to reduce only perioperative opioid use may not be effective in the reduction of the duration of postoperative ileus. Data from animal experiments reveal that the gastrointestinal tract is very sensitive to opioids, even at very low doses. The ratio between analgesic and constipating doses of morphine is approximately 4 to 1 (4 times more morphine is needed to obtain analgesic effect than to obtain slow gastrointestinal motility).[120] This gastrointestinal sensitivity to opioids is probably caused by relatively poor penetration of morphine into the brain, which may partly account for the severity of constipation in patients who receive opioids.[120] Further, repeated administration of opioids for pain relief may result in tolerance to these analgesics, but tolerance does not appear to extend to gastrointestinal motility and transit.[120] Endogenous opioids released after surgical injury may also play a role in the pathogenesis of postoperative ileus.[121] These opioids may not be affected by traditional "opioid-sparing" analgesic techniques after colonic surgery. For these reasons, simply reducing exogenous opioid use by 20% to 30% after traditional analgesic techniques may not be effective in promoting an earlier return of bowel function after major abdominal surgery.[12,115,116]

The methodology utilized in the RCTs that examined the role of parenteral opioid-sparing analgesic regimens on bowel function were limited and of poor quality and methodology. Postoperative ileus was considered a secondary endpoint in many studies, and they may have been insufficiently powered to make a definitive conclusion. Studies that evaluated the short-term (<72 hours) reduction in opioid use may not adequately assess the true incidence of postoperative ileus. Further, the definition of ileus and methods of assessment were either variable or not well defined. A correlation between some of the widely used clinical endpoints for resolution of ileus, including return of bowel sounds and passage of flatus and stool, as well as assessment of electrical activity of the colon, are still controversial.[111]

Surprisingly, only 1 published RCT to date has examined the opioid-sparing effect of the administration of an NSAID on bowel function after colon surgery.[115] NSAIDs may possess the ideal analgesic properties for abdominal surgeries because they not only reduce postoperative opioid use but also may increase gastrointestinal motility, probably by decreasing the synthesis of inhibitory prostaglandins.[122] Although this well-designed prospective, double-blind RCT demonstrated a 29% reduction in morphine use, no differences were evident in the time to first flatus or first intake of soft diet.[115] A statistical ($P < .05$), although not clinically significant, reduction occurred in the time to first bowel movement in the ketorolac group (1.5 days) compared with the morphine group (1.7 days). Perhaps

an even greater reduction in postoperative opioid use is necessary to result in a more significant earlier return of bowel function.

Evaluation of whether a reduction in epidural opioid use contributes to an earlier return of bowel function after abdominal surgery is more difficult because the beneficial effect of epidural analgesia on the duration of postoperative ileus is probably related to the local anesthetic. Epidural block with local anesthetics may improve bowel function after surgery by several mechanisms, including block of afferent and efferent inhibitory reflexes, efferent sympathetic block with concomitant increase in splanchnic blood flow, and anti-inflammatory effects after absorption of local anesthetics.[111] Therefore, the fact that virtually every RCT that examined epidural local anesthetics alone *v* parenteral opioids after colon surgery supports the findings of faster recovery from postoperative ileus with the former method of postoperative-pain management is not surprising.[110] The fact that the duration of ileus is similar with the administration of epidural opioids compared with systemic opioids[110] confirms that the pathogenesis of the reduction of postoperative ileus by epidural analgesia is probably mediated by local anesthetic block.[111] No RCTs have evaluated the effect of reduced epidural opioid use on bowel function after colon surgery. Only 1 RCT has examined the efficacy of combining a nonopioid analgesic with an epidural local anesthetic/opioid solution for colon surgery.[119] This study revealed an earlier return in bowel function with the addition of dextromethorphan to an epidural local anesthetic/opioid infusion in patients undergoing colonic surgery.[119] However, whether this improvement in bowel function was attributable to a reduction in epidural opioid use or to an interaction between dextromethorphan and the epidural local anesthetic is difficult to determine. Experimental evidence indicated that *N*-methyl-D-aspartate (NMDA) receptor antagonists may interact synergistically with local anesthetics.[123,124] Surprisingly, no RCTs have examined the effects of perioperative NSAID administration on epidural analgesia for colon surgery.

In contrast to the summit participants, ASRA members voted strongly in support of the statement, which reflects a strong perception that opioid-sparing regimens can result in an earlier return of bowel function after major abdominal surgery. This perception is likely the result of their interpretation of "opioid-sparing regimen" to mean epidural analgesia, where significant reduction in the duration of ileus has been demonstrated with local-anesthetic–containing infusions. In "less-invasive" abdominal surgery, such as abdominal hysterectomy, no correlation exists between the dose of morphine and the duration of ileus.[125] This finding may reflect the lower severity of pain and opioid use after abdominal hysterectomy when compared with colon surgery.

Future Directions

Because, as a single-modality treatment, opioid-sparing analgesic techniques by themselves are unlikely to significantly shorten the duration of postoperative ileus after colonic surgery, members of the workshop suggested that future studies are needed to evaluate a more comprehensive multimodal rehabilitation program for major abdominal surgery. As suggested by previous investigators[112,126-128] this program may include the use of minimally invasive surgery, thoracic epidural analgesia, avoidance of nasogastric tubes, early ambulation, and nutrition, in addition to opioid-sparing analgesic techniques. Further research is needed to examine the role of opioid-sparing analgesic techniques, including NSAIDs, in combination with either epidural or systemic analgesics on postoperative bowel function after major abdominal surgery.

Statement 10

Postoperative pain can be effectively controlled in patients with opioid tolerance.

Rationale and Definition of Statement

Perioperative management of acute pain in opioid-dependent patients often presents major clinical challenges. The majority of these individuals may be moderately to profoundly unresponsive to the therapeutic effects of opioid analgesics,[129-132] whereas a subset of patients may actually experience increased discomfort or hyperalgesia after opioid administration.[133,134]

Although many caregivers appreciate the implications of diminished opioid sensitivity and believe they can adequately manage these patients, others may not recognize or compensate for high-grade opioid tolerance.[129,131,135] Treatment options in this challenging situation include opioid-dose escalation, the use of neuraxial or neural block, and treatment with nonopioid analgesic adjuvants.[131,135-138] Nevertheless, the available evidence that effective management guidelines exist for providing optimal postsurgical analgesia in opioid-tolerant patients is limited. Thus, to allow for a meaningful analysis of the statement, we focused on textbook chapters, review articles, and pertinent case reports that examined this particular patient subset.

Literature Search

The literature search was conducted by use of the specific text words "postoperative pain and postsurgical pain" and yielded a total of 37,431 articles. Modifiers such as "opioid tolerance", or "opioid dependent" resulted in 159 articles. The search was initially focused by use of the descriptors "English language," "humans," "meta-analysis," and "randomized controlled trials"; however, no papers could be located. Expansion of the search to include review articles, case reports, and clinical papers yielded a total of 26 articles, each of which was examined for relevance to the statement. The reference lists of these articles were also examined.

Evidence

A total of 7 review articles and 11 clinical reports were ultimately included in this analysis. Several recommendations and patient-care guidelines were consistently mentioned in each review, including the importance of recognizing the opioid-tolerant patient, maintaining baseline opioid therapy, upward compensation in perioperative opioid dosing, the use of peripheral and central neural block, and administration of nonopioid analgesics (Table 7).[129-132,139,140] The reasons that underlie recent increases in the number of opioid-dependent patients were discussed in 4 of the reviews and included increased acceptance and prescription of opioid analgesics, concerns of analgesic undermedication, the favorable side-effect profiles of newer semisynthetic and sustained-release opioids, and morbidity associated with NSAIDs and COX-2 inhibitors (Table 8).[129,131,132,139] All of the reviews underscored the importance of patient identification. To help ensure optimal pain control, surgeons, anesthesiologists, and pain specialists need to identify opioid-dependent patients before surgical admission and develop a clear management strategy that employs liberal doses of opioid and nonopioid analgesics.[129,131,132,139,140] Clinicians should also recognize that a subset of patients may be polydrug dependent and often require alcohol, marijuana, or sizable doses of anxiolytics and other psychoactive drugs to help control pain or to provide emotional/psychological support.

Table 7. Guidelines for Effective Treatment of the Opioid-Tolerant Patient

Recognize the opioid-tolerant patient
Maintain baseline opioid therapy
Upward compensation in perioperative opioid dosing
Use of peripheral and central neural block
Administration of nonopioid analgesics

Table 8. Recent Trends That Indicate an Increased Prevalence of Opioid-Tolerant Patients Who Present for Surgery

Increased acceptance and prescription of opioid analgesics
Concerns of analgesic undermedication
Favorable side-effect profiles of newer semisynthetic and sustained-release opioids
Morbidity associated with NSAIDs and COX-2 inhibitors

Three clinical reviews stressed the importance of maintaining baseline analgesia. Patients should be instructed to take their usual dose of oral opioid on the morning of surgery. Because most sustained-release opioids provide 12 hours or more of analgesic effect, baseline requirements will generally be maintained during preoperative and intraoperative periods. Thereafter, baseline requirements may be provided orally or parenterally.[131,132,135]

With regard to the use of IV PCA, several recent reviews and clinical reports agreed that opioid-tolerant patients can effectively use such therapy as long as an adequate loading dose is provided, the incremental dose is increased in proportion to the degree of tolerance, and a basal infusion is provided.[129,131,132,136,141] Allowing substance abusers or recovering addicts to use IV PCA to control postoperative pain was initially considered controversial, as caregivers worried that self-administration might rekindle addictive behavior. More recent case reports indicate that along with oral methadone, IV PCA may be offered, provided pain intensity and opioid consumption are carefully assessed, and such therapy is supplemented with neural block and nonopioid analgesics.[132,135,136,140,141]

Several reviews and case reports advocated administration of nonopioid analgesics to reduce opioid-dose requirements and provide multimodal analgesia, although relatively few evaluations were performed in opioid-dependent patients.[131,132] Five reviews and case reports discussed the benefits of continuous neural block and neuraxial analgesia. Increased bolus doses and infusion concentrations were recommended to overcome spinal opioid-receptor down-regulation and improve analgesic efficacy, which underscores the observation that larger-than-average doses of neuraxial opioid are also required to attain adequate pain control in opioid-tolerant patients.[129,131,132,135,140] de Leon-Casasola and Lema[138,142] also recommend coadministration of local anesthetics and switching to an opioid such as sufentanil with high intrinsic binding and spinal potency.

Grading of Evidence

On the basis of the evidence in these reviews and clinical reports, members of this workshop agreed

that the level of evidence available regarding this statement was Category III (evidence obtained from a case series, case reports, or flawed clinical trials) (Table 1).

Level of Support for Statement

On the basis of available evidence, workshop members rated the level of support for this statement as Category C (poor evidence to support the statement, but recommendations may be made on other grounds) (Table 1). Reasonable, well-thought-out treatment guidelines appear to be available to optimize pain relief in opioid-dependent patients, although none has been critically tested.

In the at-large group, none of the summit participants voted "1" (accept completely), although 63% (7 of 11) voted "2" or "3," to accept the statement with some (4 of 11) or major (3 of 11) reservations, respectively. Forty-two percent (4 of 11) voted to reject either with reservations ("4") or completely ("5") (Table 1). This outcome contrasted to the vote of the ASRA membership, of whom 96% felt that evidence was sufficient to accept the statement, 36% accepting it completely ("1"). Only 4% of the ASRA respondents rejected the statement (Fig 10).

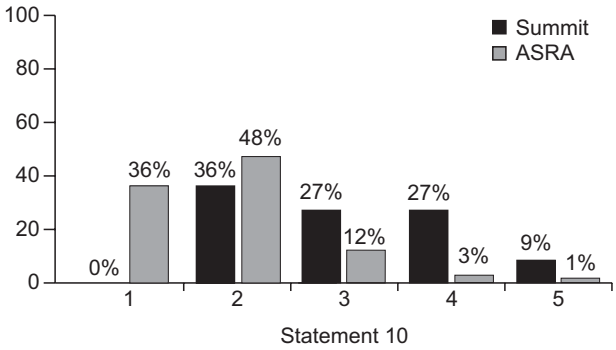

Fig 10. Voting comparison for Statement 10 (Postoperative pain can be effectively controlled in patients with opioid tolerance). Summit: 11 members of the Acute Pain Summit 2005 panel; ASRA: American Society of Regional Anesthesia and Pain Medicine members participating in Web-based survey. 1 = accept completely; 2 = accept with some reservations; 3 = accept with major reservations; 4 = reject with reservations; 5 = reject completely.

Discussion

On the basis of the available evidence, most opioid-tolerant patients can experience effective postsurgical analgesia, provided that critical treatment principles are followed. Differences in support for the statement "Postoperative pain can be effectively controlled in opioid-dependent patients" between the ASRA members and those attending the pain summit were striking, and, at first, difficult to understand. As was mentioned, many of those attending the summit felt that guidelines for patient management were anecdotal and observational and not from carefully controlled trials. Moreover, they recalled difficulties controlling pain in many highly tolerant patients. Problems included the fact that chronic pain and drug-seeking behaviors greatly influenced management of acute pain, the magnitude of opioid tolerance was difficult to assess, and many patients developed hyperalgesia after high-dose opioid administration. For these reasons, those summit participants disagreed with the ASRA respondents' perception that the statement could be accepted without reservations. Members of the summit group were, however, able to accept the statement with either minor or major reservations. Reservations included the fact that guidelines presented in several of the review articles can be followed closely, with care taken to avoid either opioid underdosing or potential for withdrawal, or overdosing and potential for hyperalgesia, yet pain control can remain poor. The fact that many ASRA members voted strongly in support of the statement may reflect a lack of experience with difficult, highly dependent patients. On the other hand, it could underscore the fact that this select group of caregivers routinely employs effective neural block in the majority of patients, thereby achieving effective analgesia while minimizing the need to administer anything other than baseline opioids.

The major issue raised by those attending the pain summit was the absolute lack of controlled data or any meta-analysis that demonstrated that adherence to published guidelines improves perioperative management and outcomes in opioid-dependent patients. With regard to epidural analgesia, no controlled trials have been performed to determine whether increased opioid dose, increased local-anesthetic concentration, or both are necessary to improve overall efficacy in opioid-dependent patients.[138,142]

Future Directions

Future directions suggested by summit participants reflect some of the limitations of relying on case reports that describe improvements in analgesic management, rather than on data collected from RCTs. Clinical trials that evaluate dose requirements after various surgical procedures in opioid-tolerant patients have yet to be performed. Studies are also needed to evaluate whether multimodal analgesic approaches, such as the perioperative use of methadone and ketamine to minimize opioid-dose escalation and development of opioid-

induced hyperalgesia will improve postsurgical outcomes.[137,143-145] Future trials should assess not only outcomes in the short-term (pain intensity, opioid consumption, treatment of side effects) but also events occurring over longer time frames (opioid dose de-escalation, opioid detoxification, return to work, etc.).

Conclusions

Many of the pain-treatment modalities we use daily have clear, scientific support for their usefulness in clinical practice. Through this critical appraisal, we can see the limitations of the existing evidence and confirm the areas in which benefit has been demonstrated. The use of PCA, continuous epidural analgesia, and continuous peripheral-nerve blocks clearly improve pain control and patient satisfaction in the postoperative period. However, improvement in other outcomes, particularly reductions in major morbidity or mortality, is less certain. A limited body of evidence that has emerged suggests technical weaknesses associated with use of PCA-infusion devices that limit their usefulness, increase expense, and lead to frequent safety concerns. Despite much rhetoric about combining multiple analgesic techniques to provide multimodal analgesia, only limited evidence suggests that this approach will improve pain control or perioperative outcomes. More studies are needed on new modalities to determine their place in therapy. Many practicing clinicians remain unfamiliar with these new modalities, and the published trials offer little guidance on how to use them in clinical practice.

Despite marked public interest and a number of national efforts to develop guidelines for acute-pain management, whether the appearance and dissemination of these guidelines have improved our ability to provide adequate postoperative pain control remains unclear. Experimental evidence points toward the need for better pain control, because current evidence indicates that poorly controlled acute pain may well increase the likelihood of chronic pain thereafter. Finally, the prevalence of opioid-tolerant patients presenting for major surgery is on the rise, and controlling pain in this population can be difficult. Limited evidence suggests that pain can be controlled in most of these patients, but widespread opinion is that adequate pain control may be difficult or impossible to achieve in some opioid-tolerant patients.

Examination of the disparities between the opinions of a large number of practicing clinicians and those of the summit participants after a detailed examination of the scientific evidence is interesting. Many of the disparities likely arose from each individual's interpretation of the statements. Despite our attempts to write discrete statements and avoid vague terminology, dual interpretations inevitably arose. The authors in each section have been careful to point out where these vagaries led to difficulties with their evidence-based analyses.

One theme about the types of evidence most likely to help guide rational use of pain therapy evolved from a number of our discussions. Although randomized, controlled trials are thought to be the "gold standard" to determine analgesic efficacy, even the largest trials are unlikely to examine more than several hundred patients. Randomized trials are unlikely to detect rare, but potentially catastrophic, outcomes. Thus, large-scale observational (cohort) studies would be especially valuable to determine the actual incidence of infrequent side effects and adverse reactions in the typical clinical setting, and future investigators should be encouraged to pursue this line of investigation.

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Appendix A: The Pain Summit survey

Acute Post-Surgical Pain Field Survey

Please tell us about the role of acute postsurgical pain in your practice.

What percentage of patients in your practice expect to have mild to moderate acute pain after surgery?
☐ 0-25% ☐ 25-50% ☐ 50-75% ☐ 75-100%

What percentage of your patients would say postsurgical pain is their greatest fear when preparing for surgery?
☐ 0-25% ☐ 25-50% ☐ 50-75% ☐ 75-100%

What percentage of your patients with acute postsurgical pain would report having a quicker recovery if their pain needs were adequately treated?
☐ 0-25% ☐ 25-50% ☐ 50-75% ☐ 75-100%

How many acute postsurgical pain patients have you seen in your practice in the past 6 months?
☐ 0-10 ☐ 11-20 ☐ 21-30 ☐ 31-50 ☐ 50+

Grade your level of support for the following statements using the scale below

1 = Accept completely
2 = Accept with some reservations
3 = Accept with major reservations
4 = Reject with reservations
5 = Reject completely

STATEMENT 1: Use of intravenous PCA leads to improved patient outcomes when compared with nurse-administered parenteral opioids.
1 2 3 4 5

STATEMENT 2: Use of continuous regional analgesic techniques leads to improved patient outcomes.
1 2 3 4 5

STATEMENT 3: The use of multimodal analgesia improves postoperative pain control and reduces analgesia-related adverse effects.
1 2 3 4 5

STATEMENT 4: Technology-related problems limit the safety and effectiveness of IV and epidural PCA.
1 2 3 4 5

STATEMENT 5: New and emerging therapies offer advantages over existing analgesic options for treating postoperative pain (grade each therapy).

Iontopheretic transdermal fentanyl
1 2 3 4 5 ☐ Unfamiliar

Extended-release epidural morphine
1 2 3 4 5 ☐ Unfamiliar

STATEMENT 6: The creation and dissemination of acute-pain guidelines has improved postoperative-pain management.
1 2 3 4 5

STATEMENT 7: Poorly controlled postoperative pain leads to an increased likelihood of chronic pain.
1 2 3 4 5

STATEMENT 8: Use of continuous postoperative epidural analgesia leads to improved patient outcomes when compared with parenteral opioids in patients with preexisting cardiovascular and pulmonary disease.
1 2 3 4 5

STATEMENT 9: Opioid-sparing analgesic regimens result in an earlier return of bowel function after major abdominal surgery.
1 2 3 4 5

STATEMENT 10: Postoperative pain can be effectively controlled in patients with opioid tolerance.
1 2 3 4 5

CME Posttest

STATEMENT 1: Use of intravenous PCA leads to improved patient outcomes when compared with nurse-administered parenteral opioids.

1. Use of patient-controlled analgesia after major surgery leads to which of the following changes in patient outcome when compared with nurse-administered parenteral opioids?
   A. Increased patient satisfaction
   B. Reduced postoperative pain
   C. Reduced duration of hospitalization
   D. Earlier return of bowel function
   E. Reduced incidence of nausea and vomiting

STATEMENT 2: Use of continuous regional-analgesic techniques leads to improved patient outcomes.

2. The use of continuous peripheral nerve blocks (perineural analgesia) after major surgery leads to which of the following changes in patient outcome when compared with systemic administration of opioid analgesics?
   A. Reduced incidence of motor block
   B. Earlier postoperative ambulation
   C. Reduced duration of hospitalization
   D. Reduced duration of stay in the Postanesthesia Care Unit
   E. Reduced incidence of opioid-related side effects

STATEMENT 3: The use of multimodal analgesia improves postoperative pain control and reduces analgesia-related adverse effects.

3. The addition of a nonsteroidal anti-inflammatory drug (NSAID) to standard IV PCA for the treatment of postoperative pain results in which of the following?
   A. Reduction in postoperative ileus
   B. Reduction in postoperative opioid requirements
   C. Reduction in postoperative pruritus
   D. Reduction in postoperative blood loss
   E. Reduction in duration of hospitalization

STATEMENT 4: Technology-related problems limit the safety and effectiveness of IV and epidural PCA.

4. Errors that have been reported with the use of infusion devices that are currently used to provide patient-controlled analgesia (PCA) include all of the following EXCEPT:
   A. Errors in programming leading to drug overdose
   B. Errors in programming leading to insufficient analgesia
   C. Errors in route of drug infusion (switch between intended epidural and intravenous route)
   D. Errors in electrical function of the infusion device leading to shock hazard to the patient
   E. Errors in drug administration (hydromorphone used in place of morphine) leading to drug overdose

STATEMENT 5: New and emerging therapies offer advantages over existing analgesic options for treating postoperative pain (grade each therapy).

Iontopheretic transdermal fentanyl
Extended-release epidural morphine

5a. Iontopheretic transdermal fentanyl provides all of the following potential benefits EXCEPT:
   A. Reduced programming errors
   B. Equivalent safety and efficacy to IV PCA morphine
   C. Reduced duration of hospitalization
   D. Needle-free system
   E. Deactivation after 24 hours or 80 doses a day

5b. Extended-release epidural morphine provides all of the following potential benefits EXCEPT:
   A. Extended duration of analgesia
   B. No risk of respiratory depression
   C. Single-dose administration
   D. No need for continuous epidural infusion
   E. Reduced need for supplemental analgesics postoperatively

STATEMENT 6: The creation and dissemination of acute-pain guidelines has improved postoperative-pain management.

6. Many institutions implemented treatment policies guided by patient pain-intensity ratings indexed with a numerical scale. The implementation of such treatment policies has been associated with which of the following?
   A. Improved pain control after surgery
   B. Improved patient satisfaction
   C. Increased events of over-sedation and fatal respiratory depression
   D. Reduced duration of hospitalization after surgery
   E. Reduced use of epidural analgesia

STATEMENT 7: Poorly controlled postoperative pain leads to an increased likelihood of chronic pain.

7. Chronic pain after major surgery is more common in patients who have all of the following characteristics during the intraoperative and postoperative periods EXCEPT:
   A. Higher pain intensity
   B. Larger incisions
   C. Greater opioid use
   D. Higher pain scores
   E. Greater blood loss

STATEMENT 8: Use of continuous postoperative-epidural analgesia leads to improved patient outcomes when compared with parenteral opioids in patients with preexisting cardiovascular and pulmonary disease.

8. Use of epidural analgesia in patients undergoing coronary artery bypass grafting (CABG) is associated with which of the following outcomes?
   A. Reduction in mortality
   B. Reduction in the incidence of myocardial infarction
   C. Reduction in the incidence of cardiac arrhythmias
   D. Reduction in blood loss
   E. Reduction in the incidence of stroke

STATEMENT 9: Opioid-sparing analgesic regimens result in an earlier return of bowel function after major abdominal surgery.

9. Earlier return of bowel function after major abdominal surgery is seen in patients who receive which of the following analgesic regimens when compared with parenteral opioid analgesia alone?
   A. A nonsteroidal anti-inflammatory drug (NSAID) in combination with IV PCA opioid
   B. Acetaminophen in combination with IV PCA opioid
   C. Continuous epidural infusion of opioid analgesic alone
   D. Continuous epidural of a combination of opioid analgesic and local anesthetic
   E. A COX-2 selective inhibitor in combination with IV PCA opioid

STATEMENT 10: Postoperative pain can be effectively controlled in patients with opioid tolerance.

10. All of the following actions have been proposed as means to improve postoperative pain control in patients with opioid tolerance EXCEPT:
    A. Maintain baseline opioid therapy throughout the perioperative period
    B. Use larger than average doses of opioid analgesics
    C. Use peripheral and central neural block whenever appropriate
    D. Administer nonopioid analgesics whenever appropriate
    E. Wean opioid analgesics promptly after surgery

Evaluation Form

Acute Postsurgical Pain Management: A Critical Appraisal of Current Practice

A CME Supplement to *Regional Anesthesia and Pain Medicine* The University of Wisconsin School of Medicine and Public Health respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form.

Please answer the following questions by circling the appropriate rating:

5 = Outstanding 4 = Good 3 = Satisfactory 2 = Fair 1 = Poor

Extent to Which Program Activities Met the Identified Objectives After completing this activity, participants should be able to:

Explain the differences in patient outcomes when comparing IV PCA versus nurse-administered parenteral opioids in patients after major surgery
5 4 3 2 1

Describe the changes in patient outcomes when administering perineural analgesia versus systemic administration of opioid analgesics in patients after major surgery
5 4 3 2 1

Explain the impact of multimodal analgesia on analgesia-related adverse effects when compared with standard IV PCA for the treatment of acute postoperative pain
5 4 3 2 1

Discuss the technology-related problems associated with IV and epidural PCA
5 4 3 2 1

Review the advantages potentially offered by newer technologies and emerging therapies
5 4 3 2 1

Discuss the impact of acute-pain guidelines on postoperative pain management
5 4 3 2 1

Describe the consequences of inadequate pain management in the postoperative setting
5 4 3 2 1

Identify the potential benefits to using epidural analgesia versus parenteral opioids in patients with preexisting cardiovascular or pulmonary disease
5 4 3 2 1

Review the effects of opioid-sparing analgesic regimens on return of bowel function after major abdominal surgery
5 4 3 2 1

Describe techniques to effectively manage postoperative pain in the opioid-tolerant patient
5 4 3 2 1

Overall Effectiveness of the Activity

Was timely and will influence how I practice
5 4 3 2 1

Will help me improve patient care
5 4 3 2 1

Stimulated my intellectual curiosity
5 4 3 2 1

Avoided commercial bias
5 4 3 2 1

Will the information presented cause you to make any changes in your practice?
____Yes ____No

If Yes, please describe any change(s) you plan to make in your practice as a result of this activity.
_____
_____

How committed are you to making these changes?
5 (Very committed) 4 3 2 1 (Not at all committed)

Additional comments about this activity:

_____

_____

Do you feel future activities on this subject matter are necessary and/or important to your practice?
____Yes ____No

Please list any other topics that would be of interest to you for future educational activities:

_____

Request for Credit

No prerequisites or fees are required for participating in and receiving CME credit for this activity. During the CME eligibility period of July 2006 to July 2007 participants must (1) study the educational activity, (2) complete the posttest by recording the best answer to each question in the answer key on the bottom of this evaluation form, (3) complete the evaluation form, and (4) mail or fax the evaluation form and answer key to University of Wisconsin School of Medicine and Public Health.

A statement of credit will be issued only upon receipt of a completed activity evaluation form and a completed posttest with a score of 70% or better. Your statement of credit will be mailed to you within 4 to 6 weeks.

I certify my actual time spent to complete this educational activity to be:

☐ I participated in the entire activity and claim 4.0 credits.

☐ I participated in only part of the educational activity and claim _____ credits.

Posttest Answer Key

1	2	3	4	5a	5b	6	7	8	9	10

Degree: ☐ MD ☐ DO ☐ PharmD ☐ RN ☐ RPh ☐ PA ☐ Other _____

Mail or fax your completed evaluation form to:
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and Public Health
750 Highland Avenue, Madison, WI 53705
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