

Postoperative pain treatment

SIAARTI Recommendations 2010

Short version *

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ABSTRACT

The aim of these recommendations is the revision of data published in 2002 in the "SIAARTI Recommendations for acute postoperative pain treatment". In this version, the SIAARTI Study Group for acute and chronic pain decided to grade evidence based on the "modified Delphi" method with 5 levels of recommendation strength.

Analgesia is a fundamental right of the patient. The appropriate management of postoperative pain (POP) is known to significantly reduce perioperative morbidity, including the incidence of postoperative complications, hospital stay and costs, especially in high-risk patients (ASA III-V), those undergoing major surgery and those hospitalized in a critical unit (Level A).

Therefore, the treatment of POP represents a high-priority institutional objective, as well as an integral part of the treatment plan for «perioperative disease», which includes analgesia, early mobilization, early enteral nutrition and active physiotherapy (Level A).

In order to improve an ACUTE PAIN SERVICE organization, we recommend:

— a plan for pain management that includes adequate preoperative evaluation, pain measurement, organization of existing resources, identification and training of involved personnel in order to assure multimodal analgesia, early mobilization, early enteral nutrition and active physiotherapy (Level A);

— the implementation of an Acute Pain Service, a multidisciplinary structure which includes an anesthetist (team coordinator), surgeons, nurses, physiotherapists and eventually other specialists;

— referring to high-quality indicators in establishing an APS and considering the following key points in its organization (Level C):

- service adoption;
- identifying a referring anesthetist who is on call 24 hours a day;
- patient care during the night and weekend;
- sharing, drafting and updating written therapeutic protocols;
- continuous medical education;
- systematic pain assessment;
- data collection regarding the efficacy and safety of the implemented protocols;
- at least one audit per year.

— a preoperative evaluation, including all the necessary information for the management of postoperative analgesia (Level C);

— to adequately inform the patient about the risks and benefits of drugs and procedures used to obtain the maximum efficacy from the administered treatments (Level D). We describe pharmacological and loco-regional techniques with special attention to day surgery and difficult populations. Risk management pathways must be the reference for early identification and treatment of adverse events and chronic pain development.

(*Minerva Anestesiologica* 2010;76:657-67)

Key words: Clinical protocols - Pain, postoperative - Risk management.

These recommendations are intended to be useful for physicians during the decision-making process. We offer fundamental advice, supported by analysis of the currently available literature, by expert opinion, and by clinical practice. Therefore, any recommendation should be periodically revised with the evolution of knowledge, technologies, and clinical practice. These recommendations are the revision of data published in 2002 in the "SIAARTI Recommendations for Acute Postoperative Pain Treatment".¹

Methodology

These recommendations include statements, together with the appropriate references, scored according to the quality of achieved clinical performance. In this way, the evidence-based data published in the literature (review, meta-analysis, guidelines) were reviewed using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.² For the first time, in this version, the SIAARTI Study Group graded evidence using the "modified Delphi" method.

Levels of evidence:

I – Large randomized trials with clear results, low risk of false positive (alpha) or false negative (beta) errors

II – Small randomized trials with uncertain results, moderate-high risk of false positive (alpha) and/or false negative (beta) errors

III – Non randomized, prospective controlled trials

IV – Non randomized, retrospective controlled trials or expert opinion

V – Case-control studies, non-controlled trials or expert opinion

Classification of strength of each recommendation:

— Level A recommendations: supported by at least two level I studies

— Level B recommendations: supported by one level I study

— Level C recommendations: supported by level II studies only

— Level D recommendations: supported by at least one level III study

— Level E recommendations: supported by level IV or V studies

We followed "Delphi Methodology, A Consensus Strategy (>75% of Study Group Adherents)," during a special session of the annual SIAARTI and Pain SIAARTI Cultural Area Congress 2006-2007-2008, with the aim of recognizing KEYSTONE STATEMENTS such as:³⁻¹¹

- Abrogation of postoperative pain therapy graduation in three levels, as used in previous guidelines;
- Adoption of the statement that the organizing model of postoperative management should be adapted to the local working environment;
- Adoption of multimodal contest-sensible analgesia, with personalized therapeutic plans and limits to standard drug prescription and to continuous infusion by elastomeric pumps;
- Multimodal analgesia must be administered to in- and outpatients who have undergone fast-track surgeries;
- A control plan that utilizes in-hospital routes and outlines the adverse events related to pain therapy should be put in place for risk-management;
- Special attention must be devoted to the prevention of chronic pain.

Postoperative pain

Analgesia is a fundamental right of the patient. The appropriate management of postoperative pain (POP) is known to significantly reduce perioperative morbidity, including the incidence of postoperative complications, hospital stay and costs, especially in high risk patients (ASA III-V), those undergoing major surgery and those hospitalized in a critical unit (Level A).¹²

Therefore, the treatment of POP must be one of the priority institutional objectives as well as an integral part of the treatment plan for «perioperative disease», which includes analgesia, early mobilization, early enteral nutrition and active physiotherapy (Level A).³

Anesthetists do not always consider the postoperative period as pertinent to their own duties and responsibilities: the actual organization of their job is the main limiting factor with regard to a professional approach to postoperative pain.

Acute pain service

In several countries, the implementation of an Acute Pain Service (APS) at the major clinical cen-

ters was recommended in order to reduce postoperative pain among patients (Level A).¹³ The Acute Pain Service is a multidisciplinary structure involving anesthetists, surgeons, nurses, physiotherapists and, eventually, other specialists.

In this organizational context, the anesthetist should play a primary role as the coordinator of the Team responsible for the treatment of acute pain, due to his specific knowledge of physiopathology and acute pain management (Level D).³⁻⁵ The implementation of an APS can improve pain control in surgical departments and seems to be able to reduce the frequency of adverse events such as postoperative nausea and vomiting (Level C).¹³

An optimal organizing model is not available for APS, but this must be adapted to local needs and opportunities. As far as cost-benefit analysis is concerned, there are some positive data for APS when used in combination with fast-track protocols. APS integration strategies and rehabilitation multimodal techniques in specific programs (fast-track surgery, clinical pathways) must be investigated further on a larger scale.

We recommend:

- a plan for pain management that involves adequate preoperative evaluation, pain measurement, organization of existing resources, and the identification and training of involved personnel to ensure multimodal analgesia, early mobilization, early enteral nutrition and active physiotherapeutic (Level A);³

- the implementation of an Acute Pain Service, a multidisciplinary structure that should comprise an anesthetist (team coordinator), surgeons, nurses, physiotherapists and, eventually, other specialists;⁵

- referring to high quality indicators in establishing an APS and considering the following key points in its organization (Level C):¹³

- service institutionalization;
- identifying a referring anesthetist who is on call 24 hours a day;
- patient care during the night and weekend;
- sharing, drafting and updating written therapeutic protocols;
- continuous medical education;
- systematic pain assessment;
- data collection regarding the efficacy and safety of the implemented protocols;
- at least one audit per year;

- a preoperative evaluation, including all the necessary information for the management of postoperative analgesia (Level C);¹⁴

- to adequately inform the patient about the risks and benefits of drugs and procedures used to obtain the maximum efficacy from the administered treatments (Level D). This information should be collected during the preoperative anesthesiologic assessment and reported in writing in the informed consent to anesthesia to adequately advise the patient regarding available procedures. It has been demonstrated that both oral and written information are able to reduce postoperative anxiety and pain. Notably, this information must be articulated in a simple way and understandable for the patient.¹⁵

Assessment and measurement of pain

We recommend:

- A periodic assessment and transcription of pain score in the case history, both at rest and during activity (Level A).¹⁶ We recommend using: NRS (Numeric Rating Scale), VAS (Visual Analogical Scale) and VRS (Verbal Rating Scale).

- In pediatric age or non-collaborative patients, the facial scale and neuro-behavioral scale are preferred (Level B).

SYSTEMIC ANALGESIA

The drugs used most frequently for the treatment of postoperative pain are acetaminophen, NSAIDs, weak and strong opiates and local anesthetics, alone or in combination with adjuvants. These drugs can be used as monotherapy or in combination, in order to take advantage of the different mechanisms and sites of action that characterize each drug.

Administration of these drugs should adhere to the principles of pharmacokinetics, pharmacodynamics and pharmacogenetics (Level A).¹⁷ Continuous infusion techniques without flow control meters must be avoided. A registration system should be implemented to record pain, analgesia efficacy, and adverse events. Such a registration system would involve data gathered from case histories, either paper or computerized.

We found that:

- Acetaminophen exhibits efficacy as an anal-

gesic (NNT 3.5-3.8 per 500-1000 mg), without significant adverse events (Level A); acetaminophen can be used in a patient with hepatic failure, in whom liver function is being monitored; in the case of renal impairment, the drug's pharmacologic profile is not affected (Level B). The combination of acetaminophen plus morphine is able to reduce the daily dose of opiate required by 20-33% (Level A); the combination of acetaminophen and tramadol demonstrated greater efficacy than acetaminophen-codeine (Level B).¹⁸⁻²⁰

— NSAIDs are indicated for the treatment of moderate pain; they are able to reduce the dosage of opiates when used in combination and to control moderate to severe pain (Level A);²¹

— COXIBs are contraindicated for patients with ischemic heart disease and/or evident cerebrovascular disease, congestive heart failure and patients who have recently undergone aortocoronary bypass (Level B);^{22, 23}

— Opiates are drugs of choice for the treatment of moderate-severe POP (Level A);²⁴

— The use of opiates can cause adverse effects in a dose-dependent manner; vomiting can be reduced with the administration of droperidol, dexamethasone, ondansetron, or propofol and with the avoidance of protoxide (Level C).²⁵

— Because tramadol induces worse respiratory depression than morphine (Level B), its combination with morphine is not recommended due to an intra-additive effect (Level C); tramadol is effective when combined with NSAIDs (Level D).²⁶

— Morphine is the gold standard among analgesics, due to the fact that it is a pure agonist of opiate receptors, morphine does not have a ceiling effect in terms of analgesic efficacy, but its use is limited by the typical adverse events induced by opiates. The initial dose should take the patient's age into consideration, while the subsequent doses should be designed to maximize efficacy. During the postoperative period, in the case of initial therapy by intravenous route, it is recommended to switch to PCA without basal infusion, which will ensure substantial efficacy, patient satisfaction, a low degree of sedation and a low incidence of complications in selected patients. Intravenous continuous infusion should be administered to hospitalized patients only, with appropriate monitoring (Level A).^{27, 28}

— Multimodal analgesia involves the use of different classes of analgesics (NSAIDs, COX2 inhibitors or acetaminophen in combination with morphine IV PCA) and induces an "opioid sparing effect", with a 40% reduction in the amount of morphine required if combined with NSAIDs and a <20% reduction if combined with acetaminophen during the first 24 hours postoperatively.

— Continuous infusion of Remifentanyl, at low doses (<0,1 mcg/kg/min), is a valid analgesic option for postoperative pain management in the ICU setting, in the first 24-48 hours, especially in patients with liver and renal disease (Level B).²⁹⁻³¹

— Oxycodone is used in POP as step-down analgesia following PCA (Level D) or in pre-anesthesia when short half-life opiates are used for minor surgery.³²

— Perioperative ketamine can reduce postoperative pain intensity (Level A), the incidence of PONV (Level B) and the dose of morphine required (by 30-50%) (Level A).³³

— Perioperative use of gabapentin/pregabalin is effective in preventing persistent postsurgical pain. These drugs reduce perioperative noxious afferent input associated with surgery and reduce spinal cord neuroplasticity associated with central sensitization (Level C).³⁴

— Systemic analgesia should be included in hospital protocols for multimodal context-sensitive analgesia.

PATIENT-CONTROLLED ANALGESIA

The intravenous patient-controlled analgesia (PCA) with opiates assures better analgesia (mean 5 mm on a VAS pain scale of 0-100 mm) and greater patient satisfaction compared with conventional treatments with parenteral opiates (Level A).³⁵

Nevertheless, intravenous PCA with opiates does not allow a reduction in opiate use or result in lower incidence of opiate-related adverse events compared with conventional treatments with parenteral opiates (Level A) (Table I).³⁶

EPIDURAL ANALGESIA

In case of postoperative pain, epidural analgesia exhibited significantly better efficacy than systemic analgesia with opiates (Level A).³⁷

Epidural analgesia with local anesthetics, alone or in combination with opiates, is able to reduce some respiratory complications such as atelectasis, to improve respiratory exchanges and to reduce pulmonary infections and paralytic ileus (Level A);³⁸ the combination of thoracic peridural analgesia plus early enteral nutrition is able to reduce postoperative protein catabolism and the incidence of peripheral bypass thrombosis (Level C).³⁹

The combination of low doses of local anesthetic and lipophilic opiates is the best therapeutic option in terms of postoperative pain control. This approach reduces the incidence of adverse events as compared to treatment with a local anesthetic, alone or in combination with morphine (Level A).⁶

Management of patients undergoing anticoagulant and/or antiplatelet therapy with epidural analgesia requires specific precautions, which are widely discussed in the SIAARTI Guidelines for Safety in Locoregional Anesthesia.⁴⁰

Epidural catheters should be managed in wards that have an established organization and operative protocols. Nurses should be required to have undergone previous training; regular daily visits should be planned, and a medical staff should be available for emergencies.

The SIAARTI study group for acute and chronic pain recommends epidural thoracic technique (for 48-72 hours) for thoracic and upper abdominal surgery, in the absence of formal contra-indications to catheter insertion (Table II).

ALR Techniques

Continuous peripheral nerve block

Continuous peripheral nerve block reduces the likelihood of adverse events in comparison to central nerve block, which can lead to severe complications such as hematoma or epidural abscess.⁴¹

Several randomized trials demonstrated the efficacy of this procedure, which offers clear benefits for the patient and minimizes adverse events.⁴²

Clinical trials showed that after major orthopedic surgery on the upper and lower limbs, continuous peripheral nerve blocks have the same efficacy as continuous epidural block; both approaches are significantly more effective than intravenous opiates (Level A).^{42, 43} Regional analgesia should

TABLE I.—*Common IV-PCA regimens for opioid-naïve patients.*

Opioid	Demand dose	Lock-out (min)	Continuous basal infusion*
Morphine	1-2 mg	6-10	0-2 mg/h
Fentanyl	20-50 mcg	5-10	0-60 mcg/h
Sufentanil	4-6 mcg	5-10	0-8 mcg/h
Tramadol	10-20 mg	6-10	0-20 mg/h

* Continuous basal infusions are not recommended for the initial setting

also be used in critical patients in order to reduce the use of sedative and opiate drugs (Level C).⁴⁴

Patient-controlled regional anesthesia

Patient-controlled regional anesthesia (PCRA) exhibited greater efficacy than basal infusion in postoperative pain control and assures better mobilization of the patient (Level C) (Table III).⁴⁵⁻⁵²

DAY SURGERY

As far as the administration route is concerned, we recommend (Level D) the following:

— intravenous route: for the first dose of acetaminophen/NSAIDs and the possible titration of morphine only

— oral route: to be used during the preoperative period and as soon as possible after surgery

— intramuscular route: contraindicated.

As regards the expected pain intensity, please refer to "Pain control in day surgery: SIAARTI guidelines":⁵³

— mild pain: local anesthetic infiltration + non-opiate drugs (acetaminophen, NSAIDs, COX2 inhibitors) (step I);

— moderate pain: step I + intermittent dose of opiate (route of administration: see above), possibly slow release (step II);

— moderate to severe pain: step II + local anesthetics by perineural route, with or without a continuous infusion catheter.⁵⁴

SPECIAL POPULATIONS

Elderly patients (Level C)

In elderly patients (>65 years), we recommend:^{55, 56}

— use of a simple semantic pain scale (absent, mild, moderate, severe) for pain assessment among cooperative patients;

TABLE II.—*Epidural analgesia: recommended drugs and doses.*

Surgery	Site of puncture	Starting dose	Top Up	Analgesia
Lower limbs surgery	L2-L3 L3-L4	1-2 ml per metamer	Lidocaine 2 % 90 min	Levobupivacaine 0.125% or Ropivacaine 0.2%
Lower abdominal surgery	The middle point of surgical incision T11-T10	Titration: 5 ml every 10 minutes	Levobupivacaine 0.5%	+
Thoracic and upper abdominal surgery	The middle point of surgical incision T7-T8	0.5-1 ml per metamer Titration: 5 ml every 10 minutes	or Ropivacaine 0.75% 120 min (1/2 starting dose)	Fentanyl 2 mcg/ml or Sufentanil 0.5-1 mcg/ml Infusion Rate: 4-8 ml/h

TABLE III.—*Common infusion modalities for continuous peripheral nerve block analgesia.*

Site of catheter's insertion	Common Local Anaesthetics and concentrations	Continuous infusion	Bolus dose
Interscalene brachial plexus	Bupivacaine 0.1% and 0.125%	5-9 ml/h	3-5 ml
Infraclavicular brachial plexus	Levobupivacaine 0.1% and 0.2%	5-9 ml/h	3-5 ml
Paravertebral	Ropivacaine 0.2%	5-10 ml/h	3-5 ml
Lumbar plexus		8-10 ml/h	5-7 ml
Femoral nerve		7-10 ml/h	5-7 ml
Sciatic nerve		7-10 ml/h	5-7 ml
Popliteal sciatic nerve		5-7 ml/h	3-5 ml

— use of neurobehavioral measures in non-cooperative patients;

— analysis of the changes in pharmacokinetics and any physiological compromise of pharmacodynamics, as well as the risks related to the use of NSAIDs/COXIBs;

— 1/3 to 2/3 reduction of the minimum effective dose of opiates; in this context, the PCA is also safe in older patients without cognitive deficits;

— peridural analgesia necessitates reduced doses of local anesthetics and opiates;

— guarantee of an analgesic plan focused on early rehabilitation and complete functional recovery.

Pediatric patients

(For advanced information, consult www.sarnepi.it, the Italian version of UK guidelines for postoperative pediatric treatment.)⁵⁷

Pain control can be achieved through the use of analgesics administered via different routes, in combination with sedation or general anesthesia, using non-pharmacologic methods.

As far as minor procedures are concerned (venipuncture, stitches, etc.), the administration of

inhaled protoxide (50%) and/or of a topical local anesthetic can be considered a safe and effective procedure (Level A). Concerning more severe procedures (lumbar puncture, bone marrow aspiration), the administration of inhaled protoxide (50%) and of a topical or local anesthetic infiltration is effective in most patients (Level A). For major procedures (fracture reduction), intravenous regional blocks using a local anesthetic are effective in most of the pediatric patients. Despite the potential for complications and the high incidence of adverse events, general anesthesia may be more appropriate in select groups of patients.

Acetaminophen and NSAIDs can be used for the treatment of moderate pain and can reduce the need for opiates after major surgery (Level A). Acetylsalicylic acid must be used carefully in febrile children due to the potential risk of Reye syndrome; furthermore, aspirin and NSAIDs can increase the risk of postoperative bleeding (Level A); serious adverse events are rare in children aged >6 months.

The PCA system is very safe and effective and can be used in cooperative children (usually >5 years of age). In day-surgery procedures, wound

infiltration with local anesthetic, caudal block or peripheral nerve block (blocking the dorsal nerve of the penis for phimosis, blocking the ilioinguinal/iliohypogastric nerve for hernia) will ensure a sufficient degree of analgesia (Level B).⁵⁸

Obese patients

Obese patients must stay in the PACU for prolonged periods in order to ensure that the ongoing analgesia is safe and effective. Prolonged stay is required due to the need for strict monitoring of sedation, respiratory rate, oxygen saturation, capnometry and PONV (Level B).⁵⁹ The use of PCA and PCEA is recommended (Level C), even if locoregional procedures (PCEA) are more difficult to implement and have a higher incidence of complications.⁶⁰

Patients with obstructive sleep apnea

In OSA patients, we recommend (Level C):^{61, 62}

- preoperative identification of at-risk patients (COPD, smokers, chronic snoring, obese) and possible planning of postoperative stay in a protected area;
- opiate-sparing analgesia techniques;
- monitoring the sedation level, as well as the respiratory rate;
- administration of supplementary oxygen by nasal CPAP;
- avoiding any sort of basal infusion of opiates;
- continuous epidural and intravenous PCA at fixed doses.

Chronic opioid abusers (COA) (Level D)

We recommend:⁵⁵

- identifying COA patients during the preoperative period;
- no reduction in the typical daily dose of opiates;
- “proactive” management of POP that involves a multimodal approach:
 - premedication with opiates, with dose titration;
 - perioperative continuous use, if possible, of locoregional anesthesia procedures;
 - full daily dose of NSAIDs and/or acetaminophen;

- full daily dose of opiates (>2-3-times the routine dosage used in POP), possibly titrated intraoperatively by target controlled infusion (TCI) and postoperatively by PCA;

- preventing the patient from missing periods of analgesia and avoiding oversedation phases, which both require a switch to the oral route in the following days;

- scheduling perioperative use of adjuvants such as alpha-2 agonists or low-dose ketamine, as well as possible opiate cycling (to methadone or buprenorphine) in the perioperative period.

Errors in the management of postoperative pain

In preparing these recommendations, particular attention has been placed on possible errors in the management of pain and on the factors that can cause its chronicization.

The most common errors in the management of pain can be classified as “evaluation and documentation errors”, “errors of treatment and control” or “educational errors” by the patient.⁶³

In each of these categories, errors can be labeled as: “ability-based”, “rules-based” or “knowledge-based” errors.⁶⁴

Ability-based errors, due to:

- *poor attention*: compliance problems of the patient, difficult communication with the patient (for example, due to language problems) or because the pain level after drug administration is not reported.

Rules-based errors:

- *application of incorrect rules*, for example, fixed schedule administration of analgesics or treatment of patients with history of drug abuse with narcotics;

- *poor application of good rules*, for example, intramuscular administration chosen over oral administration.

Knowledge-based errors:

- *for inadequate knowledge*: pain is to be expected in older people and its development is normal after a surgical procedure; patient satisfaction represents a good tool to evaluate the adequacy of pain control.

We must incorporate the philosophy of risk management into hospital plans designed to pre-

vent and treat the adverse effects of POP. At minimum, we should have hospital protocols for the prevention and treatment of opioid-mediated respiratory depression; for the prevention of technical mistakes due to PCA; for the prevention, recognition and treatment of epidural hematoma, compartment syndromes and subdural migration due to spinal and peri-nervous techniques; and for the recognition and treatment of local anesthetic plasma reabsorption (Level C).^{65, 66}

The risk factors for the development of chronic pain after a surgical procedure can be divided in categories. Here, the blue flags indicate perioperative risk factors, the yellow flags indicate psychological and environmental factors and the red flags indicate postoperative complications that may require treatment (Level C).⁶⁷

Blue flags

— Preoperative factors:

— Age, sex, pre-existing chronic pain, site and extension of the surgical procedure, previous surgical intervention, genetic predisposition.

— Postoperative factors:

Non-controlled pain, severe pain, excessive analgesic intake during the first 7 days.

Yellow flags

— Psychological factors:

Patient attitude, preoperative stress, anticipation of disease chronicization, benefits linked to the pain.

— Environmental factors:

Poverty, low educational level.

Red flags

— Postoperative factors:

- infection;
- bleeding;
- compartmental syndrome;
- injury to internal organs.

Conclusions

This publication is the fourth version of recommendations for postoperative pain treatment published by the SIAARTI Study Group on Acute Pain. The number of level A evidence studies, supported by meta-analyses and randomized con-

trolled trials, is increased in this study as compared to others. The guidelines are consistent with the practices of Italian anesthesiologists, in adherence with international reports calling for the inclusion of postoperative pain treatment in perioperative medicine. The next step must include a multidisciplinary panel that includes every type of interested specialist and patient association, with the aim of producing multidisciplinary national guidelines in adherence with the national “Hospitals Without Pain” project.

There are numerous limitations with regard to the diagnosis and treatment of postoperative pain:⁶⁸⁻⁷²

— there is a demand among the scientific community to adopt scientific methods to evaluate the intensity and quality of pain. Such scientific methods would be more sophisticated than the VAS and the Simple Semantic Scale (e.g., the new version (SFQ-2) of the brief version of the Questionnaire of Melzack), which are presumably useful for studies on the prevention of chronic surgery-related pain;⁶⁸

— there is disagreement regarding the superiority of loco-regional techniques in terms of outcome, postoperative pain quality, duration of stay and incidence of postoperative respiratory insufficiency;⁶⁹

— there is clear evidence for the potential of simple techniques such as continuous infiltration or a single-shot peri-incision with local anesthetic;⁷¹

— there is a notable emphasis on safe pathways, with the aim of reducing the incidence of opioid-mediated respiratory depression,⁶⁸ spinal hematomas and / or compartmental syndromes through the use of loco-regional techniques and antiaggregant/anticoagulant drugs.^{65, 66}

These factors engender speculation regarding the scientific validity of multimodal techniques, in consideration of the increased number of patients that need to be recruited for meaningful CRTs.⁷² Finally, these guidelines are in agreement with the new version of the Australian and New Zealand guidelines on acute pain.⁷³

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Acknowledgments—The authors wish to thank Dr. Piero Zucchi for his assistance with the manuscript.

Received on June 28, 2009; accepted for publication on June 11, 2010.

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