Published in final edited form as:
Anesth Analg. 2013 May ; 116(5): 1141–1161. doi:10.1213/ANE.0b013e318277a270.

Preventive Analgesia by Local Anesthetics: The Reduction of Postoperative Pain by Peripheral Nerve Blocks and Intravenous Drugs

Antje Barreveld, MD,
Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Jürgen Witte, MD,
Department of Anesthesiology, University of Virginia, Charlottesville, Virginia

Harkirat Chahal, MD,
Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Marcel E. Durieux, MD, PhD, and
Department of Anesthesiology, University of Virginia, Charlottesville, Virginia

Gary Strichartz, PhD
Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Abstract

The use of local anesthetics to reduce acute postoperative pain has a long history, but recent reports have not been systematically reviewed. In addition, the need to include only those clinical studies that meet minimum standards for randomization and blinding must be adhered to. In this review we have applied stringent clinical study design standards to identify publications on the use of perioperative local anesthetics. We first examined several types of peripheral nerve blocks, covering a variety of surgical procedures, and second, for effects of intentionally administered IV local anesthetic (lidocaine) for suppression of postoperative pain. Thirdly, we have examined publications in which vascular concentrations of local anesthetics were measured at different times after peripheral nerve block procedures, noting the incidence when those levels reached ones achieved during intentional IV administration. Importantly, the very large number of studies using neuraxial blockade techniques (epidural, spinal) has not been included in this review but will be dealt with separately in a later review.

The overall results showed a strongly positive effect of local anesthetics, by either route, for suppressing postoperative pain scores and analgesic (opiate) consumption. In only a few situations were the effects equivocal. Enhanced effectiveness with the addition of adjuvants was not

Corresponding Author: Gary Strichartz, PhD, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Pain Research Center BWH/ MRB611 75 Francis Street Boston, MA 02115-6110, Phone: 617 732-7802, FAX: 617 730-2801, gstrichartz@partners.org.
Current Affiliation: Department of Anesthesiology and Intensive Care, University of Muenster, Muenster, Germany
Drs. Antje M. Barreveld and Jürgen Witte contributed equally to this work.

The authors declare no conflicts of interest.

uniformly apparent. The differential benefits between drug delivery before, during, or immediately after a surgical procedure are not obvious, and a general conclusion is that the significant antihyperalgesic effects occur when the local anesthetic is present during the acute postoperative period, and its presence during surgery is not essential for this action.

Introduction

The perioperative use of analgesic drugs to reduce postoperative pain is properly termed "preventive analgesia."[1,2] (In contrast, the term "preemptive analgesia" is limited to describing effects from drugs that are administered before any surgical manipulations.) Reduced postoperative pain hastens functional recovery and hospital discharge, decreases acute morbidity and may well reduce the probability of developing chronic postoperative pain. However, it appears that the incidence of postoperative pain is under-reported and that the symptoms are under-treated.[3] *Anesthesia & Analgesia* is dedicated to a relatively exhaustive review of papers from the past 5–10 years that report criteria-documented clinical studies of preventive analgesia.[4] The present paper reviews the results of studies where local anesthetics were used for peripheral nerve blocks or intentionally given IV, during or after the surgical procedure. Results are organized by surgical procedure, inasmuch as we think that this information is best used as a resource for anesthesiologists and surgeons who are interested in reducing postoperative pain from specific procedures. The literature searches for this article extend through May 2012. We encourage the interested reader/practitioner to conduct a search of the more recent publications for a complete collection, keeping in mind the importance of inclusion criteria for discerning among clinical studies.[1]

Methods

Studies on the use of peripheral nerve blocks for acute postoperative pain control after lower and upper extremity procedures and tranversus abdominis plane (TAP) blocks were identified using the following search criteria on PubMed:

- *Search Limits*: 01/01/2005 to 06/01/2012, Clinical trial, Randomized controlled trial, Humans, English language.
- *Search Terms*: "local anesthetic AND femoral nerve block AND pain"; "local anesthetic AND lumbar plexus block AND pain"; "local anesthetic AND psoas compartment block AND pain"; "local anesthetic AND sciatic nerve block AND pain"; "local anesthetic AND intraarticular AND pain"; "local anesthetic AND periarticular AND pain"; "local anesthetic AND brachial plexus block AND pain"; "local anesthetic AND interscalene nerve block AND pain"; "local anesthetic AND transversus abdominis plane block AND pain"; "local anesthetic AND TAP block AND pain"; "local anesthetic AND nerve block AND dexamethasone AND pain"; "local anesthetic AND nerve block AND clonidine AND pain"; "local anesthetic AND nerve block AND dexmedetomidine AND pain"; "local anesthetic AND nerve block AND ketorolac AND pain"; "local anesthetic AND nerve block AND benzodiazepine AND pain"; "local anesthetic AND intraarticular AND dexamethasone AND pain"; "local anesthetic AND intraarticular AND clonidine AND pain"; "local anesthetic AND intraarticular AND dexmedetomidine AND pain"; "local anesthetic AND intraarticular AND dexamethasone AND pain"; "local anesthetic AND intraarticular AND ketorolac AND pain"; "local anesthetic AND intraarticular AND benzodiazepine AND pain."

The use of IV local anesthetics to reduce postoperative pain was searched on PubMed by the following criteria:

- *Search limits:* Randomized controlled trial, clinical trial, humans, English language (no date limits were set as there exists only a small number of published studies on this subject)
- *Search terms*: “intravenous AND local anesthetic”; “intravenous AND lidocaine”; “intravenous AND local anesthetic AND pain”; “intravenous AND local anesthetic AND postoperative pain”; “intravenous AND lidocaine AND postoperative pain”; “intravenous AND lidocaine AND pain”; “intravenous AND local anesthetic AND preventive analgesia”; “intravenous AND lidocaine AND preventive analgesia."

All studies identified using the above search criteria were evaluated for the following inclusion criteria:

1. Randomized controlled trials (except in a few instances as is noted)
2. Postoperative pain evaluation and/or rescue analgesic use
3. Methodologically sound design.[1]

References of articles thus selected were also searched for relevant studies. The studies excluded primarily investigated variations in block techniques or included opioid adjuvants in the local anesthetic mixture and were therefore not examined in this review. All nerve block studies identified were organized by surgical type to assist readers’ decision-making in choosing nerve block technique(s) and local anesthetic(s).

Results

Peripheral Nerve Blocks

The nerve block searches led to 471 journal articles. Duplicated studies were removed and all remaining studies and the references were screened for eligibility, revealing 89 studies that met inclusion criteria (Table 1, overview).

Total Knee Arthroplasty—Thirty-five studies in total knee arthroplasty (TKA) surgery examined the following local anesthetic injection or infusion techniques: (1) single-shot femoral nerve blocks (SSFNB); (2) continuous femoral nerve block catheters (CFNB); (3) sciatic nerve blocks combined with other blocks; (4) single-shot or continuous lumbar plexus blocks (SSLPB or CLPB); (5) intraarticular/periarticular (IA) injections or infusions. Of these thirty-five studies, 20 compared a specific intervention to IV patient-controlled analgesia (PCA) or “no block” control or to a placebo injection/infusion or sham block; all 19 demonstrated a positive analgesic effect of the local anesthetic(s), except one study that found no analgesic benefit of an IA infusion of 0.25% bupivacaine versus placebo.[5]

The remaining 15 studies compared different local anesthetics, local anesthetic concentrations, or techniques. For instance, the administration of a preoperative versus postoperative SSFNB did not impact pain or opioid use.[6] Bupivacaine versus ropivacaine showed similar efficacy in SSFNB with or without a single-shot sciatic nerve block.[7–9] As might be predicted, a local anesthetic injection decreases pain for the expected duration of the anesthetic and most studies examine acute postoperative pain up to 24–48 hours after surgery. With single injections, this effect did not appear to persist beyond postoperative care unit (PACU) discharge,[10,11] although opioid use was shown to be decreased up to 48 hours after the injection in elderly patients.[11] An additional study comparing a low-dose

bupivacaine plus hydromorphone epidural infusion combined with a SSFNB demonstrated decreased pain versus an epidural alone.[12]

A continuous femoral nerve catheter is often placed for knee arthroplasty and the resulting CFNB shows improved pain control versus SSFNB.[13] When administered with or without a single-shot sciatic nerve block, CFNB consistently demonstrated decreased pain and/or opioid use when compared to PCA control or placebo infusion,[14–17] and continuous sciatic nerve block proved to be superior to a single-shot nerve block.[18,19] Ropivacaine infusions for 24–48h, and up to 96h, were primarily studied, although there was no difference between ropivacaine or levobupivacaine.[20] When compared to an epidural infusion, the epidural provided superior pain control, as might be predicted given that a femoral block does not cover the entire surgical area.[21] However, if a sciatic nerve block was performed in addition to a CFNB and compared to an epidural, pain scores and/or opioid use were unchanged,[22] and as predicted a single-shot or continuous sciatic nerve block administered in addition to a CFNB was superior to a CFNB or CLPB alone.[22,23–25]

CFNBs have also been compared to IA infusions or injections and have been shown to be superior[26] or no difference when a bolus is delivered by femoral catheter every 4 hours;[27] however, the addition of an IA injection to CFNB improved analgesia when compared to a CFNB alone.[28] The majority of studies examining IA injections or infusions administered exclusively do, however, demonstrate improved analgesia versus placebo or PCA control or intrathecal morphine,[29–32] (one negative study is mentioned above[5]). There was no difference noted between IA or periarticular infusion.[33]

Finally, four studies using lumbar plexus blocks (also referred to as “psoas compartment blocks”) in TKA were identified. A CLPB with a sciatic block decreased pain when compared to a PCA[34] and even was shown to be as effective as an epidural.[35] One study using ropivacaine did not show a difference in analgesia between a CLPB versus SSLPB when both were combined with a sciatic block,[36] although another study using levobupivacaine that also used a placebo infusion did demonstrate improved pain control with a CLPB versus SSLPB[37] (Table 1, References 38 and 39, regarding TKA but not included in the text).

Anterior Cruciate Ligament Reconstruction and Arthroscopic Knee Surgery— Four studies on anterior cruciate ligament reconstruction were identified and 2 of the 3 did not show an analgesic benefit of bupivacaine given by SSFNB or IA infusion versus placebo,[40,41] whereas one study using ropivacaine and bupivacaine versus placebo did show a positive analgesic effect of SSFNB.[42] One study compared CFNB with a sciatic nerve block versus a SSFNB with a sciatic nerve block and IA infusion and found that the CFNB provided improved pain control.[43] In arthroscopic knee surgery, 6 studies meeting our search criteria were identified.[44–49] Four of the 6 compared SSLPB or IA injection to placebo or no block and showed a positive analgesic effect.[44–47] SSLPB with sciatic block was superior to SSFNB with sciatic block in arthroscopic knee surgery.[48]

Total Hip Arthroplasty—Eight studies meeting search criteria were identified (Table 1); 4 of these were compared to placebo or control and showed a positive analgesic effect of IA bolus or infusion or CLPB.[50–53] The choice of local anesthetic for CLPB or SSLPB did not affect preventive analgesia,[54,55] and extending a ropivacaine infusion beyond 24 hours did not provide additional benefit.[56] CLPB versus CFNB did not show a difference in pain control but CFNB decreased time to first ambulation.[57]

Foot and Ankle Surgery—Four studies meeting search criteria were identified, all using sciatic or popliteal blocks (Table 1). Only one study compared popliteal block to PCA

control and found a positive analgesic effect.[58] Two studies demonstrated that 0.5% or 0.75% levobupivacaine was more effective than 0.5% ropivacaine[59,60] and as long as the total dose of ropivacaine is constant, the concentration and infusion rate can be varied.[61]

Arthroscopic Shoulder Surgery—Ten studies meeting search criteria were identified and 6 of the 10 studies compared the nerve block to a control and the remaining 4 studies compared nerve block techniques (Table 1). Of the 6 controlled studies, 2 did not demonstrate an analgesic effect of local anesthetic administered by subacromial infusion versus placebo or PCA control.[62,63] Clinicians have tried adding subacromial catheters to interscalene block (ISB) to prolong the analgesic effect of ISB but this has not been shown to be superior to ISB alone.[64,65] ISB is well-accepted as effective pain management in arthroscopic shoulder surgery. A 2004 study comparing IA injection, ISB and suprascapular block versus control demonstrated most effective pain control at 24 hours with ISB,[66] whereas a 2011 study did not demonstrate any analgesic benefit after SS ISB beyond 6 hours.[65] Five of the 6 studies examined for this review have shown that ISB provides improved analgesia versus an IA/subacromial infusion or block,[64,65,67–69] whereas one study demonstrated similar pain control with continuous IA infusion for 48h when compared to single-shot ISB (SSISB), although this study could have compared continuous infusions of both interventions to ensure a more accurate comparison.[70]

Two studies in patients undergoing arthroscopic acromioplasty and/or rotator cuff repairs comparing SSISB to continuous ISB (CISB) and showed significant reduction in visual analog scale (VAS) scores and opioid consumption with CISB.[58,71] Using lower volumes of local anesthetic has been shown to provide effective analgesia with minimal postoperative motor dysfunction in patients undergoing arthroscopic shoulder surgery.[72] Therefore in arthroscopic shoulder surgery, an IA injection or infusion does not definitively improve pain control versus no intervention and is inferior to ISB. Moreover, concerns have been raised about local anesthetics impeding wound healing in the case of subacromial catheters.[69] There are also case reports of glenohumeral chondrolysis after IA pain pumps and IA local anesthetic injection[73–75] and subacromial catheters are not routinely recommended at this time.

Major/Open Shoulder Surgery—Eight studies meeting search criteria were identified and 4 studies comparing ISB versus placebo or no block demonstrated improved analgesia.[76–79] One study showed that CISB with a patient-controlled catheter (PCISB) is superior to SSISB but the benefits were noted only in the first 24 hours.[77] PCISB also was beneficial in early rehabilitation.[78]

The remaining 4 studies examined varying volumes and concentrations of local anesthetics in ISB for open shoulder surgery.[80–83] ISB is associated with a 100% incidence of hemidiaphragmatic paresis from block of the phrenic nerve.[84,85] It is contraindicated in patients with moderate to severe chronic obstructive pulmonary disease.[86] Low volume blocks, down to 5 ml from the conventional 20–30ml, decrease the incidence of hemidiaphragmatic paresis to 45%[80] and even 0%[87] with no difference in analgesic effect. Three studies compared 0.2%, 0.3%, 0.4% ropivacaine infusion.[81–83] The need for running a high concentration, low volume infusion is especially important in ambulatory patients who are discharged home with a fixed reservoir of local anesthetic with limited capacity; however, a higher concentration can lead to a denser sensory block but with unwanted motor block and side effects leading to overall lower patient satisfaction.[83] Patients receiving 0.2% received similar analgesia to 0.4% ropivacaine with less motor block and higher patient satisfaction .[81,83] There was no difference in pain scores between 0.2% and 0.3% ropivacaine; however, opioid requirements were less in the 0.3% group.[82]

Hand & Forearm Surgery—A 2004 study showed improved pain control with axillary block versus general anesthesia on the day of surgery but no difference in analgesic effect measured on postoperative days 1, 7, or 14.[88] Only one study in hand surgery patients met inclusion criteria for this review and examined low-dose anesthetic mixture with axillary block versus general anesthesia and also showed improved pain scores and decreased opioid use up to 24h postoperatively but not beyond.[89]

Transversus Abdominis Plane Block—TAP block is a relatively new technique first described by Rafi in 2001[90] and deserves briefly mentioning because it is gaining in popularity for use in pain control after laparoscopy or other open lower abdominal surgeries. A 2011 meta-analysis examined 4 studies using TAP block.[91] Twelve studies on TAP block were identified for this review and 10 of the 12 studies showed a benefit of TAP block for postoperative pain control (Table 1).[92–101] The surgeries studied included laparoscopic surgery, open appendectomy and abdominal surgery, cesarean delivery, and total abdominal hysterectomy. In 3 studies surgery was completed under spinal anesthesia while the other 9 used general anesthesia. One study compared TAP block to epidural analgesia and found similar pain scores between groups but decreased opioid use in the epidural group, suggesting that TAP block, though not superior to epidural analgesia, may be a reasonable alternative where epidural analgesia is contraindicated or not performed.[93] TAP block did not provide additional analgesic benefit in children undergoing laparoscopic appendectomy, all children received local anesthetic infiltration of port sites.[102] TAP block was also ineffective in one study where patients underwent cesarean delivery and all received intrathecal morphine, which by itself is effective pain control.[103] Intrathecal morphine, however, can cause side effects such as respiratory depression, pruritis, and nausea. TAP block therefore appears to be a valuable tool in treating postoperative lower abdominal surgical pain after general anesthesia but not after receiving intrathecal morphine. TAP block appears to be safe, can minimize side effects of traditional opioid therapy (although further studies are needed to substantiate this claim) and can be used when a neuraxial technique is contraindicated.

Local Anesthetic Nerve Block Adjuvants

Peripheral nerve blocks and local anesthetic adjuvants—Various adjuvants have been tried to improve the analgesic effects of nerve blocks. The use of epinephrine to prolong the block has been well established in clinical practice. We excluded opioid adjuvants because opioids already have an inherent strong analgesic effect and any benefit from peripheral administration could be attributed to systemic plasma effects, for instance. One study examining naloxone added to a mix of lidocaine and fentanyl or lidocaine alone in axillary nerve block for forearm surgery demonstrated prolonged sensory and motor block versus placebo or fentanyl alone.[104] The study is limited by the fact that epinephrine was not used.

Additional adjuvants have been studied in peripheral nerve blocks. A 2009 meta-analysis examined the effect of clonidine on peripheral nerve and plexus blocks and concluded that only a brief prolongation of analgesia was achieved, but with additional prolonged motor block and increased risk of side effects such as hypotension, fainting and sedation.[105] Dexmedetomidine is also an alpha-2 agonist but with alpha-2 selectivity 8 times that of clonidine. When added to local anesthetics such as levobupivacaine, it extends the sensory/motor block and analgesia duration but may lead to side effects such as hypotension and bradycardia which are expected after IV administration.[106] Its long-term effects have not been studied.

Dexamethasone has also been shown to prolong analgesia with upper extremity nerve blocks.[107–111] Its use has been recommended when epinephrine is contraindicated. Midazolam has been added to bupivacaine for brachial plexus block and showed improved postoperative analgesia, but data to support its use are limited and it caused additional sedation in subjects, likely secondary to systemic absorption.[112] Magnesium 100–150 mg when added to prilocaine in axillary plexus block prolonged sensory and motor block and was more effective than IV magnesium,[113] but one additional study examining magnesium added to bupivacaine for ISB did not demonstrate prolonged block or decreased opioid use versus placebo although decreased pain scores in the magnesium group were observed.[114] Tramadol when added to levobupivacaine for ISB also demonstrated improved analgesia when compared to receiving placebo or even intramuscular tramadol.[115] In summary, many adjuvants have been successfully added to local anesthetics to improve pain control but none of the adjuvants has been studied long term and there are insufficient data on their safety in perineural injection.

Intraarticular local anesthetic adjuvants—Various adjuvant medications to local anesthetics administered in IA infusions or IA single-shot injections for arthroscopic knee surgery have been studied. IA tramadol[116] and magnesium sulfate,[117] in addition to local anesthetics, appear to decrease pain scores and total analgesic requirements versus local anesthetics alone. IA dexmedetomidine in addition to local anesthetic showed decreased 24-hour opioid use as well as VAS scores, but this was significant only up to 6 hours postoperatively.[118] IA ketamine with local anesthetic demonstrates conflicting effects on pain scores and opioid use when compared to local anesthetics alone in arthroscopic knee surgeries.[119,120] IA morphine and ketorolac in addition to ropivacaine improved pain control versus ropivacaine alone[121] but not versus bupivacaine alone.[31] In hip surgery, IA clonidine injection in addition to local anesthetic did not however show a difference in pain scores or opioid consumption versus local anesthetic alone.[122] The use of adjuvant medications in IA local anesthetic solutions needs to be studied further in order to justify routine use.

Intravenous use of local anesthetics as preventive analgesics

Although many different local anesthetics have been used in clinical practice, only lidocaine has been considered safe for IV use because of its long history of systemic administration as an antiarrhythmic drug. Investigation of any neurological or cardiovascular toxicity after prolonged, low-dose infusion of other local anesthetics would be of great interest, as these compounds might offer some benefits.

Perioperative IV lidocaine for postoperative analgesia was examined in a 2010 review[123] and additional recently published studies meeting our search criteria were identified. For this review, sixteen randomized, double-blind placebo-controlled studies were identified that examined the IV use of local anesthetics in humans and its effect on postoperative pain (Table 2). In the majority of these studies patients received an initial bolus of lidocaine or equal amounts of saline at induction, followed by a continuous infusion of lidocaine or saline which was maintained during surgery and, in some studies, for additional time periods of 30 minutes up to 24 hours postoperatively. Surgical procedures that were studied included open and laparoscopic cholecystectomy,[124–126] radical prostatectomy,[127] major abdominal surgery such as prostatectomy, cystectomy, abdominal nephrectomy and colectomy, all combined with lymph node dissection,[128] open and laparoscopic colorectal surgery,[129–132] total hip arthroplasty,[133] ambulatory surgery,[134,135] abdominal hysterectomy,[136] inguinal herniorrhaphy,[137] laparoscopic appendectomy,[138] and breast surgery.[139] A total of 678 patients were enrolled and randomized to lidocaine or placebo administration. The bolus amount was 100 mg in two studies and 1.5 mg/kg in all other studies. Infusion rates ranged

from 1.5 – 3 mg/kg/h intraoperatively and, when given postoperatively, from 1.33 mg/kg/h to 3 mg/min.

Ten out of 13 clinical trials reported a preventive analgesic effect of lidocaine that lasted longer than 8.5 hours, which is 5.5 times the half-life of IV lidocaine (the definition of preventive effect as used by Katz et al.).[1] After laparoscopic cholecystectomy, administration of lidocaine for 24 hours reduced pain medication use in the first two postoperative days.[124,125] When given during radical prostatectomy and maintained for one hour postoperatively, a two-thirds reduction in total pain score index could be demonstrated, although the amount of pain medication used and patient satisfaction were not different from the control group.[127] After major abdominal surgery, lidocaine administration led to reduced morphine usage and lower pain scores during movement in the first 72 hours after the procedure.[128]

A preventive analgesic effect could also be demonstrated after laparoscopic colectomy. The intra- and postoperative administration of a continuous lidocaine infusion for 24 hours slightly reduced the use of pain medication and pain scores during movement between the 24^{th} and 48^{th} postoperative hours, compared to the control group.[129] When given this treatment during ambulatory surgery and for one hour after, patients used less morphine in the first 24 hours after hospital discharge compared with patients who were treated with placebo. After 24 hours however, there was no difference in the consumption of pain medication or in the pain scores.[134] The use of IV lidocaine in ambulatory laparoscopic surgery was also examined by De Oliveira et al.[135] The intraoperative administration of lidocaine improved quality of recovery and decreased pain scores in the PACU and opioid consumption in the first 24 hours after surgery. When given during inguinal herniorrhaphy, lower pain scores until 12 hours after surgery were reported, and fentanyl consumption and frequency of PCA pushes were also significantly reduced.[137] In addition to intraperitoneal instillation of lidocaine or saline, Kim et al. compared intraoperative infusion of lidocaine with intraoperative infusion of saline during laparoscopic appendectomy.[138] Patients who received lidocaine had lower pain scores for eight hours and lower fentanyl consumption until 24 hours after the end of surgery. Preventive analgesia was also demonstrated when IV lidocaine was given during breast surgery and maintained for one hour after the end of the procedure.[139] Although there was no significant difference in the consumption of analgesics, a decreased incidence of persistent postsurgical pain was reported.

Three studies with a similar study design failed to demonstrate a preventive analgesic effect of lidocaine. When lidocaine was administered IV during total hip arthroplasty and an infusion was maintained for 60 minutes postoperatively, no difference in pain scores and consumption of analgesics could be detected.[133] In a study in patients with colorectal surgery, intraoperative lidocaine administration that was continued for four hours postoperatively did not reduce overall piritramide consumption or pain intensities at rest and during coughing, although there was a trend for lower VAS scores in the lidocaine group.[130] A preventive analgesic effect could also not be demonstrated after abdominal hysterectomy. Patients who received lidocaine intraoperatively had similar opioid consumption and numeric pain ratings at all time points to those who were treated with placebo.[136]

A different study design compared thoracic epidural with IV infusion.[131] On the day before surgery, an epidural catheter was placed in 60 patients scheduled for open colonic surgery. On the day of surgery patients were randomized to one of three groups. One group received a lidocaine bolus of 2 mg/kg followed by a continuous infusion of 3 mg × kg^{-1} × h^{-} via epidural catheter and received saline IV; a second group received the same dose of lidocaine via peripheral IV catheter and saline via the epidural catheter; and the third group received saline IV as well as via the epidural catheter. Postoperative pain was managed with

morphine/ropivacaine patient-controlled epidural analgesia (PCEA). In the group treated with IV lidocaine, patients had lower pain scores at rest for four hours postoperatively compared with the saline group, and lower pain scores during coughing for twelve hours. The IV group also had higher first PCEA trigger times and lower total PCEA consumption than the control group. However, the group that received lidocaine via an epidural catheter had the best pain relief of all groups.

Swenson et al. compared the effect of IV and epidural administration of local anesthetics. [132] In this trial 42 patients undergoing open colon surgery were enrolled and divided into two groups. One group received an IV lidocaine bolus of 1.5 mg/kg during induction, followed by a continuous infusion of lidocaine, which was maintained until return of bowel function or postoperative day 5. The other group received a lidocaine bolus at induction only. Postoperative pain was managed using a thoracic epidural catheter with an infusion of bupivacaine and hydromorphone that was started within one hour of the end of surgery and maintained in the same way as the lidocaine infusion in the other group. Although IV lidocaine was as effective as epidural bupivacaine for postoperative pain control, the study design (in particular the absence of a placebo group) does not allow a determination if a preventive analgesic effect was present. Five adverse events were recorded in this trial. Two patients of the IV lidocaine group developed typical side effects of local anesthetics such as disorientation and perioral numbness, one of them had elevated lidocaine levels. After these events, the dose in the remaining patients was reduced from 3 mg/min to 2 mg/min for patients with a body weight more than 70kg and from 2mg/min to 1mg/min for patients with a body weight of less than 70kg.

Drug interactions with lidocaine were examined in patients scheduled for laparoscopic cholecystectomy randomized to four groups.[126] The first group received a single dose of the N-methyl-d-aspartate receptor antagonist, dextromethorphan, 30 minutes before skin incision and a continuous lidocaine infusion during surgery. The second group received dextromethorphan before and saline during surgery. The third group received the H1 histamine receptor blocker and serotonin-norepinephrine reuptake inhibitor chlorpheniramine before skin incision and lidocaine during surgery. The fourth group received chlorpheniramine before and saline during surgery. All infusions were terminated at the end of the procedure. Postoperative pain was treated with meperidine. Although VAS scores at rest did not demonstrate a preventive analgesic effect of lidocaine, VAS scores during coughing in patients who were treated with lidocaine were lower in the first 12 hours in the lidocaine/chlorpheniramine groups and lower in the first 24 hours in the lidocaine/dextrometorphan groups. In addition both lidocaine groups had lower total meperidine consumption than the control groups. These results also suggest a preventive analgesic effect.

In conclusion, thirteen out of sixteen studies demonstrated preventive analgesia by IV administration of lidocaine. This, effect however, could not be associated with a specific regimen or dosage.

Intravenous local anesthetic drug levels resulting from peripheral nerve blocks

Given the large doses of local anesthetics administered for major nerve blocks, and the frequent occurrence of nearby vascular structures, reasonable concern has been expressed about potential systemic drug levels and resulting toxicity. Data from studies examining these levels can also inform us about the therapeutic potential of intra- and postoperative local anesthetic. In one study in which cervical plexus block was accomplished by slow injections of lidocaine (320–460 mg) plus bupivacaine (80–115 mg), arterial lidocaine reached a peak level of ~5μg/mL at 5–10 min after injection, and then slowly declined to a value of 2–3μg/mL at 3 hr after the block.[140] Bupivacaine levels in these same patients had a

similar time course, with peak values of 1–2 μg/mL and 3 hr levels of ~0.5 μg/mL. It is noteworthy that a different study, of local anesthetic mixtures for femoral and sciatic nerve blocks, showed that the presence of lidocaine hastened the decline and reduced the peak levels of co-injected bupivacaine or ropivacaine.[8] Lidocaine levels such as these are in the range achieved for treatment of chronic pain by intentional IV delivery,[141] and are consonant with the levels resulting from the perioperative delivery of lidocaine for minimizing postoperative pain (see preceding section).

Few studies report the fraction of local anesthetic in plasma that is bound to protein. Although rapid drug dissociation from this protein-bound pool in response to the uptake of free drug by circulated tissues will almost certainly provide a larger “free fraction” than is measured at equilibrium, at least some of the total local anesthetic in plasma is unavailable. Depending on their affinity for and their dissociation rate from plasma proteins, such binding will reduce both the therapeutic and the toxic potential of IV drugs. Particularly relevant in the postoperative context is the increase that follows surgery of alpha-1 acid glycoprotein, the protein that binds local anesthetics with a high affinity. Future studies of local anesthetic levels in plasma would be more informative and useful if bound as well as total local anesthetic were reported.

Although there have been no studies of the therapeutic actions of IV longer-acting local anesthetics, these might have benefit at plasma levels 0.1 to 0.25 that of lidocaine, assuming an action at Na^+ channels that results in inhibition of abnormal action potentials.[142] Cervical plexus blocks with bupivacaine (80–115 mg) or levobupivacaine (125 mg dose) result in peak plasma levels of ~1–2μg/mL[140] and 0.4–0.8 μg/mL,[143] respectively. Brachial plexus blocks with ropivacaine, dose ~250 mg, resulted in plasma levels of 2.6–3.3μg/mL[144] while the same local anesthetic used for femoral nerve block (0.75%, 225 mg)[43] or TAP block (150 mg)[145] resulted in peak plasma levels of ~1.5 and 2 μg/mL, respectively. Relative to the known “therapeutic” concentrations of plasma lidocaine, these values of the longer-acting local anesthetics may well have therapeutic benefit, particularly when their plasma decay occurs over 3 hr or longer, as is the case for most after bolus injections for the block. Therefore, it seems probable that at least part of the reduction of postoperative pain by local anesthetics given for peripheral nerve block results from the systemic distribution of these drugs, which might be acting on the central (CNS) as well as the peripheral nervous system.

Discussion

This review documents “preventive analgesia” by local anesthetics in a large majority of randomized clinical studies. Preventive analgesia is defined as a reduction of postoperative pain that persists for more than 5.5 half-lives of a drug[1], which is ~ 8 hours for lidocaine, and 12–16 hours for bupivacaine.[146] Most of the cited studies examined pain scores and/or opioid consumption for at least 24 hour after surgery and local anesthetic administration, thus meeting the criteria for preventive analgesia.

Nerve blocks by local anesthetics improve postoperative analgesia compared to placebo or PCA. Peripheral nerve blocks appear to have better analgesic efficacy than IA infusions for both upper and lower extremity surgeries. Some of the effects of peripheral nerve block procedures may be attributed to CNS effects from the systemic distribution of these drugs secondary to peripheral nerve block. Intravenous administration of lidocaine has demonstrated a postoperative analgesic benefit but this effect is not associated with a specific regimen or dose and no studies compared IV lidocaine to a regional anesthetic technique such as an epidural or peripheral nerve block. Therefore IV lidocaine administration may be a reasonable analgesic approach when regional techniques are contraindicated or not performed.

The volume and concentration of the local anesthetic used does not appear to affect the efficacy of the block, but what seems to be important is the total dose (mass) of local anesthetic.[61,147] The timing of the block, pre- or postincision, also does not appear to be of clinical significance,[6] and this has been discussed at length by Katz and Clarke.[148] This suggests that either postoperative nerve impulse activity or slower changes in synaptic neuroplasticity in the CNS, or changes in the signaling properties of non-neuronal cells, such as microglia, in the CNS are affected by local anesthetics given for peripheral nerve block.[149,150]

What are the limitations in assessing clinical trials that validate the preventive analgesia by local anesthetics? One limitation in studying the effect of peripheral nerve blocks is the difficulty in designing double-blind, placebo-controlled studies. Such a design necessitates a sham block which is often clinically and ethically unacceptable, and therefore many studies compare the effects of different treatments but do not use a true, drug-free “control.” In addition, all studies are powered to examine different primary outcomes that were not necessarily pain scores or analgesic use, for instance. Furthermore, all studies used different local anesthetics, different drug doses and concentrations, and in the case of infusions, different rates and durations of infusions. Finally, surgical techniques are variable and surgeries performed at different institutions cannot be assumed to cause similar pain in patients.

The longer-term outcomes from local anesthetics used perioperatively are rarely assessed. Since chronic pain, persisting for more than 3 months after surgery, is an increasingly recognized syndrome, and acute pain intensity has a positive correlation to the occurrence of such chronic pain,[151, 152] one predicts that acute pain management would be an effective preventive treatment for chronic pain. Further study is desired in order to examine the long-term analgesic effects of peripheral nerve blocks or IV-administered local anesthetics.

Acknowledgments

Funding: Some salary support from NIH grant(s) (NIH/NCI CA080153) and partial support from departmental funds.

References

1. Katz J, Clarke H, Seltzer Z. Preventive analgesia: *quo vadimus*? Anesth Analg. 2011; 113:1242–1253. [PubMed: 21965352]
2. Kissin I. A call to reassess the clinical value of preventive (preemptive) analgesia. Anesth Analg. 2011; 113:977–978. [PubMed: 22021795]
3. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg. 2003; 97:534–540. [PubMed: 12873949]
4. Clarke H, Bonin RP, Orser BA, Englesakis M, Wijeysundera DN, Katz J. The Prevention of Chronic Postsurgical Pain Using Gabapentin and Pregabalin: A Combined Systematic Review and Meta-Analysis. Anesth Analg. 2012 Mar 13. PMID: 22415535 [Epub ahead of print].
5. Nechleba J, Rogers V, Cortina G, Cooney T. Continuous intra-articular infusion of bupivacaine for postoperative pain following total knee arthroplasty. J Knee Surg. 2005; 18:197–202. [PubMed: 16152868]
6. Bunburaphong P, Niruthisard S, Werawatganon T, Keeyapaj W, Vimuktanandana A, Toleb K. Postoperative analgesia for total knee replacement: comparing between pre-and postoperative "3-in-1" femoral nerve block. J Med Assoc Thai. 2006; 89:462–467. [PubMed: 16696391]
7. de Lima ESR, Correa CH, Henriques MD, de Oliveira CB, Nunes TA, Gomez RS. Single-injection femoral nerve block with 0.25% ropivacaine or 0.25% bupivacaine for postoperative analgesia after

total knee replacement or anterior cruciate ligament reconstruction. J Clin Anesth. 2008; 20:521–527. [PubMed: 19019663]

8. Cuvillon P, Nouvellon E, Ripart J, Boyer JC, Dehour L, Mahamat A, L'Hermite J, Boisson C, Vialles N, Lefrant JY, de La Coussaye JE. A comparison of the pharmacodynamics and pharmacokinetics of bupivacaine, ropivacaine (with epinephrine) and their equal volume mixtures with lidocaine used for femoral and sciatic nerve blocks: a double-blind randomized study. Anesth Analg. 2009; 108:641–649. [PubMed: 19151302]
9. Beaulieu P, Babin D, Hemmerling T. The pharmacodynamics of ropivacaine and bupivacaine in combined sciatic and femoral nerve blocks for total knee arthroplasty. Anesth Analg. 2006; 103:768–774. [PubMed: 16931694]
10. Kardash K, Hickey D, Tessler MJ, Payne S, Zukor D, Velly AM. Obturator versus femoral nerve block for analgesia after total knee arthroplasty. Anesth Analg. 2007; 105:853–858. [PubMed: 17717250]
11. Ozen M, Inan N, Tumer F, Uyar A, Baltaci B. The effect of 3-in-1 femoral nerve block with ropivacaine 0.375% on postoperative morphine consumption in elderly patients after total knee replacement surgery. Agri. 2006; 18:44–50. [PubMed: 17457713]
12. YaDeau JT, Cahill JB, Zawadsky MW, Sharrock NE, Bottner F, Morelli CM, Kahn RL, Sculco TP. The effects of femoral nerve blockade in conjunction with epidural analgesia after total knee arthroplasty. Anesth Analg. 2005; 101:891–895. [PubMed: 16116010]
13. Salinas FV, Liu SS, Mulroy MF. The effect of single-injection femoral nerve block versus continuous femoral nerve block after total knee arthroplasty on hospital length of stay and long-term functional recovery within an established clinical pathway. Anesth Analg. 2006; 102:1234–1239. [PubMed: 16551930]
14. Ilfeld BM, Mariano ER, Girard PJ, Loland VJ, Meyer RS, Donovan JF, Pugh GA, Le LT, Sessler DI, Shuster JJ, Theriaque DW, Ball ST. A multicenter, randomized, triple-masked, placebo-controlled trial of the effect of ambulatory continuous femoral nerve blocks on discharge-readiness following total knee arthroplasty in patients on general orthopaedic wards. Pain. 2010; 150:477–484. [PubMed: 20573448]
15. Shum CF, Lo NN, Yeo SJ, Yang KY, Chong HC, Yeo SN. Continuous femoral nerve block in total knee arthroplasty: immediate and two-year outcomes. J Arthroplasty. 2009; 24:204–209. [PubMed: 18534496]
16. Martin F, Martinez V, Mazoit JX, Bouhassira D, Cherif K, Gentili ME, Piriou P, Chauvin M, Fletcher D. Antiinflammatory effect of peripheral nerve blocks after knee surgery: clinical and biologic evaluation. Anesthesiology. 2008; 109:484–490. [PubMed: 18719447]
17. Seet E, Leong WL, Yeo AS, Fook-Chong S. Effectiveness of 3-in-1 continuous femoral block of differing concentrations compared to patient controlled intravenous morphine for post total knee arthroplasty analgesia and knee rehabilitation. Anaesth Intensive Care. 2006; 34:25–30. [PubMed: 16494145]
18. Wegener JT, van OOij B, van Dijk CN, Hollmann MW, Preckel B, Stevens MF. Value of single-injection or continuous sciatic nerve block in addition to a continuous femoral nerve block in patients undergoing total knee arthroplasty. Reg Anesth Pain Med. 2011; 36(5):481–488. [PubMed: 21857273]
19. Cappelleri G, Ghisi D, Fanelli A, Albertin A, Somalvico F, Aldegheri G. Does continuous sciatic nerve block improve postoperative analgesia and early rehabilitation after total knee arthroplasty? A prospective, randomized, double-blinded study. Reg Anesth Pain Med. 2011; 36(5):489–492. [PubMed: 21857276]
20. Heid F, Muller N, Piepho T, Bares M, Giesa M, Drees P, Rumelin A, Werner C. Postoperative analgesic efficacy of peripheral levobupivacaine and ropivacaine: a prospective, randomized double-blind trial in patients after total knee arthroplasty. Anesth Analg. 2008; 106:1559–1561. [PubMed: 18420876]
21. Sundarathiti P, Ruananukul N, Channum T, Kitkunasathean C, Mantay A, Thammasakulsiri J, Sodsee W. A comparison of continuous femoral nerve block (CFNB) and continuous epidural infusion (CEI) in postoperative analgesia and knee rehabilitation after total knee arthroplasty (TKA). J Med Assoc Thai. 2009; 92:328–334. [PubMed: 19301724]

22. Hunt KJ, Bourne MH, Mariani EM. Single-injection femoral and sciatic nerve blocks for pain control after total knee arthroplasty. J Arthroplasty. 2009; 24:533–538. [PubMed: 19026519]
23. Mistraletti G, De La Cuadra-Fontaine JC, Asenjo FJ, Donatelli F, Wykes L, Schricker T, Carli F. Comparison of analgesic methods for total knee arthroplasty: metabolic effect of exogenous glucose. Reg Anesth Pain Med. 2006; 31:260–269. [PubMed: 16701193]
24. Pham Dang C, Gautheron E, Guilley J, Fernandez M, Waast D, Volteau C, Nguyen JM, Pinaud M. The value of adding sciatic block to continuous femoral block for analgesia after total knee replacement. Reg Anesth Pain Med. 2005; 30:128–133. [PubMed: 15765454]
25. Morin AM, Kratz CD, Eberhart LH, Dinges G, Heider E, Schwarz N, Eisenhardt G, Geldner G, Wulf H. Postoperative analgesia and functional recovery after total-knee replacement: comparison of a continuous posterior lumbar plexus (psoas compartment) block, a continuous femoral nerve block, and the combination of a continuous femoral and sciatic nerve block. Reg Anesth Pain Med. 2005; 30:434–445. [PubMed: 16135347]
26. Carli F, Clemente A, Asenjo JF, Kim DJ, Mistraletti G, Gomarasca M, Morabito A, Tanzer M. Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. Br J Anaesth. 2010; 105:185–195. [PubMed: 20551021]
27. Affas F, Nygards EB, Stiller CO, Wretenberg P, Olofsson C. Pain control after total knee arthroplasty: a randomized trial comparing local infiltration anesthesia and continuous femoral block. Acta Orthop. 2011; 83(3):441–447. [PubMed: 21561303]
28. Krenzel BA, Cook C, Martin GN, Vail TP, Attarian DE, Bolognesi MP. Posterior capsular injections of ropivacaine during total knee arthroplasty: a randomized, double-blind, placebo-controlled study. J Arthroplasty. 2009; 24:138–143. [PubMed: 19520544]
29. Kazak Bengisun Z, Aysu Salviz E, Darcin K, Suer H, Ates Y. Intraarticular levobupivacaine or bupivacaine administration decreases pain scores and provides a better recovery after total knee arthroplasty. J Anesth. 2010; 24:694–699. [PubMed: 20571832]
30. Ong JC, Chin PL, Fook-Chong SM, Tang A, Yang KY, Tay BK. Continuous infiltration of local anaesthetic following total knee arthroplasty. J Orthop Surg. 2010; 18:203–207.
31. Gomez-Cardero P, Rodriguez-Merchan EC. Postoperative analgesia in TKA: ropivacaine continuous intraarticular infusion. Clin Orthop Relat Res. 2010; 468:1242–1247. [PubMed: 20049572]
32. Essving P, Axelsson K, Aberg E, Spannar H, Gupta A, Lundin A. Local infiltration analgesia versus intrathecal morphine for postoperative pain management after total knee arthroplasty: a randomized controlled trial. Anesth Analg. 2011; 113(4):926–933. [PubMed: 21821506]
33. Dobrydnjov I, Anderberg C, Olsson C, Shapurova O, Angel K, Bergman S. Intraarticular versus extraarticular ropivacaine infusion following high-dose local infiltration analgesia after total knee arthroplasty. Acta Ortho. 2011; 82(6):692–698.
34. Bagry H, de la Cuadra Fontaine JC, Asenjo JF, Bracco D, Carli F. Effect of a continuous peripheral nerve block on the inflammatory response in knee arthroplasty. Reg Anesth Pain Med. 2008; 33:17–23. [PubMed: 18155052]
35. Campbell A, McCormick M, McKinlay K, Scott NB. Epidural vs. lumbar plexus infusions following total knee arthroplasty: randomized controlled trial. Eur J Anaesthesiol. 2008; 25:502–507. [PubMed: 18298872]
36. Frassanito L, Vergari A, Messina A, Pitoni S, Puglisi C, Chierichini A. Anaesthesia for total knee arthroplasty: efficacy of single-injection or continuous lumbar plexus associated with sciatic nerve blocks--a randomized controlled study. Eur Rev Med Pharmacol Sci. 2009; 13:375–382. [PubMed: 19961044]
37. Watson MW, Mitra D, McLintock TC, Grant SA. Continuous versus single-injection lumbar plexus blocks: comparison of the effects on morphine use and early recovery after total knee arthroplasty. Reg Anesth Pain Med. 2005; 30:541–547. [PubMed: 16326339]
38. Paauwe JJ, Thomassen BJ, Weterings J, van Rossum E, Ausems ME. Femoral nerve block using ropivacaine 0.025%, 0.05% and 0.1%: effects on the rehabilitation programme following total knee arthroplasty: a pilot study. Anaesthesia. 2008; 63:948–953. [PubMed: 18540926]

39. Good RP, Snedden MH, Schieber FC, Polachek A. Effects of preoperative femoral nerve block on pain management and rehabilitation after total knee arthroplasty. Am J Orthop. 2007; 36:554–557. [PubMed: 18033568]
40. Matava MJ, Prickett WD, Khodamoradi S, Abe S, Garbutt J. Femoral nerve blockade as a preemptive anesthetic in patients undergoing anterior cruciate ligament reconstruction: a prospective, randomized, double-blinded, placebo-controlled study. Am J Sports Med. 2009; 37:78–86. [PubMed: 18936277]
41. Parker RD, Streem K, Schmitz L, Martineau PA. Efficacy of continuous intra-articular bupivacaine infusion for postoperative analgesia after anterior cruciate ligament reconstruction: a double-blinded, placebo-controlled, prospective, and randomized study. Am J Sports Med. 2007; 35:531–536. [PubMed: 17244900]
42. Wulf H, Lowe J, Gnutzmann KH, Steinfeldt T. Femoral nerve block with ropivacaine or bupivacaine in day case anterior crucial ligament reconstruction. Acta Anaesthesiol Scand. 2010; 54:414–420. [PubMed: 20085546]
43. Dauri M, Fabbi E, Mariani P, Faria S, Carpenedo R, Sidiropoulou T, Coniglione F, Silvi MB, Sabato AF. Continuous femoral nerve block provides superior analgesia compared with continuous intra-articular and wound infusion after anterior cruciate ligament reconstruction. Reg Anesth Pain Med. 2009; 34:95–99. [PubMed: 19282706]
44. Eroglu A, Saracoglu S, Erturk E, Kosucu M, Kerimoglu S. A comparison of intraarticular morphine and bupivacaine for pain control and outpatient status after an arthroscopic knee surgery under a low dose of spinal anaesthesia. Knee Surg Sports Traumatol Arthrosc. 2010; 18:1487–1495. [PubMed: 20130836]
45. Marret E, Gentili M, Bonnet MP, Bonnet F. Intra-articular ropivacaine 0.75% and bupivacaine 0.50% for analgesia after arthroscopic knee surgery: a randomized prospective study. Arthroscopy. 2005; 21:313–316. [PubMed: 15756185]
46. Goodwin RC, Amjadi F, Parker RD. Short-term analgesic effects of intra-articular injections after knee arthroscopy. Arthroscopy. 2005; 21:307–312. [PubMed: 15756184]
47. Hadzic A, Karaca PE, Hobeika P, Unis G, Dermksian J, Yufa M, Claudio R, Vloka JD, Santos AC, Thys DM. Peripheral nerve blocks result in superior recovery profile compared with general anesthesia in outpatient knee arthroscopy. Anesth Analg. 2005; 100:976–981. [PubMed: 15781509]
48. Atim A, Ergin A, Kurt E, Ozdemiroglu Y, Guzeldemir E. Comparison of sciatic psoas compartment block and sciatic femoral 3-in-1 block for knee arthroscopy. J Clin Anesth. 2007; 19:591–595. [PubMed: 18083472]
49. Jacobson E, Assareh H, Cannerfelt R, Anderson RE, Jakobsson JG. Knee Surg Sports Traumatol Arthrosc. 2006; 14:120–124. [PubMed: 15947913]
50. Chen DW, Hsieh PH, Huang KC, Hu CC, Chang YH, Lee MS. Continuous intra-articular infusion of bupivacaine for post-operative pain relief after total hip arthroplasty: a randomized, placebo-controlled, double-blind study. Eur J Pain. 2010; 14:529–534. [PubMed: 19781964]
51. Becchi C, Al Malyan M, Coppini R, Campolo M, Magherini M, Boncinelli S. Opioid-free analgesia by continuous psoas compartment block after total hip arthroplasty. A randomized study. Eur J Anaesthesiol. 2008; 25:418–423. [PubMed: 18028577]
52. Siddiqui ZI, Cepeda MS, Denman W, Schumann R, Carr DB. Continuous lumbar plexus block provides improved analgesia with fewer side effects compared with systemic opioids after hip arthroplasty: a randomized controlled trial. Reg Anesth Pain Med. 2007; 32:393–398. [PubMed: 17961837]
53. Murphy TP, Byrne DP, Curtin P, Baker JF, Mulhall KJ. Can a periarticular levobupivacaine injection reduce postoperative opiate consumption during primary hip arthroplasty? Clin Orthop Relat Res. 2012; 470:1151–1157. [PubMed: 21960156]
54. Ilfeld BM, Moeller LK, Mariano ER, Loland VJ, Stevens-Lapsley JE, Fleisher AS, Girard PJ, Donohue MC, Ferguson EJ, Ball ST. Continuous peripheral nerve blocks: is local anesthetic dose the only factor, or do concentration and volume influence infusion effects as well? Anesthesiology. 2010; 112:347–354. [PubMed: 20098137]

55. de Leeuw MA, Dertinger JA, Hulshoff L, Hoeksema M, Perez RS, Zuurmond WW, de Lange JJ. The efficacy of levobupivacaine, ropivacaine, and bupivacaine for combined psoas compartment-sciatic nerve block in patients undergoing total hip arthroplasty. Pain Pract. 2008; 8:241–247. [PubMed: 18503623]
56. Ilfeld BM, Ball ST, Gearen PF, Le LT, Mariano ER, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Meyer RS. Ambulatory continuous posterior lumbar plexus nerve blocks after hip arthroplasty: a dual-center, randomized, triple-masked, placebo-controlled trial. Anesthesiology. 2008; 109:491–501. [PubMed: 18719448]
57. Ilfeld BM, Mariano ER, Madison SJ, Loland VJ, Sandhu NS, Suresh PJ, Bishop ML, Kim TE, Donohue MC, Kulidjian AA, Ball ST. Continuous femoral versus posterior lumbar plexus nerve blocks for analgesia after hip arthroplasty: a randomized, controlled study. Anesth Analg. 2011; 113:897–903. [PubMed: 21467563]
58. Capdevila X, Dadure C, Bringuier S, Bernard N, Biboulet P, Gaertner E, Macaire P. Effect of patient-controlled perineural analgesia on rehabilitation and pain after ambulatory orthopedic surgery: a multicenter randomized trial. Anesthesiology. 2006; 105:566–573. [PubMed: 16931991]
59. Fournier R, Faust A, Chassot O, Gamulin Z. Levobupivacaine 0.5% provides longer analgesia after sciatic nerve block using the Labat approach than the same dose of ropivacaine in foot and ankle surgery. Anesth Analg. 2010; 110:1486–1489. [PubMed: 20304982]
60. Casati A, Vinciguerra F, Santorsola R, Aldegheri G, Putzu M, Fanelli G. Sciatic nerve block with 0.5% levobupivacaine, 0.75% levobupivacaine or 0.75% ropivacaine: a double-blind, randomized comparison. Eur J Anaesthesiol. 2005; 22:452–456. [PubMed: 15991509]
61. Ilfeld BM, Loland VJ, Gerancher JC, Wadhwa AN, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Mariano ER. The effects of varying local anesthetic concentration and volume on continuous popliteal sciatic nerve blocks: a dual-center, randomized, controlled study. Anesth Analg. 2008; 107:701–707. [PubMed: 18633055]
62. Banerjee SS, Pulido P, Adelson WS, Fronek J, Hoenecke HR. The efficacy of continuous bupivacaine infiltration following arthroscopic rotator cuff repair. Arthroscopy. 2008; 24:397–402. [PubMed: 18375270]
63. Cho NS, Ha JH, Rhee YG. Patient-controlled analgesia after arthroscopic rotator cuff repair: subacromial catheter versus intravenous injection. Am J Sports Med. 2007; 35:75–79. [PubMed: 16923824]
64. Ciccone WJ 2nd, Busey TD, Weinstein DM, Walden DL, Elias JJ. Assessment of pain relief provided by interscalene regional block and infusion pump after arthroscopic shoulder surgery. Arthroscopy. 2008; 24:14–19. [PubMed: 18182196]
65. DeMarco JR, Componovo R, Barfield WR, Liles L, Nietert P. Efficacy of augmenting a subacromial continuous-infusion pump with a preoperative interscalene block in outpatient arthroscopic shoulder surgery: a prospective, randomized, blinded, and placebo-controlled study. Arthroscopy. 2011; 27:603–610. [PubMed: 21663717]
66. Singelyn FJ, Lhotel L, Fabre B. Pain relief after arthroscopic shoulder surgery: a comparison of intraarticular analgesia, suprascapular nerve block, and interscalene brachial plexus block. Anesth Analg. 2004; 99:589–592. [PubMed: 15271745]
67. Winkler T, Suda AJ, Dumitrescu RV, Pinggera O, Weber G, Loho G, Schneider B, Wurnig C. Interscalene versus subacromial continuous infusion of ropivacaine after arthroscopic acromioplasty: a randomized controlled trial. J Shoulder Elbow Surg. 2009; 18:566–572. [PubMed: 19213575]
68. Fontana C, Di Donato A, Di Giacomo G, Costantini A, De Vita A, Lancia F, Caricati A. Postoperative analgesia for arthroscopic shoulder surgery: a prospective randomized controlled study of intraarticular, subacromial injection, interscalenic brachial plexus block and intraarticular plus subacromial injection efficacy. Eur J Anaesthesiol. 2009; 26:689–693. [PubMed: 19593887]
69. Delaunay L, Souron V, Lafosse L, Marret E, Toussaint B. Analgesia after arthroscopic rotator cuff repair: subacromial versus interscalene continuous infusion of ropivacaine. Reg Anesth Pain Med. 2005; 30:117–122. [PubMed: 15765452]

70. Webb D, Guttmann D, Cawley P, Lubowitz JH. Continuous infusion of a local anesthetic versus interscalene block for postoperative pain control after arthroscopic shoulder surgery. Arthroscopy. 2007; 23:1006–1011. [PubMed: 17868841]
71. Fredrickson MJ, Ball CM, Dalgleish AJ. Analgesic effectiveness of a continuous versus single-injection interscalene block for minor arthroscopic shoulder surgery. Reg Anesth Pain Med. 2010; 35:28–33. [PubMed: 20048655]
72. Al-Kaisy A, McGuire G, Chan VW, Bruin G, Peng P, Miniaci A, Perlas A. Analgesic effect of interscalene block using low-dose bupivacaine for outpatient arthroscopic shoulder surgery. Reg Anesth Pain Med. 1998; 23:469–473. [PubMed: 9773699]
73. Anakwenze OA, Hosalkar H, Huffman GR. Case reports: two cases of glenohumeral chondrolysis after intraarticular pain pumps. Clin Orthop Relat Res. 2010; 468:2545–2549. [PubMed: 20112077]
74. Bailie DS, Ellenbecker TS. Severe chondrolysis after shoulder arthroscopy: a case series. J Shoulder Elbow Surg. 2009; 18:742–747. [PubMed: 19186080]
75. Webb ST, Ghosh S. Intra-articular bupivacaine: potentially chondrotoxic? Br J Anaesth. 2009; 102:439–441. [PubMed: 19286766]
76. Hadzic A, Williams BA, Karaca PE, Hobeika P, Unis G, Dermksian J, Yufa M, Thys DM, Santos AC. For outpatient rotator cuff surgery, nerve block anesthesia provides superior same-day recovery over general anesthesia. Anesthesiology. 2005; 102:1001–1007. [PubMed: 15851888]
77. Goebel S, Stehle J, Schwemmer U, Reppenhagen S, Rath B, Gohlke F. Interscalene brachial plexus block for open-shoulder surgery: a randomized, double-blind, placebo-controlled trial between single-shot anesthesia and patient-controlled catheter system. Arch Orthop Trauma Surg. 2010; 130:533–540. [PubMed: 19841925]
78. Hofmann-Kiefer K, Eiser T, Chappell D, Leuschner S, Conzen P, Schwender D. Does patient-controlled continuous interscalene block improve early functional rehabilitation after open shoulder surgery? Anesth Analg. 2008; 106:991–996. [PubMed: 18292451]
79. Ilfeld BM, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Chmielewski TL, Spadoni EH, Wright TW. Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty: a randomized, triple-masked, placebo-controlled study. Anesthesiology. 2006; 105:999–1007. [PubMed: 17065895]
80. Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJ. Effect of local anaesthetic volume (20 vs 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. Br J Anaesth. 2008; 101:549–556. [PubMed: 18682410]
81. Le LT, Loland VJ, Mariano ER, Gerancher JC, Wadhwa AN, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Ilfeld BM. PAINfRE Investigators. Effects of local anesthetic concentration and dose on continuous interscalene nerve blocks: a dual-center, randomized, observer-masked, controlled study. Reg Anesth Pain Med. 2008; 33:518–525. [PubMed: 19258966]
82. Borgeat A, Aguirre J, Marquardt M, Mrdjen J, Blumenthal S. Continuous interscalene analgesia with ropivacaine 0.2% versus ropivacaine 0.3% after open rotator cuff repair: the effects on postoperative analgesia and motor function. Anesth Analg. 2010; 111:1543–1547. [PubMed: 20889941]
83. Fredrickson MJ, Price DJ. Analgesic effectivensss of ropivacaine 0.2% vs 0.4% via an ultrasound guided C5–6 root/ superior trunk perineural ambulatory catheter. Br J Anaesth. 2009; 103:434–439. [PubMed: 19608563]
84. Urmey WF, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. Anesth Analg. 1992; 74:352–357. [PubMed: 1539813]
85. Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. Anesth Analg. 1991; 72:498–503. [PubMed: 2006740]
86. Neal JM, Gerancher JC, Hebl JR, Ilfeld BM, McCartney CJ, Franco CD, Hogan QH. Upper extremity regional anesthesia: essentials of our current understanding, 2008. Reg Anesth Pain Med. 2009; 34:134–170. [PubMed: 19282714]

87. Renes SH, van Geffen GJ, Rettig HC, Gielen MJ, Scheffer GJ. Minimum effective volume of local anesthetic for shoulder analgesia by ultrasound-guided block at root C7 with assessment of pulmonary function. Reg Anesth Pain Med. 2010; 35:529–534. [PubMed: 20975468]

88. McCartney CJ, Brull R, Chan VW, Katz J, Abbas S, Graham B, Nova H, Rawson R, Anastakis DJ, von Schroeder H. Early but no long-term benefit of regional compared with general anesthesia for ambulatory hand surgery. Anesthesiology. 2004; 101:461–467. [PubMed: 15277930]

89. O'Donnell BD, Ryan H, O'Sullivan O, Iohom G. Ultrasound-guided axillary brachial plexus block with 20 milliliters local anesthetic mixture versus general anesthesia for upper limb trauma surgery: an observer-blinded, prospective, randomized, controlled trial. Anesth Analg. 2009; 109:279–283. [PubMed: 19535722]

90. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. Anaesthesia. 2001; 56:1024–1026. [PubMed: 11576144]

91. Siddiqui MR, Sajid MS, Uncles DR, Cheek L, Baig MK. A meta-analysis on the clinical effectiveness of transversus abdominis plane block. J Clin Anesth. 2011; 23:7–14. [PubMed: 21296242]

92. De Oliveira GS, Fitzgerald PC, Marcus RJ, Ahmad S, McCarthy RJ. A dose-ranging study of the effect of transversus abdominis plane block on postoperative quality of recovery and analgesia after outpatient laparoscopy. Anesth Analg. 2011; 113(5):1218–1225. [PubMed: 21926373]

93. Niraj G, Kelkar A, Jeyapalan I, Graff-Baker P, Williams O, Darbar A, Maheswaran A, Powell R. Comparison of analgesic efficacy of subcostal transversus abdominis plane blocks with epidural analgesia following upper abdominal surgery. Anaesthesia. 2011; 66:465–471. [PubMed: 21457153]

94. Atim A, Bilgin F, Kilickaya O, Purtologlu T, Alanbay I, Orhan ME, Kurt E. The efficacy of ultrasound-guided transversus abdominis plan block in patients undergoing hysterectomy. Anaesth Intensive Care. 2011; 39:630–634. [PubMed: 21823381]

95. Carney J, Finnerty O, Rauf J, Curley G, McDonnell JG, Laffey JG. Ipsilateral transversus abdominis plane block provides effective analgesia after appendectomy in children: a randomized controlled trial. Anesth Analg. 2010; 111:998–1003. [PubMed: 20802056]

96. Carney J, McDonnell JG, Ochana A, Bhinder R, Laffey JG. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. Anesth Analg. 2008; 107:2056–2060. [PubMed: 19020158]

97. Belavy D, Cowlishaw PJ, Howes M, Phillips F. Ultrasound-guided transversus abdominis plane block for analgesia after Caesarean delivery. Br J Anaesth. 2009; 103:726–730. [PubMed: 19700776]

98. McDonnell JG, O'Donnell B, Curley G, Heffernan A, Power C, Laffey JG. The analgesic efficacy of transversus abdominis plane block after abdominal surgery: a prospective randomized controlled trial. Anesth Analg. 2007; 104:193–197. [PubMed: 17179269]

99. McDonnell JG, Curley G, Carney J, Benton A, Costello J, Maharaj CH, Laffey JG. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg. 2008; 106:186–191. [PubMed: 18165577]

100. Niraj G, Searle A, Mathews M, Misra V, Baban M, Kiani S, Wong M. Analgesic efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing open appendicectomy. Br J Anaesth. 2009; 103:601–605. [PubMed: 19561014]

101. El-Dawlatly AA, Turkistani A, Kettner SC, Machata AM, Delvi MB, Thallaj A, Kapral S, Marhofer P. Ultrasound-guided transversus abdominis plane block: description of a new technique and comparison with conventional systemic analgesia during laparoscopic cholecystectomy. Br J Anaesth. 2009; 102:763–767. [PubMed: 19376789]

102. Sandeman DJ, Bennett M, Dilley AV, Perczuk A, Lim S, Kelly KJ. Ultrasound-guided transversus abdominis plane blocks for laparoscopic appendicectomy in children: a prospective randomized trial. Br J Anaesth. 2011; 106(6):882–886. [PubMed: 21504934]

103. Costello JF, Moore AR, Wieczorek PM, Macarthur AJ, Balki M, Carvalho JC. The transversus abdominis plane block, when used as part of a multimodal regimen inclusive of intrathecal morphine, does not improve analgesia after cesarean delivery. Reg Anesth Pain Med. 2009; 34:586–589. [PubMed: 19916252]

104. Movafegh A, Nouralishahi B, Sadeghi M, Nabavian O. An ultra-low dose of naloxone added to lidocaine or lidocaine-fentanyl mixture prolongs axillary brachial plexus blockade. Anesth Analg. 2009; 109:1679–1683. [PubMed: 19843808]

105. Popping DM, Elia N, Marret E, Wenk M, Tramer MR. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology. 2009; 111:406–415. [PubMed: 19602964]

106. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg. 2010; 111:1548–1551. [PubMed: 20889939]

107. Parrington SJ, O'Donnell D, Chan VW, Brown-Shreves D, Subramanyam R, Qu M, Brull R. Dexamethasone added to mepivacaine prolongs the duration of analgesia after supraclavicular brachial plexus blockade. Reg Anesth Pain Med. 2010; 35:422–426. [PubMed: 20814282]

108. Vieira PA, Pulai I, Tsao GC, Manikantan P, Keller B, Connelly NR. Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade. Eur J Anaesthesiol. 2010; 27:285–288. [PubMed: 20009936]

109. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. Anesth Analg. 2006; 102:263–267. [PubMed: 16368840]

110. Cummings KC 3rd, Napierkowski DE, Parra-Sanchez I, Kurz A, Dalton JE, Brems JJ, Sessler DI. Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine. Br J Anaesth. 2011; 107(3):446–453. [PubMed: 21676892]

111. Tandoc MN, Fan L, Kolesnikov S, Kruglov A, Nader ND. Adjuvant dexamethasone with bupivacaine prolongs the duration of interscalene block: a prospective randomized trial. J Anesth. 2011; 25:704–709. [PubMed: 21681533]

112. Jarbo K, Batra YK, Panda NB. Brachial plexus block with midazolam and bupivacaine improves analgesia. Can J Anaesth. 2005; 52:822–826. [PubMed: 16189333]

113. Gunduz A, Bilir A, Gulec S. Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med. 2006; 31:233–236. [PubMed: 16701189]

114. Lee AR, Yi HW, Chung IS, Ko JS, Ahn HJ, Gwak MS, Choi DH, Choi SJ. Magnesium added to bupivacaine prolongs the duration of analgesia after interscalene nerve block. Can J Anaesth. 2012; 59(1):21–27. [PubMed: 22012543]

115. Alemanno F, Ghisi D, Fanelli A, Faliva A, Pergolotti B, Bizzarri F, Fanelli G. Tramadol and 0.5% levobupivacaine for single-shot interscalene block: effects on postoperative analgesia in patients undergoing shoulder arthroplasty. Minerva Anestesiol. 2012; 78(3):291–296. [PubMed: 21971437]

116. Zeidan A, Kassem R, Nahleh N, Maaliki H, El-Khatib M, Struys MM, Baraka A. Intraarticular tramadol-bupivacaine combination prolongs the duration of postoperative analgesia after outpatient arthroscopic knee surgery. Anesth Analg. 2008; 107:292–299. [PubMed: 18635500]

117. Elsharnouby NM, Eid HE, Abou Elezz NF, Moharram AN. Intraarticular injection of magnesium sulphate and/or bupivacaine for postoperative analgesia after arthroscopic knee surgery. Anesth Analg. 2008; 106:1548–1552. [PubMed: 18420874]

118. Paul S, Bhattacharjee DP, Ghosh S, Dawn S, Chatterjee N. Efficacy of intra-articular dexmedetomidine for postoperative analgesia in arthroscopic knee surgery. Ceylon Med J. 2005; 55:111–115. [PubMed: 21341623]

119. Ayoglu H, Altunkaya H, Bayar A, Turan IO, Ozer Y, Ege A. The effect of intraarticular combinations of tramadol and ropivacaine with ketamine on postoperative pain after arthroscopic meniscectomy. Arch Orthop Trauma Surg. 2010; 130:307–312. [PubMed: 18982335]

120. Borner M, Burkle H, Trojan S, Horoshun G, Riewendt HD, Wappler F. [Intra-articular ketamine after arthroscopic knee surgery. Optimisation of postoperative analgesia]. Anaesthesist. 2007; 56:1120–1127. [PubMed: 17726586]

121. Ng HP, Nordstrom U, Axelsson K, Perniola AD, Gustav E, Ryttberg L, Gupta A. Efficacy of intra-articular bupivacaine, ropivacaine, or a combination of ropivacaine, morphine, and ketorolac on postoperative pain relief after ambulatory arthroscopic knee surgery: a randomized double-blind study. Reg Anesth Pain Med. 2006; 31:26–33. [PubMed: 16418021]

122. Mannion S, Hayes I, Loughnane F, Murphy DB, Shorten GD. Intravenous but not perineural clonidine prolongs postoperative analgesia after psoas compartment block with 0.5% levobupivacaine for hip fracture surgery. Anesth Analg. 2005; 100:873–878. [PubMed: 15728081]

123. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidcaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. Drugs. 2010; 70(9):1149–1163. [PubMed: 20518581]

124. Cassuto J, Wallin G, Högström S, Faxén A, Rimbäck G. Inhibition of postoperative pain by continuous low-dose intravenous infusion of lidocaine. Anesth. Analg. 1985; 64:971–974. [PubMed: 3898920]

125. Rimbäck G, Cassuto J, Tollesson PO. Treatment of postoperative paralytic ileus by intravenous lidocaine infusion. Anesth. Analg. 1990; 70:414–419. [PubMed: 2316883]

126. Wu CT, Borel CO, Lee MS, Yu JC, Liou HS, Yi HD, Yang CP. The interaction effect of perioperative cotreatment with dextromethorphan and intravenous lidocaine on pain relief and recovery of bowel function after laparoscopic cholecystectomy. Anesth Analg. 2005; 100:448–453. [PubMed: 15673874]

127. Groudine SB, Fisher HA, Kaufman RP, Patel MK, Wilkins LJ, Mehta SA, Lumb PD. Intravenous lidocaine speeds the return of bowel function, decreases postoperative pain, and shortens hospital stay in patients undergoing radical retropubic prostatectomy. Anesth. Analg. 1998; 86:235–239. [PubMed: 9459225]

128. Koppert W, Weigand M, Neumann F, Sittl R, Schuettler J, Schmelz M, Hering W. Perioperative intravenous lidocaine has preventive effects on postoperative pain and morphine consumption after major abdominal surgery. Anesth. Analg. 2004; 98:1050–1055. [PubMed: 15041597]

129. Kaba A, Laurent SR, Detroz BJ, Sessler DI, Durieux ME, Lamy ML, Joris JL. Intravenous lidocaine infusion facilitates acute rehabilitation after laparoscopic colectomy. Anesthesiology. 2007; 106:11–18. [PubMed: 17197840]

130. Herroeder S, Pecher S, Schönherr ME, Kaulitz G, Hahnenkamp K, Friess H, Böttiger BW, Bauer H, Dijkgraaf MGW, Dijkgraaf OGW, Durieux ME, Hollmann MW. Systemic lidocaine shortens length of hospital stay after colorectal surgery: a double-blinded, randomized, placebo-controlled trial. Ann. Surg. 2007; 246:192–200. [PubMed: 17667496]

131. Kuo CP, Jao SW, Chen KM, Wong CS, Yeh CC, Sheen MJ, Wu CT. Comparison of the effects of thoracic epidural analgesia and i.v. infusion with lidocaine on cytokine response, postoperative pain and bowel function in patients undergoing colonic surgery. Br J Anaesth. 2006; 97:640–646. [PubMed: 16952918]

132. Swenson BR, Gottschalk A, Wells LT, Rowlingson JC, Thompson PW, Barclay M, Sawyer RG, Friel CM, Foley E, Durieux ME. Intravenous lidocaine is as effective as epidural bupivacaine in reducing ileus duration, hospital stay, and pain after open colon resection: a randomized clinical trial. Reg Anesth Pain Med. 2010; 35:370–376. [PubMed: 20588151]

133. Martin F, Cherif K, Gentili ME, Enel D, Abe E, Alvarez JC, Mazoit JX, Chauvin M, Bouhassira D, Fletcher D. Lack of impact of intravenous lidocaine on analgesia, functional recovery, and nociceptive pain threshold after total hip arthroplasty. Anesthesiology. 2008; 109:118–123. [PubMed: 18580181]

134. McKay A, Gottschalk A, Ploppa A, Durieux ME, Groves DS. Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery. Anesth. Analg. 2009; 109:1805–1808. [PubMed: 19923506]

135. De Oliveira GS, Fitzgerald P, Streicher LF, Marcus RJ, McCarthy RJ. Systemic lidocaine to improve postoperative quality of recovery after ambulatory laparoscopic surgery. Anesth Analg. 2012 May 14. [Epub ahead of print].

136. Bryson GL, Charapov I, Krolczyk G, Taljaard M, Reid D. Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy. Can J Anaesth. 2010; 57:759–766. [PubMed: 20532723]

137. Kang H, Kim BG. Intravenous lidocaine for effective pain relief after inguinal herniorrhaphy: a prospective, randomized, double-blind, placebo-controlled study. J Int Med Res. 2011; 39(2): 435–445. [PubMed: 21672347]

138. Kim TH, Kang H, Hong JH, Park JS, Baek CW, Kim JY, Jung YH, Kim HK. Intraperitoneal and intravenous lidocaine for effective pain relief after laparoscopic appendectomy: a prospective, randomized, double-blind, placebo-controlled study. Surg Endosc. 2011 Oct; 25(10):3183–3190. [PubMed: 21487863]

139. Grigoras A, Lee P, Sattar F, Shorten G. Perioperative intravenous lidocaine decreases the incidence of persistent pain after breast surgery. Clin J Pain. 2012 Jun 13. [Epub ahead of print].

140. Tissot S, Frering B, Gagnieu MC, Vallon JJ, Motin J. Plasma concentrations of lidocaine and bupivacaine after cervical plexus block for carotid surgery. Anesth Analg. 1997; 84:1377–1379. [PubMed: 9174324]

141. Ferrante FM, Paggioli J, Cherukuri S, Arthur GR. The analgesic response to intravenous lidocaine in the treatment of neuropathic pain. Anesth Analg. 1996; 82:91–97. [PubMed: 8712433]

142. Persaud N, Strichartz GR. Micromolar lidocaine selectively blocks propagating ectopic impulses at a distance from their site of origin. Pain. 2002; 99:333–340. [PubMed: 12237212]

143. Pintaric TS, Kozelj G, Stanovnik L, Casati A, Hocevar M, Jankovic VN. Pharmacokinetics of levobupivacaine 0.5% after superficial or combined (deep and superficial) cervical plexus block in patients undergoing minimally invasive parathyroidectomy. J Clin Anesth. 2008; 20:333–337. [PubMed: 18761239]

144. Rettig HC, Lerou JG, Gielen MJ, Boersma E, Burm AG. The pharmacokinetics of ropivacaine after four different techniques of brachial plexus blockade. Anaesthesia. 2007; 62:1008–1014. [PubMed: 17845652]

145. Latzke D, Marhofer P, Kettner SC, Koppatz K, Turnheim K, Lackner E, Sauermann R, Muller M, Zeitlinger M. Pharmacokinetics of the local anesthetic ropivacaine after transversus abdominis plane block in healthy volunteers. Eur J Clin Pharmacol. 2011; 68:419–425. [PubMed: 22037563]

146. Arthur, GR. Pharmacokinetics of Local Anesthetics. In: Strichartz, G., editor. Local Anesthetics. Heidelberg, New York: Springer-Verlag; 1987. p. 165-186.

147. Bertini L, Palmisani S, Mancini S, Martini O, Ioculano R, Arcioni R. Does local anesthetic dilution influence the clinical effectiveness of multiple-injection axillary brachial plexus block?: a prospective, double-blind, randomized clinical trial in patients undergoing upper limb surgery. Reg Anesth Pain Med. 2009; 34:408–413. [PubMed: 19920416]

148. Katz, J.; Clarke, H. Preventive analgesia and beyond: Current status, evidence, and future directions. In: Macintyre, PE.; Rowbotham, DJ.; Howard, R., editors. Clinical Pain Management: Acute Pain. 2nd ed.. London: Hodder Arnold Ltd; 2008. p. 154-198.

149. Araujo MC, Sinnott CJ, Strichartz GR. Multiple phases of relief from experimental mechanical allodynia by systemic lidocaine: responses to early and late infusions. Pain. 2003; 103:21–29. [PubMed: 12749955]

150. Ji RR, Gereau RWt, Malcangio M, Strichartz GR. MAP kinase and pain. Brain Res Rev. 2009; 60:135–148. [PubMed: 19150373]

151. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and prevention. Lancet. 2006; 367:1618–1625. [PubMed: 16698416]

152. Katz J, Seltzer Z. Transition from acute to chronic postsurgical pain: risk factors and protective facors. Expert Rev Neurother. 2009; 9(5):72.

Table 1

Peripheral nerve blocks and preventive analgesia, organized by surgical procedure.

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
Total knee arthroplasty			
[18]Wegener JT *et al.* 2011	GA + ***CFNB versus CFNB+SS sciatic nerve block versus CFNB+cont sciatic nerve block (36h)***	All subjects CFNB: 0.375% levobupivacaine 20mL then 0.125% levobupivacaine 10mL/h then 6mL/h post-op and 5mL bolus q30min PRN - CFNB only *(30)* - + SS sciatic nerve block: 0.375% levobupivacaine 20mL *(30)* - + cont sciatic nerve block: 0.375% levobupivacaine 20mL then 0.125% levobupivacaine 10mL/h intraop, 6mL/h post-op and 5mL bolus q30min PRN *(30)*	- Analgesic effect: yes (both sciatic groups) - Pain: decreased NRS in both SS and cont sciatic groups versus femoral catheter alone - Analgesic use: decreased in both SS and cont sciatic groups versus femoral catheter alone on POD1 and decreased in cont sciatic group POD2
[27]Affas F *et al.* 2011	Spinal + ***SSFNB q4h bolus post-op via catheter versus IA injection (24h)***	- FNB: 0.2% ropivacaine 30mL then 15mL bolus q4h×24h (20) - IA and periarticular: 0.2% ropivacaine 150mL with ketorolac and epinephrine *(20)*	- Analgesic effect: no difference - Pain: no difference - Analgesic use: no difference
[33]Dobydnjov I *et al.* 2011	Spinal + ***IA versus periarticular catheter (24h)***	All subjects: 0.2% ropivacaine 150mL +ketorolac+epi - IA catheter: 0.5% ropivacaine 2mL/h *(18)* - periarticular catheter: 0.5% ropivacaine 2mL/h *(18)*	- Analgesic effect: no difference - Pain: no difference - Analgesic use: no difference
[32]Essving P *et al.* 2011	Spinal + ***intrathecal morphine versus IA catheter (48h)***	- IA: 400mg ropivacaine +ketorolac+epi intraop then 200mg ropivacaine +ketorolac+epi POD1 and POD2 *(25)* - control: intrathecal morphine + saline equivalent volume *(25)*	- Analgesic effect: yes - Pain: decreased VAS - Analgesic use: decreased
[19]Cappelleri G *et al.* 2011	GA + cont lumbar plexus block + ***cont sciatic nerve block versus SS sciatic nerve block (48h)***	All subjects cont lumbar plexus block: 0.125% levobupivacine 8ml/h - cont sciatic: 20mL 0.37% levobupivacaine then 0.1mL/kg/h 0.06% levobupivacaine - SS sciatic: 20mL 0.37% levobupivacaine followed by normal saline infusion	- Analgesic effect: yes (cont catheter) - Pain: decreased VAS in cont catheter group - Analgesic use: decreased in cont catheter group
[14]Ilfeld B *et al.* 2010	GA + ***CFNB*** (active drug ×96h versus active drug ×24h then placebo ×72h)	All subjects: 1.5% mepivacaine with epi 40 mL - active infusion: 0.2% ropivacaine 6mL/h PCEA 4mL q30min ×36h then portable pump 5 mL/h bolus	- Analgesic effect: yes - Pain: no overall difference in numeric scores but pain < 4 earlier during hospitalization in

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
		4 mL/h q60min PRN ×60h *(39)* - control: 0.2% ropivacaine 6mL/h, bolus 4mL q30min ×24h then saline infusion ×72h *(38)*	ropivacaine versus placebo - Analgesic use: no difference
[29]Kazak Bengisun Z *et al.* 2010	Spinal + ***IA injection versus placebo***	- 200mg bupivacaine w/ epi 150 mL solution *(20)* - 200mg levobupivacaine w/ epi 150 mL solution *(20)* - normal saline 150 mL *(20)*	- Analgesic effect: yes for both levo- and bupivacaine - Pain: decreased VAS in levo-and bupivacaine groups versus placebo - Analgesic use: decreased in levo-and bupivacaine groups versus placebo
[30]Ong JC *et al.* 2010	Anesthetic not specified + ***IA infusion versus IA injection + infusion versus PCA (48h)***	- IA infusion: 0.25% bupivacaine 4 mL/h *(16)* - IA injection + infusion: injection—normal saline 50 mL, ketorolac 30mg, morphine 10mg, bupivacaine 100mg, infusion—as above *(21)* - PCA *(17)*	- Analgesic effect: yes, no difference between IA groups - Pain: VAS decreased in IA groups versus control but no difference between infusion versus injection +infusion - Analgesic use: decreased in IA groups versus control but no difference between infusion versus injection+infusion
[31]Gomez-Cardero P *et al.* 2010	Spinal + ***IA infusion versus placebo (24h)***	- 0.2% ropivacaine 5 mL/h *(25)* - normal saline 5 mL/h *(25)*	- Analgesic effect: yes - Pain: decreased VAS up to POD3, no difference at 1 month - Analgesic use: decreased up to POD3
[26]Carli F *et al.* 2010	Spinal + ***CFNB versus IA infusion (48h)***	All subjects posterior capsule: 0.2% ropivacaine 50 mL + ketorolac 15mg + epi - CFNB: 0.2% ropivacaine 8 mL bolus then 8mL/h *(20)* - IA: 100mL bolus solution of 0.2% ropivacaine + ketorolac 30mg + epi then 0.5% ropivacaine + ketorolac 30mg + epi 0.25 mg 50 mL solution infused over 24h post-op *(20)*	- Analgesic effect: yes CFNB versus IA infusion (note: ketorolac added to IA infusion) - Pain: no difference in numeric pain scores - Analgesic use: decreased in CFNB
[22]Hunt KJ *et al.* 2009	GA + ***SSFNB versus SSFNB-sciatic***	- SSFNB: 0.5% bupivacaine 10–15 mL *(33/31)* - sciatic: 0.5% bupivacaine 10–15 mL *(31)* - sham femoral: normal saline 10–15 mL *(24)*	- Analgesic effect: yes - Pain: decreased VAS in SSFNB and SSFNB-sciatic versus sham up to POD2; decreased VAS in SSFNB-sciatic versus SSFNB on day of surgery only

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
			- Analgesic use: decreased SSFNB-sciatic versus SSFNB or sham
[15]Shum CF *et al.* 2009	Spinal + ***CFNB versus PCA (48h)***	- 0.15% ropivacaine 10 mL/h ×24 h then 5 mL/h ×24h *(17)* - 0.2% ropivacaine 10 mL/h ×24h then 5 mL/h ×24h *(18)* - PCA *(20)*	- Analgesic effect: yes - Pain: difference in VAS only at 6h post-op in CFNB groups versus PCA - Analgesic use: decreased up to 72h post-op in CFNB groups versus PCA
[8]Cuvillon P *et al.* 2009 *includes lower leg/foot sx*	MAC or GA + ***SSFNB-sciatic*** (comparison of different LAs)	- 0.5% bupivacaine 40 mL *(20)* - 0.75% ropivacaine 40 mL *(20)* - 0.5% bupivacaine 20 mL + 2% lidocaine 20 mL *(21)* - 0.75% ropivacaine 20 mL + 2% lidocaine 20 mL *(21)* *(20 mL local anesthetic with epi in each block)*	- Analgesic effect: yes in bupivacaine versus bupivacaine-lidocaine - Pain: VAS no difference - Analgesic use: decreased in bupivacaine alone versus bupivacaine-lidocaine mixture group
[21]Sundarathiti P *et al.* 2009	Spinal + ***CFNB versus epidural (48h)***	- CFNB: bolus 0.25% levobupivacaine 20 mL then 0.125% levobupivacaine 8 mL/h ×48h *(30)* - epidural: 0.125% levobupivacaine with morphine 0.0125 mg/mL at 4 mL/h ×48h *(31)*	- Analgesic effect: yes (epidural) - Pain: decreased VAS in epidural group up to 6h postop, no difference between 2 groups 6–72h postop - Analgesic use: decreased use in epidural group
[36]Frassanito L *et al.* 2009	IV sedation + ***sciatic-SSLPB versus sciatic-CLPB (48h)***	- sciatic-SSLPB: sciatic--0.6% ropivacaine 15 mL, SSLPB--0.6% ropivacaine 30 mL *(22)* - sciatic-CLPB: sciatic--bolus as above; CLPB—bolus as above, then 0.2% ropivacaine 10 mL/h *(22)*	- Analgesic effect: no difference (sciatic-SSLPB versus sciatic-CLPB) - Pain: no difference in numerical pain score - Analgesic use: no difference
[28]Krenzel *et al.* 2009	Spinal + CFNB (24h) + ***IA injection versus placebo***	- All subjects CFNB: 0.5% ropivacaine 30 mL bolus, then 0.2% ropivacaine 10mL/h - IA injection: 0.5% ropivacaine 20 mL *(35)* - Placebo: posterior capsular injection 20 mL normal saline *(32)*	- Analgesic effect: yes - Pain: no difference in pain scores (although less "severe pain" scores in IA group (pain 7–10)) - Analgesic use: decreased in IA group but only in first 12 hours
[7]de Lima E Souza R *et al.* 2008 *includes ACL reconstruction*	Spinal + ***SSFNB versus no block***	- 0.25% bupivacaine 40 mL *(30)* - 0.25% ropivacaine 40 mL *(32)* - no block *(28)*	- Analgesic effect: yes (but no difference ropiv versus bupiv) - Pain: no difference in VAS between ropiv versus bupiv, but more severe

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
			pain (8–10) in no block group - Analgesic use: decreased at 10h post-op between LAs versus no block, no difference between groups at 24h
[16]Martin F *et al.* 2008	GA + ***CFNB-sciatic versus PCA (48h)***	- CFNB: bolus 0.75% ropivacaine 20 mL then 0.2% ropivacaine 0.15 mL/kg/h ×48h, sciatic: 0.75% ropivacaine 20 mL *(20)* - PCA *(18)*	- Analgesic effect: yes - Pain: VAS decreased in block group POD1 and POD7 but not beyond - Analgesic use: decreased in block group in PACU and POD1 but not beyond
[20]Heid F *et al.* 2008	GA + ***CFNB-sciatic (72h)*** (comparison of different LAs)	- Ropiv: CFNB--bolus 0.5% ropivacaine 35 mL then 0.2% ropivacaine 5mL/h with 5 mL PCA bolus q30min PRN; sciatic--bolus 25 mL 0.5% ropivacaine *(30)* - Levobupiv: CFNB--bolus 0.3125% levobupivacaine 35 mL then 0.125% levobupivacaine 5mL/h with 5 mL PCA bolus q30min PRN; sciatic--bolus 0.3125% levobupivacaine 25 mL *(30)*	- Analgesic effect: no difference ropivacaine versus levobupivacaine - Pain: no difference in numeric pain scores - Analgesic use: no difference
[38]Paauwe JJ *et al.* 2008	GA or spinal + ***CFNB (until POD1),*** then comparison of various bupiv doses QID bolus via FNB catheter until POD2	- CFNB (all subjects): bolus 0.2% ropivacaine 20 mL then 0.1% ropivacaine 5 mL/hr until POD1 AM - bolus ropivacaine 10 mL (0.1% or 0.05% or 0.025%) QID POD1–POD2 with ropivacaine bolus 10 mL q30min PRN *(12 each group)*	- Analgesic effect: yes (with 0.1% versus lower concentration) - Pain: decreased VAS in 0.1% versus 0.025% 30min after QID bolus - Analgesic use: no difference
[35]Campbell A. *et al.* 2008	Spinal + ***CLPB versus epidural (48h)***	- CLPB: 30 mL 0.5% levobupivacaine then 0.125% levobupivacaine and clonidine 1.2mcg/mL 10 mL/h *(29)* - epidural: 4 mL 0.5% levobupivacaine, then 0.125% levobupivacaine and clonidine 1.2mcg/mL 6 mL/h *(31)*	- Analgesic effect: no difference epidural versus CLPB (note: clonidine added to both infusions) - Pain: No difference in VAS >6h postop - Analgesic use: no difference
[34]Bagry H *et al.* 2008	Spinal + ***CLPB-continuous sciatic versus PCA (48h)***	- CLPB-continuous sciatic loading dose: 2% lidocaine w/ epi 0.5 mL/kg ½ in each catheter then 0.2% ropivacaine 8 mL/h CLPB and 5 mL/h sciatic catheter ×48h *(6)* - PCA *(6)*	- Analgesic effect: yes - Pain: VAS decreased POD1 and 2 with movement and POD2 only at rest - Analgesic use: no opioid used in catheter group

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
[10]Kardash K *et al.* 2007	Spinal +/− IV sedation + ***SSFNB versus obturator nerve block versus sham block***	- SSFNB/obturator nerve block: 0.5% bupivacaine with epi 20 mL *(19/20)* - sham block (simulated postspinal) *(20)*	- Analgesic effect: yes (SSFNB) - Pain at rest: no difference in numeric pain score - Pain with movement: decreased numeric pain score at PACU discharge in SSFNB versus obturator or sham, no difference 24–48h - Analgesic use: no difference
[39]Good RP *et al.* 2007	Anesthetic not specified + ***SSFNB versus PCA***	- 0.5% bupivacaine 40 mL *(22)* - PCA *(20)*	- Analgesic effect: yes - Pain: no difference - Analgesic use: decreased in SSFNB
[9]Beaulieu P *et al.* 2006	GA + ***SSFNB-sciatic*** (comparison of different LAs)	- SSFNB-sciatic: 0.5% bupivacaine or 0.5% ropivacaine 15 mL sciatic, 25 mL SSFNB of *(25 each LA group)*	- Analgesic effect: no clear difference ropiv versus bupiv - Pain: decreased in ropiv group 7–10h post-op but decreased in bupiv group at 28h, no difference at 48h - Analgesic use: increased in PACU in bupivacaine group but up to 48h post-op no difference between groups
[17]Seet E *et al.* 2006	Spinal + ***CFNB versus PCA (48h)***	- 0.15% ropivacaine 10 mL/hr ×24 hr then 5 mL/h next 24h *(17)* - 0.2% ropivacaine 10 mL/hr ×24h then 5 mL/h next 24h *(18)* - PCA *(20)*	- Analgesic effect: yes (but ropiv concentrations with equivalent effect) - Pain: no difference in VAS - Analgesic use: decreased in both ropiv groups versus control, no difference between ropiv groups
[6]Bunburaphong P *et al.* 2006	GA + ***SSFNB pre- versus postoperative***	- pre versus post-op SSFNB: 0.2% bupivacaine 30 mL *(24 each group)*	- Analgesic effect: no difference pre versus post-op SSFNB - Pain: no difference in numeric pain score - Analgesic use: no difference
[13]Salinas FV *et al.* 2006	Spinal + ***SSFNB versus CFNB (48h)***	- SSFNB: 0.375% ropivacaine with epi 30 mL *(18)* - CFNB: 0.375% ropivacaine with epi 30 mL bolus then 0.2% ropivacaine 10 mL/h started 6h after bolus ×48h *(18)*	- Analgesic effect: yes with CFNB - Pain: decreased VAS in CFNB up to POD2 - Analgesic use: decreased in CFNB up to POD2

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
[11]Ozen M *et al.* 2006	GA + ***SSFNB versus PCA***	- femoral block: 0.375% ropivacaine 40 mL *(14)* - PCA *(14)*	- Analgesic effect: yes - Pain: decreased VAS in SSFNB up to 8h postop - Analgesic use: decreased up to 48h in SSFNB
[23]Mistraletti G *et al.* 2006	Spinal + ***CFNB-continuous sciatic versus epidural versus PCA (48h)***	- CFNB-sciatic: CFNB--2% lidocaine w/ epi 0.25 mL/kg bolus, 0.2% ropivacaine 8 mL/h ×48h; continuous sciatic: 2% lidocaine w/ epi 0.25 mL/kg bolus, 0.2% ropivacaine 4 mL/h ×48h *(9)* - epidural: 2% lido with epi 3 mL bolus then 0.1% bupivacaine with fentanyl 3 mcg/mL at 10 mL/h (rate adjusted for pain) *(9)* - PCA *(9)*	- Analgesic effect: yes (but no difference between CFNB–cont sciatic and epidural) - Pain: decreased VAS in epidural and CFNB–cont sciatic and epidural versus PCA control (up to 48h in epidural and up to discharge in block group), no difference CFNB-cont sciatic versus epidural - Analgesic use: decreased in both groups versus PCA control, no data given for CFNB-cont sciatic versus epidural
[12]Yadeau JT *et al.* 2005	Combined Spinal Epidural (CSE for 48h) + ***SSFNB versus no additional block***	- epidural (all subjects): 0.06% bupivacaine and 10mcg/mL hydromorphone 3–6 mL/h with 5 mL PCEA bolus q15min PRN *(39/41)* - SSFNB: 0.375% bupivacaine with epi 30mL *(41)*	- Analgesic effect: yes with addition of SSFNB - Pain: decreased VAS POD1 and 2 in femoral group - Analgesic use: no difference between groups
[24]Pham Dang C *et al.* 2005	GA + ***CFNB-sciatic catheter versus CFNB (36h)***	- CFNB: 0.75% ropivacaine 15 mL bolus then 0.2% ropivacaine 2–5 mL/h with 10 mL bolus q30 min PRN *(14)* - sciatic: 0.2% ropivacaine 10 mL bolus q12h × 36h *(14)*	- Analgesic effect: yes (CFNB-sciatic versus CFNB) - Pain: decreased VAS in CFNB-sciatic versus CFNB (up to 36h) - Analgesic use: decreased in in CFNB-sciatic veruss CFNB
[25]Morin AM *et al.* 2005	GA + ***CLPB versus CFNB versus CFNB-sciatic (48h)***	- CLPB: 1+ prilocaine 30 mL and 0.75% ropivacaine 20 mL *(30)* - CFNB: 1% prilocaine 30 mL (20 mL if combined with sciatic) and 0.75% ropivacaine 20 mL (10 mL if combined with sciatic) *(30)* - CFNB-sciatic: CFNB—as above; sciatic--1% prilocaine 20 mL and 0.75% ropivacaine 10 mL *(30)*	- Analgesic effect: yes (CFNB-sciatic versus CFNB and CLPB) - Pain: no difference - Analgesic use: decreased in CFNB-sciatic vs CFNB and CLPB
[37]Watson MW *et al.* 2005	Spinal + ***CLPB-sciatic versus SSLPB-sciatic +placebo infusion (48h)***	- all subjects: SSLPB 0.5% levobupivacaine 25 mL, sciatic 0.5% levobupivacaine 15 mL	- Analgesic effect: yes CLPB vs SSLPB - Pain: no difference in VAS scores

Reference	Block/Intervention	Local Anesthetic/Intervention Details (n)	Outcomes
		- CLPB: 0.1% levobupivacaine 10 mL/h *(16)* - control: normal saline 10 mL/h *(16)*	- Analgesic use: decreased in levobupiv group
[5]Nechleba J et al. 2005	Anesthetic not specified + ***IA infusion versus placebo***	- 0.25% bupivacaine infusion (rate not specified) *(15)* - saline infusion *(15)*	- Analgesic effect: no - Pain: no difference in VAS - Analgesic use: no difference
ACL reconstruction			
[42]Wulf H *et al.* 2010	GA + ***SSFNB versus placebo***	- 0.2% ropivacaine 30 mL *(75)* - 0.75% ropivacaine 30 mL *(73)* - 0.25% bupivacaine 30 mL *(72)* - placebo (normal saline) 30 mL *(34)*	- Analgesic effect: yes - Pain: decreased VAS vs placebo in all 3 LA groups only at 4h postop - Analgesic use: decreased in LA groups vs placebo up to 24h
[43]Dauri M *et al.* 2009	IV sedation + ***CFNB-sciatic versus SSFNB-sciatic + IA infusion (36h)***	All subjects sciatic: 0.75% ropivacaine 20 mL and clonidine 30 mcg - CFNB: 0.2% ropivacaine 7 mL/h *(25)* - SSFNB + IA infusion: 0.75% ropivacaine 25 mL and clonidine 30 mcg then 0.2% ropivacaine 2 mL/h ×2 catheters *(25)*	- Analgesic effect: yes CFNB versus SSFNB+IA infusion (note: ketorolac and clonidine added to IA infusion) - Pain: decreased VAS in CFNB versus SSFNB+IA infusion at 12 h with movement and at rest and at 24 hrs with movement - Analgesic use: decreased in CFNB
[40]Matava MJ *et al.* 2009	GA + intra-articular/wound local anesthetic injection + ***SSFNB versus placebo***	- all subjects: IA 0.5% bupivacaine 20 mL - SSFNB: 0.5% bupivacaine with epi 30 mL *(31)* - placebo: 2 mL saline SQ *(25)*	- Analgesic effect: no (note: all received IA bupiv 20 mL) - Pain: VAS no difference - Analgesic use: no difference
[41]Parker RD *et al.* 2007	GA + ***IA infusion versus placebo versus no block (72h)***	- 0.25% bupivacaine 4 mL/h *(21)* - normal saline 4 mL/h *(21)* - no block *(21)*	- Analgesic effect: no - Pain: no difference in VAS - Analgesic use: decreased 48–72h only in bupiv vs no block but not vs placebo
Arthroscopic knee surgery			
[44]Eroglu A *et al.* 2010	Spinal + ***IA injection versus IA morphine versus placebo***	- 0.25% bupivacaine 20 mL *(20)* - 5 mg morphine in 20 mL saline *(20)* - normal saline 20 mL *(20)*	- Analgesic effect: yes (no difference bupivacaine versus morphine) - Pain: decreased VAS in bupivacaine/morphine versus placebo but no difference between bupivacaine and morphine (up to 24h) - Analgesic use: decreased in bupiv/morphine versus

			placebo but no difference between bupiv and morphine
[48]Atim A *et al.* 2007	Sedation/GA + ***SSLPB-sciatic versus SSFNB-sciatic***	40mL solution: 0.5% bupivacaine 15 mL, 2.0% prilocaine 15 mL, 0.9% normal saline 10 mL - SSLPB-sciatic: SSLPB—40mL, sciatic—20mL *(21)* - SSFNB-sciatic: SSFNB—40 mL, sciatic—20 mL *(21)*	- Analgesic effect: yes SSLPB-sciatic versus SSFNB-sciatic - Pain: decreased tourniquet pain in SSLPB-sciatic - Analgesic use: decreased in SSLPB-sciatic
[49]Jacobson E *et al.* 2006	GA + ***IA injection*** (comparing different LAs)	- 0.25% levobupivacaine 20 mL *(40)* - 0.5% levobupivacaine 20 mL *(40)* - 1% lidocaine 20 mL *(40)*	- Analgesic effect: yes 0.5% levobupiv versus other LAs - Pain: decreased VAS in 0.5% levobupiv versus other LAs at 24h (no difference 0.25% bupiv versus lidocaine) - Analgesic use: decreased in 0.5% levobupiv versus other LAs at 24h (no difference 0.25% bupiv versus lidocaine)
[47]Hadzic A et al. 2005	sedation/GA + ***SSLPB-sciatic versus no block***	- SSLPB-sciatic: 3% 2-chloroprocaine with bicarbonate and epi SSLPB—30 mL, sciatic—20 mL - no block *(25)*	- Analgesic effect: yes - Pain: decreased VAS in block group - Analgesic use: no difference
[45]Marret E *et al.* 2005	GA + ***IA injection versus placebo***	- 0.5% bupivacaine 30 mL *(15)* - 0.75% ropivacaine 30 mL *(15)* - normal saline 30 mL *(15)*	- Analgesic effect: yes ropiv versus bupiv/saline - Pain: decreased VAS in ropiv versus bupiv/saline (no difference between bupiv versus saline) - Analgesic use: decreased in ropiv versus bupiv/saline at 24h (no difference between bupiv versus saline)
[46]Goodwin RC *et al.* 2005	GA + ***IA injection versus placebo*** (different LAs pre- and postincision)	- pre incision: 0.25% bupivacaine w/ epi 60 mL; postincision: saline 60 mL *(9)* - pre incision: 0.25% bupivacaine with epi and 1mg morphine; post incision: saline 60 mL *(7)* - pre incision: saline 60 mL; post incision 0.25% bupivacaine with epi 60 mL *(10)* - pre incision: saline 60 mL; post incision: 0.25% bupivacaine with epi and 1 mg morphine *(10)* - pre incision: saline with epi 60 mL; post incision: saline 60 mL *(8)*	- Analgesic effect: yes, no difference if morphine added - Pain: decreased pain score in bupiv and bupiv/morphine group versus placebo regardless of pre versus postincisional administration (no benefit if morphine added) - Analgesic use: decreased in bupiv and bupiv/morphine group versus placebo regardless of pre versus postincisional administration (no benefit if morphine added)

		- pre incision: 60 mL saline; post incision: saline with epi 60 mL *(10)*	
Total hip arthroplasty			
[53]Murphy TP *et al.* 2012	spinal + ***periarticular injection versus placebo***	- 0.25% levobupivacaine 60mL*(23)* - control: equivalente volumen normal saline *(25)*	- Analgesic effect: yes - Pain: no difference - Analgesic use: decreased
[57]Ilfeld BM *et al.* 2011	GA + ***CFNB versus CLPB (48h)***	- CFNB: 0.2% ropivacaine 6 mL/h, 4mL bolus q30min PRN ×48h *(25)* - CLPB: as above *(22)*	- Analgesic effect: no difference (CFNB versus CLPB) - Pain: no difference - Analgesic use: no difference
[54]Ilfeld BM *et al.* 2010	GA + ***CLPB (48h)***, comparing 2 ropiv concentrations	- all subjects: 2% mepivacaine w/ epi 15mL bolus - 0.1% ropivacaine 12 mL/h ×48h, 4 mL bolus PRN *(26)* - 0.4% ropivacaine 3mL/h ×48h,1 mL bolus PRN *(24)*	- Analgesic effect: no difference between 2 ropiv concentrations - Pain: no difference in numeric pain scores - Analgesic use: no difference
[50]Chen DW *et al.* 2010	GA + ***IA infusion versus placebo (48h)***	- 0.5% bupivacaine 24 mL bolus then 2 mL/h *(46)* - normal saline bolus 24 mL then infusion 2mL/h *(46)*	- Analgesic effect: yes - Pain: no difference in VAS scores - Analgesic use: decreased in bupiv group only POD 2 and POD 3 (no difference POD 1)
[56]Ilfeld BM *et al.* 2008	GA + ***CLPB (24h),*** then randomized to ropivacaine or placebo until POD4	- all subjects: 2% mepivacaine with epi 15 mL then 0.5% ropivacaine with epi 10 mL, then 0.2% ropivacaine 8 mL/h, bolus 4 mL q30min PRN, ×24h POD1 randomization: - 0.2% ropivacaine 8 mL/h ×72h *(24)* - placebo (normal saline) 8 mL/h ×72h *(23)*	- Analgesic effect: no difference (CLPB 24h versus 96h) - Pain: no difference in numeric pain scores - Analgesic use: no difference
[55]De Leeuw MA *et al.* 2008	GA + ***sciatic-SSLPB***, comparison of different LAs	- 0.3% levobupivacaine 50 mL *(15)* - 0.45% ropivacaine 50 mL *(15)* - 0.3% bupivacaine with epi 50 mL *(15)*	- Analgesic effect: no difference between LAs - Pain: no change in VAS scores (only significant lowering in ropiv vs levobupiv at 4h) - Analgesic use: no difference
[51]Becchi C *et al.* 2008	Spinal + ***CLPB versus IV pain med infusion (48h)***	- CLPB: 0.75% ropivacaine bolus (0.4 mL/kg) then 0.2% ropivacaine infusion 10 mL/h *(37)*	- Analgesic effect: yes - Pain: decreased pain scores block versus control up to 48h

		- control: 0.1% morphine and 0.12% ketorolac 2 mL/h IV *(36)*	- Analgesic use: decreased in block group up to 24h
[52]Siddiqui ZI *et al.* 2007	GA + ***CLPB versus PCA (36h)***	- 2% lidocaine with epi 3 mL and 0.25% bupivacaine 20 mL then 0.125% bupivacaine 10 mL/h *(17)* - PCA *(17)*	- Analgesic effect: yes - Pain: decreased in CLPB - Analgesic use: decreased in CLPB

Foot and ankle surgery			
[59]Fournier R *et al.* 2010	No anesthesia or GA + ***SS sciatic*** (comparing LAs)	- 0.5% levobupivacaine 20 mL *(40)* - 0.5% ropivacaine 20 mL *(40)*	- Analgesic effect: yes levobupiv - Pain: tourniquet pain measured but not reported - Analgesic use: decreased in levobupiv group
[61]Ilfeld BM *et al.* 2008	No anesthesia + ***continuous poplitealsciatic nerve block (48h)*** (comparing different LA concentrations)	all subjects pre-op: 1.5% mepivacaine with epi 50 mL bolus - 0.2% ropivacaine 8 mL/h, 4 mL bolus q30 min PRN *(25)* - 0.4% ropivacaine 4 mL/h, 2 mL bolus q30 min PRN *(25)*	- Analgesic effect: no difference with equal ropiv doses - Pain: no difference in numeric scores - Analgesic use: no difference
[58]Capdevila X *et al.* 2006	GA + SS popliteal block + ***cont popliteal block versus PCA (72h)*** *(note: arthroscopic shoulder surgery with ISB also studied)*	SS popliteal block (all subjects): 0.5% ropivacaine 30 mL - cont popliteal block: 0.2% ropivacaine 7 mL/hr *(15)* - basal-bolus popliteal block: 0.2% ropivacaine 5 mL/hr, 2 mL bolus q12min PRN *(15)* - PCA *(13)*	- Analgesic effect: yes (cont or basal-bolus) versus PCA - Pain: decreased (cont or basal-bolus) versus PCA - Analgesic use: decreased (cont or basal-bolus) versus PCA
[60]Casati A *et al.* 2005	No anesthesia or sedation + ***SS sciatic*** (comparing different LAs)	- 0.5% levobupivacaine 20 mL *(15)* - 0.75% levobupivacaine 20 mL *(15)* - 0.5% ropivacaine 20 mL *(15)*	- Analgesic effect: yes 0.75% levobupiv versus lower concentration LAs - Pain: decreased VAS in 0.75% levobupiv at 8h only - Analgesic use: decreased in 0.75% levobupiv versus other LAs

Arthroscopic Shoulder Surgery			
[65]DeMarco JR *et al.* 2011	GA + postoperative IA catheter (72h) + ***preoperative SS ISB versus placebo injection***	All subjects subacromial catheter: 0.5% bupivacaine 2mL/h for 72h - SS ISB: 0.5% ropivacaine 30mL *(28)* - placebo: normal saline 10mL *(25)*	- Analgesic effect: yes - Pain: decreased VAS only up to 6h postop - Analgesic use: no difference
[71]Fredrickson MJ *et al.* 2010	GA + superficial cervical plexus block + ***SS ISB versus cont ISB (48h)***	All subjects superficial cervical plexus block: 1 % lidocaine 5– 10 mL - SS ISB: 0.5% ropivacaine 30 mL - cont ISB: 0.5% ropivacaine 30 mL then 0.2%	- Analgesic effect: yes (cont versus SS ISB) - Pain: decreased numeric pain score up to POD1 cont versus SS

		ropivacaine 2 mL/hr bolus 5 mL q60 min PRN	- Analgesic use: decreased up to POD2 cont versus SS
[67]Winkler T *et al.* 2009	GA + ***continuous ISB versus subacromial infusion (48h)***	- cont ISB: 0.75% ropivacaine 10 mL bolus then 2% ropivacaine 2 mL/h *(20)* - subacromial: 0.75% ropivacaine 10 mL bolus then 2% ropivacaine 2 mL/h *(20)*	- Analgesic effect: yes ISB versus subacromial - Pain: decreased VAS at 8 and 12h post-op for ISB group, no difference after 12–43h - Analgesic use: no difference
[68]Fontana C *et al.* 2009	GA + ***IA injection versus subacromial injection versus SS ISB versus IA + subacromial injection versus no block***	- SS ISB: 0.5% levobupivacaine 30 mL with epi *(24)* - IA: 0.5% levobupivacaine 30 mL with epi *(24)* - subacromial: 0.5% levobupivacaine 30 mL with epi *(24)* - IA + subacromial: 0.5% levobupivacaine with epi 15 mL each site *(24)* - control: no block *(24)*	- Analgesic effect: yes all groups versus control (ISB overall decreased fentanyl use versus all groups) - Pain: decreased VAS in subacromial, subacromial+IA and ISB (but not IA) versus control - Analgesic use: decreased in all groups versus control at 24h (and overall decreased use in ISB versus other groups)
[62]Banerjee *SS et al.* 2008	Unspecified anesthetic + ***subacromial infusion versus placebo (48h)***	all subjects subacromial bolus: 0.25% bupiv with epi 35 mL - 0.25% bupivacaine 2 mL/h *(20)* - 0.25% bupivacaine 5 mL/h *(20)* - normal saline 5 mL/h *(20)*	- Analgesic effect: no - Pain: no difference in VAS - Analgesic use: no difference
[64]Ciccone WJ *et al.* 2008	GA + ***SS ISB versus subacromial infusion versus SS ISB + subacromial infusion versus SS ISB + saline subacromial infusion (48h)***	- SS ISB: 0.3% ropivacaine 30 mL - subacromial infusion: 0.5% buipvacaine 20 mL then 5 mL/h, 1 mL bolus PRN - SS ISB + subacromial infusion: as above - SS ISB + saline subacromial infusion: as above + saline 5 mL/h, 1 mL bolus PRN *(76)*	- Analgesic effect: yes ISB +/− subacromial infusion or placebo versus subacromial infusion alone - Pain: decreased VAS immediately post-op all SS ISB groups versus subacromial infusion alone - Analgesic use: decreased in all block groups versus subacromial infusion alone
[63]Cho NS *et al.* 2007	Unspecified anesthetic + ***subacromial infusion versus PCA (48h)***	- 0.5% bupivacaine (rate not specified)*(20)* - PCA *(20)*	- Analgesic effect: no - Pain: no difference - Analgesic use: not specified
[70]Webb D *et al.* 2007	Unspecified anesthetic + ***SS ISB versus IA infusion (48h)***	- interscalene: 0.5% bupivacaine with epi single-shot injection (volume not specified) *(29)*	- Analgesic effect: no difference ISB versus IA infusion - Pain: no difference in VAS

		- IA: 0.5% bupivacaine infusion (rate not specified) *(28)*	- Analgesic use: no difference
[58]Capdevila X *et al.* 2006	GA + SS ISB + ***cont ISB versus basal-bolus ISB versus PCA (72h)*** *(note: hallux valgus surgery with popliteal block also studied)*	SS ISB (all subjects): 0.5% ropivacaine 30 mL - cont ISB: 0.2% ropivacaine 7 mL/hr *(15)* - basal-bolus ISB: 0.2% ropivacaine 5 mL/hr, 2 mL bolus q12min PRN *(15)* - PCA *(10)*	- Analgesic effect: yes ISB (cont or basal-bolus) versus PCA - Pain: decreased ISB (cont or basal-bolus) versus PCA - Analgesic use: decreased ISB (cont or basal-bolus) versus PCA
[69]Delaunay L *et al.* 2005	SS ISB anesthetic + ***continuous ISB versus subacromial infusion (48h)***	All subjects: SS ISB 1.5% mepivacaine 30 mL bolus - cont ISB: 0.2% ropivacaine 5 mL/h, 5 mL bolus q 30min PRN *(15)* - subacromial infusion: 0.2% ropivacaine 5 mL/h, 5 mL bolus q 30min PRN *(15)*	- Analgesic effect: yes cont ISB versus subacromial infusion - Pain: decreased VAS in cont ISB up to 24h - Analgesic use: decreased in cont ISB up to 48h

Open Shoulder Surgery			
[77]Goebel S *et al.* 2010	GA + SS ISB + ***ISB patient-controlled catheter versus placebo (72h)***	All subjects: SS ISB 0.75% ropivacaine 30 mL - patient-controlled ISB: 0.2% ropivacaine bolus 10 mL q15min PRN - placebo: normal saline bolus 10 mL q15min PRN	- Analgesic effect: yes (but not beyond 24h postop) - Pain: no difference - Analgesic use: decreased (but not beyond 24h postop)
[82]Borgeat A *et al.* 2010	GA + ***cont ISB (48h)*** (comparison of different LA concentrations)	All subjects: SS ISB 0.5% ropivacaine 40 mL - 0.2% ropivacaine 14 mL/h *(40)* - 0.3% ropivacaine 14 mL/h *(40)*	- Analgesic effect: yes 0.3% versus 0.2% ropiv - Pain: VAS no difference - Analgesic use: decreased 0.3% versus 0.2% ropiv
[83]Fredrickson MJ *et al.* 2009	GA + ***cont superior trunk block*** (comparison of different LA concentrations)	All subjects: 0.5% ropivacaine 30 mL - 0.2 % ropivacaine 2 mL/h *(32)* - 0.4% ropivacaine 2 mL/h *(33)*	- Analgesic effect: no difference 0.2% versus 0.4% ropiv - Pain: no difference 0.2% versus 0.4% ropiv - Analgesic use: no difference 0.2% versus 0.4% ropiv
[81]Le LT *et al.* 2008	GA + ***SS ISB*** (comparison of different LA concentrations)	All subjects: 1.5% mepivacaine 40 mL - 0.2% ropivacaine 8 mL/h, bolus 4 mL q30min PRN *(25)* - 0.4% ropivacaine 4 mL/h, bolus 2 mL q30min PRN *(25)*	- Analgesic effect: yes 0.2% versus 0.5% ropiv - Pain: decreased pain scores POD 2 and 3 0.2% versus 0.5% ropiv - Analgesic use: decreased 0.2% versus 0.5% ropiv
[80]Riazi S *et al.* 2008	GA + ***SS ISB*** (different volumes of LA)	- 0.5% ropivacaine 5 mL *(20)*	- Analgesic effect: no difference 5 versus 20 mL 0.5% ropiv

		- 0.5% ropivacaine 20 mL *(20)*	- Pain: no difference in numeric pain score - Analgesic use: no difference
[78]Hofmann-Kiefer K *et al.* 2008	GA + ***cont ISB versus PCA (72h)***	- cont ISB: 0.75% ropivacaine 40 mL then 0.2% ropivacaine 10 mL/h, 10 mL bolus q20min PRN *(36)* - PCA *(34)*	- Analgesic effect: yes - Pain: decreased VAS up to 72h postop - Analgesic use: decreased
[79]Ilfeld BM *et al.* 2006	GA + SS ISB ***cont ISB versus placebo (48h)***	All subjects: SS ISB 1.5% mepivacaine 40 mL and 0.5% ropivacaine 10 mL - cont ISB (started 24h postop): 0.2% ropivacaine 7 mL/h, 3 mL bolus q60 min PRN *(16)* - placebo: normal saline 7 mL/h, 3 mL bolus q60 min PRN *(14)*	- Analgesic effect: yes - Pain: decreased numeric pain scores POD 1–4 - Analgesic use: decreased POD 1–4
[76]Hadzic A *et al.* 2005	GA + ***SS ISB versus no block***	- SS ISB: 0.75% ropivacaine 35–40 mL *(25)* - control: no block *(25)*	- Analgesic effect: yes, but not beyond 24h - Pain: no difference (VAS), but 4 versus 0 pain related hospital admissions in no block group versus ISB - Analgesic use: decreased

Hand/ /upper limb surgery			
[89]O'Donnell BD *et al.* 2009	***SS axillary block versus GA (no block)***	- axillary block: 2% lidocaine w/ epi 10 mL and 0.5% bupivacaine 10mL and 150mg clonidine *(50)* - control: no block with GA *(50)*	- Analgesic effect: yes - Pain: decreased VAS up to 6h postop - Analgesic use: decreased in block group

TAP block (laparosocopy, open appy, lap chole, c/s, TAH, bowel resection)			
[92]De Oliveira GS *et al.* 2011 (lap gyn)	GA + ***bilateral TAP block versus placebo injection***	- TAP: 0.25% or 0.5% ropivacaine 15mL bilateral *(47)* - placebo: normal saline equivalent volume *(23)*	- Analgesic effect: yes - Pain: decreased NRS for 0.5% ropiv group - Analgesic use: decreased in both ropiv groups
[101]El-Dawlatly AA *et al.* 2009 (lap chole)	GA + ***bilateral TAP block versus no block/PCA***	- TAP: 0.5% bupivacaine 15 mL bilateral *(21)* - no block/PCA *(21)*	- Analgesic effect: yes - Pain: no pain scores reported - Analgesic use: decreased up to 24h postop
[102]Sandeman DJ *et al.* 2011 (lap appy)	GA + ***bilateral TAP block versus no block***	All patients: 0.2% ropivacaine 1mg/kg port-site infiltration	- Analgesic effect: no - Pain: no difference

		- TAP: 0.2% ropivacaine 0.5mg/kg bilateral *(46)* - no block *(47)*	- Analgesic use: no difference
[93]Niraj G. *et al* 2011 (upper abdominal surgery)	GA/Epidural + ***Bilateral TAP catheters versus epidural analgesia (72h)***	- TAP: 0.375% bupivacaine 1mg/kg every 8 hours *(29)* - Epidural control: 0.25% bupivacaine 20mL bolus intraop then 0.125% bupivacaine with fentanyl 2mcg/mL 6mL/h with PCEA bolus 2mL q30min *(33)*	- Analgesic effect: yes (but not superior to epidural group) - Pain: no difference between groups - Analgesic use: increased in TAP group
[98]McDonnel l JG *et al.* 2007 (bowel resection)	GA + ***Bilateral TAP block versus no block***	- TAP: 0.375% levobupivacaine 20 mL bilateral *(16)* - no block *(16)*	- Analgesic effect: yes - Pain: decreased VAS up to 24h postop - Analgesic use: decreased
[95]Carney J *et al.* 2010 (open appy)	GA + ***right TAP block versus placebo injection***	- TAP: 0.75% ropivacaine 2.5mg/kg *(19)* - placebo: equivalent ropiv volume but normal saline *(21)*	- Analgesic effect: yes - Pain: decreased VAS up to 48h postop - Analgesic use: decreased up to 48h postop
[100]Niraj G *et al.* 2009 (open appy)	GA + ***right TAP block versus no block***	- TAP: 0.5% bupivacaine 20 mL *(24)* - no block *(23)*	- Analgesic effect: yes - Pain: decreased VAS up to 24h postop - Analgesic use: decreased up to 24h postop
[103]Costello JF *et al.* 2009 (c/s)	Spinal + ***bilateral TAP block versus placebo injection***	All subjects: spinal 0.375% bupivacaine 12mg + fentanyl 10mcg + morphine 100 mcg - TAP: 0.375% ropivacaine 20 mL bilateral *(47)* - placebo: normal saline 20 mL *(49)*	- Analgesic effect: no (Note: morphine given via spinal both groups) - Pain: no difference VAS - Analgesic use: no difference
[97]Belavy D *et al.* 2009 (c/s)	Spinal + ***Bilateral TAP block versus placebo injection***	All subjects: spinal 0.5% bupivacaine 11mg + fentanyl 15mcg - TAP: 0.5% ropivacaine 20 mL *(23)* - placebo: normal saline 20 mL *(24)*	- Analgesic effect: yes - Pain: decreased VAS up to 48h - Analgesic use: decreased up to 48h
[99]McDonnel l JG *et al.* 2008 (c/s)	Spinal + ***Bilateral TAP versus placebo injection***	All subjects spinal: 0.5% bupivacaine 12mg + fentanyl 25mcg - TAP: ropivacaine 1.5mg/kg total (max 150mg) bilateral *(25)* - placebo: equivalent volume normal saline *(25)*	- Analgesic effect: yes - Pain: decreased VAS - Analgesic use: decreased up to 48h
[94]Atim A *et al.* 2011 (TAH)	GA + ***bilateral TAP block versus placebo injection versus local wound infiltration***	- TAP: 0.25% bupivacaine 20mL bilateral *(18)* - placebo: normal saline equivalent volume *(18)* - control: bupivacaine 0.25% 20mL local wound infiltration *(19)*	- Analgesic effect: yes - Pain: decreased VAS up to 24h for TAP group versus placebo and control - Analgesic use: decreased in TAP group up to 24h versus placebo and control

[96]Carney J *et al.* 2008 (TAH)	GA + ***Bilateral TAP block versus placebo injection***	- TAP: 0.75% ropivacaine 1.5 mg/kg total (max 150mg) bilateral*(24)* - placebo: equivalent normal saline injection *(26)*	- Analgesic effect: yes - Pain: decreased VAS up to 48h postop - Analgesic use: decreased up to 48h postop

Analgesic Use = opioid consumption, non-opioid consumption, or combination opioid + non-opioid consumption
Bupiv = bupivacaine
Cont = continuous
CFNB = continuous femoral nerve block
CLPB = continuous lumbar plexus block
Cont ISB = continuous interscalene block
c/s = cesarean section delivery
Epi = epinephrine
GA = General Anesthesia
IA = intraarticular/periarticular
Intra-op = intraoperative
IP = intraperitoneal
IV = intravenous
LA = local anesthetics
Lap appy = laparoscopic appendectomy
Lap chole = laparoscopic cholecystectomy
Lap gyn = laparoscopic gynecologic surgery
Levobupiv = levobupivacaine
Lido = lidocaine
Open appy = open appendectomy
PCA = patient-controlled analgesia
POD = postoperative day
Post-op = postoperative
Ropiv = ropivacaine
Sciatic = sciatic nerve block
SSFNB = single-shot femoral nerve block
SS ISB = single-shot interscalene block
SSLPB = single-shot lumbar plexus block
TAH = total abdominal hysterectomy
TAP block = transversus abdominus plane block
VAS = visual analogue scale

Table 2

Perioperative IV lidocaine and preventive analgesia, grouped by surgical type

Reference	Surgical Type	IV Local Anesthetic Dosing (n)	Outcomes
[124]Cassuto J *et al.* 1985	Cholecystectomy	- Lidocaine bolus (100mg) and infusion (2mg/min for 24h) *(10)* - Equal volume of saline *(10)*	Analgesic effect: yes Pain: decreased pain scores Analgesic use: decreased POD1 and POD2
[125]Rimbäck G *et al.* 1990	Cholecystectomy	- Lidocaine bolus (100mg) and infusion (3mg/min, stopped 1t 24hr postop) *(15)* - Equal volume of saline *(15)*	Analgesic effect: yes Pain: n/a Analgesic use: decreased POD1 and POD2
[126]Wu CT *et al.* 2005	Laparoscopic cholecystecomy	4 groups: - chlorpheniramine bolus IM, saline infusion IV intraop *(25)* - dextrometorphan IM, saline infusion IV intraop *(25)* - chlorpheniramine bolus IM, lidocaine infusion 3mg/kg/h intraop *(25)* - dextrometorphan IM, lidocaine infusion 3mg/kg/h IV intraop *(25)*	Analgesic effect: yes Pain: VAS scores decreased during coughing in the first 12–24h Analgesic use: decreased
[127]Groudine SB *et al.* 1998	Radical retropubic prostatectomy	- Lidocaine bolus (1.5mg/kg) and infusion (3mg/min unless weight < 70kg, then 2mg/min until 60 min after skin closure) *(20)* - Equal volume of saline *(20)*	Analgesic effect: yes Pain: two-third reduction in total pain score index Analgesic use: no difference
[128]Koppert W *et al.* 2004	Major abdominal surgery	- Lidocaine bolus (1.5mg/kg) and infusion (1.5mg/kg/h, stopped 1hr postop) *(20)* - Equal volume of saline *(20)*	Analgesic effect: yes Pain: decreased pain scores during movement in the first 72h Analgesic use: decreased
[129]Kaba A *et al.* 2007	Laparoscopic colectomy	- Lidocaine bolus (1.5mg/kg) and infusion (2mg/kg/h intraoperatively and 1.33mg/kg/h for 24h postop) *(20)* - Equal volume of saline *(20)*	Analgesic effect: yes Pain: decreased pain during mobilization and coughing, no difference at rest Analgesic use: decreased during first 24h post-op
[130]Herroder S *et al.* 2007	Colorectal surgery	- Lidocaine bolus (1.5mg/kg) and infusion (2mg/min until 4h postop) *(31)* - Equal volume of saline *(29)*	Analgesic effect: no Pain: no difference, although trended towards decreased VAS scores Analgesic use: no difference
[131]Kuo CP *et al.* 2006	Elective surgery for colon cancer	- Lidocaine bolus (2mg/kg) and infusion (3mg/kg/h intraop, PCEA with morphine/ropivacaine postop) *(20)*	Analgesic effect: yes Pain: decreased pain scores at rest 4h postop, decreased

Reference	Surgical Type	IV Local Anesthetic Dosing (n)	Outcomes
		- Equal amounts of saline, PCEA with morphine/ropivacaine post-op *(20)*	pain scores during coughing for 12h Analgesic use: higher first PCEA trigger times and decreased opioid consumption
[132]Swenson BR *et al.* 2010	Open colon surgery	- Lidocaine bolus (1.5mg/kg) and infusion (1 mg/min in patients < 70 kg, 2 mg/min in patients > or = 70 kg, maintained until return of bowel function or post-op day 5) *(22)* - Lidocaine bolus (1.5mg/kg) and epidural analgesia (bupivacaine 0.125% and hydromorphone 6 mcg/mL, started at 10 mL/hr within 1 hr of the end of surgery, maintained until return of bowel function or postoperative day 5) *(20)*	Analgesic effect: no, absence of placebo group Pain: no difference Analgesic use: no difference
[133]Martin F *et al.* 2008	Total hip arthroplasty	- Lidocaine bolus (1.5mg/kg) and infusion (1.5mg/kg/h, stopped 1hr after skin closure) *(28)* - Equal volume of saline *(30)*	Analgesic effect: no Pain: no difference Analgesic use: no difference
[134]McKay A *et al.* 2009	Ambulatory surgery	- Lidocaine bolus (1.5mg/kg) and infusion (2mg/kg/h, continued until 1hr after arrival in the PACU) *(29)* - Equal volume of saline *(27)*	Analgesic effect: yes Pain: decreased pain at rest in PACU; no difference 24h after discharge Analgesic use: decreased in PACU, no difference 24h after discharge
[136]Bryson GL *et al.* 2010	Abdominal hysterectomy	- Lidocaine bolus (1.5mg/kg) and infusion (3mg/kg/h, until the end of surgery) *(44)* - Equal volume of saline *(46)*	Analgesic effect: no Pain: no difference Analgesic use: no difference
[135]De Oliveira GS *et al.* 2012	Ambulatory laparoscopic surgery	- Lidocaine bolus (1.5mg/kg) and infusion (2mg/kg/h, until the end of the surgical procedure) *(31)* - Equal volume of saline *(32)*	Analgesic effect: yes Pain: decreased pain scores in PACU Analgesic use: decreased first 24h
[137]Kang H *et al.* 2011	Inguinal Herniorrhaphy	- Lidocaine bolus (1.5mg/kg) and infusion (2mg/kg/h, intraoperatively) *(32)* - Equal volume of saline *(32)*	Analgesic effect: yes Pain: decreased pain scores until 12h postop Analgesic use: decreased opioid consumption and frequency of PCA button pushes
[138]Kim TH *et al. 2011*	Laparoscopic appendectomy	- IP group: Intraperitoneal instillation of lidocaine (3.5mg/kg), IV injection of saline *(25)* - IV group: Intraperitoneal instillation of saline, IV injection of lidocaine bolus (1.5mg/kg), followed by	Analgesic effect: yes Pain: decreased pain scores until 8h postop

Reference	Surgical Type	IV Local Anesthetic Dosing (n)	Outcomes
		continuous infusion (2mg/kg/h intraop) *(22)* - Control group: Intraperitoneal instillation and IV injection of saline *(21)*	Analgesic use: decreased up to 24h
[139]Grigoras A *et al.* 2012	Breast surgery	- Lidocaine bolus (1.5mg/kg) and infusion (1.5mg/kg/h, stopped 1h postop) *(17)* - Equal volume of saline *(19)*	Analgesic effect: yes Pain: decreased incidence of persistent postsurgical pain Analgesic use: no difference

Analgesic Use = opioid consumption, non-opioid consumption, or combination opioid + non-opioid consumption
Bupiv = bupivacaine
Cont = continuous
CFNB = continuous femoral nerve block
CLPB = continuous lumbar plexus block
Cont ISB = continuous interscalene block
c/s = cesarean section delivery
Epi = epinephrine
GA = General Anesthesia
IA = intraarticular/periarticular
Intra-op = intraoperative
IP = intraperitoneal
IV = intravenous
LA = local anesthetics
Lap appy = laparoscopic appendectomy
Lap chole = laparoscopic cholecystectomy
Lap gyn = laparoscopic gynecologic surgery
Levobupiv = levobupivacaine
Lido = lidocaine
Open appy = open appendectomy
PCA = patient-controlled analgesia
POD = postoperative day
Post-op = postoperative
Ropiv = ropivacaine
Sciatic = sciatic nerve block
SSFNB = single-shot femoral nerve block
SS ISB = single-shot interscalene block
SSLPB = single-shot lumbar plexus block
TAH = total abdominal hysterectomy
TAP block = transversus abdominus plane block
VAS = visual analogue scale