

Standardized Multimodal Pain Management Reduces Post-Operative Pain and Length of Stay in Hospital for Total Knee Arthroplasty: A Retrospective Review

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Citation

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Abstract

Study Objective: To evaluate the utility of multimodal pain management subsequent to general or neuraxial anesthesia following total knee arthroplasty.

Design: Retrospective review. **Setting:** University-affiliated teaching hospital. **Patients:** 389 patients (ASA physical status I-IV) scheduled for elective total knee replacement surgery over 3 year period. **Interventions and Measurements:** A total of 218 patients met inclusion criteria: 1) status-post a total knee arthroplasty 2) femoral nerve block with a continuous infusion of 0.1% ropivacaine 3) femoral catheter discontinued on post-op day 3, and 4.) follow-up with acute pain service. The study group (S) (N=105) received multimodal pain management consisting of a continuous femoral nerve blockade, celecoxib 200mg PO Q24 hrs, oxycontin 10mg PO Q12, acetaminophen 1000mg PO TID, and Percocet 5/325 1-2 tabs PO Q4-6 hr PRN (≤ 3 tabs/24hrs). The control group (NS) (N=113) received a continuous femoral nerve block with a non-standardized pain management regimen as prescribed by the orthopedic service. **Outcome measurements included:** mode of anesthesia (neuraxial vs. GA); length of surgery; time to ambulation and 90° flexion; pain score, morphine equivalents and length of stay in hospital. **Main Results:** The study group demonstrated decreased pain scores on the third post-operative day as compared to the control group (S=2.43 vs. NS=3.38, $p=0.003$, SEM + 0.215). The study group also demonstrated reduced length of stay relative to controls (S=3.64 vs. NS=4.47, $p<0.001$, SEM + 0.114). **Conclusion:** Multimodal pain management following total knee arthroplasty improved post-operative outcomes irrespective of opioids requirements or mode of anesthesia. Our results are consistent with previous work demonstrating improved patient care, superior analgesia and reduced length of stay in hospital through implementation of standardized multimodal pain management with standardized discharge criteria.

INTRODUCTION

There is an increasing focus on optimizing postoperative pain management for total knee arthroplasty (TKA) with the goal of decreased opiate requirements, shortened length stay (LOS) in hospital, reduced time to ambulation, and improved patient satisfaction [1-4]. At present, there is no definitive protocol that employs the combination of regional techniques and systemic pharmacotherapy for postoperative pain control in tricompartamental knee arthroplasty. To this end, we conducted a retrospective assessment of the benefit conferred by a standardized multimodal pain protocol following TKA performed over a three year period in our medical center. Multimodal or balanced analgesia in the setting of TKA may incorporate nerve blockade, IV and PO medications as well as a coordinated rehabilitation program. We evaluated clinical outcomes of a regimen comprised of

immediate and extended release opiates, celecoxib, and acetaminophen combined with regional femoral nerve blockade under close follow up of a dedicated multidisciplinary acute pain management team.

Pain may be treated at various neurophysiological levels [3] that span peripheral, spinal and cortical targets. Peripheral acting analgesics include local anesthetics, α_2 -adrenergic agonists, NSAIDS (including COX-2 selective inhibitors), and opioids; and these agents also act at the level of the spinal cord. Opioids, NMDA receptor antagonists (i.e. ketamine), anticonvulsants (i.e. gabapentin), and acetaminophen have been demonstrated to provide analgesia at the cortical level [5]. It is thought that acetaminophen exerts its analgesic and antipyretic through inhibition of cyclooxygenase-3 (COX-3), a close homologue of COX-1

variant [6]. Non-selective NSAIDs such as diclofenac and ibuprofen have also been shown to potently inhibit COX-3. Over the past decade, there has been both uncertainty and controversy as to the utility of the class of selective COX-2 inhibitors in the acute or immediate postoperative setting[7]. However, recent studies have demonstrated the effectiveness of this class in reducing postoperative pain[8, 9]. Ilfeld et al reported that 80-90% of patients undergoing TKA required intravenous opioids for immediate postoperative pain relief [10, 11].

Opioids delivered orally or through patient controlled analgesia have been traditionally used following TKA. However, in addition to well-known side effects stemming from this class of medication [12], opioid usage is implicated with increases in hospital costs and length of stay (LOS) [13]. Higher doses of opioids have also been associated with increased risk of adverse drug events. Several studies have shown a meaningful reduction in narcotic requirements and in-turn decreased adverse drug events using acetaminophen, celecoxib, and gabapentin as part of multi-modal pain regimens in this setting [12, 14-16]. Ketamine, a competitive NMDA receptor antagonist, has been shown to decreased opioid tolerance and delayed hyperalgesia, thought to be associated with activation of central nervous system NMDA receptors. [17-19]. Others have demonstrated a decrease in post-operative opioid requirement with concomitant use of ketamine and opioids than with opioids alone. [20-22].

It is widely accepted that continuous femoral nerve blockade improves analgesia outcomes following TKA [23]. Continuous femoral nerve blockade provides prolonged analgesia while decreasing disability and length of stay (LOS) after TKA and other major hospital-based knee procedures. According to the American Academy of Orthopaedic Surgeons, the average LOS has decreased nearly 3-fold, from 11 days in 1990 to approximately 4 days in 1996, and has since remained constant [10, 24]. In addition to decreased time to discharge readiness, femoral blockade enables more effective rehabilitation, and a decrease in post-operative complications [25].

METHODS

A retrospective chart review was conducted of 389 patients who underwent total knee replacement between 1/2008-12/2010. Institutional review board (IRB) approval was obtained for the study and signed written informed consent was obtained from all patients. A total of 218 patients met inclusion criteria: 1) status-post TKA 2) femoral

nerve block with a continuous infusion of ropivacaine 0.1% placed following surgical procedure 3) femoral catheter discontinued on POD 3 and 4.) follow-up with acute pain service. The study group (N=105) included patients receiving a standardized protocol: a continuous femoral nerve block, celecoxib 200 mg PO Q24, oxycontin 10 mg PO Q12, acetaminophen 1000 mg PO TID, and Percocet 1-2 tabs PO Q4-6 hr PRN with a maximum of 3 tabs per 24hrs for breakthrough pain >5. Percocet dosing was limited to ensure acetaminophen did not exceed 4 grams per 24 hour period. Patients included in the non-standardized protocol group received femoral nerve block with a continuous infusion combined with short acting opioids prescribed at the discretion of the primary team.

Exclusion criteria were contraindication to NSAIDs and/or acetaminophen due to renal or liver disease as well as chronic opiate usage. The control group (N=113) consisted of patients with a continuous femoral nerve block who received a non-standardized pain management regimen as prescribed by the orthopedic service.

The following parameters were recorded: mode of anesthesia (neuraxial vs. GA-ETT); length of surgery; time to ambulation and 90 ° flexion; pain score (visual analog scale) as recorded by the pain team, as well as, morphine equivalents consumed on post-op day 1-3; medication side effects and length of hospital stay (LOS).

The length of stay in hospital or discharge readiness was determined by the orthopedic surgical team. Criteria for discharge at the Maimonides Medical Center include absence of bleeding, anemia (measured with daily CBC) and indicators of infection such as wound drainage, fever and leukocytosis. Inadequate pain control also precluded discharge. [26].

Statistical analysis was performed using SPSS and SigmaStat software packages. The unpaired t-test was used to compare mean outcomes of the standardized multimodal and the non-standardized protocol. The chi-squared test was used to analyze differences in proportion of patients in the two groups for various outcomes.

RESULTS

Analysis was performed on the 218 patients meeting inclusion criteria into the study. There was no significant difference between groups with respect to anthropometric data and duration of surgery ($S 2.16 \pm 0.054$ vs. NS

2.15±0.059, p=0.855) (Table 1). There was also no significant difference between groups in terms of gender distribution (p=0.435) or modes of anesthesia (p=0.680) (Table 2). The distribution of ASA classification also did not differ statistically between the two groups: ASA I (S=1% vs. NS=0%), ASA II (56% vs. 61%), ASA III (48% vs. 51%), ASA IV (0% vs. 1%), (N=218, p=0.569) (Figure 1).

The group receiving the standardized multimodal protocol exhibited a statistically significant decrease in reported pain scores (VAS) on the third post-operative day as compared to the control group (S=2.43 vs. NS=3.38, p=0.003, SEM + 0.215) (Figure 2). Morphine requirements did not differ significantly between treatment groups, with a nonsignificant trend toward higher opioids requirements in the standardized protocol group on the first and second post-operative days (Day 1: S=15.8 vs. NS=13.1, p=0.052, SEM + 1.0 Day 2: S=13.0 vs. NS=10.7, p=0.08, SEM + 0.76 Day 3: S=7.7 vs. NS=7.9, p=0.87, SEM + 0.63). The standardized treatment group also demonstrated a shortened length of stay (S=3.64 vs. NS=4.47, p<0.001, SEM + 0.114). The standardized protocol group displayed a slight delay to ambulation of approximately four hours. (S=1.36 vs. NS=1.19, p<0.036 SEM + 0.61), which was statistically significant.

Length of stay was significantly shorter in the standardized protocol group irrespective of mode of anesthesia (Figure 3). Post-operative pain (VAS) reduction on post-operative day 3 between study groups achieved statistical significance only in patients receiving neuraxial anesthesia (p=0.01), while a trend toward statistical significance was found in patients undergoing general anesthesia (p=0.055). There was no significant difference between groups when stratified by mode of anesthesia with respect to anthropometric data, except in age in those receiving general anesthesia (S=64.8 vs. NS=69.6, p=0.02 SEM + 1.31). Simple linear regression demonstrated no significant relationship between age and length of stay either in those receiving general or neuraxial anesthesia (data not shown).

Figure 1

Table 1: There was no significant difference between treatment protocols with respect to anthropometric data and duration of surgery († unpaired t-test).

	Protocol	Mean ± SEM	P-Value †
Age	S	66.75±0.973	0.640
	NS	67.39±0.951	
Wt (kg)	S	90.89±1.92	0.102
	NS	86.60±1.77	
Ht (in)	S	63.53±0.392	0.928
	NS	63.49±0.334	
Surgery Time (hrs)	S	2.16±0.054	0.855
	NS	2.15±0.059	

Figure 2

Table 2: Gender distribution (p=0.435) and mode of anesthesia (p=0.680) did not differ significantly between standardized (S) and non-standardized (NS) treatment protocols (§Pearson's chi-square).

	Protocol	N	P-Value §
Gender			0.435
Male	S	28 (26.7%)	
	NS	25 (22.1%)	
Female	S	77 (73.3%)	
	NS	88 (77.9%)	
Type of Anesthesia			0.680
GA	S	38 (36.2%)	
	NS	44 (38.9%)	
Spinal	S	65 (61.9%)	
	NS	67 (59.3%)	
CSE	S	2 (1.8%)	
	NS	1 (1.0%)	

Figure 3

Figure 1: Study population by ASA Physical status. The distribution did not differ significantly between standardized (▨) and non-standardized (▤) treatment protocols (Pearson's chi-square $p=0.570$).

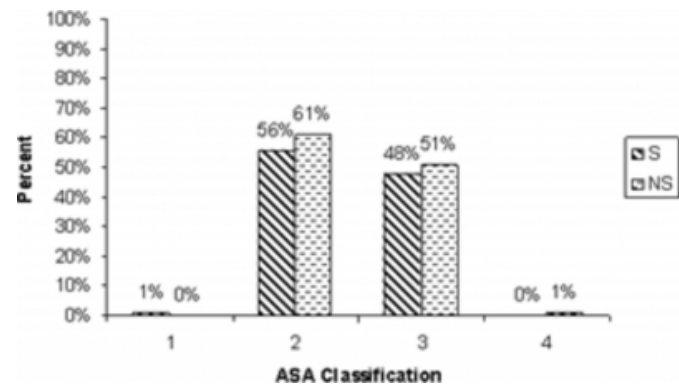


Figure 4

Figure 2: Comparison between standardized (S) and non-standardized (NS) treatment protocols for post-operative pain (VAS), morphine equivalents dosed, length of stay as well as days to 90 degree flexion and ambulation. (A) Mean pain score on postoperative day #3 was significantly higher in the NS group (S=2.43 vs. NS=3.38, $p=0.003$, SEM $\hat{A} \pm 0.215$). (B) There was a non-significant trend towards higher morphine requirements in the standardized treatment group (Day1: S=15.8 vs. NS=13.1, $p=0.052$, SEM $\hat{A} \pm 1.0$ Day 2: S=13.0 vs. NS=10.7, $p=0.08$, SEM $\hat{A} \pm 0.76$ Day 3: S=7.7 vs. NS=7.9, $p=0.87$, SEM $\hat{A} \pm 0.63$). (C) Length of stay in hospital was significantly shorter in the standardized treatment group relative to the non-standardized (S=3.64 vs. NS=4.47, $p<0.001$, SEM $\hat{A} \pm 0.114$). Time to ambulation was slightly greater in the standardized treatment protocol (S=1.36 vs. NS=1.19, $p<0.036$ SEM $\hat{A} \pm 0.61$) (Error bars indicate standard error of mean).

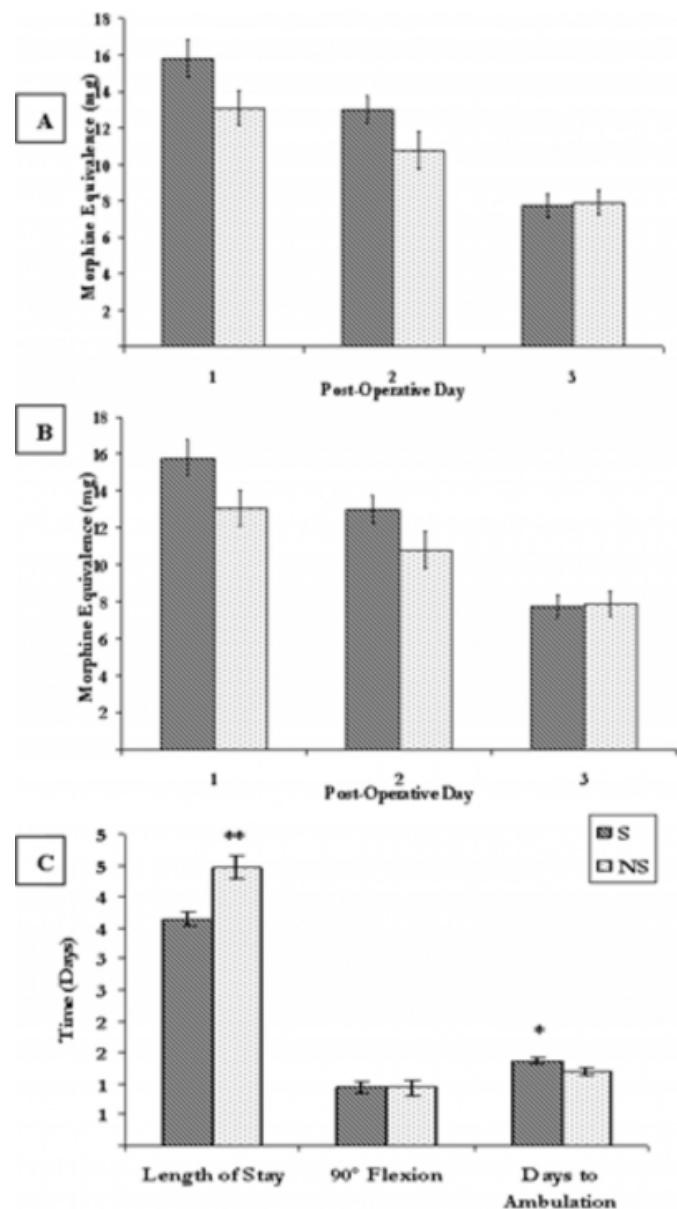
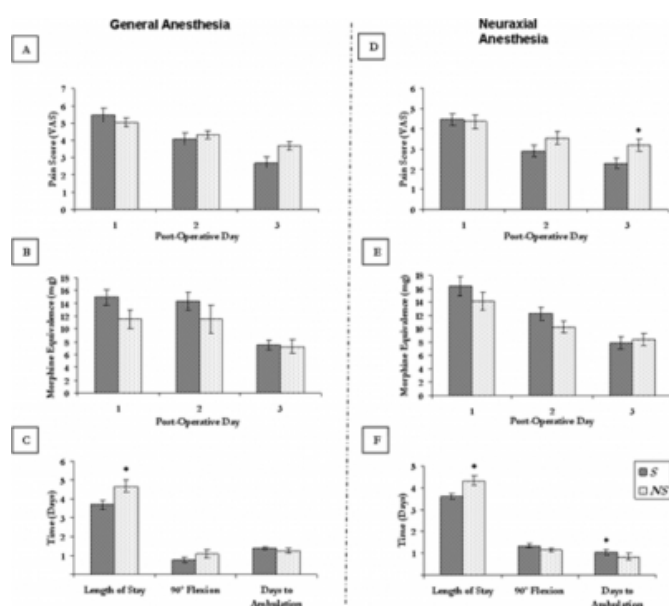


Figure 5

Figure 3: A comparison between standardized (S) and non-standardized (NS) treatment protocols with data stratified by mode of anesthesia. (A-C) General anesthesia: Hospital stay was longer in the NS group (S=3.69 vs. NS=4.68 days, $p=0.01$, SEM $\hat{A} \pm 0.215$). (D-F) Neuraxial anesthesia: Hospital stay was longer in the NS group (S=3.61 vs. NS=4.30 days, $p=0.009$, SEM $\hat{A} \pm 0.131$); postoperative pain (VAS) on day three was lower in the S group (S=2.27 vs. NS=3.18, $p=0.026$, SEM $\hat{A} \pm 0.210$); time to ambulation was slightly increased in the S group (S=1.35 vs. NS=1.15, $p=0.04$, SEM $\hat{A} \pm 0.79$).



DISCUSSION

This retrospective review demonstrates effective post-operative analgesia after TKA utilizing a standardized multimodal pain management protocol. These results, which are consistent with prior studies[12-16], indicate that multimodal pain management reduces length of stay in hospital. This outcome supports the claim that the standardized multimodal regimen confers a reduction in post-operative complications and health care costs. In the present study, all patients undergoing TKA at our medical center were subject to standardized discharge criteria and guidelines as outlined in the orthopedics and anesthesia literature [26-28]. Our results indicate patients receiving a standardized multimodal protocol exhibited lower pain scores as well as shorter hospital stays. Shorter lengths of stay have previously been associated with improved patient satisfaction; however, we were not able to assess for this endpoint in the present retrospective review [29]. We note a slight delay to ambulation in the multimodal pain group. However, this delay was not clinically meaningful given that

the standard group achieved shorter time to discharge as reflected in duration of the hospital stay. This group of patients also reported lower pain scores as compared to their counterparts not receiving the standardized multimodal pain management protocol.

Previous work has demonstrated multimodal pain management as superior to IV patient-controlled analgesia alone (PCA), in terms of degree of analgesia and length of stay [28]. Others have shown that non-opioid adjuncts reduce opioid requirements. Here, our results suggest superior analgesia as well as shortened length of stay with multimodal pain management irrespective of opioid requirement. However, it should be noted that patients receiving the non-standardized treatment protocol did not necessarily receive IV PCA and may have received other, possibly inadequate opioid regimens. Overall, the strategy of targeting multiple pain pathways within a structured acute pain management regimen provided better outcomes. Still, our results point to the utility of a structured surgery-specific pain management protocol, which also benefits from a multimodal approach.

We also observed that multimodal pain management conferred reduced length of stay irrespective of mode of anesthesia. It appears that analgesia was superior in the standardized multimodal group receiving either neuraxial ($p=0.026$) or general anesthesia, despite only a strong trend towards statistical significance in the general anesthesia group ($p=0.055$). This discrepancy may be attributable to small sampling size. It should also be noted that the time to ambulation was slightly longer in patients receiving neuraxial anesthesia with subsequent multimodal pain management as compared to those not treated with the standardized protocol (14.8% or 4 hours). As noted above, the delay of four hours may not be meaningful clinically given that the duration of stay was lower in the multimodal pain management group. Future prospective randomized trials may focus on the contribution of neuraxial anesthesia to postoperative multimodal pain management. It would also be interesting to investigate whether the time of placement of peripheral block relative to surgical procedure has any effect on outcome, and whether the peripheral component is independent of mode of anesthesia.

Taken together, our results are consistent with previous work demonstrating improved patient care, superior analgesia and reduced length of stay in hospital through implementation of standardized multimodal pain management with

standardized discharge criteria and guidelines.

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References

- Joshi GP: Multimodal analgesia techniques and postoperative rehabilitation. *Anesthesiol Clin North America* 2005, 23:185-202.
- Kehlet H, Werner M, Perkins F: Balanced analgesia: what is it and what are its advantages in postoperative pain? *Drugs* 1999, 58:793-797.
- Kehlet H, Dahl JB: The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg* 1993, 77:1048-1056.
- Woolf CJ: Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med* 2004, 140:441-451.
- Pyati S, Gan TJ: Perioperative pain management. *CNS Drugs* 2007, 21:185-211.
- Chandrasekharan NV, Dai H, Roos KL, Evanson NK, Tomsik J, Elton TS, Simmons DL: COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning, structure, and expression. *Proc Natl Acad Sci U S A* 2002, 99:13926-13931.
- Eisenach JC: Data fabrication and article retraction: how not to get lost in the woods. *Anesthesiology* 2009, 110:955-956.
- Buvanendran A, Kroin JS: Multimodal analgesia for controlling acute postoperative pain. *Curr Opin Anaesthesiol* 2009, 22:588-593.
- Boonriong T, Tangtrakulwanich B, Glabglay P, Nimmaanrat S: Comparing etoricoxib and celecoxib for preemptive analgesia for acute postoperative pain in patients undergoing arthroscopic anterior cruciate ligament reconstruction: a randomized controlled trial. *BMC Musculoskelet Disord* 2010, 11:246.
- Ilfeld BM, Le LT, Meyer RS, Mariano ER, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, et al: Ambulatory continuous femoral nerve blocks decrease time to discharge readiness after tricompartiment total knee arthroplasty: a randomized, triple-masked, placebo-controlled study. *Anesthesiology* 2008, 108:703-713.
- Ilfeld BM, Mariano ER, Girard PJ, Loland VJ, Meyer RS, Donovan JF, Pugh GA, Le LT, Sessler DI, Shuster JJ, et al: 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.
- Duellman TJ, Gaffigan C, Milbrandt JC, Allan DG: Multi-modal, pre-emptive analgesia decreases the length of hospital stay following total joint arthroplasty. *Orthopedics* 2009, 32:167.
- Oderda GM, Said Q, Evans RS, Stoddard GJ, Lloyd J, Jackson K, Rublee D, Samore MH: Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007, 41:400-406.
- Menigaux C, Adam F, Guignard B, Sessler DI, Chauvin M: Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. *Anesth Analg* 2005, 100:1394-1399, table of contents.
- Elia N, Lysakowski C, Tramer MR: Does multimodal analgesia with acetaminophen, nonsteroidal anti-inflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. *Anesthesiology* 2005, 103:1296-1304.
- Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N: Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth* 2011, 106:292-297.
- Zakine J, Samarq D, Lorne E, Moubarak M, Montravers P, Beloucif S, Dupont H: Postoperative ketamine administration decreases morphine consumption in major abdominal surgery: a prospective, randomized, double-blind, controlled study. *Anesth Analg* 2008, 106:1856-1861.
- Petrenko AB, Yamakura T, Baba H, Shimoji K: The role of N-methyl-D-aspartate (NMDA) receptors in pain: a review. *Anesth Analg* 2003, 97:1108-1116.
- Woolf CJ, Chong MS: Preemptive analgesia--treating postoperative pain by preventing the establishment of central sensitization. *Anesth Analg* 1993, 77:362-379.
- Bilgin H, Ozcan B, Bilgin T, Kerimoglu B, Uckunkaya N, Toker A, Alev T, Osma S: The influence of timing of systemic ketamine administration on postoperative morphine consumption. *J Clin Anesth* 2005, 17:592-597.
- Elia N, Tramer MR: Ketamine and postoperative pain--a quantitative systematic review of randomised trials. *Pain* 2005, 113:61-70.
- Schmid RL, Sandler AN, Katz J: Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. *Pain* 1999, 82:111-125.
- Paul JE, Arya A, Hurlburt L, Cheng J, Thabane L, Tidy A, Murthy Y: Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. *Anesthesiology* 2010, 113:1144-1162.
- Ilfeld BM, Gearen PF, Enneking FK, Berry LF, Spadoni EH, George SZ, Vandenborne K: Total knee arthroplasty as an overnight-stay procedure using continuous femoral nerve blocks at home: a prospective feasibility study. *Anesth Analg* 2006, 102:87-90.
- Chelly JE, Greger J, Gebhard R, Coupe K, Clyburn TA, Buckle R, Criswell A: Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty. *J Arthroplasty* 2001, 16:436-445.
- Davies AP: Rating systems for total knee replacement. *Knee* 2002, 9:261-266.
- Patt JC, Mauerhan DR: Outcomes research in total joint replacement: a critical review and commentary. *Am J Orthop (Belle Mead NJ)* 2005, 34:167-172.
- Ayalon O, Liu S, Flics S, Cahill J, Juliano K, Cornell C: A Multimodal Clinical Pathway Can Reduce Length of Stay After Total Knee Arthroplasty *HSS Journal* 2010, 7.
- Tokunaga J, Imanaka Y: Influence of length of stay on patient satisfaction with hospital care in Japan. *Int J Qual Health Care* 2002, 14:493-502.

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