Predictors for moderate to severe acute postoperative pain after total hip and knee replacement

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Abstract

Purpose The ability to identify and focus care to patients at higher risk of moderate to severe postoperative pain should improve analgesia and patient satisfaction, and may affect reimbursement. We undertook this multi-centre cross-sectional study to identify preoperative risk factors for moderate to severe pain after total hip (THR) and knee (TKR) replacement.

Methods A total of 897 patients were identified from electronic medical records. Preoperative information and anaesthetic technique was gained by retrospective chart review. The primary outcomes were moderate to severe pain (pain score $\geq 4/10$) at rest and with activity on postoperative day one. Logistic regression was performed to identify predictors for moderate to severe pain.

Results Moderate to severe pain was reported by 20 % at rest and 33 % with activity. Predictors for pain at

rest were female gender (OR 1.10 with 95 % CI 1.01–1.20), younger age (0.96, 0.94–0.99), increased BMI (1.02, 1.01–1.03), TKR vs. THR (3.21, 2.73–3.78), increased severity of preoperative pain at the surgical site (1.15, 1.03–1.30), preoperative use of opioids (1.63, 1.32–2.01), and general anaesthesia (8.51, 2.13–33.98). Predictors for pain with activity were TKR vs. THR (1.42, 1.28–1.57), increased severity of preoperative pain at the surgical site (1.11, 1.04–1.19), general anaesthesia (9.02, 3.68–22.07), preoperative use of anti-convulsants (1.78, 1.32–2.40) and anti-depressants (1.50, 1.08–2.80), and prior surgery at the surgical site (1.28, 1.05–1.57).

Conclusions Our findings provide clinical guidance for preoperative stratification of patients for more intensive management potentially including education, nursing staffing, and referral to specialised pain management.

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Introduction

Improvement of pain control is an international initiative promoted by multiple health organisations including WHO [1]. In the United States, the Department of Health and Human Services, National Institutes of Health, and the Institute of Medicine have joined to focus on hospital-based pain control. A major component is identification of predictors of pain that may lead to individualised care and selective application of greater expertise in pain management such as acute pain services (<http://www.iom.edu/activities/publichealth/painresearch.aspx>). Evidence based triage of patients is important due to cost concerns. Acute pain services are effective but may be relatively expensive with unfocused provision to all patients [2]. The ability to identify and focus care to patients at higher risk of moderate to severe postoperative pain should improve analgesia, improve patient satisfaction, and may affect reimbursement.

In the United States alone, approximately 436,000 total hip replacements (THR) and 680,000 total knee replacements (TKR) were performed in 2008 with an expected 673 % and 174 % increase expected by 2030 [3]. THR and TKR are typically painful procedures that have a variety of options for postoperative analgesia ranging from surgeon provided (e.g., local infiltration) to more intensive techniques (e.g., perineural catheters) requiring care from an acute pain service (APS) [4, 5]. Thus, these procedures may especially benefit from analgesic risk stratification to identify patients at risk for acute moderate to severe pain and to potentially optimise management. We undertook this multi-centre cross sectional study to identify pre-operative risk factors for moderate to severe pain after THR and TKR.

Methods

This study was a multi-centre, cross-sectional, observational study involving Hospital for Special Surgery (HSS) in New York, Rush University Medical Center (Rush) in Chicago, Massachusetts General Hospital (MGH) in Boston, and Sunnybrook Health Sciences Centre (Sunnybrook) in Toronto. Other aspects from this same protocol have been previously reported [6]. Institutional review board approval was granted at all centres, and written informed consent was obtained from all included patients. From October 10, 2007 to March 15, 2010, all patients between the ages of 18 and 99 who had undergone primary total hip or knee replacement were identified from electronic medical records. The primary outcomes were pain scores (0=no pain to 10=worst pain) at rest and with activity on postoperative day one. Moderate to severe pain was defined with a cutoff value of 4/10, as this has been previously identified as a value at which patients request additional analgesics, become

unsatisfied with pain control, and have interference with functional activity [7]. Preoperative information was gained by retrospective chart review including patient demographics, co-morbidities, home medications, and anaesthetic technique. Standard perioperative management for each site is described in the [Appendix](#).

Statistical analysis

Two identical but separate analyses were performed for moderate to severe pain at rest and with activity. Univariate analysis for differences between patients with and without moderate to severe pain was conducted by using chi-square or Fisher's exact tests for categorical variables, and t-tests or Mann–Whitney U tests for continuous variables according to the distribution of the data. Multivariate logistic regression based on the generalised estimating equations (GEE) method was built to identify the risk factors for moderate to severe pain. Unlike standard logistic regression, GEE logistic regression allows for dependence within clusters, presumably clustering by hospitals in this multi-centre study. Model fitting for multivariable logistic regression started with a full model comprised of an outcome variable of whether patients had moderate to severe pain on postoperative day one and all risk factors that were statistically or clinically significant in the univariate analysis, including gender, age, BMI, type of procedure (knee versus hip), severity of preoperative pain at the surgical site, preoperative use of opioids, anti-convulsants, and anti-depressants, smoking history, alcohol use, prior surgery at the surgical site, and general anaesthesia for both rest and activity regressions.

Backward elimination method was used for model selection. The QIC goodness of fit statistics was calculated for comparing different GEE models and the model with the smallest QIC was chosen. Odds ratio, 95 % confidence interval, and *p*-value were reported from the logistic regression. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC). Statistical significance was set at 0.05.

Results

A total of 897 patients were included in the study, and individual and composite study site demographics are displayed in Table 1. Twenty percent of patients reported moderate to severe pain at rest and 33 % with activity on postoperative day one, and distribution of pain scores are displayed in Figs. 1 and 2. Potential predictors for moderate to severe pain are displayed in Table 2. Final independent predictors for increased risk of moderate to severe pain at rest were female gender (OR 1.10 with 95 % CI 1.01–1.20),

Table 1 Perioperative characteristics of patients by institutional site

Characteristic	HSS (<i>N</i> =545)	Rush (<i>N</i> =164)	MGH (<i>N</i> =152)	Sunnybrook (<i>N</i> =36)	Combined (<i>N</i> =897)
Age, mean (SD), years	68 (11)	65 (10)	64 (12)	67 (11)	67 (11)
Gender; M/F, %	41/59	39/61	52/48	31/69	42/58
BMI, mean (SD), kg/m ²	29 (6)	32 (8)	30 (6)	28 (6)	30 (7)
Procedure, <i>N</i> (%)					
THR	270 (50)	49 (30)	92 (61)	17 (47)	428 (48)
TKR	275 (50)	115 (70)	60 (39)	19 (53)	469 (52)
Diabetes, <i>N</i> (%)	50 (9)	19 (12)	14 (9)	3 (8)	86 (10)
Prior chronic pain condition, <i>N</i> (%)	232 (43)	26 (16)	51 (34)	3 (8)	312 (35)
Home opioids, <i>N</i> (%)	106 (19)	40 (24)	28 (18)	1 (3)	175 (20)
Home anticonvulsant, <i>N</i> (%)	54 (10)	13 (8)	4 (3)	1 (3)	60 (7)
Home antidepressants, <i>N</i> (%)	88 (16)	23 (14)	36 (24)	0	147 (16)
Smoker, <i>N</i> (%)	30 (6)	5 (3)	16 (11)	32 (89)	83 (9)
Alcohol use, <i>N</i> (%)	302 (55)	94 (57)	85 (56)	0	517 (58)
Prior surgery at same hip or knee, <i>N</i> (%)	194 (36)	64 (39)	54 (36)	14 (39)	326 (36)
Preexisting pain at surgical site, <i>N</i> (%)	520 (95)	162 (99)	150 (99)	36 (100)	868 (98)
Preexisting pain worst level, mean (SD)	8.4 (1.8)	9.0 (1.3)	8.3 (1.9)	8.5 (2.3)	8.5 (1.8)
Anesthesia type, <i>N</i> (%)					
General	7 (1)	10 (6)	95 (62)	4 (11)	116 (13)
Regional	538 (99)	154 (94)	57 (38)	32 (89)	781 (87)
VAS pain score on POD1, mean (SD)					
Rest	1.5 (1.2)	3.3 (2.6)	4.0 (2.0)	2.1 (1.6)	2.3 (2.0)
Activity	2.1 (2.2)	4.7 (2.5)	6.0 (2.2)	3.3 (2.2)	3.0 (2.7)

HSS Hospital for Special Surgery, MGH Massachusetts General Hospital, BMI body mass index, POD postoperative day, THR total hip replacements, TKR total knee replacements

younger age (0.96, 0.94–0.99), increased BMI (1.02, 1.01–1.03), TKR vs. THR (3.21, 2.73–3.78), increased severity of preoperative pain at the surgical site (1.15, 1.03–1.30), preoperative use of opioids (1.63, 1.32–2.01), and general anaesthesia (8.51, 2.13–33.98). Final independent predictors for pain with activity were TKR vs. THR (1.42, 1.28–1.57), increased severity of preoperative pain at the surgical site (1.11, 1.04–1.19), general anaesthesia (9.02, 3.68–22.07), preoperative use of anti-convulsants (1.78, 1.32–2.40) and

anti-depressants (1.50, 1.08–2.80), and prior surgery at the surgical site (1.28, 1.05–1.57) (Table 3).

Discussion

We identified younger age, female gender, increased BMI, increased severity of preoperative pain at the surgical site, prior surgery at the surgical site, preoperative use of opioids,

Fig. 1 Histogram of distribution of postsurgical pain scores at rest on postoperative day 1

Fig. 2 Histogram of distribution of postsurgical pain scores with activity on postoperative day 1

Table 2 Incidence of moderate to severe pain at rest and during activity for each potential risk factor

Characteristic	Rest			Activity		
	Moderate to severe pain <i>N</i> =181	No moderate to severe pain <i>N</i> =707	<i>P</i> -value	Moderate to severe pain <i>N</i> =295	No moderate to severe pain <i>N</i> =461	<i>P</i> -value
Age, mean (SD), years	63 (12)	68 (10)	<0.001*	65 (11)	68 (10)	<0.001*
Gender; M/F, %	40/60	43/57	0.45	41/59	43/57	0.60
BMI, mean (SD), kg/m ²	32 (8)	29 (6)	<0.001*	30 (7)	29 (7)	0.04*
Procedure, <i>N</i> (%)						
THR	61 (34)	365 (52)	<0.001*	134 (45)	243 (53)	0.05
TKR	120 (66)	342 (48)		161 (55)	218 (47)	
Diabetes, <i>N</i> (%)	21 (12)	64 (9)	0.30	30 (10)	44 (10)	0.79
Prior chronic pain condition, <i>N</i> (%)	58 (32)	253 (36)	0.33	92 (31)	172 (37)	0.08
Home opioids, <i>N</i> (%)	49 (27)	126 (18)	0.005*	62 (21)	84 (18)	0.34
Home anticonvulsant, <i>n</i> (%)	17 (9)	54 (8)	0.44	29 (10)	31 (6.7)	0.12
Home antidepressants, <i>n</i> (%)	37 (20)	108 (15)	0.09	58 (20)	63 (14)	0.03*
Smoker, <i>N</i> (%)	25 (14)	57 (8)	0.02*	33 (11)	36 (8)	0.12
Alcohol use, <i>N</i> (%)	100 (55)	412 (58)	0.23	165 (56)	271 (59)	0.37
Prior surgery at same hip or knee, <i>N</i> (%)	73 (40)	248 (35)	0.16	120 (41)	45 (31)	0.006*
Preexisting pain at surgical site, <i>N</i> (%)	178 (98)	681 (96)	0.37	288 (98)	442 (96)	0.39
Preexisting pain worst level, mean (SD)	9.0 (1.4)	8.4 (1.8)	<0.001*	8.7 (1.7)	8.4 (1.8)	0.01*
Anesthesia type, <i>N</i> (%)						
General	63 (35)	53 (7)	<0.001*	57 (19)	13 (2.8)	<0.001*
Regional	118 (65)	654 (93)		238 (81)	448 (97)	
VAS pain score on POD1, mean (SD)						
Rest	5.5 (1.4)	1.4 (1.0)		5.8 (1.8)	1.3 (1.2)	
Activity	6.0 (2.4)	2.4 (2.3)		3.1 (1.9)	1.3 (1.1)	

THR total hip replacements, TKR total knee replacements

*Statistically significant

anti-depressants and anti-convulsants, use of general anaesthesia, and TKR vs. THR as risk factors for acute moderate to

severe pain. These predictors may be clinically used to stratify analgesic risk of patients and assign greater resources to high

Table 3 Risk factors for acute moderate to severe pain for rest and activity

Risk factors	Odds ratio	95 % CI	<i>P</i> value
Rest			
Female gender	1.10	1.01–1.20	0.0367
Age	0.96	0.94–0.99	0.0127
Body mass index	1.02	1.01–1.03	0.0047
Total knee replacement	3.21	2.73–3.78	<0.001
Severity of preoperative pain at surgical site	1.16	1.03–1.30	0.0133
Home opioids	1.63	1.32–2.01	<0.001
General anesthesia	8.51	2.13–33.98	0.0024
Activity			
Total knee replacement	1.42	1.28–1.57	<0.001
Severity of preoperative pain at surgical site	1.11	1.04–1.19	0.002
General anesthesia	9.02	3.68–22.07	<0.001
Preoperative anti-convulsants	1.78	1.32–2.40	<0.001
Preoperative anti-depressants	1.50	1.08–2.80	0.0163
Prior surgery in at surgical site	1.28	1.05–1.57	0.0168

risk patients. Some of these risk factors have been previously identified, which adds external validity to our findings. A recent observational study of 1,700 patients after mixed surgical procedures noted that female gender (OR 1.5) and younger age (OR 1.3) were risk factors for immediate acute pain in the recovery room [8]. A previous qualitative systematic review including 23,000 patients after mixed surgical procedures noted that preoperative pain and younger age were risk factors for increased postoperative pain [9]. This review also identified total joint replacement as a specific procedure associated with increased risk of postoperative pain, thus our specific analysis of risk factors after total hip and knee replacement addressed a high risk population.

Poor postoperative pain control has multiple potential clinical implications. Severity of acute postoperative pain has been identified in several studies to increase risk of chronic postsurgical pain after THR and TKR [10]. A separately published analysis from this same protocol noted that 53 % of patients reported chronic postsurgical pain one year after TKR and 38 % of patients one year after THR [6]. More effective control of acute pain may decrease risk for subsequent development of chronic pain, as our separate analysis noted that for every unit improvement (1/10) in quality of acute postoperative pain control, as measured on a 0–10 (0=worst, 10=best) scale, the odds of developing chronic pain decreased by 10 %. Pain control is an important determinant of patient satisfaction, and improvement in postoperative analgesia should improve patient satisfaction [11]. Quality of patient satisfaction may subsequently carry financial consequences for reimbursement. In the United States, The Centres for Medicare and Medicaid Services plan to adjust hospital reimbursement in part based on patient satisfaction with pain control [12].

After stratification for patients at analgesic risk, several multimodal clinical interventions are available for implementation. Patient education has been demonstrated to improve satisfaction with postoperative analgesia and has been incorporated into fast track recovery programs for multiple surgical procedures [13, 14]. Nursing to patient staffing ratios have been shown to affect perception of quality and patient satisfaction [15]. Thus, stratified patients may benefit from optimised nurse staffing ratios. Use of multimodal systemic analgesics such as NSAIDs, gabapentanoids, and ketamine have all been shown to reduce opioid use [16] and may be especially helpful in high analgesic risk patients.

Referral to specialised expert pain management from an acute pain service is an effective intervention. Referral to an APS allows use of higher acuity analgesic techniques such as regional analgesia techniques and multimodal analgesia which have been shown to be highly effective after THR and TKR [4, 5, 17]. However, such expert care also carries cost. A previous RCT that randomised unselected patients to routine versus APS postoperative analgesic care determined

that use of APS provided more effective analgesia but required USD 546 for each additional day of highly effective analgesia versus routine care [2]. The ability to direct such costly services in an evidence-based fashion would likely be beneficial. This expert analgesic care can be extended beyond the immediate postoperative care with demonstrated benefit. Recent publications have observed that seamlessly continuing expert pain management beyond the in-patient phase via telephone and outpatient clinic management for several weeks after surgery can improve patient satisfaction from 91 % to 99 % as measured by the commonly used Press Ganey™ survey [18].

Mechanisms for the identified predictors are speculative. Female gender, younger age, and increased BMI have been inconsistently identified as a risk factor for several different surgical procedures and underlying mechanisms are uncertain [9, 19, 20]. Other risk factors such as home use of opioids and anticonvulsants, prior surgery on the hip and knee, and greater preoperative severity of pain at the hip or knee may reflect greater severity of underlying pathology, central or peripheral sensitisation to preexisting nociception from the hip or knee [21], or opioid induced hyperalgesia [22]. Preexisting depression as reflected by home use of antidepressants has been previously described as a risk factor for severity of postoperative pain [9, 19]. Finally, the protective effect of regional versus general anaesthesia may reflect beneficial effects of preventive analgesia [21].

There are limitations to our study. Typical of any cross-sectional study is that only a single period in time (postoperative day one) was considered, and future longitudinal studies would be welcome. Our analysis was observational and can only determine associations between risk factors and severity of acute pain. Future studies are needed to determine efficacy of interventions to treat acute pain after total hip and knee replacement and longitudinal effects of such treatment on patient satisfaction and development of chronic pain.

In conclusion, our findings provide clinical guidance for preoperative selection of patients for more intensive management including education, nursing staffing, and referral to specialised pain management including regional analgesia, multimodal analgesia, and potential aftercare follow up. Identification and optimised management of high risk patients should improve quality of analgesia and patient satisfaction scores.

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Conflict of interest The authors declare that they have no conflict of interest.

Appendix

At HSS, patients typically received patient controlled epidural analgesia (PCEA) with 0.06 % bupivacaine with hydromorphone 10 mcg/ml or clonidine 1 mcg/ml after central neuraxial anaesthesia. Initial settings were continuous infusion of 4 ml/h, bolus dose 4 ml, lockout time ten minutes, and one hour lockout of 20 ml. TKR patients also receive a single shot femoral nerve block with 30 ml 0.25 % bupivacaine. Patients were assessed twice a day by our Acute Pain Service (APS) consisting of an anaesthetist attending and a pain specialist registered nurse. Patients were typically started on oral analgesics on the night of surgery, and the continuous infusion was decreased as tolerated until successful conversion to oral analgesics only. For example, most patients having unilateral total knee replacement had their continuous infusion decreased to 2 ml/h on the morning of postoperative day (POD) one and then decreased to 0 ml/h on the evening of POD1 followed by discontinuing the PCEA on the morning of POD2. Meloxicam (7.5–15 mg qday) was administered as a standard adjunct analgesic unless contraindicated by active cardiovascular disease, liver disease, renal disease, or sensitivity to NSAIDs. Analgesic adjuncts such as pregabalin were prescribed at the discretion of the APS. There were standing orders for nalbuphine 5 mg iv as an anti-pruritic and ondansetron 4 mg iv as an anti-emetic. Patients undergoing THR and TKR are enrolled in multi-disciplinary clinical pathways that initiate physical therapy either on the afternoon of surgery or morning of POD1. Both pathways target BID ambulation on POD1 followed by progressively more activity. The TKR pathway includes continuous passive motion devices BID. For pharmacological deep venous thrombosis (DVT) prophylaxis, a nomogram [23] is used to dose coumadin to achieve an INR of 1.8–2.5 on postsurgical day 4.

At Rush University Medical centre, patients typically received PCEA with 0.1 % bupivacaine with fentanyl 5 mcg/ml after spinal anaesthesia. Initial settings were continuous infusion of 6 ml/h, bolus dose 1 ml, lockout time 15 min, and one hour lockout of 10 ml. Patients were assessed twice a day. Patients were typically started on oral analgesics on the night of surgery, and the continuous infusion was decreased as tolerated until successful conversion to oral analgesics only. On POD2, the epidural was discontinued and patients commenced on oxycodone extended release 10 mg BID. Preoperative and postsurgical celecoxib (200 mg day) was administered as a standard adjunct analgesic unless contraindicated by active cardiovascular disease, liver disease, renal disease, or sensitivity to NSAIDs. Analgesic adjuncts such as pregabalin were prescribed at the discretion of the APS. For

pharmacological deep venous thrombosis (DVT) prophylaxis, a nomogram [23] is used to dose coumadin to achieve an INR of 1.8–2.5 on POD4.

At MGH, patients undergoing TKR typically receive spinal anaesthesia using 3 ml of bupivacaine 0.5 % and THR patients receive general anaesthesia. A portion of patients are placed on IV PCA hydromorphone 0.2 mg q10 min with no basal rate (1 h max=1.5 mg) titrated to adequate pain control over the first 24 h. These patients are then usually converted to oral analgesics on POD1 with oxycodone 5 mg/acetaminophen 325 mg 1–2 tabs q4h PRN. The rest of the patients are started on oral analgesics immediately in the postoperative period with additional oxycodone extended release 10 mg BID. Most patients in addition were prescribed NSAID's either as ketorolac or ibuprofen 400–600 mg q8h PRN. After THR, 68 % of patients received acetaminophen 650 mg q6h PRN pain post-operatively. Physical therapy for both TKR and THR patients is typically started on POD1 with at least BID ambulation and followed by progressively increased activity. If the patient receives PCEA, passive range of motion is performed BID in TKR patients until the epidural catheter is discontinued. For pharmacological DVT prophylaxis, patients are usually started on scheduled subcutaneous heparin or subcutaneous dalteparin.

At Sunnybrook, patients typically received acetaminophen 1,000 mg, celecoxib 400 mg, and gabapentin 600 mg approximately two hours prior to surgery. TKR patients receive either a femoral nerve block or a catheter accompanied with a sciatic nerve block prior to surgery. Central neuraxial (90 % are spinal) anesthesia is used. Postoperative analgesia consist of IV PCA with hydromorphone, oxycodone extended release 10 mg q8 h×12 doses, and oxycodone 5–15 mg q 2 h prn after the IV PCA is discontinued. Additional analgesics are celecoxib 200 mg BID×8 doses, acetaminophen 100 mg q 6 h×4 days, and gabapentin 200 mg q8 h×12 doses. For the TKR patients with a femoral nerve catheter, ropivacaine 0.15 % is infused at 5 ml/h until 0600 POD2. Routine prn medications for nausea are ondansetron, procchlorperazine, and dimenhydrinate. Diphenhydramine is routinely used on a prn basis for pruritus. Both pathways target BID ambulation on POD1 followed by progressively more activity. For pharmacological deep venous thrombosis (DVT) prophylaxis, rivaroxaban 10 mg po daily is started on POD1 for 15 days.

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