A REAL WORLD MANAGEMENT OF PATENTS WITH OSTEOARTHRITIS KNEE UNDERGOING TOTAL KNEE REPLACEMENT – A RETROSPECTIVE STUDY IN THAILAND (ARMOR STUDY)

Thanainit Chotanaphuti[*], *Viroj Kawinwonggowit*[**], *Chamroonkiat Leelasestaporn*[***], *Sombat Rojvitroj*[****]

[*]**Department of Orthopedics, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Bangkok, Thailand**

[**]**Department of Orthopedics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand**

[***]**Bumrungrad International Hospital, Bangkok, Thailand**

[****]**Bangkok Dusit Medical Services PLC, Bangkok, Thailand**

Abstract

Background: In Thailand, total knee replacement (TKA) is a common clinical intervention to manage patients with OA (osteoarthritis). Public and private hospitals tend to exhibit different patterns of TKA use. Hence, knowledge with regard to TKA practice patterns, use and treatment outcomes in different hospitals in Thailand will improve the understanding of clinical management of OA and patient care.

Objectives: The primary objective of the study was to examine the patterns of pain management during pre-operative, hospital admission for TKA, and postoperative periods (surgery to 3 months after discharge) for patients receiving TKA in public and private hospitals. The data were collected from various hospitals and subjected to analysis.

Methods: This retrospective observational multi-center chart review study was conducted in public (n=2) and private (n=2) hospitals in Thailand. A total of 220 patients diagnosed with knee OA (ICD-10 code, M17.0 and 17.1) who had undergone TKA were included in the study. The estimated ratio of patients from public and private hospitals was 1:1. Patient medical charts were accessed with the Ethics Committee's approval. De-identified patient data were extracted from the chart and entered into a paper Case Report Form (CRF). Patients with history of major cardiovascular events and bilateral total knee replacement were excluded from the study.

Results: At clinical baseline, cyclooxygenase-II (COX-II) inhibitors followed by traditional nonsteroidal anti-inflammatory drugs (tNSAIDs) were the preferred drug classes for pain management irrespective of hospital type or age group. At operation, use of pain control drugs was comparable between public and private hospitals. The use of concomitant drugs such as antithrombotic agents was observed to be frequent in both the hospital types and different age groups. After surgery, use of opioids was the highest among other drug classes followed by COX-II inhibitors and tNSAIDs; however, the use of opioids decreased faster daily compared with COX-II inhibitors which remained constant until 4 days after surgery. Among discharge pain control medications, analgesics and opioids were used extensively followed by COX-II inhibitors; however, the use of NSAIDs was very limited because of associated complications. During the follow-up period, opioids were the most commonly prescribed drug class in both hospital types; use of COX-II inhibitors was significantly higher in private hospitals The same trend of drug use was observed by age group (both >70 and <70 years of age). The proportion of patients with complications was observed more in public hospitals as compared with private settings. In the present study, patients receiving COX-II-inhibitors combined with other pain control medications reported lower pain scores than average after surgery. The clinical outcome distribution among patients receiving multiple pain control drugs during discharge was observed to be better compared with other combined regimens or analgesics alone.

Conclusion: Pain management is one of the most important and challenging aspects of TKA. The patterns of pain management during pre-operative, during operation and postoperative stages differed. The use of COX-II inhibitors followed by NSAIDs was observed to be higher in the pre-operative stage, while use of opioids was higher after surgery and follow-up period compared with COX-II inhibitors.

Keywords : Total knee arthroplasty, Total knee replacement, Knee osteoarthritis, Pain management

J Southeast Asian Med Res 2018; 2(1): 45-57.
http://www.jseamed.org

Correspondence to:
Chotanaphuti T, Department of Orthopedics, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Bangkok, 10400, Thailand; Phone: 662- 17 2460066 Ext 93459; Fax:662-6444940;
Email: tanainit@hotmail.com

Introduction

Osteoarthritis (OA) is one of the most common musculoskeletal disorders that impact patients' quality of life. It causes permanent disability, especially among the elderly. [1] Research on defining optimal outcomes in pain management is still in its infancy and more understanding is needed. Generally, the main treatment goals for management of pain, both acute and chronic, are to relieve pain, facilitate function and improve quality of life. Achieving a pain-free state is challenging and unrealistic as a treatment goal. For optimal results, the treatment plan should be tailored to the needs, desires and circumstances of individual patients.

Nonoperative therapies, namely, pharmacological and nonpharmacological treatment modalities, [2-5] have been found to be effective and convenient in helping OA patients achieve pain relief. In Thailand, traditional nonsteroidal anti-inflammatory drugs (tNSAIDs) and selective cyclooxygenase (COX)-II inhibitors are usually prescribed to patients with OA to control pain. Due to the low cost, tNSAIDs are one of the most common drugs used for pain relief among patients with OA. Although tNSAIDs are effective in controlling pain in mild to moderate OA, they were also found to cause peptic ulceration and life threatening complications such as hemorrhage and perforation due to its nonselective action on COX-I. The risk of these side effects increases with long term use. Recently, COX-II selective inhibitors have been recommended for pain management among patients with high risk of adverse drug events from tNSAIDs. [6-9] This is because COX-II inhibitor drugs only inhibit the COX-II isoenzyme, which is released during inflammation. Therefore, COX-II inhibitor drugs are able to control pain without increasing the risk of bleeding and gastrointestinal complications. However, in Thailand, patients with OA pain have limited access to COX-II inhibitors due to the lack of reimbursement. The COX-II inhibitor drugs are currently in a controlled list of government drug use evaluation (DUE). The study by Philip G and colleagues indicated that approximately 54% patients had moderate to severe pain while on the currently prescribed pain treatments (most commonly NSAIDs, followed by paracetamol and opioids); and therefore, presents a high unmet need in the pain management in patients with knee OA [10]. Therefore, when more serious joint deformity occurs and pain is uncontrolled, operative options like total knee arthroplasty (TKA) or total knee replacement are considered.

TKA is an elective surgery, indicated for disability, pain and limited function from OA, rheumatoid arthritis, or any type of arthritic knee deformity. This surgery has to be considered in light of the patient's symptoms, current health status and radiographic evidence of primary or inflammatory degenerative joint disease. The latter is shown as narrowed joint space, osteophytes (spurring) and bone cysts, squaring of condyles and bone sclerosis. [11] As TKA is an elective surgery, the decision to pursue TKA could be subjective, depending upon the physician's opinion /practice and patients' conditions, as well as patients' response to other treatment options. [12] No age or weight limit exists for a patient to undergo TKA. Operations have been successfully performed among young patients with juvenile arthritis and among elderly patients with degenerative arthritis. [12] Postoperative pain management is also important, as related research has demonstrated that poor acute pain control after TKA could

lead to long term chronic pain.[13] Therefore, effective acute pain control with analgesia or anesthesia techniques should be provided.

Methods

This study was a retrospective, observational multi-center chart review study conducted in public and private hospitals in Thailand. Patient data were identified and extracted using ICD-10 and/or procedural codes that were used at each institution.

Study population

A total of approximately 220 male and female patients with OA were included in this study. The study was conducted in four medical centers in Bangkok – two public hospitals (Phramongkutklao Hospital and Ramathibodi Hospital) and two private hospitals (Bangkok Hospital and Bumrungrad Hospital). A hundred and ten patients were selected from public and private sectors. Eligible patients comprised patients with OA who had undergone TKA between January 2014 and December 2015, and were randomly selected for chart review. All related data were extracted from the chart and entered into an approved paper Case Report Form (CRF). The Ethics Committee's approval was obtained from each institute before accessing patient medical charts.

Inclusion Criteria

Patients' inclusion criteria included aged >35 years, with a diagnosis of OA of the knee (ICD-10 code, M17.0 and 17.1) and who had undergone unilateral total knee replacement. Patients had a regular clinical record at the study site.

Exclusion Criteria

Patients' exclusion criteria included having a history of major cardiovascular events, i.e., acute MI, unstable angina, congestive heart failure, history of total knee replacement (same side) or bilateral total knee replacement. Patients with incomplete/insufficient data required for the primary objective were also excluded.

Data collection

Investigators and designees extracted data from medical charts of eligible patients. Paper CRFs were used in this study. In compliance with Thailand FDA and relevant private information protection laws, confidentiality of protected health information was maintained by all parties throughout the study. All data were secured against unauthorized access. Data were de-identified with a unique identifier on each patient's CRF and other study records were sent to MSD.

Statistical analysis

Before conducting analyses for specific objectives, descriptive statistics for all demographic characteristics, hospital type and presence of comorbidities were carried out. These included mean, standard deviation, median, interquartile range and minimum/maximum for continuous variables and proportions with standard deviations for categorical variables. Statistical significance was set at $p<0.05$.

Sample Size Calculation

The sample size of 220 was estimated using Yamane's formula. Based on a population of 390 patients, precision of ± 5% and 95% confidence level, at least 197 subjects were required for the study.

Results

The results were reported according to primary and secondary objectives. The primary objectives were to examine the use of drugs to manage pain during pre-operative, operation and postoperative periods. The secondary objectives were to evaluate resource use, pain score, clinical outcomes and waiting time to TKA.

Demographics of study population

Table 1 shows the demographics of eligible patients. Though the baseline characteristics of the patients visiting public and private hospitals were comparable, differences were observed in the presentation of symptoms, with private hospitals seeing more patients presenting severe symptoms. Symptom severity was assessed based on clinical judgment recorded in a chart.

Table 2 depicts the proportion of patients with different insurance schemes. The majority of the patients visiting public hospitals were covered under the CSMBS insurance scheme (66.36%), followed by UCS (10.9%). Approximately 87% patients visiting private hospitals incurred out-of-pocket expense compared with only 20% patients visiting public hospitals.

Table 1. Baseline characteristics of patients visiting public and private hospitals

Characteristics	All patients (%)	Public Hospital (%)	Private Hospital (%)	*p*-value
Arthritis	0.45	0.00	0.91	0.3171
Autoimmune diseases	0.00	0.00	0.00	1
Other metabolic syndrome	10.91	9.09	12.73	0.3876
CNS	0.91	0.91	0.91	1
Respiratory disease	0.45	0.91	0.00	0.3171
Other**	19.55	29.09	10.00	.00038*

*Statistical significance at $p<0.05$

** Others include Delirium, BPH, AIHA, Glaucoma, Anemia and CVA

Table 2. Different insurance schemes and reimbursement statuses

		All patients		**Public Hospital**		**Private Hospital**	
		n	**%**	**n**	**%**	**n**	**%**
Gender	Male	53	24.09	20	18.18	33	30.60
	Female	167	75.91	90	81.82	77	70
Public Insurance Scheme or source of funding for QA treatment	Universal Coverage Scheme (UCS or 30 Baht-Scheme)	12	5.46	12	10.91	0	0
	Social Security Scheme (SSS)	3	1.37	3	2.73	0	0
	Civil Servant Benefit Scheme (CSMBS)	73	33.18	73	66.36	0	0
	None	132	60.0	22	20	110	100
Private insurance	yes	10	4.55	1	0.91	9	8.18
Out-of-pocket	yes	118	53.64	22	20	96	87.27
Reimburse from employer	yes	5	2.28	0	0	5	4.55

Pain management during the pre-operative period

Table 3 compares the patterns of pain management for OA by hospital type (public and private hospitals) at clinical baseline. Public hospitals were more likely to prescribe COX-II inhibitors, tNSAIDs and opioids, as well as combined therapies including tNSAIDS+COX-II inhibitors and tNSAIDS+opioids compared with private hospitals. Private hospitals were also more likely to prescribe paracetamol (9.09%) than public hospitals (4.55%).

Table 4 details the proportion of patients on various therapies by age group (≥70 versus <70 years) at clinical baseline. Patients aged ≥70 years were more likely to be prescribed opioids (5.88%) as compared with patients aged <70 years (2.97%). Similarly, tNSAIDS+COX-II inhibitors were prescribed more frequently among patients aged ≥70 years.

Table 3. Percentage of patients on pain drug therapy at clinical baseline by hospital type

Drug Class	% of patients receiving drug therapy at clinical baseline			
	All patients (n=220)	Public Hospital (n=110)	Private Hospital (n=110)	*p*-value
Paracetamol	6.82	4.55	9.09	0.1827
tNSAIDs	10.45	11.82	9.09	0.5091
COX-II inhibitors	17.27	23.64	10.91	0.0127*
Opioids	4.55	6.36	2.73	0.1972
Paracetamol+ tNSAIDs	1.82	0.91	2.73	0.3137
Paracetamol+ COX-II inhibitors	5.91	9.09	2.73	0.0460*
Paracetamol+ Opioids	1.82	2.73	0.91	0.3137
tNSAIDs+ COX-II inhibitors	3.64	6.36	0.91	0.0312*
tNSAIDs+ Opioids	1.82	3.64	0	0.0439*
COX-II inhibitors + Opioids	1.36	2.73	0	0.0817
Paracetamol+ tNSAIDs+ COX-II inhibitors	1.36	0.91	1.82	0.5617
Other medications	9.55	10.91	8.18	0.4918
No pain medication	33.64	16.36	50.91	<0.0001*

*Statistical significance at $p<0.05$

Table 4. Proportion of patients on drug class at medication after operation by hospital type (discharge clinical baseline by age group medication)

Drug Class	% of patients on therapy at clinical baseline by age group		
	≥70 years old (n=119)	≤70 years old (n=101)	*p*-value
Paracetamol	9.24	3.96	0.1223
tNSAIDs	11.76	8.91	0.4921
COX-II inhibitors	19.333	14.85	0.3821
Opioids	5.88	2.97	0.3028
Paracetamol+ tNSAIDs	0	3.96	0.0288*
Paracetamol+ COX-II inhibitors	5.04	6.93	0.5544
Paracetamol+ Opioids	1.68	1.98	0.8685
tNSAIDs+ COX-II inhibitors	4.20	2.97	0.6279
tNSAIDs+ Opioids	1.68	1.98	0.8685
COX-II inhibitors + Opioids	1.68	0.99	0.6608
Paracetamol+ tNSAIDs+ COX-II inhibitors	0.84	1.98	0.4685
Other medications	10.92	7.92	0.4514
None prescribed	27.73	40.59	0.0447

*Statistical significance at $p<0.05$

Pain management during operation

Drug use pattern related to TKA during operation by hospital type. While both public and private hospitals prescribed antibiotics, differences were observed in the prescription of other concomitant drugs. While antihistamines and bone and muscle-related drugs were often prescribed in public hospitals, private hospitals were more likely to prescribe antithrombotic and GI-related drugs than public hospitals.

The use of pain control drugs at discharge was almost similar in both public and private hospitals. Among concomitant drugs, the use of bone-related drugs (38% vs. 5%, $p<0.0001$) and antibiotics (77% vs. 35%, $p<0.0001$) were higher in public hospitals compared with private hospitals. However, the use of antithrombotic drugs was almost twice as high in private hospitals compared with public hospitals (65% vs. 35%, $p<0.0001$). On average, physicians prescribed discharge pain medication for 9.13 days across hospitals.

Table 5 shows the pain control drug prescription during discharge by hospital type. In public hospitals, the majority of patients received analgesic drugs (71%) or analgesic +opioids (50%), whereas patients in private hospitals were more likely to receive COX-II inhibitors during discharge. At discharge, private hospitals prescribed more COX-II inhibitors than public hospitals ($p=0.0006$).

Table 5. Distribution of pain control drugs related to TKA during operation by hospital type and operation by hospital types (discharge medication)

Drug type	% of patients on discharge medication after operation			
	All patients (n=220)	Public Hospital (n=110)	Private Hospital (n=110)	*p*-value
COX-II inhibitors	40.5	29.1	51.8	0.0006*
tNSAIDS	18.2	1.8	34.5	0.0059*
Muscle relaxant	12.7	12.7	12.7	0.00068*
Opioids	26.4	18.2	34.5	0.138
Analgesic drug plus opioid	47.7	50.0	45.5	0.5
Analgesic drug	62.7	70.9	54.5	0.0121*
Others**	9.1	5.5	12.7	0.064

*Statistical significance at $p<0.05$

** Others include perskindol spray and repagril

Pain management in the postoperative period (follow-up period)

Among all drug classes, opioids were the most frequently prescribed in the postoperative period (at three-month follow-up) in both public and private hospitals. Private hospitals relied more on prescribing COX-II inhibitors (71% vs. 47%, $p=0.0004$), tNSAIDs (42% vs. 21%, $p=0.0009$) and analgesics (90% vs. 75%, $p=0.0028$) as compared with public hospitals.

In pre-operative, during admission, and postoperative periods, both public and private hospitals had similar testing requirements. Therefore, the laboratory measurements were comparable for patients attending public and private hospitals.

The rate of complications in the postoperative setting was higher in public hospitals as compared with private settings (2.73% vs. 0.91%). Private hospital patients were more likely to report urinary tract infection (UTI) while patients from public hospitals were more likely to report deep vein thrombosis (DVT), pulmonary embolism and congestive heart failure (CHF).

Pain score

During the pre-operative period, mean pain score at public and private hospitals were comparable (2.32 vs.2.99, respectively).

Table 6 summarizes the pain score and drug use pattern to control pain after surgery by hospital type. Use of opioids decreased daily in both public and private hospitals.

However, the use decreased at a higher rate in public hospitals as compared with private ones. Pain score was comparatively higher in public hospitals than private hospitals and decreased over subsequent days in both hospital types.

Table 7 shows the mean time from decision to TKA was shorter in private hospitals compared with public hospitals (22.9 days vs. 171.5 days, $p < 0.0001$).

Table 6. Pain score and drugs used to control pain after surgery

Day		All patients	Public Hospital	Private Hospital
Day 1	Mean pain score	3.78	4.79	2.76
	IV tNSAIDs (%)	11.36	13.64	9.09
	Oral tNSAIDs (%)	10.91	2.73	19.09
	Opioids (%)	69.09	70.00	68.18
	COX-II (%)	36.36	22.73	50.00
	Paracetamol (%)	54.55	47.27	61.82
	Others* (%)	22.27	23.64	20.9
Day 2	Mean pain score	3.44	4.15	2.63
	IV tNSAIDs (%)	5.94	5.45	6.42
	Oral tNSAIDs (%)	11.82	1.82	21.82
	Opioids (%)	64.55	62.73	66.36
	COX-II (%)	35.21	24.55	45.87
	Paracetamol (%)	53.64	45.45	61.82
	Others* (%)	22.27	23.64	20.91
Day 3	Mean pain score	2.80	3.22	2.3
	IV tNSAIDs (%)	1.99	1.00	2.97
	Oral tNSAIDs (%)	13.18	1.82	24.55
	Opioids (%)	53.91	50.00	61.82
	COX-II (%)	33.77	22.00	45.54
	Paracetamol (%)	47.75	32.27	58.18
	Others* (%)	14.55	10.00	19.09
Day 4	Mean pain score	2.48	2.78	2.22
	IV tNSAIDs (%)	1.90	0	3.80
	Oral tNSAIDs (%)	8.18	0	16.36
	Opioids (%)	31.36	23.64	39.09
	COX-II (%)	32.05	21.05	43.04
	Paracetamol (%)	37.92	28.57	47.27
	Others* (%)	7.73	4.55	10.91
Day 5	Mean pain score	2.08	2.79	1.73
	IV tNSAIDs (%)	1.45	0	2.90
	Oral tNSAIDs (%)	6.82	0	13.64
	Opioids (%)	20.00	10.91	29.09
	COX-II (%)	25.72	16.67	34.78
	Paracetamol (%)	22.73	8.18	32.27
	Others* (%)	4.55	0.91	8.18

*Others include analgesic combination drugs, neurology, muscle relaxant drugs

Table 7. Mean time to TKA (from TKA decision date to surgery)

Time to TKA (from TKA decision date to surgery)	All patients (%)	Public Hospital (%)	Private Hospital (%)
Mean (day)	97.2	171.5	22.9
Min (day)	0	8	0
Max (day)	695	695	187
SD (day)	130.85	147.2	39.2

Length of hospital stay (post TKA)

Average admission duration (post TKA until discharge) after TKA in both public and private hospitals was also studied. The majority of patients (~85%) stayed in hospitals around three to six days. Only 8% of patients stayed in hospitals for one to two days.

Clinical Assessment of knee function after TKA during the postoperative (follow-up) period

Table 8 reports the clinical assessment and patient reported outcomes (PRO) including pain assessment during the postoperative (follow-up) period in both public and private hospitals. More patients in public hospitals experienced pain as compared with private hospitals, albeit not statistically significant (6.4% vs. 3.6%, p = 0.3412). A significantly higher proportion of patients were found able to walk but with a cane in private hospitals compared with public hospitals (17.3% vs. 7.3%, p = 0.0238).

Overall, patients who were prescribed analgesics only were the most likely to experience pain (21%), followed by analgesics+ analgesics plus opioid combination (12%). A high proportion of patients (ranging from 64% to 79%) reported overall good outcomes while on COX-II inhibitor combinations. A lower proportion of patients on COX-II inhibitor combinations (ranging from 0%-14%) reported issues with flexion/extension compared with the overall range of 0% to 63%. No patient reported issues with surgery wound while on COX-II inhibitor combination, except for COX-II inhibitors + analgesics plus opioid (12% of patients reported some issues).

Table 8. Pain outcomes in public and private hospitals after TKA during the postoperative (follow-up) period

Assessment	All patients (%) (n=220)	Public Hospitals (%) (n=110)	Private Hospitals (%) (n=110)	p-value
Reported pain	5.0	6.4	3.6	0.3412
Overall good outcomes	63.2	60.9	65.5	0.4777
Reported some issue with flextion/extention	15.9	18.2	13.6	0.3523
Able to walk but need cane	12.3	7.3	17.3	0.0238*
Reported some issue with flextion/extention	2.3	0.9	3.6	0.1770

*Statistical significance at p<0.05

Discussion

The objectives of the study were to examine the patterns of pain management during pre-operative, hospital admission for TKA, and postoperative periods among patients with knee OA receiving unilateral TKA in public and private hospitals. The baseline characteristics for patients visiting public and private hospitals were largely comparable. Notable differences between the two groups were: (i) severity of OA, with more patients presenting severe OA in private hospitals (78%) than in public hospitals (59%) and (ii) out-of-pocket expenses, with more private hospital patients (87%) incurring private expenses than public hospital patients (20%).

In this study, baseline medication was collected to elicit an understanding on the OA treatment before TKA. The present study showed that among patients overall (both public and private hospitals combined), at clinical baseline, use of COX-II inhibitors was highest followed by tNSAIDs. By hospital type, use of COX-II inhibitors and combined therapies including paracetamol+ COX-II inhibitors, tNSAIDS+COX-II inhibitors and tNSAIDS + opioids were higher in public than private hospitals. In contrast, paracetamol prescriptions were almost twice in private hospitals compared with public hospitals (9.09% vs. 4.55%). Of note, 50% of patients from private hospitals had no record of OA medication for pain management. No statistically significant differences were observed in the medications prescribed to both aged ≥70 years and <70 years, which could indicate a consistent treatment guideline regardless of age. However the proportion of patients receiving COX-II inhibitors was higher compared with tNSAIDs. This could be due to the side effect caused by the long term use of tNSAIDs. During the operation period, among patients overall, use of antibiotics followed by GI related drugs and antithrombotics were observed to be high. Use of pain control drugs at operation was similar between public and private hospitals (20% vs. 20.9%). The present study also showed a high use of antithrombotics as concomitant drugs during the perioperative period across hospitals and different age groups. The findings are consistent with the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, which recommend the use of antithrombotic drugs as a prophylaxis measure to reduce the outcomes of fatal and symptomatic pulmonary embolism and symptomatic DVT in patients with TKA.(14) The pattern of drug use at operation was similar across different age groups, except for bone- and muscle-related drugs, which was significantly reported to be higher among patients aged ≥70 years, compared with patients <70 years of age (25.21% vs. 9.9%). The multimodal approach was commonly used to achieve synergistic effects in managing pain for patients with TKA.[15] In this study, various combinations of pain control drugs were used in Thai clinical practice after surgery. Among the different combinations, in both public and private hospitals combined, opioids combinations (with paracetamol and with COX-II inhibitors) were found to be the most common combined pain regimen to be used after surgery. Patients who received COX-II inhibitors as one of their pain control regimens reported lower pain scores than the mean pain scores in the cohort, particularly on Day 1 after surgery and therefore, could be considered as the most effective pain control combined regimen. Patients receiving COX-II inhibitors combined with other drugs reported the lowest average score within five days after surgery. This finding was consistent with the study conducted by Peter Lierz et al. demonstrating that the pain intensity among patients taking COX-II inhibitor (etoricoxib) was reduced during the first postoperative day. Approximately 97% of patients in the etoricoxib group achieved successful pain management compared with only 73% patients in placebo group.[16] It was also observed that use of opioids was gradually decreased in both public and private hospitals. This could be explained by the potential side effects of opioids and the narrow risk-benefit ratio. Opioids should be used sparingly and only for short duration, as long term use may lead to dependence and addiction.[17] In contrast, COX-II inhibitors were consistently prescribed during the first four days after surgery.

The present analysis showed that among different drug categories prescribed at discharge, among patients overall, the highest proportion were on pain control drugs followed by antibiotics. A similar trend was followed by public and private hospitals individually. Among the pain controlled medications prescribed at hospital discharge, analgesics and opioids were used extensively followed by COX-II inhibitors among patients overall as well as in both the public and private hospitals analyzed separately. The prescription

of COX-II inhibitors, tNSAIDs and opioids were higher in private hospitals compared with public hospitals. The use of tNSAIDs was limited during the discharge period in both public and private hospitals. This could be because of the concern for postsurgical gastrointestinal or bleeding complications, the most common adverse event of tNSAIDs.[7, 8, 18] Therefore, COX-II inhibitor is one of the primary choices for controlling pain after surgery. A randomized, double-blind study conducted by Rasmussen and colleagues suggested that the use of etoricoxib (COX-II inhibitor) resulted in superior analgesic effect compared with placebo in the acute postsurgical setting.[19] On average, physicians prescribed discharge pain medication for 9.13 days across studied hospitals. At three-month follow-up, most patients from all studied hospitals had good overall outcomes and were able to walk with a cane. Some were found to have issues with flexion/ extension and experienced mild pain symptoms, which are common symptoms during the first few months after surgery.[20] The prescribing patterns were almost similar for both age groups, except that patients aged <70 years (63.37% vs. 55.46%) being more likely to be prescribed with COX-II inhibitors than those aged ≥70 years. Complication rates were also higher in public hospitals as compared with private settings (2.73% vs. 0.91%). The complications reported were mainly UTI, DVT, pulmonary embolism and CHF. During the follow-up period, among different pain medications prescribed, opioids were the most commonly prescribed drug class among patients overall as well as in public and private hospitals analyzed separately, with the use being higher in private hospitals. Use of COX-II inhibitors, tNSAIDs and opioids was also observed to be higher in private hospitals as observed during the discharge period. These findings were consistent with public and private payers.

Among patients overall (both public and private hospitals combined), clinical outcome distribution during the follow-up period among patients receiving a combination of pain control drugs during discharge tended to be better compared with other combined regimens or analgesics alone. Considering the types of pain control drugs, the results demonstrated that patients with discharge prescriptions of COX-II inhibitors combined with other pain treatments were more likely to achieve pain control than patients receiving analgesics (paracetamol) alone or analgesics plus opioids during the follow-up visit. No patient receiving COX-II inhibitors, tNSAIDs or opioids in both hospital types reported any issues with surgery wound. Patients taking opioids were most likely to report some issues with flexion/extension, while patients on COX-II inhibitors were the least likely. This was consistent with the finding from a study by Arendt-Nielsen et al., reporting that patients with knee OA on COX-II inhibitor (etoricoxib) therapy experienced improvement in pain control during walking/stair climbing and reported lower general pain scores compared with those taking placebo.[21] Although this constituted a retrospective study, the results indicated the potential benefit of using COX-II inhibitors as a postoperative pain management therapy for patients undergoing TKA.

Notably, in the present study, among the overall patient population, the average time to TKA from decision to surgery was almost three months. The average waiting time observed to TKA from decision to surgery was almost seven times higher in public hospitals (~6 months) compared with private hospitals (<1 month). The maximum waiting time was almost two years in public hospitals, while less than one year time in private hospitals. Although patients are covered under national health insurance in principle, many chose to seek treatment from private hospitals providing shorter waiting times. The long waiting time at the public hospitals could have also encouraged patients to seek informal care or self-medicate.[22] This could imply a high unmet need in the public sector in view of insufficient facilities, and availability of effective OA treatment in Thailand.

The study results showed approximately one fourth of patients (both public and private hospitals combined) underwent TKA surgery on both knees during the study period; this number was higher in public hospitals compared with private hospitals (33.64% vs. 17.27%). No significant difference was found in the proportion of patients undergoing surgery on the first knee (either left/right) by hospital type. Among patients overall (both private and public hospitals combined), a higher proportion of surgeries were on the left knee compared to the right knee among patients who underwent surgery on the second knee. While private hospitals followed the same trend, the

opposite trend was followed by public hospitals. Several limitations should be noted when interpreting these results. The retrospective nature of the study limited the amount of information for analysis.[23, 24] Particularly, the data could only provide an initial descriptive understanding of the clinical treatment pattern. Therefore, we were unable to conclude a causal relationship between intervention and treatment outcomes. In addition, the hospitals included in this study were located in metropolitan Bangkok. However, given that they were all tertiary care hospitals, they are reflective of the best medical practices in Thailand. Another limitation was the different methods for collecting pain scores. While three hospitals used VAS, one center recorded it as NRS. Nonetheless, since NRS is a segmented numeric version of VAS [25], VAS scores were similar to NRS scores and the final data were represented using the NRS scale. Finally, the study could not capture the data for patients who might have undergone surgery on the second knee after the study period. In addition, patients who underwent surgery in private hospitals may have received drug from elsewhere, which were not recorded in the chart.

Conclusion

At clinical baseline (before TKA), COX-II inhibitors were the most common drugs prescribed for pain management, irrespective of hospital type or age group; the use of COX-II inhibitors monotherapy/combination regimens was higher in the public than the private sector. At operation, the use of pain control drugs was similar for both public and private hospitals; antibiotics were highly prescribed drug during this period. After surgery, use of opioids was highest, followed by COX-II inhibitors and analgesics. COX-II inhibitors were more likely to be used in the private sector. The multimodal approach was found to be effective in managing pain during the different stages of TKA. Pain score after surgery for patients taking combined regimens of COX-II inhibitors was observed to be lower than those taking other drugs. Compared with public hospitals, lower pain scores were observed in private hospitals. At discharge, analgesics and opioids were the most commonly prescribed classes, followed by COX-II inhibitors. In terms of clinical outcomes, patients prescribed with COX-II inhibitors combined with other pain control treatment reported less pain than patients taking only analgesics or analgesics plus opioids. Patients taking COX-II inhibitors reported no issue with surgery wound and were the least likely to report issues with flexion/extension. During follow-up visit, a majority of patients were on opioids followed by analgesics and COX-II inhibitors in both public and private hospitals. In conclusion, this study provided an initial understanding of pain management among patients with OA undergoing TKA in public and private hospitals.

Acknowledgement

The study was supported by Merck Sharp & Dohme Corp.

References

1. Farr Ii J, Miller LE, Block JE. Quality of life in patients with knee osteoarthritis: A commentary on nonsurgical and surgical treatments. Open Ortho J 2013; 7: 619-23.
2. Conaghan PG, Dickson J, Grant RL. Care and management of osteoarthritis in adults: summary of NICE guidance. BMJ 2008; 336: 502-503.
3. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 2012; 64: 465-74.
4. Rhon D, Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008; 16: 1585; author reply 1589.
5. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 2010; 18: 476-99.
6. Wallace JL. NSAID gastropathy and enteropathy: distinct pathogenesis likely necessitates distinct prevention strategies. Br J Pharmacolo 2012; 165: 67-74.
7. Turajane T, Wongbunnak R, Patcharatrakul T, Ratansumawong K, Poigampetch Y, Songpatanasilp T. Gastrointestinal and cardiovascular risk of non-selective

NSAIDs and COX-2 inhibitors in elderly patients with knee osteoarthritis. J Med Assoc Thai 2009; 92 (Suppl 6): S19-26.

8. Masso Gonzalez EL, Patrignani P, Tacconelli S, Garcia Rodriguez LA. Variability among nonsteroidal antiinflammatory drugs in risk of upper gastrointestinal bleeding. Arthritis Rheum 2010; 62: 1592-601.
9. Turajane T, Chaweevanakorn U, Sungkhun P, Larbphiboonpong V, Wongbunnak R. Cost-utility analysis and economic burden of knee osteoarthritis treatment: the analysis from the real clinical practice. J Med Assoc Thai 2012; 95 (Suppl 10): S98-104.
10. Conaghan PG, Peloso PM, Everett SV, Rajagopalan S, Black CM, Mavros P, et al. Inadequate pain relief and large functional loss among patients with knee osteoarthritis: evidence from a prospective multinational longitudinal study of osteoarthritis real-world therapies. Rheumatology (Oxford) 2015; 54: 270-77.
11. Van Manen MD, Nace J, Mont MA. Management of Primary Knee Osteoarthritis and Indications for Total Knee Arthroplasty for General Practitioners. J Am Osteopath Assoc 2012; 112: 709-15.
12. AAOS. American Academy of Orthopaedic Surgeons: Total Knee Replacement. 2015; http://orthoinfo.aaos.org/topic.cfm?topic=a00 389. Accessed 30 Jan 2016.
13. McCartney CJ, Nelligan K. Postoperative pain management after total knee arthroplasty in elderly patients: treatment options. Drugs Aging 2014; 31: 83-91.
14. Falck-Ytter Y, Francis CW, JohansonNA, Curley C, Dahl OE, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2 Suppl): e278S-e325S.
15. Korean Knee Society. Guidelines for the management of postoperative pain after total knee arthroplasty. Knee Surg Relat Res 2012; 24: 201-7.
16. Lierz P, Losch H, Felleiter P. Evaluation of a single preoperative dose of etoricoxib for postoperative pain relief in therapeutic knee arthroscopy: a randomized trial. Acta Ortho 2012; 83: 642-7.
17. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg 2013; 3: 191-6.
18. Schafer AI. Effects of nonsteroidal antiinflammatory drugs on platelet function and systemic hemostasis. J Clin Pharmacolo 1995; 35: 209-19.
19. Rasmussen GL, Malmstrom K, BourneMH, Jove M, Rhondeau SM, Kotey P, et al. Etoricoxib provides analgesic efficacy to patients after knee or hip replacement surgery: a randomized, double-blind, placebo-controlled study. Anesth Analg 2005; 101: 1104-11.
20. Choi YJ, Ra HJ. Patient Satisfaction after Total Knee Arthroplasty. Knee Surg Relat Res 2016; 28: 1-15.
21. Arendt-Nielsen L, Egsgaard LL, Petersen KK. Evidence for a central mode of action for etoricoxib (COX-2 inhibitor) in patients with painful knee osteoarthritis. Pain 2016; 157: 1634-44.
22. Rosenwald K, Ertl K, Fletcher KE, Whittle J. Patterns of arthritis medication use in a community sample. J Prim Care Community Health 2012; 3: 272-7.
23. Anthonisen NR. Retrospective studies. Can Respir J 2009; 16: 117-8.
24. Euser AM, Zoccali C, Jager KJ, Dekker FW. Cohort studies: prospective versus retrospective. Nephron Clin Pract 2009; 113: c214-7.
25. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: VisualAnalog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res 2011; 63 (S11): S240-52.