

## Research Article

# Local infiltration analgesia with bupivacaine reduces postoperative pain and opioid consumption after joint replacements in a Vietnamese Hospital

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## ABSTRACT

Knee and hip replacements are two major surgeries, which can lead to severe postoperative pain. An effective pain relief is essential to ensure an expected recovery outcome. Local infiltration analgesia with bupivacaine (LIB) has been investigated and accepted globally. However, this has been a new method in Vietnam, and recently applied at Thong Nhat Hospital. The objective of this study was to evaluate the effectiveness of LIB in management of postoperative pain, compared with conventional regimen in patients undergoing knee or hip replacements. A retrospective cohort study was conducted using medical records of patients undergoing either knee or hip replacement. Patients with renal or hepatic failure, a history of drug addiction, or allergy to any study medications were excluded. Patients were randomly selected from two groups – conventional pain control (n = 40) and LIB pain control (n = 40). LIB regimen included spinal anesthesia during surgery, local injection of bupivacaine before wound closure, and analgesia such as opioid, NSAIDs and gabapentin after surgery as needed. Local injection of bupivacaine was not performed in the conventional group. There were no significant differences between two study groups with respect to baseline characteristics. Patients in LIB group had significantly lower rate of severe pain in the first day after surgery ( $p < 0.001$ ), lower opioid consumption in the first three postoperative days ( $p < 0.05$ ), lower rate of severe pain in the first day after surgery ( $p < 0.001$ ), earlier ambulation ( $p = 0.004$ ), lower length of hospital stay ( $p = 0.039$ ), lower rate of sleep disturbance ( $p = 0.018$ ), and lower rate of respiratory depression ( $p = 0.043$ ), compared with those in conventional group. Our study suggests that LIB provided effective pain relief with less opioid consumption and an earlier functional recovery.

## 1. INTRODUCTION

Knee and hip replacements are two common orthopedic surgeries, and can cause severe postoperative pain, which probably leads to delayed recovery, prolonged hospitalization and adverse effects in motor function without an inappropriate pain treatment.

There are many conventional types of pain control after joint replacements for Vietnamese patients such as opioid regimen,

epidural analgesia, and femoral nerve block, but they still remain some disadvantages. For instance, opioids is considered as broad spectrum analgesic agents affecting a large number of organ system and influencing a wide range of body function, and therefore can cause numerous adverse effects such as sedation, nausea, physical dependence, and respiratory depression, especially among the elderly, who is at high risk of knee and hip replacements, due to increasing plasma concentrations<sup>1</sup>. In addition, both epidural analgesia and femoral nerve block are reported to effect negatively in walking ability<sup>2,3</sup>.

On the other hand, local infiltration analgesia considered as part of multimodal therapy was recorded to have a good result in postoperative pain control with fewer side effects as well as advantages in cost-effectiveness and ease-of-use in comparison with conventional methods. It is unlikely to epidural analgesia and femoral nerve block which requires professional training, this method can be performed by every surgeon without further training. Many studies have shown positive results from various medications and combinations for local infiltration analgesia, including ropivacaine, morphine, ketorolac, and epinephrine<sup>4-6</sup>. Local infiltration with bupivacaine (LIB) was also highlighted. Researchers have found that LIB reduces postoperative opioid consumption, which can lead to lower risk of adverse drug-related events. Besides, LIB also effect positively in recovery outcomes such as increasing patient satisfaction, and decreasing lengths of mobilization and hospital stay<sup>7</sup>.

Although LIB has been introduced globally for many years, it has been carefully applied recently in Vietnamese hospitals. There is a deficiency of researches comparing data between conventional regimens and LIB in Vietnam.

Therefore, the aim of this study was to evaluate the effectiveness related to improve postoperative opioid consumption, postoperative pain and recovery outcomes of LIB (with local injection of bupivacaine before wound closure) in management of pain after knee or hip replacements, compared with conventional regimen (without local injection of bupivacaine before wound closure).

## 2. MATERIALS AND METHODS

### 2.1. Study settings

This was a retrospective cohort study using medical records of patients undergoing

knee or hip replacements at Thong Nhat hospital. The protocol of this study was approved by the Institutional Review Board of the Thong Nhat Hospital (Project Number: 69 IRB/ QDBVTN 07022016)

### 2.2. Participants:

According to the following inclusion and exclusion criteria

#### *Inclusion criteria*

- Patients undergoing knee or hip replacement from January 1<sup>st</sup>, 2014 to May 10<sup>th</sup>, 2016.
- Aged 18 years or older.

#### *Exclusion criteria*

- Patients with a history of drug addiction (using more than 30 mg/day morphine or an equivalent dose of opioid within a month).
- Patients who are allergic to any study medications.

### 2.3. Sample size

A required sample size for each group was calculated using the formula:

$$n = \frac{2C}{(ES)^2}$$

C = 7.85 ( $\alpha = 0.05$ , CI 95% and  $\beta = 0.2$ , power = 0.8); ES =  $(\mu_1 - \mu_0)/\sigma_0$

$\mu_1$ ,  $\mu_0$  are average opioid consumptions (morphine IV, mg) during 24 hours after surgery of LIB pain control group and conventional pain control group, respectively.  $\sigma_0$  is standard deviation of average opioid consumption during 24 hours after surgery of conventional pain control group.

According to the study of Chen DW, et al.<sup>8</sup>,  $\mu_1$  was 2.50 mg,  $\mu_0$  was 4.50 mg, and  $\sigma_0$  was 2.51 mg. Therefore, the minimum sample size for each group was 25. In this study, we selected 40 patients in each group.

### 2.4. Study process

From January 1<sup>st</sup>, 2014 to May 10<sup>th</sup>, 2016, there were 176 medical records of patients undergoing knee and hip replacements in Orthopedic Department of Thong Nhat Hospital collected. 80 Patients were then randomly

selected from 176 medical records using SPSS into two groups – study group (LIB pain control group, n = 40) and conventional group (conventional pain control group, n = 40). LIB regimen included spinal anesthesia during surgery, local injection of bupivacaine before wound closure, and analgesia such as opioid, NSAIDs and gabapentin after surgery as needed. Local injection of bupivacaine before wound closure was not performed in conventional group. These two regimens were applied in the study hospital based on the WHO guideline<sup>9</sup> and availability of drugs in pharmacy.

Demographic data, including age, gender, comorbidities, pre-operative American Society of Anaesthesiologists' (ASA) classification of Physical Health – ASA score, causes of surgery, surgical methods, and operation time was collected for each patient.

On the operative day, amount of spinal fentanyl and patient's psychological consultation were also collected. On the first three postoperative days (POD1, 2, and 3), opioid consumption (morphine IV, mg) was recorded, and the Verbal Rating Scale (VRS) was used to measure pain level, including no pain, mild pain, moderate pain and severe pain. In addition, ambulation day and sleep disturbance were recorded. In this study, we defined ambulation day as the postoperative day that patient was recorded "physiotherapy practice" on nursing documentation, and sleep disturbance as that a patient could not sleep well at night after surgery and was prescribed diazepam.

Dosages of additional opioid drugs prescribed after surgeries were assessed until patients discharged from hospital. As patients were prescribed with different opioids, dosages of opioids were converted into opioid equivalents of intravenous morphine (morphine IV, mg) as follow<sup>10</sup>:

- Morphine IV : fentanyl IV = 100 : 1 (10 mg morphine = 100 mcg fentanyl)

- Fentanyl IV : sufentanyl IV = 5 : 1 (25 mcg fentanyl = 5 mcg sufentanyl)

- Morphine IV : tramadol = 1 : 10 (10 mg morphine = 100 mg tramadol)

- Tramadol PO : tramadol IV = 1.2 : 1 (12 mg tramadol PO = 10 mg tramadol IV)

Adverse drug events such as nausea, vomiting, respiratory depression, urinary retention, constipation, and others were also recorded. Discharge eligibility was met when a patient is conscious, have stable vital signs and can walk with crutches or with assistance of technician in 3 continuous days.

## 2.5. Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) Program, version 22.0. Patient's data were presented as mean  $\pm$  S.D., median (interquartile range 25-75%) or percentage. Comparison between LIB group and conventional study group the severe pain rate in the first postoperative day, rate of sleep disturbance, and adverse event rates were assessed using Chi-square test. T-test or Mann Whitney test was used to test for significant differences in means of ambulation days, opioid consumption, and length of hospital stay. The level of statistical significance was specified at  $p < 0.05$ .

## 3. RESULTS

### 3.1. Baseline characteristics of two study groups

Among 80 patients, 52.5% were female. Median age was 77 years old (67 – 84), with 85% patients aged 65 years and older. Chronic diseases were common among patients with 70% having at least one of them. Hypertension (60%) and cardio vascular diseases (26.3%) ranked the highest. There was no significant difference between two study groups with respect to demographic data. Pre-operative ASA score of patients was at level 2 and 3 (22.5% and 77.5%, respectively) without significant differences between two study groups. Most patients suffered from femoral head fracture (56.3%) and knee osteoarthritis (35%). There were three surgical methods recorded, including total knee replacement (35%), partial hip replacement (41.2%), and total hip replacement (23.8%). There were also no significant differences between two study groups in causes and methods of surgery. The baseline characteristics of patients were presented in Table 1.

Overall, baseline characteristics of patients between two groups were not statistically different. However, amount of spinal fentanyl in study group was significantly lower than conventional group ( $p = 0.046$ ).

### 3.2. Opioid consumption after surgery

In this study, patients were prescribed intravenous opioid as sufentanyl, fentanyl, or tramadol in the first 3 days after surgery. Opioid dosages were adjusted to individual pain level.

**Table 1.** Patients' baseline characteristics

Baseline characteristics		All patients in the study (n = 80)	Study group (n = 40)	Conventional group (n= 40)	p value (compare study and conventional group)
Age, years	Median	77 (67 – 84)	76.5 (67 – 84)	77 (70 – 83)	0.544
	< 65	12 (15%)	8 (20%)	4 (10%)	0.210
	≥ 65	68 (85%)	32 (80%)	36 (90%)	
Gender	Female	42 (52.5%)	22 (55%)	20 (50%)	0.654
	Male	38 (48.5%)	18 (45%)	20 (50%)	
Comorbidities	Hypertension	48 (60%)	20 (50%)	28 (70%)	0.068
	Diabetes	32 (40%)	6 (15%)	6 (15%)	1.000
	Respiratory diseases	4 (5%)	1 (2.5%)	3 (7.5%)	0.615
	Cardio vascular diseases	21 (26.25%)	11 (27.5%)	10 (25%)	0.799
	Gastro intestinal diseases	2 (2.5%)	1 (2.5%)	1 (2.5%)	1.000
	Others	6 (7.5%)	1 (2.5%)	5 (12.5%)	0.201
Type of surgery	Knee replacement	28 (35%)	16 (40%)	12 (30%)	0.348
	Hip replacement	52 (65%)	24 (60%)	28 (70%)	
Cause of surgery	Knee osteoarthritis	28 (35%)	16 (40%)	12 (30%)	0.348
	Femoral head fracture	45 (56.3%)	21 (52.5%)	24 (60%)	0.499
	Others	7 (8.7%)	3 (7.5%)	4 (10%)	1.000
Surgical methods	Total knee replacement	28 (35%)	16 (40%)	12 (30%)	0.282
	Partial hip replacement	33 (41.2%)	13 (37.5%)	20 (40%)	
	Total hip replacement	19 (23.8%)	11 (32.5%)	8 (20%)	
Median operation time, min (IQR), minutes		100 (80 – 130)	95 (80 – 130)	100 (80 – 125)	0.599
Pre-operative ASA	2	18 (22.5%)	12 (30%)	6 (15%)	0.108
	3	62 (77.5%)	28 (70%)	34 (85%)	
Pre-operative psychological consultation	Yes	66 (82.5%)	34 (85%)	32 (80%)	0.556
	No	14 (17.5%)	6 (15%)	8 (20%)	
Spinal fentanyl, mcg (min – max)		30.0 ± 13.07 (10 – 100)	26.88 ± 6.47 (10 – 50)	33.13 ± 16.86 (10 – 100)	<b>0.046</b>

\*Study group: LIB pain control group

Conventional group: conventional pain control group

Median age and operation time were compared using Mann-Whitney test. Rates of respiratory diseases, gastro intestinal diseases, and others (comorbidities) were compared using Fisher exact test. Chi – square test was used for others.

On the following days, if patients still suffered from severe pain, Ultracet PO (Ultracet: 37.5 mg tramadol + 325 mg paracetamol) would have been added. In order for comparison, dosages of opioid were converted into opioid equivalents of intravenous morphine.

Opioid consumption in POD 1 of study group was  $16.72 \pm 6.96$  mg, compared with  $20.88 \pm 5.17$  of conventional group ( $p = 0.03$ ). Similarly, in POD 2 and POD 3, opioid consumption of study group were significantly lower than conventional group ( $7.41 \pm 7.12$  mg vs  $12.63 \pm 5.55$  mg and  $5.25 \pm 6.32$  mg vs  $10.25 \pm 4.80$  mg, respectively) ( $p < 0.001$ ). (Table 2)

In addition, proportion of patients using more than 10 mg morphine IV in the first 24 hours after surgery was significantly lower in study group (67.5%), compared with conventional group (97.5%) ( $p < 0.001$ ). Multiple regression analysis was used to analyze the associated factors, including method of pain management, age, gender and pre-operative consultation with opioid consumption in POD 1, 2, and 3. The result showed that postoperative opioid consumption was not depended on age, gender, and pre-operative psychological consultation, but depended on pain management method (with LIB regimen). Patients experienced LIB consumed

**Table 2.** Pain control outcomes comparing between LIB group (study group) and conventional analgesia group (conventional group)

Pain control outcomes	Study group	Conventional group	p value	
<b>Opioid consumption, mg</b>				
POD1	16.72 ± 6.96 (0 – 25)	20.88 ± 5.17 (10 – 50)	<b>0.030</b>	
POD2	7.41 ± 7.12 (0 – 25)	12.63 ± 5.55 (0 – 25)	<b>&lt; 0.001</b>	
POD3	5.25 ± 6.32 (0 – 25)	10.25 ± 4.80 (0 – 20)	<b>&lt; 0.001</b>	
During the first 3 post- operative days	29.38 ± 15.88 (0 – 75)	43.75 ± 9.85 (0 – 75)	<b>&lt; 0.001</b>	
Patients consumed ≥ 10 mg/ 24h postoperatively	67.5%	97.5%	<b>&lt; 0.001</b>	
<b>Postoperative pain, %</b>				
POD 1	Severe	30	77.5	<b>&lt; 0.001</b>
	Moderate	60	20	<b>&lt; 0.001</b>
	Mild	10	2.5	0.359
POD 2	Severe	7.5	20	0.105
	Moderate	50	75	<b>0.021</b>
	Mild	42.5	5	<b>&lt; 0.001</b>
POD 3	Severe	0	0	
	Moderate	25	62.5	<b>0.001</b>
	Mild	75	37.5	<b>0.001</b>
<b>Median ambulation day (IQR), days</b>	5 (4 – 7)	7 (5 – 10)	<b>0.004</b>	
<b>Median length of hospital stay (IQR), days</b>	14 (9 – 17)	15 (12 – 21)	<b>0.039</b>	
<b>Patients with Sleep disturbance, %</b>	12.5%	35%	<b>0.018</b>	
<b>ADEs, %</b>				
Nausea and vomiting	0%	7.5%	0.241	
Respiratory depression	5%	20%	<b>0.043</b>	
Urinary retention	50%	60%	0.369	
Constipation	0%	10%	0.116	

less opioid after surgery. The results of multiple regression analysis were represented in Table 3.

### 3.3. Severe pain rate after surgery

Postoperative pain was measured by The Verbal Rating Scale (VRS) with 3 pain level documented, including mild pain, moderate pain and severe pain. On POD 1, the severe pain rate of patients in study group was 30%, compared with 77.5% in conventional group ( $p < 0.001$ ). Besides, percentages of patients suffered from moderate pain were also significantly lower in conventional group in POD 2 (50% vs 75%) and POD 3 (25% vs 62.5%) ( $p < 0.05$ ). (Table 2)

### 3.4. Ambulation day

The medium time required for ambulation was 5 and 7 days in study group and conventional group, respectively. The difference was statistically significant ( $p = 0.004$ ) (Table 3).

### 3.5. Length of hospital stay

The median length of hospital stay after

surgery in study group was significantly lower than conventional group (14 days vs 15 days,  $p = 0.039$ ). (Table 2)

### 3.6. Sleep disturbance

In our study, 23.8% patients have sleep disturbance at least once after surgery. There was a significantly lower percentage of patients recorded sleep disturbance in study group (12.5%), compared with conventional group (35.0%) ( $p = 0.018$ ). (Table 2)

### 3.7. Adverse event rates

There were 4 adverse drug events documented, including constipation, urinary retention, respiratory depression, and nausea and vomiting. Among them, urinary retention was the most popular adverse drug event (in 55% of all patients). The proportion of patients suffered from respiratory depression in study group (5%) was significantly lower than conventional group (20%) ( $p = 0.043$ ). Meanwhile, the differences in other adverse drug events were not statistically significant between two study groups (Table 2).

**Table 3.** Factors associated with opioid consumption

Factors	R	R <sup>2</sup>	Coef (B)	CI 95% of Coef (B)		p value
				Lower limit	Upper limit	
<b>POD1</b>						
Age			0.370	-0.095	0.168	0.579
Gender (female)			1.922	-0.832	4.676	0.169
Pre-operative consultation (yes)	0.364	0.132	0.554	-3.125	4.243	0.776
LIB regimen (yes)			-4.206	-6.974	-1.437	<b>0.003</b>
<b>POD2</b>						
Age			0.098	-0.038	0.233	0.155
Gender (female)			-1.215	-4.057	1.627	0.397
Pre-operative consultation (yes)	0.431	0.186	1.065	-2.742	4.872	0.579
LIB regimen (yes)			-5.014	-7.870	-2.157	<b>0.001</b>
<b>POD3</b>						
Age			0.076	-0.044	0.197	0.212
Gender (female)			-0.671	-3.199	1.857	0.598
Pre-operative consultation (yes)	0.436	0.190	-0.693	-4.080	2.693	0.685
LIB regimen (yes)			-4.778	-7.319	-2.236	<b>&lt; 0.001</b>
<b>Summary of three first postoperative days</b>						
Age			0.210	-0.072	0.493	0.142
Gender (female)			0.036	-5.896	5.967	0.991
Pre-operative consultation (yes)	0.507	0.257	0.925	-7.020	8.871	0.817
LIB regimen (yes)			-13.997	-19.959	-8.034	<b>&lt; 0.001</b>

#### 4. DISCUSSION

Most patients in our study were aged 65 years and over (85%). Median age of patients in our study (77 years old) was higher than those involved in Peters CL, et al. study<sup>11</sup> (59 years old) and Chen DW, et al. study<sup>8</sup> (54 years old). This was because most patients in Thong Nhat hospital were veterans. A study of Healey M, et al.<sup>12</sup> showed that older patients seemed to suffer more severe postoperative pain. In addition, changing in pharmacokinetic makes the elderly become more sensitive to opioid. However, the difference in age between two groups in this study was not statistically significant ( $p = 0.201$ ). Proportion of female was higher than male in this study (52.5% vs 47.5%). Although gender is an element that affects postoperative pain, there was no statistically significant difference between two study groups ( $p = 0.645$ ). Pre-operative ASA score of patients in this study were at level 2 and 3 (22.5% and 77.5%, respectively), similarly to Shen SJ, et al.<sup>13</sup> (38.9% and 61.1%, respectively). This was appropriate due to large amount of patients in this study was the elderly. According to Kinjo S, et al. study<sup>14</sup>, ASA is one element to predict postoperative pain. However, the difference in pre-operative ASA of patients in two study groups was not statistically significant.

All knee replacement patients were suffered from knee osteoarthritis, and underwent total knee replacement. Meanwhile, among hip replacement patients, femoral head fracture was the most common cause (45/52, 86.5%). This was similar to Kim NTT, et al. study<sup>15</sup> (82.1%), and could be explained by lower bone density of the elderly. There were no significant differences between two study groups with respect to causes and methods of surgeries.

According to Gagliese LJM<sup>16</sup>, the longer operative time, the more painful after surgery was expected. However, the difference in operative time between two groups in this study was not statistically significant ( $p = 0.599$ ).

Most patients in our study (82.5%) were pre-operative consulted about surgical method, analgesic regimen and expected outcome. Although a study of Mamie C, et al.<sup>17</sup> showed that patients suffered less postoperative pain if they were consulted before surgery, this element was not significantly different between two study groups ( $p = 0.556$ ).

In this study, LIB was used as a part of multimodal regimen, along with spinal fentanyl. Patients in study group used less spinal fentanyl, compared with conventional group 26.88 mcg vs 33.13 mcg, respectively) ( $p = 0.046$ ). Therefore, LIB showed its very first benefit in lowering opioid consumption, spinal fentanyl in particular.

Totally, there were no significant difference between two study groups with respect to demographic data, comorbidities, pre-operative ASA, causes of joint replacements, surgery methods, operation time, and pre-operative patient psychological consultation ( $p > 0.05$ ), and thus patients characteristics between two study groups are similar as well as statistical interferences are eliminated.

In this study, postoperative opioid consumption was the main outcome. LIB was revealed to significantly reduce opioid consumption in the first 3 days as well as total consumption in the first 3 days postoperatively. Mean opioid consumption during first 24 hours after surgery in study group and conventional group was 16.72 mg and 20.88 mg, respectively. The difference was statistically significant ( $p = 0.030$ ). The same result was revealed by Chen DW, et al. study<sup>8</sup> and Shen SJ, et al. study<sup>13</sup>. According to Chen DW, et al.<sup>8</sup>, experience of clinical practice indicated that patients experience the most discomfort from the end of general anesthesia to when the first dose of oral pain medication was given. It also indicated that the LIB filled the gap for pain management in this period, and reduced pain in the most painful period postoperatively (the immediate postoperative period). Similarly, mean opioid consumption in POD 2 and 3, and a total amount used in the first 3 postoperative days were lower in study group, compared to conventional group ( $p < 0.001$ ). Other studies such as those of Goyal N, et al.<sup>18</sup> also had the same outcome which remained the conclusion of positive impact of local infiltration. In addition, this therapy was found to be quite reliable as proportion of patients using more than 10 mg morphine IV in the first 24 hours after surgery was lower in study group (67.5%) than conventional group (97.5%) ( $p < 0.001$ ). Similarly to this study, in a study among knee replacement, Essving P, et al.<sup>19</sup> concluded that proportion of patients using more than 5 mg morphine IV in local infiltration analgesia group was less than those in conventional group (0% vs 41.7%, respectively) ( $p < 0.01$ ). These results in this study indicate that LIB had reduced opioid consumption after surgery.

On the other hand, according to Burns JW, et al.<sup>20</sup>, various factors such as age, gender, and pain relief expectation can influence the requirements for postoperative analgesia. Therefore, in this study, multiple regression analysis was used to evaluate those factors on opioid consumption in POD 1, 2, and 3. Either

age, gender or pain relief expectation had no significant effect on POD 1, 2, and 3 opioid consumptions ( $p > 0.05$ ). Meanwhile, it was dependent on pain management protocol (LIB protocol) ( $p = 0.003$ ,  $p = 0.001$ , and  $p < 0.001$  on POD1, 2, and 3, respectively). The administration of intravenous opioid has been playing a main role for postoperative pain management. This, however, are commonly associated with many complications and adverse drug events such as sedation, nausea, vomiting, respiratory depression, gastro intestinal diseases, and urinary retention. Meanwhile, knee and hip replacements are popular among the elderly who are sensitive to those unwanted effects. Therefore, decrease in opioid consumption of LIB is meaningful for patients.

Although postoperative analgesia is a key factor to evaluate efficacy of pain management, other clinical outcomes such as postoperative pain, functional recovery, and complication have been taken account in some recent studies. These elements were also investigated in this study.

The result showed that patients in study group, compared with conventional group, suffered less severe pain on POD 1 (30% vs 77.5%,  $p < 0.001$ ), and moderate pain on POD 2 (50% vs 75%,  $p = 0.021$ ), and POD 3 (25% vs 62.5%,  $p = 0.001$ ). Study of Shen SJ, et al.<sup>13</sup> among knee replacement patients had similar result with significantly lower numeric rating scale (NRS) data of bupivacaine group than control group (4.5 vs 7.9,  $p = 0.001$ ). According to Chen DW, et al. study<sup>8</sup> among hip replacement patients, pain scores of the study group were also significantly lower than those of the control group at each time point assessed during the first 12 hours postoperatively ( $p < 0.001$ ). This indicated that LIB had produced a good pain relief in the first 3 days after surgery.

Earlier functional recovery will bring satisfaction as well as prevent patients from some unwanted complications such as paralytic ileus, venous thromboembolism, and pneumonia. In this study, median ambulation day of study group was 5 days, significantly lower than 7 days of conventional group ( $p = 0.004$ ). This indicated earlier recovery of LIB which was also found in other studies such as Essving P, et al.<sup>19</sup> ( $p < 0.05$ ) and Fu P, et al.<sup>21</sup> ( $p < 0.001$ ). This was explained, according to Chaumeron A, et al.<sup>22</sup> that LIB affects in less functional limitation of quadriceps which leads to earlier mobilization.

Besides, medium length of hospital stay of study group was 14.3 days, significantly lower

than 18.7 days of conventional group ( $p = 0.039$ ). The similar result was also found in other studies such as Kazak BZ, et al.<sup>23</sup> (2.5 days vs 4.5 days, respectively,  $p < 0.05$ ) and Essving P, et al.<sup>19</sup> (1 day vs 3 days, respectively,  $p < 0.001$ ). Another study of Chen DW, et al.<sup>8</sup> showed that percentage of patients with less than 6 days of hospitalization was significantly higher in LIB group (98.5%) than in control group (47.9%) ( $p < 0.001$ ). Therefore, along with earlier ambulation, LIB also provided shorter length of hospitalization.

The sleep disturbance rate of study group was significantly lower compared with conventional group ( $p = 0.018$ ). Stress and painful experiences are main reasons of postoperative sleep disturbance which brings dissatisfaction and negative effects on mental and physical status, as well as slows down rehabilitation process. An effective pain management improves sleep quality, and this can indicate that LIB had positive impact on both patient emotion and their recovery.

Urinary retention was the most common adverse event among patients in this study (55%), and respiratory depression ranked the second (12.5%). High rate of urinary retention was caused by painful experience and orbicularis spasm. It was also a common ADE of spinal anesthesia which was a part of multimodal pain regimen, along with LIB. Respiratory depression rate was significantly lower in study group (5%) than conventional group (20%) ( $p = 0.043$ ). It could be explained by the decrease in opioid consumption which leads to less opioid-related complications. Meanwhile other ADEs such as urinary retention, nausea and vomiting, and constipation were similar between two groups ( $p > 0.05$ ). This indicated that LIB was safe. In addition, lower rate of respiratory depression was meaningful because knee and hip replacements were common among the elderly.

In conclusion, this study demonstrated better pain control for study group. Patients in LIB had lower opioid consumption in the first 3 days, lower postoperative pain, earlier ambulation, shorter length of hospital stay, lower rate of sleep disturbance, and lower rate of respiratory depression.

Despite these encouraging findings, the retrospective of this study shows its weakness when monitoring data passively in short term (within 3 days after surgery) in one center, and assessing pain qualitatively instead of quantitatively. A prospective study with validated patient assessment tools and long term

monitoring in multiple centers can be suggested for further studies.

## 5. CONCLUSION

The use of simple method, LIB, shows positive impact on decrease opioid consumption, pain control, earlier functional recovery, sleep quality as well as lower rate of respiratory depression – an opioid-related complication among patients undergoing knee or hip replacements. Therefore, it can be an option to be substituted for conventional pain control regimen.

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### Conflict of interest

We have no conflict of interest to declare.

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### Ethical approval

The protocol of this study was approved by the Institutional Review Board of the Thong Nhat Hospital (Project Number: 69 IRB/ QDBVTN 07022016)

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