



# Blood Loss-Related Functional Outcome in Post-Operative Total Knee Arthroplasty: Prospective Cohort Study

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## Abstract

**Objective:** Current blood management programs for knee arthroplasty recommend avoiding blood transfusions and setting criteria for hemoglobin (Hb) < 7 g/dl or < 8 g/dl inpatients who have cardiac diseases or specific situations that do not concern the pre-operative HB level. This cutoff is safe for hemodynamically stable patients and those without cardiovascular complications. However, no study has shown the result of functional outcome, which is the primary objective of total knee arthroplasty (TKA).

**Methods:** We conduct an 18-month prospective cohort study on patients diagnosed with primary OA knee and indicated for surgical treatment with total knee arthroplasty at a single medical school hospital. Patients were divided into two groups of HB loss <20% or ≥20%. Timed up and go information was collected and compared at pre-operative period and post-operative day 1, 2, 3 and 14.

**Results:** A total of 154 patients were analyzed. No significant different in patient characteristics was found between the Hb loss <20% group (group 1, n=120) and HB loss ≥20% group (group 2, n=34). Comparison of mean TUG between the two groups found no significant difference on post-operative day 1 ( $81.34 \pm 20.09$  and  $84.99 \pm 25.59$  ( $P=0.45$ )), 2 ( $56.85 \pm 11.12$  and  $59.06 \pm 13.67$  ( $P=0.39$ )), 3 ( $44.14 \pm 8.20$  and  $45.66 \pm 9.19$  ( $P=0.35$ )) and 14 ( $31.92 \pm 6.02$  and  $34.04 \pm 5.99$  ( $P=0.07$ )).

**Conclusion:** No significant difference in physical outcomes was found between the two groups. Current blood transfusion criteria after total knee arthroplasty can be used without concern about the physical outcome at the early post-operative period.

**Keywords:** blood loss, knee arthroplasty, total knee arthroplasty, functional outcome, timed up and go



# ความสัมพันธ์ระหว่างการสูญเสียเลือด และสมรรถภาพการทำงานของร่างกาย ในผู้ป่วยหลังผ่าตัดเปลี่ยนผิวข้อเข่าเทียม

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## บทคัดย่อ

**วัตถุประสงค์:** แนวทางการจัดการเลือดในผู้ป่วยที่จะเข้ารับการผ่าตัดเปลี่ยนผิวข้อเข่าเทียมแนะนำให้หลีกเลี่ยงการให้เลือด โดยตั้งเกณฑ์การให้เลือดคือ ค่าฮีโมโกลบินน้อยกว่า 7 มิลลิกรัมต่อเดซิลิตร หรือน้อยกว่า 8 มิลลิกรัมต่อเดซิลิตร ในผู้ป่วยที่มีโรคหัวใจร่วมด้วย โดยไม่ได้สนใจค่าฮีโมโกลบินก่อนผ่าตัด เนื่องจากมีรายงานว่าเกณฑ์การให้เลือดนี้ปลอดภัยสำหรับผู้ป่วยที่มีการไหลเวียนของเลือดปกติ และไม่มี ความแตกต่างในภาวะแทรกซ้อนทางหัวใจ และหลอดเลือด แต่ยังไม่มีการวิจัยใดที่แสดงผลของสมรรถภาพร่างกายซึ่งเป็นเป้าหมายหลักของการผ่าตัดเปลี่ยนผิวข้อเข่าเทียม

**วิธีดำเนินการวิจัย:** รูปแบบการศึกษาเป็นแบบตามแผน ชนิดไปข้างหน้า เก็บข้อมูลประมาณ 18 เดือน ในผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นโรคข้อเข่าเสื่อมชนิดปฐมภูมิที่ได้รับการวางแผนการรักษาด้วยการผ่าตัดเปลี่ยนผิวข้อเข่าเทียม ซึ่งจะถูกแบ่งเป็นสองกลุ่มคือกลุ่มที่สูญเสียฮีโมโกลบินน้อยกว่าร้อยละ 20 (กลุ่มที่ 1) และกลุ่มที่สูญเสียฮีโมโกลบินมากกว่าหรือเท่ากับร้อยละ 20 (กลุ่มที่ 2) โดยเวลาในการเดิน การทดสอบความสามารถในการทรงตัว (timed up and go test) จะถูกบันทึกและเปรียบเทียบในวันก่อนเข้ารับการผ่าตัด หลังเข้ารับการผ่าตัดวันที่ 1, 2, 3 และ 14

**ผลการวิจัย:** ผู้เข้าร่วมงานวิจัยทั้งหมด 154 ราย ประกอบด้วยกลุ่มที่ 1 120 ราย และกลุ่มที่ 2 34 ราย ค่าเฉลี่ยของเวลาในการเดิน การทดสอบความสามารถในการทรงตัว (timed up and go test) ของทั้งสองกลุ่มไม่มีความแตกต่างกันอย่างมีนัยสำคัญในช่วงหลังการผ่าตัดวันที่ 1 (81.34+/-20.09 และ 84.99+/-25.59 (P=0.45)) วันที่ 2 (56.85+/-11.12 และ 59.06+/-13.67 (P=0.39)), วันที่ 3 (44.14+/-8.20 และ 45.66+/-9.19 (P=0.35)) และวันที่ 14 (31.92+/-6.02 และ 34.04+/-5.99 (P=0.07))

**สรุป:** งานวิจัยนี้ไม่พบความแตกต่างอย่างมีนัยสำคัญในด้านสมรรถภาพร่างกายระหว่างทั้งสองกลุ่ม เกณฑ์การให้เลือดหลังการผ่าตัดเปลี่ยนผิวข้อเข่าเทียมในปัจจุบันสามารถใช้ได้โดยไม่ต้องคำนึงถึงสมรรถภาพร่างกายในระยะหลังการผ่าตัดช่วงแรก

**คำสำคัญ:** การเสียเลือด การผ่าตัดเปลี่ยนผิวข้อเข่าเทียม ข้อเข่าเทียม สมรรถภาพร่างกาย การทดสอบความสามารถในการทรงตัว

## Introduction

Total knee arthroplasty (TKA) is a common orthopedic operation for the treatment of knee joint osteoarthritis to relieve pain and improve functional outcome. The number of these operations has increased over the time due to a high success rate and satisfaction<sup>1</sup>. However, some complications occur after TKA, one of which is anemia due to blood loss<sup>2</sup>. Prasad N<sup>3</sup> reported that the mean total estimated blood loss after TKA is about 1,000 ml, and 20% of patients who undergo TKA required a blood transfusion<sup>4</sup>.

Blood transfusion is related to many complications, such as infection, risk of disease transmission, hemolytic reaction, fluid and hemodynamic overload, acute lung injury, coagulopathy, allergic reaction, increase length of hospitalization, and an increased incidence of prosthetic joint infection<sup>5-6</sup>. The present strategy is to reduce the need for blood transfusion. Many studies and blood management programs only recommend transfusion when hemoglobin (Hb) <7 g/dl or <8 g/dl in patients who have cardiac diseases or in a specific situation; this criteria is safe for hemodynamically stable patients and those without cardiovascular complication<sup>4,7-10</sup>. Tavarez Cardozo et al.<sup>11</sup> suggested transfusion when Hb loss > 20% from baseline due to the increased risk of tissue hypoperfusion. However, no research has shown the result of functional outcome, which is the primary objective of TKA.

To date, no single best functional outcome has emerged for TKA. Physical functional outcome can be assessed in the early post-operative period<sup>12</sup> using "Timed up and go" (TUG) test, which has excellent test-retest reliability, validity and easy to use<sup>13-14</sup>. This study aimed to analyze the relationship between Hb loss and TUG in the early post-operative period. We hypothesize that patients with Hb loss >20% may have poorer TUG than those with Hb loss <20%. If a significant difference is found, then the blood management program and transfusion criteria might have to be reconsidered to improve functional outcome.

## Methods

After being approved by the Institutional Review Board of Navamindradhiraj University, Thailand, this prospective study was conducted from 1<sup>st</sup> September 2018 to 1<sup>st</sup> February 2020. Male and female patients aged between 55-80 years diagnosed with primary osteoarthritis of knee joint and indicated for surgical treatment with unilateral total knee arthroplasty using cruciate-retaining (CR) technique was included.

Exclusion was performed in two steps. First is pre-operation: patients presenting contralateral symptomatic osteoarthritis of knee that has not been corrected, patients with hip or spine problems that affect gait, patients with motor power below grade 4, and patients with hematologic disease were excluded. The second step is the first day after operation: patients with hemodynamic instability, orthostatic hypotension, nausea vomiting score > 1, and pain score > 3; patients who received blood transfusion; and patients who cannot walk by themselves at post-operative day 1 was further excluded.

After the patient was assigned for TKA and met the inclusion criteria, informed consent was obtained from all participants. Data on patient characteristic including age, gender, body weight, BMI, pre-operative Hb and TUG were collected as baseline. Patient with ASA classification 3 must consult a medical doctor and anesthesiologist for pre-operative evaluation. All the patients met the physiotherapist for quadriceps exercise teaching and post-operative rehabilitation program before surgery. Spinal anesthesia and spinal anesthesia with intrathecal morphine were used as anesthetic method. Standard TKA was performed by a single surgeon in the supine position, anterior midline incision, mid-vastus approach, CR technique. If intra-op balancing cannot be achieved and converted to cruciate sacrifice technique, then the patients were excluded. A tourniquet was used in all cases and deflated before the closure of the wound to achieve hemostasis. Meticulous closure was performed after a Radivac suction drain was inserted inside the joint. The drain was removed at 24 hr post-operation. Cocktail periarticular injection with

lidocaine and ketorolac was used for all patients. All participants underwent the same post-operative protocol including intravenous fluid management, pain control, venous thromboembolism (VTE) prophylaxis and rehabilitation program.

At post-operative day 1,2,3 and 14, data including vital signs, shock index, pain score, nausea vomiting score, orthostatic hypotension and TUG were collected. TUG was assessed by only one researcher. Hb was collected at 2 weeks pre-operation as baseline and post-operateday 1 and 3. The participants were divided into two groups with Hb loss <20% or ≥ 20%. Clinical data including TUG were compared between the two groups.

Statistical analyses were performed using SPSS version 26 on windows 10 platform. All data were compared using independent t-test or chi-square tests depending on their variable types.

A P-value of ≤0.05 was considered statistically significant. The sample size of Hb change ≥ 20% (n=34) and Hb change < 20% (n=120) provided 80% power to detect 20% differences in TUG.

### Results

A total of 183 patients were included in this study. Among which, 29 were excluded (three had lumbar spine pain, ten due to post-operative pain score more than 2, four due to nausea vomiting score more than 1, two have post-operative thromboembolism event, two have post-operative delirium, one change anesthetic method to general anesthesia due to failed spinal anesthesia, and seven due to post-operative blood transfusion). Data of the remaining 154 patients were analyzed. Hb loss ≥ 20% group had 34 patients, and Hb loss < 20% group had 120 patients. Patients' characteristics are shown in Table 1.

**Table 1:**

Patients characteristics

	Hb change <20% n = 120	Hb change > 20% n = 34	Total n = 154	P-value
<b>Age (years)</b>	68.03 ± 7.03	70.74 ± 6.67	68.63 ± 7.02	0.05
<b>Gender</b>				
male	13 (10.8%)	4 (11.8%)	17 (11%)	0.88
female	107 (89.2%)	30 (88.2%)	137(89%)	
<b>Side</b>				
right	69 (57.5%)	17 (50%)	86 (55.8%)	0.44
left	51 (42.5%)	17 (50%)	68 (44.2%)	
<b>Body weight (kg)</b>	64.85 ± 11.64	63.74 ± 11.98	64.6 ± 11.69	0.63
<b>BMI (kg/m<sup>2</sup>)</b>	26.85 ± 4.29	26.64 ± 4.55	26.80 ± 4.33	0.81
<b>ASA classification</b>				
1	19 (15.8%)	4 (11.8%)	23 (15%)	0.11
2	68 (56.7%)	15 (44.1%)	83 (54%)	
3	33 (27.5%)	15 (44.1%)	48 (31%)	
<b>Anesthetic method</b>				
SB	11 (9.2%)	2 (5.9%)	13 (8%)	0.55
SB+MO	109 (90.8%)	32 (94.1%)	141 (92%)	
<b>operative time (min)</b>	120.12 ± 15.28	122.12 ± 19.27	120.56 ± 16.20	0.53
<b>preop Hb (g/dl)</b>	12.69 ± 1.13	12.53 ± 1.28	12.65 ± 1.16	0.48
<b>preop TUG (sec)</b>	14.74 ± 3.46	15.38 ± 3.50	14.89 ± 3.46	0.34

BMI= Body mass index, ASA= American Society of Anesthesiologists classification, SB= Spinal Block, SB+MO= Spinal Block with Morphine, Hb= Hemoglobin, TUG= Time Up and Go mean +/- Standard deviation, number and percentage.

In this study, 17 patients were male (11%) and 137 were female (89%). Between the two groups, no significant differences were observed in the number and proportion of male and female patients ( $P = 0.88$ ). No significant differences were also noted in other patient characteristics including gender, side, body weight, BMI, ASA classification, anesthetic method, operative time, and pre-operative Hb and TUG as shown in Table 1.

Pre-operative Hb levels ranged from 8.9 to 15.3 g/dL with mean 12.65 g/dL. Post-operative Hb mean was 10.83 g/dL with a range from 7 to 13.4 g/dL. Calculated percentage of Hb changed in this population ranged from 3.82% to 33.11% with Mean 14.43%. We excluded 7 patients from this study due to blood transfusion, 6 of them were Hb changed more than 20%, one of them had Hb change 13.73% but the Hb level was 6.7 and received blood transfusion follows the guideline.

The pre-operative TUG in this population ranged from 9.01 to 22.70 (mean =  $14.89 \pm 3.46$ ), which markedly increased to 43.32-145.70 (mean =  $82.14 \pm 21.39$ ) in post-operative day 1. TUG then slightly decreased in post-operative days 2 (37.93 - 82.07, mean =  $57.34 \pm 11.71$ ), 3 (28.56 - 64.11, mean =  $44.47 \pm 8.42$ ), and 14 (21.03 - 43.37, mean =  $32.39 \pm 6.06$ ). Comparison of the mean TUG between the two groups showed no significant difference on post-operative day 1 ( $P = 0.45$ ), day 2 ( $P = 0.39$ ), day 3 ( $P = 0.35$ ), and day 14 ( $P = 0.07$ ). The TUG results are summarized in Table 2.

Four patients with post-operative complication were excluded. No other complications were observed in the study population. The mean length of hospital stay was 5.1 days with a range of 4 - 8 days, and no significant difference was observed between the two groups ( $P = 0.50$ ).

## Discussion

In this study, we found that the Hb loss decreased from  $12.65 \pm 1.16$  g/dL to  $10.83 \pm 1.25$  g/dL, indicating that the mean Hb loss was about 14.43% after unilateral TKA. This result slightly lower than that from the systematic review of Donat R. Spahn<sup>8</sup>, who stated that Hb will decrease by about 22.06%, and Narayana Prasad<sup>3</sup>, who stated that Hb will decrease by 20.08% after unilateral TKA. The less Hb loss may be because the current population was subjected to CR technique, which induces lower blood loss than cruciate sacrifice<sup>15</sup>, and was injected with tranexamic acid<sup>16</sup>, which was not mentioned in the previous studies. Although this study calculate Hb loss on post-operative day 3, which is a day before Hb reaches the lowest level<sup>17</sup>, we believe that this change does not affect the results and treatment of the patient from the lowest day, day 4.

**Table 2:**

Timed up and go

	Minimum	Maximum	Mean±SD	Hb change <20% n=120	Hb change >20% n=34	P-value
TUG day 1	43.32	145.70	$82.14 \pm 21.39$	$81.34 \pm 20.09$	$84.99 \pm 25.59$	0.45
TUG day 2	37.93	82.07	$57.34 \pm 11.71$	$56.85 \pm 11.12$	$59.06 \pm 13.67$	0.39
TUG day 3	28.56	62.11	$44.47 \pm 8.42$	$44.14 \pm 8.20$	$45.66 \pm 9.19$	0.35
TUG day 14	21.03	43.37	$32.39 \pm 6.06$	$31.92 \pm 6.02$	$34.04 \pm 5.99$	0.07

Mean ± Standard deviation

The primary result of this study is TUG. The mean pre-operative TUG was  $14.89 \pm 3.46$  s, which is slightly faster than the  $16.7 \pm 7.7$  reported by Givens, DL, et al.<sup>18</sup> We think that the low mean and narrow standard deviation resulted from the exclusion of patients with contralateral knee pain, hip pain and low back pain because of the effect of these conditions on TUG<sup>19</sup>. Comparison of TUG between the two groups of study did not find significant differences on post-operative days 1, 2, 3 and 14. On post-operative day 14, a nearly statistically significant difference was observed ( $P = 0.07$ ). This finding may be due to multiple uncontrollable factors, such as inflammation, anesthetic drug, and fatigue, that occur during the early post-operative period day 1 - 3 and might have an effect on TUG. On day 14, these factors may have disappeared, leading to TUG improvement and differences between the two groups. Qi Zhou et al.<sup>17</sup> reported that after surgery, Hb levels dramatically decrease in the first 4 days then start to recover up to 93.56% by 6 weeks. Therefore, at the period of 2 to 6 week post-operation, Hb does not return to its baseline level. The TUG in this period may have exhibited a different result. In future studies, the follow up time should be extended for further observation. On the basis of the result on day 14 ( $P = 0.07$ ), Hb loss is possibly related to TUG. However, we cannot analyze this correlation because of the small sample size.

The advantages of this study are its prospective study design and the comparison of the results of physical performance between the two blood loss groups, which has never been reported before. However, this work also has limitations. First, this research used the changes in Hb level to represent blood loss outcome; this parameter is not accurate for calculating blood loss<sup>20</sup>, but is easy to use in clinical practice. Second, this study used only TUG as an outcome, which represents only the physical outcome. This work only focus

on physical performance after blood loss, self-reported measures of function such as WOMAC score, KSS score, and Oxford knee score, were not employed because their results are based on patient perceptions of function and are not related to physical performance<sup>21</sup>, and among the physical outcomes TUG after TKA has improvement, reaching a plateau earlier than others with excellent test-retest reliability and validity<sup>22</sup>. The third and fourth limitations are the small sample size, which cannot be used to analyze correlations, and the short follow up of 2 weeks, which does not cover the time when Hb level is low as described above.

## Conclusion

No significant different in physical outcome was observed between the patients with Hb loss  $< 20\%$  and  $\geq 20\%$  after TKA. Therefore, the criteria for post-operative blood management program and blood transfusion in TKA can be used as recommended due to their safety in case of cardiovascular events, reduced transfusion complications, and no difference in physical outcome.

## Conflict of interest

The authors declare no conflict of interest in this study.

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