

Original Research Article

The relationship between tourniquet time and IL-6, D-Dimer and visual analogue scale in total knee arthroplasty

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ABSTRACT

Background: The use of tourniquet during TKA aside from having several advantages, is also accompanied by several risks. This study was performed to prove the relation between the duration of tourniquet application to inflammatory response, pro-thrombotic condition, and pain response of the patients undergoing TKA procedures.

Methods: This study is a cross-sectional analytical experimental research. A femoral tourniquet was applied to 34 primary osteoarthritis (OA) patients undergoing the standard procedure of TKA and the duration of tourniquet application data was noted and collected. Pain assessment was performed by using Visual Analogue Scale (VAS), whereas blood samples are taken from the patients and IL-6 cytokine and D-dimer levels were identified at 12 hours and 24 hours post-operatively. Statistical analysis (Pearson correlation) was performed to see the correlation of tourniquet duration to the VAS, IL-6, and D-dimer serum level at 12 hours and 24 hours post-operatively.

Results: The result of this study showed a positive correlation between the duration of tourniquet use with IL-6 at 12 hours post operation ($r=0.359$) and 24 hours post operation ($r=0.658$); with D-dimer at 12 hours post operation ($r=0.491$) and 24 hours post operation ($r=0.483$); and with VAS at 12 hours post operation ($r=0.647$) and 24 hours post operation ($r=0.507$) with $p<0,05$. A positive correlation was found between tourniquet time and IL-6, D-dimer and VAS.

Conclusions: The duration of tourniquet cut-off time of more than 122.5 minutes elevates IL-6 and D-Dimer which increases the risk for SIRS and DVT.

Keywords: Ascorbic acid, Interleukin-6, Open fractures, *Staphylococcus aureus*

INTRODUCTION

Total Knee Arthroplasty (TKA) is a general surgical procedure performed to treat patients with pain due to osteoarthritis and rheumatoid arthritis. The TKA operating incident in 2013 increased in Europe with an estimated 91,703 cases in England, Wales and Northern Ireland. Currently, majority of TKA procedures are carried out with the help of a tourniquet device that is installed around the thigh.¹⁻³

The use of tourniquet in lower limb surgery in the orthopedic field has developed rapidly since it was first introduced. One of the complications of using a tourniquet is increased pain due to tourniquet inflation. Another complication is the increase in several proinflammatory cytokines due to the occurrence of reperfusion syndrome. Tissue damage induces a local and systemic response characterized by the release of mediators such as pro-inflammatory cytokines to maintain immune integrity and stimulate reparative

mechanisms. The acute phase response begins locally at the site of surgical trauma by macrophages and monocytes, which release proinflammatory cytokines, specifically Tumor Necrosis Factor alpha (TNF α) and Interleukin-1 beta (IL-1 β). In tissues during the acute phase response caused by trauma, TNF- α and IL-1 β cytokines stimulate the production and release of other cytokines, including Interleukin-6 (IL-6) which reaches a peak of 4-48 hours after surgery.^{1,2,4}

In addition to increasing cytokines, a number of physiological disorders that occur with the use of tourniquets can predispose patients to thrombotic conditions. The use of tourniquet can induce an increase in circulating thrombotic markers such as D-Dimer, tissue plasminogen activator, angiotensin-converting enzyme, antithrombin-III and protein C.^{1,5}

The use of tourniquet during TKA besides having benefits also cannot be separated from some of the risks and adverse effects it may caused. Determining the duration of use of a safe tourniquet is very important to prevent the occurrence of complications of reperfusion syndrome which can trigger inflammatory reactions and tissue damage. The use of tourniquet in a safe period of time is expected to minimize the incidence of complications such as post-operative pain associated with blood vessel and nerve suppression, muscle damage, and a number of other physiological disorders that predispose to thrombotic conditions.^{1,5,6} This study was performed to prove the relation between the duration of tourniquet application to inflammatory response, pro-thrombotic condition, and pain response of the patients undergoing TKA procedures.

METHODS

This study is a cross-sectional analytical experimental research. This study was conducted to patients with primary OA of the knee who failed conservative treatment and agreed to undergo TKA in our centre during the period of July 2017 to September 2018. The other inclusion criteria was the age range of 50-65 years old, the usage of femoral tourniquet with the duration of

less than three hours, physical status class I or II based on the American Society of Anaesthesiologists Classification (ASA Class), using the spinal or epidural anaesthesia procedure. Patients with history of chronic inflammatory or autoimmune joint diseases, neoplasm, thromboembolism, thrombocytopenia, heart disease, and stroke, and those who used the general anaesthesia procedure were excluded from this study.

A consecutive sample selection was carried out, resulting in 34 subjects. A femoral tourniquet was applied to 34 primary OA patients undergo TKA and the duration of tourniquet application data was noted and collected. Pain assessment was performed by using Visual Analogue Scale (VAS), whereas blood samples are taken from the patients and IL-6 cytokine and D-dimer levels were identified using ELISA method. The pain assessment and the measurement of the laboratory parameters were performed at 12 hours postoperatively after the first epidural analgesia and 24 hours postoperatively after the second epidural analgesia. Pain assessment by using VAS was performed at inpatient ward of Sanglah General Hospital whereas the examination of IL-6, D-Dimer and VAS was carried out at the Clinical Pathology Laboratory at Sanglah Hospital.

The data was collected and statistical analysis by Pearson correlation was performed to see the correlation between tourniquet duration to VAS, IL-6, and D-dimer serum level at 12 hours and 24 hours post-operatively. The analysis was performed by using SPSS for Windows version 22.

RESULTS

The subjects of this study consists of 34 patients with primary osteoarthritis (OA) of the knee who failed conservative treatment and agreed to undergo TKA and femoral tourniquet application. 4 (11.8%) male patients and 30 (88.2%) female patients, with a range of age 50 years to 81 years and a mean age of 66.5 years. Based on the duration of tourniquet application time range from 105 to 150 minutes with mean duration is 130.7 minutes (Table 1).

Table 1: Descriptive statistics of age, sex and duration of tourniquet.

Subject characteristics	Mean \pm SD (n=34)	Minimum	Maximum	P
Age	66.588 \pm 7.336	50.00	81.00	0.602
Sex				0.550
Male	4 (11.8%)			
Female	30 (88.2%)			
Long duration of tourniquet	130.735 \pm 12.740	105.00	150.00	0.001

In 12 hours post operatively, the mean of IL-6 level, D-dimer level, and VAS score were 437.219 mcg/L, 16.917 mcg/L, and 5.382 respectively, were as in 24 hours post

operatively, the mean of IL-6 level, D-dimer level, and VAS score were 365.180 mcg/L, 5.085 mcg/L, and 4.411 respectively (Table 2). The data of all variables were normally distributed.

Table 2: Descriptive statistics for IL-6, D-Dimer and VAS levels at 12 hours and 24 hours postoperatively.

Variable	Mean \pm SD (n=34)	Minimum	Maximum	P
IL-6 level				0.000
24 hours post operatively	365.180 \pm 89.947	200.06	500.00	
12 hours post operatively	437.219 \pm 44.785	345.99	500.00	
D-dimer level				0.000
24 hours post operatively	5.085 \pm 1.559	2.30	8.64	
12 hours post operatively	16.917 \pm 1.868	12.28	19.83	
Vas score				0.014
24 hours post operatively	4.411 \pm 1.616	2.00	8.00	
12 hours post operatively	5.382 \pm 1.435	3.00	8.00	

Pearson correlation test was performed to assess the strength and direction of the linear relationship between tourniquet application duration and the IL-6 level, D-dimer level, and VAS respectively. The test results showed that there is a positive correlation between the duration of the tourniquet with IL 6, D-dimer and VAS levels. Correlation coefficient (r) between the duration of use of tourniquet with IL-6 levels 24 hours postoperatively was 0.658, whereas with IL-6 12 hours postoperative levels was 0.359 and statistically significant with p values of 0.000 and 0.037 respectively ($p < 0.05$). The value of the correlation coefficient (r) between the duration of tourniquet use with 24-hour postoperative D-dimer levels was 0.483 while the 12-hour postoperative D-dimer levels were 0.491 and statistically significant with p values of 0.004 and 0.003 ($p < 0.05$). While the value of the correlation coefficient (r) between the duration of use of tourniquet with a 24-hour postoperative VAS value was 0.507 and with a 12-hour postoperative VAS value was 0.647 and statistically significant with p values of 0,000 and 0.002 ($p < 0.05$) (Table 3).

Table 3: Correlation between long time tourniquet with each variable.

Variable	Pearson correlation	P
Long duration of tourniquet with il-6 level		
24 hours post operative	0.658	0.000
12 hours post operative	0.359	0.037
Long duration of tourniquet with d-dimer level		
24 hours post operative	0.483	0.004
12 hours post operative	0.491	0.003
Long duration of tourniquet with vas score		
24 hours post operative	0.507	0.002
12 hours post operative	0.647	0.000

Value Based on de Vaus (2002), the correlation coefficient mentioned above can be concluded that there is the strongest correlation between the duration of tourniquet use with IL-6 24 hours postoperatively and the VAS value 12 hours after surgery.

DISCUSSION

In this study, higher IL-6 levels were obtained at 12 hours postoperatively and proved to be significantly different as compared to IL-6 levels at 24 hours postoperatively. The value of the correlation coefficient (r) between the duration of the use of tourniquet and IL-6 level 24 hours postoperatively is 0.658, whereas IL-6 12 hours postoperative level is 0.359 and statistically significant with p values of 0.000 and 0.037 respectively ($p < 0.05$). Linear relationships with significant positive correlations were found especially between the duration of the use of tourniquets with IL-6 levels at 24 hours postoperatively.

The acute phase response begins locally at the site of surgical trauma by macrophages and monocytes, which release proinflammatory cytokines, specifically TNF α and IL-1 β . In cytokine tissue during acute trauma-induced phase responses, TNF α and IL-1 β stimulate the production and release of other cytokines, including IL-6, which reaches a peak of 4-48 hours after surgery.⁷⁻¹⁰ A consistency with previous studies has shown that the tourniquet in TKA does not worsen systemic improvement in C-reactive protein. However, the findings by Matziolis et al., In a study showed an excessive inflammatory response occurred within 24 hours after the tourniquet release process at TKA. Thus, the systemic inflammatory response to the tourniquet at TKA depends on the first 24 hours after surgery.^{7,9,11}

In this study, higher D-Dimer levels were obtained at 12 hours postoperatively and proved to be significantly different as compared to D-Dimer levels at 24 hours postoperatively in patients undergoing primary TKA surgery.

The value of the correlation coefficient (r) between the duration of the use of the tourniquet and the D-Dimer level 24 hours postoperatively is 0.483 while the D-Dimer level 12 postoperative hours is 0.491 and are statistically significant with the p values of 0.004 and 0.003 ($p < 0.05$) respectively.

In the research of Tick L.W et al, it was also mentioned that with an increase in D-Dimers above 4 µg / mL there was a higher risk for DVT. This is also supported by research carried out by Naem M.A et al, where all of the samples obtained increased D-Dimer on the first post-operative day. In this study the intersection was obtained at 122.5 minutes. Where if the use of a tourniquet exceeds 122.5 minutes then the D-dimer level 24 hours postoperatively will be more than 4 g / mL and the risk of DVT.^{10,12-14}

In this study higher VAS values were obtained at 12 hours postoperatively and proved to be significantly different compared to VAS values at 24 hours postoperatively in patients undergoing primary TKA surgery. The value of the correlation coefficient (r) between the duration of use of the tourniquet and the VAS value 24 hours postoperatively is 0.507 and 12 hours postoperatively is 0.647 and statistically significant with p values of 0.000 and 0.002 respectively (p<0.05). Linear relationships with significant positive strong correlations were obtained mainly between the length of the tourniquet installation and the VAS value at 12 hours postoperatively. A statement from Tai et al., 2012 which states that the use of tourniquet at TKA can reduce the time of surgery and bleeding and cause extensive muscle damage which can cause the effects of postoperative pain. In contrast to the research conducted by Marcos George et al, 2016, in his study there was no significance between the use of tourniquet and pain complications with a p value of 0.174.¹⁵⁻¹⁸

CONCLUSION

A strong positive relationship between the duration of tourniquet use with IL 6, D-Dimer and VAS scales are obtained. The clinical and practice duration of tourniquet use should be a parameter that must be considered to minimize the inflammatory response, prothrombotic conditions and postoperative pain in TKA procedure. This study can be used as a baseline to examine the role of tourniquet duration on inflammatory responses, prothrombotic conditions and postoperative pain. A similar study with higher number of samples can be conducted in the future.

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