

Risks of Propofol-based Total Intravenous Anesthesia Compared with Local Anesthesia in Patients Undergoing Percutaneous Transluminal Angioplasty in The Lower Extremity

Wejpisit Wongwiwattananon, M.D., Jatuporn Pakpirom, M.D., Raviwan Akarapatima, M.D.

Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Received 17 February 2020 • Revised 23 April 2020 • Accepted 24 April 2020 • Published online 15 June 2020

Abstract:

Objective: This study aimed to determine the risks of propofol-based total intravenous anesthesia (TIVA) compared to local anesthesia (LA) in patients undergoing percutaneous transluminal angioplasty (PTA) in a lower extremity.

Material and Methods: A retrospective cohort study was conducted in 231 patients who underwent PTA in the lower extremity using either propofol-based TIVA or LA between January 2016 and September 2018. The outcomes of interest included perioperative major adverse cardiac events (MACE) and minor perioperative complications. Risk factors analysis was performed using a univariate logistic regression and backward stepwise multivariate logistic regression.

Results: Although the rate of perioperative MACE was two times higher in the propofol-based TIVA group (7.8%) than the LA group (3.9%), no significant difference was found (p -value=0.221). The propofol-based TIVA group had a significantly higher incidence of all minor perioperative complications than the LA group (77.6% vs 13.6%, p -value<0.001). Multivariate analysis found that low body mass index (BMI) and American Society of Anesthesiologists classification III were independent factors associated with perioperative MACE, while propofol-based TIVA, body weight (or BMI), hypertension, diabetes mellitus, previous coronary artery disease, and previous congestive heart failure were associated with perioperative minor complications.

Conclusion: Based on this study, no significant differences in perioperative MACE were found using either TIVA or LA. However, TIVA produced a significantly higher incidence of perioperative minor complication than LA. Close intraoperative monitoring should be implemented when using propofol-based TIVA in patients undergoing PTA in the lower extremity.

Keywords: critical limb ischemia, local anesthesia, percutaneous transluminal angioplasty, peripheral artery disease, propofol-based total intravenous anesthesia

Contact: Wejpisit Wongwiwattananon, M.D.
Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University,
Hat Yai, Songkhla 90110, Thailand.
E-mail: wejpisit@gmail.com

J Health Sci Med Res 2020;.....
doi: 10.31584/jhsmr.2020747
www.jhsmr.org

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Introduction

Approximately 202 million people had peripheral artery disease in 2010 and more than half of them were in either low-income or middle-income countries.¹ Due to aging populations, a growing number of vascular patients have multiple medical conditions that can cause an increase in the risks of doing conventional surgical revascularization procedures in the lower extremity. Hence, there has been a shift toward less invasive procedures using percutaneous transluminal angioplasty (PTA) to revascularize peripheral arterial disease in the lower extremities.²

The advantages of PTA over surgical revascularization at the lower extremities include lower morbidities, less cardiovascular stress, and the ability to perform the procedure under local anesthesia (LA).³⁻⁶ In particular regions, such as the United States of America, PTA is performed under local anesthesia and sedation in an interventional radiology suite rather than under general anesthesia. However, European countries prefer performing the procedure under general anesthesia in an operating theater. This might be because of higher patient expectations and patient anxiety under local anesthesia.^{7,8} Therefore, propofol-based total intravenous anesthesia (TIVA) is the preferable choice to overcome patient anxiety during the procedure. At our institute, PTA in a lower extremity had been performed with only local anesthesia by interventional radiologist in the past 10 years because of unavailable personnel from the anesthesiology department. Recently, anesthesiologist had provided service for interventional radiologist, which then almost all cases routinely underwent PTA with propofol-based TIVA because of the mutual preference of the interventional radiologists and the anesthesiologists.

It was reported that the choice of anesthetic technique could impact the perioperative outcomes in certain operations.⁹⁻¹¹ Nevertheless, the choice of the anesthetic technique in other procedures may favor

locoregional anesthesia, but the current evidence remains controversial.¹²⁻¹⁹ Several studies of PTA in the lower extremity focused mostly on long-term surgical outcomes.²⁰⁻²⁴ However, the number of studies which considered perioperative major adverse cardiac events (MACE) along with other minor perioperative complications is limited.^{25,26} In addition, the effect on cardiovascular and respiratory depression of propofol-based TIVA in patients undergoing PTA in the lower extremity can be unpredictable because of advanced age and multiple medical comorbidities. The aim of this study was to determine the risks of propofol-based TIVA in patients undergoing PTA in the lower extremity.

Material and Methods

A retrospective cohort study was conducted in a university-based tertiary care hospital and is the referral center for vascular intervention in southern Thailand. Approval for the study was received from the Ethics Committee of the Faculty of Medicine, Prince of Songkla University. Eligible patients were identified from the hospital information system database from January 2016 to September 2018 using search terms with specific International Classification of Diseases, Tenth Revision (ICD-10) codes that included (1) peripheral artery disease, unspecified (I739) and (2) performing PTA under ICD-9-AM with the codes 3950 and 8848. The patients included in the study were over 18 years old who underwent PTA in their lower extremity and underwent the procedure under either propofol-based TIVA or LA. Those who had continuous infusion of vasopressor before the operation were excluded from the study. All of the procedures in our hospital were performed in the interventional radiology suite. All patients in the LA group received local infiltration by an interventional radiologist at the femoral puncture site without an attending anesthesiologist, whereas propofol-based TIVA was provided by the anesthesia team.

Both groups received the same standard American Society of Anesthesiologists (ASA) monitoring, which included pulse oximetry, blood pressure, and electrocardiogram. In addition, the end-tidal capnography was monitored in the propofol-based TIVA group. The interval of blood pressure recording time was every 15 minutes in the LA group, and every 5 minutes in the propofol-based TIVA group. Every patient in both groups received supplemental oxygen before the procedure.

The primary outcomes were perioperative MACE and minor perioperative complications. Perioperative MACE was defined and recorded if patients developed the following perioperative events: (1) fatal arrhythmia (ventricular tachycardia, ventricular fibrillation, and complete heart block); (2) congestive heart failure (CHF); (3) myocardial infarction; (4) stroke; (5) cardiac arrest; and (6) death. Minor perioperative complications were defined as: (1) hypotension; (2) arrhythmia; (3) airway intervention; (4) vasopressor requirement during operation; and (5) continuous vasopressor infusion during and within 24 hours of the operation. Hypotension was defined as mean arterial pressure <65 millimetre of mercury (mmHg) or 20.0% of baseline in hypertensive patients. Any airway interventions needed during the operation or within 24 hours after the operation that included positive pressure ventilation with a facemask, laryngeal mask airway insertion, or endotracheal intubation were defined as airway intervention. Operation time was the duration the patient remained in the operation room.

Baseline patient characteristics, underlying diseases, and surgical factors were reviewed and recorded from the anesthetic and medical records in the hospital information system as independent variables. Patient characteristic information included age, sex, body weight, height, body mass index (BMI), and ASA classification. Other collected data included underlying diseases including diabetes, hypertension, previous CHF, previous coronary artery

disease (CAD), previous stroke, and creatinine >2 milligram per deciliter (mg/dL). Also recorded were the clinical presentations that were either intermittent claudication or critical limb ischemia and the site of arterial occlusion.

The sample size was calculated based on the formula of the two-proportion difference of prevalence of perioperative MACE between 1.0% of LA²⁶ and 12.0% of propofol-based TIVA. A total of 231 patients were required of which 154 patients were in the LA group and 77 patients were in the propofol-based TIVA group to provide 80.0% power. The level of significance was set at 0.05 and the ratio between the LA group and propofol-based TIVA group was equal to 2:1. For the statistical analysis, we used R software v.3.4.5 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables, such as age, height, body weight, and operative time are reported as mean±standard deviation (S.D.) or median (interquartile range; IQR) depending on which one was appropriate for distribution of the data. Discrete variables are reported as frequency and percentage. The chi-square test or Fisher's exact test was used as appropriate to compare the difference of categorical variables between the two groups. Unpaired student *t*-test or Mann-Whitney U test was used to test the difference of continuous variables between the two groups. Univariate analysis and backward stepwise multivariate logistic regression were used to find the associated factors of perioperative MACE and minor complications.

Results

The baseline patient characteristics of 231 patients that included underlying diseases, surgical factors, and clinical presentation are presented in Table 1. The mean±S.D. age of the patients was 69.9±13.0 years (range 30–97 years) and 64.1% were male. The proportion of ASA classification III is higher in the propofol-based TIVA group. More than half of the patients had hypertension and diabetes mellitus while almost one quarter of the

Table 1 Baseline patient characteristic, underlying diseases, and clinical presentations

Patient characteristics	n=231
Age, years, mean±S.D.	69.9±13.0
Sex	
Male	148 (64.1)
Female	83 (35.9)
Body weight, kg, mean±S.D.	56.8±10.8
Height, cm, mean±S.D.	160.8±8.2
Body mass index, kg/m ² , mean±S.D.	21.9±3.6
ASA classification	
ASA class I	3 (1.3)
ASA class II	115 (49.8)
ASA class III	113 (48.9)
Underlying disease	
Hypertension	177 (76.6)
Diabetes mellitus	120 (51.9)
Previous CAD	45 (19.5)
Previous CHF	15 (6.5)
Previous stroke	20 (8.7)
Creatinine >2 mg/dL	56 (24.2)
Clinical presentation	
Claudication	54 (23.4)
Critical limb ischemia	177 (76.6)

Data are presented as n (%) unless indicated otherwise.

S.D.=standard deviation, kg=kilogram, cm=centimeter, m²=square meter, ASA=American Society of Anesthesiologists, CAD=coronary artery disease, CHF=congestive heart failure, mg/dL=milligram per deciliter, n=number

patients had impaired renal function (creatinine >2 mg/dL). The majority of cases presented with critical limb ischemia (76.6%) which was more than claudication (23.4%). The median IQR operation time in the propofol-based TIVA group was higher than the LA group [135 (105,165) vs 125 (105,150)] without significant difference (p-value=0.293). There was no statistically significant difference in the baseline characteristics between the LA group and the propofol-based TIVA group, except the LA group had a significantly higher number of patients with diabetes mellitus than the propofol-based TIVA group (58.4% vs 39.0%, p-value=0.008) (Table 2).

Perioperative complications, including MACE and minor perioperative complications in both the LA group and propofol-based TIVA group are presented in Table 3. Although the rate of perioperative MACE in the propofol-based TIVA group (7.8%) was two times higher than the LA group (3.9%), no significant difference was found (p-value=0.221). However, a statistically significantly higher proportion of patients were found to have minor complications (hypotension, arrhythmia, airway intervention, vasopressor needed, and continuous vasopressor infusion) in the propofol-based TIVA group than in the LA group.

Table 2 Patient characteristics and underlying diseases for both the local anesthesia group and propofol-based total intravenous anesthesia group

Patient characteristics	Local anesthesia (n=154)	Propofol-based TIVA (n=77)	p-value
Age, years, median (IQR)	71 (61.0, 79.0)	74 (64.0, 80.0)	0.243
Sex			0.734
Male	97 (63.0)	51 (66.2)	
Female	57 (37.0)	26 (33.8)	
Body weight, kg, median (IQR)	58 (50.0, 65.0)	54 (47.0, 63.0)	0.123
Height, cm, mean±S.D.	160.6±7.7	161±9.2	0.722
Body mass index, mean±S.D.	22.2±3.5	21.3±3.8	0.068
ASA classification			0.019
ASA classification I-II	87 (56.4)	31 (40.3)	
ASA classification III	67 (43.5)	46 (59.7)	

Table 2 (continued)

Patient characteristics	Local anesthesia (n=154)	Propofol-based TIVA (n=77)	p-value
Hypertension	116 (75.3)	61 (79.2)	0.621
Diabetes mellitus	90 (58.4)	30 (39.0)	0.008
Previous CAD	28 (18.2)	17 (22.1)	0.597
Previous CHF	11 (7.1)	4 (5.2)	0.777
Previous stroke	12 (7.8)	8 (10.4)	0.679
Creatinine >2 mg/dL	42 (27.3)	14 (18.2)	0.175
Received fentanyl	43 (27.9)	77 (100.0)	<0.001
Fentanyl dosage, mcg, median (IQR)	0 (0.0, 30.0)	100 (75.0, 125.0)	<0.001
Received midazolam	11 (7.1)	33 (42.9)	<0.001
Midazolam dosage, mg, median (IQR)	0 (0.0, 0.0)	0 (0.0, 1.0)	<0.001
Propofol dosage, mg, median (IQR)	0 (0.0, 0.0)	454 (298.0, 724.0)	

Data are presented as n (%) unless indicated otherwise.

TIVA=total intravenous anesthesia, IQR, interquartile range, kg=kilogram, S.D.=standard deviation, ASA=American Society of Anesthesiologists, CAD=coronary artery disease, CHF=congestive heart failure, mg/dL=milligram per deciliter, n=number; mcg=microgram; mg=milligram

Table 3 Perioperative complications in the local anesthesia group and propofol-based total intravenous anesthesia group

Perioperative complications	Local anesthesia (n=154)	Propofol-based TIVA (n=77)	p-value
Perioperative MACE	6 (3.9)	6 (7.8)	0.221
Fatal arrhythmia	1 (0.6)	2 (2.6)	0.258
Myocardial infarction	3 (1.9)	1 (1.3)	1.000
Congestive heart failure	2 (1.3)	2 (2.6)	0.602
Stroke	0 (0.0)	1 (1.3)	0.333
Cardiac arrest	3 (1.9)	0 (0.0)	0.553
Death	2 (1.3)	2 (2.6)	0.602
Minor complications	21 (13.6)	59 (77.6)	<0.001
Hypotension	18 (11.7)	58 (75.3)	<0.001
Arrhythmia	5 (3.2)	10 (13.0)	0.011
Airway intervention	2 (1.3)	11 (14.3)	<0.001
Vasopressor needed	3 (1.9)	38 (49.4)	<0.001
Continuous vasopressor	3 (1.9)	10 (13.0)	0.001

Data are presented as n (%).

TIVA=total intravenous anesthesia, MACE=major adverse cardiac events, n=number

The six MACE cases in the LA group were due to postoperative, non-ST elevated myocardial infarction (NSTEMI) in three cases, cardiac arrest; mainly from massive bleeding of surgical complications in two cases, and perioperative congestive heart failure, probably related to volume overload in one case. Likewise, in the propofol-based TIVA group, the MACE were NSTEMI with CHF in one case, acute postoperative ischemic stroke in one case, hypoxic arrest due to airway obstruction from over sedation at recovery room in one case, profound hypotension with ventricular tachycardia after bolus dose of propofol intraoperatively in one case, two cases with uncontrolled labile blood pressure (severe hypertension;

then profound hypotension), acidosis from reperfusion syndrome, congestive heart failure and surgical complications (retroperitoneal hemorrhage).

We performed univariate and multivariate analyses to find the independent risk factors of perioperative MACE (Table 4 and Table 5, respectively). We found that BMI and ASA classification \geq III were associated with the incidence of perioperative MACE. However, no associations were found between patient characteristics and underlying diseases that included hypertension, diabetes mellitus, previous CAD, previous CHF, previous stroke, and creatinine >2 mg/dL, or clinical presentation and technique of anesthesia with perioperative MACE.

Table 4 Univariate analysis of independent risk factors associated with perioperative and postoperative major adverse cardiac events and non-major adverse cardiac events outcomes

MACE	Yes (n=12)	No (n=219)	p-value
Age, years, median (IQR)	71 (62.8, 85.2)	72 (61.0, 79.0)	0.346
Body weight, kg, median (IQR)	49.5 (44.8, 53.2)	57 (49.0, 65.0)	0.056
Height, cm, mean \pm S.D.	162.6 \pm 8.4	160.7 \pm 8.2	0.433
BMI, kg/m ² , mean \pm S.D.	19.3 \pm 2.6	22.1 \pm 3.6	0.011
ASA classification			0.014
I-II	2 (16.7)	116 (53.0)	
\geq III	10 (83.3)	103 (47.0)	
Hypertension	10 (83.3)	167 (76.3)	0.737
Diabetes mellitus	5 (41.7)	115 (52.5)	0.663
Previous CAD	4 (33.3)	41 (18.7)	0.256
Previous CHF	2 (16.7)	13 (5.9)	0.178
Previous stroke	2 (16.7)	18 (8.2)	0.278
Creatinine >2 mg/dL	5 (41.7)	51 (23.3)	0.169
Clinical presentation			1.000
Claudication	3 (25.0)	51 (23.3)	
Critical limb ischemia	9 (75.0)	168 (76.7)	
Technique of anesthesia			0.221
Local anesthesia	6 (50.0)	148 (67.6)	
TIVA	6 (50.0)	71 (32.4)	

Data are presented as n (%) unless indicated otherwise.

MACE=major adverse cardiac events, IQR, interquartile range, S.D.=standard deviation, kg=kilogram, cm=centimeter, m²=square meter, BMI=body mass index, ASA=American Society of Anesthesiologists, CAD=coronary artery disease, CHF=congestive heart failure, mg/dL=milligram per deciliter, TIVA=total intravenous anesthesia, n=number

Table 5 Multivariate analysis of independent factor associated with major adverse cardiac events

Factor	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Body mass index	0.78 (0.65, 0.95)	0.77 (0.64, 0.94)	0.005
ASA classification III (Ref: classification I-II)	5.63 (1.21, 26.29)	6.6 (1.37, 31.66)	0.018
Technique of anesthesia (Ref: local anesthesia)	2.08 (0.65, 6.69)	1.81 (0.48, 6.85)	0.387

OR=odds ratio, CI=confidence interval, ASA=American Society of Anesthesiologists

Table 6 Multivariate analysis of independent factors associated with minor perioperative complications

Factor	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Propofol-based TIVA	21.98 (10.82, 44.67)	65.24 (22.77, 186.9)	<0.001
Body weight	0.95 (0.93, 0.98)	0.92 (0.88, 0.96)	<0.001
Hypertension	2.81 (1.33, 5.96)	4.52 (1.37, 14.86)	0.009
Diabetes mellitus	1.1 (0.64, 1.9)	3.42 (1.27, 9.25)	0.010
Coronary artery disease	2.63 (1.35, 5.12)	2.76 (1.02, 7.48)	0.043
Previous CHF	5.82 (1.79, 18.93)	7.66 (1.77, 33.07)	0.005

OR=odds ratio, CI=confidence interval, TIVA=total intravenous anesthesia, CHF=congestive heart failure

After that, a further analysis to identify the risk factors of perioperative minor complications was done and we found that using propofol-based TIVA, body weight (or BMI), history of hypertension, history of diabetes mellitus, previous CAD, and previous CHF were associated with perioperative minor complications (Table 6).

Discussion

The risks of perioperative MACE and minor complications were demonstrated in patients undergoing PTA in lower extremities; using both propofol-based TIVA provided by anesthesiologist and LA anesthesia carried out by an interventionist. Significant higher events of minor complications, mainly due to propofol side effects, was shown in the propofol-based TIVA than that of the LA group.

Sedation and anesthesia are essential procedures for performing surgical intervention. However, the mechanisms of various sedatives or anesthetic drugs used are different, and result in a variation of side effects which require vigorous monitoring of the hemodynamic status for the principles of patient safety.²⁵ One randomized-controlled trial study²⁶ in 40 patients underwent PTA found that propofol-based TIVA had less respiratory depression than midazolam and no significant difference in blood pressure with no incidence of hypotension when achieved the same level of sedation at conscious sedation, however the dosage of propofol in the study was considerably low (46.7 ± 24.2 mg) compared to our current practice.

The perioperative MACE in our study was found in 3.9%, which was in the range of previous studies; which was reported to be 1.0–6.6.^{27,28} The difference of

incidence detected might be because of different patient characteristics, regimens of anesthesia or definitions of perioperative MACE. The perioperative MACE could be resulted from the combined multifactorial causes of which a previous study suggested a cardiac risk index for predicting major noncardiac surgery²⁹, and the guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery.³⁰

Our study found that BMI and ASA classification III were an independent risk factor of perioperative MACE in patients who underwent PTA in the lower extremity. A previous retrospective study, that had similar results with this study, showed no association between the patient's age and perioperative MACE in patients who underwent PTA in the lower extremity.²⁷ In our study, low BMI was the independent factor that had a significant association with perioperative MACE. This could imply that obese patients possibly had closer monitoring during the perioperative care than non-obese patients in our practice; therefore, the term "obesity paradox"³¹ might be considered. A previous study in CAD also reported that patients who had a BMI between 30 and 40 kg/m² had a decrease in all-cause mortality.³² In contrast, the multivariate analysis in a previous study²⁸ found that diabetes mellitus and chronic renal failure were independent factors associated with perioperative MACE. This might be explained by the relatively lower sample size and incidence of perioperative MACE in our study.

Propofol-based TIVA was the independent risk factors associated with perioperative minor complications in patients who underwent lower extremity PTA in our study. These perioperative minor complications can lead to life-threatening events if not promptly managed³³ which require an experienced anesthesiologist, well-prepared resuscitation equipment, and standard monitoring including capnography.³⁴ These actions would provide a prompt response to any event during the procedure, especially

anesthesia in the remote area that usually have limited resources.

The results of our study suggested that MACE as well as minor perioperative complications were not uncommon, particularly in patients using propofol-based TIVA. These complications should be acknowledged and carefully prevented; even when propofol-based TIVA is performed by an experienced anesthesiologist.

There are several limitations because this is a retrospective cohort study. Firstly, the different interval of blood pressure recording time between two groups might affect the result. The propofol-based TIVA group received more frequent blood pressure monitoring and might be one of the reasons that we found a higher incidence of hypotension, however it could not fully explain the higher incidence of vasopressor used. Secondly, this study may have selection bias that unintentionally excluded patients who had severe cardiopulmonary compromise because this condition is a contraindication to perform propofol-based TIVA, which they underwent general anesthesia with endotracheal tube with balanced technique with volatile anesthetics instead. Thirdly, the induction and maintenance rate of propofol-based TIVA was not documented in the anesthetic record since the optimal dosage is adjusted by the attending anesthesiologist according to the condition of the patient. The other limitation is that we could not assess the depth of anesthesia or sedation in the propofol-based TIVA group because this is a retrospective cohort study and the patients who received propofol-based TIVA in our institute did not routinely monitor the bispectral index or record the clinical assessment of sedation depth. Lastly, we calculated the sample size based on the prevalence of the outcomes from previous studies which were quite different compared to our findings. Hence, the main reason of the non-significant difference of MACE between groups might be from the insufficient sample size to detect a

difference between the groups. From our results, the power of two independent proportions was calculated and it was considerably low at 23.1%.

Conclusion

The occurrence of perioperative, major adverse cardiac events was not significantly different between patients undergoing PTA in the lower extremity between those using propofol-based TIVA and those using local anesthesia. However, minor perioperative complications, such as hypotension, arrhythmia, airway intervention or the need of vasopressor were more likely to be found in propofol-based TIVA, therefore, close intraoperative monitoring is important and complications during the propofol-based TIVA procedure in patients who undergo PTA in the lower extremity should be prevented.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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