Incidence of Perioperative Myocardial Infarction in Patients Who Underwent Preoperative Evaluation by Internist for Intermediate and High Risk Non-Cardiac Surgery

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Background: *Incidence of perioperative myocardial infarction (PMI) in patients who underwent intermediate to high risk surgery is varied from 1 to 9 percent based on previous studies.*
Objective: *To study the incidence of PMI among patients who undergo preoperative evaluation by internists for intermediate to high risk non-cardiac surgery.*
Material and Method: *This study is a cross-sectional study, performed at Thammasat Hospital for one year. Eligible patients were subjects older than 20 years old who underwent elective intermediate to high risk non-cardiac surgery with preoperative cardiovascular evaluation. The primary outcome was the incidence of PMI which diagnosed based on definition of Third universal definition of myocardial infarction ESC/ACCF/AHA/WHF 2012. The secondary outcome was the incidence of elevated high sensitivity cardiac Troponin T (hs-cTnT).*
Results: *Fourty-five patients (median age 66 years, female 68.9%) were eligible for this study. Most of them underwent orthopedic surgery (88.9%). Three female patients developed PMI, represented as 6.7%. In multivariate logistic regression analysis, CrCl <30 mL/min/1.73m^2 was an independent factor associated with PMI [adjusted odd ratio 82.00 (95% CI 3.64-1,846.00; p = 0.006)]. Twenty-two patients (48.9%) had elevated hs-cTnT.*
Conclusion: *Incidence of PMI was similar to the previous study, and eGFR less than 30 mL/min/1.73m^2 was an independent factor for PMI.*

Keywords: *Perioperative myocardial infarction, Preoperative evaluation*

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Perioperative myocardial infarction (PMI) is one of the major complication in perioperative period and associated with high morbidity and mortality. The presentations are often subtle, so PMIs are late recognized by physician, resulting in 30 to 70% mortality[1]. After the utilization of hs-cTnT assays, physicians can use this cardiac marker with clinical history and electrocardiographic findings to readily recognized myocardial infarction, hence reducing the mortality of PMIs. Many studies[2-4] demonstrated that onset of PMIs is within the first 24 hours after surgery and the elevation of cardiac troponin also start within 24 hours[3].

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Incidence of perioperative myocardial infarction (PMI) in patients who underwent intermediate to high risk surgery is about 1 to 9% based on previous studies performed in Thailand and other countries[5,6]. Preoperative cardiovascular evaluation in order to identify patients at risk is the key to prevent PMI and reduce mortality. There are many risk prediction tools used to predict perioperative cardiac mortality, one of the most simple and well-known tool is Lee index, developed in 1999[4]. It contained five independent risk factors including history of IHD, history of cerebrovascular disease, heart failure, insulin-dependent diabetes and preoperative serum creatinine >2 mg/dL. Lee index uses serum creatinine as one of independent factors, but the same serum creatinine level may not represent the same estimated glomerular filtration rate (eGFR) in different patients and may have different risk in developing perioperative cardiac complication. To date, there are still no study mentioned

which cutoff level of eGFR is associated with perioperative cardiac complication including PMI.

There are two accepted mechanisms that can explain the pathophysiology of PMI[7]. The first is acute coronary syndrome (Type I MI) that caused by spontaneous plaques rupture, and the second is myocardial oxygen supply-demand imbalance (type II MI). Based on knowledge on pathophysiology, intraoperative factors such as intraoperative hypotension, intraoperative blood loss may have to be taken into account as factors that may increase risk of PMI. Studies in these intraoperative factors are still lacking, and were not mentioned in Lee index as well.

This research was designed to study the incidence of PMI among intermediate and high risk elective non-cardiac surgery and to find factors associated with PMI.

Material and Method

Study design

Study design was a cross-sectional study, performed at Thammasat University Hospital conducted during July 2013 to 2014. Sample size of at least 45 patients was calculated by using the incidence of PMI in previous study[5].

The study protocol was approved by Thammasat University Hospital ethics committee. Patients who were enrolled in the study need to sign an informed consent, before taking blood sample for hs-cTnT and performing 12-leads ECG at ward and within 24 hours after surgery.

Data collection

Forty-five patients who were planned to undergo intermediate or high risk elective non-cardiac surgery were recruited to the study if they were older than 20 years, had no active cardiac condition defined in ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation[6], and have no recent MI (within 6 weeks). Every recruited patient was interviewed and investigated to obtain baseline characteristic data included functional capacity, underlying disease, clinical risk factors based on Lee index, body mass index, eGFR (calculated using CKD-EPI formula), family history of coronary artery disease (CAD), smoking behavior, preoperative ECG. The patients were then undergone cardiac assessment by internal medicine residents and cardiologist followed the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and also 2009 ACCF/AHA Focused Update on Perioperative Beta Blockage Incorporated Into the ACC/AHA 2007 Guidelines. After the operation finished and patients were transferred to ward, an ECG and serum hs-cTnT were immediately obtained and were repeated at 24 hours after surgery. We also recorded intraoperative factors such as intraoperative blood loss, intraoperative blood pressure (to record the episodes of intraoperative hypotension) as we hypothesized these factors as intraoperative factors associated with PMI.

Perioperative myocardial infarction (PMI)

The diagnosis of PMI were made by adopting the Third Universal Definition of Myocardial infarction[8]. The patients who developed PMI were managed according to ACS protocol.

Intraoperative hypotension

Using the same definition as reported in anesthetic literatures as a decrease in systolic or mean arterial pressure more than 25% from baseline[7].

Preoperative ECG abnormalities

ECG that might represent previously injured myocardium, which included ST segment depression, T wave inversion, and pathologic Q wave.

Outcome

The primary outcome was the incidence of PMI. The secondary outcome was the incidence of patients with elevated hs-cTnT which defined as a cutoff level more than 0.014 ng/ml.

Statistical analysis

Data were analyzed using SPSS version 13.0.

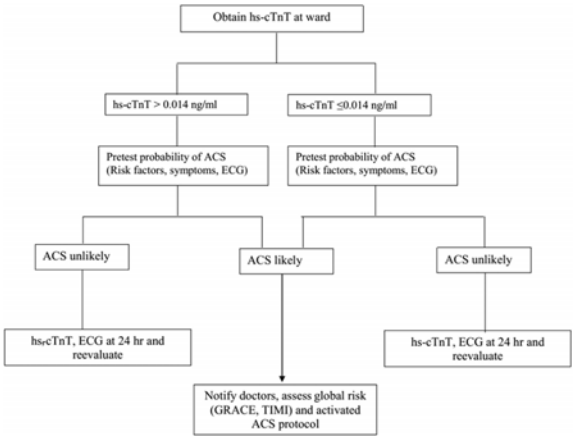

Fig. 1 Protocol for managing patients at ward.

The associations between PMI and various risk factors were calculated using Chi-square and Fisher's exact tests. The *p*-value of less than 0.05 was defined as statistically significance. Multiple cutoff levels of eGFR and intraoperative amount of blood loss were analysed to find the most statistic significant cutoff levels which associated with PMI.

Results

Fourty-five patients were recruited (median age 66 years, female 69%). Majority of these patients underwent orthopedic surgery (89%) while the others underwent general surgery. Only one patient had clinical risk factors more than two (2%). Hs-cTnT was found elevated in 22 patients (49%). Intraoperative hypotension was found in 26 patients (58%). Three patients had eGFR ≤30 ml/min/1.73m^2 (6.7%) and 6 patients (13%) had intraoperative blood loss ≥500 ml.

Table 1 showed baseline characteristic of patients who developed PMI. There were three female patients developed PMI, represented as 6.7% of incidence. Among three patients with PMI, one patient underwent intra-abdominal surgery and the other two underwent orthopedic surgery. One of the three patients had 3 clinical risk factors of Lee index, the other two patients had 0 and 1 clinical risk factors. Two of the three patients had episodes of intraoperative hypotension, and had GFR of less than 30 ml/min/1.73 m^2 as well. None of them who developed PMI had angina pectoris. Time from surgery to developed PMI were recognized at 4 hr, 24 hr, and 24 hr respectively. All of the three patients had new ST segment change at postoperative period suggestive of myocardial infarction and one of them was classified as high risk category based on GRACE risk score.

Table 2 showed relationship between the PMI and clinical risk factors. The eGFR ≤30 mL/min/1.73 m^2 (CKD-EPI) and intra-operative blood loss ≥500 ml were statistically significant associated with PMI. Interestingly, number of clinical risk factors based on

Table 1. Baseline characteristic of patients who developed PMI

	Patient No.1	Patient No.2	Patient No.3
Age (year)	66	82	75
Gender	Female	Female	Female
Type of surgery	Intra-abdominal	Orthopedic	Orthopedic
Clinical risk factors	3	1	0
BMI (kg/m^2)	21	21	27
CAD	Yes	No	No
CVA/TIA	No	No	No
CHF	No	No	No
PAD	No	No	No
Family history of CAD	No	Yes	No
eGFR (ml/min/1.73m^2)	15	17	76
Insulin dependent DM	Yes	No	No
HT	Yes	No	No
DLP	Yes	Yes	No
Smoking	No	No	No
Functional capacity ≤4 METS	Yes	Yes	No
Preoperative ECG	Normal	Abnormal	Normal
Intraoperative hypotension[1]	No	Yes	Yes
Intraoperative blood loss (ml)	30	1,270	500
Elevated hs-cTnT at ward	Yes	No	No
Elevated hs-cTnT at 24 hr after surgery	Yes	Yes	Yes
Time from surgery when PMIs were recognized (hr)	4	24	24

[1] Defined as a decreased in MAP >25% from baseline

BMI = body mass index, CAD = coronary artery disease, CVA/TIA = cerebrovascular disease/transient ischemic attack, CHF = congestive heart failure, PAD = peripheral arterial disease, eGFR = estimated glomerular filtration rate, HT = hypertension, DLP = dyslipidemia, DM = diabetes mellitus, ECG = electrocardiogram, hs-cTnT = high sensitivity cardiac troponinT, MAP = mean arterial pressure

Lee index were not statistically significant associated with PMI.

In multivariate logistic regression analysis, eGFR ≤30 ml/min/1.73m^2 was an independent factor associated with PMI [adjusted odd ratio 82.00 (95% CI 3.64 to 1,846.00; $p = 0.006$)], as shown in Table 3.

Twenty-two patients (49%) had elevation in hs-cTnT. Dyslipidemia, serum creatinine ≥2 mg/dL, intraoperative hypotension and intraoperative blood loss ≥500 ml were statistically significant associated with hs-cTnT elevation, as shown in Table 4.

In multivariate logistic regression analysis, intraoperative hypotension was an independent factor associated with hs-cTnT elevation [adjusted odd ratio 3.709 (95% CI 1.021 to 13.472; $p = 0.046$)] as shown in Table 5.

Discussion

The study showed the incidence of PMI among intermediate and high risk elective non-cardiac surgery was 6.7%, which was similar to those reported in previous study at Thammasat University Hospital[6].

The author had observed that decrease in eGFR was the factor associated with PMI, especially eGFR ≤30 ml/min/1.73m^2 was found to be an independent factor associated with PMI[adjusted odd ratio 82.00 (95%CI 3.64 – 1846.00; $p = 0.006$)]. Multiple mechanisms may be explained why patients with renal dysfunction

Table 2. Relationship between the PMI and clinical risk factors

Risk factors	All (n=45)	Periop MI (n=3)	Non-MI (n=42)	*p*-value
Male	14 (31%)	0	14 (31%)	0.54
Female	31 (68%)	3 (7%)	28 (62%)	0.54
Age ≥75	9 (20%)	2 (4%)	7 (16%)	0.097
BMI ≥23	29 (64%)	1 (2%)	28 (62%)	0.285
CAD	7 (16%)	1 (2%)	6 (13%)	0.405
CHF	1 (2%)	0	1 (2%)	1.0
eGFR ≤30 ml/min/1.73m^2	3 (7%)	2 (4%)	1 (2%)	0.009
Insulin dependent DM	7 (16%)	1 (2%)	6 (13%)	0.405
CVA	3 (7%)	0	3 (7%)	1.0
Fam Hx CAD	8 (18%)	1 (2%)	7 (16%)	0.452
HT	34 (76%)	1 (2%)	33 (73%)	0.146
DLP	35 (78%)	2 (4%)	33 (73%)	0.539
Smoking	15 (33%)	0	15 (33%)	0.54
ECG abnormal at baseline	13 (29%)	1 (2%)	12 (27%)	1.0
Clinical risk score ≥3	1 (2%)	1 (2%)	0	0.067
Clinical risk score ≥2	3 (7%)	1 (2%)	2 (4%)	0.19
METs<4	9 (20%)	2 (4%)	7 (16%)	0.097
Intraoperative hypotension*	28 (62%)	2 (4%)	26 (56%)	1.0
Blood loss ≥500 ml	6 (13%)	2 (5%)	4 (9%)	0.043
Elevated hs-cTnT	22 (49%)	3 (7%)	19 (42%)	0.109

* Defined as a decreased in MAP >25% from baseline

BMI = body mass index, CAD = coronary artery disease, CVA/TIA = cerebrovascular disease/transient ischemic attack, CHF = congestive heart failure, PAD = peripheral arterial disease, eGFR = estimated glomerular filtration rate, HT = hypertension, DLP = dyslipidemia, DM = diabetes mellitus, ECG = electrocardiogram, hs-cTnT = high sensitivity cardiac troponinT, MAP = mean arterial pressure

Table 3. Multivariate logistic regression analysis of factors that were statistically significant associated with PMI

Factors	Adjusted OR	95% CI	*p*-value
eGFR ≤30 ml/min/1.73m2	82.00	3.64 – 1846.00	0.006

eGFR = estimated glomerular filtration rate

Table 4. Relationship between the elevation hs–cTnT and clinical risk factors

Risk factors	All (n=45)	Elevated hs-cTnT (n=22)	Non-elevated (n=23)	*p*-value
Male	14 (31%)	8 (18%)	6 (13%)	0.454
Female	31 (69%)	14 (31%)	17 (38%)	
Age ≥75	9 (20%)	6 (13%)	3 (7%)	0.284
BMI ≥23	29 (64%)	1 (2%)	28 (62%)	0.285
CAD	7 (16%)	5 (11%)	2 (4%)	0.243
CHF	1 (2%)	0	1 (2%)	1.0
Cr ≥2mg/dL	4(9%)	4(9%)	0	0.049
eGFR ≤30 ml/min/1.73m^2	3 (7%)	3 (7%)	0	0.109
Insulin dependent DM	7 (16%)	4 (9%)	3 (7%)	0.699
CVA	3 (7%)	0	3 (7%)	0.233
Fam Hx CAD	8 (18%)	6 (13%)	2 (4%)	0.135
HT	34 (76%)	19 (42%)	15 (33%)	0.099
DLP	35 (78%)	20 (44%)	15 (33%)	0.038
Smoking	15 (33%)	9 (20%)	6 (13%)	0.292
ECG abnormal at baseline	13 (29%)	8 (18%)	5 (11%)	0.279
Clinical risk score ≥3	1 (2%)	1 (2%)	0	0.489
Clinical risk score ≥2	3 (7%)	2 (4%)	1 (2%)	0.608
MET<4	9 (20%)	7 (16%)	2 (4%)	0.071
Intraoperative hypotension*	28 (62%)	17 (38%)	11 (24%)	0.042
Blood loss ≥500 ml	6 (13%)	6 (13%)	0	0.009

Cr = serum creatinine

* Defined as a decrease in MAP >25% from baseline.

Table 5. Multivariate logistic regression analysis of factors that were statistically significant associated with hs-cTnT elevation

Factors	Adjusted OR	95% CI	*p*-value
Decreased in MAP ≥ 25% from baseline	3.709	1.021-13.472	0.046

MAP = mean arterial pressure

have increase risk of myocardial infarction, including PMI. Renal dysfunction promotes atherosclerosis by inducing inflammation and vascular calcification, furthermore uremia also causes an excess thrombin generation and increase the rate of coronary thrombotic events[8]. Also, some studies showed that decline in eGFR causes diminish in vascular elasticity and subsequently causes an impaired in endothelium–vasodilatory response, increasing rate of ischemic events[8-11].

Intraoperative factors that statistically associated with PMI in this study was intraoperative blood loss, which could be explained by myocardial oxygen supply-demand imbalance described previously. Intraoperative hypotension and number of clinical risk factors (based on Lee index) were not statistically significant associated with PMI possibly due to small sample size.

Twenty-two patients (49%) were found to have elevation hs-cTnT. As we known that not all elevation of cardiac troponin results from myocardial infarction, even from ischemic etiology there are many conditions other than ACS, such as hypoxia or hypoperfusion. As expected, the data showed intraoperative hypotension was an independent factor associated with an elevation in hs-cTnT. However, an elevation in hs-cTnT per se was not statistically associated with PMI. So inappropriate overdiagnosis of PMI based on cardiac troponin alone may lead to adverse complication. A previous studies found an association between elevation in cardiac troponin and long-term survival[12].

An intermediate or long-term follow-up of this group of patients should be focused in the near future study to obtain more knowledge on cardiovascular outcomes.

Conclusion

The incidence of PMI among intermediate and high risk elective non-cardiac surgery was similar to previous studies. The cutoff value of eGFR ≤30 ml/min/1.73 m^2 was an independent factor associated with PMI. There were an association between intraoperative blood loss ≥500 ml and PMI.

We still encourage the use of risk prediction tools such as Lee index as it was one of the most validated and simple risk prediction tool nowadays. But to be more accurate than Cr >2 mg/dL as described in Lee index, the cutoff value of eGFR ≤30 ml/min/1.73 m^2 should be used as alternative criteria to classify risk for developing PMI. Moreover, physicians should also consider intraoperative factors such as intraoperative hypotension and intraoperative blood loss as key factors that might be associated with PMI and give awareness on these risks.

Study limitations

This study had some limitations from small numbers of patients and type of surgical procedures are limited to orthopedic and general surgeries. So, the incidence of PMI from this study might have some bias from this reason.

What is already known on this topic?

PMI is underdiagnosed by its clinical presentation which are often subtle.

What this study adds?

This study describes the incidence of PMI in real world practice even receiving preoperative evaluation by internist or cardiologist. The data also showed the incidence of elevation of serum hs-cTnT during perioperative period, which are higher than our expectation.

This data might be helpful to predict prognosis if there are more data from short-term or long-term follow up study will be continued.

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Potential conflicts of interest

None.

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อุบัติการณ์การเกิดภาวะกล้ามเนื้อหัวใจขาดเลือดระหว่างและหลังการผ่าตัดในผู้ป่วยกลุ่มที่มีความเสี่ยงจากการผ่าตัดปานกลางและสูงจากการผ่าตัดประเภทอื่นนอกเหนือจากการผ่าตัดหัวใจหลังจากได้รับการเตรียมการผ่าตัดโดยอายุรแพทย์ในโรงพยาบาลธรรมศาสตร์

ปวินท์ ศิริแสงชัยกุล, อิงอร อรุณากูร

ภูมิหลัง: *อุบัติการณ์ของการเกิดภาวะกล้ามเนื้อหัวใจขาดเลือดระหว่างและหลังการผ่าตัดประเภทอื่นนอกเหนือจากการผ่าตัดหัวใจ พบได้ตั้งแต่ 1-9 เปอร์เซ็นต์จากการศึกษาที่ผ่านมา*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณา เก็บรวบรวมข้อมูลทั้งสิ้น 1 ปี โดยจะศึกษาผู้ป่วยที่มีอายุตั้งแต่ 20 ปีขึ้นไป ที่ได้รับการเตรียมการผ่าตัดโดยอายุรแพทย์ เพื่อจะเข้ารับการผ่าตัดประเภทอื่นนอกเหนือจากการผ่าตัดหัวใจที่มีความเสี่ยงของการผ่าตัดปานกลางถึงสูง ซึ่งจะวัดผลการศึกษาหลักเป็นอุบัติการณ์ของการเกิดภาวะกล้ามเนื้อหัวใจขาดเลือด ระหว่างและหลังการผ่าตัด และผลการศึกษารองเป็นอุบัติการณ์ของการเพิ่มระดับ hs-cTnT ในเลือด*

ผลการศึกษา: *ผู้เข้าร่วมวิจัยทั้งสิ้น 45 คน เป็นเพศหญิงร้อยละ 68.9 มีอายุโดยเฉลี่ย 66 ปี โดยการผ่าตัดส่วนใหญ่เป็นการผ่าตัดทางกระดูกและข้อ คิดเป็นร้อยละ 88.9 ทั้งนี้พบผู้ป่วยที่ได้รับการวินิจฉัยภาวะกล้ามเนื้อหัวใจขาดเลือดระหว่างและหลังการผ่าตัดทั้งสิ้น 3 ราย เป็นเพศหญิง คิดเป็นอุบัติการณ์ร้อยละ 6.7 และพบผู้ป่วยที่มีการเพิ่มระดับ hs-cTnT ในเลือดทั้งสิ้น 22 ราย คิดเป็นอุบัติการณ์ร้อยละ 48.9 นอกจากนี้ยังพบว่าค่าการกรองของไตที่ต่ำกว่าระดับ 30 มิลลิลิตรต่อนาทีต่อ 1.73 ตารางเมตร เป็นปัจจัยเสี่ยงที่สัมพันธ์กับการเกิดภาวะกล้ามเนื้อหัวใจ ขาดเลือดระหว่างและหลังการผ่าตัดอย่างมีนัยสำคัญ*

สรุป: *อุบัติการณ์ของการเกิดภาวะกล้ามเนื้อหัวใจขาดเลือดระหว่างและหลังการผ่าตัด มีค่าใกล้เคียงกับผลการศึกษาเดิมและพบว่าค่าการกรองของไตที่ต่ำกว่าระดับ 30 มิลลิลิตรต่อนาทีต่อ 1.73 ตารางเมตร เป็นปัจจัยเสี่ยงที่มีความสัมพันธ์กับการเกิดภาวะดังกล่าว*