Original Article

Can Postoperative ST-Segment Change and Blood Pressure Variability Predict Short-Term Mortality in Patients Following Major Vascular Surgery?

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Objective: To evaluate the association between the ST-segment abnormality, blood pressure variability (BPV), and short-term mortality in patients who had undergone major vascular surgery.

Materials and Methods: A prospective cohort study of 71 patients that underwent major vascular surgery between June 2011 and May 2013 at Maharaj Nakorn Chiang Mai Hospital was completed. Blood pressure was recorded for the first week after surgery, as well as electrocardiograms at baseline and for the first four post-operative days. The association between abnormality of ST-segment, BPV, and short-term mortality were analyzed.

Results: Nine (13%) patients had ST-segment change and 18 (25%) patients had BPV in the first week of post-operation. The median follow-up was 11 months. Thirteen (18%) patients died during follow-up. Post-operative ST-change was associated with a significantly increased risk of short-term mortality (hazard ratio (HR) 24.74, 95% confidence interval (CI) 6.23 to 98.27). BPV was also associated with short-term mortality (HR 4.65, 95% CI 1.31 to 16.49). In addition, the risk of stroke in patients with BPV was 20.6 times higher than those without BPV.

Conclusion: ST-change and BPV after major vascular surgery were associated with a significantly increased risk of short-term mortality.

Keywords: ST-segment change, Blood pressure variability, Major vascular surgery, Mortality

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Patients undergoing major vascular surgery are at constant risk of developing myocardial infarction. Mortality in these patients is best predicted by post-operative myocardial infarction rather than by other traditional pre-operative clinical predictors[1,2]. Making the diagnosis of silent myocardial infarction (SMI) for such patients is difficult because up to 94% occurs without signs and asymptomatically[3-5]. Electrocardiogram (ECG) remains a good screening tool to identify ischemia events of the heart[6]. ST-segment analysis accompanied by a release of cardiac enzymes have been proved to be a reliable tool in detecting SMI[7]. Recent studies in patients suffering from unstable angina show increased cardiac enzymes levels before the manifestation of myocardial infarction[8]. These results suggest that ECG and cardiac enzymes may be a useful tool to indicate ischemic myocardial damage in the post-operative period. However, the information about using ECG as part of predicting short-term mortality after vascular surgery is uncertain.

The occurrence of blood pressure fluctuations over time has been documented since the eighteenth century, but the clinical importance of this phenomenon is only now being recognized[9]. Several studies[10-12] have suggested that an increase of blood pressure variability (BPV) is associated with an increase in

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subsequent cardiovascular events/complications. This can probably be explained by increased stress on the walls of the heart and the blood vessels. Variability in blood pressure also has an important role in the progression of organ damage and in triggering of vascular events[13]. Guidelines for diagnosis and treatment focus only on underlying mean blood pressure[14]. However, these guidelines are inconsistent, and no short-term prognostic study is available for patients after major vascular surgery. The aim of the present study was to determine the short-term mortality of patients undergoing major vascular surgery with postoperative ST-segment change and BPV.

Materials and Methods

The sample size calculation was estimated based on our experience and an audit study, which is conducted by The Vascular Anaesthesia Society of Great Britain and Ireland (alpha 0.05, power 80%, hazard ratio 3.5 to 4.5, mortality 20%)[15]. After approval by the local ethics committee and written informed consent, 71 patients underwent elective major vascular surgery between June 2011 and May 2013 at the Maharaj Nakorn Chiang Mai Hospital were prospectively investigated. Exclusion criteria were digoxin/digitoxin medication, left bundle branch block, left heart hypertrophy, atrial flutter or fibrillation, preexisting ST depression in the preoperative 12-lead ECG, or cerebrovascular disease. The major vascular surgery included open abdominal aortic aneurysm repair, infrainguinal arterial bypass, carotid artery procedure, and lower extremities amputations. Demographic and health-related information was obtained through a written history and a physical examination performed preoperatively by studied personnel and reviewed of the preoperative medical record on the presence of clinical risk factors and chronic cardiac medication used with classes of antihypertensive medications. The main clinical characteristics are reported in Table 1.

Baseline preoperative ECG was performed one day before surgery. After the operation, post-operative ECG and creatine kinase-MB (CK-MB), and cardiac Troponin-T were obtained for the first four postoperative days (at 0, 24, 48, 72-hour). All patterns of ST-segment change and rising cardiac enzymes defined as post-operative ischemic complications were analyzed by the same experienced cardiologist, who was blinded as to the clinical signs.

One day before surgery, blood pressure was recorded every two hours by a nurse with a mercury sphygmomanometer. Mean blood pressure of each patient was calculated and recorded for one week, during the post-operative period, the same standardized protocol and equipment were used for measuring blood pressure. The standard deviation and coefficient of variation of systolic and diastolic blood pressure across study times were calculated to assess of BPV.

During the post-operative period, the occurrence of any cardiac symptoms was documented, and all post-operative complications were recorded. The post-operative period ended at discharge. From June 2011, a follow-up of all 71 patients survived major vascular surgery for at least 30 days was started. Details of all post-operative vascular events and deaths were recorded during follow-up. Stroke was defined as a neurological deficit with symptoms continuing for 24 hours, or leading to death with no apparent cause other than vascular. Short-term mortality and survival were determined at six months for each follow-up patients.

All data were analyzed by using a Stata version 11.0. Baseline characteristics and other continuous variable data were analyzed with t-test/Mann Whitney U test. To compare categorical data, Fisher's exact tests were used. The short-term survival was presented as Kaplan-Meier's curve. Effect of BPV on stroke was presented by risk ratio (RR) and 95% confidence interval (CI). All statistically significant data were defined as p-value less than 0.05.

Results

Seventy-one patients, including 47 men and 24 women, with a mean age of 68 years, were studied prospectively. Nine (13%) patients showed ST-segment change on ECG during the first four days after surgery, and 15 (21%) patients also had elevated CK-MB and troponin-T levels. BPV was observed in 18 (25%) patients during the first week of post operation. When evaluating possible risk factors for the development of ST-change, the presence of any underlying diseases was not significantly associated with an increased frequency of ST-change. There was a significant association in revascularization in patients who had post-operative BPV.

The median follow-up was 11 months (25^{th} to 75^{th} percentile, 1.3 to 20 months). Thirteen (18%) patients died during follow-up. Nine died from cardiac causes. The cause of non-cardiac death was complications from a stroke in one patient, secondary sepsis in two patients, and renal failure in one patient. All developing post-operative complications during the time of follow-up were recorded and are shown

Table 1. Baseline characteristics

Characteristics	ST-change on EKG, n (%)		p-value	BP variability, n (%)		p-value
	No (n=62)	Yes (n=9)		No (n=53)	Yes (n=18)	
Demographics						
Age (years), Mean±SD	67.7±11.3	69.5±12.3	0.650	70±10.4	61.8±12.2	0.008
Male	44 (70.9)	3 (33.3)	0.053	39 (73.5)	10 (55.5)	0.042
Female	18 (29.0)	6 (66.6)		14 (26.4)	8 (44.4)	
Type of surgery			0.755			0.075
AAA repair	33 (53.2)	4 (44.4)		29 (54.7)	8 (44.4)	
Infrainguinal bypass	22 (35.5)	4 (44.4)		21 (39.6)	5 (27.8)	
Carotid artery procedure	3 (4.8)	0 (0.0)		1 (1.89)	2 (1.11)	
Amputation	4 (6.6)	1 (11.1)		2 (3.77)	3 (16.7)	
Medical history						
Hypertension	48 (77.4)	6 (66.7)	0.439	41 (77.4)	13 (72.2)	0.751
Diabetes mellitus	10 (16.1)	2 (22.2)	0.643	8 (15.1)	4 (22.2)	0.485
Dyslipidemia	24 (38.7)	4 (44.4)	0.732	21 (39.6)	7 (38.9)	1.000
Chronic kidney disease	14 (22.6)	0 (0.0)	0.189	12 (22.6)	2 (11.1)	0.494
COPD	5 (8.6)	2 (22.2)	0.214	6 (11.3)	1 (5.6)	0.670
Chronic smoking	15 (24.6)	2 (22.2)	1.000	6 (11.3)	1 (5.6)	0.670
Chronic cardiac medication						
ASA	33 (53.2)	7 (77.8)	0.282	30 (56.6)	10 (55.6)	1.000
ACEI	9 (14.5)	2 (22.2)	0.622	5 (9.43)	6 (33.3)	0.025
β-blocker	11 (17.7)	6 (66.7)	0.005	9 (17.0)	8 (44.4)	0.027
Statin	41 (66.1)	4 (44.1)	0.272	34 (64.2)	11 (61.1)	1.000
Diuretic	3 (4.84)	1 (11.1)	0.426	3 (5.7)	1 (5.7)	1.000
CCB	19 (30.6)	2 (22.2)	0.716	16 (30.2)	5 (27.8)	1.000
Nitrate	4 (6.45)	2 (22.2)	0.164	2 (3.8)	4 (22.2)	0.033

BP=blood pressure; EKG=electrocardiography; SD=standard deviation; AAA=abdominal aortic aneurysm; COPD=chronic obstructive pulmonary disease; ASA=aspirin; ACEI=angiotensin-converting-enzyme inhibitor; CCB=calcium channel blockers

Table 2. Analysis of association between ST-change, BP variability, and postoperative complication

	ST-change on EKG, n (%)		p-value	BP variability, n (%)		p-value
	No	Yes		No	Yes	
Stroke	6 (9.7)	2 (2.22)	0.266	1 (1.9)	7 (38.8)	<0.001
Pneumonia	3 (4.8)	3 (3.33)	0.024	4 (7.6)	2 (11.1)	0.639
Sepsis	10 (16.1)	4 (44.4)	0.068	9 (17.0)	5 (27.8)	0.324
Rhabdomyolysis	2 (3.2)	2 (22.2)	0.076	2 (3.8)	2 (11.1)	0.265
Renal failure	6 (9.7)	2 (22.2)	0.266	5 (9.4)	3 (16.7)	0.409

BP=blood pressure; EKG=electrocardiography

in Table 2. Based on traditional diagnostic criteria of post-operative myocardial infarction from the same cardiologist, three (8%) patients receiving abdominal aortic operations, and six (18%) patients receiving infrainguinal bypass and lower extremity amputations were interpreted as myocardial infarction during the first four post-operative days. All of these patients also had significant elevated CK-MB and Troponin-T

Table 3. Hazard ratio of ST-change and BPV in 6 months mortality

Factors	HR	95% CI	p-value
ST-change	24.74	6.23 to 98.27	<0.001
BPV	4.65	1.31 to 16.49	0.017
Elevated cardiac enzyme	19.25	4.06 to 91.22	<0.001
Myocardial infarction	24.75	6.23 to 98.27	<0.001

HR=hazard ratio; CI=confidence interval; BPV=blood pressure variability

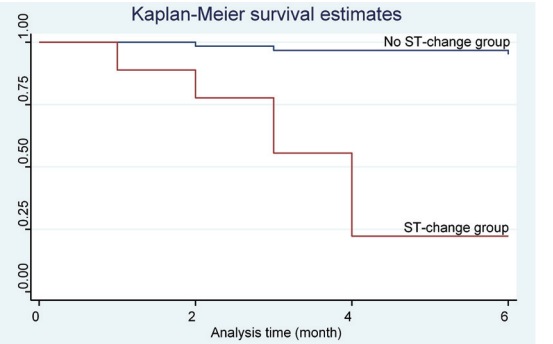

Figure 1. Kaplan-Meier survival estimates by ST-change. Upper line represented no ST-change group and lower line represented ST-change group.

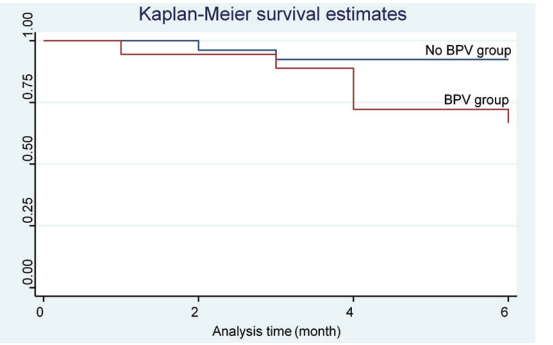

Figure 2. Kaplan-Meier survival estimates by BP variability (BPV). Upper line represented no BPV group and lower line represented BPV group.

levels. ST-change was associated with a significantly increased risk of short-term mortality in the univariable analysis, hazard ratio 24.74 (95% CI 6.23 to 98.27, p<0.001), as shown in Table 3. If analyzed in patients who only had elevated CK-MB and Troponin-T levels, there was no significant increased risk of short-term mortality. After recruitment in the present study using the Kaplan-Meier survival curve, patients' survival significantly decreased in the fourth month of follow-up (median survival time of four months), as shown in Figure 1.

BPV for each participant was defined using the standard deviation and coefficient of variation across time. The mean of the standard deviation for systolic/diastolic blood pressure was 11.7/4.3 mmHg. Eight (21%) patients had abdominal aortic operations, eight (24%) patients had infrainguinal bypass and lower extremities amputations, and two (66%) patients had carotid artery operations. BPV was less associated with short-term mortality when compared with ST-change, but had a significantly increased risk of short-term mortality with a hazard ratio of 4.65 (95% CI 1.31 to 16.49, p=0.017). BPV in post-operative patients was also strongly associated with an increased risk of stroke, RR 20.6 (95% CI 2.72 to 156.30, p=0.003). Survival of post-operative patient with BPV is shown in Figure 2.

Discussion

Post-operative myocardial infarction complications are a major healthcare challenge because of doubtful detection because of altered pain perception caused by residual anesthetics, analgesics, or incisional pain[16]. Previously, several investigations have shown that elevated levels of abnormal cardiac troponin after major vascular surgery identified patients as having increased risks of peri-operative and short-term cardiac complications[17-19]. Many studies have shown that BPV correlates closely with target-organ damage[10,11] and that the effect was independent of mean blood pressure values[20,21]. However, there were no such studies or comments about mortality in those groups of patients. Therefore, the authors designed a study on the association of ST-change, BPV, and short-term mortality.

After the same cardiologist interpreted the ST-change in the study population, the incidence of post-operative myocardial infarction occurred in more than 13% of the patients who underwent successful major vascular surgery, mostly without any signs and symptoms. A median follow-up at 11 months found that patients who had developed post-operative ST-change were 24.7 times more likely to die within six months of surgery compared with patients without ST-change. The strong association between ST-change and short-term mortality suggested that clinically meaningful post-operative ischemia may have been missed in a significant number of vascular surgery patients. Thus, routine post-operative ECG monitoring and cardiac enzymes surveillance may alert clinicians to patients at

high-risk for cardiovascular complications and death before the occurrence of a morbid and mortality event.

BPV for each participant was defined using the standard deviation and coefficient of variation across visits. Mortality was assessed through May 31, 2013 (median follow-up 11 months; n=6 deaths). Higher levels of short-term (one-week) variability in systolic blood pressure were associated with increased mortality over the six months follow-up with a hazard ratio of 4.65 (95% CI 1.31 to 16.49). Data suggested that BPV for post-operative major vascular surgery patients may have some utility and may help predict the short-term mortality rate. The authors had known the importance of BPV, rather than pressure alone, as a warning prognostic for stroke. Stroke was defined as a neurological deficit with symptoms continuing more than 24 hours, or leading to death with no apparent cause other than vascular. Effect of BPV on stroke events in post-operative major vascular surgery in the presented had a significantly high-RR of 20.6 (95% CI 12.72 to 156.30). The findings from the present suggested that such variability was associated with increased mortality and stroke events in post-operative vascular surgery patients.

There are some limitations to this study. First, the intermitted blood pressure measurement (every two hours) by a non-invasive method did not allow for the fastest or shortest blood pressure changes to be measured[22]. Second, the mortality study in the death population included a number of non-cardiovascular deaths. These limited the power of the study to statistically demonstrate the relationship between the study phenomena under investigation and fatal cardiovascular events. However, the results on the importance of erratic blood pressure variability for the risk of stroke were reflected by those post-operative patients who developed BPV, of which the number was 20.6 times higher than normal post-operative patients. Lastly, the sample size of the presented was small (large CI). Additional large research is needed to confirm these results, identify the putative mechanisms involved in this association, and evaluate approaches to reduce variability in blood pressure and its clinical sequelae.

Conclusion

Developing of ST-change and BPV after major vascular surgery were associated with a significantly increased risk of short-term (6-months) mortality. Moreover, post-operative BPV provided important prognostic information on stroke events. Routine post-operative ECG surveillance and consideration of BPV was useful for identifying patients who had increased risk for morbidity and mortality. Further research is needed to determine whether the intervention could improve the outcome for post-operative major vascular patients with ST-change and BPV.

What is already known on this topic?

ECG and cardiac enzymes may be a useful tool to indicate ischemic myocardial damage in the post-operative period. In addition, an increase in BPV is associated with an increase in subsequent cardiovascular events/complications. However, the information about using ECG as part of predicting short-term mortality after vascular surgery is uncertain.

What this study adds?

ST-change and BPV after major vascular surgery were associated with a significantly increased risk of short-term mortality and BPV also provided important prognostic information on stroke events.

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Conflicts of interest

The authors declare no conflict of interest.

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