J Korean Surg Soc 2013;84:178-184
http://dx.doi.org/10.4174/jkss.2013.84.3.178

JKSS
Journal of the Korean Surgical Society

pISSN 2233-7903 · eISSN 2093-0488

ORIGINAL ARTICLE

Cardiac risk factors of revascularization in chronic atherosclerotic lower extremity ischemia

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Purpose: To identify the risk factors of major adverse cardiac event (MACE) in patients with chronic atherosclerotic lower extremity ischemia (CALEI) undergoing revascularization without noninvasive stress testing (NIST). **Methods:** From January 2007 to January 2012, patients with CALEI who underwent revascularization were retrospectively reviewed. Emergent operations, revision procedures for previous surgery, or patients with active cardiac conditions were excluded. NIST was not performed for patients without active cardiac conditions. Cardiac risk was categorized into low, intermediate and high risk, according to the Lee's revised cardiac risk index. MACE was defined as acute myocardial infarction or any cardiac death within 30 days after surgery. **Results:** A total of 459 patients underwent elective lower extremity revascularization procedures (240 open surgeries, 128 endovascular procedures, and 91 hybrid surgeries). The treated lesions comprised of 18% aorto-iliac, 58% infrainguinal, and 24% combined lesions. With regard to cardiac risk, low-, intermediate- and high risks were 67%, 32% and 2%, respectively. MACE was developed in 7 patients (2%). High or intermediate risk group by the Lee's index was related to postoperative MACE. Subgroup analysis for open surgery or hybrid surgery group identified female gender as an independent risk factor of MACE (P = 0.049; odds ratio, 5.168; confidence interval, 1.011 to 26.423). **Conclusion:** The Lee's index was a useful predictor of MACE. MACE is more common in female patients than male patients after open or hybrid surgery. Routine preoperative NIST is not suggested for all patients undergoing revascularization for CALEI, especially for those in the low risk group.

Key Words: Peripheral arterial disease, Postoperative complications, Myocardial infarction, Risk factors

INTRODUCTION

Cardiac complications are important causes of morbidity and mortality in vascular surgery, and the reported rate of cardiac morbidity is often greater than 5% [1]. For these reasons, preoperative cardiac risk evaluation is an important part of vascular surgery. The American College of Cardiology (ACC) and the American Heart Association (AHA) introduced guidelines to detect and manage perioperative cardiac risk and to prevent cardiac complications after vascular surgery [2]. For preoperative noninvasive stress testing (NIST), the guidelines recommended that patients with active cardiac conditions (Table 1) should be evaluated and treated (class I). Patients who do not have

Received September 18, 2012, Revised December 17, 2012, Accepted January 6, 2013

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active cardiac conditions are stratified into 3 groups by the Lee's revised cardiac risk index (Table 2) [3]. NIST may be considered for patients with high (class IIa) or intermediate (class IIb) risk, if it will change management.

However, in practice, NIST is sometimes performed without considering patient conditions. This study was aimed to identify the risk factors of postoperative major adverse cardiac event (MACE) when NIST is not performed before revascularization in chronic atherosclerotic lower extremity ischemia (CALEI).

METHODS

Patients

From January 2007 to January 2012, all patients with CALEI who underwent revascularization procedures in Daegu Catholic University Medical Center were retrospectively reviewed. Excluding emergent or urgent operations, nonatherosclerotic etiology, revision procedures for previous vascular or endovascular surgery or active cardiac conditions, 459 patients were enrolled in this study.

Patient demographic data, coexisting disease and treatment factors including procedure type (open surgery, endovascular treatment, and hybrid surgery), treated lesions and operation time were investigated. According to the Lee's index, patients were categorized into 3 groups (low-, intermediate-, and high-risk group).

Preoperative cardiac evaluation

First, careful history taking was done to identify prior angina pectoris or myocardiac infarction, heart failure, arrhythmia and valvular heart disease. Physical examination, routine blood test, electrocardiography (ECG), chest X-ray and echocardiography were performed routinely. However, NIST (e.g., exercise ECG, adenosine MIBI scan and so on) or coronary angiography was not part of the routine examination. The only indication of NIST or coronary angiography was active cardiac conditions.

Table 2. The Lee's revised cardiac risk index categorizes the risk of cardiac events in patients undergoing surgery

Risk factors, No.[a]	Risk category
0	Low
1–2	Intermediate
≥3	High

[a]The Lee's index uses six criteria: high-risk surgery, ischemic heart disease, congestive heart failure, cerebrovascular disease, insulin- dependent diabetes mellitus, and renal failure [3].

Table 1. Active cardiac conditions

Condition	Example
Unstable coronary syndromes	Unstable or severe angina[a] (CCS class III or IV)[b] Recent MI[c]
Decompensated HF (NYHA functional class IV; worsening or new-onset HF)	
Significant arrhythmias	High-grade atrioventricular block Mobitz II atrioventricular block Third-degree atrioventricular heart block symptomatic ventricular arrhythmias supra ventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR greater than 100 beats per minute at rest) symptomatic bradycardia Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient greater than 40 mmHg, aortic valve area less than 1.0 cm^2, or symptomatic) Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

CCS, Canadian Cardiovascular Society; MI, myocardial infarction; HF, heart failure; NYHA, New York Heart Association; HR, heart rate.
[a]According to Campeau [4]. [b]May include "stable" angina in patients who are unusually sedentary. [c]The American College of Cardiology National Database Library defines recent MI as more than 7 days but less than or equal to 1 month (within 30 days).

Definitions and outcome assessment

Acute myocardiac infarction (AMI) was defined as the presence of 2 or more of the following 3 criteria: 1) typical chest pain, 2) elevated cardiac enzyme, and 3) typical change in serial ECG. MACE was defined as AMI or any cardiac death after treatment. Primary outcome was MACE occurring within 30 days after treatment.

Statistics

To identify the independent risk factors of MACE, univariate and multivariate analyses were performed using the SPSS ver. 12.0.1 (SPSS Inc., Chicago, IL, USA). The association between categorical clinical variables and MACE was analyzed by the chi-square test or Fisher exact test. Binary logistic regression model was used for multivariate analysis. P-value < 0.05 was considered statistically significant.

Table 3. Patient characteristics (n = 459)

Variable	Value
Age (yr)	69 (42–93)
Gender (male)	381 (83)
Indication, critical limb ischemia	
Claudication	275 (60)
Rest pain	40 (9)
Ischemic tissue loss	144 (31)
Smoking	239 (52)
Hypertension	288 (63)
Diabetes	180 (39)
Insulin-dependent	33 (7)
Chronic renal insufficiency (Cr > 2 mg/dL)	24 (5)
Ischemic heart disease	49 (11)
Prior cerebrovascular disease	75 (16)
Prior congestive heart failure	15 (3)
Left ventricular wall motion abnormality	54 (12)
Left ventricular ejection fraction (<50%)	18 (4)
Lee's revised cardiac risk index	
Low	303 (66)
Intermediate	147 (32)
High	9 (2)

Values are presented as mean (range) or number (%).

Table 4. Treatment details

Variable	Value
Operation time (min)	181 (30–620)
Anesthesia	
General	121 (26)
Regional	338 (74)
Treated lesions	
Aorto-iliac	113 (25)
Aorto-iliac + infrainguinal	91 (20)
Infrainguinal	255 (56)
Treatment types	
Open surgery	240 (52)
Endovascular treatment	128 (28)
Hybrid surgery	91 (20)

Values are presented as mean (range) or number (%).

RESULTS

A total of 459 patients underwent elective lower ex-

Table 5. Univariate analysis

Variable	MACE (-) (n = 452)	MACE (+) (n = 7)	P-value
Age (>70 yr)	205 (45)	5 (71)	0.255
Gender (female)	74 (16)	4 (57)	0.018
Indication, critical limb ischemia	179 (40)	5 (71)	0.122
Smoking	236 (52)	3 (43)	0.715
Hypertension	284 (63)	4 (57)	0.715
Diabetes	177 (39)	3 (43)	1.000
Cr (>2 mg/dL)	24 (5)	0 (0)	1.000
Ischemic heart disease	46 (10)	3 (43)	0.029
Prior cerebrovascular disease	72 (16)	3 (43)	0.090
Prior congestive heart failure	13 (3)	2 (29)	0.019
Left ventricular wall motion abnormality	51 (11)	3 (43)	0.038
Left ventricular ejection fraction (<50%)	16 (4)	2 (29)	0.027
High or intermediate risk[a)]	151 (33)	5 (71)	0.048
Operation time (hr)			0.397
<4	330 (73)	4 (57)	
≥4	122 (27)	3 (43)	
Anesthesia			0.082
General	117 (26)	4 (57)	
Regional	335 (74)	3 (43)	
Treated lesions			0.769
Aorto-iliac	112 (25)	1 (14)	
Aorto-iliac + infrainguinal	89 (20)	2 (29)	
Infrainguinal	251 (56)	4 (57)	
Treatment types			0.136
Open	234 (52)	6 (86)	
Hybrid	90 (20)	1 (14)	
Endo	128 (28)	0 (0)	

Values are presented as number (%).
MACE, major adverse cardiac event.
[a)]According to the Lee's revised cardiac risk index.

tremity revascularization procedures for CALEI during the study period. The mean age of patients was 69 years (range, 42 to 93 years) and 83% was male. Forty percent of patients had critical limb ischemia. Regarding the Lee's index, 67% of patients were at low risk, 32% intermediate risk, and 2% high risk. Other patient demographic data are shown in Table 3.

Table 6. Multivariate analysis

Variable	P-value	OR	CI
Female	0.066	4.426	0.907–21.694
Ischemic heart disease	0.0446	2.032	0.328–12.569
Prior congestive heart failure	0.146	4.425	0.597–32.814
Left ventricular wall motion abnormality	0.359	2.346	0.379–14.511
Left ventricular ejection fraction (<50%)	0.230	3.409	0.461–25.223

OR, odds ratio; CI, confidence interval.

Table 7. Univariate analysis, subgroup analysis

Variable	MACE (−) (n = 324)	MACE (+) (n = 7)	P-value
Age (>70 yr)	154 (48)	5 (71)	0.255
Gender (female)	46 (14)	5 (71)	0.018
Indication, critical limb ischemia	134 (41)	5 (71)	0.122
Smoking	176 (54)	3 (43)	0.715
Hypertension	197 (61)	4 (57)	0.715
Diabetes	110 (34)	3 (43)	1.000
Cr (>2 mg/dL)	14 (4)	0 (0)	1.000
Ischemic heart disease	31 (10)	3 (43)	0.029
Prior cerebrovascular disease	47 (15)	3 (43)	0.090
Prior congestive heart failure	10 (3)	2 (29)	0.019
Left ventricular wall motion abnormality	34 (11)	3 (43)	0.038
Left ventricular ejection fraction (<50%)	11 (3)	2 (29)	0.027
High or intermediate risk[a]	105 (32)	5 (71)	0.043
Operation time (hr)			0.397
<4	226 (64)	4 (57)	
≥4	118 (36)	3 (43)	
Anesthesia			0.082
General	98 (30)	4 (57)	
Regional	226 (70)	3 (43)	
Treated lesions			0.769
Aorto-iliac	57 (18)	1 (14)	
Aorto-iliac + infrainguinal	78 (24)	2 (29)	
Infrainguinal	189 (58)	4 (57)	
Treatment types			0.136
Open	234 (72)	6 (86)	
Hybrid	90 (28)	1 (14)	

Values are presented as number (%).
MACE, major adverse cardiac event.
[a]According to the Lee's revised cardiac risk index.

All procedures were done by two vascular surgeons. Treatment details are summarized in Table 4. The mean operation time was 181 minutes. The treated lesions comprised of 18% aorto-iliac, 58% infrainguinal, and 24% combined lesions. Fifty-two percent of the cases were open surgery, 28% were endovascular treatment and 20% were hybrid surgery.

Seven patients (1.5%) had a MACE. AMI developed in 6 patients. There were 5 cardiac deaths due to AMI (4 patients) and congestive heart failure (1 patient). All MACE occurred in patients who underwent open or hybrid surgery (2.1%, 7/331). There was no MACE in the endovascular treatment group.

On univariate analysis, female gender, ischemic heart disease, congestive heart failure, ejection fraction <50%, left ventricular wall motion abnormality in echocardiography, intermediate or high risk by the Lee's index showed association with MACE (Table 5). However, no independent risk factors of postoperative MACE were determined by the binary logistic regression model (Table 6).

Subgroup analysis was done excluding the endovascular treatment group that had no MACE (Tables 7, 8). Female gender was identified as an independent risk factor of postoperative MACE (P = 0.049; odds ratio [OR], 5.168; confidence interval [CI], 1.011 to 26.423) besides the Lee's index.

DISCUSSION

Peripheral arterial disease (PAD) is one of the clinical

Table 8. Multivariate analysis, subgroup analysis

Variable	P-value	OR	CI
Female	0.049	5.168	1.011–26.423
Ischemic heart disease	0.506	1.943	0.274–13.786
Prior congestive heart failure	0.124	4.963	0.645–38.716
Left ventricular wall motion abnormality	0.575	1.867	0.210–16.577
Left ventricular ejection fraction (<50%)	0.204	4.558	0.210–16.577

OR, odds ratio; CI, confidence interval.

manifestations of systemic atherosclerosis. Therefore, a significant portion of PAD patients have coexisting or subclinical coronary artery disease (CAD). In a multicenter, cross-sectional PAD detecting program in the United States (US), the prevalence of CAD in PAD patients was 52.9% [5]. In the Reduction of Atherothrombosis for Continued Health Registry, 51.6% of PAD patients had a concomitant CAD [6]. This means that modification of atherosclerotic risk factors is important in the long term and perioperative cardiovascular risk is high in the short term.

In the US, the ACC/AHA guidelines for perioperative cardiovascular evaluation for noncardiac surgery were first introduced in 1996 and updated two times in 2002 and 2007 [2,7,8]. One of the changes was the role of NIST. In 1996, a reversible defect on NIST was considered a predictor of postoperative MACE, and CAG with possible revascularization was recommended. However, the 2002 guidelines announced that indications of preoperative PCI for noncardiac surgery are similar to those of PCI in general because there were no controlled trials comparing perioperative cardiac outcomes for patients treated with preoperative PCI versus medical therapy.

The second multicenter Dutch Echoardiographic Cardiac Risk Evaluation study assessed the value of NIST in intermediate risk patients [9]. All patients received beta-blockers to achieve a resting heart rate of 60 to 65 beats/min. There was no difference between the no NIST group and NIST group in cardiac death or MI at 30-days after surgery (1.8% vs. 2.3%, P = 0.62). In 2004, the Coronary Artery Revascularization Prophylaxis trial was published [10]. The study randomly assigned 510 patients scheduled for vascular surgery into the following two groups: coronary artery revascularization before surgery versus no revascularization before surgery. The rate of postoperative MI, defined by the elevated troponin level, was not different (12% vs. 14%, P = 0.37). Regarding the long-term outcome, mortality rate was not different at 2.7 years after randomization, (22% vs. 23%, P = 0.92).

In the revised ACC/AHA 2007 guidelines [2] based on the above mentioned trials, the only class I recommendations of NIST are active cardiac conditions (unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease). Moreover, coronary revascularization is no longer recommended before surgery for patients with stable CAD. The European Society of Cardiology guidelines [11] have been recently published and they are not different to the ACC/AHA guidelines.

Our policy is not different from the guidelines. NIST or CAG are considered only for patients with active cardiac conditions. In our recent retrospective review of 459 patients who underwent revascularization for CALEI without preoperative NIST, 66% were at low risk, 32% at intermediate risk and 2% at high risk. MACE was 1.5% which was not higher than previous reports. Because high risk group was only 2%, it is assumed that routine NIST is not necessary at least for intermediate and low risk patients. There was no MACE after endovascular treatment. Multivariate analysis failed to identify the risk factors of postoperative MACE. Subgroup analysis of the open or hybrid surgery group showed that female gender was the only significant risk factor of MACE after surgery (P = 0.049; OR, 5.168; CI, 1.011 to 26.423).

In this study, the intermediate or high risk group was related to postoperative MACE by univariate analysis. Although the Lee's index has been widely used to assess perioperative cardiac risk since its first introduction in 1999, it still has some limitations. Ford et al. [12] conducted a meta-analysis of 24 studies that reported the association of the Lee's index with MACE or death in the hospital or within 30 days of surgery. In their systemic review, the Lee's index discriminated moderately well between patients at low versus high risk for cardiac events after mixed noncardiac surgery. However, its performance was considerably diminished when it was used in patients who underwent vascular noncardiac surgery. They emphasized the necessity of high-quality research in perioperative medicine.

For these reasons, many researchers are trying to find predictors of perioperative cardiac complications. Welten et al. [13] pointed out a limitation of the Lee's index. They claimed that the Lee's index does not include patient age. They announced that the prognostic value of the Lee's index was reduced in elderly patients (>75 years), based on the retrospective analysis of 2,642 patients who had under-

gone vascular surgery. They suggested that the revised risk of operation (low, low-intermediate, high-intermediate and high-risk procedures) and hypertension could improve the prediction of MACE as well as age.

The Vascular Study Group of New England (VSGNE) proposed a new cardiac risk prediction model specifically for vascular surgery patients [14]. Besides the 6 risk factors of the Lee's index, the VSGNE model included additional risk factors of increasing age, smoking, chronic obstructive pulmonary disease, abnormal preoperative cardiac stress test, and long-term beta-blocker treatment. The authors reported that the Lee's index underestimated in-hospital cardiac events in patients undergoing vascular surgery and their new index was more accurate than the Lee's index in predicting postoperative cardiac events.

Based on our results, the Lee's index was a significant predictor of postoperative MACE and female patients have a higher risk of MACE than male patients after open or hybrid surgery. Routine preoperative NIST is not necessary in all patients undergoing revascularization for CALEI, especially for patients in the low risk group and for those undergoing endovascular treatment.

Besides the small number of high risk patients, our study has several limitations. The most important one is the retrospective design of the study. Also, we did not include a treatment group who underwent NIST. Therefore, it is impossible to compare no NIST group and the NIST group. However, we think that this study has significance as a large observational study of patients with CALEI in Korea.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. L'Italien GJ, Cambria RP, Cutler BS, Leppo JA, Paul SD, Brewster DC, et al. Comparative early and late cardiac morbidity among patients requiring different vascular surgery procedures. J Vasc Surg 1995;21:935-44.
2. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. J Am Coll Cardiol 2007;50:1707-32.
3. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043-9.
4. Campeau L. Letter: grading of angina pectoris. Circulation 1976;54:522-3.
5. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286:1317-24.
6. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA 2006;295:180-9.
7. Eagle KA, Brundage BH, Chaitman BR, Ewy GA, Fleisher LA, Hertzer NR, et al. Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). J Am Coll Cardiol 1996;27:910-48.
8. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). J Am Coll Cardiol 2002;39:542-53.
9. Poldermans D, Bax JJ, Schouten O, Neskovic AN, Paelinck B, Rocci G, et al. Should major vascular surgery be delayed because of preoperative cardiac testing in intermediate-risk patients receiving beta-blocker therapy with tight heart rate control? J Am Coll Cardiol 2006;48:964-9.
10. McFalls EO, Ward HB, Moritz TE, Goldman S, Krupski WC, Littooy F, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med 2004;351:2795-804.
11. Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Sur-

gery; European Society of Cardiology (ESC), Poldermans D, Bax JJ, Boersma E, De Hert S, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. Eur Heart J 2009;30:2769-812.
12. Ford MK, Beattie WS, Wijeysundera DN. Systematic review: prediction of perioperative cardiac complications and mortality by the revised cardiac risk index. Ann Intern Med 2010;152:26-35.
13. Welten GM, Schouten O, van Domburg RT, Feringa HH, Hoeks SE, Dunkelgrun M, et al. The influence of aging on the prognostic value of the revised cardiac risk index for postoperative cardiac complications in vascular surgery patients. Eur J Vasc Endovasc Surg 2007;34:632-8.
14. Bertges DJ, Goodney PP, Zhao Y, Schanzer A, Nolan BW, Likosky DS, et al. The Vascular Study Group of New England Cardiac Risk Index (VSG-CRI) predicts cardiac complications more accurately than the Revised Cardiac Risk Index in vascular surgery patients. J Vasc Surg 2010;52:674-83.e3.