Prediction of major cardiac events after vascular surgery

Danielle M. Gualandro, MD, PhD,[a] Christian Puelacher, MD,[b] Giovanna LuratiBuse, MD,[c,d] Gisela B. Llobet, MD,[a] Pai C. Yu, MD, PhD,[a] Francisco A. Cardozo, MD,[a] Noemi Glarner, MSc,[b] Andres Zimmerli, MD,[b] Jaqueline Espinola, MD,[e] Sydney Corbière, MD,[b] Daniela Calderaro, MD, PhD,[a] Andre C. Marques, MD, PhD,[a] Ivan B. Casella, MD, PhD,[f] Nelson de Luccia, MD,[f] Mucio T. Oliveira, MD, PhD,[g] Andreas Lampart, MD,[c] Daniel Bolliger, MD,[c] Luzius Steiner, MD,[c] Manfred Seeberger, MD,[h] Christoph Kindler, MD,[e] Stefan Osswald, MD,[b] Lorenz Gürke, MD,[i] Bruno Caramelli, MD,[a] *and* Christian Mueller, MD,[b] on behalf of the GREAT network, *São Paulo, Brazil; Basel, Aarau, and Zurich, Switzerland; and Düsseldorf, Germany*

ABSTRACT

Objective: Predicting cardiac events is essential to provide patients with the best medical care and to assess the risk-benefit ratio of surgical procedures. The aim of our study was to evaluate the performance of the Revised Cardiac Risk Index (Lee) and the Vascular Study Group of New England Cardiac Risk Index (VSG) scores for the prediction of major cardiac events in unselected patients undergoing arterial surgery and to determine whether the inclusion of additional risk factors improved their accuracy.

Methods: The study prospectively enrolled 954 consecutive patients undergoing arterial vascular surgery, and the Lee and VSG scores were calculated. Receiver operating characteristic curves for each cardiac risk score were constructed and the areas under the curve (AUCs) compared. Two logistic regression models were done to determine new variables related to the occurrence of major cardiac events (myocardial infarction, heart failure, arrhythmias, and cardiac arrest).

Results: Cardiac events occurred in 120 (12.6%) patients. Both scores underestimated the rate of cardiac events across all risk strata. The VSG score had AUC of 0.63 (95% confidence interval [CI], 0.58-0.68), which was higher than the AUC of the Lee score (0.58; 95% CI, 0.52-0.63; $P = .03$). Addition of preoperative anemia significantly improved the accuracy of the Lee score to an AUC of 0.61 (95% CI, 0.58-0.67; $P = .002$) but not that of the VSG score.

Conclusions: The Lee and VSG scores have low accuracy and underestimate the risk of major perioperative cardiac events in unselected patients undergoing vascular surgery. The Lee score's accuracy can be increased by adding preoperative anemia. Underestimation of major cardiac complications may lead to incorrect risk-benefit assessments regarding the planned operation. (J Vasc Surg 2017;66:1826-35.)

More than 300 million major surgeries are performed annually worldwide.[1] Patients submitted to arterial vascular surgery have an especially high risk of cardiac complications because of a high concomitant prevalence of atherosclerosis.[2,3] Cardiac events including myocardial infarction (MI), acute heart failure (AHF), and major arrhythmias after vascular surgery are a major concern for physicians and patients as they are associated with an increase in mortality, length of stay, and cost.[4,5] Therefore, predicting cardiac events is essential to provide patients with the best medical care and also to assess the risk-benefit ratio of surgical procedures.

From the Interdisciplinary Medicine in Cardiology Unit, Cardiology Department,[a] and Emergency Department,[g] Heart Institute (InCor), and Vascular and Endovascular Surgery Division, Clinics Hospital,[f] University of São Paulo Medical School, São Paulo; the Department of Cardiology,[b] Department of Anesthesiology,[c] and Department of Vascular Surgery,[i] University Hospital Basel, Basel; the Department of Anesthesiology, University Hospital Düsseldorf, Düsseldorf[d]; the Department of Anesthesiology, Kantonsspital Aarau, Aarau[e]; and the Department of Anesthesiology, Clinic Hirslanden, Zurich.[h]

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Correspondence: Danielle M. Gualandro, MD, PhD, Interdisciplinary Medicine in Cardiology Unit, Cardiology Department, Heart Institute (InCor), University of São Paulo Medical School, Av Dr Eneas de Carvalho Aguiar, 44 São Paulo, SP 05403-000, Brazil (e-mail: danielle.gualandro@incor.usp.br).

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Although the use of clinical risk scores to predict postoperative cardiac events is recommended by most guidelines,[6-8] there is no specific recommendation for patients undergoing arterial vascular surgery. The Revised Cardiac Risk Index, developed by Lee et al (Lee score),[9] is widely used to estimate cardiac risk for different procedures but may underestimate risk in patients submitted to arterial vascular surgery.[10] The Vascular Study Group of New England Cardiac Risk Index (VSG) is a dedicated score to predict cardiac risk in patients submitted to vascular surgery, specifically developed for this population.[11] The Lee and VSG scores were developed in selected populations (ie, undergoing elective surgery and specific types of procedures). Their accuracy in real-world unselected patients undergoing vascular surgery is largely unknown.

The aim of our study was to evaluate the performance of the Lee and VSG scores for the prediction of major cardiac events in unselected patients undergoing arterial surgery. Our secondary aim was to determine whether the inclusion of additional risk factors improves their accuracy.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of prospectively collected multicenter registry data.
- **Take Home Message:** Risk stratification for cardiac events after arterial vascular surgery was underestimated by both the Revised Cardiac Risk Index and the Vascular Study Group of New England Cardiac Risk Index. Using receiver operating characteristic curves, the area under the curve was 0.63 for the Vascular Study Group and 0.58 for the Revised Cardiac Risk Index. The addition of preoperative anemia to the Revised Cardiac Risk Index increased the area under the curve to 0.61.
- **Recommendation:** This study suggests that commonly used cardiac risk indices for arterial vascular surgery underestimate the risk of cardiac events.

METHODS

Study design and overview. The Global Research on Acute Conditions Team (GREAT) Perioperative Initiative is an ongoing prospective international collaboration aiming to improve cardiovascular perioperative care. For this analysis, individual patient data from two prospective cohorts were pooled. From September 2012 to March 2016, we included consecutive patients undergoing arterial vascular surgery at the Clinics Hospital, University of São Paulo Medical School, Brazil, for whom a preoperative cardiologic consultation was requested. In São Paulo, there is a special routine for patients undergoing arterial surgery in which patients are systematically seen by cardiologists before surgery. From October 2014 until October 2015, consecutive patients undergoing vascular surgery at Basel University Hospital, Switzerland, were included. The University Hospital of Basel has implemented a perioperative troponin screening in clinical routine since October 2014 in patients at high perioperative cardiovascular risk undergoing major noncardiac surgery. All screened patients are registered in a dedicated prospective database. The protocol was approved by the local ethics committees, and informed consent was not required.

Patients. We included patients undergoing all vascular arterial surgeries: open or endovascular (for aorta, peripheral artery, visceral artery, and carotid artery diseases and amputations due to limb ischemia), emergent, urgent, or elective. Patients who were not submitted to arterial surgery or patients who underwent renal transplantation were excluded (Supplementary Fig, online only).

Preoperative assessment and scores. Patients were submitted to clinical evaluation, and the Lee[9] and VSG[11] scores were applied (Figs 1 and 2). The Lee score is routinely used for preoperative evaluation in clinical practice and was taken into account by the attending physician to guide perioperative management according to local guidelines.[6,8] Preoperative additional cardiac tests were done at the discretion of the attending physician, following local guidelines.[6,8]

Previous coronary artery disease (CAD) was considered if the patient had history of MI, angina pectoris, or myocardial revascularization (coronary artery bypass graft surgery or percutaneous coronary intervention) or evidence of CAD on myocardial perfusion imaging (presence of fixed or reversible perfusion defects) or coronary angiography. Preoperative chronic heart failure (CHF) was considered if there were clinical symptoms consistent with CHF regardless of left ventricular ejection fraction (LVEF), LVEF <50% assessed by echocardiography, or LVEF <45% assessed by gated single-photon emission computed tomography obtained during myocardial perfusion imaging. In cases with diagnostic uncertainty, B-type natriuretic peptide (BNP) or N-terminal proBNP levels were used if available. In patients with CHF diagnosis, New York Heart Association functional class was obtained by cardiologists. Smoking status included current and former smokers. Anemia was diagnosed according to World Health Organization criteria as hemoglobin levels <12 g/dL for women and <13 g/dL for men.[12]

Perioperative surveillance. Perioperative surveillance included serial measurements of high-sensitivity cardiac troponin T (hs-cTnT; Roche Diagnostics, Indianapolis, Ind) once daily up to the second or third day after surgery and 12-lead electrocardiography daily in São Paulo and in

- ✓ High-risk surgery (intra-thoracic, intra-peritoneal or suprainguinal vascular surgery)
- ✓ Coronary artery disease
- ✓ Chronic heart failure
- ✓ Cerebrovascular disease
- ✓ Diabetes on insulin
- ✓ Creatinine levels > 2.0mg/dL

Class	Points	Predicted Cardiac Events (%)
I	0	0.4
II	1	0.9
III	2	6.6
IV	≥ 3	11

Fig 1. Revised Cardiac Risk Index by Lee.

Age ≥ 80 anos	4 pts	Creatinine > 1.8 mg/dL	2 pts
Age 70-79 anos	3 pts	Current or previous smoking	1 pt
Age 60-69 anos	2 pts	Diabetes on insulin	1 pt
Coronary artery disease	2 pts	Chronic use of β-blockers	1 pt
Chronic heart failure	2 pts	Previous CABG or PCI	-1pt
COPD	2 pts		

Points	Predicted Cardiac Events (%)
0 – 3	2.6
4	3.5
5	6
6	6.6
7	8.9
≥8	14.3

Fig 2. Vascular Study Group of New England Cardiac Risk Index (VSG). *CABG,* Coronary artery bypass graft surgery; *COPD,* chronic obstructive pulmonary disease; *PCI,* percutaneous coronary intervention; *pts,* points.

case of hs-cTnT elevations in Basel. Additional electrocardiography and hs-cTnT measurements were performed whenever clinically indicated. The hs-cTnT was selected because of its improved diagnostic accuracy compared with other less sensitive cardiac troponin assays in the diagnosis of MI.[13] Patients were followed up until hospital discharge.

Clinical end points. The primary end point was a composite of cardiac events, including perioperative MI, AHF, clinically relevant arrhythmias, and cardiac arrest until hospital discharge. All end points were adjudicated by two cardiologists. MI was diagnosed according to the third universal definition of MI.[14] AHF was diagnosed by the attending physician, clinical symptoms, physical examination findings, chest radiography, BNP or N-terminal proBNP blood concentrations, and echocardiography.[15] Arrhythmias (atrial fibrillation or flutter, supraventricular tachycardia, ventricular tachycardia) were considered clinically significant if requiring drug therapy or electrical cardioversion. We chose this combined end point because it is the same end point used in the derivation of the Lee and VSG scores.[9,11]

Statistical analysis. Categorical variables are presented as frequencies (percentages) and were compared by χ^2 test or Fisher test, as appropriate. Numerical variables are reported as medians and interquartile range and were compared by Mann-Whitney test. We evaluated the incidence of the combined end point in each category of each cardiac risk score. Confidence intervals (CIs) for incidence of the end point were calculated using the standard formula.

For our primary analysis, comparison of the risk scores, receiver operating characteristic (ROC) curves for each cardiac risk score were constructed and the areas under the curve (AUCs) compared by the method of DeLong.[16] CIs were constructed using bootstrap. Sensitivity analysis for the AUC of both scores was done by excluding patients undergoing emergency or urgent surgeries. A post hoc subgroup analysis of patients undergoing open or endovascular procedures was also performed.

For our secondary analysis, to determine new variables independently related to the occurrence of cardiac events after surgery, two binary logistic regression models for each score were created including the scores and variables preselected by literature research (urgency, anemia, preoperative medication use).[6-9,11,17-21] As power estimation for our regression analysis, we chose to include a maximum number of covariables of 1 variable per 10 events.[22] The same variables were included in both models, except for variables that were already part of the respective score, such as type of surgery in the Lee score or smoking status in the VSG score. Variables with a *P* value <.05 were then added to the scores, and ROC curves of the scores including the new variables were constructed. AUCs of the modified scores and of the original scores were compared.

P values of <.05 were considered to indicate statistical significance. Analyses were performed using SPSS 22 (IBM, Armonk, NY) and R software (version 3.1.3, pROC).[23]

RESULTS

There were 1226 patients evaluated, and 272 were excluded (Supplementary Fig, online only). Baseline characteristics and outcome of patients divided by hospital are shown in Table I. Baseline characteristics of 954 patients included with and without a cardiac event are shown in Table II. About one-third of patients underwent aortic aneurysm repair, one-third lower extremity bypass or angioplasty, and one-fourth carotid procedures (Table III). Overall, 71% of patients underwent elective surgery, 24% urgent, and 5% emergent (within 1 day).

The primary end point of major cardiac events occurred in 120 (12.6%) patients. MI occurred in 66 (6.9%) patients, AHF in 46 (4.8%), clinically relevant arrhythmias in 24 (2.5%), and cardiac arrest in 13 (1.4%). The primary end point and MI incidence according to type of surgery are shown in Table III.

Table I. Baseline characteristics and outcome divided by hospital

	All patients (N = 954)	São Paulo cohort (n = 743)	Basel cohort (n = 211)	*P* value
Male gender	687 (72)	540 (73)	147 (70)	.39
Age, years, median (IQR)	70 (63-76)	68 (62-75)	74 (68-79)	<.001
Diabetes	324 (34)	261 (35)	63 (30)	.15
Insulin	111 (12)	82 (11)	29 (14)	.28
Hypertension	795 (83)	627 (84)	168 (80)	.10
Active or former smoker	725 (76)	564 (76)	161 (76)	.90
CAD	377 (40)	286 (39)	91 (43)	.22
CABG or PCI	175 (18)	138 (19)	37 (18)	.73
PAD	954 (100)	743 (100)	211 (100)	—
CHF	154 (16)	128 (17)	26 (12)	.09
NYHA FC ≥II[a]	54 (6)	54 (7)	NA	
History of stroke or TIA	232 (24)	195 (26)	37 (18)	<.001
COPD	90 (9)	51 (7)	39 (19)	<.001
Creatinine,[b] mg/dL, median (IQR)	1.1 (0.8-1.4)	1.1 (0.9-1.4)	1 (0.8-1.4)	.008
CRF in dialysis	32 (3.4)	25 (3)	7 (3)	.97
Anemia[c]	393 (41)	275 (37)	118 (56)	<.001
Hemoglobin,[c] g/dL, median (IQR)	13 (12-14)	13.2 (11.9-14.3)	12.4 (10.3-14)	<.001
Preoperative medications				
ASA,[c]	774 (81)	637 (86)	137 (65)	<.001
Clopidogrel	78 (8)	47 (6.3)	31 (15)	<.001
Statins	845 (89)	713 (96)	132 (63)	<.001
Beta blockers	516 (54)	409 (55)	107 (51)	.27
ACEI or ARB	556 (58)	425 (57)	131 (62)	.20
Preoperative cardiac assessment				
Myocardial perfusion imaging	375 (39)	355 (48)	20 (10)	<.001
Normal perfusion	201 (21)	201 (27)	0	<.001
Fixed perfusion defects	104 (11)	100 (14)	4 (2)	
Reversible perfusion defects	70 (7)	54 (7)	16 (8)	
Coronary angiography	67 (9)	39 (5)	28 (13)	<.001
Transthoracic echocardiography	392 (41)	392 (53)	NA	NA
Wall motion abnormalities	96 (10)	96 (13)	NA	NA
Primary end point	120 (12.6)	102 (13.7)	18 (8.5)	.045

ACEI, Angiotensin-converting enzyme inhibitor; *ARB,* angiotensin receptor blocker; *ASA,* aspirin; *CABG,* coronary artery bypass graft surgery; *CAD,* coronary artery disease; *CHF,* chronic heart failure; *COPD,* chronic obstructive pulmonary disease; *CRF,* chronic renal failure; *IQR,* interquartile range; *NA,* not available; *NYHA FC,* New York Heart Association functional class; *PAD,* peripheral artery disease; *PCI,* percutaneous coronary intervention; *TIA,* transient ischemic attack.
Values are reported as number (%) unless otherwise indicated.
[a]n = 743.
[b]n = 952.
[c]n = 953.

As for postoperative surveillance, 5% of patients did not have postoperative troponin values available. Median length of hospital stay was 5 days (interquartile range, 3-8 days). Seventy-one patients died in the hospital, resulting in an in-hospital all-cause mortality rate of 7.4%.

Accuracy of established scores. The incidence of the primary end point according to risk strata for each cardiac risk score is shown in Table IV and Fig 3. The observed risk was substantially higher than that predicted by both scores, particularly in the lower strata. Prognostic accuracy as quantified by the AUC was low for both scores. ROC curves for the Lee (AUC, 0.58; 95% CI, 0.52-0.63) and VSG (AUC, 0.63; 95% CI, 0.58-0.68) scores are shown in Fig 4. Comparison of the two AUCs showed the VSG score to be superior to the Lee score ($P = .03$). Sensitivity analysis showed similar results when we analyzed only the 620 patients (78 events, 12.6%) submitted to elective surgery: AUC was 0.58 (95% CI, 0.51-0.65) for the Lee score and 0.61 (95% CI, 0.55-0.67) for the VSG score.

Subgroup analysis of the type of approach (endovascular vs open) did not show different accuracy of the scores.

Table II. Clinical characteristics of all patients with and without cardiac events

	All patients (N = 954)	No cardiac events (n = 834)	Cardiac events (n = 120)	*P* value
Male gender	687 (72)	604 (72)	83 (69)	.46
Age, years median (IQR)	70 (63-76)	69 (63-75)	71 (63-78)	.04
Diabetes	324 (34)	277 (33)	47 (39)	.20
Insulin	111 (12)	93 (11)	18 (15)	.35
Hypertension	795 (83)	687 (82)	108 (90)	.04
Active or former smoker	725 (76)	626 (75)	99 (82.5)	.07
CAD	377 (40)	313 (38)	64 (53)	.001
CABG or PCI	175 (18)	140 (17)	35 (29)	.001
PAD	954 (100)	—	—	
CHF	154 (16)	121 (15)	33 (28)	<.001
NYHA FC ≥II[a]	54 (8)	34 (5)	20 (20)	.02
History of stroke or TIA	232 (24)	204 (25)	28 (23)	.79
COPD	90 (9)	79 (10)	11 (9)	.92
Creatinine,[b] mg/dL, median (IQR)	1.1 (0.8-1.4)	1.1 (0.8-1.4)	1.2 (1.0-1.5)	.004
CRF in dialysis	32 (3.4)	29 (4)	3 (3)	.79
Anemia,[c]	393 (41)	323 (39)	70 (58)	<.001
Hemoglobin,[c] g/dL, median (IQR)	13 (12-14)	13 (12-14)	12 (11-14)	<.001
Preoperative medications				
ASA[c]	774 (81)	669 (80)	105 (88)	.06
Clopidogrel	78 (8)	72 (9)	6 (5)	.17
Statins	845 (89)	734 (88)	111 (93)	.15
Beta blockers	516 (54)	441 (53)	75 (63)	.05
ACEI or ARB	556 (58)	481 (58)	75 (63)	.32
Preoperative cardiac assessment				
Myocardial perfusion imaging	375 (39)	327 (39)	48 (40)	.89
Normal perfusion	201 (21)	176 (21)	25 (21)	.50
Fixed perfusion defects	104 (11)	87 (10)	17 (14)	
Reversible perfusion defects	70 (7)	64 (8)	6 (3)	
Coronary angiography	67 (9)	59 (9)	8 (8)	.72
Transthoracic echocardiography	392 (41)	320 (38)	72 (60)	NA
Wall motion abnormalities	96 (10)	70 (8)	26 (22)	

ACEI, Angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *ASA*, aspirin; *CABG*, coronary artery bypass graft surgery; *CAD*, coronary artery disease; *CHF*, chronic heart failure; *COPD*, chronic obstructive pulmonary disease; *CRF*, chronic renal failure; *IQR*, interquartile range; *NA*, not available; *NYHA FC*, New York Heart Association functional class; *PAD*, peripheral artery disease; *PCI*, percutaneous coronary intervention; *TIA*, transient ischemic attack.
Values are reported as number (%) unless otherwise indicated.
[a]n = 743.
[b]n = 952.
[c]n = 953.

In patients submitted to endovascular procedures, AUC was 0.56 (95% CI, 0.48-0.65) for the Lee score and 0.64 (95% CI, 0.56-0.72) for the VSG score; and in patients submitted to open procedures, AUC was 0.59 (95% CI, 0.52-0.66) for the Lee score and 0.62 (95% CI, 0.56-0.68) for the VSG score.

Additional variables related to cardiac events. Independent risk factors for the primary end point in the Lee score model (Table V) were smoking (odds ratio [OR], 1.8; 95% CI, 1.1-3.1; $P = .03$), preoperative anemia (OR, 2.0; 95% CI, 1.3-3.0; $P = .001$), and the Lee score itself (OR, 1.3; 95% CI, 1.0-1.5; $P = .04$). In the VSG score model (Table V), besides the VSG score (OR, 1.2; 95% CI, 1.1-1.4; $P < .001$), only anemia remained an independent predictor of the primary end point (OR, 1.9; 95% CI, 1.3-2.9; $P = .002$).

Adding anemia improved the accuracy for prediction of the primary end point only for the Lee score (Fig 5): AUC for the Lee score plus anemia of 0.61 (95% CI, 0.58-0.67; $P = .002$ for comparison with the original Lee score). This power-up effect was not significant for the VSG score: AUC for the VSG score plus anemia was 0.65 (95% CI, 0.60-0.70; $P = .10$ for comparison with the original VSG score). AUCs of the Lee score plus anemia and the VSG score were similar (0.61 vs 0.63, respectively; $P = .50$). Adding smoking to the Lee score did not

Table III. Observed primary end point and perioperative myocardial infarction (*MI*) according to type of surgery

Type of surgery	All patients, No. (%)	Cardiac events, No. (%)	Perioperative MI, No. (%)
Open aortic aneurysm repair	107 (11.2)	16 (15.0)	10 (9.3)
Endovascular aortic aneurysm repair	200 (21.0)	32 (16.0)	11 (5.5)
Lower extremity bypass	219 (23.0)	33 (15.1)	23 (10.5)
Lower extremity angioplasty	109 (11.4)	14 (12.8)	5 (4.6)
Carotid endarterectomy	151 (15.8)	15 (9.9)	12 (7.9)
Carotid stenting	82 (8.6)	3 (3.7)	2 (2.4)
Amputations	37 (3.9)	5 (13.5)	2 (5.4)
Others	49 (5.1)	2 (4.1)	1 (2.0)

Table IV. Observed primary end point according to risk strata for each cardiac risk score and predicted risk

Cardiac risk scores	All patients, No. (%)	Observed cardiac events, No. (% [95% CI])	Predicted risk, %
Lee score			
I	139 (14.6)	11 (8 [4-12])	0.4
II	337 (35.3)	39 (12 [8-15])	0.9
III	285 (29.9)	33 (12 [8-15])	6.6
IV	193 (20.2)	37 (19 [14-25])	11.0
VSG score			
0-3	237 (24.8)	11 (5 [2-7])	2.6
4	181 (19.0)	15 (8 [4-12])	3.5
5	166 (17.4)	31 (18 [13-25])	6.0
6	124 (13.0)	21 (16 [10-23])	6.6
7	98 (10.3)	15 (15 [8-22])	8.9
>8	148 (15.5)	27 (18 [12-24])	14.3

CI, Confidence interval; *VSG*, Vascular Study Group of New England Cardiac Risk Index.

improve accuracy measured by AUC (AUC for the Lee score plus smoking was 0.59; 95% CI, 0.54-0.65).

DISCUSSION

In this collaborative prospective observational study, we aimed to evaluate the performance of two preoperative risk scores in unselected patients undergoing vascular surgery. We report three major findings. First, both scores substantially underestimated the rate of major cardiac events across all risk strata. Second, both scores had low accuracy in a real-world setting of unselected patients undergoing vascular surgery, but the VSG score provided better discrimination compared with the Lee score. Third, addition of anemia to the Lee score improved its accuracy and equalized it to the VSG in this sample.

In a real-world unselected population, both Lee and VSG scores substantially underestimate cardiac risk. This is of major concern, as underestimation of major cardiac complications including MI, AHF, cardiac arrest, major arrhythmias, and cardiac death invariably leads to incorrect risk-benefit assessments by physicians and patients regarding the planned operation.

We have found a much higher overall cardiac event rate than observed in the derivation cohorts (12.6% vs 6.3% for the VSG score and 2%-2.5% for the Lee score).[9,11] Vascular patients have previously been shown to have a higher risk of cardiac complications[18]; therefore, it was expected that our overall cardiac event rate would be higher than in the original paper of Lee et al. However, the finding of a much higher cardiac event rate than in the VSG cohort was unexpected. There are some possible explanations for this finding.

First, surveillance and diagnostic criteria of MI were different among studies. In our cohort, we performed routine surveillance with hs-cTnT measurements after surgery because of its diagnostic superiority compared with less sensitive assays,[13] which allowed us to identify the majority of MIs in the first days. As in >50% of cases MI patients do not complain of chest pain,[24,25] most MIs will be missed without routine screening.[26] In a recent registry that included 88,791 patients submitted to nonemergent vascular operations, the overall incidence of MI was 1.6%.[17] Previous studies also reported lower overall procedure-specific perioperative MI rates than ours, most likely because of better surveillance in our prospective study.[19,21] As there is no specific universal definition for MI after noncardiac surgery, the difference in incidence of MI in several studies depends on the diagnostic criteria and the cardiac troponin assay used.[14]

Second, differences between cohorts, such as baseline characteristics of the included patients and type of surgery, need to be considered. Overall, our population was older and had a higher prevalence of known CAD and CHF, consistent with current daily clinical practice. Forty percent of the VSG's original population had a Lee score below class II, whereas only 14% of our population had a Lee score below class II.[11] The type of surgery is also a major issue. Our inclusion criteria were broader than those from the VSG cohort, which just included nonemergent carotid endarterectomy, open or endovascular infrarenal abdominal aortic aneurysm (AAA) repair, and lower extremity bypass.[11] Half of the VSG population was submitted to carotid endarterectomy, whereas only 24% of our population underwent carotid surgery.[11] If we compare the VSG cohort's results only for open AAA

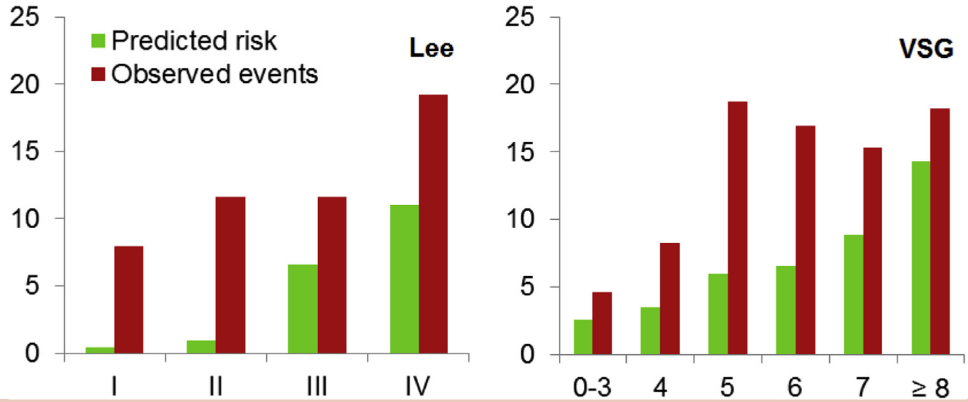

Fig 3. Combined end point according to risk strata for the Lee score (*left*) and the Vascular Study Group of New England Cardiac Risk Index (*VSG*) score (*right*), predicted event rate (*green*) vs observed event rate (*red*).

repair, their complication rate ranged from 19% to 22%, similar to ours (15%). In addition, one-third of our patients underwent urgent/emergent procedures, which are usually associated with higher complication rates.

Underestimation of cardiac risk has serious implications for clinical practice. The decision to proceed to surgery or not is based on the risk-benefit ratio. The benefit of elective surgery depends on the vascular disease's complication rate. The annual risk of AAA rupture depends on its diameter and ranges from 0.5% to 5% in AAAs between 4.0 and 4.9 cm to 30% to 50% in AAAs with a diameter ≥8.0 cm.[27] In patients with peripheral artery disease and claudication, only 1% to 2% will progress to critical limb ischemia in 5 years.[28] For patients with asymptomatic carotid stenosis, the absolute benefit in stroke prevention for revascularization is 1% to 2% per year.[29] Previous randomized trials comparing carotid endarterectomy with medical therapy were performed before improvements in medical therapy.[30,31] It has been suggested that intensive medical treatment has reduced the annual rate of stroke from 2% to 5% to 1%.[32,33] Awareness that patients classified as intermediate risk by the Lee or VSG score have cardiac event rates around 10% is extremely important for the decision of the best treatment choice (surgery vs medical treatment).[8] Other comorbidities that could compromise quality of life and may improve with surgery, such as chronic pain and poor mobility, also have to be taken into account in this decision. Nevertheless, knowledge of the rate of complications is important so that physicians and patients together make an informed decision to improve global patient care. For patients undergoing urgent or emergent surgery, canceling or postponing surgery is not an option, but estimation of cardiac events rate can also add important clinical information. Indeed, the knowledge that cardiac risk is higher than predicted empowers the evaluating physician to suggest measures to reduce risk, such as giving statins, referring the patient to the intensive care unit after surgery, and recommending surveillance for improving diagnosis and treatment of cardiac events.

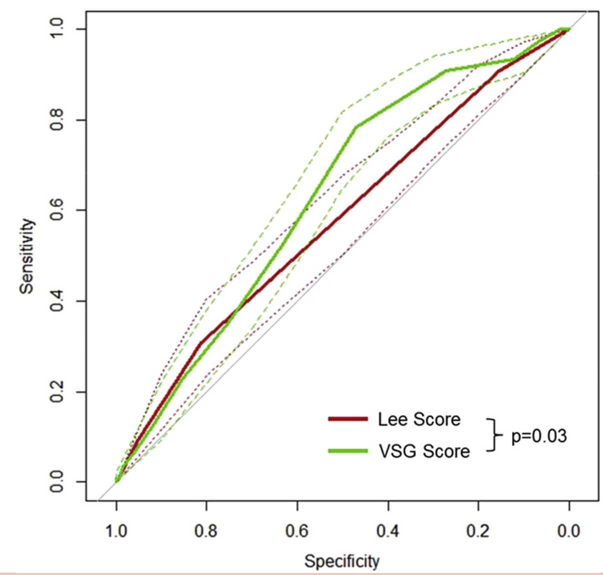

Fig 4. Receiver operating characteristic (ROC) curves of Lee score (*red*) vs Vascular Study Group of New England Cardiac Risk Index (*VSG*) score (*green*) with 95% confidence intervals (CIs) for sensitivity.

Unfortunately, both scores had low to moderate accuracy in our population of unselected patients submitted to vascular surgery. This finding may at least in part be explained by the fact that both scores do not take into account the intraoperative period. It is well known that intraoperative complications, including hypotension and bleeding, are associated with the development of postoperative major cardiac events including death.[20,34] Nevertheless, the VSG score had a better accuracy than the Lee score to predict cardiac events, a finding that is in line with previous studies.[10,11] In addition, the Lee score could not discriminate well between the patients classified in class II and III risk strata. As the Lee score had been part of the routine clinical preoperative evaluation to guide management at the participating institutions,[6,8] classifying a patient as Lee class ≥III may have led to

Table V. Logistic regression models for prediction of primary outcome including Lee score and Vascular Study Group of New England Cardiac Risk Index (*VSG*) score

	OR	95% CI	*P* value
Lee score			
Age	1.2	1.0-1.4	.066
Female sex	1.4	0.9-2.2	.137
Hypertension	1.5	0.7-2.9	.283
Urgency/emergency	1.4	0.9-2.1	.158
Smoking	**1.8**	**1.1-3.1**	**.026**
COPD	0.8	0.4-1.7	.610
ASA	1.6	0.9-3.0	.102
Statins	1.3	0.6-2.9	.450
Beta blockers	1.2	0.8-1.9	.303
ACEI or ARB	1.1	0.7-1.6	.756
Lee score	**1.3**	**1.0-1.5**	**.041**
Anemia	**2.0**	**1.3-3.0**	**.001**
VSG score			
Female sex	1.3	0.9-2.1	.195
Hypertension	1.5	0.8-3.0	.213
Urgency/emergency	1.3	0.8-2.1	.236
Suprainguinal surgery	1.1	0.7-1.8	.616
Stroke or TIA	0.9	0.5-1.4	.607
ASA	1.7	0.9-3.0	.088
Statins	1.5	0.7-3.2	.299
ACEI or ARB	1.1	0.7-1.6	.770
VSG score	**1.2**	**1.1-1.4**	**<.001**
Anemia	**1.9**	**1.3-2.9**	**.002**

ACEI, Angiotensin-converting enzyme inhibitor; *ARB,* angiotensin receptor blocker; *ASA,* aspirin; *CI,* confidence interval; *COPD,* chronic obstructive pulmonary disease; *OR,* odds ratio; *TIA,* transient ischemic attack. The boldface entries are independent risk factors for the primary end point.

changes in perioperative clinical care that could have an impact on outcome.

We have shown that the presence of anemia is a strong predictor for cardiac events. Several previous studies have demonstrated that preoperative anemia is a predictor of short- and long-term mortality after noncardiac surgery, including vascular surgery.[35-41] However, the evidence for preoperative anemia as a predictor of cardiac events after all types of vascular surgery is still limited. In a retrospective study including 360 patients undergoing peripheral arterial reconstructive surgery, Oshin and Torella reported that preoperative hemoglobin levels were related not only to mortality but also to cardiac events after surgery.[42] In a large retrospective study evaluating 31,857 elderly patients (>65 years old) of the National Surgical Quality Improvement Program (NSQIP) database undergoing elective, mostly open vascular procedures, Gupta et al have demonstrated that low preoperative hematocrit values were related to mortality and to perioperative MI or cardiac arrest within 30 days.[41] In our prospective study, we not only confirm that preoperative anemia (as defined

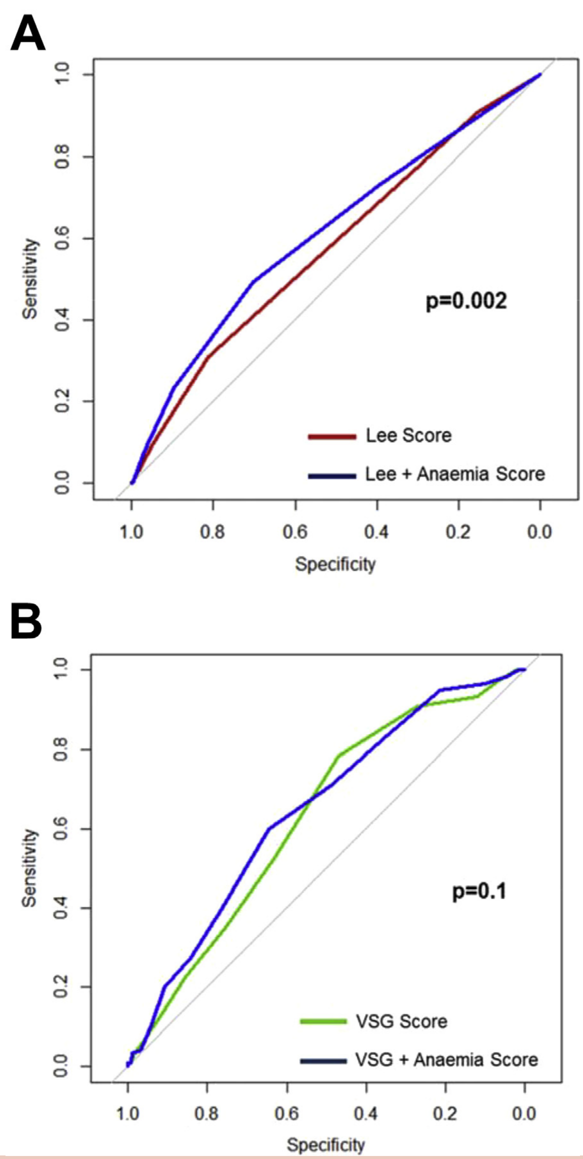

Fig 5. A, Receiver operating characteristic (ROC) curves of Lee score (*red*) vs Lee score plus anemia (*blue*). **B,** ROC curves for Vascular Study Group of New England Cardiac Risk Index (VSG) score (*green*) vs VSG score plus anemia (*blue*).

by World Health Organization criteria) is an independent predictor of cardiac events in patients undergoing open or endovascular vascular procedures but also provide a way to use this information in clinical practice. Although the VSG score alone had better accuracy than the Lee score alone in our population, it was equivalent to the Lee score plus anemia. The Lee score is simpler to calculate than the VSG score, and it is the score recommended by most guidelines.[6,8] As hemoglobin level is routinely measured before surgery, incorporation of this biomarker as a power-up in the Lee score is a simple and no-cost way of improving cardiac risk prediction.

Our study has some limitations. First, our patients came from two tertiary centers to which patients usually are referred when they have a more severe vascular disease or important cardiac or noncardiac comorbidities. In the University of São Paulo, we included patients for whom cardiac consultation was requested, and although it is common practice at our institution for vascular surgeons to request cardiac evaluation for all patients, we may have missed patients in the lower risk strata. Second, we did not evaluate the NSQIP,[43] MI/cardiac arrest,[21] and Vascular Quality Initiative[17] risk scores that are more complex and accurate than the Lee and VSG scores. These scores have to be done online or using mobile applications and evaluate only risk of MI and cardiac death, both factors limiting practical clinical use.[17,21,43] Currently, with improvement of surgical and anesthetic techniques, patients undergoing noncardiac surgery are increasingly older and have more comorbidities; therefore, it is also important to estimate the risk of other common cardiac complications besides MI and cardiac arrest, such as AHF and arrhythmias.

All risk prediction scores have advantages and limitations. They also were tested in different populations with different surgical procedures and predict different outcomes. Nevertheless, their use is recommended by most guidelines.[6-8] It is up to the attending physician to be aware of the individual strengths and limitations and to choose the most appropriate one, depending on clinical context. Using more than one risk score with different end points (VSG score plus NSQIP, for example) could be a good option to improve risk prediction and patient care. However, it is extremely important to be aware that the incidence of cardiac events is probably higher than predicted to make appropriate risk-benefit assessments regarding surgery.

CONCLUSIONS

The Lee and VSG scores have low accuracy and underestimate the risk of major perioperative cardiac events in unselected patients undergoing vascular surgery, which can at least partly be increased for the Lee score by the addition of preoperative anemia. Underestimation of major cardiac complications may lead to incorrect risk-benefit assessments by physicians and patients regarding the planned operation.

AUTHOR CONTRIBUTIONS

Conception and design: DG, CP, BC, CM
Analysis and interpretation: DG, CP, GLB, JE, SC, AM, IC, NL, MO, AL, DB, LS, MS, CK, SO, LG, BC, CM
Data collection: DG, CP, GL, PY, FC, NG, AZ, DC
Writing the article: DG, CP
Critical revision of the article: DG, CP, GLB, GL, PY, FC, NG, AZ, JE, SC, DC, AM, IC, NL, MO, AL, DB, LS, MS, CK, SO, LG, BC, CM
Final approval of the article: DG, CP, GLB, GL, PY, FC, NG, AZ, JE, SC, DC, AM, IC, NL, MO, AL, DB, LS, MS, CK, SO, LG, BC, CM
Statistical analysis: DG, CP, CK
Obtained funding: CM
Overall responsibility: DG
DG and CP contributed equally to this article and share co-first authorship.

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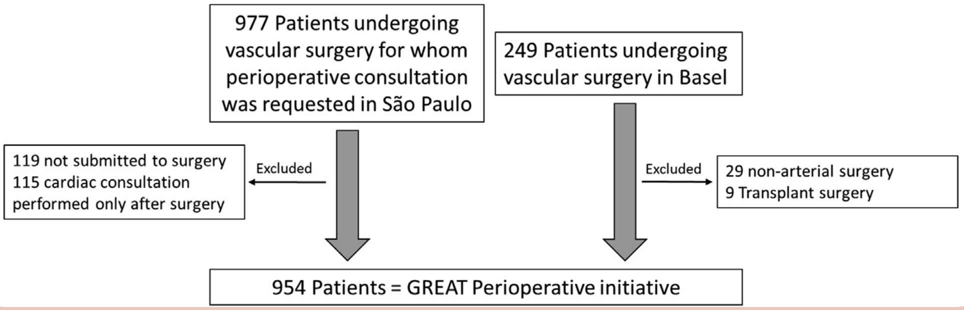

Supplementary Fig (online only). Patient flow chart. *GREAT,* Global Research on Acute Conditions Team.