Non-Coronary Arterial Disease (IX)

Coronary Risk Assessment in the Management of Patients Undergoing Noncardiac Vascular Surgery

Olaf Schouten, Jeroen J. Bax, and Don Poldermans

Section Sponsored by Laboratorio Dr Esteve

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Patients scheduled for noncardiac vascular surgery are at significant risk of cardiovascular morbidity and mortality due to underlying symptomatic or asymptomatic coronary artery disease. This review will give an overview of current preoperative cardiac risk assessment strategies for patients undergoing noncardiac vascular surgery. Clinical cardiac risk scores are useful tools for the simple identification of patients with an increased perioperative cardiac risk. These risk scores include factors such as age, history of myocardial infarction, angina pectoris, congestive heart failure, cerebrovascular events, diabetes mellitus, and renal dysfunction. Based on these cardiac risk scores further cardiac testing might be warranted in patients at increased risk. Recent developments in laboratory tests, noninvasive cardiac imaging, cardiac stress testing, and invasive cardiac imaging in the preoperative work-up of vascular surgical patients are reviewed.

Key words: Surgery. Cardiac complications. Risk factors.

INTRODUCTION

Patients scheduled for noncardiac vascular surgery are at significant risk of cardiovascular morbidity and mortality due to underlying symptomatic or asymptomatic coronary artery disease. As was shown by Hertzer et al in their landmark study in 1984 of 1000 patients undergoing noncardiac vascular surgery, 61% of all patients had at least 1 coronary artery with a stenosis of 50% or more.1 In fact, only 8% of all patients had a normal coronary angiogram. Importantly, there...
was no difference between patients who presented with an abdominal aneurysm, lower extremity ischemia, or cerebrovascular disease. More recent studies using functional tests such as dobutamine stress echocardiography confirmed the high incidence of coronary artery disease in vascular surgical patients. In a study population of 1097 vascular surgical patients with at least 1 cardiac risk factors, the incidence of wall motion abnormalities at rest was nearly 50% while one fifth of patients had stress induced myocardial ischemia.

The high prevalence of coronary artery disease in vascular surgical patients explains the high incidence of perioperative cardiac events in this patient population. Though recent developments in anesthesiological and surgical techniques, eg, locoregional anesthesia and endovascular treatment modalities, have improved postoperative cardiac outcome considerably, perioperative cardiac complications remain a significant problem. The incidence of perioperative myocardial infarction is around 5% and the prevalence of symptomatic perioperative myocardial ischemia as assessed by serum troponin I or serum troponin T in major vascular surgery is even 15% to 25%.

Patients undergoing vascular surgery are also susceptible to cardiovascular events during long-term follow-up after the surgical procedure. Over half of all long-term deaths in this population are attributable to cardiac events. The preoperative work up of vascular patients should be considered as an excellent opportunity to identify patients at increased long-term risk and treat them appropriately to lower the long-term risk for cardiovascular events. After all, the patient should live long enough to enjoy the benefits of the vascular surgical intervention.

This review will provide an overview of the current status of preoperative work-up of patients undergoing non-cardiac vascular surgery.

### Clinical Cardiac Risk Scores

#### Non-Cardiac Surgery

The first, most simple, and least costly step in preoperative cardiac risk stratification is the identification of clinical cardiac risk factors. In the last 3 decades much attention has been given to the identification of patients at risk by using simple clinical cardiac risk factors. This research has led to numerous cardiac risk indices for noncardiac surgical procedures (Table 1).

In 1977 Goldman et al proposed the first cardiac risk stratification model based on prospectively collected data. In this study of 1001 patients, 9 independent predictors were found to be correlated with postoperative life-threatening and fatal cardiac events.

#### Table 1. Risk Factors According to the Classifications of Goldman, Lee, and Boersma for Adverse Postoperative Outcome in Patients Undergoing All Types of Noncardiac Surgical Procedures

<table>
<thead>
<tr>
<th>Goldman et al, 1977</th>
<th>Lee et al, 1999</th>
<th>Boersma et al, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-threatening and fatal cardiac complication</td>
<td>Major adverse cardiac event</td>
<td>Cardiovascular death</td>
</tr>
<tr>
<td>Third heart sound or jugular venous distention</td>
<td>Congestive heart failure</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Myocardial infarction in the preceding 6 months</td>
<td>Ischemic heart disease</td>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>&gt;5 PVCs per minute at any time before operation</td>
<td>Cerebrovascular disease</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Other than sinus rhythm or presence PACs</td>
<td>Insulin dependent diabetes mellitus</td>
<td>Insulin dependent diabetes mellitus</td>
</tr>
<tr>
<td>Age over 70 years</td>
<td>Renal failure</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Intraperitoneal, intrathoracic, or aortic operation</td>
<td>High-risk surgery</td>
<td>Surgical risk according to the AHA/ACC classification</td>
</tr>
<tr>
<td><strong>Emergency operation</strong></td>
<td><strong>Important valvular aortic stenosis</strong></td>
<td><strong>Poor general medical condition</strong></td>
</tr>
<tr>
<td>No. patients in original report: 1001</td>
<td>No. patients in original report: 2893</td>
<td>No. patients in original report: 108 593</td>
</tr>
<tr>
<td>AUC in original report: 0.77</td>
<td>AUC in original report: 0.77</td>
<td>AUC in original report: 0.85</td>
</tr>
</tbody>
</table>

*PVC indicates premature ventricular contraction; PAC, premature atrial contraction.*

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Schouten O et al. Preoperative Cardiac Risk Assessment

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complications: preoperative third heart sound or jugular venous distention; myocardial infarction in the preceding 6 months; more than 5 premature ventricular contractions per minute documented at any time before operation; rhythm other than sinus rhythm or presence of premature atrial contractions on preoperative electrocardiogram; age over 70 years; intraperitoneal, intrathoracic, or aortic operation; emergency operation; important valvular aortic stenosis; and poor general medical condition. The incidence of adverse cardiac events was 1% in the group at lowest risk (class I), and increased to 7%, 14%, and 78% in class II, III, and IV patients respectively. However, it must be noted that only 18 patients were in the group at highest risk. The Goldman index has a 96.8% negative predictive value, and thus is an excellent tool to rule out coronary artery disease (CAD). The value of the Goldman index for diagnosing patients with CAD on the other hand was less optimal, ie, a positive predictive value of 21.6%.

In 1986 Detsky et al prospectively validated and modified the Goldman index and presented a simple normogram, introducing the pre-test likelihood of perioperative cardiac events for cardiac risk stratification. The Detsky modified multifactorial risk index has been in use ever since and is considered to be a good and practical index.

In 1999 Lee et al reviewed the performance of several clinical risk indices in patients who underwent elective noncardiac surgery. They found that the Goldman risk index and the Detsky modified cardiac risk index had a similar performance for predicting major cardiac complications. However, when the Goldman risk index was revised and validated, the predictive value of the risk index had substantially improved. In the validation cohort the ROC area improved from 0.70 for the original Goldman index to 0.81 for the Revised Cardiac Risk Index by Lee et al. The Revised Cardiac Risk Index identified 6 predictors (high-risk surgery, ischemic heart disease, congestive heart failure, cerebrovascular disease, insulin dependent diabetes mellitus, and renal failure) of major cardiac complications, and based on the presence of 0, 1, 2, or 3, or more of these predictors, the rate of major cardiac complications was estimated to be 0.4%, 0.9%, 7%, and 11%, respectively. Interestingly the Lee index has better prognostic value than the Goldman and Detsky indices though the number of cardiac risk factor variables in the Lee index is smaller. This might be explained by the improvement of perioperative care in the time between the development of the Goldman and Lee risk indices. Nowadays, the Lee index is considered the most relevant index for predicting perioperative cardiac risk in noncardiac surgery by many clinicians and researchers. However, the patients studied by Lee et al can hardly be considered as an average noncardiac surgical population. Thoracic, vascular and orthopedic patients were overrepresented in this study population.

Recently, Boersma et al developed the Erasmus Risk Index, a further refinement of the Revised Cardiac Risk Index. This index was based on an administrative database of 108 593 patients undergoing all types of noncardiac surgery during a period of 10 years at a university medical center in the Netherlands. Of these patients 1877 (1.7%) died in hospital, including 543 cardiovascular deaths. Applying the Revised Cardiac Risk Index in this population the corresponding odds ratio (OR) for patients without risk factors, 1, 2, or ≥3 were 1 (reference), 2.0, 5.1, and 11.0 respectively, with a C statistic for the prediction of cardiovascular mortality of 0.63. Importantly, if more precise data about the type of operation was introduced in the model the C statistic significantly increased to 0.79. Adding age resulted in an even better C index of 0.83. These data suggest that the Revised Cardiac Risk Index by Lee et al is probably suboptimal for identifying patients with greater cardiac risk, perhaps because it excluded emergency operations and perhaps because the type of surgery, which is one of the main determinants of adverse cardiovascular outcome, was considered in only 2 subtypes: high risk, including intraperitoneal, intrathoracic, and suprainguinal vascular procedures; and all remaining nonlaparoscopic procedures, mainly including orthopedic, abdominal, and other vascular procedures. In the study by Boersma et al it was found that a more subtle classification, as suggested by the American Heart Association/American College of Cardiology guideline committee, resulted, at least retrospectively, in a substantially better risk discrimination.

### Non-Cardiac Vascular Surgery

Patients undergoing non-cardiac vascular surgery are at high risk for postoperative cardiac complications due to underlying coronary artery disease. Several risk indices have been developed to stratify vascular surgical patients based on clinical cardiac risk factors (Table 2). In general, patients undergoing carotid artery stenosis repair have the least cardiac risk, followed by lower extremity revascularization procedures, and abdominal aortic procedures. Some risk indices only describe major noncardiac vascular surgical procedures, a term commonly used for lower extremity and abdominal aortic surgery.
The Glasgow aneurysm score, described in 1995, was one of the first cardiac risk scores dedicated to only vascular surgical procedures. In a retrospective study of 500 randomly chosen patients scheduled for open abdominal aortic aneurysm repair potential preoperative risk factors were related to postoperative in-hospital mortality. In multivariate analysis age, shock, myocardial disease, cerebrovascular disease, and renal disease were independently associated with adverse perioperative outcome.

One year after the introduction of the Glasgow aneurysm score, the Leiden Risk Model was proposed by Steyerberg et al. This study group composed a clinical prediction rule for perioperative mortality, using several risk factors obtained from literature. These risk factors included age, gender, a history of myocardial infarction, congestive heart failure, ischemia on the electrocardiogram, pulmonary disease, and renal dysfunction. Data from 246 patients undergoing open abdominal aortic aneurysm repair were used to validate the prediction rule. In the prediction rule, cardiac, renal, and pulmonary co-morbidity were found to be the most important risk factors, while age had only a moderate effect on perioperative mortality.

A total of 1081 consecutive patients undergoing major elective vascular surgery was used for the development and validation of a Bayesian model for preoperative cardiac risk assessment by L’Italien et al in 1996. The outcome for this study was a combination of nonfatal myocardial infarction and cardiac death. Using 567 patients as a derivation cohort the following risk factors were identified as predictors for adverse postoperative outcome: myocardial infarction, congestive heart failure, angina pectoris, prior coronary revascularization, diabetes mellitus, and age >70 years. Importantly, the validation cohort of 514 patients showed a prognostic accuracy of 74%. Patients classified as low, intermediate, and high risk had cardiac event rates of 3%, 8%, and 18% respectively.

Patients enrolled in the DECREASE I trial were used for the development of a risk score for elective major vascular surgery in 2001. This study identified 7 independent clinical risk factors for the combination of postoperative cardiac death and nonfatal myocardial infarction: a history of myocardial infarction, angina pectoris, congestive heart failure, diabetes mellitus, renal dysfunction, cerebrovascular events, and age >70 years.

For patients not on beta-blocker therapy the risk of perioperative cardiac events increased by each risk factor added, ranging from 1.0% in patients without risk factors, to 2.2%, 4.5%, 9.2%, 18.0%, and 32.0% for 1, 2, 3, 4, and ≥5 risk factors respectively.

Recently Kertai et al used a total of 2310 patients to develop a Bayesian model for the prediction of all-cause perioperative mortality in patients undergoing all types of open vascular surgery.
including emergency surgery. The information of 1537 patients were used to develop the risk score: the “customized probability index.” Risk factors associated with postoperative all-cause death were ischemic heart disease, congestive heart failure, cerebrovascular events, hypertension, renal dysfunction, chronic pulmonary disease, and type of vascular surgery, ie, ruptured AAA, elective AAA, lower extremity, and carotid. The final logistic regression model with the 9 independent predictors (including beta-blocker and statin use) of perioperative mortality was used to create a variable-weight index where scores were assigned on the basis of parameter estimates of the individual predictors. The type of surgery was a strong risk factor; patients with a ruptured abdominal aortic aneurysm had the worst outcome (43 points), followed by elective thoracoabdominal and abdominal aortic surgery (26 points), lower extremity arterial bypass surgery (15 points), and carotid surgery (0 points). It should be noted that all procedures in the risk model were open surgical procedures. Risk factors based on medical history, ordered in descending risk, were: renal dysfunction (16 points), congestive heart failure (14 points), ischemic heart disease (13 points), cerebrovascular event (10 points), hypertension (7 points), and pulmonary disease (7 points). Based on the sum of scores of surgical risk (0-46 points), medical history (0-67 points), and the score for cardioprotective medication (statins: 10 points and beta-blockers: 15 points) an overall cardiac risk can be calculated.

ADDITIONAL LABORATORY TESTING

Apart from those measurements indicating clinical risk factors (for example, serum creatinine for renal failure, fasting glucose for diabetes mellitus, etc) currently no routine laboratory measurements are related to perioperative cardiac complications.

Recent studies showed that increased plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) or B-type natriuretic peptide (BNP) are associated with adverse postoperative outcome. NT-proBNP is increased in patients with left ventricular dilatation caused by fluid overload (eg, heart failure and renal dysfunction), pressure overload (eg, aortic valve stenosis), and myocardial ischemia, which might explain the excellent relation with adverse postoperative outcome. In a study of 1590 patients scheduled for all types of noncardiac general surgery by Dernellis et al raised levels of BNP, ie >189 pg/mL, were independently associated with a staggering 34 fold increased risk for postoperative cardiac events. Similar results were found by Feringa et al in their report on the prognostic value of NT-proBNP in 170 patients scheduled for major vascular surgery. Patients with a NT-proBNP level >533 pg/mL had an independent 17-fold increased risk for postoperative cardiac events, even after adjustment for preoperative dobutamine stress echocardiography results. Gibson et al confirmed the predictive value of BNP in 149 major vascular surgical patients: using receiver-operator curve analysis a BNP concentration of 108.5 pg/mL best predicted the likelihood of cardiac events, with a sensitivity and specificity of 87%. The true value of either BNP or NT-proBNP in the preoperative screening setting must be confirmed in large scale prospective trials such as the recently started multinational DECREASE VI trial.

Diabetes mellitus is a common risk factor in patients scheduled for vascular surgery with prevalence of approximately 50% if all patients are thoroughly screened. Diabetes mellitus is known to be a strong predictor for perioperative events. Therefore fasting glucose values should be obtained from all patients scheduled for vascular surgery and glucose loading testing should be considered in all. Recently it was shown that the level of preoperative glycosylated hemoglobin in diabetic patients is strongly related to perioperative cardiac outcome. In the same patient population it was also shown that in patients with high preoperative glycosylated hemoglobin it is more difficult to regulate glucose values in the perioperative period. This might partly explain the strong relation between preoperative glycosylated hemoglobin and outcome, since it is known from critically ill patients and patients with myocardial infarction that tight glucose control is of eminent importance. In a large case-control study by Noordzij et al in noncardiac nonvascular surgical patients it was also shown that random preoperative glucose levels were associated with postoperative outcome. Those with a random glucose level ≥11.1 mmol/L had a 4-fold increased risk for perioperative cardiovascular death. Importantly, glucose levels of 5.6-11.1 mmol/L were independently associated with a 3-fold increased risk for perioperative cardiovascular events. Recently Sarveswaran et al found that preoperative asymptomatic troponin release in patients with symptomatic peripheral arterial disease is associated with a poor postoperative prognosis. Preoperative troponin release may be elevated because of asymptomatic myocardial ischemia, a condition often observed in patients scheduled for major vascular surgery. As was already noted by Landesberg et al in 1993, over 40% of patients planned for major vascular surgery experience silent myocardial ischemia preoperatively.
as assessed by continuous 12-lead ECG recording, also in asymptomatic patients.\textsuperscript{22} Notably, both Landesberg et al and Kertai et al previously showed that even low levels of asymptomatic troponin elevations in the perioperative period are associated with worse long-term outcome in patients undergoing major vascular surgery.\textsuperscript{23,24}

In most risk indices renal insufficiency is taken into account. For example, the serum creatinine cut-off value Lee et al used is 2.0 mg/dL (177 mmol/L).\textsuperscript{7} However, it might be argued that patients with less pronounced renal insufficiency also do worse compared to patients with normal serum creatinine values. A continuous variable for creatinine would probably be better, though not very user-friendly in every day practice. Recent studies have also shown that glomerular filtration rate might be a better predictor than serum creatinine since this takes into account the different creatinine concentrations between sexes.\textsuperscript{25}

### ADDITIONAL NONINVASIVE CARDIAC TESTING

If there is evidence or suspicion of CAD at physical examination, eg, valve abnormalities or left ventricular dysfunction, or a high cardiac risk score further cardiac testing might be required. The most simple, inexpensive form of cardiac imaging is resting echocardiography, for the detection of impaired left ventricular function and valve stenosis, and sclerosis. Impaired left ventricular function was long considered a strong predictor for adverse perioperative cardiac events. However, due to improved perioperative care it is no longer a strong predictor for short-term outcome but remains a significant predictor for long-term adverse cardiac events. The presence of aortic stenosis is associated with a fivefold increased risk of perioperative cardiac events.\textsuperscript{26} Also, the severity of aortic stenosis is related to an increased risk of perioperative events. Considering this, it is important to detect the presence and significance of valve disease. Though physical examination is reliable in detecting abnormal heart sounds, the estimation of the severity of stenosis by physical examination alone is difficult and echocardiography is recommended in patients with abnormal heart sounds.

### ADDITIONAL NONINVASIVE CARDIAC STRESS TESTING

According to the guidelines of the American College of Cardiology/American Heart Association, preoperative cardiac exercise or pharmacological stress testing is recommended for: patients with intermediate pre-test probability of CAD; prognostic assessment of patients undergoing initial evaluation for suspected or proven CAD; evaluation of subjects with significant change in clinical status; demonstration of proof of myocardial ischemia before coronary revascularization; evaluation of adequacy of medical treatment; and prognostic assessment after an acute coronary syndrome.\textsuperscript{27} For stress testing, the evaluation of exercise capacity when subjective assessment is unreliable seems to be a valid reason as well. Patients with CAD or at risk for CAD can be frequently found in the group of patients with limited every day exercise—for example, patients with severe intermittent claudication. In these patients pharmacological stress echocardiography or nuclear imaging are elegant ways to exclude subclinical CAD.

The sensitivity and specificity of available exercise and pharmacological stress tests were compared in several meta-analyses. The meta-analysis of Kertai et al showed a trend in favor of dobutamine stress echocardiography, though other tests had satisfying sensitivity and specificity as well.\textsuperscript{28} An upcoming elegant new diagnostic tool is dobutamine stress magnetic resonance imaging, though no randomized trials or large series have reported the sensitivity and specificity of this test yet.

In this era of new cardioprotective medical therapies, ie, beta-blockers and statins, the key question is which patient should undergo additional stress testing and which patient can be send for surgery without prior cardiac stress testing. The recently published Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study II (DECREASE II) evaluated the value of preoperative cardiac testing in intermediate-risk patients on beta-blocker therapy with perioperative tight heart rate control scheduled for major vascular surgery.\textsuperscript{29} A total of 1476 vascular surgical patients were screened for this study. Based on the risk score of Boersma et al patients were divided into 3 risk groups: low cardiac risk (no risk factors), intermediate cardiac risk (1 or 2 risk factors), and high cardiac risk (≥3 risk factors). All 770 intermediate risk patients were randomly assigned to preoperative cardiac stress-testing or no-testing. Results of preoperative testing and coronary revascularization were discussed with the attending physicians, and hemodynamic management was implemented accordingly. Importantly all patients in the DECREASE II study received beta-blocker therapy aiming at a tight heart rate control, ie, a heart rate of 60-65 beats per minute, irrespective of stress test results. Of the 386 patients randomized...
to cardiac stress-testing, 287 (74%) had no stress inducible myocardial ischemia, 65 (17%) had limited ischemia, and 34 (9%) had extensive ischemia. No difference in 30-day outcome was observed in intermediate-risk patients with and without testing, 2.3% versus 1.8% (OR = 0.78, 95% confidence interval [CI], 0.28-2.1). The upper limit of the 90% CI of the absolute risk difference in favor of cardiac testing was 1.2%, indicating non-inferiority of the no-testing strategy. In intermediate-risk patients with extensive ischemia revascularization did not improve 30-day outcome (25.0% vs 9.1% events, OR = 3.3, 95% CI, 0.5-24; \( P = .32 \)). Also, no difference in 2-year outcome was observed in intermediate-risk patients with and without testing, 4.3% versus 3.1% (\( P = .30 \)). The DECREASE II study indicates that cardiac testing of intermediate-risk patients prior to major vascular surgery, as recommended by the guidelines of the ACC/AHA,27 provided no benefit in patients on beta-blocker therapy with tight heart rate control. Importantly, the strategy of no-testing brought the operation almost 3 weeks forward.

**ADDITIONAL INVASIVE CARDIAC TESTING**

Guidelines of the American College of Cardiology /American Heart Association (ACC/AHA)27 recommend coronary angiography for patients with high-risk noninvasive test results, and myocardial revascularization in patients with prognostic high-risk anatomy in whom long-term outcome is likely to be improved.27 This recommendation was supported by the Coronary Artery Surgery Study that showed a reduced incidence of non-fatal myocardial infarctions after previous bypass surgery among vascular surgery patients compared to those treated medically, 8.5% versus 6.0% (\( P = .001 \)). More recently, the data from the Bypass Angioplasty Revascularization Investigation trial showed that bypass surgery and percutaneous coronary intervention had similar low rates of postoperative cardiac events in noncardiac surgery.31 However, these studies were not designed to assign the optimal strategy in severely ill patients with extensive coronary artery disease immediately prior to major noncardiac surgery. In addition, these studies could not address the concern of delaying the noncardiac surgical procedure because of testing, revascularization, and initiation of antiplatelet therapy since the time between revascularization and noncardiac surgery in these studies was respectively 4.1 and 2.4 years.

The randomized Coronary Artery Revascularization Prophylaxis (CARP) trial was the first study that addressed the strategy of prophylactic revascularization compared to optimal medical therapy in patients with clinically stable coronary artery disease who were scheduled for major noncardiac vascular surgery.32 This trial showed that prophylactic revascularization was safe but did not improve perioperative or long-term outcome. The long-term (median follow-up 2.7 years) mortality was 22% in patients allocated to prophylactic coronary revascularization, compared to 23% in the medical only strategy, \( P = .92 \). Also the incidence of perioperative non-fatal myocardial infarction was similar, respectively 12% and 14%, \( P = .37 \). However, it must be noted that the majority of patients in the CARP trial had only 1 or 2 vessel disease. The recently conducted DECREASE V randomized pilot study in which the majority of patients had 3-vessel disease also showed no perioperative and long-term (follow-up 1 year) benefit of prophylactic coronary revascularization.33 The findings of both CARP and DECREASE V support the current guidelines of the ACC/AHA on perioperative management in high-risk patients37 to reserve revascularization only for cardiac unstable patients. After successful noncardiac surgery these patients should be regularly screened for the presence of ischemic complaints and aggressive anti-ischemic therapy, both medical and invasive, should be considered. In these patients at high risk scheduled for major noncardiac vascular surgery prophylactic revascularization might be switched to late revascularization, preventing the delay of surgery.

**REFERENCES**


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