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Preoperative cardiac risk assessment for vascular surgery: Can it make a difference?

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Angiographically significant coronary artery disease (CAD) is common among patients with aortic and peripheral vascular disease. This burden of CAD predisposes the vascular surgery patient to cardiac complications in the post-operative period. Routine clinical evaluation seems to be neither sensitive nor specific for cardiac risk estimation, especially in a group of patients who are often unable to exercise due to lower limb claudication. Preoperative cardiac risk assessment may represent an opportunity not only to predict operative risk, but also to prognosticate long-term outcome and initiate cardiac care. Despite the obvious rationale for its use, however, the optimum strategy for cardiac risk assessment before high-risk vascular surgery and its utility remain controversial.

The role of preoperative risk assessment is to provide the patient and the surgeon with an accurate risk estimate so that informed consent may be obtained. The encounter provides an opportunity to intervene by reducing the estimated risk and to change overall prognosis. This review attempts to establish the utility of this process in somewhat reverse order. Instead of describing the various available methods that provide risk estimates, we will address the ability of diagnostic testing to alter risk first, for if we do not have strategies to alter the risk that is estimated, the process of risk stratification would only be useful to obtain informed consent. Once we can demonstrate that we are able to alter risk, we can evaluate indices that predict severity of CAD and develop an optimal protocol for risk assessment. The following sections will discuss pre-operative interventions that may change outcome in the vascular surgery patient.

Coronary angiography and revascularization

The Cleveland Clinic series[1] showed that in 1000 consecutive patients who were to have major peripheral vascular surgery, preoperative coronary angiography was normal in only 8% of patients. Interestingly, 27% had nonsignificant stenosis (<50% stenosis), 23% had single vessel, 20% had two-vessel, and 22% had 3-vessel, or left main disease.

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Table 1: Outcome of 1,961 patients in the CASS Registry who underwent coronary revasculation prior to high-risk non-cardiac surgery.

Number	395 No CAD	965 CAD & CABG	582 CAD & med
Outcome			
Peri-op MI	0.8%	0.8%	2.7%
Operative mortality	1.0%	1.7%	3.3%

Table 2: Major outcomes (mortality, nonfatal MI, stroke, uncorrected vascular disease, and cost) of 3 strategies performed in patients prior to elective vascular surgery (VS).

Plan	Mortality	MI	Stroke	Uncorrected vascular disease	Cost
No cath*	3.5%	4.5%	.5%	0%	$24,300
Cath 1†	3.8%	5.9%	1.1%	1.2%	$43,800
Cath 2‡	3.4%	5.6%	1.1%	5.2%	$41,800

* No pre-op coronary angiography (CA) or coronary revascularization (CR) and proceed directly to VS

† CA, followed by selective CR; perform VS in patients with inoperable CAD

‡ CA, followed by selective CR; cancel VS in patients with severe inoperable CAD

Although randomized data on surgical outcomes following revascularization do not exist, the Coronary Artery Surgery Study (CASS) registry provides some insight into outcomes following coronary artery bypass grafting (CABG). The CASS registry[2] reported a total of 3,368 patients who underwent major noncardiac operations after enrollment in the registry. Of these patients, 1,961 underwent high-risk noncardiac surgery; the outcomes of these patients are described in Table 1. In patients who had coronary revascularization, there was a reduction in the perioperative MI rate from 2.7% to .8% and operative mortality decreased from 3.3% to 1.7%. Although at first glance revascularization seems beneficial, these data are nonrandomized and do not take into account the mortality and morbidity of angiography and CABG.

As there is a lack of randomized data to answer the question of the benefit of preoperative revascularization, Mason et al[3] built a decision analysis model with event rates from major angiography, CABG, and percutaneous transluminal coronary angioplasty (PTCA) literature in North America and Europe. Their objective was to determine whether preoperative coronary angiography and revascularization would improve short-term outcomes in patients undergoing noncardiac vascular surgery. Patients undergoing elective vascular surgery who had either no or mild angina and a positive dipyridamole-thallium scan result were included. The three strategies prior to vascular surgery were:

- To proceed directly to vascular surgery.
- To perform coronary angiography followed by selective coronary revascularization before proceeding to vascular surgery and to cancel vascular surgery in patients with severe inoperable CAD.
- To perform coronary angiography followed by selective coronary revascularization before proceeding to vascular surgery and to perform vascular surgery in patients with inoperable CAD.

Major outcomes were calculated within three months and included mortality, nonfatal MI, stroke, uncorrected vascular disease, and cost (Table 2). In this decision analysis model, proceeding directly to vascular surgery led to the lowest morbidity and cost. The coronary angiography strategy performed in patients with inoperable CAD led to higher mortality with vascular surgery. In a subset of patients with a predicted operative mortality >5% and an operative mortality for CABG of <3-4%, the coronary angiography strategy led to lower mortality.

Decision analysis indicates vascular surgery without preoperative coronary angiography generally leads to better outcomes. Preoperative coronary angiography. therefore, should be reserved for patients whose estimated mortality from vascular surgery is substantially higher than average if one takes into account only short-term outcome. However, the benefits of revascularization are mainly realized with time and if the patient will have a long-term ben-

efit from revascularization — independent of the procedure — then revascularization should precede the procedure.

Medical intervention in the preoperative period

The only randomized data concerning medical intervention is the use of atenolol in the perioperative period.[4] This study was a randomized, double-blind, placebo-controlled trial that compared the effect of atenolol with that of a placebo on overall survival and cardiovascular morbidity in patients with, or at risk of, CAD who were undergoing noncardiac surgery. Approximately 40% of these patients had peripheral vascular surgery. Atenolol was given intravenously before and immediately after surgery, and orally thereafter for the duration of hospitalization. Patients were followed over the subsequent two years.

Overall mortality in the 192 patients after discharge (atenolol vs placebo) over 6 months was 0 vs 8%, ($p<0.001$); over 12 months 3% vs. 14%, ($p=0.005$); and over 24 months 10% vs. 21%, ($p=0.019$). Event-free survival throughout the two-year study period was 68% in the placebo group and 83% in the atenolol group ($p=0.008$).

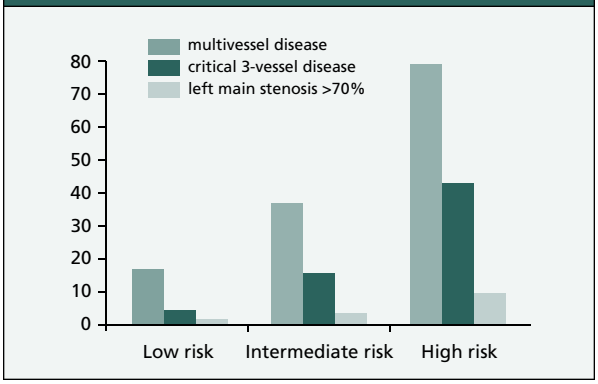
There were no differences in perioperative events and this trial was not powered to look at differences in the perioperative period. Although the rationale of a short perioperative treatment plan that results in a long-term benefit is questionable, based on this study, ACP/ACC recommendations now include use of perioperative beta-blockade.[5]

Although there is definite long-term benefit from perioperative intervention —be it medical or CABG — short-term benefits have not been definitely demonstrated. Accurately predicting which patient populations will benefit from these interventions may allow the clinician to change the risk and alter overall prognosis.

Do clinical risk indices estimate CAD severity and identify patients who would benefit from intervention?

Surgical risk has been stratified by several investigators. The widely used criteria include the Goldman, Eagle and Detsky index. Although these indices have limitations when applied to the individual, vascular surgery patient, it is generally felt that it is possible to identify those at very low risk. Preoperative clinical indices to stratify cardiac risk have not been validated angiographically.

Figure 1: A gradient of risk for severe stenosis was seen with increasing numbers of clinical markers



Paul et al[6] prospectively studied the concordance of clinical risk with severity of coronary stenosis and attempted to develop and validate a preoperative clinical index to exclude the presence of significant coronary stenosis. They studied 878 consecutive patients, including the derivation and validation sets.

"Severe" stenosis was defined as three-vessel (≥50% stenosis in each), two-vessel (≥50% stenosis in one when the other is ≥70% stenosis of the left anterior descending), or left main disease (≥50%); "critical" stenosis was three-vessel (≥70% stenosis in each) and/or left main stenosis ≥70%.

A preoperative clinical index (diabetes mellitus, prior MI, angina, age >70 years, congestive heart failure) was used to stratify patients. A gradient of risk for severe stenosis was seen with increasing numbers of clinical markers and is described in Figure 1. The following prediction rules were developed from this data set.

The predictive value for the absence of severe coronary stenoses was 96% for patients with no history of diabetes, prior angina, previous MI, or a history of congestive heart failure.

Similarly, the predictive value for the absence of critical coronary stenoses was 94% for patients with no prior angina, previous MI, or history of congestive heart failure. The

authors concluded that by reliably identifying a large proportion of patients with a low likelihood of significant stenoses, prediction rules can help to substantially reduce healthcare costs associated with preoperative cardiac risk assessment for noncardiac surgery. However, it is the patient that does not fit the low-risk category that is the norm in this population and the optimal method to stratify this patient still remains controversial. The strategies include resting ECG, resting ventricular function, and pharmacologic perfusion imaging.

Is there an optimal protocol to risk stratify the vascular surgery patient?

The ACC and the AHA have jointly produced guidelines for cardiac evaluation before noncardiac surgery. The guidelines suggest a stepwise approach that is summarized as follows:

- Urgency: if the surgery is urgent, risk stratification to be performed in the postoperative setting.
- If the patient has been revascularized in the last five years and is clinically stable, proceed to surgery.
- If the patient has had a favorable cardiac evaluation in the past two years and no change in status, investigations are not necessary.
- If the patient has an unstable coronary syndrome or major risk predictor such as decompensated CHF, significant arrhythmias, or severe valvular disease, cancel or delay surgery until the problem is diagnosed and treated.
- If the patient has intermediate predictors of risk such as age >70, MI by history or EKG, angina, CHF or diabetes mellitus, consider his/her functional status and surgery specific risks.
- If the patient is unable to perform 4 metabolic equivalents (METS) or has multiple markers of risk, proceed to noninvasive testing. If the anticipated surgical risk is high and noninvasive tests suggest significant CAD, consider a path of coronary angiography with a view to revascularization. The information gained during preoperative evaluation should be used for long-term therapy and follow-up, with primary and secondary prevention of coronary artery disease.

Although the ACC/AHA Guidelines have not been tested prospectively, Bartels et al[7] prospectively evaluated a cardiac risk stratification protocol in patients undergoing high-risk vascular surgery. Their protocol followed the ACC/AHA guidelines in 203 patients scheduled for aortic surgery. Endpoints of the study were cardiac mortality/morbidity and cost-effectiveness. Patients were stratified into low (n = 101), intermediate (n = 79), and high (n = 23) cardiac risk after clinical predictors.

After stratification, the degree of estimated functional capacity assessed by treadmill exercise and daily living activities and expressed by METs was critical for further cardiac evaluation. In intermediate-risk patients with an estimated functional capacity <5 METs and in all high-risk patients, noninvasive cardiac testing and/or subsequent medical care were performed. Noninvasive testing was considered necessary in 41 patients, coronary angiography in 7, and myocardial revascularization in 1, cancellation in 2 . Overall hospital mortality was 3.5%. Cardiac mortality and morbidity were 1% and 12.4%, respectively. The authors concluded that cardiac risk stratification for high-risk vascular surgery patients according to a protocol similar to the ACC/AHA Guidelines demonstrated excellent clinical outcome.

Summary and conclusion

Patients undergoing peripheral vascular procedures generally represent a higher-risk group with respect to future cardiac events. While short-term outcome is more difficult to modify favorably than long-term outcome, various diagnostic strategies and interventions can be deployed. In general, higher-risk patients, based on previous history or clinical evidence, should undergo further testing including coronary angiography and revascularization.

References

1. Hertzer NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular surgery patient. A classification of 1000 coronary angiograms and results of surgical management. *Ann Surg* 1984;199:223-33.
2. Foster ED, Davis KB, Carpenter JA, et al. Risk of noncardiac operation in patients with defined coronary disease: The Coronary Artery Surgery Study (CASS) registry experience. *Ann Thoracic Surg* 1986;41:42-50.
3. Mason JJ, Owens DK, Harris RA, et al. The role of coronary angiography and coronary revascularization before noncardiac vascular surgery. *JAMA* 1995;273:1919-1925.
4. Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med* 1996:335;1713-1720.
5. Eagle KA, Brundage BH, Chaitman BR, 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.
6. Paul SD, Eagle KA, Kuntz KM, et al. Concordance of preoperative clinical risk with angiographic severity of coronary artery disease in patients undergoing vascular surgery. *Circulation* 1996;94:1561-1566.
7. Bartels C, Bechtel JFM, Hossman V, et al: Cardiac risk stratification for high risk vascular surgery. *Circulation* 1997;95:2473-2475.

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Abstracts of Interest

Picotamide, an antithromboxane agent, reduces cardiovascular events in diabetics with peripheral vascular diseases: A cumulative analysis on 518 patients

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Study aim: Picotamide is an antiplatelet drug that inhibits platelet thromboxane A2 synthesis and antagonises thromboxane A2 receptors. Three double-blind, placebo-controlled randomised trials, carried out in type 2 diabetic patients with peripheral vascular diseases have been recently published (*Br J Clin Pharmacol* 1996; *Stroke* 1995; *Diabetes* 1998). Aim of this presentation was to evaluate the effects of picotamide in comparison to placebo on major cardiovascular events by means of a cumulative analysis of these studies.
Patients and methods: These trials enrolled a total of 518 patients with type 2 diabetes mellitus, followed for a minimum of 1.5 to a maximum of 6 years (1016 patients/year). Two hundred and seventy patients were treated with picotamide and 248 with the corresponding placebo. Each trial evaluated the occurrence of major (death, acute myocardial infarction, stroke, amputation) and minor (TIA, CABG, worsening of vasculopathy and angina pectoris) vascular events using the same standardised criteria. Clinical events were validated by an independent review committee. Patients were given either picotamide (300 mg t.i.d.) or the corresponding placebo in each trial.
Results: In comparison with placebo-treated patients, the incidence of major and minor events were significantly lower in picotamide group (17 events vs. 42; risk reduction: -60%; $p<0.0001$; x^2 test). There were 21 major cardiovascular events in placebo patients and 9 in the picotamide group (-58% risk reduction) ($p<0.024$). Minor events occurred in 21 patients in placebo group and in 8 patients in picotamide (-72% risk reduction) ($p<0.01$).
Conclusion: This cumulative analysis showed that picotamide, in comparison to placebo, significantly reduced the risk of cardiovascular events in diabetic patients with peripheral vascular disease.

Betaxolol, a new, long-acting beta-blocker, suppresses intraoperative myocardial ischemia during vascular surgery in patients with preoperative ischemia and coronary artery disease

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Although beta-blockade is recommended in patients with CAD to prevent perioperative coronary events during vascular surgery, little information is available from prospective studies to demonstrate their effects on ischemic indices. Accordingly, we prospectively evaluated the antiischemic effects of betaxolol (a long-acting, cardioselective beta-blocker) in patients with CAD undergoing major vascular surgical procedures. Of the 198 consecutive patients evaluated, 58 patients with angiographically proved CAD and evidence of myocardial ischemia were enrolled in the study and started on betaxolol (10-20 mg) given for at least 10-14 days preoperatively. All 58 patients underwent 48-hr ambulatory ECG monitoring at baseline and during vascular surgery, intraoperative and in the immediate postoperative period. The mean ± SD values for number of ischemic events, total duration (min) per 48 hours, and average duration (min) per event are shown in the table:

	Number of events	Total duration	Average duration
Baseline	2.6±3	90±140	22±24
Betaxolol	0.2±0.6	9.5±23	2.2±7
p-value	<0.0001	<0.0001	<0.0001

Betaxolol completely suppressed ischemia in 76% of the patients.
Conclusion: These results demonstrate that preoperative treatment with betaxolol is highly effective in suppressing myocardial ischemia during the intraoperative and immediate postoperative period. Future studies should examine relative benefits of medical therapy with long-acting beta-blockers such as betax-

ololol in reducing the risk of coronary events in patients undergoing major vascular surgical procedures.

Exercise workload capacity identifies patients at low risk for perioperative cardiovascular events and long-term mortality

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Previous studies have shown that increased levels achieved on exercise tests correlate with decreased risk of perioperative cardiac complications. This study examined whether the inexpensive and widely available supine bicycle test can be used to 1) identify patients who may proceed directly to vascular surgery without the risks and expense of additional testing and 2) indicate long-term survival.

Methods: A consecutive series of 149 patients with known or suspected coronary artery disease (CAD) underwent supine exercise radionuclide angiography prior to vascular surgery. Patients achieved high peak capacity if their peak workload was >300 kg-m/min for females or >400 for males.

Results: High peak capacity was attained by 59 (40%) patients comprised of significantly fewer females (12% vs 38%, $p<0.01$) and persons over 65 (42% vs. 71%, $p<0.01$) than the 90 low-capacity patients. Eleven cardiovascular (CV) events (5 cardiac deaths, 5 MIs, 1 cardiac arrest) occurred, none among the high-capacity patients ($p<0.01$). After adjusting for age, high peak capacity remained significantly associated with lower CV-event risk (OR = 0.14, 95% CI = [0.01, 0.78]). There were 53 deaths during 4 years of follow-up with significantly longer survival among the high-capacity patients ($p = 0.01$). After adjusting for age and gender, long-term mortality remained significantly lower in the high-capacity patients (RR = 0.41, 95% CI = [0.22, 0.80]).

Conclusion: In preoperative assessment for vascular surgery, patients who achieved high peak capacity exhibited significantly lower risk for both the occurrence of perioperative CV events and long-term mortality.

Value of dobutamine stress echocardiography in risk stratification of patients with clinical predictors of "Intermediate to High Risk" for peripheral vascular surgery

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There is a divergence of opinion regarding noninvasive stress testing in patients with two or more clinical predictors of risk of complications from peripheral vascular surgery (age >70 years, prior MI, angina, CHF, diabetes, ventricular arrhythmias requiring treatment). Recent AHA/ACC guidelines classify these patients as being at intermediate risk, other studies suggest a high risk of complications. This has resulted in variable approaches with some centers performing stress testing and others proceeding directly with coronary angiography. We performed preoperative Dobutamine stress echocardiograms (DSE) in 117 patients, mean age 58.3 ± 9.5 years, 71 males, with two or more of above mentioned clinical predictors. The follow-up period was 11.8 ± 6.9 months and the perioperative and long-term events included unstable angina, MI, coronary revascularization, CHF, arrhythmias requiring hospitalization and cardiac death. Out of 85 patients with no inducible ischemia by DSE, 7 patients (8.2%) had a total of 10 events compared to a total of 12 events in 10 of 32 (31%) patients with DSE positive for ischemia ($p<0.005$). None of the 7 patients with a negative DSE had MI or death and only 1 patient had perioperative CHF with the remaining complications being long term. Seven of 32 patients with a positive DSE had major complications with 6 MI's and 1 death, 4 of these complications were in the perioperative period. Following adjustment for all clinical predictors, the independent risk ratio of a positive DSE was 4.6.

Conclusion: The data indicate that in patients classified clinically as being at intermediate to high risk for complications from vascular surgery, a negative DSE can identify patients at lower risk of perioperative complications thus obviating the need for preoperative intervention in these patients.

Perioperative prognostic value of dipyridamole echocardiography before vascular surgery: A large scale multicenter study on 397 patients

Rosa Sicari, Ana Djordjevic-Dikic, Eugenio Picano, et al. Pisa, Italy.

Patients undergoing major vascular surgery are at relatively high risk of cardiac events, and pharmacological stress echocardiography is increasingly used for perioperative risk stratification. The aim of the study was to evaluate the value of dipyridamole echodcardiography test (up to 0.84 mg/kg over 10′) in predicting cardiac events in large scale, multicenter observational study design. We studied 397 patients (mean age 66 ± 7 years) prior to vascular surgery by dipyridamole stress echocardiography in 8 different centers. No major complications occurred during the test. Sixty-three (16%) had a positive test. Perioperative events occurred in 20 patients (5%); 4 deaths, 5 myocardial infarctions and 11 unstable angina. Sensitivity and specificity of dipyridamole stress echocardiography for predicting cardiac events were 80% and 88%, respectively, with a positive predictive value of 25% and negative predictive value of 99%. When only hard cardiac events were considered, by multivariate analysis only rest/stress difference in wall motion score index was a significant predictor (hazard ratio = 75.6, $p <0.001$). In conclusion, dipyridamole stress echocardiography provides an effective preoperative screening test for the risk stratification of patients undergoing major vascular surgery, mainly due to the extremely high negative predictive value.