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Preoperative Risk Assessment: Many Studies, Few Solutions

Is a Cardiac Risk Assessment Paradigm Possible?

Developing preoperative assessment strategies for surgical patients with or at risk for cardiac disease is both a critical goal and challenging task. More than 28 million people in the United States undergo surgery, at a cost of more than $300 billion annually—one-third of the entire U.S. health-care budget of $900 billion. Additionally, approximately 9 million surgical patients have or are at risk for cardiovascular disease, resulting in in-hospital or long-term cardiovascular complications for 1.5 million patients and additional costs exceeding $20 billion annually.[1,2] Over the next three decades, aging will exacerbate both risk and costs by increasing the surgical population older than age 65 yr from 7 to 14 million, and the number of procedures to nearly 40 million per year.[3]

Key to reducing perioperative cardiovascular morbidity and costs is the preoperative identification of high-risk patients likely to suffer postoperative complications. To be effective, preoperative testing must be able to simulate the myriad intraoperative and postoperative stresses encountered, particularly those associated with myocardial infarction. However, the multiple etiologies potentially associated with perioperative myocardial infarction make this a particularly daunting task (fig. 1).[1] Added to these are the stresses of the complex, prolonged perioperative period related to oxygen supply and demand, thrombosis, and other factors. Moreover, even in a relatively homogeneous population presenting for surgery, the relative contribution of any factor likely will vary markedly from patient to patient. Thus, preoperative risk assessment is inherently limited by the difficult (if not impossible) goal of tailoring risk identification to the requirements of individual patients. Most current preoperative tests are designed to emphasize only one or two perturbations, ignoring others that might be important for identifying additional or confounding pathophysiologic conditions in the patient for whom the test is being performed. For example, dipyridamole thallium scintigraphy assesses the effects of coronary redistribution but not of increases in heart rate, decreases in blood pressure, or alteration in thrombosis. Yet, in any given patient, it may be these latter factors and not redistribution phenomena *per se* that are most likely to precipitate adverse outcome. Thus, the ideal preoperative assessment paradigm must be comprehensive and patient-specific.

History of Preoperative Assessment Testing

With recognition that perioperative myocardial infarction was an important problem, investigators in the early 1950s explored the value of historical and clinical preoperative variables for prediction of outcome, finding that recent myocardial infarction and current congestive failure were consistent predictors.[1] In the mid-1970s, the concept of risk indexes was introduced and developed by combining such historical and preoperative clinical information. These approaches, emphasizing the chronic disease state, enhanced assessment but remained limited by an inability to assess the stress response. Nonroutine preoperative cardiac stress testing emerged, first exercise stress testing and radionuclide ventriculography, followed by ambulatory electrocardiography, perfusion scintigraphy, and stress echocardiography. During the last two decades, more than 50 trials of varying scope attempted to establish the prognostic value of such tests, with initially encouraging results. However, some limitations existed, including design and methodologic problems that rendered interpretation of the results and extrapolation of findings to more than specific study populations difficult (table 1). Most recently, dipyridamole thallium scintigraphy and ambulatory Holter electrocardiography have received considerable attention. At costs as great at high at $1,500 per test (for scintigraphy), we have an obligation to evaluate critically the true prognostic value of these nonroutine tests.

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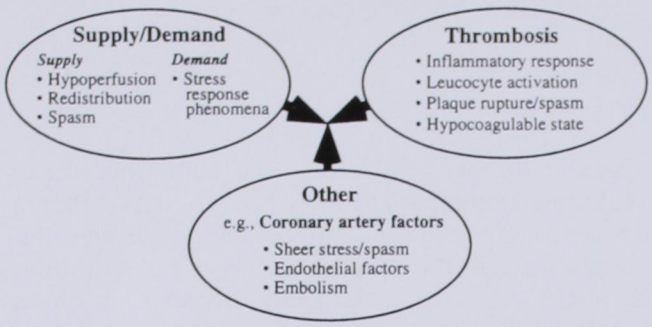

Fig. 1. Categories of potential etiologies for myocardial infarction occurring in patients undergoing noncardiac surgery. (See reference 1 for specific citations.)

Dipyridamole Thallium Scintigraphy

Because patients undergoing vascular surgical procedures are among those at greatest risk but are unable to exercise, pharmacologic methods for simulating the physiologic effects of exercise have been developed, including those that induce coronary vasodilation, *e.g.*, dipyridamole. Early studies conducted in nonsurgical patients indicated that dipyridamole thallium scintigraphy was useful for diagnosis of coronary artery disease and prediction of long-term events, such as myocardial infarction. Subsequent studies in patients undergoing vascular surgery demonstrated that nearly all perioperative adverse events were associated with scintigraphy redistribution defects at sensitivities exceeding 80% and negative predictive values near 100%.[4] For example, Boucher *et al.*[5] documented that all adverse outcomes (n = 8) after noncardiac surgery occurred in the 16 of 48 patients who had preoperative redistribution defects. Confirmation of such results by others produced more widespread practice of routinely performing dipyridamole thallium scintigraphy in patients undergoing peripheral vascular surgery.[1]

In 1991, Mangano *et al.*[6] challenged the use of routine testing based on the failure of previous investigators to blind scintigraphic findings from the treating clinicians and other limitations. In a prospective study of 60 patients undergoing elective vascular surgery that blinded all treating clinicians to scintigraphy results, they assessed not only adverse outcome but also several measures of perioperative myocardial ischemia. Unlike their predecessors, they found no association between redistribution defects and adverse cardiac outcomes; that is, 54% of adverse outcomes occurred in patients without redistribution defects, and the risk of adverse outcome was not significantly greater in patients with such defects (relative risk 1.5, 95% CI 0.6–3.9, $P = 0.4$). Additionally, they found no association between redistribution defects and perioperative ischemia—the majority of perioperative electrocardiogram and transesophageal echocardiographic ischemic episodes were not associated with redistribution defects. They suggested that adverse outcomes after surgery, particularly myocardial infarction, were due to various causes, including increases in indexes of myocardial oxygen demand, thrombosis, and other etiologies not specifically tested by dipyridamole thallium scintigraphy. They concluded that routine preoperative screening with this test may not be warranted. Only a large-scale study conducted in 457 patients by Baron *et al.*[7] resolved the resulting controversy, confirming that no significant association existed between thallium redistribution defects, perioperative myocardial infarction, or other adverse events in patients undergoing abdominal aortic surgery.

Combined, these two studies indicated that routine use of thallium scintigraphy was not appropriate for all vascular surgery patients but also recommended, with others, that the predictive value of thallium scintigraphy could be improved by identifying subsets of patients, quantifying scintigraphy data, and examining multiple segments, differing views, or differing coronary artery territories.[4] Subsequent studies applying quantitative techniques indicate prognostic value using these alternatives. Most recently, investigators have focused on delineating subsets of patients who may benefit from scintigraphic identification of risk status (*e.g.*, low *vs.* high) using clinical markers. For example, Eagle *et al.*[8] have delineated a subset of variables to develop a paradigm based on the clinical history. At the extremes of risk (no clinical variables *vs.* multiple variables present), outcome event rates were clearly predicted by clinical markers, with scintigraphy failing to provide additional information. However, scintigraphy provided useful information for patients at moderate risk (three or four risk factors). Thus, it appears that dipyridamole thallium scintigraphy can benefit preoperative risk assessment, and in addition, subset identification and quantitation of results should be an essential part of the assessment paradigm.

Table 1. Preoperative Risk Factors: Nonroutine Diagnostic Tests

Factor	Author, Year	
	Supported	Refuted
Exercise-stress testing		
Electrocardiography	Gage 1977, Cutler 1979, 1981, von Knorring 1986, McPhail 1988	Carliner† 1985, Gerson† 1985, 1990
Radionuclear	Jain 1985, Gerson 1985, Kopecky 1986, Freeman 1989	—
Ambulatory electrocardiography	Raby 1989, Pasternack 1989, Ouyang 1989, Mangano 1990	—
Echocardiography		
Precordial	—	Halm 1994
Stress	Lalka 1992, Poldermans 1993, Langan 1993, Tischler 1991, Davila-Roman 1993	—
Transesophageal	—	—
Radionuclear ventriculography	Pasternack 1984, 1985, Gerson 1985, Kopecky 1986, Freeman 1989	Kazmers 1988, 1988 Franco 1989, McCann 1989, McEnroe 1990, Baron 1994
Dipyridamole-thallium scintigraphy	Boucher 1985, Brewster 1985, Cutler 1987, Leppo 1987, Eagle 1987, 1989, Lette‡ 1989, Leveinson‡ 1990, Lane‡ 1989	London 1988, Mangano 1991, Baron 1994
Magnetic resonance imaging/spectroscopy	—	—
Cardiac catheterization	Hertzer 1984, 1985, Hollier 1984	—

Adapted with permission from Mangano.[1]

† Supportive for exercise tolerance.

‡ Supportive for quantitation of scintigraphy.

Ambulatory (Holter) Electrocardiography

During normal daily activities, ST-segment changes in patients with coronary artery disease typically are asymptomatic (silent) and appear to be unrelated to increases in heart rate. Ambulatory ST-segment changes also may be associated with abnormalities in myocardial perfusion and future cardiac events. In surgical patients, preoperative Holter electrocardiography has revealed ST-segment changes in 18–40% of patients with or at risk for coronary disease, with most (>75%) events being clinically silent.[1] For example, Raby *et al.*[9] found that 38% (12 of 32) of patients with preoperative ST-segment changes had postoperative cardiac events *versus* only 1% (1 of 144) in patients without such changes. Similarly, Mangano *et al.*[10] found that preoperative ST-segment change was a univariate predictor of outcome in 474 men with or at risk for coronary artery disease. Results of multivariable analysis differed, suggesting that preoperative Holter electrocardiography may not be sufficiently sensitive to define a low-risk subgroup. Studies to date therefore indicate that Holter electrocardiography may be prognostic of outcome in certain subsets of patients with or at risk for coronary artery disease, but its role, especially relative to that of other diagnostic tests, remains to be established.

The Current Study

In this issue of ANESTHESIOLOGY, Fleisher *et al.*[11] examine the relative merits of dipyridamole thallium scintigraphy and ambulatory Holter electrocardiography for preoperative assessment of perioperative risk in 180 patients undergoing vascular and nonvascular surgery. This study has a number of strengths, including comparative technology assessment and in-hospital and long-term outcome assessment. As with most of the trials assessing this technology, blinding of the scintigraphy results was difficult and not incorporated into the study design, perhaps affecting the interpretation of findings. The study results suggest that nonquantitative dipyridamole thallium scintigraphy and ambulatory Holter electrocardiography have near-equivalent value, both

being marginally predictive of either in-hospital or long-term outcome. Using likelihood ratios (LR, which are not dependent on prevalence of disease and thus are good indicators of prognostic value), they derived positive and negative likelihood ratios indicating only borderline prognostic value ($P = 0.05$) for both tests. Their reported value (LR 1.8) is less than those of most previous investigators' (LR 2.4–5)[4,5] but greater than the likelihood ratios documented by Mangano *et al.*[6] (LR 1.4) and Baron *et al.*[7] (LR 1.0).

Also noteworthy are the results regarding positive and negative predictive value, secondary measures used to assess technology in this study. The finding of an 18% positive predictive value is less than that reported by most other studies (23–50%), most likely reflecting differences in disease prevalence and suggesting limited value for the test. The finding of a >90% negative predictive value, although appearing supportive of the value of the test, is neither supportive nor surprising. Any preoperative test should have high (*e.g.*, >90%) negative predictive value simply because less than 10% of patients have outcomes (*i.e.*, >90% will not have outcomes).

Fleisher *et al.*[11] also report "strongly positive" dipyridamole thallium findings that demonstrate an increase in likelihood ratio (LR 3.5) for in-hospital events and an association with long-term outcome. This "quantitation" of scintigraphy results (in effect delineating an at-risk subset) markedly enhanced test specificity (improving it from 65% to 89%). Consistent with Eagle *et al.*[8] and others,[4] these findings indicate that subset identification and/or quantification of testing may improve predictive accuracy. The long-term predictive accuracy demonstrated for dipyridamole thallium scintigraphy is consistent with nonsurgical studies and most likely reflects the long-term impact of the chronic disease state and not necessarily the effects of surgery, which may be transient. Finally, results of this study by Fleisher *et al.*[11] emphasize that no preoperative test is "perfect," for, even in combination, the stresses imposed by redistribution or ambulation do not completely reflect the broad spectrum of physiologic changes encountered by the surgical patient, including hypercoagulation and persistent tachycardia, neither of which are induced by dipyridamole or ambulation. Thus, this study adds to our cumulative experience, emphasizing the challenges of risk strategy development.

Conclusions

In conclusion, preoperative assessment is the cornerstone of perioperative management of the high-risk patient undergoing surgery. Multiple tests exist and evolve as our understanding of the etiologies of adverse outcome changes. Because no single test can encompass the array of historical and preoperative clinical markers or the myriad pathophysiologic changes occurring during the prolonged perioperative period, we must attempt to devise paradigms that will permit us to effectively identify subsets of patients who will benefit from such testing, as well as the specific type of test(s) that are most meaningful for each subset. Perhaps equally important is defining subsets of patients in whom testing is not effective. Large-scale trials assessing testing technologies are essential to determine their true prognostic value and, in the present (and likely future) cost-containment economy, to ensure their cost-effectiveness.

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References

1. Mangano DT: Perioperative cardiac morbidity. ANESTHESIOLOGY 72:153–184, 1990
2. National Center for Health Statistics: Health United States 1988: Public Health Service. Washington, D.C., U.S. Government Printing Office, 1989. DHHS publication (PHS) 89–1232:10–17, 66, 67, 100, 101, 1989
3. Mangano DT: Perioperative cardiac morbidity—epidemiology, costs, problems, and solutions. West J Med 161:87–89, 1994
4. Mangano DT, Goldman L: Preoperative assessment of the patient with known or suspected coronary disease. N Engl J Med 333:Dec 28, 1995
5. Boucher CA, Brewster DC, Darling RC, Okada RD, Strauss HW, Pohost GM: Determination of cardiac risk by dipyridamole-thallium imaging before peripheral vascular surgery. N Engl J Med 312:389–394, 1985
6. Mangano DT, London MJ, Tubau JF, Browner WS, Hollenberg M, Krupski W, Layug E, Massie B, SPI Research Group: Dipyridamole thallium-201 scintigraphy as a preoperative screening test: A re-examination of its predictive potential. Circulation 84:493–502, 1991
7. Baron JF, Mundler O, Bertrand M, Vicaut E, Barré E, Godet G, Samama CM, Coriat P, Kieffer E, Viars P: Dipyriamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med 330:663–669, 1994
8. Eagle KA, Coley CM, Newell JB, Brewster DC, Darling RC, Strauss HW, Guiney TE, Boucher CA: Combining clinical and thallium data

optimizes preoperative assessment of cardiac risk before major vascular surgery. Ann Intern Med 110:859–866, 1989

9. Raby KE, Goldman L, Creager MA, Cook EF, Weisberg MC, Whittemore AD, Selwyn AP: Correlation between preoperative ischemia and major cardiac events after peripheral vascular surgery. N Engl J Med 321:1296–1300, 1989

10. Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM, SPI Research Group: Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. N Engl J Med 323:1781–1788, 1990

11. Fleisher LA, Rosenbaum SH, Nelson AH, Jain D, Th Wackers FJ, Zaret BL: Preoperative dipyridamole thallium imaging and ambulatory electrocardiographic monitoring as a predictor of perioperative cardiac events and long-term outcome. ANESTHESIOLOGY 83: 906–917, 1995