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PREOPERATIVE ASSESSMENT OF CARDIOVASCULAR RISK PRIOR TO NON-CARDIAC SURGERY

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I. DEFINITION OF THE PROBLEM

Twenty five million patients in the United States undergo noncardiac surgery annually (Ref. 1) with approximately 50,000 (0.2%) experiencing perioperative myocardial infarctions(Ref. 2). The average cost per in-hospital myocardial infarction is $12,000 yielding a total cost of 600 million dollars annually due to perioperative myocardial infarction. Furthermore,forty per cent (20,000) of these patients will die from their cardiac events (Ref. 2) and none of these patients are candidates for contemporary myocardial infarction management, i.e., thrombolytic therapy, due to recent surgery.

One in four Americans has some form of cardiovascular disease (Ref. 3) and 10% of the population is over 65. Of the 25 million noncardiac procedures performed, one million patients will have definite evidence of coronary artery disease (e.g., angina or pathological Q waves) , 3 million will have positive risk factors for coronary artery disease and 4 million will be over the age of 65. (Ref. 2) Twenty-five per cent of the non-cardiac procedures are identified as major and include intra-abdominal operations, major vascular procedures, thoracic, neurologic and orthopedic cases. [See Figure 1]

Because of the aging of the population and the development of improved medical and surgical approaches to manage cardiac disease, more patients with severe cardiac disease are alive and well and are presenting for noncardiac procedures. As a consequence, the necessity for cardiac assessment prior to surgery is increasing.

The major cardiac problems to be dealt with at the time of surgery are ischemic heart disease, congestive heart failure, or serious arrhythmias. These entities will therefore encompass the bulk of this discussion.

II. MAGNITUDE OF THE PROBLEM

The overall recognized infarction rate after noncardiac surgery is <1% (Ref 2, 4). This would suggest that the "problem" is of limited scope and magnitude. Moreover, it also attests to the safety and effectiveness of anesthetic techniques in contemporary medicine. Unfortunately, certain patient populations and certain procedures are associated with higher than anticipated risks for cardiac complications and as a consequence represent situations that should undergo careful preoperative assessment. The most worrisome populations are the elderly and those with pre-existing cardiac disease. Those procedures that subject the patient to highest risk include vascular, major intraabdominal and intrathoracic procedures.

An area where the problem of associated coronary artery disease is most worrisome is in the setting of peripheral vascular disease. Initially recognized in 1939 and now well established, the incidence of clinical coronary artery disease in patients undergoing surgery for peripheral vascular disease is approximately 50% (Ref 5,6,7). In a series of 1000 consecutive patients from the Cleveland Clinic, of those patients *without* clinically suspected coronary disease, 37% had important coronary artery disease as demonstrated by angiographic criteria (i.e., >70% stenosis of one or more coronary arteries)[Ref. 6]. Seventy-eight per cent with clinically suspected disease had angiographically demonstratable coronary disease. Thirty-four per cent of those with clinically suspected disease and 14% of those without clinically suspected disease required surgical therapy for severe coronary artery disease. (Ref. 6)

Even with clinically stable coronary disease, up to 21% of patients operated on for peripheral vascular indications will experience clinical events (Ref. 8), esp., myocardial infarctions. Fifty per cent of these post-operative myocardial infarctions are fatal, an event rate that far exceeds that of isolated myocardial infarction and approximates that of the most severe infarcts (Killup Class IV). It is therefore not acceptable to proceed with major noncardiac surgery,e.g., vascular procedures, when the likelihood of a perioperative event is excessive.

Beyond the acute perioperative period, the presence of coronary artery disease in survivors of peripheral vascular surgery significantly reduces survival compared to the general population. Approximately 50% of late deaths in patients with peripheral vascular disease are cardiac (Ref. 5,9). Therefore, in this population, associated coronary artery disease contributes to both short and long-term morbidity and mortality.

III. CARDIOVASCULAR PATHOPHYSIOLOGY OF ISCHEMIA

Myocardial ischemia at a basic level is the outcome of myocardial oxygen consumption out of proportion to coronary blood flow. Major determinants of myocardial oxygen consumption include heart rate, contractile state and wall tension. The minor components include basal energy metabolism and electrical activity (arrhythmias)[Ref 10].

At rest the myocardium receives 10% of total cardiac output. Arteriovenous oxygen difference across the cardiac bed is near maximal at rest so increased delivery of O_2 must occur via increased coronary perfusion. In the absence of coronary atherosclerosis, coronary blood flow can increase by 600% principally through a very precise autoregulation of coronary vasomotor tone (Ref 11). These profound effects are likely to be mediated by myocardial metabolites, esp., adenosine and hypoxia (Ref 10,12). This system is especially characteristic in coronary arteriolar vessels as opposed to epicardial coronary arteries. In addition to the decrease in epicardial blood flow and drop in coronary perfusion pressure caused by coronary atherosclerosis, there is an even greater problem with loss of coronary vasomotor regulation (Ref 13). This limits increases in coronary blood flow via vasodilation.

Heart rate is another important variable. Myocardial blood flow is not constant during the cardiac cycle. Systole causes extrinsic myocardial compression which impairs delivery of blood via intramural and subendocardial vessels. The majority of perfusion therefore occurs during diastole(Ref 14). Given that the duration of diastole shortens with increased heart rate, episodes of tachycardia will make the myocardium susceptible to ischemia.

The basal metabolic rate of cardiac muscle is not constant but rather varies according to underlying cardiac pathology or lack thereof. Normally, resting myocardium consumes 2ml O_2/min per 100 gm tissue. Wall tension however is a variable of O_2 consumption and is expressed by LaPlace's Law:

"... the average circumferential wall stress is related directly to the product of intraventricular pressure and internal radius and inversely to wall thickness".

This is expressed as :

$$\text{wall tension} = (Pb/h)\ X\ (1\text{-}b^2/2c^2)\ \text{ or } Pa/\ 2h$$

[ellipsoidal ventricle and spherical ventricle].

{P=pressure; h=wall thickness; a = radius of endocardial surface; b=minor ventricular axis; c=major ventricular axis}.(Ref 15)

Therefore a large dilated ventricle with thin ventricular walls and elevated end-diastolic pressure (e.g., congestive heart failure due to systolic dysfunction; severe valvular regurgitation; dilated cardiomyopathy) has the greatest basal metabolic rate. Similarly, the ventricle with thickened walls (hypertensive heart disease with left ventricular hypertrophy; hypertrophic cardiomyopathy) will also exhibit increased metabolic rates. In these settings when O_2 demand is increased, the concomitant presence of significant coronary atherosclerosis will further increase the risk of myocardial ischemia.

When ischemia occurs, myocardial metabolism shifts to anerobic mechanisms and cardiac lactate production is greatly increased. Prolonged ischemia leads to decreases in ventricular compliance which eventually causes ventricular dysfunction (Ref 14). This is initially manifest as diastolic dysfunction. This will cause an abrupt increase in venticular filling pressures follwed by ventricular dilation, systolic dysfunction and cardiovascular failure.

Ideally, monitoring of LV end-diastolic pressure(LVEDP) would identify early ischemia during operation and allow for appropriate intervention but this is not acceptable because of the need for intra-arterial cannulation and the risk of thrombosis and embolization. The measurement of pulmonary capillary wedge pressure (PCWP) is used as an indirect measure of LVEDP but rests on the assumption that the mitral valve is not stenotic and that left atrial anatomy is normal (e.g., cor triatriatum would yield spurious values). Attempts to follow pulmonary artery diastolic pressure (PAD) are even less reliable because one must also assume that the pulmonary circulation is normal since pulmonary hypertension will cause a disparity between PAD and PCWP measurements. Levine et al. at this institution have demonstrated that central venous pressures approximate PCWP in normal adults without cardiovascular disease, specifically without left ventricular disease. However, in patients with known left ventricular disease, the CVP measurement cannot be used to approximate left-sided pressures because of vastly different ventricular compliances between the right and left ventricles in disease states (Ref 16). In Cohen's review of 130 patients undergoing major vascular procedures with Swan-Ganz catheters in place, fifty per cent of patients had PCWP measurements significantly higher than CVP measurements. (Ref 17)

Typical Causes for Perioperative Increases in Myocardial O2 Demand

1. tachycardia
2. hypertension
3. anemia
4. stress
5. sympathomimetic drugs

Typical Causes for Perioperative Decreases in Myocardial O2 Supply

1. hypotension
2. tachycardia (i.e., decreased diastolic filling)
3. hypoxemia
4. acute coronary artery thrombosis or spasm

IV. SURGICAL MORBIDITY/MORTALITY DUE TO CARDIAC DISEASE

The overall incidence of myocardial infarction after noncardiac surgery in the general population is 0.7%(Ref 2,5). For specific populations however this risk is substantially increased: vascular surgery is associated with a 15% infarction rate(Ref 2,6) and patients with recent prior infarcts have reinfarction rates up to 37% after noncardiac surgery(Ref 18). The incidence could be higher since the diagnosis of post-operative myocardial infarction is not always evident. A number of these events are silent and pathologically are subendocardial. The "silent" character of these events may be due to residual anesthetic effects, competing pain stimuli or underlying co-existent pathology (e.g., diabetes).

Pathophysiologically, actual <u>infarction</u> is due to complete occlusion of a coronary vessel (Ref 19). Since we now know that 90% of all infarctions are due to coronary artery thrombosis(Ref 19), a mechanism must be postulated that is present during the peri-, intra- or post-operative period that precipitates thrombosis. Simply altering the supply/demand equation unfavorably is not sufficient. It has been proposed that shear forces within the coronary vessels are increased in the perioperative period (Ref 2). This promotes plaque rupture of pre-existent atherosclerotic lesions leading to the release of platelet mediators, e.g., serotonin and thromboxane, and the eventual development of increased platelet aggregation (Ref. 20). Surgery may cause changes in blood viscosity and the tendancy towards thrombosis. Stress associated with surgery may also elicit the release of catecholamines and other vasoactive substances with vasoconstrictor properties.(Ref 2,20)

The development of <u>congestive heart failure</u> (without concomitant myocardial infarction) is estimated to vary from 3-5% of patients undergoing non-cardiac surgery(Ref 18, 21). The incidence is highest in patients with prior myocardial infarction and in the older patient. The pathophysiology includes ischemia, transient papillary muscle dysfunction, and changes in afterload and preload as a result of peri-operative events. Both endogenous release of catecholamines during surgical stress and exogenous administration of catecholamines contribute to elevations of afterload (Ref 22). Positive pressure ventilation may lead to reductions in venous return and subsequent reductions in cardiac output. Post-operative infection, acidosis, alkalosis and anesthetic agents all represent myocardial depressants. A particularly worrisome problem occurs in the patient with chronic heart failure who has significant secondary pulmonary hypertension. The risk of right ventricular failure is increased and may lead to biventricular dysfunction. Management issues for the patient with CHF will be discussed below.(Also, see Ref. 22)

Although reports of associated arrhythmias during the perioperative period vary widely, the incidence of serious arrhythmias ranges from 1-6%.(Ref 2, 23) The administration and withdrawal of anesthesia is associated with a nearly 50% incidence of supraventricular or ventricular arrhythmias(Ref 23). When serious arrhythmias do occur, immediate consideration must be given to electrolyte abnormalities, acid-base status and oxygenation. Possible myocardial ischemia and infarction must then be considered.

V. BENEFIT/MORTALITY OF REVASCULARIZATION

The decision to proceed with coronary artery bypass surgery prior to major non-cardiac surgery represents the crux of the problem with pre-operative assessment.

Clearly patients with multi-vesssel disease, reduced LV function and active ischemia derive benefit from surgical revascularization as compared to medical therapy. The European Coronary Surgery Study showed 8 year survival rates of 85% for patients with peripheral vascular disease and coronary artery disease treated with surgery and only 52% survival for those treated medically (Ref. 24). Patients without peripheral vascular disease who were treated medically had an 81% survival rate.

For patients who have prior coronary artery bypass surgery, their operative mortality for major non-cardiac surgery is reduced to 1-1.5%(Refs. 5,7,40). These data would seemingly support revascularization prior to major non-cardiac surgery.

Unfortunately, coronary revascularization in the patient with peripheral vascular disease is not benign. As these patients are usually >60 years old, their cardiac surgery is complicated by both advanced age and peripheral vascular disease. In the CASS Registry, patients >65 experienced a 5.2% surgical mortality(Ref 25). The Mayo Clinic has reported an 11% mortality in octagenarians which increases to 16.7% in the setting of peripheral vascular disease(Ref 26). In Hertzer's series of 1000 consecutive patients at the Cleveland Clinic with peripheral vascular disease, the CABG mortality rate for those with peripheral vascular disease was 5.2% (Ref 6).

It is critical to note that in patients with suspected coronary artery disease operated on for peripheral vascular indications without prior coronary revascularization, the operative mortality is 6.8%(Ref. 5). Therefore the patient faces similar operative risks with CABG prior to vascular procedures or with vascular procedures without prior CABG.

VI. IDENTIFICATION OF THE PATIENT AT RISK

Initial attempts to identify those patients at increased risk for post-operative cardiac complications invovled retrospective analysis of surgical cases.

Goldman identified the first such constellation of pre-operative clinical parameters associated with adverse surgical outcomes(Ref 21, 27,28). Principle among these pre-operative clinical indicators were: 1.) previous myocardial infarction; 2.) congestive heart failure; 3.)arrhythmias; 4.) advanced age and 5.) type of surgery.

Those patients with a myocardial infarction within the preceding six months before non-cardiac surgery experienced a 30% reinfarction rate at three months and a 15% reinfarction rate from 3-6 months (Ref 27). Other investigators have described a reinfarction rate of 36% within three months of a prior myocardial infarction and 26% within six months(Ref 18). Previous myocardial infarction represents an even greater risk if intrathoracic, intraperitoneal or aortic procedures are contemplated.

Congestive heart failure represented a major risk for cardiac complications due to non-cardiac surgery as well. The likelihood of developing post-operative pulmonary edema was significantly related to physical findings of a third heart sound and jugular venous distention and to symptoms of increasing severity based on the New York Heart Association classification. Table I illustrates Goldman's original data on the likelihood of developing post-operative pulmonary edema based on preoperative signs and symptoms of congestive heart failure.

TABLE I

CORRELATION BETWEEN SIGNS AND SYMPTOMS OF PREOPERATIVE HEART FAILURE AND PERIOPERATIVE PULMONARY EDEMA AFTER NONCARDIAC SURGERY

no history of CHF	2%
compensated CHF (no evidence by exam or CXR)	6%
left heart failure by clinical exam or CXR findings	16%
jugular venous distention and signs of left heart failure	30%

third heart sound gallop	35%
symptoms by NYHA class	
Class I	0
Class II	7%
Class III	6%
Class IV	25%

[adopted from Goldman et al. Medicine 1978; 57:357-370]

Preoperative arrhythmias predicted an increased risk for adverse post-operative outcomes in Goldman's original data but the events noted were not recurrent arrhythmias but rather ischemic episodes and/or heart failure. Therefore the presence of arrhythmias serve primarily as a marker of ventricular dysfunction. New perioperative supraventricular tachycardia occurred in 6% of patients after intrathoracic, intraperitoneal or aortic procedures. See Table II.

TABLE II

RISK OF CARDIAC COMPLICATIONS AFTER NONCARDIAC SURGERY

	Intrathoracic, intraperitoneal or aortic procedures	other major noncardiac procedures
New perioperative SVT	6%	2%
Pulmonary edema	5%	0.4%
perioperative myocardial infarction	2.5%	1%
Cardiac death	2.5%	1%

[adapted from Goldman et al., 1978]

In Goldman's data, the risk of a perioperative cardiac event was increased tenfold for patients older than 70. Complications were also four times more likely for emergent procedures as compared to elective procedures.

These data were ultimately tabulated into Goldman's landmark multifactorial index score to estimate cardiac risk in noncardiac surgery. This has served as a benchmark among internists for the preoperative assessment of surgical patients. It should be recognized however that the data were derived retrospectively and the population of 1001 patients represents a reference population that may have higher or lower risks of cardiac disease than individual patients being evaluated for surgery. This is particularly the case for operative procedures for patients at highest risk, i.e., vascular surgery cases. This is not a shortcoming of Goldman's original work but rather an expression of Bayes' theorem---

... the likelihood of a true positive test or actual disease is both a function of the sensitivity of the test <u>and</u> the incidence of the disease in the population tested.

* Therefore in populations with an expected higher incidence of coronary disease or congestive heart failure, one <u>cannot</u> rely on the Goldman criteria.
For applicable patients, Table III reviews the classic Goldman criteria:

<u>TABLE III</u>

MULTIFACTORIAL INDEX SCORE TO ESTIMATE CARDIAC RISK IN NONCARDIAC SURGERY

	POINTS
third heart sound or jugular venous distention on preoperative exam	11
Q wave or non-Q wave myocardial infarction within six months prior to operation	10
Premature ventricular beats, >5/min; documented at any time	7
Rhythms other than sinus or presence of premature atrial contractions	7
Age > 70	5
Emergency operation	4
Intrathoracic, intraperitoneal or aortic sites of surgery	3
Important valvular aortic stenosis	3
Poor general medical condition*	3

*defined as one or more of the following: potassium <3.0meq/L; HCO3 <20meq/L; BUN >50mg/dL; Cr >3.0 mg/dL; pO2 <60mmHg; pCO2 >50mmHg; elevated SGOT.

SCORING GOLDMAN CLASS	NONE OR MINOR CARDIAC EVENTS	LIFE-THREATENING EVENTS	DEATH
Class I; 0-5 points; low-risk	99%	0.7%	0.2%
Class II; 6-12 points	93%	5%	2%
Class III; 13-25 points	87%	11%	2%
Class IV; >26 points	22%	22%	**56%**

Although not well validated, this index continues to represent one of the principle mechanisms to assess preoperative risk in general surgical populations. In one series of 1000 patients > 70 years old who underwent noncardiac surgery, 29 of 34 post-operative deaths were in Goldman class III or IV.(Ref. Weathers LW and Paine R. '81).[Ref. 29]

In 1986, Detsky et al prospectively evaluated a modified version of the Goldman criteria by adding additional variables, simplifying the scoring and using particular risks for specific surgical procedures (Ref 30,31). The modified index is indicated below (table IV):

<u>TABLE IV</u>

MODIFIED MULTIFACTORIAL INDEX (DETSKY et al)

Variable	**Points**
myocardial infarction within 6 months	10
myocardial infarction after 6 months	5
class III angina	10
class IV angina	20
unstable angina within 3 months	10
pulmonary edema within one week	10
any prior history of pulmonary edema	5
critical aortic stenosis (determined by objective criteria)	20
PAC's or rhythm other than sinus on pre-operative ECG	5

PVC's >5/min	5
poor general status (same definitions as Goldman et al)	5
age > 70	5
emergency operation	10

An important contribution of the Detsky scoring method was the inclusion of the pretest probability of a cardiac event for the planned operation and an emphasis that this may vary from procedure to procedure and more importantly from institution to institution. This allows one to adjust for particular expertise with certain procedures and inexperience with others. By calculating this pretest probability of disease, a more accurate assessment of cardiac risk is theoretically possible. Typical pretest probabilities for cardiac death, nonfatal myocardial infarction and nonfatal pulmonary edema at Toronto General Hospital (tertiary care referral type) included: 13.2% for vascular procedures; 13.6% for orthopedic procedures; 8% for intrathoracic and intraperitoneal procedures; 2.6% for head and neck procedures; and 1.6% for TURP and cataract surgery.

A nomogram is then used to integrate the index score from the above table and the pretest probability for the planned procedure yielding a posttest probability of a postoperative cardiac event. [See Figure 2]. In their series of 455 consecutive patients this revised index was evaluated prospectively and found to adequately predict postoperative outcomes in general surgical populations (Ref 31). However, in higher risk populations, this scoring system has also demonstrated significant limitations(Ref 32). It has been due to the limitations of these and other systems (Dripps [Ref 33], American Society of Anesthesiologists[Ref 34], Cooperman[Ref 35]) that other modalities have been sought to improve preoperative assessment of patients at risk for cardiac complications.

VII. PREDICTORS OF POOR OUTCOME

PREOPERATIVE FACTORS:

The clinical history remains a major contributor to the assessment of cardiac risk prior to planned non-cardiac surgery. As previously stated, advanced age, documented prior myocardial infarction, especially recent infarctions, and congestive heart failure relate well to increased operative risk. Additionally, preoperative electrocardiographic abnormalities, evidence of ischemia on stress testing or ambulatory monitoring, and left ventricular dysfunction all add substantially to the preoperative assessment of patients undergoing noncardiac surgery. The presence of one or more of these factors is often enough to warrant an altered surgical approach, e.g., invasive perioperative monitoring, less aggressive procedure, or conservative care.

congestive heart failure

The presence of congestive heart failure increases the cardiac risk of noncardiac surgical procedures (Ref. 21). The clinical diagnosis can be easily made by observing a combination of usual signs and symptoms consistent with systemic venous hypertension, pulmonary venous congestion and reduced cardiac output. Although the diagnosis is not difficult to establish, it is disturbing that even among experienced observers the correlation of physical findings with hemodynamic evidence of heart failure is poor.

Stevenson has evaluated the reliability of physical findings in a referral population of patients with chronic CHF(Ref 36). She demonstrated that the combination of rales, edema and elevated jugular venous pressures has only a 58% sensitivity for the detection of patients who hemodynamically will demonstrate pulmonary capillary wedge pressures of >22mmHg. Specificity however was 100% (i.e., no false postives but an unacceptable number of false negatives). Forty-four per cent of the patients studied with PCWP $\geq$ 35mmHg had no physical evidence of congestion. A narrow pulse pressure did correlate with a cardiac index less than 2.2 L/min/m2 and 96% of patients with chronic heart failure demonstrated a third heart sound. As a consequence, it is recommended that the preoperative physical exam in patients with chronic heart failure should encompass a search for evidence of congestion, (rales, JVP elevation, edema), as well as direct evidence of LV dysfunction, (S3, narrow pulse pressure).

electrocardiography

Preoperative electrocardiography is mandated in many medical centers at considerable cost. Not all data is entirely supportive of its use however. In Goldman's original study (Ref. 21, 27), a host of electrocardiographic abnormalities were analyzed and none were found to be independently related to postoperative cardiac events in a multivariate analysis. However, Carliner et al. in a series of 200 patients undergoing noncardiac surgery demonstrated that ST/T wave abnormalities, left ventricular hypertrophy and pathological Q waves were related to postoperative events(Ref 37). More recently, Eagle has included the presence of pathological Q waves as one of the five risk factors for cardiac events after non-cardiac surgery(see discussion below, Ref 38).

exercise electrcardiography

For those patients who are able to exercise, the exercise ECG can predict those at high and low perioperative risk. Patients who can attain >75% predicted heart rate response to exercise at a good workload, and have a normal exercise ECG have been shown to have an extraordinarily low risk of perioperative myocardial infarction even among patients with peripheral vascular disease (Ref. 39). Among patients with postive ECG stress tests prior to noncardiac surgery, up to 27% will experience postoperative myocardial infarctions (Ref. 40).

ambulatory electrocardiographic monitoring

The findings of preoperative ischemia on ambulatory ECG monitoring ("Holter" monitoring) has also been shown to predict postoperative cardiac events. Thirty-seven per cent of patients with spontaneous episodes of ischemia on preoperative monitoring experienced postoperative events compared to less than 1% of those without post-operative ischemia (Ref. 41). In Raby's study, the sensitivity of ambulatory monitoring for predicting a post-operative event was 92% and the specificity was 88% (Ref. 41). Clinical correlates of preoperative ischemia included advanced age, positive risk factors for coronary artery disease, prior history of angina, myocardial infarction, or bypass surgery and congestive heart failure.(Ref 41)

left ventricular dysfunction

Objective measures of left ventricular function prior to noncardiac surgery yield important information regarding the likelihood of perioperative events.

Pasternack et al (Ref 42) in a series of 100 patients undergoing vascular surgical procedures demonstrated the following correlation of perioperative events with ejection fractions:

EJECTION FRACTION	INCIDENCE OF PERI-OP MYOCARDIAL INFARCTION
>56%	0%
36-55%	19%
<36%	75%

Although these data emanate from a high-risk population, it is evident that even for patients undergoing highest risk operations, the presence of normal ventricular function at rest predicts a favorable post-operative cardiac event rate. For general surgical procedures, a 75% incidence of cardiac events is probably overestimated.

INTRAOPERATIVE AND POSTOPERATIVE FACTORS

In addition to preoperative markers of increased perioperative risk, *intraoperative and postoperative* events may be as important or moreso in predicting cardiac morbidity/mortality.

ischemia

The Perioperative Ischemia Research Group has identified that electrocardiographic evidence of ischemia in the first 48 hours post-operatively imparts a 9.2-fold increase in the odds of an ischemic event. In a series of 474 patients 41% had post-opeative ischemic changes and 97% of these were clinically silent. N.B., that 90% of these ischemic episodes were <u>not</u> detected by the clinical staff.(Ref 43)

In a separate study of a small number of high-risk patients, 53% of patients with silent ischemia experienced post-operative events of either myocardial infarction or congestive heart failure (Ref. 44). Episodes of silent ischemia are quite common in the population undergoing vascular procedures. Pasternack et al. have reported on 200 consecutive patients undergoing carotid or vascular procedures(Ref 45). Greater than 60% of patients experienced ischemic changes during the perioperative period but the event rate was decidely less than the previously identified rates of 35-50%. Postoperative events were most strongly related to the frequency of ischemic episodes and the duration of ischemic episodes as a per cent of total time monitored.

The disparate results of the detection of ischemia by ECG criteria from one study to the next points out the limitation of assessing perioperative ischemia as a marker for cardiac events. First, the electrocardiographical definition of ischemia varies from 0.5-2.0mV depending upon the investigator. There is no consistency of technique in monitoring. Single lead (V5), three lead, four lead and 12 lead monitoring have all been described. Obviously sensitivity will vary inversely with the amount of ST displacement accepted as ischemia and will vary directly with the number of monitored leads. All ECG monitoring systems employ filters to eliminate noise and artifact but these filters may also eliminate ST changes or distort the ECG baseline. Moreover certain operations will make ECG location suboptimal (e.g., thoracic procedures). (See Ref. 10)

Because of these limitations, we do not routinely use continuous ECG ambulatory monitoring to assess preoperative ischemia and only use standard telemetry available in ICU settings in the post-operative period.

intraoperative echocardiography

Theoretically, transesophageal echocardiography will detect new segmental wall motion abnormalities consistent with intraoperative cardiac events. Available data are limited and inconsistent. Wall motion abnormalities have been described including severe hypokinesis that are indicative of myocardial ischemia (Ref. 46). However, others have been unable to demonstrate a consistent relationship of WMA with ECG changes or hemodynamic events suggesting either clinically insignificant ischemic episodes, noncardiac disturbances of ventricular synergy or technical limitations. (Ref. 47,48)

hemodynamic alterations

Additional markers of poor post-operative outcome include: post-operative tachycardia; intraoperative hypotension (greater than 20% reduction); mean arterial pressure/heart rate ratio < 1; and pulmonary capillary wedge pressure >18mmHg. An often overlooked variable for assessing outcome after noncardiac surgery is the timing of cardiac events (Ref. 18). Although the greatest stress/risk appears to be at the time of operation, the actual peak incidence of post-operative events is on the third thru fifth post-operative day.

Accordingly, the highest risk patients should undergo prolonged post-operative monitoring. (Ref 18)

SUMMARY OF POOR PREDICTORS OF POST-OPERATIVE OUTCOME

PREOP

1. CLINICAL EVIDENCE OF PRIOR MYOCARDIAL INFARCTION OR CONGESTIVE HEART FAILURE

2. MEASURED LEFT VENTRICULAR EJECTION FRACTION <0.35

3. POSITIVE EXERCISE ECG STRESS TEST

4. EVIDENCE OF SPONTANEOUS EPISODES OF ISCHEMIA

INTRAOP AND POSTOPERATIVE

5. EVIDENCE OF ISCHEMIA BY ECG MONITORING

6. ADVERSE HEMODYNAMICS
- **drop in blood pressure > 20%**
- **increase in heart rate post-op by 20%**
- **elevated left ventricular filling pressures, >18mmHg**

7. POST-OPERATIVE MONITORING < 48 HOURS

VIII. CARDIAC RISK ASSESSMENT IN HIGH RISK PATIENTS

Despite the foregoing data including multifactorial risk scoring and predictors of poor outcome, certain subsets of patients remain with a poorly defined operative risk. This is either due to a very high incidence of pre-existing coronary disease or due to a very high risk procedure. The prototypical case is that of the patient undergoing vascular surgery, especially aortic procedures, who has no overt cardiac symptoms or signs and is unable to exercise due to claudication.

Several studies have clearly identified the limited utility of virtually all of the risk scoring systems for high-risk populations(Ref 32,49,60). Given the high cardiac morbidity and mortality of these patients it has even been suggested that all patients being considered for vascular surgical procedures undergo diagnostic cardiac catheterzation (Ref. 6). The total cost for this procedure in Dallas area hospitals is $6000(Ref 50). With 350,000 vascular procedures per year in this country, this one endeavor alone would represent an annual cost of 2.1 billion dollars. Considering the aforementioned limitations of cardiac surgery in patients with vascular disease, it would hardly seem appropriate to proceed with pre-operative cardiac catheterization in all patients.

An alternative approach has been to increase the sensitivity of the diagnosis of coronary artery disease by using perfusion imaging. Thallium (Tl)-201 is a potassium analog that is avidly taken up by myocardial tisuue in direct proportion to myocardial blood flow (Ref. 51). If injected during a time of ischemia the myocardium will not take up Tl-201 because of regional reductions in myocardial blood flow. Computer-assisted acquisition of Tl-201 uptake demontrates the spatial orientation of Tl-201 distribution and allows for fairly accurate prediction of the absence or presence of coronary disease and yields data on the likelihood of single versus multivessel coronary artery disease. For routine clinical applications, exercise stress testing with the adjunct of Tl-201 imaging has a sensitivity and specificity of approximately 85-90% in experienced laboratories.(Ref 51).

In brief, the study is performed by subjecting the patient to a stimulus, either physiologic (exercise testing, hand grip, cold pressor) or pharmacologic (dipyridamole, adenosine), that will either increase heart rate, oxygen consumption or myocardial blood flow. At a point considered to be peak exercise or peak hyperemia, a bolus of radiolabeled Tl-201 is injected and initial images of thallium distribution are obtained. Since this is a "cold" scan, defects will appear that will either represent infarcted muscle or ischemic muscle. Late imaging done at 4 hours (with possible repeat imaging at 24 hours) detects evidence of "redistribution", i.e., thallium uptake in segments that on initial studies were hypoperfused. These segments are considered to be ischemic whereas persistent defects are consistent with permanently scarred muscle (infarcted).

For patients unable to exercise, pharmacological equivalents of stress testing are available. The original agent employed was dipyridamole, either oral or the recently released intravenous form. Dipyridamole causes coronary vasodilation by blocking the uptake and metabolism of adenosine which is a potent mediator for coronary vasodilation(Ref 52). The administration of dipyridamole followed by Tl-201 imaging has been reported to have a diagnostic sensitivity equivalent to that of exercise testing with Tl-201 (Ref. 53). More recently the direct administration of adenosine has been popularized and purportedly yields better quality images and a diagnostic sensitivity of 90% (Ref 54, 55).

The first report of the utility of dipyridamole-Tl-201 imaging was from Boucher et al. at the Massachusetts General Hospital. In this major study, 54 patients undergoing vascular surgical procedures underwent dipyridamole-Tl-201 testing. Fifty per cent of the patients with reperfusion abnormalities experienced post-operative cardiac events compared to **no events** in the patients with either normal scans or fixed defects suggestive of scar only and not ischemia (Ref 56). Importantly, none of the events would have otherwise been predicted by preoperative clinical factors.

In a study of 70 patients evaluated prospectively who were undergoing aortic surgery, the relative benefits of routine exercise stress testing versus dipyridamole Tl-201 imaging were compared. 10/60 patients had a positive stress test and 31/60 had myocardial ischemia on Tl-201 imaging. Of 50 patients with nondiagnostic stress tests results, 17 had significant cardiac complications. Only 3 of 29 patients with negative Tl-201 results had cardiac events . (Ref. 57)

Mode of Testing	Sensitivity	Specifity
Exercise Stress Testing	23%	89%
Dipyridamole Tl-201	86%	68%

Ref. McPhail et al

These data would suggest that the problem of preoperative assessment in high risk patients might be alleviated by dipyridamole-Tl-201 scans. However, the low specificity of the test results in a number of patients with abnormal scans who do not experience adverse post-operative cardiac events but may still be required to undergo pre-operative catherterization based on the abnormal scan.

It has been suggested however that further refinement of the selection of patients to be tested can be achieved by combining clinical characteristics and thallium results thus improving the specificity of thallium testing. Eagle et al. reported on 111 consecutive patients undergoing vascular surgery. The first 61 patients all had dipyridamole-Tl-201 testing prior to operation. Forty-four per cent of the patients with reversible defects experienced post-operative cardiac events while none of those with normal scans experienced events. The remaining 50 patients were then stratified into low-risk versus high-risk based on the presence of only one of the following clinical indicators: previous myocardial infarction; angina; congestive heart failure; and diabetes. There were no clinical events in the patients without any of the foregoing clinical markers. Nearly 50% of those with one or more clinical indicators had a postive Dipyridamole-Tl test and 50% of those patients experienced clinical events.(Ref 58)[See Figures 3,4]

The addition of clinical information therefore improved the specificity of the test (i.e., fewer false postive events). Eagle et al. expanded on these observations with a report on 254 consecutive patients who were evaluated retrospectively to identify markers of post-operative events. Five clinical variables and two dipyridamole-thallium variables were identified as markers of events (Ref. 38):

<u>EAGLE'S CLINICAL MARKERS</u>

1. Q waves on ECG
2. History of ventricular ectopy
3. Diabetes
4. Advanced age
5. Angina

<u>DIPYRIDAMOLE THALLIUM MARKERS</u>

1. Thallium redistribution
2. Ischemic ECG changes during thallium testing

With these markers, post-operative events (angina, myocardial infarction, pulmonary edema and cardiac death) occurred in 3% of patients with no clinical markers. Death was not one of the events in this group. In patients with one or two positive clinical markers, 15% experienced cardiac events and 50% of those patients with three or more clinical markers experienced post-operative events. In the group with one or two positive clinical markers, a negative thallium scan was associated with a 3% incidence of post-operative events but a postive scan was associated with a 30% incidence of post-operative events. These results are summarized in the following table (TABLE V):[Also see Figure 5]

TABLE V

ALGORITHM TO DETERMINE POST-OPERATIVE EVENT RISK

Eagle's Classification	*event risk*
no clinical indicators	3%
one or two clinical indicators normal thallium distribution	3%
one or two clinical indicators abnormal thallium distribution	30%
three or more clinical indicators	50%

Ref. Eagle KA et al. 1989.

The specificity of thallium testing for predicting a post-operative event has also been shown to be improved by analyzing both the extent of myocardial segments involved and the severity of reversibility in involved segments. Lette et al. (Ref 59) initially reported a favorable post-operative event rate in "low-risk" positive scans vs. an extraordinary event rate (80%) in "high-risk" scans in a group of 66 patients. These same authors have more recently described their results in 125 patients undergoing elective vascular procedures. None of the patients with normal thallium scans or fixed defects experienced nonfatal myocardial infarction or death. Twenty-one per cent of those with positive scans experienced events (13/62 patients). Those patients with multiple areas of reperfusion, severe intensity of reperfusion or left ventricular dilitation after administration of thallium experienced an 85% event rate compared to only 5% if the thallium abnormalities were isolated or small (Ref 60). Unfortunately, there is presently no accepted standard to assess extent or severity of reversibility and although these data are noteworthy they cannot be universally applied. However, a "markedly positive scan" from a reliable nuclear laboratory would appear to raise the level of concern for post-operative events considerably.

Although the foregoing data rely heavily on redistribution abnormalities, even the presence of fixed defects indicative of myocardial scar may be an important preoperative finding. McEnroe et al. (Ref 61) have described a high perioperative event rate (47%) even in patients with fixed defects. This may actually be representative of the less than 100% sensitivity of Thallium scanning, i.e., false negative studies. These cases are likely best explained by technical considerations and as recent data have suggested, can be overcome with thallium reinjection prior to delayed imaging and with 24 hour imaging in addition to 4 hour imaging.(Ref 62,63)

Although these data appear to be conclusive, significant questions on the appropriate use of the test remain primarily because preoperative thallium testing is expensive ($1,000/test). Recently an even more important question has been raised regarding the actual independent predictive value of the test.

Virtually all of the foregoing studies were done in an unblinded fashion and were done in a referral population of patients at increased risk. Both of these factors may have increased the sensitivity of the test substantially. Mangano et al. (Ref 64) have reported on a series of 60 unselected, consecutive patients undergoing vascular procedures all of whom had preoperative thallium studies, perioperative monitoring of myocardial ischemia with electrocardiography and intraoperative monitoring of wall motion with transesophageal echocardiography. Physicians were blinded to results of the thallium scans. Under these circumstances the sensitivity of redistribution defects on thallium scans to predict post-operative events (including ischemia determined by ECG and TEE) was reduced to 47% and the specificity remained at 66%.

These data do not however negate the overwhelming literature supporting the use of dipyridamole thallium testing. It does however point out the absolute requirement that the test be applied in the appropriate patient population, which is primarily those at intermediate risk.

Pooled data from four studies (Ref 65) using myocardial infarction or death as an endpoint in patients undergoing vascular surgery clearly demonstrates the value of preoperative risk assessment with Tl-201 scintigraphy. 575 patients experienced 54 events (9.4%) with 87% of these events correlated with redistribution defects.

IX. MANAGEMENT OF THE HIGH RISK PATIENT

The result of a careful preoperative assessment will result either in proceeding with the planned procedure, altering the procedure or foregoing the procedure because of prohibitive risk. This can represent a difficult management decision because the planned procedure is often one that is deemed to be medically necessary despite the high risk.

For the high risk patient several options are available. For the patient with symptomatic cardiac disease with multiple pre-operative risk factors and/or positive stress test or thallium results, there should be no hesitation to consider cardiac catheterization. However, *cardiac catheterization should only be performed in those patients whose clinical presentation would warrant catheterization independent of any planned or contemplated surgical procedure.* In the patient with severe coronary disease, coronary artery bypass grafting significantly reduces the subsequent post-operative cardiac event rate after noncardiac surgery. There is no data to support or refute the benefit of coronary angioplasty prior to noncardiac surgery and it therefore should be used only when it is otherwise indicated.

For the patient undergoing major noncardiac surgery without prior revascularization, several options are available:

I. Proceeding with the planned procedure

Perioperative hemodynamic monitoring is strongly advised in the high-risk patient undergoing noncardiac surgery. Mangano et. al. observed an infarction rate of 5% and a death rate of 2% in their series of 60 patients undergoing vascular procedures without prior revascularization (Ref 64). All patients underwent arterial cannulation and variations in blood pressure and heart rate were tightly controlled so that fewer than 10% of patients experienced tachycardia(>100 beats/min), hypertension (>160mmHg for > 5 min) or hypotension (<90mmHg for > 5 min).

Rao et al. have reported a reinfarction rate reduction of 36% to 6%, in patients undergoing noncardiac surgery with a prior history of myocardial infarction (Ref. 18). In this study, pulmonary artery catheterization was done and PCWP was maintained at less than 18mmHg. Cohen has reported on 130 patients undergoing major abdominal vascular procedures all of whom underwent pulmonary artery and arterial catheterization. The overall mortality rate was 1.5% (Ref.17). Seventy-three per cent of patients required vasoactive therapy to alter systemic vascular resistance, pulmonary capillary wedge pressure, or heart rate. The following hemodynamic subsets were identified:

TABLE VI

subset	measurement	assessment of cardiac function
I	cardiac index >2.5 LVSWI >40 SVR <1800	GOOD
II	cardiac index <2.5 LVSWI >40 SVR >1800	ADEQUATE
III	cardiac index <2.5 LVSWI < 40 SVR>2000	POOR

cardiac index expressed as L/min/m^2;
SVR=systemic vascular resistance, dynes-sec-cm^{-5};
LVSWI=left ventricular stroke work index {measure of LV systolic function, expressed as gm-m/m^2/beat; derived by LVSW=[(mean arterial pressure-pulm capillary wedge pressure)X stroke volume/beat X 0.0136]; normal: 45 gm-m/m^2/beat}

(Adapted from Cohen et al. Amer Jnl of Surg 146:176, 1983.)

Although these are small studies, it appears reasonable that patients at high risk should undergo careful hemodynamic monitoring at the time of surgery. Additional considerations clearly must include careful assessment for evidence of ischemia and prolonged post-operative monitoring since the highest risk of infarction is on the 3rd-5th post-operative day.

Despite its frequently recommended use, no convincing data are available to support the prophylactic use of parenteral nitroglycerin in high-risk patients(Ref 66,67). It is more efficacious to continue anti-anginal medications at the time of surgery and to reserve parenteral nitrates for documented episodes of ischemia.

II. Altering the planned procedure

When surgery is necessary in a high-risk patient, a risk-benefit ratio must be assessed. When the risk is excessive, conservative or less aggressive procedures may be desirous. For patients with vascular disease, this may include extra-anatomic bypass(Ref 40), amputation or percutaneous peripheral angioplasty. In some settings, these latter two options represent a substantial portion of vascular procedures. Tunis et al. (Ref 68) recently reported that 20% of vascular procedures done in Maryland from 1979-1989 were peripheral angioplasties and 20% were amputations.

III. Aborting the planned procedure

Although least attractive, this may reluctantly be the best option for patients at high risk who are being evaluated for non-emergent procedures. When the cause for withholding surgery is cardiac, every attempt should be made to improve the cardiac condition since it is likely that cardiac disease will limit that patient's quality and quantity of life.

X. SUMMARY AND PROPOSED ALGORITHM

The assessment of preoperative cardiac risk prior to noncardiac surgery can be one of the more challenging assignments for the Family Practitioner, Internist or Cardiologist. Although the event rate is not excessive, certain populations at higher risk do require careful assessment. The principle issues to consider are the likelihood of cardiac disease in the patient undergoing evaluation and the risk of the planned procedure.

Patients at low risk for heart disease who are undergoing low risk surgery need little more than a clinical assessement and no specific testing is required or recommended. Patients at highest risk for cardiac complications should have the indications for surgery closely reviewed and consideration given to alternative treatment options. In particular those with symptomatic cardiac disease should be considered for aggressive cardiac management prior to major noncardiac surgery. For the patient at intermediate risk, further clarification of risk can be obtained by assessing LV function and testing for either spontaneous or provocable ischemia. Surgery may then proceed with appropriate precautions or may be delayed pending resolution of newly discovered cardiac problems.

ALGORITHM

I. GENERAL SURGICAL PROCEDURES

A. Determine clinical risk by multifactorial scoring system
  rec: Detsky Score

B. Determine usual surgical outcome for planned procedure

C. Derive estimate of post-operative event rate

if low risk: proceed with operation
high risk: consider other treatment options; proceed with cardiac workup

intermediate risk: obtain assessment of LV function and stress test

LVEF > 0.35 and normal ETT: proceed with surgery
LVEF < 0.35 and abnormal ETT: treat as high risk
LVEF < 0.35 <u>or</u> abnormal ETT:proceed with cardiac workup

D. Perioperative management for intermediate risk patients
  1. careful blood pressure monitoring (intra-arterial cannulation)
  2. intraoperative electrocardiographic monitoring

3. avoidance of hypotension, tachycardia
4. prolonged post-operative monitoring

E. Perioperative management of high risk patients
1. Invasive hemodynamic monitoring
2. limitation of blood pressure and pulse variations to <10%-20%
3. Maintenance of LV filling pressures (PCWP) <18mmHg
4. Maintenance of cardiac output > 2.2 L/min/m2
5. as per intermediate risk patients

II. HIGH RISK SURGICAL PROCEDURES (e.g. VASCULAR)

A. Assess presence of following clinical markers
1. pathological Q waves
2. prior myocardial infarction
3. angina pectoris
4. ventricular ectopy
5. diabetes
6. congestive heart failure

B. Evaluate LV function

C. Determine risk as follows:
1. Low risk-no clinical markers and normal LV function
2. Intermediate risk- 1-3 clinical markers and LVEF >0.35
3. High risk- > 3 clinical markers and/or LVEF <0.35

D. Proceed as follows:
1. Low risk: *proceed with planned procedure with:*
   a. intraoperative BP and ECG monitoring
   b. prolonged post-operative ECG monitoring

2. Intermediate risk: obtain dipyridamole or adenosine Tl-201 scan
   a. normal scan or fixed defect:
      1. *proceed with procedure*
      2. monitoring as with low risk
   b. small or limited reperfusion abnormality
      1. *proceed with planned procedure*
      2. *strongly advise invasive hemodynamic monitoring*
   c. markedly positive scan:
      treat as high risk

3. High risk
    a. if cardiac symptoms are present, proceed with work-up
    b. if no cardiac symptoms consider (case by case):
        1. proceed with cardiac work-up
        2. readdress indications for surgery
        3. proceed with less aggressive surgery
        4. defer surgery
        5. consider surgery only with strict hemodynamics

Figure 1. (From Reference #2)

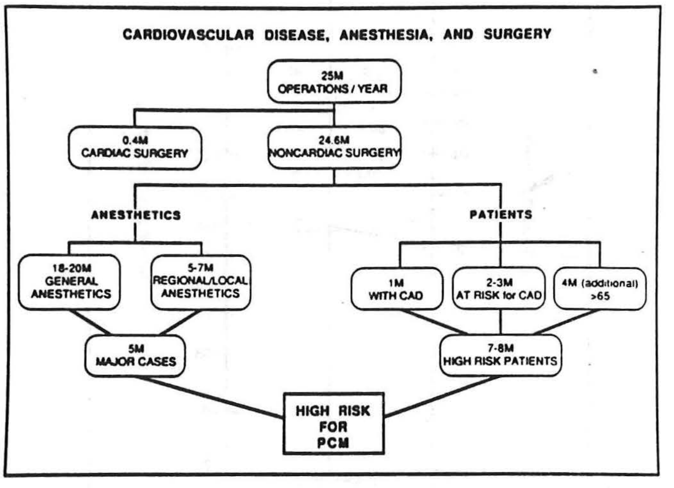


Figure 2. (From Reference #30)

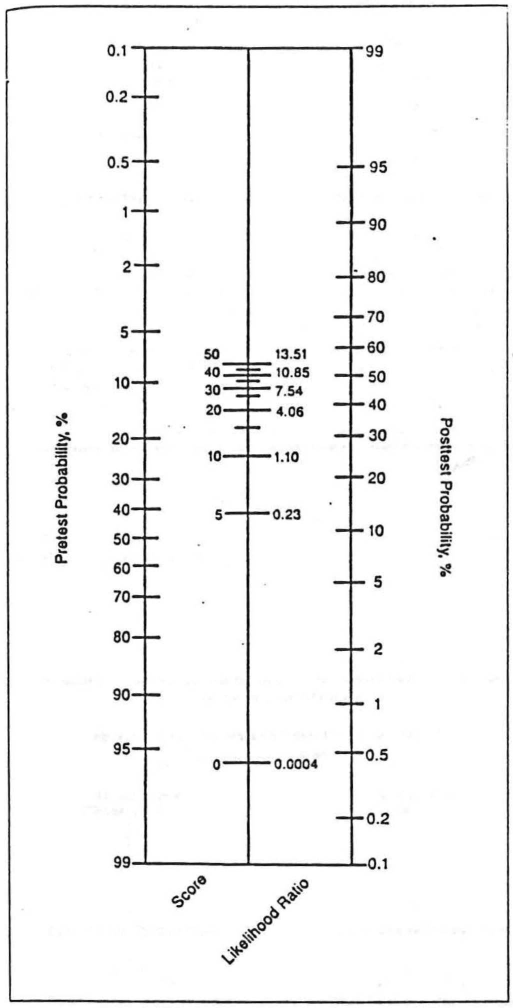


Figure 3. (From Reference #58)

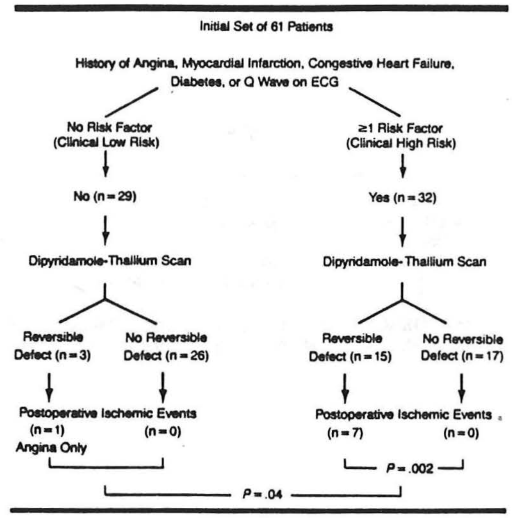


Figure 4. (From Reference #58)

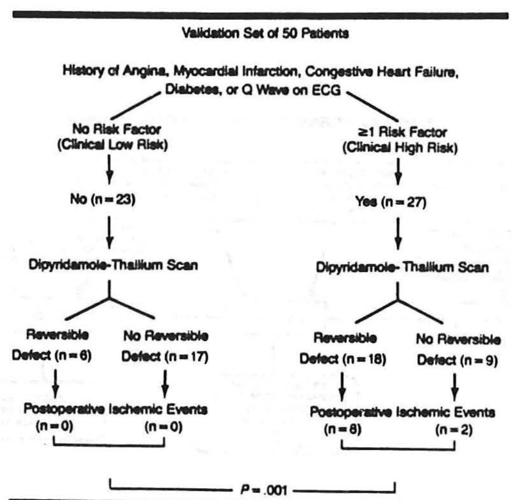


Figure 5. (From Reference #38)

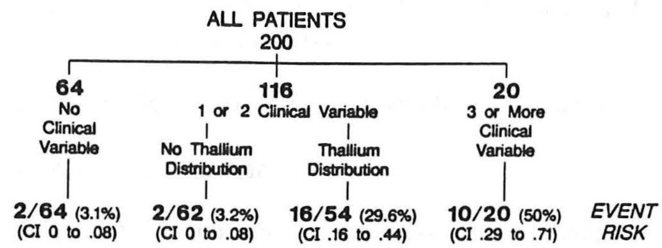
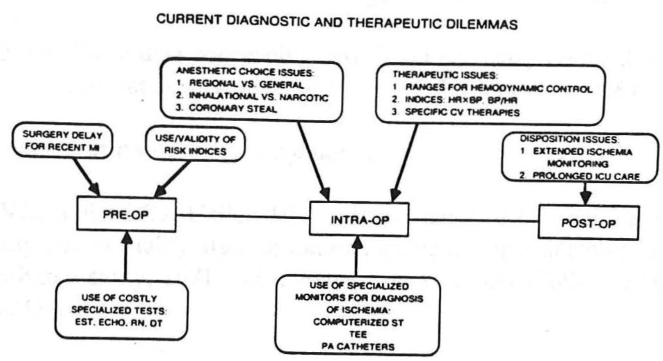


Figure 6. (From Reference #2)



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Appendix 1. Clinical scoring systems

Test	No. of points
Goldman Cardiac Operative Risk Index[21]	
History	
Age > 70 years	5
Myocardial infarction < 6 months	10
Aortic stenosis	3
Physical examination: (third heart sound, S3 gallop or signs of congestive heart failure)	11
Electrocardiogram:	
Any rhythm other than sinus	7
> 5 premature ventricular contractions/mn	7
Poor general medical condition:	3
$Po_2 < 60$	
$Pco_2 > 50$	
K+ < 3	
BUN > 50	
Creatinine > 3 (> 260 mmol/l)	
Bedridden	
Operation:	
Emergency	4
Intrathoracic or intraabdominal or aortic	3
Total points = 0 to 53	

Goldman Classification	Total Points
1	0-5
2	6-12
3	13-25
4	> 25

Test	No. of points
Detsky Modified Multifactorial Risk Index[30]	
Coronary artery disease	
Myocardial infarction within 6 months	10
Myocardial infarction more than 6 months	5
Canadian Cardiovascular Society angina	
Class III	10
Class IV	20
Unstable angina within 6 months	10
Alveolar pulmonary edema	
Within 1 week	10
Ever	5
Valvular disease	
Suspected critical aortic stenosis	20
Arrhythmias	
Rhythm other than sinus (may have APBs)	5
More than five PVCs before surgery	5
Poor general medical status	5

Age over 70 years	5
Emergency operation	10

Total score: 0 to 120

Goldman classification	Total points
1	0-15
2	16-30
3	> 30

Eagle Vascular Surgery Low Risk Clinical Markers[38]

The patient is considered to be at low risk for operation if the following five clinical markers are absent: history of angina, clinical of electrocardiographic evidence of prior myocardial infarction, diabetes, and congestive heart failure.

Cooperman Equation[35]

$P = \text{antilog}_2\ [C_1 \times X_1) + (C_2 \times X_2) + \ldots\ldots + C]$

X_1 = angina ($C_1 = 0.46$)

X_2 = congestive heart failure ($C_2 = 1.02$)

X_3 = arrhythmia ($C_3 = 0.62$)

X_4 = previous myocardial infarction ($C_4 = 0.64$)

X_5 = cerebrovascular accident ($C_5 = 1.15$)

X_6 = abnormal electrocardiogram ($C_6 = 1.25$)

Dripps-American Surgical Association Physical Status Score[33]

1 = normal healthy patient for elective operation
2 = mild systemic disease
3 = severe systemic disease with limited activity but not incapacitated
4 = incapacitating systemic disease which is a constant threat to life
5 = moribund patient not expected to survive 24 hours with or without operation

Eagle Equation[38]

Probability of postoperative event = $\dfrac{e^{score}}{1 + e^{score}}$

Calculation of score — e: base of natural logarithm

0.077 x Age - 10	
+1	if history of angina
+1.4	if Q wave on electrocardiogram
+1.2	if history of ventricular ectopic activity
+1.0	if diabetes
+1.3	if ischemic electrocardiographic changes during dipyridamole infusion
+2.3	if redistribution of thallium

Total = score

Appendix 2. Recommendations for Antibiotic Prophylaxis (Reference Circulation 83: 1175-1177; 1991.)

TABLE 1. Cardiac Conditions*

Endocarditis prophylaxis recommended
Prosthetic cardiac valves, including bioprosthetic and homograft valves
Previous bacterial endocarditis, even in the absence of heart disease
Surgically constructed systemic-pulmonary shunts or conduits
Most congenital cardiac malformations
Rheumatic and other acquired valvular dysfunction, even after valvular surgery
Hypertrophic cardiomyopathy
Mitral valve prolapse with valvular regurgitation
Endocarditis prophylaxis not recommended
Isolated secundum atrial septal defect
Surgical repair without residua beyond 6 months of secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus
Previous coronary artery bypass graft surgery
Mitral valve prolapse without valvular regurgitation†
Physiologic, functional, or innocent heart murmurs
Previous Kawasaki disease without valvular dysfunction
Previous rheumatic fever without valvular dysfunction
Cardiac pacemakers and implanted defibrillators

*This table lists selected conditions but is not meant to be all-inclusive.

†Individuals who have a mitral valve prolapse associated with thickening and/or redundancy of the valve leaflets may be at increased risk for bacterial endocarditis, particularly men who are 45 years of age or older.

Table 2. Dental or Surgical Procedures*

Endocarditis prophylaxis recommended
Dental procedures known to induce gingival or mucosal bleeding, including professional cleaning
Tonsillectomy and/or adenoidectomy
Surgical operations that involve intestinal or respiratory mucosa
Bronchoscopy with a rigid bronchoscope
Sclerotherapy for esophageal varices
Esophageal dilatation
Gallbladder surgery
Cystoscopy
Urethral dilatation
Urethral catheterization if urinary tract infection is present†
Urinary tract surgery if urinary tract infection is present†
Prostatic surgery
Incision and drainage of infected tissue†
Vaginal hysterectomy
Vaginal delivery in the presence of infection†
Endocarditis prophylaxis not recommended‡
Dental procedures not likely to induce gingival bleeding, such as simple adjustment of orthodontic appliances or fillings above the gum line
Injection of local intraoral anesthetic (except intraligamentary injections)
Shedding of primary teeth
Tympanostomy tube insertion
Endotracheal intubation
Bronchoscopy with a flexible bronchoscope, with or without biopsy
Cardiac catheterization
Endoscopy with or without gastrointestinal biopsy
Cesarean section
In the absence of infection for urethral catheterization, dilatation and curettage, uncomplicated vaginal delivery, therapeutic abortion, sterilization procedures, or insertion or removal of intrauterine devices

*This table lists selected procedures but is not meant to be all-inclusive.

†In addition to prophylactic regimen for genitourinary procedures, antibiotic therapy should be directed against the most likely bacterial pathogen.

‡In patients who have prosthetic heart valves, a previous history of endocarditis, or surgically constructed systemic-pulmonary shunts or conduits, physicians may choose to administer prophylactic antibiotics even for low-risk procedures that involve the lower respiratory, genitourinary, or gastrointestinal tracts.

Table 3. Recommended Standard Prophylactic Regimen for Dental, Oral, or Upper Respiratory Tract Procedures in Patients Who Are at Risk*

Drug	Dosing regimen†
Standard regimen	
Amoxicillin	3.0 g orally 1 hour before procedure; then 1.5 g 6 hours after initial dose
Amoxicillin/penicillin-allergic patients	
Erythromycin	Erythromycin ethylsuccinate, 800 mg, or erythromycin stearate, 1.0 g orally 2 hours before procedure; then half the dose 6 hours after initial dose
or	
Clindamycin	300 mg orally 1 hour before procedure and 150 mg 6 hours after initial dose

*Includes those with prosthetic heart valves and other high-risk patients.

†Initial pediatric doses are as follows: amoxicillin, 50 mg/kg; erythromycin ethylsuccinate or erythromycin stearate, 20 mg/kg; and clindamycin, 10 mg/kg. Follow-up dose should be one half the initial dose. **Total pediatric dose should not exceed total adult dose.** The following weight ranges may also be used for the initial pediatric dose of amoxicillin: <15 kg, 750 mg; 15–30 kg, 1,500 mg; and >30 kg, 3,000 mg (full adult dose).

TABLE 4. Alternate Prophylactic Regimens for Dental, Oral, or Upper Respiratory Tract Procedures in Patients Who Are at Risk

Drug	Dosing regimen*
Patients unable to take oral medications	
Ampicillin	Intravenous or intramuscular administration of ampicillin, 2.0 g, 30 minutes before procedure; then intravenous or intramuscular administration of ampicillin, 1.0 g, *or* oral administration of amoxicillin, 1.5 g, 6 hours after initial dose
Ampicillin/amoxicillin/penicillin-allergic patients unable to take oral medications	
Clindamycin	Intravenous administration of clindamycin, 300 mg, 30 minutes before procedure and intravenous or oral administration of 150 mg 6 hours after initial dose
Patients considered high risk and not candidates for standard regimen	
Ampicillin, gentamycin, and amoxicillin	Intravenous or intramuscular administration of ampicillin, 2.0 g, plus gentamicin, 1.5 mg/kg (not to exceed 80 mg), 30 minutes before procedure; followed by amoxicillin, 1.5 g orally 6 hours after initial dose; alternatively, the parenteral regimen may be repeated 8 hours after initial dose
Ampicillin/amoxicillin/penicillin-allergic patients considered high risk	
Vancomycin	Intravenous administration of 1.0 g over 1 hour, starting 1 hour before procedure; no repeated dose necessary

*Initial pediatric doses are as follows: ampicillin, 50 mg/kg; clindamycin, 10 mg/kg; gentamicin, 2.0 mg/kg; and vancomycin, 20 mg/kg. Follow-up dose should be one half the initial dose. **Total pediatric dose should not exceed total adult dose.** No initial dose is recommended in this table for amoxicillin (25 mg/kg is the follow-up dose).

TABLE 5. Regimens for Genitourinary/Gastrointestinal Procedures

Drug	Dosing regimen*
Standard regimen	
Ampillicin, gentamycin, and amoxicillin	Intravenous or intramuscular administration of ampicillin, 2.0 g, plus gentamicin, 1.5 mg/kg (not to exceed 80 mg), 30 minutes before procedure; followed by amoxicillin, 1.5 g orally 6 hours after initial dose; alternatively, the parenteral regimen may be repeated once 8 hours after initial dose
Ampicillin/amoxicillin/penicillin-allergic patient regimen	
Vancomycin and gentamycin	Intravenous administration of vancomycin, 1.0 g, over 1 hour plus intravenous or intramuscular administration of gentamicin, 1.5 mg/kg (not to exceed 80 mg), 1 hour before procedure; may be repeated once 8 hours after initial dose
Alternate low-risk patient regimen	
Amoxicillin	3.0 g orally 1 hour before procedure; then 1.5 g 6 hours after initial dose

*Initial pediatric doses are as follows: ampicillin, 50 mg/kg; amoxicillin, 50 mg/kg; gentamicin, 2.0 mg/kg; and vancomycin, 20 mg/kg. Follow-up dose should be one half the initial dose. **Total pediatric dose should not exceed total adult dose.**