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The role of cardiopulmonary exercise testing in preoperative evaluation of surgical patients

The situation is, therefore, that the internist believes he can diagnose heart disease in life but can only state in a general way the patient’s chance under operation; while the surgeon may deny this ability to discover heart disease while the patient is alive, but confidently makes such a diagnosis if the patient dies.

H. B. Sprague, 1929

If this has a familiar ring then you should read on. Whilst this statement was made in 1929, the modern translation would still represent the feelings of many people today. One group would believe the first part and one group the second part. The true sceptic would of course believe both.

By virtue of the fact that the anaesthesia literature contains numerous articles discussing the best approach for preoperative assessment of major non-cardiac surgery with many urging caution and a rethink of the problem, it is clear that the problem has not yet been solved! For example, some authors strongly recommend perioperative beta-blockade and others are not so sure. A recent systematic review, with meta-analyses, goes further and concludes that there is insufficient evidence to recommend perioperative beta-blockade in any type of surgery for the prevention of death, myocardial infarction or stroke. How can there be such diversity of opinion with no resolution of such a common and serious problem? We believe that the reason for this is that too much attention has been focused on myocardial ischaemia as a risk factor. We also believe it is time to rethink the myocardial ischaemia paradigm which dominates most discussions on preoperative
evaluation. We hope that this article will offer a new perspective on these issues.

The current paradigm

The current paradigm for reduction of cardiac risk in non-cardiac surgery (preoperative testing for myocardial ischaemia and perioperative management including beta-blockade) targets only ischaemic heart disease. As explained by Kertai and colleagues, plaque rupture accounts for only half of perioperative myocardial events, and prediction of perioperative myocardial infarction based on location and severity of coronary lesions is unreliable. We contend that perioperative cardiac morbidity in non-cardiac surgery has a different cause than cardiac morbidity in the non-operative setting. London and colleagues suggest the myocardial oxygen supply–demand balance as another mechanism for major cardiac complications in non-cardiac surgery. The actual mechanism is unclear; they postulate a variety of aetiological factors, among which are impaired ventricular function and reduced coronary perfusion pressure. They acknowledge that ‘limited physiologic data collection, most notably markers of the stress response or delineation of ventricular function have frustrated efforts to determine causal mechanisms’.

Non-cardiac surgery is a broad definition and encompasses procedures with large variations in postoperative stress response. Risk must be stratified according to patient-specific factors but also the surgery-specific risk, i.e. the increased oxygen demand as a consequence of surgery. As London and colleagues imply, the conventional paradigm ignores the important relationship between postoperative oxygen consumption and ventricular function. Preoperative evaluation must embrace more than just risk factor analysis for ischaemic heart disease; it should involve detection of all cardiac disease and, most importantly, objective assessment of functional capacity. The current obsession with one element of patient-specific risk, coronary artery disease, distracts attention from these other components of risk.

How do postoperative complications present?

The commonest presentation of postoperative cardiac complications is well known to most perioperative physicians; it is the patient who is hypotensive, tachycardic, oliguric and hypoxaemic in the ward two or three days following major surgery. This is often accepted as a manifestation of myocardial ischaemia progressing to perioperative myocardial infarction. However, these symptoms are equally those of a heart unable to meet the
increased oxygen consumption of major surgery. We have already defined this syndrome as postoperative cardiac failure. Under conditions of increased global oxygen demand following major surgery, it is probable that a heart with decreased functional reserve would exhibit signs of myocardial distress and damage. This would include sustained elevation of heart rate, arrhythmia, perhaps cardiac troponin release and ECG evidence of ischaemia.

Release of cardiac structural protein, i.e. troponins, does not necessarily imply myocardial infarction. Goto and colleagues state that ‘cardiac markers are quite sensitive to changes in left ventricular haemodynamic dysfunction’, and that ‘concentrations of the marker proteins appear to be related to left ventricular filling pressures’. Both of these conditions pertain to the postoperative period. Further, as Ammann and colleagues state, ‘the most important question is whether raised troponins reflect reversible or irreversible myocardial injury and how necrosis could be distinguished from reversible myocardial damage’. The end result of postoperative stress on a heart with decreased functional reserve may well be a progression to perioperative myocardial infarction, or to acute left ventricular dysfunction with overt pulmonary oedema or even to cardiac arrest. In these situations, as suggested by Sprague, the diagnosis of ischaemic heart disease is made belatedly but with great confidence. However, as Kertai and colleagues submit, correct postoperative diagnosis is frustrated by limited physiologic data collection.

A more frequent pathway of postoperative demise, as found in our studies with monitoring of cardiopulmonary function and oxygen consumption postoperatively, i.e. with physiologic data collection, is dysfunction of other organ systems, a consequent requirement for haemodynamic support and a late progression to multiple organ failure. This is the sequence of primary postoperative cardiac failure, not primary myocardial ischaemia. The management of postoperative cardiac failure requires first a recognition that the morbidity is being caused by a failing heart which, in our view, would contraindicate beta-blockade; and secondly that treatment may require invasive monitoring and pharmacological support, which may include inotropes but rarely beta-blockade.

The diagnosis of postoperative cardiac failure should, of course, be made before progression to cardiac morbidity or to organ failure. Ideally, preoperative identification of patients at risk of this problem will result in modification of postoperative management, i.e. triage to monitored care in an intensive care unit, well before the patients at risk identify themselves by exhibiting the postoperative morbidity described above.
Cardiopulmonary exercise testing

We have shown that most perioperative cardiac morbidity in major non-cardiac surgery is related to cardiac failure, i.e. outcome is determined by the functional capacity of the cardiopulmonary system as determined by cardiopulmonary exercise testing (CPET).19

Performing the cardiopulmonary exercise test

Cardiopulmonary exercise testing involves computerised analysis of gas exchange and ECG data during exercise. The CPET is non-invasive. It consists of an exercise test with a progressive graded work rate and simultaneous breath-by-breath measurement, at the mouth, of inspired and expired concentration of oxygen and carbon dioxide, and inspiratory and expiratory gas flow. With this information oxygen uptake and carbon dioxide output may be derived. In addition a 12-lead electrocardiograph (ECG) is obtained continuously.

Our preference is to use a ‘zero watt’ cycle ergometer as the method of exercise. Compared to a treadmill, the cycle has the advantages of better isolation of lower limb musculature, less effect of movement artifact and greater safety because the subject is supported. Further, the workload can be varied in a step, incremental or ramp manner; these factors contribute to a more precise estimation of workload. A ‘zero watt’ cycle does not mean that the patient is performing no work, only that the patient is performing no ‘extrinsic’ work. The size of the patient, or more accurately the weight of the lower limbs, will dictate how much ‘intrinsic’ work is performed at ‘zero’ watts. The intrinsic work performed by the ‘average’ patient is approximately 25 watts. All the CPET at our laboratory were performed using a zero watt cycle ergometer (Corival, Lode®, Groningen, Netherlands) and a Cardi-O2 metabolic cart (MedGraphics Cardi-O2®, Medical Graphics Corporation, St Paul, MN, USA) and a computerised 12-lead ECG (Mortara ELI-100XR®, Mortara Instruments; Milwaukee, WI, USA). The manufacturers supplied upgraded software on a regular basis. The software of the metabolic cart was configured for continuous display of oxygen uptake, carbon dioxide output, work rate in watts, heart rate/VO₂ slope, ventilatory equivalents for oxygen and carbon dioxide (i.e. Ve/VO₂ and Ve/VCO₂), minute and tidal volumes and flow/volume loops and oxygen pulse (VO₂/HR), which is related to stroke volume.

The protocol for CPET was always the same. The metabolic cart was calibrated before each test and a medical specialist experienced in CPET supervised and reported all tests. Resuscitation equipment was available. A
12-lead ECG was obtained at rest and continuously during exercise and into the recovery period. The patient was seated on the cycle ergometer and the mouthpiece inserted (Fig. 1.1). Baseline gas exchange data were collected for approximately one minute. The patient then cycled against a zero watt extrinsic load for three minutes; for the next six minutes the extrinsic load was increased progressively using a ramp protocol to achieve the
predicted maximum work rate. The algorithm for this was derived from Wasserman and colleagues.\textsuperscript{21} It is of note that the duration of the test was slightly shorter than is often used in younger patients. Almost all patients tested were over 60 years of age and many over 80 years. We have found it difficult to motivate the elderly to cycle for much longer than nine minutes. All tests were symptom limited. The test was ceased if the ECG showed greater than 2 mm ST depression 60 ms after the J-point in any lead or if the patient became distressed. No effort was made to determine the peak aerobic capacity.

The primary determinant of cardiac function in our studies was the anaerobic threshold (AT). This was estimated using the ‘V-slope’ method described by Beaver and colleagues.\textsuperscript{22} The anaerobic threshold is the point of oxygen uptake where anaerobic ATP (adenosine triphosphate) generation is needed to supplement aerobic metabolism. The anaerobic threshold has been used to define grading of cardiac failure.\textsuperscript{23} Secondary criteria were determination of the nadir of the $V_E/V_O_2$ slope, the inflection point of the respiratory exchange ratio (RER), and the $V_O_2$ at which there was an increase in end-tidal oxygen concentration. All results were entered into a custom configured database that allowed calculation and graphical representation of derived data. The CPET is used to determine overall cardiopulmonary function and the precise cause of exercise limitation. As oxygen uptake is a function of ventricular performance, CPET may be used to define cardiac failure accurately without using ‘estimates’ or surrogates. As survival from major surgery is very dependent on cardiopulmonary function, as we will show later, CPET is used to accurately assess risk prior to major surgery. Much physiological data are accumulated during the test, which may be displayed graphically on a computer in ‘real time’ or stored for later analysis. This allows for comparison of two variables independent of time (bivariate analysis), which is the true power of CPET. There are 15 graphs, systematically arranged into nine panels: the ‘nine panel plot’ (Fig. 1.2). This plot is used to display the cardiovascular, ventilatory, ventilation/perfusion and metabolic responses to exercise. It is normally displayed in colour. For example, if oxygen uptake is plotted against work rate in watts, the slope of the line (or $\Delta V_O_2$/Work) gives a global assessment of exercise limitation. Similarly, carbon dioxide elimination plotted against oxygen uptake ($V_CO_2$ vs. $V_O_2$) is the basis for the ‘V-Slope’ method for determination of the anaerobic threshold. Ventilation/perfusion matching is evaluated by analysis of the relationship of oxygen uptake or carbon dioxide elimination to minute volume ($V_E/V_O_2$ or $V_E/V_CO_2$). The slope of the HR/$V_O_2$ plot is related to stroke volume and improves the accuracy of ECG diagnosis of myocardial ischaemia over ST segment analysis alone.\textsuperscript{24} While these variables are not well known to most
doctors, the normal responses to exercise are well defined; with appropriate display of data from CPET it is possible to determine the functional state of the entire cardiopulmonary system.

The risk factors

Cardiac failure not myocardial ischaemia

In a study of 548 consecutive elderly patients having major non-cardiac surgery and assessed by preoperative CPET, we examined outcome in relation to both cardiopulmonary function and myocardial ischaemia.19 The incidence of myocardial ischaemia in these tests was 132 patients out of 548 (24%); most occurred as ‘silent’ ischaemia, i.e. without symptoms of chest pain. Of the nine deaths in the study attributable to cardiopulmonary causes,
only one was caused directly by myocardial infarction. Only two deaths occurred in patients who had myocardial ischaemia, the other seven deaths occurred in patients with no evidence of ischaemia but with poor ventricular function. More importantly, there were no deaths related to cardiopulmonary causes in any patient with adequate ventricular function, defined as an anaerobic threshold above 11 ml.kg\(^{-1}\).min\(^{-1}\), even if myocardial ischaemia was present. If myocardial ischaemia were the dominant factor causing perioperative complications, such morbidity would occur predominantly in those patients with ischaemia. This is not the case in any of our published studies or unpublished series, now embracing over 1600 patients.

We conclude that it is the functional capacity of the heart and lungs, not the diagnosis of myocardial ischaemia, that determines the ability to support postoperative oxygen demand and thus influences morbidity and mortality after major surgery. Therefore, unlike the current paradigm for preoperative risk assessment, measurement of functional capacity and identification of cardiac failure is of prime importance.

Is myocardial ischaemia of no importance?

We do not intend to suggest that myocardial ischaemia is not significant. Myocardial ischaemia may well be a cause of poor functional capacity and thus, indirectly, perioperative death. However, we have shown that myocardial ischaemia is important only if it limits ventricular function. Myocardial ischaemia in the presence of good functional capacity (defined as an AT greater than 11 ml.kg\(^{-1}\).min\(^{-1}\)) was not associated with postoperative deaths in three published studies, one of 187 patients, one of 214 patients, and one of 548 patients, or a further unpublished series of 751 patients. The many studies that suggest myocardial ischaemia as the main cause of morbidity did not evaluate ventricular function preoperatively in an objective fashion, if at all. Most studies make assumptions of the likelihood of myocardial ischaemia on a history of risk factors for coronary artery disease. When morbidity occurs it is attributed to coronary artery disease on the basis of these risk factors.

Risk factors for heart failure are often based on a history of hospital admission for acute left ventricular dysfunction. However, risk factors for cardiac disease in general, as well as for myocardial ischaemia, have the common end point of impaired ventricular function. It is our hypothesis that the patients who exhibit morbidity and mortality may well do so as a consequence of occult heart failure. This is by no means an uncommon problem. Ignorance of heart failure as a major contributing factor to postoperative morbidity and mortality has other important consequences, not the least of which is that therapy is directed solely at prevention of myocardial
ischaemia, including recommendations therefore for beta-blockade. A more logical approach would be to optimise cardiac performance and not just to concentrate on therapy for possible myocardial ischaemia.

Another perspective on myocardial ischaemia and cardiac failure

Our hypothesis emphasising the importance of heart failure in perioperative morbidity and mortality is supported by recent work from Hernandez and colleagues\(^3\) in a series involving a study population of 3300 and a control group of 44,500. They showed that patients identified preoperatively with coronary artery disease (CAD) without heart failure, had a similar mortality to the general population (6.6% vs. 6.2%, \(p = 0.518\), i.e. no significant difference) following major non-cardiac surgery. By way of contrast, those patients with heart failure had substantial morbidity and mortality (11.7% vs. 6.6%, \(p < 0.001\)). There were other significant findings related to readmission rates of the two groups. Heart-failure patients were readmitted more frequently for non-surgical reasons than the CAD group, with heart failure being the most common cause for this. Hernandez and colleagues\(^3\) make the important point that ‘the diagnosis of coronary disease was less important in heart failure patients because those with and without coronary disease had similarly poor outcomes’.

Assessment of functional capacity

The American College of Cardiology and the American Heart Association (ACC/AHA) Guidelines for Perioperative Cardiovascular Evaluation for Noncardiac Surgery\(^1\) state, ‘For patients with or without intermediate clinical risk factors, consideration of functional capacity (as determined by history of daily activities) and level of surgery-specific risk allows a rational approach to identifying which patients may most benefit from further non-invasive testing.’ The guidelines also point out the reliability of functional status in prediction of cardiac events. They then state, ‘If the patient has not had a recent exercise test, \([\text{our italics}]\) then functional capacity may be estimated from the ability to perform the activities of daily living.’ Whilst this may be possible at the extremes of function it is not correct for the ‘average’ patient in the middle ranges of function, i.e. making a distinction between NYHA (New York Heart Association) class II and class III is extremely difficult, much more so than the distinction between class I and class IV. This was shown by Dunselman and colleagues in 1988 in a paper comparing CPET with clinical evaluation.\(^3\) The conclusion of that study was that ‘only data from exercise studies showed differences between the groups’. We consider that making a distinction between NYHA class II and class III is crucial for accurate preoperative assessment.
In all the studies that we have performed, the mean AT for patients over 60 years of age is 12.3 ml.kg\(^{-1}\) min\(^{-1}\) of oxygen uptake (Fig. 1.3).

Using CPET data, Weber and Janicki\(^{23}\) classified cardiac failure into five groups. In terms of AT, the range from no heart failure to significant heart failure is between 14 ml.kg\(^{-1}\) min\(^{-1}\) to 8 ml.kg\(^{-1}\) min\(^{-1}\). In our series the mean, plus or minus one standard deviation, encompasses this range (Fig. 1.4). As our data show, patients at risk of perioperative cardiac morbidity have an AT of less than 11 ml.kg\(^{-1}\) min\(^{-1}\) of oxygen uptake;\(^{19}\) an AT of 11 ml.kg\(^{-1}\) min\(^{-1}\) is within one standard deviation of the mean of our entire study population. Further, one standard deviation of any five-year