Cardiopulmonary exercise testing before abdominal aortic aneurysm surgery: a validated risk prediction tool?

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In 2008 the European Society for Vascular Surgery published a report which acted as a wakeup call, by suggesting the UK to be a significant mortality outlier for Abdominal Aortic Aneurysm (AAA) surgery, in comparison to other European and Australian countries.¹ This precipitated a collaborative venture between several key stakeholders including; the Vascular Society, Vascular Anaesthesia Society of Great Britain and Ireland and British Society of Interventional Radiology, with the remit of improving outcomes in aortic aneurysm repair across the UK. Publication of the National Abdominal Aortic Aneurysm Quality Improvement Programme (NAAAQIP) in 2011² and subsequent improvements in healthcare delivery, have demonstrated impressive national mortality improvements over the last 3 yrs.

Incorporated into the NAAAQIP were specific care pathways and treatment protocols, with significant emphasis given to preoperative assessment and appropriate patient selection for surgery. A major inclusion was the recommendation for formal risk assessment to aid in this process, whilst allowing patients to make an informed choice in proceeding with intervention, choice of intervention (open or endovascular repair) or simply to decline surgery.³ Effective risk assessment is a significant challenge to clinicians and is not restricted to patients undergoing aortic surgery. Increasing importance placed on outcome measurements, in particular patient reported outcomes after Darzi’s report of 2008, High Quality Care for All,⁴ and the publication of Consultant outcome data across many surgical specialties, has precipitated an almost global search for the ideal preoperative risk prediction tool.

An understanding of what is implied by the term ‘risk’ provides a useful starting point. In a patient being considered for major vascular surgery this would be the likelihood of harm, or an unwanted event, or outcome occurring consequent to the particular intervention. In this setting most authorities would consider the unwanted outcome or event to be perioperative death or major complication. Two challenges are apparent. First the balance of risk needs to be considered with respect to 3 potential strategies, open repair, endovascular repair or conservative management. Second, mortality represents a dichotomous measure for the individual surgeon and institution, however it lacks patient focus and sensitivity. Accepting these different requirements exist, one concludes that a single risk assessment tool is unable to cover all needs. It is therefore appropriate to focus discussion on risk prediction with surgery, whilst accepting that this needs to be balanced against the option of conservative treatment. A more patient-centric outcome measure would also be a major step forwards, with functional ability and health related quality of life (HRQOL) on hospital discharge representing possible options. Non-fatal postoperative complications are known to closely correlate with functional independence and HRQOL on hospital discharge,⁵,⁶ however, as a medical community we remain inconsistent at robustly recording this. Indeed, complications are not presently collected and reported as part of the NAAAQIP dataset.

We must therefore focus attention on preoperative risk prediction, utilizing outcome measures that we are able to robustly collect and record. In this setting the ideal preoperative risk prediction tool would be non-invasive, reliable, easy to interpret, and comfortable to patients whilst carrying a low associated risk. In addition, it would be able to reliably and accurately predict the outcome of interest across a broad range of high-risk surgical procedures. This is a tall order, with a wide variety of potential candidates available – none of which is a perfect or precise fit.

In a recent issue of the BJA, Grant and colleagues⁷ add to the growing literature in this area. Cardiopulmonary exercise testing (CPET) is widely used in the UK for the objective measurement of functional capacity and risk assessment before major surgical procedures, including AAA repair. Test results are taken to infer a patients’ ability to cope with the metabolic demands of surgery,⁸ with a growing number of publications defining various cut-off values for different CPET variables, to predict mortality and major morbidity.⁹–¹⁴ Accepting this to be the outcome of interest, could CPET represent the ideal preoperative risk prediction tool to allow patients and the wider multidisciplinary team an opportunity to reach informed conclusions about appropriate surgical selection and assist in shared decision-making before AAA surgery?

In consideration of this, and when evaluating available published literature, it is prudent to have a scientific and intellectual framework to allow for rigorous evaluation of CPET before its wholesale adoption into clinical practice. The American Heart Association (AHA) has defined a phased evaluation strategy appropriate for the adoption of novel risk markers (Table 1).¹⁵
Whilst this was conceived with the assessment of biomarkers in mind, the approach described is equally applicable to other clinical settings, such as risk assessment and can be used to evaluate preoperative CPET.

Utilizing this framework it may reasonably be argued that, for AAA surgery, CPET achieves the first of the criteria in Table 1. A number of studies have demonstrated an association between CPET measured variables and postoperative outcome in aortic aneurysm repair. In a cohort of 415 patients undergoing aortic surgery, an anaerobic threshold (AT) of <10.2 ml kg$^{-1}$ min$^{-1}$ identified patients at increased risk of early death after surgery. A retrospective cohort study of 230 patients found an AT of >11 ml kg$^{-1}$ min$^{-1}$ to correlate with improved postoperative survival in open aortic surgery, a shorter length of stay and improved survival in both open and endovascular patients.

The second criterion for evaluation is prospective validation. Prentis and colleagues published a prospective, blinded, single centre study of 185 patients demonstrating an association between an AT <10 ml kg$^{-1}$ min$^{-1}$, postoperative complications and length of hospital stay, in patients undergoing open aortic surgery. The same study identified an association between AT and length of stay in patients undergoing endovascular repair. Further blinded prospective assessments of CPET in the surgical setting are required, but will prove a challenge. Anxiety about preoperative morbidity and mortality leads to surgeons and anaesthetists being reluctant to accept the methodological rigor of blinding and the majority of studies of preoperative tests are therefore at risk of bias.

The third criterion asks if the test adds incremental value to existing risk assessment protocols. Studies that address this are not available at the time of writing. Some data are available on the extent to which CPET results add value to information, from other clinical risk factors. A study of 415 patients (who underwent CPET before open or endovascular AAA repair) found an AT <10.2 ml kg$^{-1}$ min$^{-1}$, open aortic surgery, inducible cardiac ischaemia and anaemia to be independently associated with an increased risk of death within 30 days of surgery. The study by Prentis and colleagues, alluded to above, included backward multiple logistic regression modeling to identify variables associated with postoperative complications in open aortic surgery. The inclusion of additional variables did not add to the predictive value of an AT <10 ml kg$^{-1}$ min$^{-1}$. This result is striking, but in clinical practice some estimate of surgical risk (either formal or informal) is made on clinical history and other information before a CPET is performed. In statistical terms we need to know if the results of CPET improve risk prediction, when routinely available data such as clinical history are forced into the model. It is particularly important to ask if CPET results add value to existing tools such as the Revised Cardiac Risk Index (RCRI). A single centre study of patients undergoing open aortic surgery demonstrated associations between mid-term survival and CPET measured variables, and also between mid-term survival and the RCRI. However, it did not test the question of whether CPET added incremental value to the RCRI. Evidence from studies that include other types of surgery is also inconclusive. A single centre study of 100 patients undergoing major non-cardiac surgery compared ASA score, the RCRI, AT, peak oxygen consumption (VO2peak), estimated GFR, plasma B-type natriuretic peptide and C-reactive protein, for the prediction of postoperative complications. On the basis of univariate analyses, AT and VO2peak had greater predictive value than either scoring systems or biomarkers. However, the study had insufficient power to allow multivariate analyses, including several different predictors in one model.

The fourth criterion for evaluation, asks if the test changes predicted risk sufficiently to modify therapy. The studies discussed above show an association between CPET measured variables and outcome that informs the discussion of patient management in many units. Nevertheless, the current data do not prove that CPET adds value to other existing risk assessment tools. In the context of current recommendations for UK practice for formal discussion of all patients being considered for AAA surgery in a multidisciplinary team meeting including surgeons, radiologists and anaesthetists the incremental value of CPET therefore remains unproved.

The fifth and sixth criteria listed in Table 1 require its examination in a randomised controlled trial. To the authors’ knowledge this has not been undertaken.

To summarize, the currently available data give face validity to the use of preoperative CPET for the prediction of complications in patients undergoing aortic aneurysm repair but, as with many other preoperative tests, its value is not rigorously proved.

Does the work of Grant and colleagues published in a recent issue of the BJA provide additional evidence for the use of CPET as a risk prediction tool in aortic surgery? Whilst this reasonably sized cohort study was weighted in favor of EVAR, it included older patients with limited functional capacity and IHD, representing a realistic contemporary vascular population. The study was not blinded and knowledge of the CPET results could have led to high-risk patients being denied surgery or receiving extended high-dependency or intensive care. This may have weakened the reported association between CPET variables and outcome. Data from a previous smaller study were included in the cohort presented here. This increases the power of the statistical analysis, but reduces the number of subjects that this work adds to the published literature. As with many other publications this paper does not explore AT and VO2peak as continuous variables within a multivariate model. This is presumably because of constraints in sample size, but weakens the analysis. Within these constraints, this work adds weight to proof of concept.

Table 1 AHA phased evaluation strategy for the adoption of novel risk markers

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<tr>
<th>Phase</th>
<th>Description</th>
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<tr>
<td>1. Proof of Concept</td>
<td>Do novel marker levels differ between subjects with and without outcome?</td>
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<td>2. Prospective Validation</td>
<td>Does the novel marker predict development of future outcomes in a prospective cohort or nested case-cohort/case-cohort study?</td>
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<tr>
<td>3. Incremental Validation</td>
<td>Does the novel marker add predictive information to established, standard risk markers?</td>
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<td>4. Clinical Utility</td>
<td>Does the novel risk marker change predicted risk sufficiently to recommend therapy?</td>
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<td>5. Clinical Outcome</td>
<td>Does use of novel risk marker improve clinical outcomes, especially when tested in RCT?</td>
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<tr>
<td>6. Cost Effectiveness</td>
<td>Does use of the marker improve clinical outcomes sufficiently to justify the additional costs of testing and treatment?</td>
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and validates findings in other studies,\textsuperscript{11, 19} for the utility of VO\textsubscript{2}peak and ventilatory equivalents for carbon dioxide (VE/\textsubscript{VCO\textsubscript{2}}), as independent predictors of reduced survival. It does not meet the need for testing of CPET in a randomised controlled trial. The study does, however, offer useful insights into the dilemma of which CPET measured variables to use for risk prediction.

The issue of inconsistency in the selection of CPET variables and choice of thresholds for risk prediction has been highlighted in systematic reviews.\textsuperscript{8, 20} A number of other studies have been added to the evidence base since these were published, but the criticism that a number of different CPET measured variables have been proposed for preoperative risk prediction remains valid. These include AT, VO\textsubscript{2}peak, and VE/\textsubscript{VCO\textsubscript{2}} at AT. It may be argued that CPET offers an integrated assessment of the cardio-respiratory system that is not encapsulated in one variable. This argument needs to be translated into a practical approach to risk prediction. In the study by Grant and colleagues, cut-off threshold values were set for AT, VO\textsubscript{2}peak, and VE/\textsubscript{VCO\textsubscript{2}} and the authors conducted an analysis based on the number of sub-threshold CPET variables recorded in each test. The analysis reflects the approach to the interpretation of preoperative CPET tests by many practitioners, with a larger number of variables outside of the predicted range being associated with increasing concerns regarding fitness for surgery. It prompts us to suggest that a consensus meeting, or similar process is required to agree a common definition of a ‘sub-optimal’ preoperative CPET, to be examined in future prospective studies using this tool.

The scope of preoperative CPET extends significantly beyond risk prediction based on cut-off thresholds. Superiority of CPET for identification of cardiac ischaemia\textsuperscript{21} and functional heart failure\textsuperscript{22} over more traditional cardiac investigations has been demonstrated. Respiratory limitation and demarcation of obstructive vs restrictive ventilatory disease is also feasible.\textsuperscript{23} Where clinical doubt exists, CPET can be particularly useful to identify whether underlying pathology is cardiac or respiratory in nature. The dynamic, integrated nature of CPET represents a particularly useful way of identifying significant cardiorespiratory pathology in the preoperative setting, which may impact on outcome after surgery. Appropriate specialist referral can subsequently be instigated and unproved static cardiorespiratory investigations (e.g. echocardiography and pulmonary function tests avoided). It could be argued that these factors add incremental value to existing available tests in the preoperative period from a purely clinical perspective, but this requires formal statistical validation.

Although not specifically relating to vascular surgery, the recently updated ACC/AHA guideline document on perioperative cardiovascular evaluation and management before noncardiac surgery, has for the first time made recommendations with respect to preoperative CPET: ‘Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedures in whom functional capacity is unknown.’ They conclude that benefit of preoperative CPET may be greater than risk (Level of evidence B, IIb), however ‘additional studies with broad objectives are required.’\textsuperscript{24}

In conclusion, current data support an association between CPET measured variables and mortality/major morbidity after aortic surgery, but further work is required to formally validate the use of preoperative exercise testing for risk prediction. This should be conducted in the context of a rigorous intellectual framework that compares CPET with other risk prediction tools and places it in the context of the patient pathway. Such research will be greatly facilitated by work to develop a national (or indeed international) consensus on the selection and reporting of CPET variables for preoperative risk prediction.

\textbf{Declaration of interest}

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\textbf{References}


The Fourth National Audit Project of the Royal College of Anaesthetists and Difficult Airway Society (NAP4)1 2 identified three important issues around SADs: (i) pulmonary aspiration is the most common cause of major airway complications in anaesthesia, and aspiration associated with SADs is an important contributor to this; (ii) the vast majority (>80%) of SADs used in UK anaesthetic practice are first-generation devices [the cLMA or equivalent laryngeal masks (LMs)]; and (iii) important complications are associated with use of (first-generation) SADs in obese patients. It is highly likely that there is increasing use of SADs in our ever more obese anaesthetic population. The questions of greatest importance regarding SADs for routine anaesthetic practice are therefore around safety rather than efficacy.

It has recently been stated that the LMA has ‘stood the test of time’. It is true that the cLMA—and many similar LMs—remain in everyday use with a low rate of complications. The question, however, arises as to whether the cLMA should remain the predominant SAD in anaesthetic practice. The cLMA was devised more than 30 yr ago, and the prefix ‘classic’ might now indicate that it is a ‘vintage’ device rather than a ‘state-of-the-art’ one. The evidence suggests that many of the newer SADs have performance characteristics that do improve efficacy compared with the ‘vintage LMA’ and have the potential to increase safety. The cLMA is an example of a first-generation SAD (a simple airway tube); second-generation devices are defined as ‘those with specific design features intended to reduce the risk of aspiration’, and it is time to consider whether second-generation devices should now be our first choice. There are three main problems with SADs: difficult insertion; leakage during positive pressure ventilation; and the risk of aspiration of gastric contents. Many second-generation SADs now outperform the first-generation LMAs and LMs in all these domains,