Royal College of Surgeons of England
ADVANCING SURGICAL CARE

Letters and Comments

Cardiorespiratory fitness in patients undergoing elective open surgery for abdominal aortic aneurysm: does it really fail to predict short-term postoperative mortality?

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COMMENT ON
DM Bailey, GA Rose, RMG Berg *et al*. Cardiorespiratory fitness fails to predict short-term postoperative mortality in patients undergoing elective open surgery for abdominal aortic aneurysm.
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Dear Sir,

We read with great interest and anticipation the recent paper by Bailey *et al* titled 'Cardiorespiratory fitness fails to predict short-term postoperative mortality in patients undergoing elective open surgery for abdominal aortic aneurysm'.[1] Upon examination of the findings, it is apparent that there were no deaths during the study period. As such, it is impossible to predict an outcome that did not occur! We suggest that this study was not appropriately designed or powered to detect the outcome of interest, and that the conclusion, which is reflected in the title of the paper, cannot be substantiated.

We do acknowledge the difficulties in designing a study to detect hard endpoints such as mortality. This is exacerbated in the setting of abdominal aortic aneurysm (AAA) repair, where outcomes may vary between countries and clinical centres and are influenced by the presentation of patients (eg aneurysm size, symptomatic vs. asymptomatic), and the type of repair procedures used (emergency vs elective, open surgery vs. endovascular repair [EVAR]). Data from the Vascular Services Quality Improvement Programme report that the risk of death after elective open infrarenal AAA repair in the UK is approximately 4%.[2] The study by Bailey *et al* included 109 patients, 79 of whom underwent open AAA repair performed by a single surgeon at a single centre.[1] While there is a place for single-centre studies, it is unlikely that the outcomes reported are representative of that across the UK, or globally. Importantly, the low number of patients included in their study would not be sufficient to replicate the findings of previous studies that have included much larger cohorts (n=230-415) and demonstrated that measures of cardiorespiratory fitness are able to identify patients at increased risk of death within 30 days following AAA open repair.[3,4]

While the authors suggested that advances in patient treatment and surgery strategies may explain the low death rate and therefore render cardiopulmonary fitness a less sensitive predictor of short-term mortality, we maintain that the study was too small and was underpowered.

Cardiopulmonary exercise testing (CPET) provides the opportunity to assess various markers of cardiorespiratory fitness, including peak oxygen consumption ($\dot{V}O_2$peak), ventilatory threshold ($\dot{V}$T), and the ventilatory equivalents for carbon dioxide ($\dot{V}E/\dot{V}CO_2$) and oxygen consumption ($\dot{V}E/\dot{V}O_2$). The prognostic sensitivity of cardiorespiratory fitness differs depending on the measurement that is used,[5] and is specific to the population and the conditions of the CPET protocol[6,7]; and in the case of AAA repair it is also specific to the type of repair procedure used (open vs EVAR).[8] Bailey and colleagues are commended for investigating the influence of clamp position (infrarenal vs. suprarenal) on the sensitivity of cardiorespiratory fitness to detect *morbidity* outcomes following open AAA repair. However, the authors applied a generic dichotomous threshold ($\dot{V}O_2$peak $<15 ml.kg^{-1}.min^{-1}$) to characterise 'unfit' patients, based on previous recommendations that have been established for patients with lung cancer.[9] The authors did not report $\dot{V}$T, and notably ventilatory (or anaerobic) threshold measures have previously been associated with 30-day postoperative mortality in patients undergoing open AAA repair.[3,4]

Given the emerging and important role of CPET in the risk assessment of patients with abdominal aortic aneurysm, it is essential that clinical decision making is based on robust evidence. While the study by Bailey *et al* adds some new insight into the impact of cardiorespiratory fitness on *morbidity* following open AAA repair, the study was not sufficiently designed or powered to investigate the impact on *mortality*.[1], As such, the conclusion of the study cannot be substantiated, and we suggest that the title and conclusion of the paper should be corrected to more accurately reflect the outcomes of the study.

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AUTHORS' RESPONSE

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RESPONSE TO:
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ORIGINAL ARTICLE:
DM Bailey, GA Rose, RMG Berg *et al*. Cardiorespiratory fitness fails to predict short-term postoperative mortality in patients undergoing elective open surgery for abdominal aortic aneurysm *Ann R Coll Surg Engl* 2020; **102:** 536–539.
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Dear Sir,

We are grateful for the correspondence by Harwood *et al* and appreciate the opportunity to put our findings into further clinical perspective.[1] The practical message that we wanted to convey was originally intended for the surgeon engaging with a busy clinical practice. The fact that our article has attracted attention from health and exercise scientists stands further testament to the complexities underlying systemic oxygen transport, highlighting the need to integrate multiple specialist disciplines to advance our understanding and better inform the care of patients with abdominal aortic aneurysms (AAA).

We accept their primary criticism and were pleased, if not indeed surprised, that our data collected prospectively in a busy clinical setting demonstrated no mortality at 30 days in those patients classified as 'unfit' according to our cardiopulmonary exercise testing (CPET) 'cut-off' metrics. Indeed, the current risk of death after elective open (infrarenal) AAA repair in the UK would have equated to approximately 3 deaths in the 79 patients examined. Given such a low event rate, it is clear from the outset that our study was not adequately 'powered' from a statistical perspective to detect differences in mortality though we take the opportunity herein to place further emphasis on what we originally intended to be our primary 'take-home' message. Incidentally, a total of ~2,292 patients would be required in order to detect a (fit vs. unfit) difference in mortality of 50% (ie from 4% to 2%) with 80% power at $p<0.05$ according to established statistical methods.[2]

Although many studies focus on 30-day postoperative mortality, the longer term outcome is far more important to patients, particularly elective AAA repair.[3] Patients are unlikely to commit themselves to major high-risk surgery based on results at 30 days postoperatively. Focusing postoperative mortality prediction on 30 days may be misleading with modern perioperative care.

In our study, the decision to proceed with surgery in 'unfit' patients was taken after careful consideration of our CPET data, albeit tempered with specialist clinical (anaesthetic and critical care) input and a full discussion with the patient given the 'potential' for increased morbidity as indicated by preoperative CPET. Our findings are clinically important in that some and possibly increasing numbers of surgical units may well have turned down these patients for surgical intervention, classifying them as inoperable and unfit for surgery. Furthermore, if these unfit patients return to hospital symptomatic from their AAA, they may well be denied surgical intervention.

The 'unfit' patients in our study survived surgery albeit with a higher postoperative morbidity and increased hospital length of stay. Yet importantly, they go on to enjoy a significantly prolonged length and quality of life. Rather than apologise for our findings, we argue that the 'unfit' patient should always be considered by experienced clinicians as to whether they proceed to surgery and the decisions of operability, should not solely be dictated by a 'single-point' estimate of cardiorespiratory fitness as defined by CPET metrics (more on this later). *Dura est manus cirurgi, sed sanans* (the hand of the surgeon is hard, but healing) with surgery considered by many as much of an art as it is informed by sound science. The diagnostic ability of CPET facilitates the optimisation of known/hidden comorbidities and the enhanced perioperative care of these patients.

Indeed, Harwood *et al*'s (finer) point highlighting the limitations imposed by generic dichotomous thresholds for $\dot{V}O_2$peak for fitness stratification is well made, although the best available, given the lack of available data at least in the AAA setting. As stated by Moran *et al*,[4] a $\dot{V}O_2$peak cut-off point of 15ml/kg/min was considered 'a good starting point' originally informed by the study of Hartley *et al*[5] and supported by others[6] including our own work in AAA patients.[7] Variations in thresholds clearly exist, confounded