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Predicting survival after surgery: a matter of life and death

The quantification of risk is now embedded in our approach to the assessment of the high-risk surgical patient, although this has not always been the case. The past fifty years have seen a dramatic change in approach [1]. In 1957, Dripps and colleagues suggested that the quantification of peri-operative risk was not possible, due to the myriad factors involved [2]. Ten years later, the 1967 edition of the American College of Surgeons publication *Manual of Preoperative and Postoperative Management* distinguished between good-, intermediate- and poor-risk patients [3]. The 1977 publication of the Goldman cardiovascular risk scoring system [4] ushered in the approach whereby a number of factors are selected using statistical methods and combined to give a quantitative estimate of peri-operative risk. The publication of the Cardiac Risk Index marked a move to a probabilistic approach that sought to quantify risk but acknowledged that the outcome for an individual patient could not be predicted with certainty. In their review of the changes in approach to the definition of surgical risk, Neuman and Bosk report that by 1987, the Goldman Risk Index had been cited 224 times [1]. The decades since have seen the development of a substantial body of work based on this approach, with the development of general risk prediction tools such as the Lee Cardiovascular Risk Score, the POSSUM score and surgery-specific tools such as the Glasgow Aneurysm Score [5-7]. All of these focus on the risk of complications or mortality in the immediate postoperative period. In this edition of *Anaesthesia*, Carlisle and colleagues present a validation study of a clinical risk prediction tool that predicts not the likelihood of major complications and death, but the patient's chances of survival based on data from four centres on patients undergoing aortic surgery [8].

Carlisle has previously drawn attention to the fact that patients' concerns about outcome extend 'beyond one lunar orbit': people do not undergo elective surgery in order to gain only an additional 30 days of life but to improve their long-term survival and wellbeing [9]. He has constructed a clinical risk prediction tool that takes an actuarial approach based on the UK Office for National Statistics (ONS) Life Tables. For a person of a given age and sex, the ONS tables give an estimate of mortality rate and life expectancy. The tool produced by Carlisle modifies this estimate to take in to account the presence of various clinical risk factors, renal function, and the patient's exercise capacity. The tool provides an estimate of the likelihood of death with and without surgery, both in the next month and for longer periods. The model allows an estimate to be made of the extent to which an operation may shorten or lengthen the patient's life. Thus, it is potentially able to inform care more than tools that offer only an estimate of the percentage of patients who will suffer morbidity or mortality following surgery.

The study of outcome from aortic aneurysm repair is particularly apposite, since this is a prophylactic procedure done not to cure a disease such as cancer but to prevent aneurysm rupture. The patient will not be better immediately after surgery and may be considerably worse. Clinical decision-making is rendered more complex by the fact that there is more than one surgical option, and patients may be offered either open or endovascular repair, which have differing short- and long-term risk profiles. Therefore, questions of long-term survival with and without intervention are thrown into sharp relief.

This risk calculator presents a new paradigm for balancing the risks and benefits of surgery, and raises questions over the role of exercise testing in pre-operative risk assessment, the appropriateness of modifying lifetable mortality estimates with data from other risk tools, and the process by which the model was constructed. These will be considered below.

Cardiopulmonary exercise testing (CPET) has become established as a component of risk stratification before aortic aneurysm surgery in many centres. There is a body of evidence to support an association between estimates of functional capacity derived from CPET and complications following aortic surgery [10-18]. The work of Barakat et al. published in this issue of Anaesthesia adds to this evidence by demonstrating associations between a decreased anaerobic threshold and cardiac complications and between increased ventilatory equivalents for carbon dioxide and pulmonary complications. However, studies supporting the use of CPET are relatively small, generally including only a few hundred patients, and most were not blinded. A systematic review published in 2012 made the point that there is variation between studies both in the variables chosen to quantify functional capacity (generally anaerobic threshold or peak $\dot{V}O_2$) and in the cut-off values used to classify patients [19]. These issues remain unresolved. One group has suggested an approach based on the number of variables outside of the normal range [12]. It is also important to question whether knowledge of the results of a CPET test improve risk stratification after the impact of clinical risk factors, such as a history of ischaemic heart disease or renal impairment, has been taken into account. Studies that include multivariate analyses of the impact of both CPET-derived variables and other risk factors have yielded inconsistent results [12, 16, 17]. Although, strictly speaking, the model of Carlisle et al. predicts survival rather than the risk of complications, it includes multivariate analyses of multiple risk factors and supports the evidence that data from CPET contributes to pre-operative risk stratification [9]. Questions remain as to which CPET variables and cut-off values should be used for risk assessment and the added value offered by CPET when other risk factors are taken into account.

This predictive model uses CPET-derived variables to model predicted life expectancy, rather than the risk of complications, and is based on work that demonstrates an association between functional capacity and life expectancy [20]. Although such studies involve many hundreds of patients, they were not conducted in surgical populations and possible geographic variability is not taken into account. Correction for functional capacity is made after adjustments have been applied for cardiovascular risk factors. Since the effects of cardiovascular disease may be reflected in reduced functional capacity, it is possible that the approach adopted by Carlisle et al. includes a double adjustment for the effect of cardiovascular disease.

The inclusion of clinical risk factors, such as a history of heart failure or previous myocardial infarction, in the model will make intuitive sense to all who are familiar with the approach taken to modelling the risk of peri-operative risk complications in tools such as the Revised Cardiac Risk Index [6]. The inclusion in the model of a history of renal dysfunction, stroke, heart failure and myocardial infarction reflects the findings of studies of the risk of cardiovascular disease and death. For example, these risk factors appear in an analysis of predictors of death, myocardial infarction and disabling stroke using data from the ACTION trial, one of several references cited [21]. However, it is not clear how the weights given to these variables in Carlisle's model (increasing mortality hazard by 1.5 times in each case) are derived. The hazard ratios for the risk of death attributable to previous

myocardial infraction and to stroke in the analysis of the data from ACTION are 1.15 and 1.7 respectively. It is also not clear why factors such as smoking and diabetes are excluded from the Carlisle model.

Overall, the approach taken to the construction of the model is plausible but cannot automatically be assumed to be valid. Despite this, Carlisle et al.'s study suggests that the model yields valid results in an external population of patients [8]. There are some constraints. It is not clear if data from patients in the Torbay dataset used in the validation study had also been used in the derivation of the model, and complete data were not available from all centres. There was significant variation between centres; in particular, there appeared to be a systematic difference in the results of CPET tests from one centre.

Neither the model proposed by Carlisle et al., nor other currently available risk prediction tools, can fully inform the discussion with the patient of the risks and benefits of surgery. Health-related quality of life declines after both open and endovascular aortic aneurysm repair [22] but generally recovers over the next 6-12 months, although a proportion of patients experience long-term reduction in health-related quality of life. In such cases, the patient might regret accepting surgery, especially if the risks of aneurysm rupture were modest. The Carlisle model is based on the likelihood of survival with and without surgery and does not purport to predict the likelihood of postoperative complications, nor offer information on the likely impact of surgery on quality of life. Research on the prediction of quality-of-life outcomes after surgery is challenging but is sorely needed.

Concepts such as of the risk of complications following surgery or the impact of medical interventions on life expectancy can be difficult to explain to patients not used to thinking in probabilistic terms. A recent editorial in this journal has explored these challenges and the use of concepts such as micromorts and mircolives to translate abstract mathematical descriptions of risk into concrete estimates of change in life expectancy [23]. Even the best mathematical models cannot provide all the information necessary to inform a decision to undergo surgery. Patients do not consider the offer of surgery in purely probabilistic or mathematical terms, and may make choices that are mathematically nonsensical but entirely appropriate in human terms. Taking an example from obstetrics, mathematical modelling suggests that a trial of labour is the most appropriate strategy for mothers who have undergone previous caesarean section, because of the low risk to the mother and the high rate of successful vaginal delivery. However, when offered a choice, mothers heavily favoured repeat caesarean section, as they prioritised avoiding even very low risks to the infant [24]. Similarly, whilst a mathematical consideration of risk may indicate it is better not to intervene on a small aneurysm in an elderly patient, many patients and surgeons find inaction challenging. All clinicians who regularly attend a vascular multidisciplinary team meeting will be familiar with the dilemma of the how best to serve the interests of the high-risk patient who, despite advice that the risks outweigh the benefits, are adamant that they want an operation because anxiety about possible aortic rupture is destroying their quality of life. It is notable that in the EVAR2 trial of endovascular repair versus best medical therapy in high-risk patients with abdominal aortic aneurysms, there was a significant crossover in the group of patients randomised to best medical care, with a quarter of such patients undergoing aneurysm repair [25].

In a second paper published in this journal Carlisle applies the model underling the risk calculator to simulate survival in AAA patients with aneurysms ranging from 45-85 mm in diameter and with a spectrum of hazard of

death from any cause at presentation ranging from 0.5 to 2% per month. These simulations suggest that there is significant benefit in offering early aneurysm repair to a low risk patient with an aneurysm 45 mm in diameter. There seems to be little benefit in offering AAA repair to some higher risk patients even when they present with an aneurysm that is significantly greater than 55 mm in diameter. In many such cases intervention may shorten rather than lengthen life. These conclusions rest on the reliability of the risk model. If valid the inevitable conclusion is that the current approach of taking 55 mm as the diameter that should trigger considering of AAA repair in men requires re-examination. The studies upon which this is based are now more than 20 years old and much has changed in the interim. As Carlisle himself points out, life expectancy has increased over this period so that the potential benefits of appropriate AAA management are significantly greater.

To summarise, the approach to modelling survival presented by Carlisle et al. is unorthodox. The modelling process is not clear and no explanation is given as to why particular values were selected for the coefficients in the model. The model describes only survival and gives no information about the likelihood of complications. It is, however, pragmatic and has face validity, and its construction reflects clinical thinking about peri-operative risk and outcome. Carlisle et al.'s validation study suggests that the model's predictions are consistent with clinical outcomes but further studies are required. Studies of the model nested within data collection for national surgical registries, such as the National Vascular Registry, could be attempted. If these also validate the tool, it should then be tested in a randomised controlled trial, although the logistics will be challenging. However, by modelling survival rather than the risk of complications, the model offers a valuable and insightful alternative approach to assessing the risks and benefits of surgery. If widely implemented, it would represent a paradigm shift just as great as that wrought by the introduction of the Goldman Cardiac Risk Index. Such a change should rest on a rigorous and robust evidence base.

Competing interests

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S. J. Howell

Senior Lecturer in Anaesthesia

Leeds Institute of Biomedical & Clinical Sciences

St James's University Hospital

Leeds, UK

Email: S.Howell@leeds.ac.uk

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