Chronic kidney disease: a gateway for perioperative medicine

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In this issue of the BJA, Mases and colleagues1 on behalf of the Spanish ANESCARDIOCAT perioperative research group2 add important data to the expanding perioperative literature describing chronic kidney disease (CKD) as a consistent associate with postoperative morbidity. This post hoc observational study confirms the findings of a previous meta-analysis, showing an increased risk of perioperative major cardiovascular events in patients with estimated glomerular filtration rate (eGFR) ≈ 45 ml min⁻¹ 1.73 m⁻².3 These data extend the perioperative CKD literature by assessing major adverse cardiac and cerebrovascular events (MACCE) in surgical populations other than vascular surgery,3 the chief focus of previous studies primarily due to the perceived higher event rate for MACCE in this population. At this juncture, it is worth bearing in mind that the ANESCARDIOCAT study defined MACCE without routine high-sensitivity troponin sampling—which may therefore underestimate the true magnitude of the association between CKD and cardiac ischaemic events.4 Indeed, the first cohort of the international VISION study (Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study) suggests an association between postoperative troponin leak and degree of chronic renal dysfunction in ~15 000 patients.2 Both studies therefore reinforce the consistently negative impact of CKD on outcomes after non-cardiac surgery. Taken together with other recent studies, it is clear that even asymptomatic preoperative kidney impairment is associated with clinically significant increases in postoperative morbidity and mortality, as demonstrated in elective orthopaedic5 and major abdominal surgery.7 Thus, CKD defines a significant but substantial minority of patients who can be readily identified with real-time, objective, cheap, and prognostically important renal function tests that should be a key feature of every preoperative assessment.

By virtue of several creatinine-based prediction equations, the robust assessment of renal function is readily available (several web-based resources and apps are available; the calculators provided by the National Institute of Health National Kidney Disease Education Program are an excellent resource: http://www.nkdep.nih.gov). Of the purely creatinine-based equations, CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula has emerged as the most robust calculator. CKD-EPI classifies fewer individuals as having CKD and is superior for quantifying the risk for mortality compared with the MDRD (Modification of Diet in Renal Disease) study equation across a broad range of populations.8 The measurement of cystatin C—which provides a measure of renal reserve that is independent of age, sex, and lean muscle mass—may further refine risk assessment in CKD.9 Since the categorization by the National Kidney Foundation of CKD into five stages of increasing severity (Table 1), CKD has consistently been associated—in a ‘dose-dependent’ fashion—with excess all-cause mortality and cardiovascular pathology in the general population of all healthcare systems/countries examined.10 UK-specific epidemiology makes similarly sobering reading. The NEOERICA (New Opportunities for Early Renal Intervention by Computerised Assessment) project found that the age-standardized prevalence of stage 3–5 CKD is 10.6% for females and 5.8% for males in the UK.11 The key repeated finding is that the majority of patients with CKD do not progress to end-stage renal failure, but rather sustain fatal cardiovascular complications prematurely. Most alarmingly, despite the clear association with excess morbidity and mortality, patients are frequently unaware of having CKD as exemplified by the US REGARDS (REasons for Geographic And Racial Differences in Stroke) cohort study.12 In REGARDS, <10% of 3803 adults with coronary artery disease—and in routine contact with tertiary level medical providers—were aware of having CKD.

Impact of CKD on cardiovascular disease

Compelling epidemiological data show that CKD confers increased risk of cardiovascular morbidity and mortality, irrespective of age, gender, and ethnic group. While CKD in the UK population certainly associates with increased risk of hypertension, diabetes, and cardiovascular disease, an important recent study interrogating a large (1 268 029) patient cohort showed the true importance of recognizing CKD in relation to cardiovascular morbidity and mortality.13 In this cohort, the rate of myocardial infarction was lower in those with diabetes—without CKD—than in those with CKD without diabetes. The rate of incident myocardial infarction in people...
Immediate perioperative challenges associated with CKD

The Journal has previously published an extensive review of how CKD may affect anaesthetic practice, with detailed anaesthetic scrutiny of fluid balance, haemodynamic monitoring, and autonomic dysfunction clearly becoming increasingly important in patients with minimal renal reserve. Since that review, a recent meta-analysis has confirmed that CKD confers an increased risk of perioperative bleeding, as has been reported for bleeding in non-surgical settings. Further examination of the recently completed Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) Study will provide definitive contemporary data to substantiate the relationship between CKD stages and (higher sensitivity) troponin-defined perioperative cardiovascular events. Importantly, this 40 000 patient observational study enrolled patients undergoing a broad range of non-cardiac surgical procedures, not just non-vascular surgery.

### The dangers of CKD preceding end-stage renal failure

The dose–response relationship between CKD, significant non-cardiac postoperative morbidity associated and prolonged hospital stay mirrors similar studies in the general medical population, where CKD increases the risk of adverse outcomes after percutaneous coronary intervention. Factors other than renal drug clearance can also alter drug effects, including a substantially higher frequency of adverse drug reactions to water-soluble drugs in elderly patients with unrecognized CKD. As proof of principle, interventional studies in separate healthcare systems have demonstrated that clinical decision support systems targeted at appropriate drug dosing in CKD reduce the hospital length of stay.

### A critical opportunity for perioperative medicine

The early identification of individuals with CKD, especially those populations with a high risk for CKD and related adverse outcomes, is a major public healthcare challenge. Both the identification and subsequent implementation of evidence-based interventions may slow or prevent the progression to advanced stages of the disease, reduce the risk of cardiovascular disease, multiple other complications, and improve quality of life.
surgery, particularly in an ageing population with frequently undiagnosed or unrecognized CKD, a role for perioperative medicine in deciphering the impact of progressive stages of CKD on postoperative and general healthcare outcomes is self-evident. The NEOERICA study of computerized records found that for a general practice of 10,000 patients, around 150 patients with stages 3–5 CKD would be identified—over and above those patients already known to have CKD. Indeed, perioperative medicine finds itself in an unrivalled position to contribute in helping define a new strategy to address CKD progression. Central to this role is the use of standardized, population-based definitions to define CKD, which has often been lacking in previous perioperative studies. Understanding how immediate and longer-term postoperative outcomes impact on CKD progression can help elucidate mechanisms through which CKD alters renal and extra-renal disease. The perioperative environment provides an ideal, controlled human model to enable further mechanistic understanding of why CKD patients are more prone to cardiac, infectious, and drug/pharmacokinetic-related morbidity. In this way, experimental perioperative medicine can provide important mechanistic insights that translate to the wider CKD population. Thus, not only should CKD be regarded as a robust marker of increased perioperative risk of morbidity, but also a key element underlying the emergence of perioperative medicine as a preventive translational speciality. For example, the NEOERICA study identified that arterial pressure was appropriately controlled in only 20% of diabetic patients with stage 3–5 CKD. The REGARDS study highlighted the need for subspeciality clinicians routinely assessing renal function to be cognizant of the wider implications of CKD in order to educate and inform their patient population. Effective perioperative medicine should be in the vanguard of directing readily available interventions and the targeting of specialist resources to address these clear deficiencies. Thus, both acute and longer-term outcomes for patients with CKD can be positively influenced by perioperative medicine. Adopting the routine practice of applying creatinine to calculate eGFR using the MDRD or CKD-EPI nomogram—or merely noting the increasingly commonly automated reporting of estimated GFR—can help firmly establish the contribution of academic and clinical perioperative medicine to surgical patient care well beyond the perioperative period.

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References
Error modelling in anaesthesia: slices of Swiss cheese or shavings of Parmesan

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Accidents in complex systems occur through the concatenation of multiple factors; each may be necessary, but only when all are present are conditions sufficient to produce an accident. In 1990, James Reason, then a professor of Psychology at the University of Manchester, provided a crucial contribution to this idea by proposing a ‘model’ of how accidents could be seen as the result of interrelations between real time ‘unsafe acts’ by front-line operators and latent conditions. Holes can appear in multiple levels of the system. When these holes line up, as in multiple slices of Swiss cheese, an accident can occur. A key facet of this model is the suggestion that by preventing any one hole in the Swiss cheese, the eventual adverse event could have been prevented.

The Swiss cheese model has been further developed and explored in other complex high-risk industries, including aviation, nuclear power, and, increasingly, healthcare. For example, the 2002 Überlingen plane crash involved the midair collision of a cargo plane and a passenger jet at 35 000 feet. Reviews of the circumstances leading up to the collision identified numerous ‘holes’ involving the International Civil Aviation Authority, the air traffic control organization and culture, and pilot training. These holes included aspects of workload, workflow, training, equipment, and communication.

Multiple checks of patient identification and the surgical checklist are designed to prevent wrong site, wrong side procedures. A risk of utilizing the Swiss cheese model is the thought that any single error, in this process, can be mitigated by the protective actions of the system, other personnel within the system, or both. Obtaining consent for a procedure on the ‘wrong’ side will be corrected by marking the site, and other checks along the surgical pathway. If the system prevents poor practices contributing to adverse events, pressures to change may be resisted.

In healthcare, though, a large numbers of errors are unredeemable. Many of these errors may decrease the probability, or even possibility, of an optimal outcome. A safe blood transfusion service involves numerous checks at multiple levels. However, some of the key steps in the process are not able to be prevented, identified, or corrected by other parts of the system. A significant deviation from procedure may be unrecoverable. A mislabelled specimen may only be salvageable if the patient is known, by the laboratory, to have a different blood group. Failure to adequately check the blood and patient documentation, at the time of administration, may only be discovered after an adverse effect has occurred.

A recent report outlined the consequences of a delayed diagnosis. After 18 months of treating a plantar wart, a biopsy diagnosed a melanoma. In court, the plaintiff was unable to prove, on the balance of probabilities that the delay contributed to the development of distant metastases. However, it makes biological sense that a significant delay in diagnosis could lead to an increased possibility of metastatic spread.

A similar case involved a 6-yr-old girl, who, in 1990, developed headache and drowsiness. Two weeks later, during a second hospital admission, she became drowsy, with nonresponsive pupils. A CT scan revealed a brain tumour. The trial judge held that it could not be proven that the delay had caused Ms Tabet’s brain damage, but found that negligence made a 25% contribution towards her ultimate brain damage. He held that she was entitled to damages for the lost chance of a better medical outcome. That chance was assessed as a 40% chance of a better medical outcome, and