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ORIGINAL ARTICLE

Perioperative management of adult cadaveric and live donor renal transplantation in the UK: a survey of national practice

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ABSTRACT

Background. There is a limited evidence base and no national consensus regarding the perioperative management of patients undergoing renal transplantation. We developed an electronic survey to capture an overview of renal transplant perioperative practice across UK renal transplant centres and determine the need for future guidelines on patient management.

Methods. A 29-question survey was developed to encompass the entire renal transplant perioperative pathway and input was sought from clinicians with expertise in renal transplant surgery, anaesthesia, nephrology and intensive care. The survey was sent to lead renal anaesthetists at each of the 23 transplant centres across the UK.

Results. A 96% response rate was achieved with 22 out of 23 centres returning complete responses. There was limited evidence of guideline-based approaches to preoperative workup. Questions regarding intraoperative fluid management, blood pressure targets, vasopressor administration and central venous pressure (CVP) monitoring identified a broad range of practice. Of note, the routine use of goal-directed fluid therapy based on cardiac output estimation was reported in six (27.3%) centres, while nine centres (40.9%) continue to target a specific CVP intraoperatively. In all, 12 (54.5%) centres perform transversus abdominis plane blocks with fentanyl-based patient-controlled analgesia as the most common mode of postoperative analgesia. A single centre reported a renal transplant-specific Enhanced Recovery after Surgery programme for cadaveric organ recipients.

Conclusions. This questionnaire highlighted a high degree of heterogeneity in current UK practice as regards the perioperative management of renal transplant recipients. Development of evidence-based national consensus guidelines to standardize the perioperative care of these patients is recommended in order to improve patient outcomes and focus areas of future research.

Keywords: anaesthesia, perioperative care, renal transplant, survey

INTRODUCTION

Patient outcomes after major surgery can be improved considerably through the delivery of effective perioperative care [1]. Patients undergoing renal transplantation are increasing in age and multi-morbidity [2], with a unique pathophysiology that mandates effective evidence-based perioperative practice. Although significant research effort has been put into improving the management of patients undergoing major surgery, the majority of these studies exclude renal transplant recipients [3, 4]. This has resulted in a limited evidence base to inform the perioperative care of this complex patient cohort.

Currently, there is little national consensus on the perioperative management of patients undergoing renal transplantation and efforts to address this are hampered by the lack of a national body or representation to engender communication between transplant centres. To provide an evidence base to highlight the importance of this consensus, we developed a survey to generate an overview of current national practice across UK renal transplant units and identify areas of heterogeneity in management.

MATERIALS AND METHODS

An electronic survey was sent to the lead renal anaesthetist at each of the 23 centres performing adult cadaveric renal transplantation across the UK, between February 2018 and April 2018. Where this individual could not be identified, an anaesthetist with a renal transplant interest was sought.

The survey was developed to encompass the entire perioperative episode of patients undergoing renal transplantation. Input regarding content was sought from clinicians with expertise across this clinical spectrum, including transplant surgery, anaesthesia, nephrology and intensive care medicine. A total of 29 questions were included, divided into pre-, intra- and postoperative management. Closed questions designed to generate unambiguous responses were developed with free-text options to expand on answers given.

Information was requested regarding:

- the presence of pre-assessment guidelines and the use of cardiac risk assessment testing;
- (ii) preoperative dialysis;
- intraoperative fluid management;
- (iv) intraoperative monitoring and haemodynamic targets;
- vasoactive drugs; (v)
- (vi) management of reperfusion; and
- analgesia.

All 29 questions are presented in Appendix 1.

The survey was assessed via the National Research Ethics Service decision-making tool and did not meet current UK definitions for research requiring ethics committee approval [5]. The survey was registered with the local audit and clinical governance department.

RESULTS

Complete survey responses were obtained from 22 out of 23 adult renal transplant centres (96% response rate). All but one centre identified a site-specific guideline for the perioperative management of renal transplantation; these guidelines were predominately under the auspices of anaesthesia and nephrology.

Preoperative workup

Despite the presence of site-specific perioperative guidelines for the management of these patients there was significant heterogeneity in the indications for, and modality of, preoperative cardiorespiratory function testing performed. Of the 22 centres, 5 (22.7%) do not routinely perform cardiorespiratory investigations and where these are implemented they are performed on a case-by-case basis without defined indications or criteria. In the remaining centres, the selected testing modality showed broad variation based on local expertise and availability. The most commonly requested investigations include transthoracic echocardiography (TTE), cardiopulmonary exercise testing, pulmonary function and stress echo (Table 1). A single centre (4.5%) routinely requests cardiology review prior to transplantation, whereas the remaining centres identified common indications for cardiology referral as age >50 years and the presence of pre-existing diabetic and cardiovascular disease.

Perioperative management

Dialysis. The majority of centres (63.6%) dialyse preoperatively to the recipient's 'dry weight'. Three centres (13.6%) stated that they target a post-dialysis body weight 1-2 kg above the recipient's dry weight, whereas the others do not specify a preoperative dialysis target weight.

Grade of anaesthetist. The grade of the most senior anaesthetist managing a cadaveric renal transplant showed variation between centres and according to the time of day. During normal working hours, 81.8% of centres provide consultant-led care. Between 12 a.m. and 8 a.m. the most senior anaesthetist managing these cases was a post-fellowship registrar in 16 (72.7%) centres. In two (9.1%) centres, out-of-hours care was provided by a pre-fellowship registrar, with the four (18.2%) remaining centres providing consultant-led care at all times of

Fluid management and cardiac output optimization. Survey responses identified a wide range of, and variability in, practice as regards intraoperative fluid administration. While most centres routinely use a balanced salt solution (plasmalyte, compound sodium lactate and the haemodialysis fluid 'hemosol'), eight (36.4%) centres reported the use of 0.9% saline as their primary intravenous fluid (Figure 1). One centre (4.5%) uses hypertonic 1.26% sodium bicarbonate as intraoperative maintenance. Fluid administration via a fixed-rate infusion pump was only used in one centre with all others opting for free-flow systems.

Goal-directed fluid therapy based on cardiac output (CO) estimation was described as routine practice in six (27.3%) centres. The remaining centres all used CO systems to guide fluid

Table 1. Responses to the question: which tests do you routinely request to assess preoperative cardiopulmonary function in patients to be listed for renal transplantation (select all that apply)?

Investigation	Number of centres (%)
TTE	10 (45.5)
Stress echo	4 (18.2)
Cardiopulmonary exercise test	2 (9.1)
Pulmonary function tests	2 (9.1)
Myocardial perfusion scan	1 (4.5)
6-min walk test	0 (0)
Shuttle test	0 (0)
Coronary angiogram	0 (0)

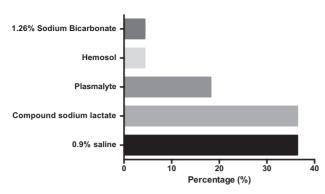


FIGURE 1: Responses to the question: which intravenous fluid is predominantly used intraoperatively during renal transplantation in your centre?

Table 2. Responses to the free-text question: if a specific MAP or SBP is targeted, please give details

Free-text responses

Patient dependent

Above 100-110 mmHg systolic post-reperfusion

Patient's baseline MAP

MAP >80 mmHg

Dependent on patient's preoperative blood pressure and surgical communication

10% variability around the baseline MAP

SBP >110 mmHg

SBP >120 mmHg 20 min prior to reperfusion and onwards

Within 10% of preoperative blood pressure

Patient's usual SBP

administration on a patient-specific basis though no centres identified defined criteria for patient selection. The modalities of CO estimation employed were predominately arterial pressure wave analysis, such as LiDCOrapid and Flotrac (11 centres, 50%), and oesophageal Doppler (9 centres, 40.9%), with a single centre implementing non-invasive Finapres technology.

Central venous catheters. Three-quarters of centres regularly insert a central venous catheter (CVC) into renal transplant recipients and half of all centres would place a CVC in addition to an existing patent dialysis line. In all, nine centres (40.9%) target a specific central venous pressure (CVP) intraoperatively; the target CVP showed wide variation, with reported values from 7 to 17 cm H_2O .

Blood pressure management. A total of 13 centres (59.1%) target either a specific mean arterial pressure (MAP) or systolic blood pressure (SBP), but there was a wide variety in the targets described (Table 2). Quoted MAP targets varied between 10% and 20% of baseline recipient MAP, with two centres (9.1%) stating an MAP target >80 mmHg for all cases. A total of three centres (13.6%) target the recipient's preoperative SBP, aiming to maintain this throughout the case.

Two (9.1%) centres reported the routine insertion of arterial lines, with the remainder only doing so where arterial waveform methods of CO estimation were employed, as above. The vasoactive agents employed intraoperatively are predominately ephedrine and metaraminol in 11 and 15 centres, respectively (Figure 2). Phenylephrine and noradrenaline are reserved as secondary agents. One centre (4.5%) reported the frequent use of dopamine infusions.

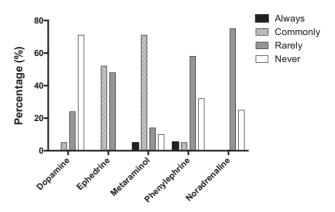


FIGURE 2: Responses to the question: regarding vasoactive drugs, does your centre use the following frequently, rarely or never: dopamine, ephedrine, metaraminol, phenylephrine and noradrenaline.

Reperfusion. Forced diuresis with furosemide was reported as routine practice in 3 (13.6%) centres, whereas 11 centres (50% of responses) stated an institutional avoidance of its use for this indication. The administration of mannitol was more common, with routine use reported in nine (40.9%) centres, whereas only five centres (22.7%) stated that it was never used.

Analgesia. Transversus abdominis plane blocks are used routinely in 12 (54.5%) centres and of these two-thirds are sited by the anaesthetist (the remainder under direct vision by the operating surgeon). In all, two centres (9.1%) used a local anaesthetic infusion via a surgically inserted catheter between wound layers. Twenty (90.9%) centres provided patient-controlled analgesia postoperatively, with the majority of these (13 centres, 65%) using fentanyl as the first choice opioid, 5 (25%) using morphine and 2 (10%) oxycodone.

Postoperative care

A dedicated renal ward was the most common postoperative destination for renal transplant recipients (13 centres, 59.1%), while a renal- or transplant-specific high dependency unit provided postoperative care in the remaining centres. Several sites stipulated that high-risk recipients would be cared for in a general intensive care unit setting, decided on a case-by-case basis, although no predetermined criteria were used for patient selection.

A renal transplant-specific Enhanced Recovery after Surgery (ERAS) programme was in place in only one centre (4.5%) for cadaveric organ recipients and four centres (18.2%) for live donor recipients.

Practice according to transplant centre surgical volume

There was no evidence of standardization in practice between the nine largest volume transplant centres, which each performed >150 renal transplants in 2017/18 [6]. For example, regarding preoperative assessment, four of these nine centres (44.4%) reported a locally developed approach to preoperative investigation with no routine tests. Furthermore, one (11.1%) large-volume centre reported the routine use of CO estimation to guide fluid administration intraoperatively (oesophageal Doppler), while there was marked variation in implementing forced diuresis at reperfusion and vasopressor use. Of the four UK centres reporting the existence of an ERAS protocol for livedonor recipients, two were large-volume centres.

DISCUSSION

There is a clear heterogeneity in current UK practice regarding the management of renal transplant recipients throughout the entire perioperative period. Of note, this variation in practice is independent of transplant centre surgical volume, where it would be reasonable to expect defined protocols produced by experienced clinicians. Although the majority of centres have developed guidelines for the perioperative management of cadaveric renal transplantation, these are centre specific and disparate in their content.

There are some components of current practice identified in the survey for which there is evidence of an association with harm. The routine administration of chloride-rich solutions has been associated with impaired diuresis, decreased renal blood flow and development of metabolic acidosis compared with buffered salt solutions [7-9]. Hyperchloraemic acidosis is associated with acute kidney injury (AKI) following abdominal surgery, which may be attenuated by reducing the intraoperative chloride load [10]. It follows that the perioperative use of physiologically balanced replacement fluids is associated with a reduction in the need for dialysis and a reduced incidence of hyperkalaemia when compared with 0.9% saline in renal transplant surgery [11].

While renal transplant surgery generally involves much smaller fluid losses than major intra-peritoneal surgery [12], transplant recipients have an increased risk of fluid overload, especially in the anuric cohort. Despite this it remains common practice to give significant crystalloid volume expansion prior to renal vessel clamping with the aim of decreasing postoperative acute tubular necrosis. However, no published evidence supports the pursuit of positive fluid balance to improve renal outcomes [13], with retrospective data showing perioperative fluid administration of >2500 mL as strongly and independently associated with chronic allograft dysfunction [14]. This indiscriminate fluid administration approach is facilitated by ongoing debate regarding the utility of CO-based goal-directed fluid administration and use of approaches such as CVP targeting [15, 16].

Management of renal graft reperfusion is highly heterogeneous and not in keeping with the current evidence. There is no evidence in the general or post-renal transplantation population that forced diuresis with furosemide shortens AKI duration, reduces the need for dialysis or improves outcomes [17, 18]. The evidence base concerning the use of furosemide and mannitol is outdated, retrospective or contains a small number of patients, and thus their relevance to current practice is unclear [19, 20]. Similarly, the routine administration of mannitol must be weighed against the associated risks with accompanying hydration if the patient is anuric.

There is conflicting evidence regarding the effects of dopamine in the perioperative period. The majority of studies fail to show any significant benefit when administered to renal transplant recipients [21, 22]. Although recent evidence suggests that low-dose dopamine may increase renal plasma flow, urine flow rate and creatinine clearance [23], these findings have not been reproduced. Dopamine administered to live donor recipients incurs no outcome advantage in either recipient or donor [24].

We have shown that current out-of-hours care of these patients is often provided by more junior clinicians. Hence, a particular focus on trainee education, competence and confidence is required. Care of renal transplant recipients is poorly represented in the current anaesthetic curriculum and this requires redress.

Despite a growing evidence base within some specific domains of perioperative management of renal transplant recipients, controversy and variation in clinical practice persist. These debates are not unique to UK practice; indeed controversy over aspects of perioperative care for the renal transplant recipient is also evident in continental Europe, with several areas of management still under discussion and investigation [25, 26].

Though more up-to-date and robust research is required, significant improvements can be made to patient outcomes through better use and implementation of the evidence base already available through systematic review. Additional nationallevel consensus is also required and should be developed through the use of collaborative tools such as Delphi consensus methodology [27]. This should seek to generate guidelines covering the entire perioperative pathway of renal transplant recipients. Non-standardized, outdated practice has the potential to impact negatively on patient outcomes; the development of an ERAS programme is likely to resolve some of the uncontrolled variation in current practice and would be expected to enhance outcomes. The feasibility of an ERAS programme for deceased donor renal transplant recipients has been demonstrated [28], and there is emerging evidence pointing towards improved postoperative outcomes [29] alongside a wealth of existing literature to support the approach in other surgical specialties [30].

CONCLUSION

This survey has demonstrated a high degree of heterogeneity in current UK practice as regards the perioperative management of renal transplant recipients. It has also highlighted a number of non-standardized and potentially outdated practices. The formation of a working party and development of evidencebased national consensus guidelines are recommended to focus future research targets and standardize the perioperative care of these complex patients.

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CONFLICT OF INTEREST STATEMENT

None declared.

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Appendix 1

Table A1. Complete set of questions sent electronically to each transplant centre

-	Question Question details	
1	Transplant unit (select option)	
2	What is your job title?	
3	Does your centre have a specific guideline for the perioperative management of renal transplantation? • Yes	
	• No	
	If yes, which speciality(ies) is responsible for it?Unsure/do not know	
4	Which tests do you routinely request to assess preoperative cardiopulmonary function in patients to be listed for renal transplantation (select all that apply)? • Transthoracic echo (TTE)	
	Pulmonary function tests (PFTs)	
	• Stress echo	
	Myocardial perfusion scan (MPS)	
	Cardiopulmonary exercise test	
	Coronary angiogram	
	6-min walk	
	• Shuttle test	
-	• Other (please specify)	
5	Are patients routinely assessed by a cardiologist prior to transplantation?	
	• Always	
	If previous history of cardiovascular disease	
	• If patient >50 years old	
	• Not routinely	
	Other (please specify)	
6	For patients requiring haemodialysis prior to transplantation, does your centre aim to dialyse to dry weight pre-op?	
	• Yes	
	• No	
	• If no, please give detail (i.e. 1 kg over dry weight)	
7	Generally, what is the level of the most senior anaesthetist managing a cadaveric renal transplant in the following situations: Normal working hours Monday–Friday (8 a.m.–6 p.m.)	
	Between the hours of 6 p.m. and 12 a.m.	
	• Between the hours of 12 a.m. to 8 a.m.	
8	Which intravenous fluid is predominantly used intraoperatively in your centre?	
	• 0.9% saline	
	• Plasmalyte	
	Compound sodium lactate	
	Hemosol (solution for haemodialysis)	
	Other (please specify)	
9	What do you anticipate the average operative blood loss to be during renal transplant?	
	• 0-250 mL	
	• 250–500 mL	
	• 500–750 mL	
	• >750 mL	
10	How do you manage intraoperative fluid administration:	
10	Fixed continuous infusion with infusion pump	
	Continuous infusion with infusion pump	
	Boluses on top of infusion Boluses only	
11	• Boluses only	
11	Does your centre regularly use cardiac output (CO) monitoring to guide fluid management during renal transplantation?	
,	• Yes	
	• No	
	• Sometimes	
	Comments	

886 | C.M. Morkane et al.

Table A1. (continued) Ouestion Question details number 12 If your centre does regularly use CO monitoring, which method is employed (select all that apply): · Oesophageal Doppler • Arterial waveform analysis (i.e. LiDCOrapid, Flotrac) • Non-invasive (i.e. Finapres, ClearSight) • Bioimpedence, bioreactance • Other (i.e. PPV (pulse pressure variation), SVV (stroke volume variation)), please state what 13 Do you regularly use CVCs (central venous catheters) in patients undergoing renal transplantation? Yes No If you answered yes to Question 13, would you use an existing dialysis line (if present) or place a separate central line? 14 • Yes, I would place a separate CVC line • No, I would use an internal jugular line dialysis if present 15 If you answered yes to Question 13, do you target a specific CVP value or range? • Yes No • If yes, what is you CVP target 16 Do you routinely insert arterial lines into patients undergoing renal transplantation? • Yes No Comments Do you target specific intraoperative MAP (mean arterial pressure) or SBP (systolic blood pressure) values in renal transplant recipients? 17 • Yes No • If a specific MAP or SBP is targeted, please give details 18 Regarding vasoactive drugs, does your centre use the following always, commonly, rarely or never: • Dopamine Ephedrine Metaraminol • Phenylephrine • Noradrenaline 19 Regarding the vasoactive drugs in Question 18, does your centre use boluses, infusions or a combination? · Boluses only · Infusion only • Boluses plus infusion 20 Do you regularly use furosemide to promote diuresis during renal transplantation? Routinely · Occasionally • Never 21 Do you use mannitol? Routinely Occasionally Never Which neuromuscular blockers do you regularly use for renal transplants? 22 23 If you use rocuronium, is there local guidance on the use of sugammadex in patients with renal disease? • Yes No If yes, please give details Regarding postoperative analgesia, do you use transversus abdominis plane (TAP) blocks regularly? 24 • Yes No If you answered yes to Question 24, TAP blocks are predominantly inserted by 25 • The anaesthetist following induction of anaesthesia · The anaesthetist at the end of surgery • By the surgeon intra-op

- Other (please specify)
- 26 Regarding postoperative analgesia, do you use patient-controlled analgesia (PCA)?
 - Yes
 - No
 - PainBuster/infusions into the TAP via catheter

(continued)

Table A1. (continued)

• Neither

Question Question details number 27 If you answered yes to Question 26, the opioid of choice in a PCA for analgesia post-renal transplantation is: • Morphine • Oxycodone • Other (please specify) What is the postoperative destination of renal transplant recipients in your centre? 28 • Specific renal high dependency unit (HDU) • General critical care unit • Renal ward • General medical or surgical ward • Other (please specify) Do you have a specific enhanced recovery programme for: 29 • Cadaveric renal transplant recipients • Live related recipients • Both