

MR. JOEY JUNARTA (Orcid ID : 0000-0002-9411-1478)

Article type : Original Article

Original article

Role of a cardio-renal multi-disciplinary team meeting in managing cardiovascular risk in patients on kidney transplant waitlists

Authors: Joey Junarta^{1,2}, Maria Fernandez¹, Isaac Chung¹, Ahmad Salha¹, Bayiha D. Klaud Francheska¹, Racquel Lowe-Jones¹, Rajan Sharma², Sami Firoozi², Debasish Banerjee^{1,2}

Institutions: ¹Renal and Transplantation Unit, St George's University Hospitals NHS Foundation Trust, ²Cardiology Clinical Academic Group, Molecular and Clinical Sciences Research Institute, St George's, University of London

Running title: CV risk management on kidney transplant waitlist Word count: Abstract 197, Body 3523 Tables: 6 Figures: 4

Address of correspondence: Joey Junarta MBBS BSc (Hons) St George's Hospital Blackshaw Road, Tooting, London, SW17 0QT, UK Telephone +44 2087251673 Fax +44 2087252068 Email: joeyjunarta@hotmail.com

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the <u>Version of Record</u>. Please cite this article as <u>doi:</u> 10.1111/ctr.14061

This article is protected by copyright. All rights reserved

Abstract

Background: Waitlisted kidney transplant patients suffer from excess cardiovascular events. The benefits of regular cardiac investigations, potentially harmful and expensive, are unknown. We investigate the effectiveness of a cardio-renal MDT in managing high cardiovascular risk waitlisted transplant patients to prevent events and enable transplantation.

Methods: Clinical outcomes in waitlisted transplant candidates managed by our cardio-renal MDT protocol were compared against our standard protocol. Data compared include the transplantation, event, and death rates, cost of cardiac investigations and procedures, and graft, patient survival, and re-hospitalisation rates in transplanted patients.

Results: 207 patients were studied (81 standard, 126 cardio-renal MDT). Over 2.7 years, the cardio-renal MDT protocol transplanted more patients than the standard group (35% vs. 21%; p=0.02). The managing cost per patient per year was higher in the standard group (£692 vs. £610). This was driven by more echocardiograms and more tests per patient in the standard group (p<0.01). There was no difference in adverse events or death. There was no difference in re-hospitalisation, graft or patient survival rate in transplanted patients.

Conclusions: Our cardio-renal MDT was effective in managing high-risk kidney transplant candidates with greater rates of transplantation and low rates of events at a lower cost.

Key words: end stage renal disease, chronic kidney disease, cardiovascular disease, kidney transplantation, cardiorenal syndrome

Background

Patients on the kidney transplant waitlist suffer from multiple co-morbidities associated with endstage renal disease (ESRD). This incurs a high cardiovascular event and mortality rate despite already having undergone cardiovascular evaluation to be listed for transplantation [1, 2]. Currently, there is no established protocol on when and how to utilise cardiac investigations in waitlisted transplant candidates. Indeed, cardiac investigations may be used to screen for patients with asymptomatic coronary artery disease (CAD). This may enable the correction of it before being listed again. Occasionally, investigated patients are deemed unsuitable due to unmodifiable cardiac risk and poor prognosis and are subsequently removed from the waitlist. This is to prevent premature cardiovascular mortality at transplantation or soon after. However, screening is potentially harmful and is costly.

The lack of evidenced-based screening methods prompted the start of two randomised controlled trials aiming to determine the optimal strategy to monitor and maintain cardiac fitness in waitlisted patients. The CADScreening trial (NCT02082483) is investigating the benefits of routine screening for CAD in waitlisted patients with myocardial perfusion scintigraphy (MPS) or dobutamine stress echo (DSE) versus selective screening based on symptoms. The CARSK trial (NCT03674307) tests the hypothesis that no further screening after waitlist entry is non-inferior to regular screening for CAD in preventing adverse cardiac events.

As a unit, we have a risk stratification protocol for patients before waitlisting for kidney transplantation. This protocol is relatively successful, evidenced by low peri-transplant death and cardiac event rates [3]. Our protocol introduced a cardio-renal multi-disciplinary team (MDT) meeting evaluation for all patients on the transplant waitlist. This study aims to investigate the effectiveness of a structured cardio-renal MDT in managing high cardiovascular risk patients on the kidney transplant waitlist to prevent pre-/peri-transplant cardiovascular events and enabling successful transplantation. This includes rationalising cardiac investigations in such patients to provide safe kidney transplantation yet minimize invasive investigations.

Materials and methods

This study was an observational audit that compared two cohorts of patients. The control group was managed by our standard protocol, while our cardio-renal MDT managed the interventional cohort. All patients on the kidney transplant waitlist at St. George's University Hospitals NHS Foundation Trust between 1 October 2011 and 31 September 2014 were included in the standard protocol group. Patients were followed from 1 October 2011 to 30 April 2016. All patients on the kidney transplant waitlist at St. George's University Hospitals NHS Foundation Trust between 1 October 2014 and 30 September 2017 were included in the cardio-renal MDT group. Patients were followed from 1 October 2014 to 11 May 2019. This study was approved by the hospital's Clinical Effectiveness and Audits Committee. As it is an audit, all data is anonymised, and informed consent was not necessary.

Prior to waitlisting, each patient underwent cardiac investigation and risk stratification according to our unit protocol [3]. Patients were classified as either high-risk (>60 years old or significant CAD [previous myocardial infarction, angiogram with >50% stenosis] or previous cerebrovascular accident (CVA) or significant peripheral vascular disease or had diabetes mellitus) or low-risk (those without defined high-risk features).

Waitlisted patients managed with our standard protocol involved being closely followed by their primary nephrologist. The primary nephrologist would determine the initiation of any inter-disciplinary management with cardiology regarding transplant needs. The decision to review patients and examine them in a clinical setting was determined based on clinical need by individual nephrologists and cardiologists. This includes decisions involving the evaluation of patients using cardiac testing.

Waitlisted patients managed with our cardio-renal MDT protocol were closely followed by a primary nephrologist and cardiologist. Patients were also reviewed and examined in a clinical setting based on clinical need throughout the follow-up period. However, patients were additionally routinely discussed in cardio-renal MDT meetings that occurred 4 times a year. Twelve to 14 patients were discussed in a single meeting with each patient discussed for approximately 5 minutes. The meetings were attended by kidney transplant nurses, 1 interventional cardiologist, 1 non-interventional cardiologist and nephrologists caring for the patients.

High-risk patients were routinely discussed every 2 years since waitlisted while low-risk patients were routinely discussed every 5 years since waitlisted. Any patient deemed complex by a nephrologist or cardiologist where the decision to maintain waitlist status was not straightforward were discussed in addition to the specified routine intervals. For example, patients with a very complicated history of CAD or were suffering from angina at the time.

The meeting would begin with the nephrologists presenting the patient's relevant clinical findings and the patient's specific concerns if necessary. The cardiologists would then present all the cardiac investigations. Each patient discussion leads to 3 possible outcomes. First, a patient is deemed too high-risk for surgery and was advised to be removed from the list. The second outcome is to re-evaluate a currently asymptomatic patient on the waitlist, usually with a non-invasive test. The third outcome is the decision to investigate a patient with complex findings or is currently symptomatic. This often prompted advice for coronary angiogram (CA) or invasive cardiac intervention.

The following are the definitions of a positive test: echocardiogram (echo) (wall motion or valvular abnormality), exercise stress echocardiogram (ESE) ($\geq 2x17$ segments abnormal), DSE ($\geq 2x17$ segments abnormal), CA ($\geq 50\%$ stenosis in any vessel).

Statistical analyses were conducted using IBM SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Kaplan-Meier curves and Cox regression analysis were used to compare the cardiac event rates between different groups, including diabetics vs. non-diabetics and those who tested DSE positive vs. DSE negative. Events included acute coronary syndrome, CVA, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), or death.

Results

Baseline characteristics of patients discussed

A total of 81 patients were included in the standard protocol group. There were 126 kidney transplant candidates included in the cardio-renal MDT group. Twenty-nine patients were discussed more than once, which resulted in 164 cardio-renal MDT meeting patient episodes. Table 1 shows the baseline characteristics of all patients. There was no difference in any clinical or laboratory characteristics between groups. Four patients had previous renal transplants in the standard protocol group. Two patients had previous renal transplants in the standard protocol group.

Procedures performed

Table 2 compares the type and number of cardiac procedures performed between groups. Throughout the study period, 114 and 127 cardiac investigations were done in the standard and cardio-renal MDT groups. Twenty-three percent of patients received no cardiac intervention, 33% had a single intervention, and 43% had multiple interventions in the standard protocol group. Thirty-five percent of patients received no cardiac intervention, 44% had a single intervention, and 21% had multiple interventions in the standard protocol group, more patients underwent multiple interventions (43% vs. 21%; p<0.01). There was also more echo performed in the standard protocol group. There was no difference in the number of DSE, ESE, CA, PCI, or CABG performed.

In the cardio-renal MDT group, 96 cardiac procedures were performed as a direct outcome of the MDT discussion. Nine echo, 5 ESE, and 61 DSE were conducted in the repeat evaluation of asymptomatic patients (Figure 1). Thirteen CA, 4 PCIs, and 4 CABGs were conducted in the immediate evaluation of symptomatic patients (Figure 2). Non-invasive testing in asymptomatic patients (echo, ESE, DSE) resulted in a further 19 CA, 10 PCI, and 2 CABG (Figure 1).

Patients removed from the transplant waitlist

In the standard protocol group, 12 patients were deemed unsuitable for transplantation and removed from the transplant waitlist. One patient died of a myocardial infarction at the end of follow-up. In the cardio-renal MDT group, 7 patients were deemed unsuitable for transplantation and were removed from the transplant waitlist. Six patients were still alive at the end of follow-up. One patient died of myocardial

infarction. Our cardio-renal MDT removed fewer patients based on cardiovascular risk compared to our standard protocol (7 vs. 12; p=0.02).

Clinical outcomes – transplantation rate and adverse events

Table 3 compares clinical outcomes between groups. Importantly, more patients were transplanted over the follow-up period if they were managed in the cardio-renal MDT group as opposed to the standard protocol group (35% vs. 21%; p=0.02). There was no difference in mortality or the number of adverse events between groups.

In the standard protocol group, there was no difference between transplanted and non-transplanted patients with respect to the following: age (p=0.16), body mass index (BMI) (p=0.09), diabetes status (p=0.81), smoking status (p=0.15), gender (p=0.33), hypertension (p=0.23), haemoglobin (p=0.54), urea (p=0.92), parathyroid hormone (PTH) (p=0.23), phosphate (p=0.21), ferritin (p=0.80), length of follow-up (p=0.39), or positive DSE (p=0.09). Transplanted patients had higher creatinine (p=0.04) and cholesterol (p=0.01) and lower calcium (p<0.01) at baseline. There was no difference in those who experienced events and those who did not with respect to the following: age (p=0.17), BMI (p=0.30), diabetes status (p=0.59), smoking status (p=0.97), gender (p=0.23), hypertension (p=0.90), haemoglobin (p=0.43), creatinine (p=0.78), urea (p=0.90), PTH (p=0.94), calcium (p=0.71), phosphate (p=0.86), ferritin (p=0.07), or positive DSE (p=0.88). Those who suffered events had higher cholesterol (p=0.01) and shorter follow-up (p<0.01).

In the cardio-renal MDT group, there was no difference between transplanted and non-transplanted patients with respect to the following: age (p=0.83), body mass index (BMI) (p=0.29), diabetes status (p=0.85), smoking status (p=0.45), gender (p=0.08), hypertension (p=0.48), haemoglobin (p=0.01), creatinine (p=0.36), urea (p=0.10), cholesterol (p=0.98), parathyroid hormone (PTH) (p=0.52), calcium (p=0.33), phosphate (p=0.71), ferritin (p=0.52), length of follow-up (p=0.19), or positive DSE (p=0.43). There was no difference in those who experienced events and those who did not with respect to the following: age (p=0.65), BMI (p=0.75), smoking status (p=0.11), gender (p=0.20), hypertension (p=0.75), creatinine (p=0.81), urea (p=0.18), cholesterol (p=0.31), PTH (p=0.42), calcium (p=0.45), phosphate (p=0.01) and those with events had lower haemoglobin (p=0.02) and shorter follow-up (p<0.00).

Diabetics were more likely to experience events as shown by the Kaplan-Meier analysis in Figure 3 (Log-rank test; p<0.01) and was the only significant variable on Cox regression when adjusted for age, gender, hypertension, cholesterol, and BMI (p=0.01). Those with positive DSE results tended to have more events (Figure 4), but this was not statistically significant (Log-rank test; p=0.09).

Clinical outcomes – morbidity and mortality in transplanted patients

Table 4 summarizes the long term clinical outcomes in transplanted patients between the two groups. There was no difference in hospitalisation rates 1 year after transplantation between groups. In the cardio-renal MDT group, 18 patients were hospitalised at least once 1 year after transplantation. There were 23 hospitalisations, of which 4 were due to cardiac causes. Three were due to acute coronary syndrome, and 1 was due to heart failure exacerbation. In the standard protocol group, 7 patients were hospitalised at least once 1 year after transplantation. There were 9 hospitalisations, of which none were due to cardiac causes. There was no difference in the number of total hospitalisations between the two groups (p=0.67). There was no difference in graft or patient survival at 1 or 2 years after transplantation between groups. *Cost analysis*

Tables 5 and 6 show the cost of investigations in the standard protocol and cardio-renal MDT protocol groups [4]. Notably, cardiac stress testing is significantly cheaper than CA, PCI, or CABG. The total cost of cardiac evaluation and intervention for maintaining 81 patients active on the list under the standard protocol was £151,483 or £692/patient/year. The cost of maintaining patients under the cardio-renal MDT protocol was £207,652. The cost at £610/patient/year is more economical compared to patients managed under the standard protocol.

Peri-transplant event rates

In the cardio-renal MDT group, 2 patients (6%) suffered from adverse events within thirty days of kidney transplant surgery, as defined previously [5, 6]. One patient had atypical chest pain and a troponin T rise 13 days after surgery. While the other suffered ischaemic chest pain 5 days after surgery. Both were treated conservatively. No peri-transplant events occurred in patients managed with the standard protocol.

Discussion

This study demonstrates the efficacy of a cardio-renal MDT in managing high cardiovascular risk patients on the kidney transplant waitlist. Over the same duration of 2.7 years, the cardio-renal MDT group transplanted more patients than the standard protocol group (35% vs. 21%; p=0.02) with only 2 perioperative events. No difference existed between transplanted and non-transplanted patients regarding baseline clinical or laboratory characteristics in the cardio-renal MDT group. In the standard protocol group, those who were transplanted had higher creatinine and cholesterol and lower calcium, demonstrating that those who were transplanted had worse renal function and metabolic risk factors. There was no

difference in adverse events or mortality between the two groups. There was also no difference in morbidity or mortality in transplanted patients, namely patient and graft survival and re-hospitalisation rate. Importantly, the cost of cardiovascular investigations and interventions was cheaper in the cardio-renal MDT group at £610/person/year vs. £692/person/year in the standard protocol group. The increased cost in the standard protocol group was driven by a higher number of echo conducted and a greater number of patients undergoing multiple cardiac tests. Ultimately, the cardio-renal MDT conducted a more tailored cardiac evaluation, which omitted unnecessary echo. The cardio-renal MDT identified 7 very high-risk patients on the list and removed them. Only 1 of these patients died upon follow-up. In doing so, we were able to prevent the high likelihood of these patients suffering from peri-operative adverse events. Additionally, this allowed donor kidneys to be allocated to more suitable candidates who would benefit. Overall, the cardio-renal MDT accepted a higher risk patient population where it refused fewer patients for transplantation compared to our standard protocol. Having a vested cardiology group involved allowed these patients to be transplanted without suffering from worse post-transplant adverse outcomes. Presumably, increased multi-disciplinary team working pre-transplantation allowed for timelier and directed cardiac care post-transplantation. The average cost over 2.7 years to maintain the kidney transplant waitlist with the cardio-renal MDT protocol was £1,634 per patient. DSE costs 10x less than CA, with PCI and CABG being even more expensive. Thus, the DSE was useful in ruling out disease to prevent conducting more invasive and costly cardiac investigations and procedures. Diabetics on the kidney transplant waitlist have a 2% higher mortality rate per year compared to their non-diabetic counterparts [7]. This is consistent with our study, where diabetics suffered more adverse events. We also showed that patients with positive DSE tended to have more events, but this was not statistically significant. This agrees with previous studies done [3, 8].

The optimal screening method and modality to optimise cardiovascular risk in transplant candidates is not agreed upon. The sensitivity and specificity of DSE in detecting underlying CAD in patients with ESRD has been reported to range from 0.44-0.89 and 0.71-0.94, respectively [9]. In comparison, the sensitivity and specificity of MPS were 0.29-0.92 and 0.67-0.89, respectively [9]. Indeed, it has been shown that MPS was only useful for cardiovascular risk stratification in kidney transplant candidates that were determined to be intermediate-risk, not low or high-risk [10]. In light of this, Mann et al. argued that CA is more useful in assessing cardiovascular risk in transplant candidates [11].

The contrasting approach by Kumar's group versus Kasiske's group is an example of the lack of clarity to manage these patients best [12, 13]. Kumar et al. investigated cardiac survival after pre-emptive coronary angiography in ESRD patients before transplantation [12]. Their pre-transplant practice involves an aggressive approach to invasive cardiac investigations in transplant candidates, where screening CA is conducted liberally, including in all patients >50 years old or with diabetes. In patients who went CA screening and were deemed suitable for waitlist entry, overall survival three years after CA was 97.2% in

those eventually transplanted. At the same time, it was 80.7% in those still awaiting transplantation [12]. Ultimately, survival was comparable to our approach, where screening was not restricted to solely invasive and expensive CA. In contrast, Kasiske et al. found that a risk-stratified approach to screening waitlisted kidney transplant candidates effectively avoided unnecessary testing [13]. In their retrospective review of 514 patients, 43.6% were categorised as low risk and did not undergo cardiac screening [13]. In these patients, the incidence of an ischaemic heart disease (IHD) event after waitlisting (before or after transplantation) was 0.5% at 1 year, 3.5% at 3 years, and 5.3% at 5 years [13]. 56.4% of patients were categorised as high-risk and underwent non-invasive stress testing or coronary angiography, which resulted in 6.2% and 2.8% of these patients to undergo prophylactic angioplasty or CABG, respectively [13]. Overall, the incidence of an IHD event after listing in these patients was 3.5% at 1 year, 8.1% at 3 years, and 19.7% at 5 years [13]. Importantly, of the 68 patients who suffered from an IHD event after being waitlisted, 80.6% underwent screening [13]. Yet, only 9% of patients screened underwent coronary angioplasty or CABG [13]. The authors concluded that in light of the relatively low proportion of screened patients who subsequently had an intervention, screening might not be cost-effective in preventing IHD events. Regardless, comparing these two contrasting approaches to our study, our cardio-renal MDT approach was effective and cost-sensitive, considering the transplantation, event, and mortality rate. Teamwork between cardiologists, nephrologists, and kidney transplant nurses improved care by aggregating and combining a greater amount of knowledge and expertise to make targeted clinical decisions and execute tasks more efficiently. This was evidenced by conducting fewer investigations that lowered cost, and transplanting more patients compared to our standard protocol over the same period. Therefore, it may be more useful to evaluate patients using a multi-modal approach rationalised in a structured MDT discussion instead of restricting assessment using a single pre-specified cardiac investigation or withholding screening altogether. It is important to stress that the annual mortality rate of those who remained on our waiting list is below national averages when managed with the standard or cardio-renal MDT protocol [7].

Previously, it has been shown that a multi-disciplinary approach can be useful in cardiac risk stratifying kidney transplant candidates [14]. Depending on whether patients were determined to be low, intermediate, or high-risk, cardiac testing was performed, which may include an exercise stress test, myocardial perfusion imaging, or CA [14]. Similar to our study, any abnormality on non-invasive testing led to more invasive evaluation and/or intervention. However, there was no mention of the long term outcomes resulting from this multi-disciplinary approach, including the transplantation, event, and mortality rate. Furthermore, a cost-analysis was not done. Therefore, it is difficult to determine the actual efficacy of the study's approach.

Recently, the Cardiovascular Work Group of the Kidney Pancreas Community of Practice of the American Society of Transplantation aimed to summarise key factors that may contribute to sub-optimal cardiovascular care in kidney transplant patients, including during the period of active transplant listing [15]. They stressed that despite the guidance available endorsed by organisations such as the American College of Cardiology, the American Heart Association, the National Kidney Foundation, and the American Society of Transplantation, the management of cardiovascular risk pre- and post-kidney transplantation vary widely amongst different transplant centers [15-17].

Several reasons may explain this. Firstly, there is a paucity of robust data on the optimal screening and management methods for CAD in CKD, as well as the optimal frequency to reassess coronary ischemia in asymptomatic patients [15]. It is unsurprising that this is the case, considering that CKD patients are often excluded from major cardiovascular trials. Screening for cardiac disease in kidney transplant candidates may be important for two reasons. Firstly, to identify patients with asymptomatic CAD to enable either the correction of it or removal of the patient from the list, with the end goal of preventing premature cardiovascular mortality at transplantation or soon after. Secondly, to avoid the misallocation of scarce donor allografts into those who experience early mortality.

Another reason is that the waitlisted patient invariably falls into a "no man's" land, where the responsibility of cardiovascular risk ownership is unclear in the setting of a fragmented model of care consisting of the transplant nephrologist, the evaluating cardiologist, and the referring nephrologist [15]. Thus, the Cardiovascular Work Group urge the development of proactive care models and cardiovascular screening trials to address the waitlisted population of patients [15]. The CADScreening (NCT02082483) and CARSK trial (NCT03674307) will hopefully provide greater insight into the best way to detect cardiovascular disease in such patients. In the meantime, our study shows that a structured cardio-renal MDT meeting is useful in rationalising cardiac investigations in waitlisted candidates. Furthermore, our protocol replaces the fragmented care actively waitlisted patients experience with a more holistic approach where the whole multi-disciplinary team shares responsibility for cardiovascular risk optimisation.

Limitations

Our study was an observational study without randomisation. Hence, it is hypothesis generating and may need data from a prospective randomised study before being universally accepted.

Conclusions

This is the first study to have evaluated the cost and effectiveness of a standardised cardio-renal MDT meeting in managing cardiac risk amongst kidney transplant candidates. Our cardio-renal MDT managed a group of very high-risk patients at a lower cost but was able to transplant more patients over the same follow-up period compared to our standard protocol. The overall cost was £610/year/patient in the cardio-renal MDT group, and this was achieved using mostly non-invasive cardiac tests and limiting invasive cardiac testing or intervention.

	List of abbrev	viations
	ESRD:	end-stage renal disease
	CAD:	coronary artery disease
	MPS:	myocardial perfusion scintigraphy
	DSE:	dobutamine stress echo
	MDT:	multi-disciplinary team
	CVA:	cerebrovascular accident
	CA:	coronary angiogram
	Echo:	echocardiogram
	ESE:	exercise stress echocardiogram
	PCI:	percutaneous coronary intervention
	CABG:	coronary artery bypass graft
	IQR:	interquartile range
	BMI:	body mass index
	PTH:	parathyroid hormone
	LVSF:	left ventricular systolic function
	LVEF:	left ventricular ejection fraction
	MRI:	magnetic resonance imaging
Q	IHD:	ischaemic heart disease

Acc

This article is protected by copyright. All rights reserved

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the St. George's University Hospitals NHS Foundation Trust Clinical Effectiveness and Audits Committee. This article does not contain any studies with animals performed by any of the authors. As it is an audit, all data is anonymised and informed consent was not necessary.

Consent for publication: Not applicable.

Availability of data and materials: Data is safely kept in a password protected security system at St. George's University Hospitals NHS Foundation Trust. The datasets used and/or analysed during the current study are de-identified and available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests. The results presented in this paper have not been published previously in whole or part, except in abstract form.

Funding: The authors have no sources of funding for this research to declare.

Authors' contributions: DB design, data collection, manuscript, supervision. SF design, manuscript, supervision. RS design, manuscript, supervision. JJ data collection, analysis, manuscript. MF data collection, analysis, manuscript. IC data collection, analysis, manuscript. AS data collection, analysis, manuscript. BF data collection, analysis, manuscript. RL data collection, analysis, manuscript. All authors read and approved the final manuscript.

Acknowledgements: Not applicable.

References

1. Machnicki G, Pinsky B, Takemoto S, et al. Predictive ability of pretransplant comorbidities to predict long-term graft loss and death. Am J Transplant 2009, 9(3):494-505.

2. Sapir-Pichhadze R, Tinckam KJ, Laupacis A, et al. Immune Sensitization and Mortality in Wait-Listed Kidney Transplant Candidates. J Am Soc Nephrol 2016, 27(2):570-578.

3. Ramphul R, Fernandez M, Firoozi S, et al. Assessing cardiovascular risk in chronic kidney disease patients prior to kidney transplantation: clinical usefulness of a standardised cardiovascular assessment protocol. BMC Nephrol 2018, 19(1):2-017-0795-z.

4. NHS Improvement: National tariff payment system 2017/18 and 2018/19.
https://improvement.nhs.uk/resources/national-tariff-1719/ (2019). Accessed 14 Jun 2019.

5. Twerenbold R, Badertscher P, Boeddinghaus J, et al. 0/1-Hour Triage Algorithm for Myocardial Infarction in Patients With Renal Dysfunction. Circulation 2018, 137(5):436-451.

6. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012, 60(16):1581-1598.

7. Matas AJ, Smith JM, Skeans MA, et al. OPTN/SRTR 2013 Annual Data Report: kidney. Am J Transplant 2015, 15 Suppl 2:1-34.

8. Herzog CA, Marwick TH, Pheley AM, et al. Dobutamine stress echocardiography for the detection of significant coronary artery disease in renal transplant candidates. Am J Kidney Dis 1999, 33(6):1080-1090.

9. Lentine KL, Costa SP, Weir MR, et al. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. J Am Coll Cardiol 2012, 60(5):434-480.

10. Galvao De Lima JJ, Wolff Gowdak LH, de Paula FJ, et al. The role of myocardial scintigraphy in the assessment of cardiovascular risk in patients with end-stage chronic kidney disease on the waiting list for renal transplantation. Nephrol Dial Transplant 2012, 27(7):2979-2984.

11. Mann DM, Fernandez S, Mondal Z, et al. Role of Coronary Angiography in the Assessment of Cardiovascular Risk in Kidney Transplant Candidates. Am J Cardiol 2016, 118(5):679-683.

12. Kumar N, Baker CS, Chan K, et al. Cardiac survival after pre-emptive coronary angiography in transplant patients and those awaiting transplantation. Clin J Am Soc Nephrol 2011, 6(8):1912-1919.

13. Kasiske BL, Malik MA, Herzog CA. Risk-stratified screening for ischemic heart disease in kidney transplant candidates. Transplantation 2005, 80(6):815-820.

14. Szabo RP, Varga I, Balla J, et al. Cardiovascular Screening and Management Among Kidney Transplant Candidates in Hungary. Transplant Proc 2015, 47(7):2192-2195.

15. Rangaswami J, Bangalore S, Kaplan B, et al. Cardiovascular disease care fragmentation in kidney transplantation: a call for action. Kidney Int 2019, 96(3):568-571.

16. Danovitch GM, Hariharan S, Pirsch JD, et al. Management of the waiting list for cadaveric kidney transplants: report of a survey and recommendations by the Clinical Practice Guidelines Committee of the American Society of Transplantation. J Am Soc Nephrol 2002, 13(2):528-535.

17. Lentine KL, Schnitzler MA, Brennan DC, et al. Cardiac evaluation before kidney transplantation: a practice patterns analysis in Medicare-insured dialysis patients. Clin J Am Soc Nephrol 2008, 3(4):1115-1124.

 Table 1. Baseline clinical and laboratory characteristics.

Characteristic	Standard protocol (N=81)	Cardio-renal MDT protocol (N=126)	P-value
Age	59.42 (11.14)	61.15 (8.12)	0.16
Body mass index	29.08 (5.76)	28.15 (4.6)	0.19
Male	44 (54.32%)	75 (59.52%)	0.42
Diabetes mellitus	45 (55.56%)	77 (61.11%)	0.42
Hypertension	76 (93.83%)	121 (96.03%)	0.37
Smoking status past/present/never	47/9/25 (58.02%/11.11%/30.86%)	70/12/44 (55.56%/9.52%/34.92%)	0.82
Haemoglobin (g/L)	108.07 (17.15)	108.18 (14.63)	0.96
Cholesterol (mmol/L)	4.08 (1.19)	4.02 (1.16)	0.69
Parathyroid hormone (pmol/L)	47.72 (58.04)	44.54 (39.20)	0.62
Calcium (mmol/L)	2.20 (0.18)	2.34 (1.64)	0.44
Phosphate (mmol/L)	1.48 (0.38)	1.50 (0.32)	0.77
Ferritin (mcmol/L)	312.60 (343.73)	385.97 (337.08)	0.12

Legend: MDT multi-disciplinary team. Data presented as mean (standard deviation) or number

(percentage %)

Acce

This article is protected by copyright. All rights reserved

 Table 2. Type and number of cardiac procedures performed.

Procedure	Standard protocol (N=81)	Cardio-renal MDT protocol (N=126)	P-value
Echocardiogram	30 (37.04%)	9 (7.14%)	< 0.01
Exercise stress echocardiogram	0	5 (3.97%)	0.11
Dobutamine stress echocardiogram	49 (60.49%)	61 (48.41%)	0.08
Coronary angiogram	20 (24.69%)	32 (25.40%)	0.29
Percutaneous coronary intervention	9 (11.11%)	14 (11.11%)	0.52
Coronary artery bypass graft	6 (7.41%)	6 (4.76%)	0.79

Legend: Data presented as number (percentage %)

 Table 3. Long term clinical outcomes.

Outcome	Standard protocol (N=81)	Cardio-renal MDT protocol (N=126)	P-value
Transplanted	17 (20.99%)	44 (34.92%)	0.02
Adverse event	29 (35.80%)	42 (33.33%)	0.66
Death	8 (9.88%)	16 (12.69%)	0.21

Legend: Data presented as number (percentage %)

Table 4. Long term clinical outcomes in transplanted patients.

Outcome	Standard protocol (N=17)	Cardio-renal MDT protocol (N=44)	P-value
Hospitalised 1 year after transplantation	7 (41.18%)	18 (40.91%)	0.99
Graft survival 1 year after transplantation	17 (100%)	42 (95.45%)	0.37
Graft survival 2 years after transplantation	16 (94.11%)	42 (95.45%)	0.83
Patient survival 1 year after transplantation	17 (100%)	43 (97.72%)	0.53
Patient survival 2 years after transplantation	16 (94.11%)	43 (97.72%)	0.48

Legend: Data presented as number (percentage %)

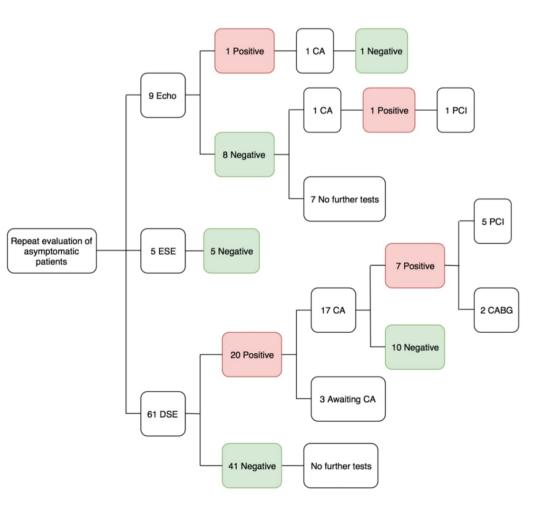
Table 5. Cost for procedures calculated from NHS best practice tariffs in the standard protocol group.

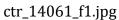
Procedure	Number	Cost per procedure (£)	Cost (£)
Echocardiogram	30	58	1,740
Exercise stress echocardiogram	0	250	0
Dobutamine stress echocardiogram	49	250	12,250
Coronary angiogram	20	2,751	55,020
Percutaneous coronary intervention	9	4,025	36,225
Coronary artery bypass graft	6	7,708	46,248
Total cost			151,483
Cost per patient			1,870
Cost per patient per year			692

Table 6. Cost for procedures calculated from NHS best practice tariffs in the cardio-renal MDT protocol group.

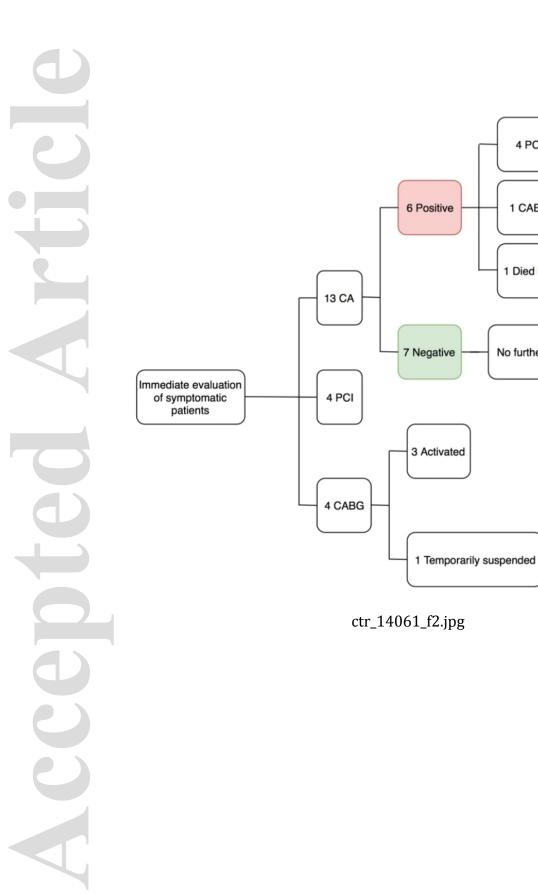
Procedure	Number	Cost per procedure (£)	Cost (£)
Echocardiogram	9	58	522
Exercise stress echocardiogram	5	250	1,250
Dobutamine stress echocardiogram	61	250	15,250
Coronary angiogram	32	2,751	88,032
Percutaneous coronary intervention	14	4,025	56,350
Coronary artery bypass graft	6	7,708	46,248
Total cost			207,652
Cost per patient			1,648
Cost per patient per year			610

ACCE





This article is protected by copyright. All rights reserved

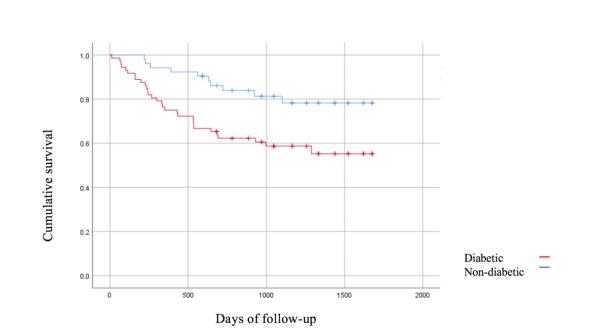


4 PCI

1 CABG

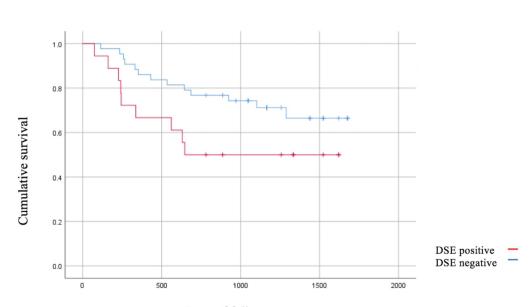
No further tests

1 Died before planned CABG



ctr_14061_f3.jpg

j,



Days of follow-up

ctr_14061_f4.jpg

D'C'