# Renal transplant recipient and deceased-donor risk profiles at Wits Donald Gordon Medical Centre, Johannesburg, South Africa: A 9-year review

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**Background.** Renal transplantation is the gold-standard therapy for end-stage renal disease. Decision-making around the acceptance of deceased-donor organs is complex and time sensitive. Risk scoring systems for both donors and recipients attempt to simplify the allocation of renal grafts to the most appropriate recipient.

**Objectives.** To investigate the role of these transplant risk scores in the South African (SA) setting.

**Methods.** A total of 188 adult deceased-donor organ referrals over the 9-year period 1 January 2013 - 31 December 2021 were included. The Kidney Donor Risk Index (KDRI) and the UK KDRI were calculated for each donor. Recipients who were allocated these grafts were characterised, and the Hennepin Transplant Risk Score and the Kidney Transplant Morbidity Index (KTMI) were calculated.

**Results.** The median (interquartile range) KDRI was 1.2 (0.9 - 1.6), confirming that low- to average-risk donors were being utilised. Similarly, the median UK KDRI was 0.9 (0.8 - 1.2). Both these scores performed poorly in predicting graft and patient survival, with a *C*-statistic of 0.5. Renal recipient risk scores also demonstrated low- to average-risk patients being transplanted, with a median Hennepin score of 2 - 4 points and a KTMI of 2 points. These recipient scores predict increased recipient mortality at high scores, albeit with low sensitivity, and were not significantly associated with graft survival.

**Conclusion.** Deceased-donor and renal recipient risk scores commonly used internationally performed poorly in predicting graft survival in our cohort, and should be used with caution in the SA setting. A conservative approach to organ donor referral and utilisation as well as renal transplant recipient listing was noted.

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End-stage renal disease presents a major challenge to the South African (SA) healthcare system, with a renal replacement therapy (RRT) patient prevalence of 146 per million population as per the 2020 South African Renal Registry.[1] A minority of patients receiving RRT access transplantation services, with only 20.7% reported to have received a functioning renal graft as of December 2020, after a median duration of RRT of 5.8 years.

Kidney transplantation is the RRT of choice in the treatment of end-stage renal failure. Transplantation has been validated internationally as superior to dialysis in terms of patient survival and costs, with patients in the dialysis group suffering significantly more all-cause mortality.[2,3] Access to donor organs is severely restricted nationally and internationally, and while living-donor renal transplantation has the potential to expand the donor pool, many patients do not have access to a medically fit living donor and remain dependent on having a graft allocated to them from the deceased-donor pool.

Deceased donors are historically classified into standard and extended criteria. Extended-criteria donors (ECDs) are those aged >60 years, or between the ages of 50 and 59 years with two or more of the following criteria: hypertension, renal insufficiency, or death by cerebrovascular accident. The relative risk of graft loss when allocated an ECD renal graft is 1.7, resulting in a 1-year graft survival rate of ~83% v. 90% for a graft from a standard-criteria donor (SCD).[4] This classification allows for informed consenting of the recipient when allocating a higher-risk graft to a specific recipient. It is worth noting that virtually all patients with end-stage renal failure will benefit from transplantation, irrespective of the recipient risk profile and the graft allocated.[3]

In an attempt to improve on the dichotomous nature of the ECD v. SCD classification, Rao *et al.*[5] developed the Kidney Donor Risk Index (KDRI).[5] Independent donor risk factors included in the KDRI score are donor age, height, weight, ethnicity, history of hypertension or diabetes, cerebrovascular accident as cause of death, preterminal creatinine level, and hepatitis C serology. Patients who received a graft from a high-KDRI donor (>1.45) had a 5-year graft survival rate of 63%, compared with 82% for those who received a graft from a donor with a KDRI <0.79.[5]

The UK KDRI was subsequently developed in 2012, showing equivalent predictive ability to the KDRI but with a reduction in the risk factors independently associated with graft loss and recipient mortality. A total of five variables are considered, namely donor age and weight, history of hypertension, length of hospital stays, and adrenaline use at the time of donation.[6] Several scoring systems have since been developed, some requiring only clinical data and others requiring histopathological information.[7] Matching donor and recipient risk profiles may ensure that the maximum benefit is obtained from renal allografts.

When assessing the recipient risk profile, international demographics demonstrate an ageing recipient population with associated comorbidities.[8,9] The Hennepin Transplant Risk Score

and the Kidney Transplant Morbidity Index (KTMI) have both been validated for the risk stratification of kidney transplant recipients. The Hennepin score assesses four parameters, namely recipient age, Karnofsky performance score, history of hypertension, and metabolic risk factors such as diabetes mellitus and dialysis vintage (length of time on dialysis). An above-average risk classification (2 - 4 points) confers a 4 times increased likelihood of adverse events, and a high-risk classification (≥8 points) translates to an 11 times increased risk.[10] The KTMI considers nine parameters, namely recipient age, dialysis dependence and vintage, history of diabetes, coronary artery disease, cerebrovascular disease, peripheral vascular disease, retransplant status, and dependence on others to perform activities of daily living, to assess recipient pretransplant comorbidity status, and has shown a linear decrease in graft survival and patient survival as scores increase.[11]

To date, kidney donor and recipient risk profiles using the established risk scoring classification systems have not been established for the SA population. This study aimed to describe the risk profile of deceased-donor renal grafts on offer to our programme in conjunction with risks present in the renal recipient population at the time of transplant, and to assess the predictive value of the KDRI, UK KDRI, KTMI and Hennepin score in predicting outcomes in the SA setting.

## Methods

Deidentified data from the REDCap database at the Wits Donald Gordon Medical Centre Kidney Transplant Research Database were analysed. Ethical approval was obtained from the University of the Witwatersrand's Human Research Ethics Committee (ref. no. M190880 (R14/49)). Adult recipients (>18 years) of deceased-donor, kidney-only grafts during the 9-year period 1 January 2013 - 31 December 2021 were included, allowing for a minimum follow-up period of 1 year to 31 December 2022. The corresponding deceased-donor demographic information as well as data elements for the abovementioned donor risk scores were collected and analysed.

The effect of each risk score (categorised as well as in continuous form) on patient and graft survival was assessed by Cox proportional hazards regression analysis. Performance of the score was evaluated by calculation of the concordance index (*C*-statistic) for recipient and graft survival at 1 year. The effect of transplant year was analysed similarly. Comparison of risk scores between ECD status and transplant year was performed using the Kruskal-Wallis test. Data analysis was carried out using SAS version 9.4 for Windows (SAS Institute, USA). A 5% significance level was used.

## Results

### Deceased-donor data

A total of 188 referred deceased-donor kidneys were accepted for transplantation by our programme during the study period and included in the study. The majority of deceased donors were in the 18 - 49-year age group (*n*=123/188; 65.4%) with 34.6% aged >49 years (*n*=65). The current allocation agreement dictates that one suitable kidney is allocated to a patient listed on the deceased WDGMC waiting list, and the other to the public sector where an independent team performs the transplant. No data are currently available on the outcomes of grafts not allocated to the WDGMC Transplant Unit. In terms of race, 146 donors were white (77.7%) and 18 were black (9.6%), with the remainder falling into other groups. Donors had a median (interquartile range (IQR)) height of 172 (165 - 179) cm and a median weight of 75 (65 - 90) kg, and the gender distribution was 58.0% male to 42.0% female. Of the deceased donors, 40 (21.3%) were known to have had hypertension and 13 (6.9%) to have had diabetes, and 1 tested hepatitis C antibody positive (0.5%). The cause of death was reported as a cerebrovascular incident in 60 cases (31.9%) and as traumatic brain injury in another 60 (31.9%), with 68 deaths (36.2%) being from other causes. Only brain-dead donors were procured during this time period, with no cases of donation after cardiac death being recorded as ECDs.

Of the cases with sufficient data to analyse, 131/167 (78.9%) were classified as SCDs and 36/167 (21.7%) as ECDs. The average hospital length of stay prior to organ donation was 3 (range 2 - 7) days, the median (IQR) terminal creatinine level 96.38 (64.55 - 153.85) μmol/L, and the rate of adrenaline dependence at the time of donation 40.4%.

### Recipient data

The majority of recipients fell into the 35 - 49-year age group (*n*=84/188; 44.7%); 42 (22.3%) were aged <35 years and 62 (33.0%) >50 years. Recipients were predominantly male (*n*=120; 63.8%) and black (*n*=97; 51.6%). A normal body mass index (BMI) was recorded in 71 patients (37.8%), with 56 (56.9%) being overweight (BMI >25 kg/m$^2$), of whom 37 (29.0%) were obese (BMI >30 kg/m$^2$).

Most recipients scored as minimally disabled by their disease, with 9.0% requiring assistance with activities of daily living. Cardiovascular morbidity as defined in the Hennepin score and KTMI was documented in 15.4% of patients, with 29/188 having at least one of the following: pulmonary hypertension, atrial fibrillation, history of an abnormal cardiac stress test, myocardial infarct, cardiac revascularisation, or peripheral vascular disease. Anticoagulation therapy at the time of transplant was infrequent at 12.2%.

The major modality of RRT at the time of listing was haemodialysis, and 48.9% had been on an RRT modality for >4 years. In 175 cases (93.1%) the transplant was the patient's first, and recipients spent an average of 11 days in hospital between the transplant and discharge.

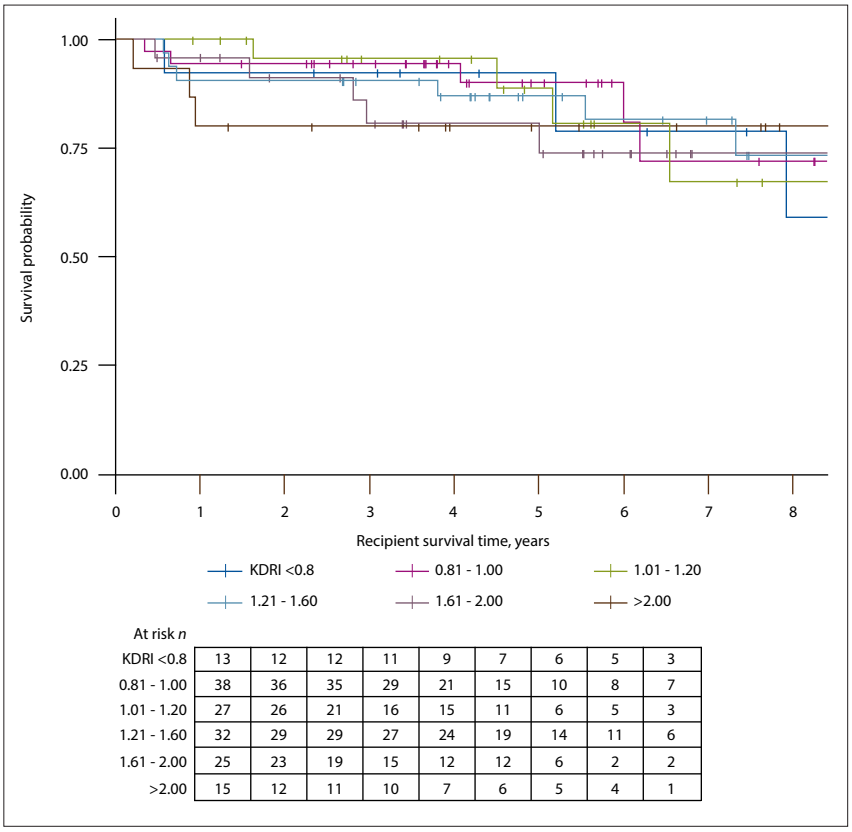
### Deceased-donor risk score analysis

The median (IQR) KDRI score calculated for the cohort was 1.2 (0.9 - 1.6). Grafts with a below-average risk for adverse events (graft loss or recipient mortality) (KDRI <1) comprised 30.0% of the grafts accepted. Grafts with a KDRI of 1.4 - 2.0 (increased risk of adverse events of 40 - 100% compared with the standard donor defined in the KDRI) comprised 27.5%. There was no statistically significant association between KDRI and recipient or graft survival in our cohort (Figs. 1 and 2). Unadjusted, considering KDRI as continuous, the hazard ratio (HR) for graft failure was 1.06 (95% confidence interval 1.0004 - 1.13) for every 0.1-unit increase in KDRI score. Median recipient survival at 1 year (94%), 3 years (90%) and 5 years (85%) did not differ statistically between risk groups.

The median (IQR) UK KDRI in this cohort was 0.9 (0.8 - 1.2). Unadjusted, there was no significant association between UK KDRI (categorised or considered as a continuous variable) and recipient or graft survival.

### Renal recipient risk score analysis

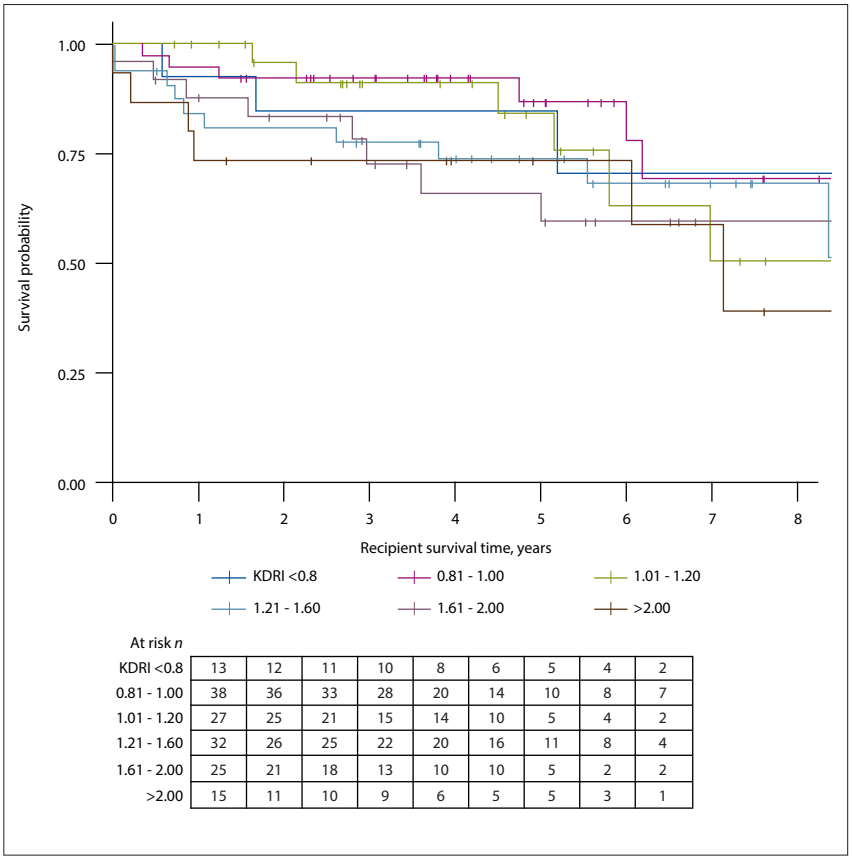
Recipient profiles were analysed using the Hennepin transplant recipient criteria. The majority of recipients (77.7%) were classified as average risk (scoring 2 - 4 points), with 3.2% of recipients identified as low risk (0 - 1 points) and 13.9% as high risk (5 - 8+ points). The median Hennepin score was 2, indicating an average-risk candidate. Unadjusted, there was a significant increased likelihood of death for a score of 5 - 8 v. 0 - 2 ($p$=0.0047) (Fig. 3). There was no significant association between the categorised score and graft survival (Fig. 4). Unadjusted, considering the score as continuous, the HR for death increased with increasing Hennepin score.




At risk *n*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| KDRI <0.8 | 13 | 12 | 12 | 11 | 9 | 7 | 6 | 5 | 3 |
| 0.81 - 1.00 | 38 | 36 | 35 | 29 | 21 | 15 | 10 | 8 | 7 |
| 1.01 - 1.20 | 27 | 26 | 21 | 16 | 15 | 11 | 6 | 5 | 3 |
| 1.21 - 1.60 | 32 | 29 | 29 | 27 | 24 | 19 | 14 | 11 | 6 |
| 1.61 - 2.00 | 25 | 23 | 19 | 15 | 12 | 12 | 6 | 2 | 2 |
| >2.00 | 15 | 12 | 11 | 10 | 7 | 6 | 5 | 4 | 1 |

*Fig. 1. Recipient survival over time per KDRI category. (KDRI = Kidney Donor Risk Index.)*




At risk *n*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| KDRI <0.8 | 13 | 12 | 11 | 10 | 8 | 6 | 5 | 4 | 2 |
| 0.81 - 1.00 | 38 | 36 | 33 | 28 | 20 | 14 | 10 | 8 | 7 |
| 1.01 - 1.20 | 27 | 25 | 21 | 15 | 14 | 10 | 5 | 4 | 2 |
| 1.21 - 1.60 | 32 | 26 | 25 | 22 | 20 | 16 | 11 | 8 | 4 |
| 1.61 - 2.00 | 25 | 21 | 18 | 13 | 10 | 10 | 5 | 2 | 2 |
| >2.00 | 15 | 11 | 10 | 9 | 6 | 5 | 5 | 3 | 1 |

*Fig. 2. Graft survival over time per KDRI category. (KDRI = Kidney Donor Risk Index.)*

When assessing recipient risk using the KTMI, 145 patients (77.2%) scored 0 - 3, conferring an >80% likelihood of graft survival and a 92% likelihood of patient survival at 3 years. In our cohort, the median KTMI was 2, with 85.4% graft survival and 93.7% patient survival.[10] Unadjusted, there was a significant increased likelihood of death for a score of 3 - 6 v. 0 - 1 ($p$=0.046). There was no significant association between the categorised score and graft survival. Considering the score as continuous, the HR for death increased with increasing KTMI score.

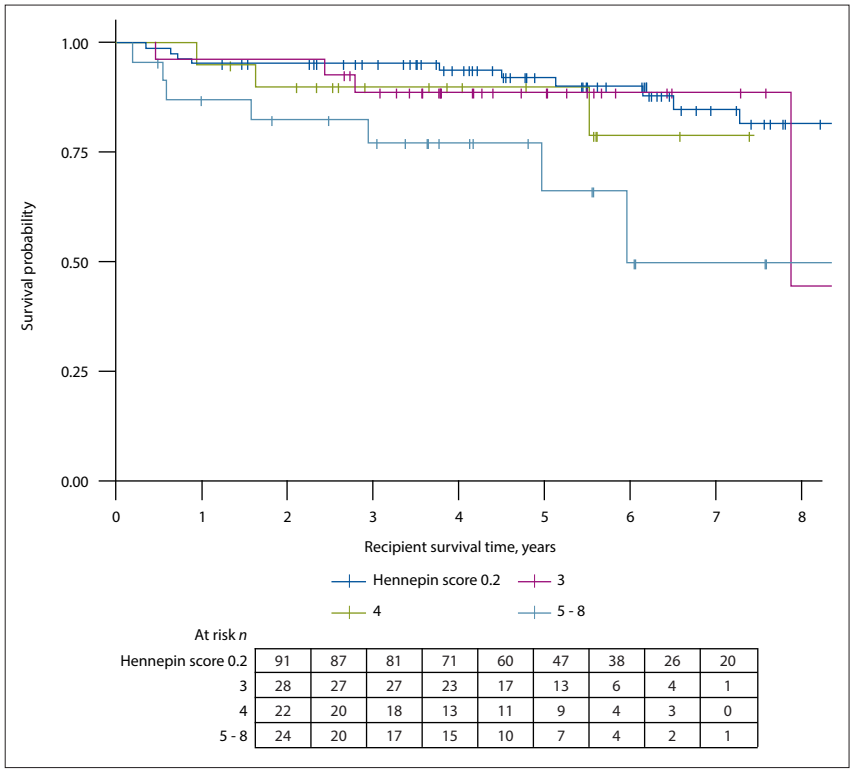
The *C*-statistic for all scores at 1 year was poor at 0.5. There was no significant association between transplant year and patient or graft survival.

The association between each risk score and transplant year and ECD status was analysed. ECDs had higher median risk scores in the KDRI and UK KDRI compared with non-ECDs ($p$<0.01), and the median risk scores in 2015 were significantly higher than in other years for both donor scoring systems. Similarly, no significant differences in patient or graft risk scores were noted between different years.

## Discussion

Acceptance of deceased-donor kidneys is often complex and time pressured, with decisions potentially contributing to graft and patient survival, but equally contributing to the unnecessary discarding of organs or a delay in transplantation. In an attempt to optimise these processes, various scoring systems attempt to simplify acceptance. The accuracy and applicability of these scoring systems in the SA context has not yet been defined. This study characterised deceased-donor kidneys and their subsequent recipients over a 10-year period and applied four of the most commonly used risk stratification methods in use: the KDRI and UK KDRI for donors, and the KTMI and Hennepin risk score for recipients.

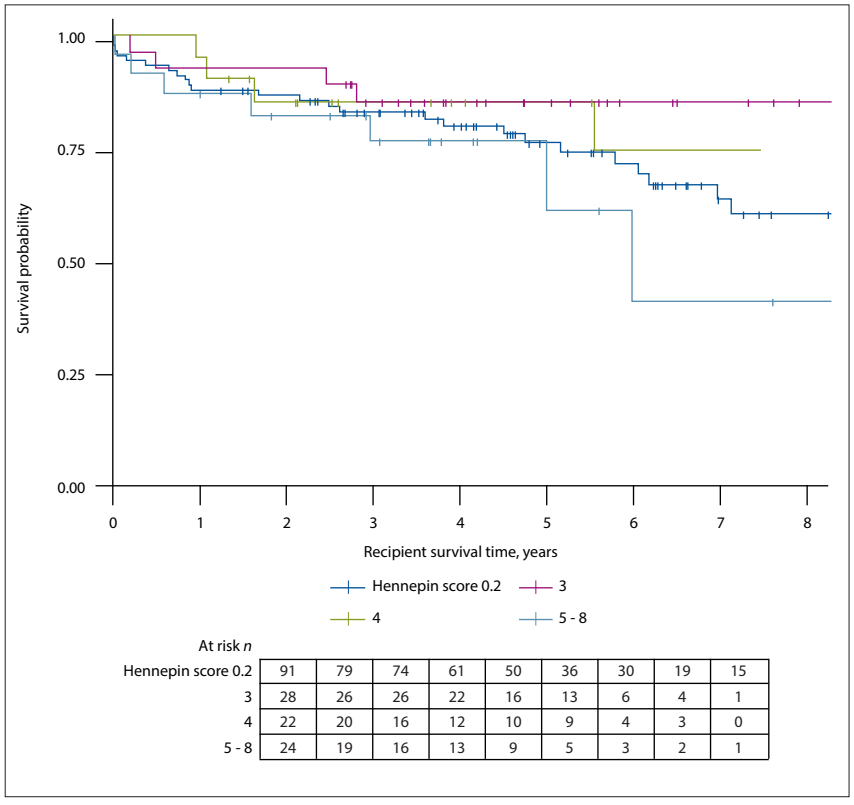
The majority of the deceased donors were aged <49 years, but a significant proportion (34.5%) were >50 years old, an age group where extended-criteria parameters may be applied. A total of 20.7% met extended criteria, with 21.3% of these hypertensive, 26.5% with renal impairment, and 31.9% having suffered a cerebrovascular event as the cause of death. This number is relatively low by international standards, with many European countries now reporting ECD rates in excess of 60%, and may reflect missed opportunities for organ donor referral in SA, where potential donors are




At risk *n*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Hennepin score 0.2 | 91 | 87 | 81 | 71 | 60 | 47 | 38 | 26 | 20 |
| 3 | 28 | 27 | 27 | 23 | 17 | 13 | 6 | 4 | 1 |
| 4 | 22 | 20 | 18 | 13 | 11 | 9 | 4 | 3 | 0 |
| 5 - 8 | 24 | 20 | 17 | 15 | 10 | 7 | 4 | 2 | 1 |

*Fig. 3. Recipient survival over time per Hennepin Transplant Risk Score bracket.*




At risk *n*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Hennepin score 0.2 | 91 | 79 | 74 | 61 | 50 | 36 | 30 | 19 | 15 |
| 3 | 28 | 26 | 26 | 22 | 16 | 13 | 6 | 4 | 1 |
| 4 | 22 | 20 | 16 | 12 | 10 | 9 | 4 | 3 | 0 |
| 5 - 8 | 24 | 19 | 16 | 13 | 9 | 5 | 3 | 2 | 1 |

*Fig. 4. Graft survival over time per Hennepin Transplant Risk Score bracket.*

not identified and referred by treating teams because they erroneously perceive a medical contraindication to successful donation. While only one patient with active hepatitis C was accepted for donation, it is well known that with access to direct-acting antivirals for recipients, many similar donor organs could be allocated safely.

The majority of donors were white (77.7%), while most kidney graft recipients were black (51.6%). This population discrepancy highlights a gap in community education and advocacy around organ donation in this recipient population.

Renal transplant recipients were predominantly male (63.8%), much in keeping with recent international literature,[12] highlighting a gender discrepancy in access to transplantation. According to SA data from 2020, only 40.2% of patients on RRT were female, whereas there is an overall female predominance of 51.1% in the SA population.[1] More than half of the recipients were classified as overweight or obese, but despite associated postoperative and post-transplant complications,[13] obese patients still have a significantly lower risk of mortality after transplant than if they remain on dialysis.[14] Cardiovascular comorbidity was noted in only 15.4% of patients, which may indicate a conservative approach to listing potential recipients. Conversely, more than half of the patients who underwent a transplant had a dialysis vintage >4 years, indicating lack of living donors and long waiting times. The retransplantation rate in our cohort of recipients was 6.9%, significantly below the international standard, where 67% of patients with graft failure receive a second transplant.

In the cohort studied, both the KDRI and the UK KDRI had poor discriminatory value in predicting outcomes, with a *C*-statistic of 0.5. Research has similarly shown that risk scoring systems such as the Remuzzi grading, KDRI and Nyberg grade could not determine a significant difference in graft survival in other cohorts. Only the Maryland Aggregate Pathology Index (MAPI) score, which requires a renal biopsy, correlated with graft outcome.[7]

The European Renal Association-European Dialysis and Transplantation Association (ETA-EDTA) demonstrated an incremental increase in the crude KDRI of donors annually from 1.31 in 2005 to 1.47 in 2015.[12] Our research does not show the same trend, with a median score of 1.2 across the study period, 2015 being an outlier year at 1.6. This finding could infer that only patients who are relatively low risk are referred for transplantation and that our centre is more conservative when considering deceased-donor kidneys for acceptance. In the face of severe organ shortages, a more liberal approach to organ acceptance may be indicated. Access to *ex vivo* organ perfusion technologies would increase the rate of acceptance of marginal organs.

The Hennepin recipient risk score offers an objective measure to consistently select appropriate recipients.[10] The median score in our study population was 2, translating to an average-risk candidate. This score is slightly higher than in the Hennepin County study that initially validated this score, which conferred an average risk of 1.33. This unit-specific score would indicate that a large population of higher-risk recipients are not considered for listing in our programme, and as such do not get access to transplantation. Both the recipient risk scores studied showed statistically significant correlations between recipient mortality and high Hennepin and KTMI scores, making these useful tools in risk-stratifying patients. However, these scores were not useful in predicting graft survival.

## Conclusion

An overall conservative approach to referral of potential donors, as well as to accepting deceased-donor referrals and listing renal transplant recipients, was noted in this study. Applying deceased-donor risk scores is of little value, and they performed poorly in predicting outcomes in the context of our health system. Renal recipient scores, however, showed significant value in predicting recipient mortality, but not graft survival. Risk stratification systems should be applied with caution in the SA setting.

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**Author contributions.** FvdS: principal investigator; MB: article write-up and editing; PG: statistical analysis; BS, MdJ, RB, JL: article editing.

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**Conflicts of interest.** None.

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