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Nonutilization of Kidneys From Donors After Circulatory Determinant of Death

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Background. The expansion of donation after circulatory determination of death (DCDD) programs and unmet demands for kidney transplantation indicate that there is a need to improve the efficiency and utilization of these organs. **Methods.** We studied all DCDD donors retrieved for kidney transplantation in Australia between 2014 and 2019 and determined the factors associated with nonutilization using least absolute shrinkage and selection operator and random forest models. Self-organizing maps were used to group these donors into clusters with similar characteristics and features associated with nonutilization were defined. **Results.** Of the 762 DCDD donors, 116 (15%) were not utilized for kidney transplantation. Of the 9 clusters derived from self-organizing map, 2 had the highest proportions of nonutilized kidneys. Factors for nonutilization (adjusted odds ratio [95% confidence interval], per SD increase) were duration from withdrawal of cardiorespiratory support till death (1.38 [1.16-1.64]), admission and terminal serum creatinine (1.43 [1.13-1.85]) and (1.41 [1.16-1.73]). Donor kidney function and duration of warm ischemia were the main factors for clinical decisions taken not to use kidneys from DCDD donors. **Conclusions.** Donor terminal kidney function and the duration of warm ischemia are the key factors for nonutilization of DCDD kidneys. Strategies to reduce the duration of warm ischemia and improve post-transplant recipient kidney function may reduce rates of nonutilization.

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INTRODUCTION

The growth of patients with stage V chronic kidney disease is outstripping the capacity for kidney transplantation. The number of patients on the deceased donor transplant waiting list continues to increase with the availability of donor organs not matched by growing demands. Currently, 5% to 7% of patients are dying each year while waiting for a kidney transplant.[1] Efforts to increase deceased donor kidney transplantation have seen a dramatic rise in the utilization of donation after circulatory determination of death (DCDD) donor kidneys.[2,3] In Australia and New Zealand, the number of kidneys transplanted from controlled DCDD donors has substantially increased over the last decade. These donors comprised over 30% of all deceased donor kidneys and transplants in 2019.[4] Similar patterns are observed in the United States and Europe, with over 20%

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of all deceased donor kidney transplants from the DCDD pathways.[5] As donation rates increase, donor demographics are also likely to change. There are more older donors with comorbid conditions such as hypertension and diabetes over the last 5 y.[5] A key challenge with the use of these kidneys from the DCDD pathway is the inherent risk of organ nonutilization after retrieval.[6] Prior work using data from the Australia and New Zealand Organ Donation (ANZOD) registry found kidneys from DCDD were twice as likely to be discarded after retrieval compared with kidneys from donation after brain death (DBD) donors, adjusted for other donor characteristics and era of donation.[7]

Although kidneys from DCDD may experience a higher risk of delayed graft function (DGF),[8] a large-scale observational study has shown comparable medium and longer-term patient and graft survival between recipients who have received kidneys from DCDD and DBD donors.[9] Given the substantial survival advantage associated with kidney transplantation (compared with dialysis treatment) for patients with kidney failure,[10] the reasons for the higher probability of nonutilization among DCDD donors are important to understand. Prior studies have found that center level characteristics such as the number of prevalent patients on the waiting list and the incidence of patients with kidney failure are key factors that may have contributed to the observed organ acceptance behavior within individual centers,[4] but the impact of many predonation and donor-related factors remain uncertain. These factors are also likely to be clustered in a systematic but nonlinear pattern. Knowledge and understanding of these features are required to inform future clinical practice, guide donation, and procurement agencies to identify potential donors that are likely to be nonutilized and assist key stakeholders within the donation and transplantation sector to make more informed choices, while maintaining efficiency within the allocation process and resources. Using novel machine learning clustering algorithms, this study therefore aimed to define the predonation and donor-related factors for nonutilization of kidneys from controlled DCDD donors.

MATERIALS AND METHODS

Study Population

All actual controlled DCDD kidney donors in Australia between 2014 and 2019 were included. The electronic donor record (EDR) system was introduced in 2014, therefore, details of the predonation hemodynamic records were not available before 2014. The EDR contains premortem, perimortem, and postmortem information of all donors from all jurisdictions in Australia who were consented for organ donation in Australia and is managed and held by Australian Organ and Tissue Authority in Canberra. Multiorgan DCDD transplants were excluded. An actual donor is defined as a donor for whom the organ retrieval procedure has commenced (ie, surgical incision has occurred) for the purpose of transplantation.[11] Deidentified donor data were sourced from the ANZOD and the Australia and the New Zealand Dialysis and Transplant registries and the deidentified data set was prepared by the Australia and the New Zealand Dialysis and Transplant registry. These data were not reidentifiable. The institutional board and the human research ethics committee of the University of Western Australia approved the conduct of the study (ethics reference: RA/4/20/4743). The relevant state-based jurisdictions of DonateLife (Organ and Tissue Authority) and Ministry of Health have granted approval for the conduct of this study. This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies.[12]

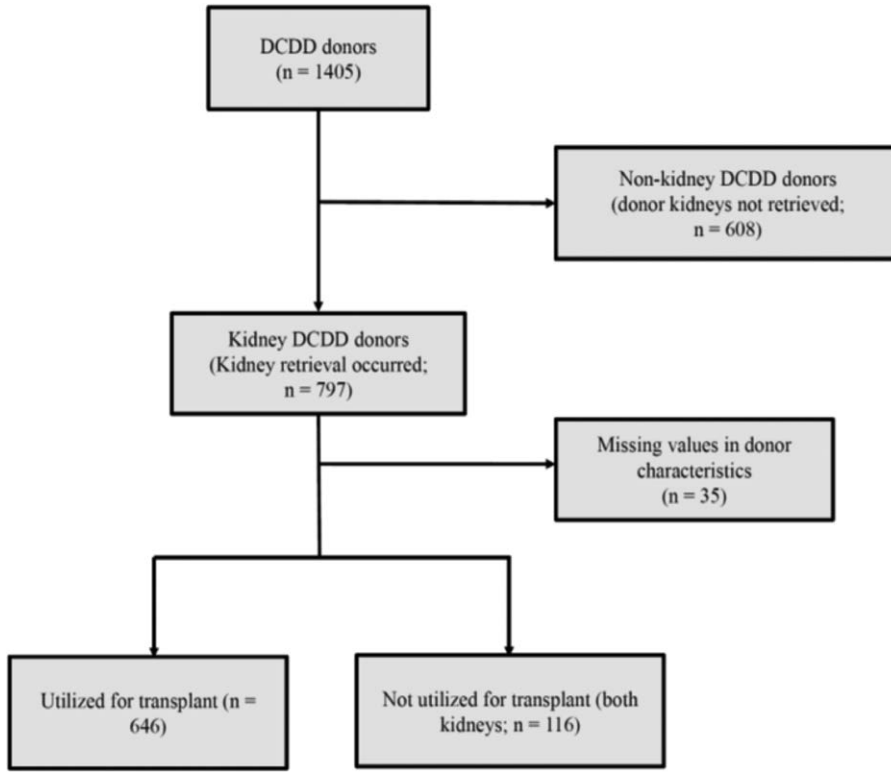

FIGURE 1. Cohort flow of the donation after circulatory determination of death (DCDD) donors retrieved and utilized for transplantation.

TABLE 1.

Baseline characteristics of the kidney donors from the DCDD pathway between 2014 and 2019

	N	Overall (N = 762)	Utilized (N = 646)	Nonutilized (N = 116)	*P*
Donor age (yes, SD)	762	47 (16)	47 (16)	49 (16)	0.2
Death to cold perfusion (SD), min	762	10.1 (3.7)	10.1 (3.6)	11.0 (3.7)	0.005
Cardiac arrest with prior downtime, n (%)	762				0.2
No		372 (49)	310 (48)	62 (53)	
Yes—Unwitnessed		167 (22)	139 (22)	28 (24)	
Yes—Witnessed		223 (29)	197 (30)	26 (22)	
Donor gender, n (%)	762				0.3
Female		278 (36)	230 (36)	48 (41)	
Male		484 (64)	416 (64)	68 (59)	
Donor diabetes, n (%)	762				0.002
No diabetes		692 (91)	596 (92)	96 (83)	
Type I (insulin dependent)		9 (1.2)	5 (0.8)	4 (3.4)	
Type II (non insulin or insulin requiring)		61 (8.0)	45 (7)	16 (14)	
Donor hypertension history, n (%)	762	204 (27)	160 (25)	44 (38)	0.005
Donor smoking history, n (%)	762				0.6
Never		276 (36)	233 (36)	43 (37)	
Former		189 (25)	157 (24)	32 (28)	
Current		297 (39)	256 (40)	41 (35)	
Donor cancer history, n (%)	762	73 (9.6)	54 (8.4)	19 (16)	0.011
Creatinine admission (SD), μmol/L	762	95 (63)	88 (42)	129 (121)	<0.001
Creatinine terminal (SD), μmol/L	762	101 (104)	90 (82)	158 (175)	<0.001
Urea admission (SD), μmol/L	762	6.45 (5.07)	6.18 (4.8)	7.98 (6.1)	<0.001
Urea terminal (SD), μmol/L	762	8.9 (6.4)	8.4 (5.7)	11.5 (9.2)	<0.001
Oliguria last 12 h <20 mL/h, n (%)	762	60 (7.9)	48 (7.4)	12 (10)	0.4
Donor anti-HCV serology test result, n (%)	762				<0.001
Negative		737 (97)	631 (98)	106 (91)	
Not done		8 (1.0)	7 (1.1)	1 (0.9)	
Positive		17 (2.2)	8 (1.2)	9 (7.8)	
Donor NAT HCV test result, n (%)	762				<0.001
Indeterminate		1 (0.1)	0 (0)	1 (0.9)	
Negative		714 (94)	611 (95)	103 (89)	
Not done		45 (5.9)	35 (5.4)	10 (8.6)	
Positive		2 (0.3)	0 (0)	2 (1.7)	
Donor NAT HBV test result, n (%)	762				0.01
Indeterminate		1 (0.1)	0 (0)	1 (0.9)	
Negative		706 (93)	605 (94)	101 (87)	
Not done		50 (6.6)	38 (5.9)	12 (10)	
Positive		5 (0.7)	3 (0.5)	2 (1.7)	
Donor HBsAg test result, n (%)	762				0.02
Negative		756 (99)	643 (99.5)	113 (97.4)	
Not done		5 (0.7)	3 (0.5)	2 (1.8)	
Positive		1 (0.1)	0 (0)	1 (0.8)	
Donor HBcAb test result, n (%)	762				0.04
Negative		58 (7.6)	49 (7.8)	9 (7.8)	
Not done		701 (92)	596 (92)	105 (91)	
Positive		3 (0.4)	1 (0.2)	2 (1.2)	
Donor cause of death categories, n (%)	762				0.12
Cerebral hypoxia/ischemia		328 (43)	278 (43)	50 (43)	
Cerebral infarct		60 (7.9)	49 (7.6)	11 (9.5)	
Intracranial hemorrhage		174 (23)	144 (22)	30 (26)	
Nonneurological condition		64 (8.4)	50 (7.7)	14 (12)	
Other neurological condition		17 (2.2)	16 (2.5)	1 (0.9)	
Traumatic brain injury		119 (16)	109 (17)	10 (8.6)	
Ventilation duration (SD), h	762	170 (763)	175 (823)	142 (226)	0.3
Donor BMI, mean (SD)	762	28 (7)	28 (7)	29 (8)	0.2
Donor state, n (%)	762				0.7
NSW/ACT		231 (30)	197 (30)	34 (29)	
QLD		120 (16)	106 (16)	14 (12)	
SA/NT		51 (6.7)	43 (6.7)	8 (6.9)	
VIC/TAS		314 (41)	263 (41)	51 (44)	
WA		46 (6.0)	37 (5.7)	9 (7.8)	
WCRS duration, mean (SD)	762	23 (16)	22 (14)	28 (22)	0.12

ACT, Australian Capital Territory; BMI, body mass index; DCDD, donation after circulatory determination of death; HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; NAT, nucleic acid testing; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia; WCRS, withdrawal of cardiorespiratory support.

Data Collection

The ANZOD registry comprise of all deceased donor data and include age, sex, ethnicity, viral serological status (hepatitis B and C virus), smoking history, prior comorbid conditions (history of diabetes, cancer, and hypertension), body mass index (BMI), primary cause of donor death, ventilation (in hours), withdrawal of cardiorespiratory support (WCRS) duration (in minutes) (defined as the time from WCRS until death), presence or absence of oliguria (defined as urine output of <20 mL/h in the preceding 12 h), terminal urea (in mmol/L), terminal creatinine (in μmol/L) and donor state. In Australia, determination of death according to circulatory criteria is through observation of absent arterial pulsatility for a minimum of 3 min and a maximum of 5 min, using intra-arterial pressure monitoring and confirmed by clinical examination (absence of heart sounds and central pulses). In cases without an arterial line, electrical asystole is observed for a minimum of 3 min and a maximum of 5 min on the electrocardiogram and confirmed by clinical examination. During the timeframe of this study period, machine perfusion was not used routinely.

Outcome Measures

The outcome measure of this study was the nonutilization status of both kidneys (both kidneys not used) from DCDD donors after the kidneys have already been retrieved. We did not include nonutilization of a single kidney as the outcome of interests because the reasons for nonutilization of both kidneys are likely to be different to those whereby only a single kidney was used. Additionally, the purpose of this work was to define the global donor issues that were related to nonutilization rather than other structural, anatomical or pathological issues related to the individual kidneys in donors that were deemed suitable for use.

Statistical Analysis

Donor characteristics were expressed as number (proportion) for categorical data, or as mean (SD) for continuous data. Student *t* test and χ^2 test were used to evaluate the associations between donor characteristics and kidney nonutilization for continuous and categorical variables, respectively.

The clinical features were selected using 2 prediction models, least absolute shrinkage and selection operator (LASSO) and random forest, by 5-fold cross validation with 20-time repetition. For LASSO, the feature scores were determined by the percentage of being selected in the cross validation, whereas for random forest, the feature scores were calculated by the average of the feature importance. The feature scores derived from the 2 methods were highly correlated, with Pearson correlation, $r = 0.86$. For each LASSO model, the lambda was determined by the one with minimum 10-fold cross validation error using cv.glment() in R package glmnet. Random forest model was performed using randomForest() in R package randomForest using the default hyperparameter settings (ntree = 500, mtry = sqrt [number of features in the data]). We then selected the clinical features with LASSO feature scores greater than 0.8 and random forest feature scores >10 to fit the multivariable logistic regression model to determine the predictive predonation and donor-related factors for nonutilization of kidneys from DCDD donors. The variables were first transformed to z-score before fitted to the logistic regression model to derive the odds ratio per SD. The prediction models were evaluated by area under receiver operating characteristics curve (AUC-ROC), accuracy rate,

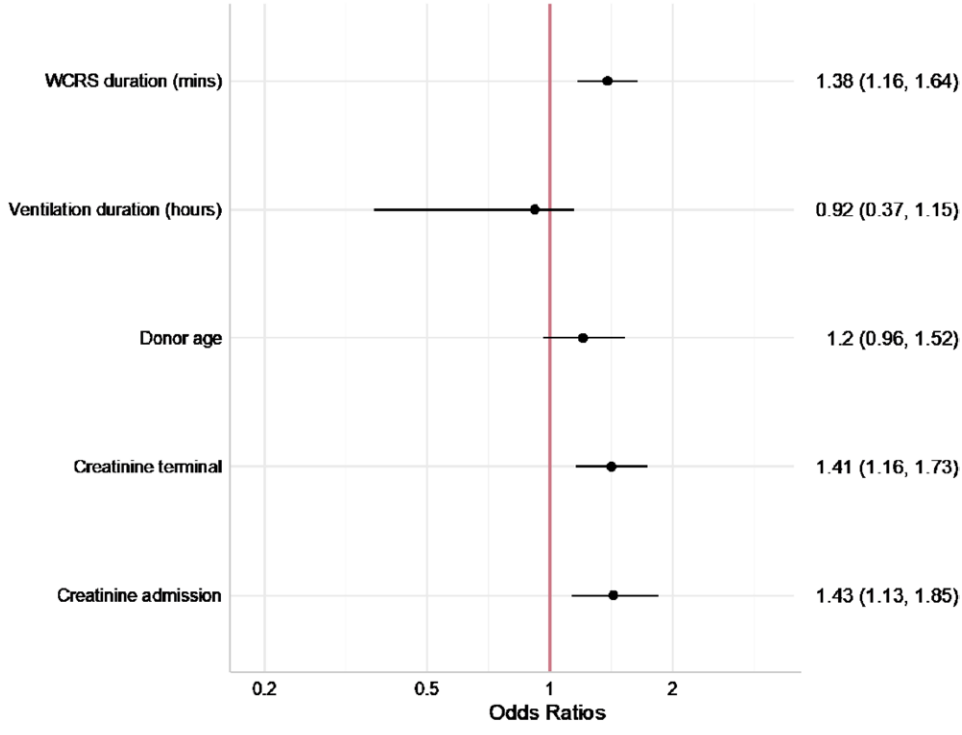

FIGURE 2. Factors predicting nonutilization of kidneys from the donation after circulatory determination of death (DCDD) pathways selected by logistic regression modeling. WCRS, withdrawal of cardiorespiratory support. *WCRS duration, donor age, terminal and admission serum creatinine were defined as per standard deviation increase in the unit of measures of interest. Point estimates are shown for each selected covariate, expressed as adjusted odds ratio (solid circles) and 95% confidence intervals.

balanced accuracy rate by 5-fold cross validation, repeated by 20 times. The models were fitted by upsampling to account for the imbalance of the 2 classes. Interactions between donor age and other donor characteristics were also examined in the final prediction model. Finally, self-organizing map (SOM) analysis was performed with a three-by-three grid to group the actual donors into clusters based on the similarity of their characteristics. SOM is a form of unsupervised neural network models and has been widely used for clustering, dimension reduction, and feature reduction and selection.[13] It also enables projection of complex, nonlinear relationship of high-dimension data set to a low-dimensional space while preserving most of the topological structure of the data. The SOM approach has allowed researchers to overcome the challenges of nonlinearity and skewed data distribution within a multivariable data set.[14] It involves the discovery of natural grouping within the data, where existing or new features can be mapped and identified as individual clusters for the prediction of nonutilization of kidneys from controlled DCDD donors. We have chosen the SOM because it has the practical value for visualizing our complex, multidimensional correlated data by representing the final output into 2-dimensional.

RESULTS

Baseline Characteristics of the Controlled DCDD Donors

There were 762 actual DCDD kidney donors between 2014 and 2019 with complete information on donor characteristics (n = 35 had incomplete donor details). Of these, 646 (85%) were utilized for kidney transplantation and 116 (15%) were not utilized (Figure 1). Donors of kidneys that were not utilized for kidney transplantation were more likely to have diabetes (17.4% versus 7.8%), hypertension (38% versus 25%), or positive hepatitis C serology (7.8% versus 1.2%) and hepatitis B serology (0.9% versus 0%) compared with those that were utilized for transplantation (Table 1). The primary causes of donor death, WCRS duration, the states in which the donors were retrieved, and the mean ventilation hours were similar between the 2 groups.

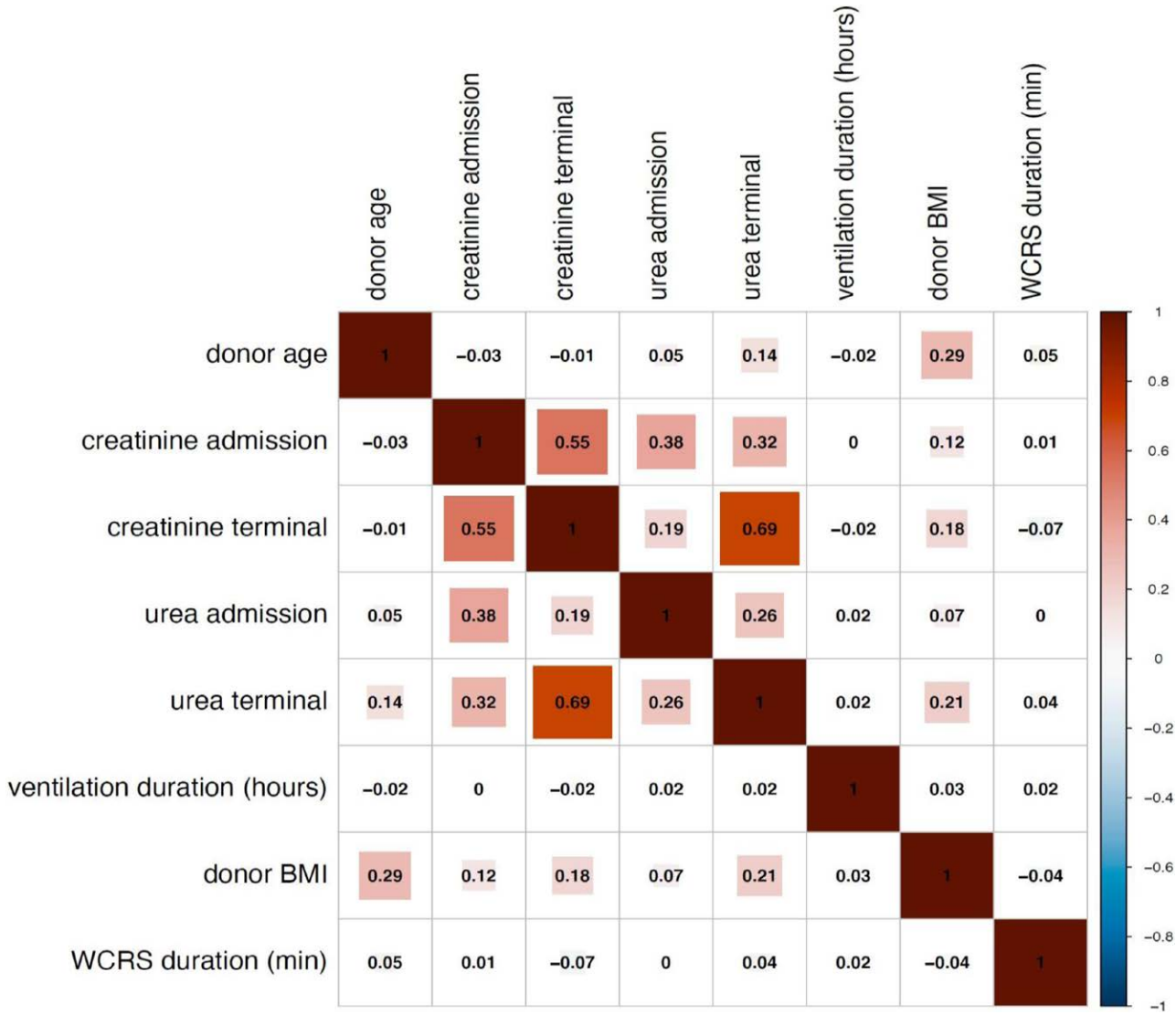

FIGURE 3. Correlation matrix of the key variables in the prediction models. Table of correlation matrix showing the correlation coefficients between selected donor and donation pathway variables, with 0 indicating no linear correlation between 2 variables and 1 indicating a perfect correlation between 2 variables. BMI, body mass index; WCRS, withdrawal of cardiorespiratory support.

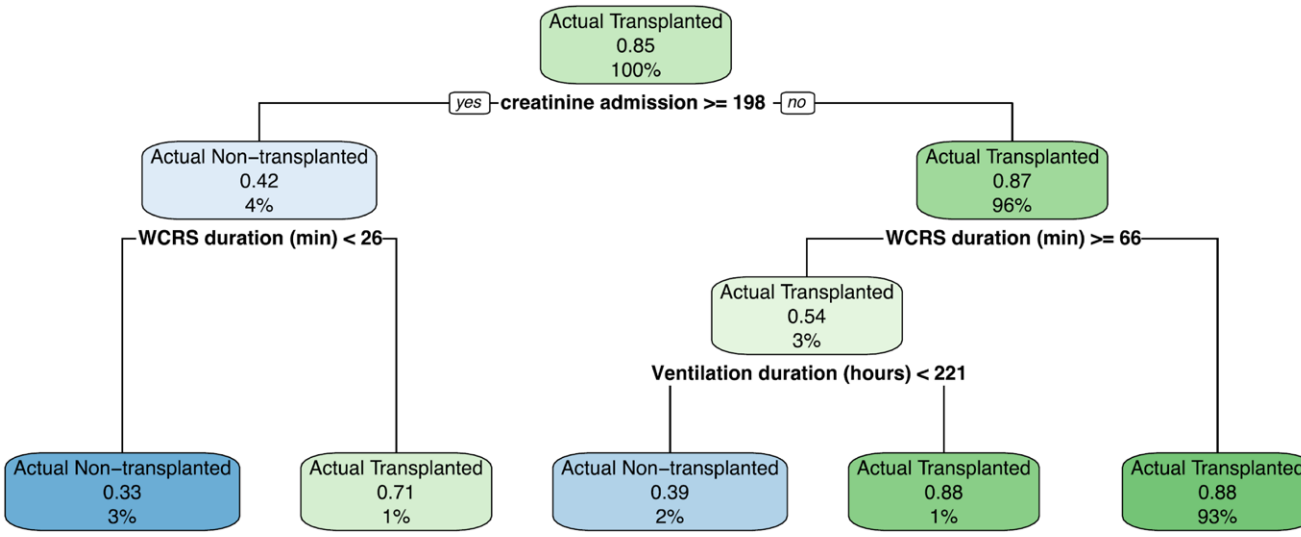

FIGURE 4. Decision tree for the classification of utilization and nonutilization of donor kidneys for transplantation. A decision tree showing the possible outcomes (utilization and nonutilization of actual donation after circulatory determination of death deceased donor kidneys) of each conditional event of admission creatinine, withdrawal of cardiorespiratory support (WCRS) duration, and ventilation hours.

Predictive Factors for Nonutilization of Kidneys From DCDD Donors

Factors for nonutilization defined (adjusted odds ratio, per SD increase, [95% confidence interval]) were WCRS duration (1.38 [1.16-1.64]), admission and terminal serum creatinine (1.43 [1.13-1.85]) and (1.41 [1.16-1.73]), donor age (1.2 [0.96-1.52]) and ventilation duration preceding death (0.92 [0.37-1.15]) (Figure 2). Terminal and admission serum creatinine levels were only moderately correlated and were, therefore, included in the same model (Figure 3). There were no interactions between admission serum creatinine and donor age (P = 0.13), and between terminal serum creatinine levels and donor age (P = 0.49).

Classifier for Utilization and Nonutilization of Kidneys for Transplantation

The decision tree indicates the classifier that defined utilization versus nonutilization was the admission serum creatinine

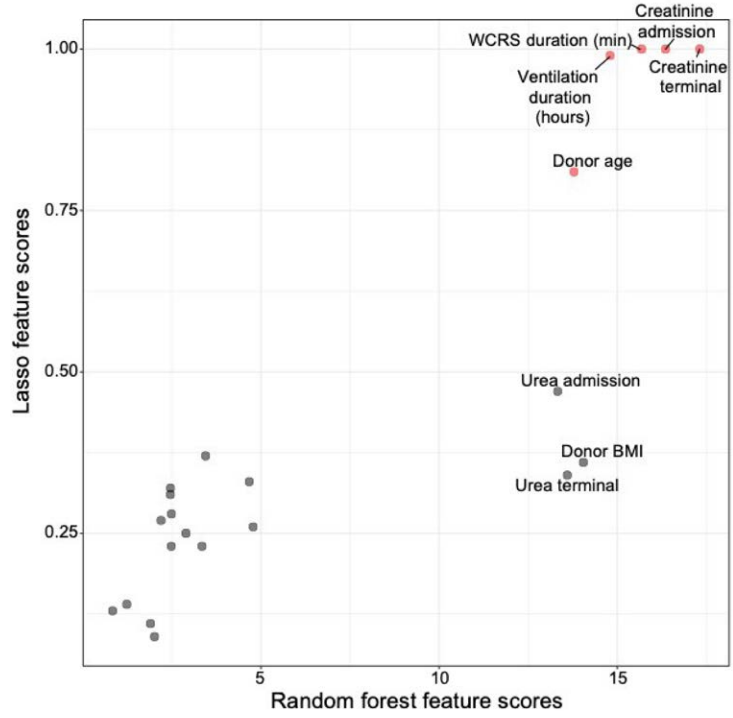

FIGURE 5. Variables of importance selected by the least absolute shrinkage and selection operator (LASSO) and the random forest models for the prediction of nonutilization of kidneys from the donation after circulatory determination of death (DCDD) pathways. The selection of the important covariates in the prediction models of nonutilization of actual DCDD deceased donor kidneys using LASSO (vertical axis) and random forest analyses (horizontal axis). The most influential covariates identified were admission and terminal creatinine, withdrawal of cardiorespiratory support (WCRS) duration, and donor ventilation duration (top right region). BMI, body mass index.

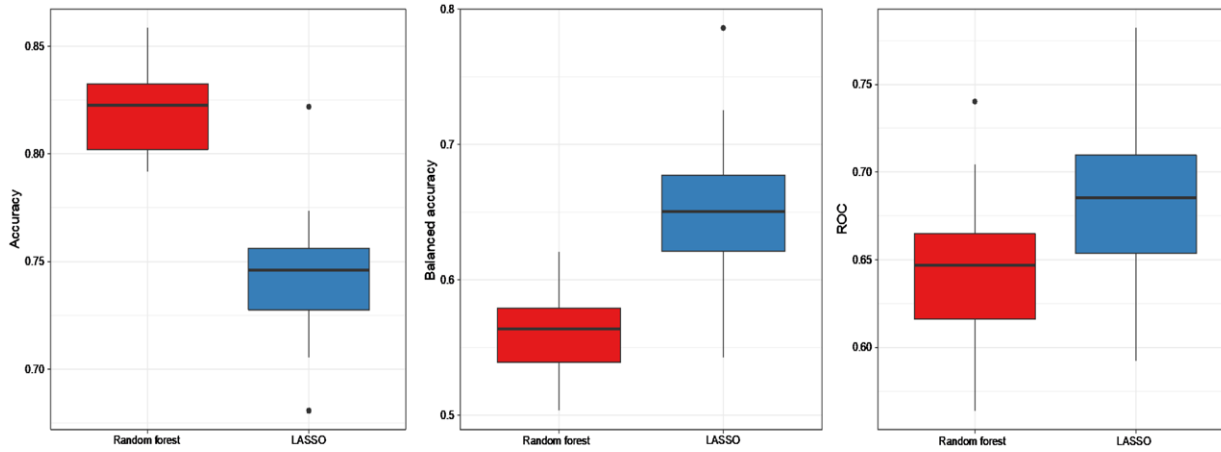

FIGURE 6. Classification cross validation findings of the random forest and the least absolute shrinkage and selection operator (LASSO) models prediction model for nonutilization of kidneys from the donation after circulatory determination of death (DCDD) pathway. Performance characteristics (accuracy [left panel], balanced accuracy [middle panel], receiver operating characteristic [ROC; right panel]) of the LASSO and random forest models in the prediction of nonutilization of actual DCDD deceased donor kidneys. Both models showed similar overall performance characteristics.

and it can be interpreted as follows. The color and name of the code predicts the class that most of the actual donors were assigned to. The first numerical value represents the percentage of the donors that were utilized for transplantation. The second numerical value indicates the percentage of actual donors with the prespecified characteristics (such as WCRS duration and admission serum creatinine) within the entire cohort. In this decision tree, the primary split point was 198 μmol/L (Figure 4). Four percent of all actual donors had admission serum creatinine ≥198 μmol/L. Of these, for the majority, kidneys were not utilized (58%), but 42% were transplanted. In contrast, 87% of all actual donors with serum creatinine <198 μmol/L had kidneys utilized for transplantation. Furthermore, only 1% of all actual donors with serum creatinine ≥198 μmol/L and a WCRS duration of >26 min. In this highly selected group of actual donors, the majority (71%) were utilized.

Performance of the Classification Models for the Prediction of Nonutilization of Kidneys From DCDD

In the random forest model, variables with the highest feature importance scores were the WCRS duration, terminal

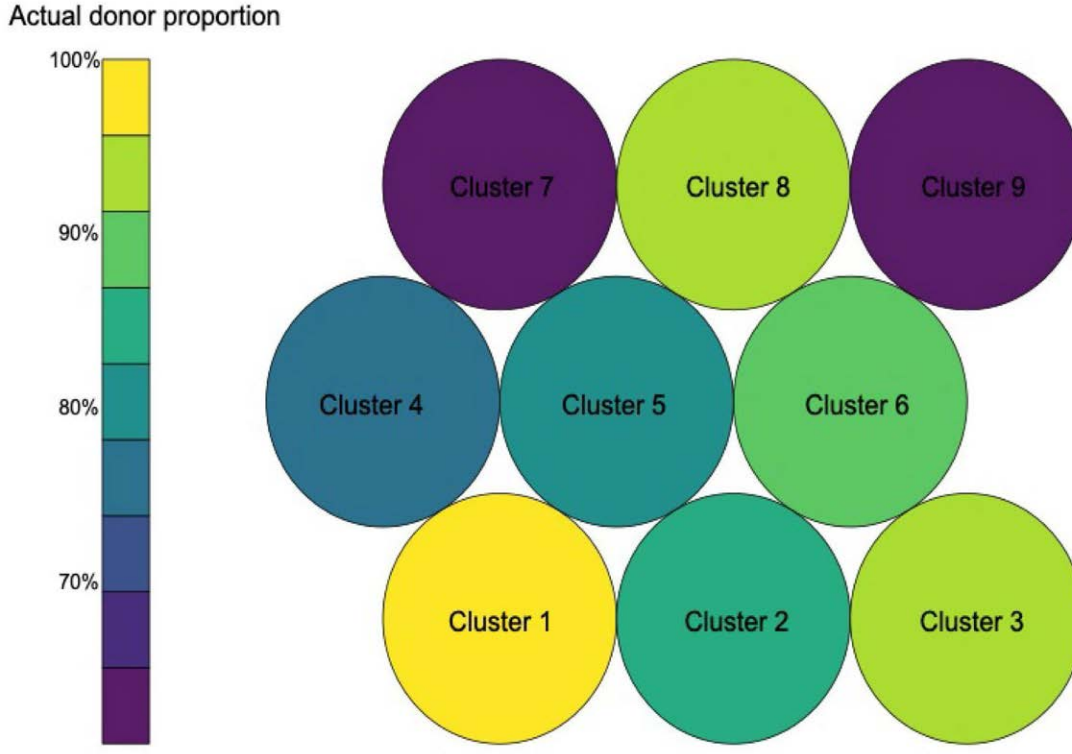

FIGURE 7. Characterization of nonutilized kidneys from donors of the donation after circulatory determination of death (DCDD) pathway using self-organizing maps. Self-organizing map showing the classification of data into clusters (clusters 1–9 represented by individual circles) according to the similarity between the data: donor utilization rates are 100%, 85%, 91%, 76%, 78%, 89%, 61%, 94%, and 64% for cluster 1–9.

and admission serum creatinine, donor age, total ventilation duration (hour) and donor BMI. In the group LASSO model, the key variables of importance were terminal serum urea and creatinine, total ventilation duration (hours), serum urea and creatinine on admission, donor age, donor BMI, WCRS duration, the time from death to cold abdominal perfusion and the state in which the donors resided and died subsequently. The variables selected by the random forest model were donor age, ventilation duration in hours, terminal and admission serum creatinine and urea, donor BMI and the WCRS duration (Figure 5). The random forest model had similar performance characteristics (cross validation accuracy: 81.9%; balanced accuracy: 0.56; AUC-ROC [0.65, 0.59-0.71]), as the LASSO model (accuracy: 74.2%; balanced accuracy: 0.6; AUC-ROC [0.69, 0.63-0.75]) (Figure 6). The variables of importance across the 2 models were (in descending order): admission and terminal serum creatinine levels, WCRS duration, total ventilation duration in hours, donor age and donor BMI.

Characterization of Nonutilized Kidneys From DCDD Donors

Using the SOM analysis on the donor characteristics, 9 different clusters of actual donors were classified into kidneys that were utilized for transplantation or discarded (Figure 7). Baseline characteristics of the DCDD donors stratified by the 9 clusters are shown in Table S1 (**SDC**, http://links.lww.com/TXD/A424). Donors that belonged to clusters 7 and 9 had the highest proportion of nonutilized kidneys with the following features: highest serum terminal and admission serum creatinine and urea levels, urea admission, and urea terminal, whereas cluster 9 has the longest WCRS duration (min) (Figure 8). The characteristics of each cluster are now provided in Figure 9.

DISCUSSION

In this large contemporary study of donors from the controlled DCDD pathway in Australia, approximately 10% of kidney donor pairs were nonutilized after retrieval. The 3 main factors that determined nonutilization of kidneys for transplantation were higher terminal and admission serum creatinine levels and longer WCRS duration preceding death. Other donor characteristics such as cancer history, prior hepatitis B and C infection, causes of death and geographical location of the donors were not the core determinants for nonutilization.

Nonutilization of deceased donor organs is a major impediment in patient access to transplantation. Prior research in Australia, the United States, and Europe has shown an increasing trend of nonutilization of kidneys (from donors of the DBD as well as the DCDD pathways).[1,5,7] Reasons for the increase in kidney nonutilization are unclear, but this has been attributed to other unmeasured factors such as fear of donor-transmitted disease,[15] poor perfusion at the time of retrieval, and logistic reasons including the lack of beds and operating lists.[16] Our study suggests that donor kidney function and the duration of warm ischemia are the 2 key variables that influence clinical decision-making. Although serum terminal creatinine may not be the optimal measure for predicting outcomes after transplantation, it is an important variable within the kidney donor profile index and is now used widely globally to predict post-transplant allograft survival.[17] In combination with other donor-related variables, the kidney donor profile index scores can correctly classify graft survival in about 70% of the times.[17] Apart from using biochemical measures, some have advocated other ways to assess organ quality before allocation, including renal histology, and the organ perfusion status.[18] Biopsy data were not available in this data set, but the key concerns with biopsy at retrieval are the risk of delayed decisions and the prolonged cold ischemic times,

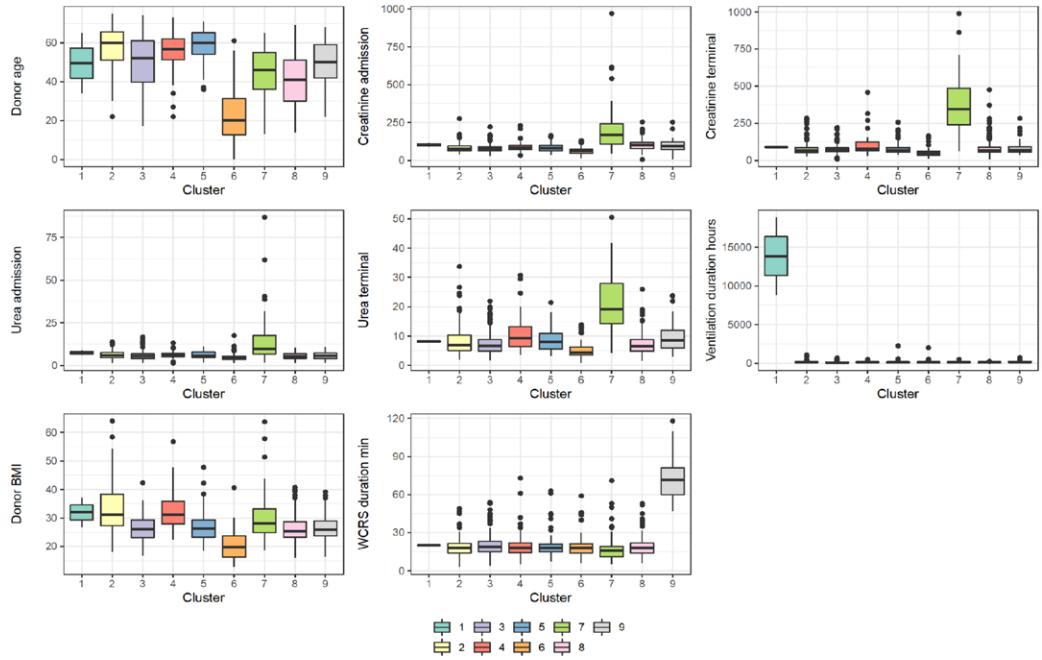

FIGURE 8. Key features of the nonutilized donation after circulatory determination of death (DCDD) clusters. Figure showing the clusters with the highest proportion of nonutilized actual DCDD deceased donor kidneys, according to selected donor and donation pathway characteristics. Donors of clusters 7 and 9 have the highest proportion of nonutilized kidneys. BMI, body mass index; WCRS, withdrawal of cardiorespiratory support.

which may further damage the marginal kidney.[19] Others have also shown inconsistent findings between biopsy features and longer-term allograft outcomes.[20] The decision to accept a less-than-ideal donor kidney is challenging because it is difficult to accurately quantify the risk of accepting a deceased donor kidney, which may not result in optimal patient and allograft outcomes, compared with the risk of dying (approximately 5%–10% annually) on the waiting list while waiting for a better organ.[21,22] These uncertainties may have led to a more judicious approach to acceptance and many centers have taken a more risk averse approach to avoid poorer outcomes, and the impact on center-specific metrics and league-tables.[16] However, transplant centers need to be aware of the unintended consequences jeopardizing access to transplantation, particularly for older potential candidates with comorbidities. Our previous research indicates that transplantation for selected patients who may have considerable coexisting illness is cost-effective and achieves substantial survival gains compared with the alternative of dialysis.[10]

Using novel unsupervised machine learning approaches, we have extended previous research by defining the distinctive features of the 2 clusters of DCDD donors that were not utilized for transplantation. One of these clusters uniquely belonged to donors that had longer WCRS duration, and the others were predominated by donors with poorer admitted and terminal kidney function. Previous investigations suggested a direct association between longer duration of functional warm ischemia, defined as the first recorded time of systolic blood pressure <50 mm Hg to cold perfusion, and increased risk of slow graft function, and premature graft loss in kidney from DCDD donors.[23,24] Prior work has indicated a longer time from WCRS until death was associated

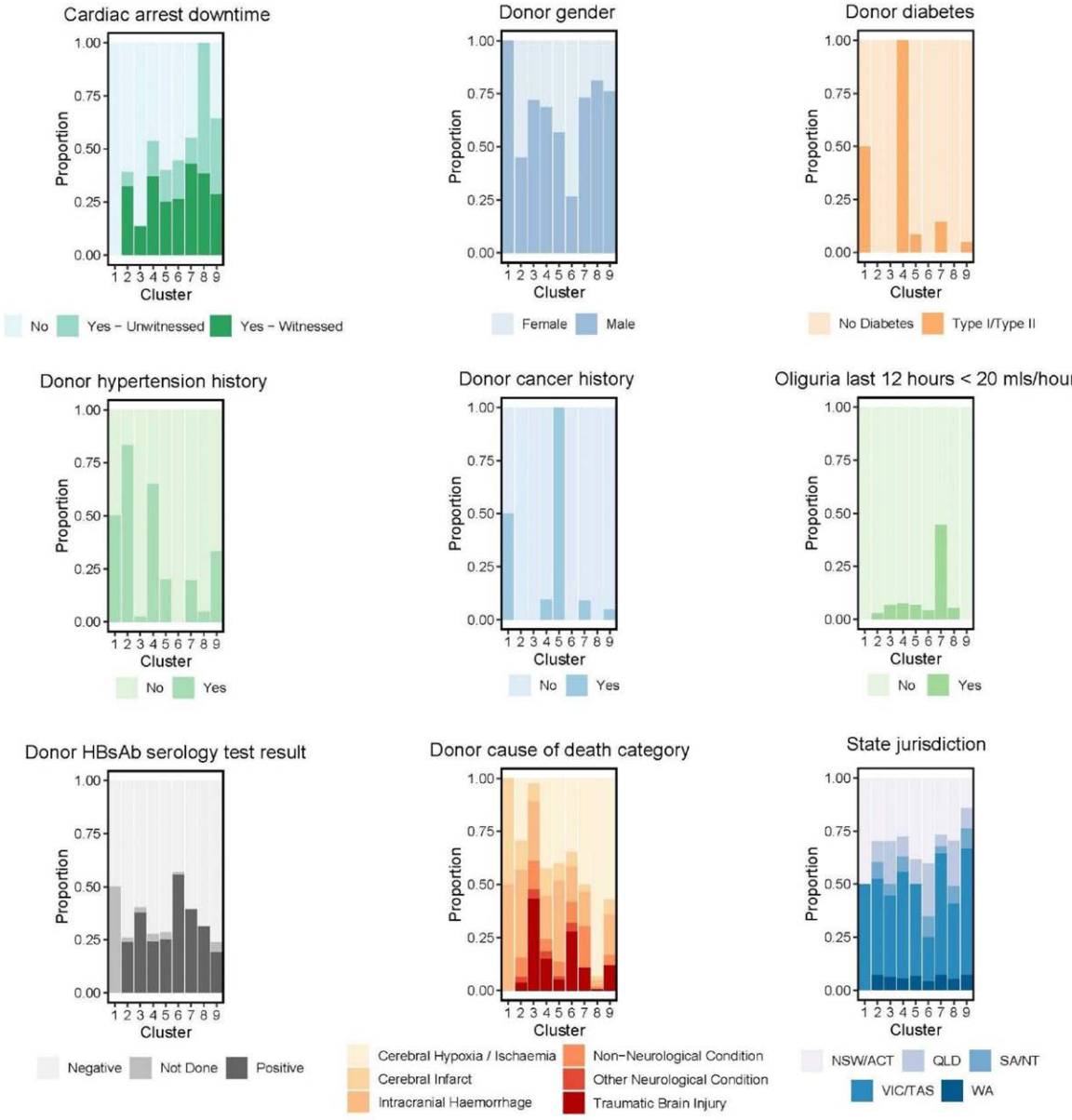

FIGURE 9. Characteristics of the individual clusters. This figure shows the characteristics of the individual clusters. For example, donors in cluster 1 did not experience any cardiac down time, were mostly female, and were not oliguric, and most died from cerebral infarct/hypoxia. ACT, Australian Capital Territory; HBsAb, hepatitis B surface antibody; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia.

with increased risk of primary nonfunction, particularly in DCDD donors where the duration of systolic blood pressure <80 mm Hg exceeded 20 min before cold perfusion.[25] Novel organ preservation and re-conditioning strategies using machine perfusion techniques have been shown to be effective in improving organ utilization by reducing the risk of DGF and primary nonfunction for both DCDD and DBD donors and may offer considerable benefits compared with cold perfusion alone.[26,27] It is also important to note that although kidneys from donors with acute kidney injury (AKI) are more likely to be discarded, recent work have reported comparable longer-term graft survival in recipients who have received kidneys from donors with and without AKI. A recent registry-based analysis found that donor AKI was associated with DGF, but not with death-censored or overall graft loss after a median follow-up time of 5 y.[28] This finding was consistent across all AKI stages after accounting for potential confounding using propensity-score matching. It is therefore important for transplanting centers to consider the use of these donor kidneys with AKI, particularly donors without considerable comorbidities.

This study has several strengths. It is one of the largest cohorts of DCDD donors with near complete repeated measures of demographics, donor characteristics as well as hemodynamic details during the predonation phase. We have used several novel machine learning approaches to determine the variable importance in these data-driven models. We acknowledge that the importance ranking may fluctuate between models, but we have provided a robust perspective on the relative importance of each of the predictors aggregated across the multiple models and have found the consistent factors across the LASSO, tree-based, random forest and the SOM analyses. These findings have major clinical implications. Using our data, donor procurement agencies can now accurately identify donor kidneys from the DCDD pathway that are at risk of nonutilization and then devise an algorithm that includes a tailored and fast-tracked approach of offering the potential candidates and centers that may accept them.[29]

Our study also has some potential limitations. The EDR and ANZOD registry do not collect the granular details regarding the specific reasons for nonutilization and refusal after allocation, details regarding at risk donor behaviors, other measures of kidney qualities such as donor histological biopsy data, perfusion status at the time of retrieval, and measures of the duration of cold ischemia of the nonutilized kidneys because these kidneys were never transplanted. Although prospective comparative outcomes data (including the risk of DGF, short- and longer-term graft loss) of kidneys with similar qualities that have been transplanted subsequently would have provided valuable information to inform clinical decision-making, it is not feasible and ethical to test and evaluate this hypothesis in a trial setting.

In conclusion, we have shown that donor kidney function and warm ischemia are the key predictive factors for nonutilization. Transplant clinicians are generally risk averse and reluctant to accept kidneys at risk of primary nonfunction, DGF or poorer future graft function. Potential strategies to reduce nonutilization rates in Australia may include implementation a fast-track policy to expediate the allocation of these less-than-ideal kidneys to centers that have the resources and capacity to test novel organ preservation interventions, and those that have accepted these donors in the past, circumventing other centers who are less willing to accept these organs.

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