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ORIGINAL ARTICLE

Poor organ quality and donor–recipient age mismatch rather than poor donation rates account for the decrease in deceased kidney transplantation rates in a Germany Transplant Center

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Summary

Kidney transplantation is limited not by technical or immunological challenges but by lack of donor organs. Whereas the number of patients on waiting list increased, the transplantation rate decreased. We analyzed the development of decline rates and reasons as well as the fate of declined organs. In total, 1403 organs offered to 1950 patients between 2001 and 2010 were included. Of 440 organs offered between 2009 and 2011 that were declined, we investigated whether these organs were transplanted elsewhere and requested delayed graft function, creatinine, graft and patient survival. Data were compared to results of transplantations at the same time at our center. Decline rate increased from 47% to 87%. Main reasons were poor organ quality and donor–recipient age or size mismatch. Of the rejected organs, 55% were transplanted at other centers with function, graft and patient survival equivalent to patients transplanted at our center during that period. The number of decline has increased over time mainly due to a growing number of marginal donors accounting for poor organ quality or a mismatch of donor and recipient. If proper donor–recipient selection is performed, many organs that would otherwise be discarded can be transplanted successfully.

Introduction

Today kidney transplantation is the gold standard for the treatment of patients with end-stage renal disease, whose success nowadays is limited not by technical or immunological challenges, but by the lack of donor organs. This discrepancy between organ supply and demand is resulted in dramatically increasing waiting times, associated with elevated morbidity and mortality for patients on the waiting list [1,2]. Despite this demand, reported discard rates of explanted organs are growing [3]. Despite varying between donation areas [4], up to half of the recovered expanded donor kidneys are discarded in the United States [5]. In the Eurotransplant (ET) area in 2011, of 2365 suitable donor organs, 99.9% were offered, 93.5% were accepted, and only 88.5% were transplanted.

Due to the lack of organs, some authors claim that not only the number of donors but also the number of organs recovered and transplanted per donor should be maximized [6]. It is estimated that the number of potential medically suitable organ donors varies from 38 to 55 per million people and year [7]. The organ allocation in Germany is carried out by ET according to the Eurotransplant Kidney Allocation System (ETKAS) [8].

The final decision whether or not to accept a kidney is predominantly made by transplant surgeons [9], based on the anticipated cold ischemia time (CIT), age- and weight-matching, and cause of brain death [10]. Although recipients of extended criteria donor (ECD) kidneys have a 77% higher risk of graft failure than patients receiving a conventional transplant [11], marginal kidneys doubled the deceased transplant volume between 2005 and 2011 [12]. This seems to be justifiable as patients longer than 4 years on the waiting list have a better survival after transplantation of an ECD-kidney compared to remaining on the waiting list.

However, no specific criteria exist that determine which kidney to accept for which patient.

In this work, we analyze the development of the number of donor organs offered to patients in our center, the decline rate, and the reasons for decline over the time period from 2001 to 2010. We present data on the follow-up of kidneys that we declined for one of our patients and that were then transplanted elsewhere.

Patients and methods

Patients

The transplant center Freiburg of the Department for General and Visceral Surgery performs deceased and living donor kidney transplantations as well a pancreas transplantation. There are around 400 patients on the waiting list for kidney transplantation (ranging from $n = 387$ in 2001 to $n = 420$ in 2010) and an annual transplantation rate of deceased donor organs (excluding combined pancreas–kidney transplantation) of $n = 81$ in 2001 to $n = 64$ in 2010.

Between the years 2001 and 2010, 1403 organs of deceased donors were offered by ET to 1950 patients; of those, 745 organs were accepted and 658 organs were declined.

We retrospectively analyzed the development of the decline rate and reasons of organ offers over time, according to the documentation in the patient files.

Of 183 organs offered in the years 2009 and 2010 that were not accepted by our center, ET numbers were submitted to the Deutsche Stiftung Organ transplantation (German Organ Transplantation Foundation) (DSO), who investigated whether these organs were transplanted at other centers in Germany and submitted a questionnaire to those centers, requesting delayed graft function rates, organ function (creatinine), graft, and patient survival. These data were compared to data of patients transplanted at the same time at our transplant center, receiving a deceased donor organ.

Reasons for organ decline were specified according to the ET classification system, being poor organ quality, age/size mismatch, recipient associated (immunological or nonimmunological), incompatible virology, reserve or center offer, or others.

Poor organ quality summarizes organs with macroscopical or microscopical pathologies as well as donor specific criteria. In the definition from the year 2002, a marginal (or ECD) donor is defined as a donor older than 60 years without comorbidities or a donor over the age of 50 with at least two comorbidities such as a history of hypertension, death from cerebrovascular disease, or a terminal serum creatinine level >1.5 mg/dl [13].

A clear definition for incompatible age or size does not exist. In our center, we did not observe any case of incompatible size in this collective. The main reason was therefore age mismatch, without defining a critical value, but considering the summation of age mismatch, cause of death, creatinine value, history of cardiac arrest/resuscitation, hypertension, and expected CIT.

In order to gain time in the allocation process, a primary kidney offer is routinely addressed to a second patient, in case the organ is declined for the first patient. This procedure is called secondary or reserve offer. In case the standard allocation is not successful, rescue allocation rules are applied. In case of a competing center, the offer is send to at least three transplant centers. The center that accepts first gets the organ. This procedure is not used in case of an urgent allocation, for example, instable donor or long CIT.

Data

Data were collected in a database using SPSS (SPSS for Windows, version 15.0; SPSS Inc., Chicago, IL, USA), and evaluation was performed by retrospective analysis.

Univariate survival was analyzed by the Kaplan–Meier method with a log-rank test for comparison of subgroups. A P-value of <0.05 was regarded as statistically significant.

The study was approved by the local ethics committee under the registration number 198/14.

Results

The number of patients on the waiting list remained stable over the years in this study ($n = 387$ in 2001 and $n = 420$ in 2010). In the same period, the annual number of transplantations of deceased donor organs decreased from $n = 81$ in 2001 to $n = 64$ in 2010. This fact is probably not due to a drop in donation rates.

After a decrease in donor organs between the years 2001 and 2004, the number of available donor organs increased again, raising in total by 22% from 2001 to 2010 (from $n = 135$ in 2001 to $n = 165$ in 2010) (Fig. 1, gray bars). The number of organ offers increased in the same time period by 54%, meaning that if we declined an organ, it was often offered to another patient in our center. The decline

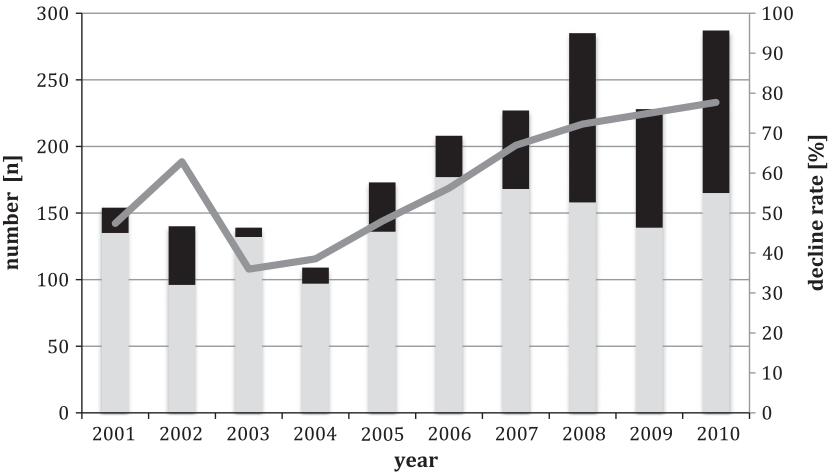

Figure 1 Total number of available donor kidneys per year (gray bars), total number of organ offers (gray + black bars), decline rate [%] of organ offers (gray line on secondary axis).

rate therefore increased dramatically from 47% to 87% between the years 2001 and 2010 (Fig. 1, gray line).

Overall, 1403 organs of deceased donors were offered in this time period to 1950 patients. Of those, 745 organs were accepted and 658 organs were declined. Each organ that was not accepted was thus offered to an average of 1.8 patients, and 1205 offers were declined.

Reasons for organ decline according to the ET classification system were poor organ quality, incompatible age/size mismatch, recipient associated (immunological or nonimmunological), incompatible virology, reserve or center offer, or others. In the year 2010, poor organ quality accounted for 56% of declines, and in 30%, incompatible age or size mismatch was the reason for not accepting the organ offer. Both factors clearly increased since 2001, when poor organ quality was in 47% the reason for decline and incompatible age or size mismatch in 4% (Fig. 2). At the same time, the percentage of donors over 65 years increased from 10% to 38% (Fig. 3).

Of 183 organs that were not accepted at the transplant center Freiburg in the years 2009 and 2010, 100 (54.6%) were transplanted at other centers, 98 of those as single organ, and 2 as dual organ transplants. Three organs had a primary nonfunction and 32% of patients required dialysis after transplantation, 25% more than one dialysis.

In the same time period (2009–2010), 121 kidney transplants of deceased donor organs were performed in Freiburg. Creatinine at the time of discharge was 1.6 ± 0.9 mg/dl for patients transplanted in Freiburg and 2.1 ± 0.9 mg/dl for patients transplanted elsewhere ($P < 0.01$). Interestingly, 1 year after transplantation, creatinine had fallen to 1.6 ± 0.8 mg/dl in patients transplanted elsewhere, which was no longer significantly different from the best creatinine of the kidneys transplanted in Freiburg (1.6 ± 0.9 mg/dl, NS), and 1-year graft survival of kidneys transplanted in Freiburg was 86% vs. 92% for kidneys that were declined in Freiburg but transplanted elsewhere ($P = 0.119$) (Fig. 4). Patient survival 1 year after transplantation was not worse for patients transplanted in Freiburg than elsewhere (96% vs. 98%, $P = 0.095$). Causes of death for patients transplanted in Freiburg were cardiovascular ($n = 3$), unknown ($n = 2$), cancer ($n = 1$), SAB ($n = 1$), and accident ($n = 1$); 2 patients that were transplanted elsewhere died from sepsis.

The kidneys that were declined in Freiburg but transplanted elsewhere differed in various characteristics

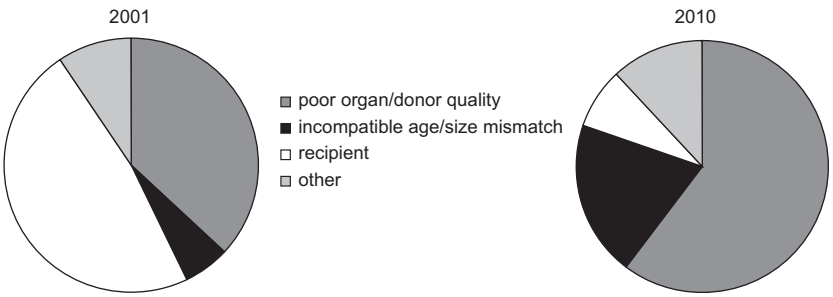

Figure 2 Reasons for decline.

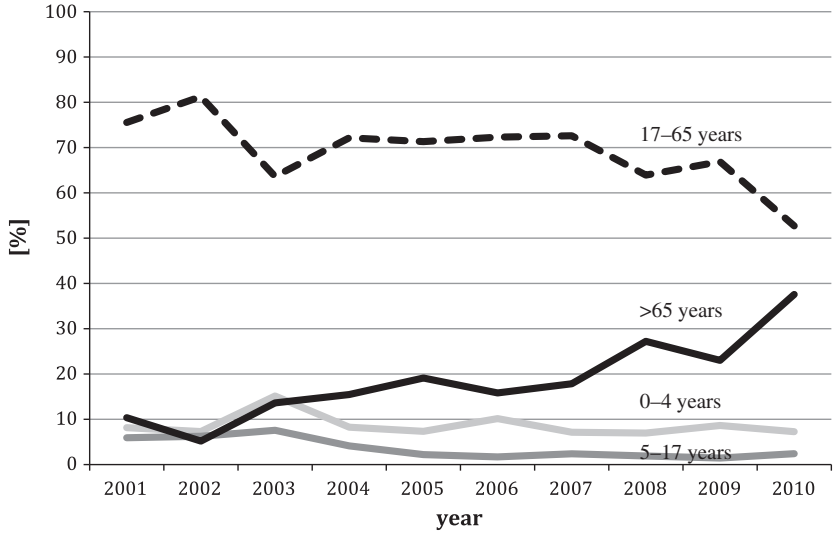

Figure 3 Development donor ages between the years 2001 and 2010.

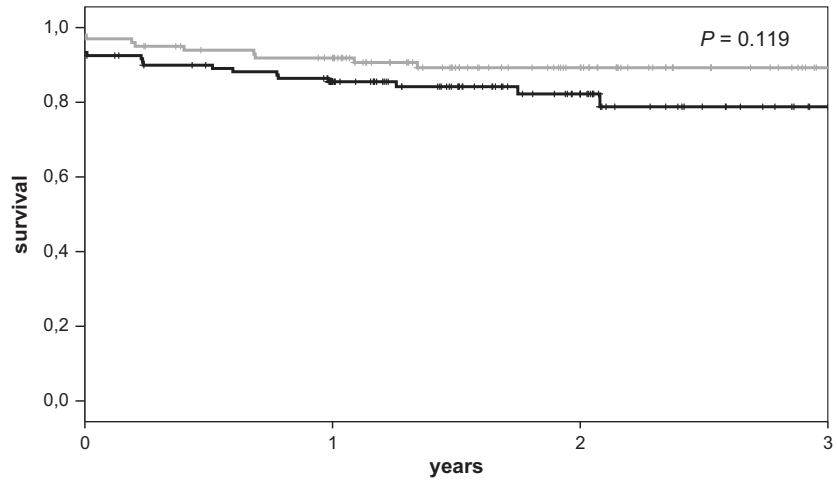

Figure 4 Graft survival of organs transplanted in the years 2009 and 2010 at GFRTP (black) and elsewhere (gray).

significantly from those transplanted in Freiburg. The donors that were declined were significantly older (55 vs. 49 years) and had more often a history of hypertension (45% vs. 30%) or diabetes (14% vs. 3%) and a higher creatinine at the time of organ donation (1.1 vs. 0.9 mg/dl). Hypotensive periods or cardiopulmonary resuscitation (CPR) was more often observed in donors of kidneys transplanted in Freiburg. The number of donated organs was higher in patients whose organs were accepted in Freiburg. The distance from the organ donor to Freiburg (as a parameter for estimated CIT) was significantly longer in organs that were declined than in organs that were accepted (309 vs. 410 km) (Table 1).

Discussion

While the number of patients on the waiting list is increasing, the number of transplantations performed decreased by over 20% from 2001 to 2010. This fact is probably not due to a drop in donation rates, as the number of available organs simultaneously increased by 22% (135 in 2001 vs. 165 in 2010). The decline rate of organ offers, in contrast, increased dramatically. Reasons for decline were mainly poor organ quality (56%) and incompatible age/size mismatch (30%). The percentage of donors over 65 years. increased from 10% to 38% during that time. Older donors are known to be associated with a higher risk of overall

Table 1. Characteristics of organ donors of the years 2009 and 2010 that were accepted in the transplant center Freiburg or declined in Freiburg but transplanted elsewhere.

Characteristics	Transplanted in Freiburg	Transplanted elsewhere	*P*
Male/female	73/43	108/73	0.626
Donor age [years]	49 ± 17	55 ± 24	0.041
Donor BMI [kg/m^2]	26 ± 5	26 ± 6	0.831
Hospital stay [day]	4 ± 4	5 ± 4	0.156
No. of offered organs	4.6 ± 1.7	3.9 ± 1.6	<0.001
Creatinine admission [mg/dl]	0.9 ± 0.3	0.9 ± 0.4	0.573
Creatinine donation [mg/dl]	0.9 ± 0.3	1.1 ± 0.8	<0.001
Hypotensive periods/CPR [%]	38	25	<0.001
Catecholamines [%]	85	85	0.188
Blood transfusion [%]	17	22	0.774
Distance donation to Freiburg [km]	309 ± 255	410 ± 301	0.003
Hypertension [%]	30	45	0.036
Smoking [%]	41	30	0.053
Diabetes [%]	3	14	0.006
Malignancy [%]	7	13	0.074
Drugs [%]	1	3	0.148

graft failure. Transplantation of young donor kidneys results in an additional two to three mean graft function years compared to patients receiving kidneys from older donors [14]. Age matching is therefore important. The increased donor age in our center may therefore partially explain the augmented decline rate.

The decision whether to accept an organ or not is made predominantly by the transplant surgeon on the basis of a risk-benefit assessment [10] and is also practiced at our center. Individual preferences of patients are currently less respected [9], although it is regarded as an essential component of patient care to allow patient participation in medical decisions. The time patients were on the waiting list correlated inversely with their emphasis on quality and function of the donor kidney [9] as physical and psychological quality of life is declining over time on dialysis [15]. Ojo *et al.* demonstrated that even the transplantation of marginal organs may improve the survival of patients by 5 years in comparison with remaining on dialysis [16]. Early transplantation is therefore important for patients survival and economically as healthcare cost is lower after transplantation compared to dialysis [17].

Which patients in particular benefit from transplantation, even if an ECD organ is offered, needs to be judged based on a validated clinical tool. Several donor risk indices have been developed [18–22], of which the kidney donor risk index (KDRI) has a greater predictive value for short-term outcome than pathology [23]. Although these indices may help with organ allocation and informed consent [19], they are not yet established in clinical practice. Nevertheless, we could show in our collective that organ donors we declined were older, higher creatinine values at the time of donation and had more often a history of diabetes or hypertension.

Even in standard criteria donors, McCullough *et al.* [24] described a decline in average post-transplant lifetime and life-year gains through transplantation. To achieve the maximum lifetime of a transplanted kidney, not only the organs have to be assessed, but also the recipients. The recipient risk score, based on diabetes, age, time on dialysis, and history of angina, is the first comorbidity score developed specifically for renal transplant recipients [25]. The calculation of life years from transplant (LYFT), defined as the extra years of life that a patient can expect to live after transplantation compared to remaining on dialysis [26], and consecutively prioritizing candidates with higher LYFT, may help to increase the benefit from donated kidneys [26]. However, the estimation of LYFT for recipients in combination with the KDRI as a tool for optimized allocation is not yet accepted [14].

In contrast, a system that identifies kidneys that are difficult to allocate according to the disposition of transplant centers to accept marginal organs in order to avoid waisted time [27] and higher discard rates [28], a new allocation system that offers organs with a kidney donor risk index (KDRI) >85% to a wider geographic area has been implemented in the United States [5].

There are seven studies that investigated the outcome of donor kidneys that were rejected in one center but transplanted in another center [29–34]. The number of patients assessed varied from 22 to 170. Organ donors were younger than in our study, between 40 and 59 years with the control groups slightly younger than the study groups.

Cold ischemia times ranged from 13 to 28 h in these studies. Frei *et al.* have described a rise of risk for graft failure of 3% per hour of CIT [35]. That factor should also account for an allocation to centers willing to accept marginal kidney organs in order to shorten CIT. A change in allocation policy from a point system to an evidence-based system, especially for marginal organs, might help to improve equity and efficiency [36]. In our collective, the distance of the donor to our transplant center was regarded as a parameter of estimated CIT and was significantly longer in organs we declined than in organs we accepted.

One of the most important factors regarding not only the long-term outcome of the grafts but also the mortality of patients is the delayed graft function [37,38]. Measures aiming at the reduction of delayed graft function are therefore of utmost importance. One point may be the reduction of CIT, but other possibilities should also be considered. Perfusion systems, for example, may reduce the rate of delayed

graft function and improve 1-year graft survival. They may therefore be helpful, especially in ECD kidneys [39].

Of 183 organs that were not accepted at the transplant center Freiburg, 100 (54.6%) were transplanted at other centers in Germany. One-year patient survival at the transplant center Freiburg was 96% compared to 98% for patients transplanted at other centers. According to the CTS registry, 1-year patient survival is 95%, being equivalent to our results. As to graft survival, we could show equivalent results for organs having been rejected at our center and transplanted elsewhere and in Freiburg: 86% vs. 92% ($P = 0.119$). Both values are within the range of the CTS registry with 90% 1-year graft survival.

Two organs have been transplanted as dual organs. This is in accordance with Derweesh *et al.* [40], who suspected that 5–10% of kidneys are discarded due to suspected insufficient nephron mass, and Lu *et al.* reasoned that the organ pool could be expanded using dual transplantation [41]. The KDRI might be helpful to distinguish which organs can be transplanted as single organs and which ones benefit from dual transplantation [42].

Regarding organ function, there was no difference in best creatinine or creatinine 1 year after transplantation, respectively. One year after transplantation creatinine had fallen to 1.6 ± 0.8 mg/dl in patients transplanted elsewhere, which was not significantly different from the best creatinine of the kidneys transplanted in Freiburg (1.6 ± 0.9 mg/dl, NS). The same results could be shown by Friedersdorff *et al.*, who described that in 31% of patients rejected in Berlin and transplanted elsewhere, creatinine values were below 1.47% and 94% under 2.97 mg/dl [10].

Summarizing all studies dealing with this topic, it seems that, although the collective of potential donors and recipients has changed over time, acceptance criteria of transplant centers remained the same. This contributes to increased decline rates. Beside measures to improve organ quality or the donation and allocation process, transplant centers may also adapt their acceptance criteria to the current situation.

Although this study is limited by its design, it has to be assumed that currently some kidneys are discarded unnecessarily. A national registry specific for the follow-up of nonstandard risk donors, as already implemented in Spain [43], could help to obtain further insight into the risk-benefit assessment.

In accordance with all other authors who studied the outcome of initially declined organs, we conclude that the critical revision of donor criteria might reduce the number of discarded donor organs [29] and that our own acceptance criteria should be less strict [10,30–32,44].

Conclusion

The number of declined donor organs is increasing over the past decade, mainly due to a growing number of marginal donors accounting for poor organ quality or a mismatch of donor and recipient, particularly concerning the age. If proper donor–recipient selection is performed, many organs, that would otherwise be discarded, can be transplanted successfully.

Authorship

DT-H: designed the study, interpreted data and wrote the paper. CT and SA: collected data. CS and OD: designed the study. UTH and DB: critically revised the manuscript. PP: designed the study, critically revised the manuscript.

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