**Transplantation Publish Ahead of Print**

**DOI: 10.1097/TP.0000000000003964**

# Kidney Transplantation after Rescue Allocation - the Eurotransplant Experience: A Retrospective Multicenter Outcome Analysis

**Running title**: Kidney Transplantation after Rescue Allocation

Assfalg, Volker MD[1,2,#]; Miller, Gregor MSc[3,#]; Stocker, Felix MD[1,2]; van Meel, Marieke[4]; Groenevelt, Tiny[4]; Tieken, Ineke MD[4]; Ankerst, Donna PhD[3]; Renders, Lutz MD[1,5]; Novotny, Alexander MD[1,2]; Hartmann, Daniel MD, MSc[1,2]; Jell, Alissa MD[1,2]; Rahmel, Axel MD[4§]; Wahba Roger MD[6]; Muehlfeld, Anja MD[7]; Bouts, Antonia MD, PhD[8]; Ysebaert, Dirk MD, PhD[9]; Globke, Brigitta MD[10]; Jacobs-Tulleneers-Thevissen, Daniel MD, PhD[11]; Piros, László MD, PhD[12]; Stippel, Dirk MD[6]; Heller, Katharina MD[13]; Eisenberger, Ute MD[14]; van Laecke, Steven MD, PhD[15]; Weimer, Rolf MD[16]; Rosenkranz, Alexander R. MD[17]; Berger, Stefan MD[18]; Fischer, Lutz MD[19]; Kliem, Volker MD[20]; Vondran, Florian MD[21]; Sester, Urban MD[22]; Schneeberger, Stefan MD, MBA[23]; Harth, Ana MD[24]; Kuypers Dirk MD, PhD[25]; Függer, Reinhold MD[26]; Arnol, Miha MD, PhD[27]; Christiaans, Maarten MD[28]; Weinmann-Menke, Julia MD[29]; Krüger, Bernd MD[30]; Hilbrands, Luuk MD[31]; Banas, Bernhard MD, MBA[32]; Hakenberg, Oliver MD[33]; Minnee, Robert MD, PhD, MSc[34]; Schwenger, Vedat MD, MHBA[35]; Heyne, Nils MD[36]; van Zuilen, Arjan MD, PhD[37]; Reindl-Schwaighofer, Roman MD, PhD[38]; Lopau, Kai MD[39]; Hüser, Norbert MD[1,2*]; Heemann, Uwe MD[1,5*]

1. TransplanTUM Munich Transplant Center, Technical University of Munich, TUM School of Medicine, Klinikum rechts der Isar, Ismaningerstr. 22, D-81675 München, German
2. Department of Surgery, Technical University of Munich, TUM School of Medicine, Klinikum rechts der Isar, Ismaningerstr. 22, D-81675 München, Germany
3. Department of Mathematics, Technical University of Munich, Chair of Mathematical Modeling of Biological Systems, Boltzmannstr. 3, D-85748 Garching, Germany



Downloaded from http://journals.lww.com/transplantjournal by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC1y0abggQZXdgGj2MwlZLeI= on 02/16/2022

ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

4. Eurotransplant International Foundation, P.O. Box 2304, NL-2301 CH Leiden, The Netherlands
5. Department of Nephrology, Technical University of Munich, TUM School of Medicine, Klinikum rechts der Isar, Ismaningerstr. 22, D-81675 München, Germany
6. Department of General Visceral Cancer and Transplant Surgery, Transplant Center Cologne, University of Cologne Faculty of Medicine and University Hospital of Cologne, Kerpener Str. 62, D-50937 Cologne, Germany
7. Department of Nephrology, Universitätsklinikum Aachen, Pauwelsstraße 30, D-52074 Aachen, Germany
8. Department of Pediatric Nephrology, Emma Children's Hospital, Amsterdam UMC, Meibergdreef 9, NL-1105 AZ, Amsterdam, The Netherlands
9. Department of Surgery, Antwerp University Hospital & University of Antwerp, Drie Eikenstraat 655, B-2650 Edegem (Antwerpen), Belgium
10. Department of Surgery, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Augustenburger Platz 1, D-13353 Berlin, Germany
11. Department of Surgery, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Laarbeeklaan 101, B-1090 Brussels, Belgium
12. Department of Transplantation and Surgery, Semmelweis University, School of Medicine, Baross u. 23, H-1082 Budapest, Hungary
13. Medizinische Klinik 4, Universitätsklinikum Erlangen-Nürnberg, Transplantationszentrum Erlangen-Nürnberg, Ulmenweg 18, D-91054 Erlangen, Germany
14. Department of Nephrology, University Hospital Essen, University Duisburg-Essen, Hufelandstraße 55, D-45147 Essen, Germany



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

15. Renal department, University Hospital Gent, C. Heymanslaan 10, B-9000 Gent, Belgium
16. Department of Internal Medicine, Nephrology and Renal Transplantation, University Clinic of Giessen and Marburg (UKGM), Campus Giessen, Klinikstrasse 33, D-35392 Giessen, Germany
17. Universitätsklinik für Innere Medizin, Medizinische Universität Graz, Auenbruggerplatz 15, A-8036 Graz, Austria
18. Division of Nephrology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, NL-9700RB Groningen, The Netherlands
19. Department of Visceral Transplant Surgery, University Medical Center Hamburg-Eppendorf, Martinistraße 52, D - 20246 Hamburg, Germany
20. Department of Internal Medicine, Division of Nephrology, Transplantationszentrum Hannoversch Münden, Klinikum Hann. Münden, Vogelsang 105, D-34346 Hann. Münden, Germany
21. Department for General, Visceral and Transplant Surgery, Hannover Medical School, Carl-Neuberg-Str. 1, D-30625 Hannover, Germany
22. Internal Medicine IV - Nephrology and Hypertension, Saarland University Medical Center and Saarland University Faculty of Medicine, D-66421 Homburg, Germany
23. Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria
24. Medizinische Klinik I, Kliniken der Stadt Köln gGmbH, Lehrstuhl für Innere Medizin II, Uniklinik WItten/Herdecke, Ostmerheimerstr. 200, D- 51109 Köln, Germany
25. Department of Nephrology, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium
26. Department of Surgery, Ordensklinikum Elisabethinen Linz, Fadinger Strasse 1, A-4020 Linz, Austria



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

27. Department of Nephrology and Renal Transplantation, University Medical Centre Ljubljana, Zaloska 7, SLO-1000 Ljubljana, Slovenia
28. Division of Nephrology, Maastricht University Medical Centre, Department of Internal Medicine, P. Debyelaan 25, NL-6229 HX Maastricht, The Netherlands
29. Schwerpunkt Nephrologie und Nierentransplantation, Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Langenbeckstraße 1, D-55131 Mainz, Germany
30. Department of Nephrology, Universitätsmedizin Mannheim, Medizinische Fakultät Mannheim der Universität Heidelberg, Theodor-Kutzer-Ufer 1-3, D-68167 Mannheim, Germany
31. Department of Nephrology, Radboud university medical center, P.O. Box 9101, NL-6500 HB Nijmegen, The Netherlands
32. Department of Nephrology, Universitätsklinikum Regensburg, Universitäres Transplantationszentrum, Franz-Josef-Strauß-Allee 11, D-93042 Regensburg, Germany
33. Department of Urology, University Hospital Rostock, Schillingallee 35, D-18057 Rostock, Germany
34. Department of Surgery, Division of HPB & Transplant Surgery, Erasmus MC Transplant Institute, Dr. Molewaterplein 40, NL-3015 GD Rotterdam, The Netherlands
35. Department of Nephrology, Klinikum der Landeshauptstadt Stuttgart, Katharinenhospital, Kriegsbergstr. 60, D-70174 Stuttgart, Germany
36. Department of Internal Medicine IV, Section of Nephrology and Hypertension, Tübingen University Hospital, Otfried-Müller-Str. 10, D-72070 Tübingen, Germany
37. Department of Nephrology, University Medical Center Utrecht, NL-3508 Utrecht, The Netherlands



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

38. Department of Internal Medicine III, Division of Nephrology and Dialysis, Medical University of Vienna, Währinger Gürtel 18-20, A-1090 Wien, Austria

39. Dep. Internal Medicine 1, Div. Nephrology, University hospital Wuerzburg, Oberdürrbacher Str. 6, D-97080 Würzburg, Germany

§. Present address: Deutsche Stiftung Organtransplantation (DSO), Deutschherrnufer 52, D-60594 Frankfurt am Main, Germany

#, Volker Assfalg and Gregor Miller contributed equally to this work

*, Norbert Hüser and Uwe Heemann contributed equally to this work

**Financial disclosures:** The authors declare no financial disclosures resulting in conflicts of interest. For further details please check the conflict of interest statements uploaded in the Editorial Manager.

**Competing interest declaration:** The authors declare no conflict of interests.

**Declaration:**All results presented in this paper have not been published previously in whole or part.

**Authorship:**

VA, NH, UH: study idea, design, manuscript

VA, GM, FS, MvM, TG, IT, AR, NH, UH: study performance

VA, GM, FS, DA, LR, AN, DH, AJ, RW, NH, UH: data analyses, manuscript

All authors: data ascertainment, manuscript discussion, manuscript revisions

**Corresponding author:** PD Dr. med. Volker Assfalg TransplanTUM, Munich Transplant Center Technical University of Munich TUM School of Medicine Klinikum rechts der Isar Department of Surgery Ismaningerstr. 22 D-81675 Munich, Germany phone +49-(0)89-4140-2121 fax +49-(0)89-4140-4870 e-mail volker.assfalg@tum.de



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Abbreviations:**

| | |
|---|---|
| AM | acceptable mismatch program |
| CIT | cold ischemia time |
| CCO | competitive center offer |
| CMV | cytomegalovirus |
| DDRT | deceased donor renal transplantation |
| DwFG | death with functioning graft |
| ECD | expanded criteria donor |
| ET | Eurotransplant International Foundation, Leiden, The Netherlands |
| ETKAS | Eurotransplant Kidney Allocation System |
| ESP | Eurotransplant Senior Program |
| HR | hazard ratio |
| PNF | primary non-function |
| PRA | preformed antibodies |
| RA | rescue allocation |
| REAL | recipient oriented extended allocation |
| SA | standard allocation |
| SHR | subdistribution hazard ratio |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**ABSTRACT**

**Background:** At Eurotransplant (ET), kidneys are transferred to 'rescue allocation' (RA), whenever the standard allocation (SA) algorithms Eurotransplant kidney allocation system (ETKAS) and Eurotransplant senior program (ESP) fail. We analyzed the outcome of RA.

**Methods:** Retrospective patient clinical and demographic characteristics association analyses with graft outcomes for 2,421 recipients of a deceased donor renal transplantation (DDRT) after RA versus 25,475 after SA from 71 centers across all ET countries from 2006 to 2018.

**Results:** Numbers of DDRTs after RA increased over the time, especially in Germany. RA played a minor role in ESP vs. ETKAS (2.7% vs. 10.4%). RA recipients and donors were older compared to SA recipients and donors, cold ischemia times were longer, waiting times were shorter, and the incidence of primary non-function was comparable. Among ETKAS-recipients, HLA matching was more favorable in SA (mean 3.7 vs. 2.5). In multivariate modeling, the incidence of death with a functioning graft (DwFG) in ETKAS was reduced in RA compared to SA (subdistribution hazard ratio 0.70, 95% confidence interval [0.60-0.81], $p<0.001$) whereas other outcomes (mortality, graft loss) were not significantly different. None of the three outcomes were significantly different when comparing RA with SA within the ESP program.

**Conclusions:** Facing increased waiting times and mortality on dialysis due to donor shortage, this study reveals encouragingly positive DDRT outcomes following RA. This supports the extension of RA to more patients and as an alternative tool to enable transplantation in patients in countries with prohibitively long waiting times or at risk of deterioration.

Supplemental Visual Abstract; http://links.lww.com/TP/C297



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

## INTRODUCTION

Allocation schemes for deceased donor kidney transplantation (DDRT) are based on scientifically proven risk factors for graft and recipient outcome as well as ethical principles. These algorithms rank potential recipients on the waiting list for every allocation procedure. At the Eurotransplant International Foundation (ET), immunological matching, waiting time, cold ischemia time (CIT), age, urgency and preformed antibodies (PRA) are the defining factors [1-3].

Death on the ET waiting list ranges between 4.2% and 5.4% (mean 4.7%) for the last 15 years. This high mortality, which is a consequence of persistent and increasing donor shortage and high numbers of patients on the waiting list [4] resulted in the acceptance and transplantation of kidneys from comorbid donors with indefinite and disputable outcome. During the last two decades, 'expedited' or 'rescue allocation' (RA) rules have been established and refined repeatedly by most organizations worldwide to reduce the number of discarded grafts and increase transplant numbers [1-3]. Currently, 22.6% of all kidneys offered within ET are finally discarded and the median age of these donors is 61 years.

ET, the largest European organ allocation organization, defined distinct rules for RA following logistic and/or medical reasons which allow to deviate from the standard allocation (SA) programs 'Eurotransplant Kidney Allocation System' (ETKAS) and 'Eurotransplant Senior Program' (ESP)[2,5]. The ETKAS is destined for all candidates irrespective of their age and considers waiting time, HLA match, a regional/national bonus to favor shorter CITs, a pediatric bonus, and a high urgency bonus. However, the ESP is an alternative program only for candidates beyond 64 years of age, which abstains from HLA matching and only takes account of waiting time and preferably short CITs by regional allocation of kidneys from donors older than 64 years. Both SA programs transfer grafts to RA to prevent loss of potentially transplantable organs [5].

The reasons for switching over to RA may be very inhomogeneous and can derive from



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

different reasons:

- repeated rejection of the offer for all candidates of five different centers e.g., due to donor-related reasons such as presumed inadequate quality of the graft or problems with the procurement process
- non-acceptance of the organ five hours after procurement
- logistics do not allow for a timely transplantation causing an increased CIT
- impending loss of the organ for transplantation
- or an interaction of these factors [2,6].

In addition, a subsequent 'cascade effect' of repeated declines has been reported in case of the subjective negative assessment of an offer and decline by one center [7].

However, even though kidneys offered via RA recently turned out to be of inferior histopathological quality [8] and characteristics of RA transplants are inhomogeneous, the outcome was demonstrated to be comparable to SA in small single center analyses [7,8].

In RA, centers may self-select suitable recipients by themselves either from an ET-generated ranking list within the Recipient Oriented Extended Allocation (REAL) program, which abides by the ETKAS SA criteria, or from an in-house list for Competitive Center Offers (CCO) [2], documenting the reasons for selecting the recipient for transparency and scrutiny. The detailed regulations on RA within ET can be looked up online in reference 5.

CCOs provide centers the opportunity to allocate grafts according to the match list or by specific in-house rules, such as urgency, need, or expected transplant outcome. The potential benefits from the transplantation of kidneys from expanded criteria donors (ECD) [9] to non-immunized recipients >40 years of age with diabetes and hypertension – the most perilous comorbidity cluster – have been described repeatedly [10-12]. A recent study showed that benefits of RA for selected recipients with impaired health status were most likely attributable to reduced waiting times [8], the strongest established modifiable risk factor for outcomes [13].

Current increases in both the number of kidneys offered via RA and the needs for donor



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

kidneys across most countries, particularly in Europe, forces transplant physicians to identify and quantify the benefits of RA for selected target candidates. Hitherto, the outcomes from RA transplants have not been analyzed by comprehensive trials with sufficiently large case numbers. Therefore, this multicenter study was initiated to reveal the outcomes of RA from 71 ET kidney transplant centers in comparison to outcomes from SA within the same area.

## MATERIALS AND METHODS

Long-term outcomes of RA kidney-only transplantations from brain death deceased donors (DDRT) within ETKAS and ESP in the ET area between January 2006 and May 2018 were investigated after approval of the study by the ET authorities (14046KAC14). During this time period a total of 50,835 SA and 3,498 RA DDRTs were performed.

All ET transplant centers were requested to return follow-up data to increase data completeness at the ET registry as previously performed by the ET community for comparable issues [14,15]. The request was issued between January and September 2019 and ascertained date of last follow-up, graft loss with date of loss, patient's death with date of death, as well as patient's death with functioning graft (DwFG), sequence of organ transplantation, and underlying renal disease, respectively. DwFG data provide insights into the concomitant health status of the affected recipients by accounting for the number of deaths not associated with graft failure. Information on sex, age at transplant, HLA match, waiting time, transplant period, country where the transplantation was performed, and general information on the overall ET waiting list and transplantations were obtained from the ET database.

Individual records with missing follow-up were assumed to have data missing at random and removed for statistical analyses [16], other exclusions are shown in Figure 1. Missing follow-up was defined, whenever no more information was available after transplantation. Cases with errors or contradictory information in the dataset were excluded as well. Non-informative censoring was assumed for all time-to-event analyses [17].



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

Within the investigated period and the restricted data set, 821 patients were repeatedly transplanted, including 179 RA patients. Re-transplantations were considered as independent observations. Mean (median) follow-up times for both SA- and RA-DDRTs were 1838.5 (1674) versus 1516.3 (1157) days, respectively. Follow-up acquisition was terminated on July 3rd, 2020 and reported follow-up was capped at 10 years after transplantation for all analyses. ET data protection policy required patient and center anonymization at the ET registry department, which provided anonymized data to the study statisticians and principal investigators.

Recipient survival was counted from day of transplant to day of death and not censored for graft loss. Graft loss was defined as return to dialysis after successful transplantation. All outcome parameters were censored for patient loss to follow-up. Cumulative incidence curves were calculated for recipient death, DwFG, and graft loss, the latter two accounting for competing risks of each other. Censored patient survival and cumulative incidence of DwFG and graft loss were compared for all investigated subgroups defined by clinical and demographic parameters. For factors with more than two groups in this analysis, Bonferroni correction was applied to account for multiple pairwise comparisons. For patient survival, Cox proportional hazards models were used [18]. For analyses of DwFG and graft loss, the Fine Gray proportional regression model was used with semiparametric random effects for competing risks [19-21]. Multivariable models for patient survival, DwFG, and graft loss included covariates previously identified [22] to affect graft failure and mortality after DDRT, such as age and gender of the recipient, waiting time, CIT, diabetes, transplant count, and HLA matches for comparison between RA and SA [4,8,13-15,23-27]. Both univariable and multivariable models were fit to all endpoints, with 95% CIs reported for hazard ratios. Primary non-function (PNF) was assumed when graft failure was recorded within 90 days after transplantation. Patients who died on the day of transplantation (SA: n=1; RA: n=1) and transplants with PNF were henceforth excluded from investigations on graft loss and DwFG.



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

The number of HLA matches including HLA-A, -B, and -DR loci was analyzed with regards to transplant outcome and further subdivided: all matches with at least one -DR plus at least one -A or one -B match were assigned to the group of 'favorable matches'; all others were defined as 'unfavorable matches'.

To account for relevant numbers of recipients with missing follow-up, a subgroup analysis was performed to determine statistically higher rates of missing follow-up with respect to the allocation modus. The chi square test with Monte Carlo simulations was used to test for differences in the categorical variables related to follow-up (Table S1 http://links.lww.com/TP/C296 ).

All analyses were performed at the two-sided level of significance of 0.05 using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria) [21,28]. All data ascertainments and analyses were performed in accordance with ethical standards as laid down in the Declaration of Helsinki.

**RESULTS**

Demographic and transplant-specific data on SA and RA transplantations are given in Table 1 and the densities of recipient age for RA and SA are depicted in Figure 2A. The steep increase in SA recipients starting at 65 years originates from the ESP. RA recipients from the ETKAS waiting list as well as from the ESP list were significantly older than recipients after SA, received organs from older donors, had a worse HLA match and a prolonged CIT, but waiting time was shorter in each case. Notably, PNF-rates were comparable between SA and RA (Table 1). Considering recipients from the ETKAS waiting list only, the mean HLA match was higher for all HLA-A, -B, and -DR, in sum, and the frequency of favorable matches was superior (Table 2).

The numbers and proportions of RA increased markedly over the analyzed time periods (Figure 2B). Kidneys from RA were mainly allocated to candidates on the ETKAS waiting list and rarely for ESP-listed recipients (93.2% vs. 6.8%). RA played a minor role in ESP- as



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

compared to ETKAS-listed patients (2.7% vs. 10.4%; Table 1). Germany had by far the most transplants within ET with respect to SA (59.1%), but especially with respect to RA (75.8%; Table 1).

With regards to cases with or without follow-up, no differences could be revealed for SA between left versus right organs, but significant differences were found for recipient age, donor age, allocation program, CIT, recipient sex, donor sex, renal disease, matching, waiting time, transplant count, transplantation period, and country. Among RA recipients, follow-up was less frequently noted in cases with unknown CIT, male donors, long waiting time, and later transplantation periods, and from Germany (Table S1 http://links.lww.com/TP/C296 ).

Table 3 gives an overview on patient survival, DwFG, and graft loss with regards to allocation modus and transplant-specific variables in univariate testing. Figure 3 displays the cumulative incidence curves of outcome of ETKAS-listed candidates with regards to RA vs. SA. Transplant outcome after RA between the different ET member countries did not reveal any statistical differences in subgroup analyses due to low case numbers in most countries (Table 1). However, waiting time of ETKAS-listed patients was by far the longest in Germany (mean 2410 days vs. <1600 days in all other ET member countries).

In univariate analyses, mortality and DwFG within ten years after RA were significantly higher as compared to SA for the analyzed period, but graft loss was similar (Table 3). Notably, patients with diabetes and prolonged waiting time displayed an increased mortality hazard and increased cumulative incidence of DwFG, but not with respect to graft loss. Survival and graft loss turned out to be worse in recipients of a second graft. DDRTs in recipients with cystic disease, favorable HLA match, organs from younger donors, and with shorter CITs showed superior outcomes in all three categories (Table 3).

The univariate analysis of transplant-specific continuous variables and the multivariate analysis of patient survival, DwFG, and graft loss of recipients from the ETKAS waiting list with regards to known influencing variables including the allocation modus can be found in



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

Table 4A and 4B. Remarkably, in the multivariate analysis both survival and graft loss after RA turned out to be comparable to SA (p=0.090 and p=0.885), whereas RA even showed reduced cumulative incidences for DwFG (subdistribution hazard ratio, SHR: 0.70; 95% CI: 0.60-0.81; p<0.001). Diabetes was associated with higher mortality and DwFG incidence. Re-transplantation was also associated with increased incidence of graft loss.

Notably, in subanalyses for recipients from the ESP waiting list, patient survival, DwFG and graft loss after RA were also comparable to SA (Table 4C). Furthermore, HLA match, CIT, and re-transplantation were not associated with any outcomes, whereas long waiting times as well as diabetes showed a positive association with mortality and DwFG.

Finally, the respective impact of the two crucial factors 'increasing donor age' and 'prolonged CIT' on patient survival, DwFG, and graft loss was exemplarily investigated for a fictitious reference recipient: 55-year-old, non-diabetic, female, favorable HLA match, waiting time of 5 years, and first transplantation (Table 5). In this prediction model, the risk of a prolonged CIT was markedly less critical than an older age of the donor.

**DISCUSSION**

Survival of recipients after DDRT has been demonstrated to be superior to that of patients on dialysis and candidates awaiting DDRT [4]. Shorter waiting time is the strongest modifiable factor for increasing transplant outcome [13]. Therefore, any candidate awaiting DDRT should ideally be transplanted as soon as possible and with an adequate graft. In contrast, organ shortages and demographic changes evidently impede this desirable goal. To cope with these challenges in kidney transplant supply and maintain acceptable transplant numbers, ET implemented the ESP and RA algorithms during the past decades. In contemporary practice, transplant physicians are pushed to accept kidneys from older donors with more comorbidities. The transplant outcomes of kidneys from ECDs have been repeatedly evaluated [10-12], revealing a survival benefit in unsensitized patients older than 40 years with diabetes or hypertension, particularly due to shortened waiting times [12], but data on survival



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

and graft loss after RA DDRTs are scarce. Kidneys transplanted after RA have been reported to originate from older donors with a higher rate of diabetes, hypertension, fulfilled ECD criteria [6,8], and both increased acute and chronic histopathological changes were observed in zero-time biopsies from RA kidneys [8]. DDRTs after RA were characterized by a prolonged CIT, worse HLA matching, increased CMV transmission risk, but a reduced waiting time [8], which was validated by this study.

As the proportion of DDRT after RA increased markedly over time, this option apparently acquired greater importance in the ET kidney transplant centers. We therefore performed this comprehensive long-term ET multicenter study to resolve the question of RA DDRT outcome, thus far only addressed in single center reports [8,29,30].

**Demographic and transplant specific characteristics of rescue-allocated DDRTs**

This ET multicenter study confirmed the previously observed significantly older age of RA DDRT recipients and donors [8,29,30] in a comprehensive patient collective and even in case of distinction between ETKAS- and ESP-listed recipients. Notably, RA plays a minor role in recipients within the ESP until now (Table 1).

Considering the evidently crucial role of an 'excellent donor' and a favorable HLA match for younger recipients and the shorter waiting time within the ESP, it may be assumed that centers referred to RA especially in cases with an urgent need for a transplant due to deterioration and risk of delisting. Those patients typically suffer from comorbidities like hypertension and diabetes [8,11]. They are likely to be either too young to apply for the ESP (mean 57.4 years) to benefit from the shorter waiting time within this programme or already qualified for the ESP, but their advanced age (mean 69.3 years; Table 1) and limiting frailty [31] signal risk of imminent delisting. Considering this, transplant physicians obviously tended towards accepting RA offers, condoning increased donor age, prolonged CITs, and unfavorable HLA matching, just to escape this dilemma and shorten waiting time (Table 1). Despite the evidentially negative, though reasonable, compromises PNF turned out to be



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

comparable between RA and SA as previously reported [8], which additionally encourages acceptance of RA offers. The question is whether a recommendation should be made for RA kidneys to be considered for more candidates apart from older patients and those with comorbidities, frailty, and an increased risk of delisting or higher risk of mortality after transplant [32-35].

Favorable HLA matching is essential for long-time graft and patient survival [15,23,27] and is credited with extra allocation points in the ETKAS, but ignored in the ESP [2], which concentrates on shorter CITs by regional allocation to reduce harm to organs from older donors [2]. This survey confirmed worse HLA matches and inferior HLA favorability of RA DDRTs of recipients listed within the ETKAS program (Table 2) [8,29]. Furthermore, less advantageous CMV-constellations were just recently identified in a single center study [8]. Taking this into account, preferring a recipient with a more favorable match in CCOs in future and assumingly better HLA matches in REAL versus CCO might even have an additional positive impact on outcome (Table 4B). Notably, right kidneys were significantly more frequent in RA which possibly might derive from apprehended technical problems due to the shorter vein and repeated decline in different centers [7]. Overall patient and graft outcome after RA including PNF was comparable to SA despite prolonged CITs, older recipient and donor age, inferior HLA matches, and assumingly higher CMV-risk. This observation must be ascribed to the pivotal impact of shortened waiting times in RA [8,13].

**Use of kidney transplants from RA in the course of time and among ET countries**

The increasing use of kidneys from RA, especially since 2014 (Figure 2B), correlates unambiguously with the mounting need for more grafts, which is aggravated by both the demographic change over the last decades and consecutively more comorbidities of the donors. Today, every tenth DDRT within the ET area originates from RA compared to a range of rates between 4.8% and 26.4% previously reported in single centers [7,8,29,30]. Furthermore, the effect of legal regulations concerning organ donation on the use of kidneys



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

from RA was confirmed by this survey. The opting-in approach with its specific consent of the individual and deplorably low donation rates fosters the observed significantly longer waiting times and higher rate of RA in Germany (11%), whereas countries with the opting-out approach hardly use organs from RA (Table 1). However, despite an increased use of RA kidneys, decline rates of all kidneys offered before RA was initiated were comparable between the member states.

Facing the previously identified major benefit of shortened waiting times on transplant outcome [13] despite marginal grafts in RA [8,10-12] repeatedly declined in different centers for various reasons [7], DDRT through RA is reasonable and should be continued especially in countries with considerably prolonged waiting times due to organ shortage.

**Rescue-allocated kidney recipient survival**

Most encouragingly, multivariate analyses adjusting for potential confounding factors revealed comparable patient survival and decreased DwFG in ETKAS-listed recipients of RA versus SA DDRTs (Table 4B) despite worse recipient-, donor-, and transplant-specific characteristics in RA DDRT (Table 1). These results strongly encourage transplant physicians to continue DDRT via RA and debilitate any concerns of causing harm to recipients by use of RA grafts which might derive from the mentioned characteristics in RA and the univariate analysis (Table 3, Figure 3). According to our data, more attention should be directed to favorable HLA matching, younger donor age, and short CIT. Whenever possible, these factors should be taken into consideration and a recipient with a better HLA match should be prioritized in CCOs, especially in young recipients. Just recently, an easily practicable algorithm for acceptance of RA offers and careful selection of eligible RA recipients was demonstrated to yield excellent outcome [8]. Taken together, this offers the chance to include these variables into allocation (e.g. REAL), provide more safety to the centers concerning acceptance or decline, and improve RA outcome in future.

In the face of a limited pool of grafts, we urgently have to accelerate transportation and



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

implement virtual crossmatching to reduce CITs whenever reasonable. Prospectively, even more RA grafts might be transplanted this way and allow for a reduction in waiting time – the key to reducing mortality [13].

Recipients with diabetic nephropathy and recipients of a re-transplantation showed inferior outcome in multivariate analyses as previously reported [10-12,15](Table 4B). If donor numbers markedly increased and waiting times decreased, survival of these poor prognosis patients could potentially increase.

According to the multivariate analysis, senior recipients of RA DDRT clearly profited from RA as survival and DwFG were comparable to SA. Notably, patient survival after RA was borderline significantly better compared to SA (Table 4C). These findings underline our explicit recommendation to continue and even extend RA use. In ESP-listed recipients, HLA matching and donor age had no impact on survival, but short waiting times were favorable, which facilitates the selection of appropriate RA recipients in this subgroup. Short waiting times must be expected to have a significant impact on outcome after DDRT and naturally prevent death on the waiting list in seniors.

**Graft survival after rescue-allocated DDRTs**

Fortunately, 10-year graft survival after RA DDRT was comparable to SA in the multivariate analysis even despite proven inferior histopathological acute and chronic tissue damages, worse HLA matching and elevated CMV-risk, longer CITs, older donor age, and significantly more adverse comorbidities and fulfilled ECD-criteria in RA donors as reported before [8]. Therefore, the acceptance of RA kidneys should be extended especially in countries with long waiting times. With regards to the multivariate analysis (Table 4B, C) and predictions (Table 5), all efforts need to be made to avoid loss of grafts from young donors by even accepting prolonged CITs. The effect of worse HLA matching and increased CMV transmission risk in RA [8] is apparently less weighty on overall graft outcome than expected.

In senior recipients graft survival after RA was equivalent to results from ESP SA and HLA



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

matching may equally be neglected. Adding this to the excellent survival data, RA can be recommended for senior candidates as a potentially useful tool to provide these patients with a graft before deterioration, delisting, or death on the waiting list with increasing age and comorbidities in future [13,31,32,36].

**Limitations**

The major limitation of this study is the retrospective data assessment from a non-compulsory database. Contribution to data completeness differs between the ET member countries. While in some countries, including the Netherlands and Belgium, data reporting to ET is compulsory, in others, such as Germany, it is up to the centers. This explains the suboptimal data completeness in some parts, for example, the high rate of SA recipients without follow-up from Hungary and Germany. However, by use of statistical censoring, missing follow-up was correctly compensated for in the analyses and thanks to the participation of 71 transplant centers, data completeness was considerable after return of the questionnaires.

Unfortunately, relevant parameters, such as delayed graft function, rejection, biopsy-proven rejections, one-year glomerular filtration rate (GFR), concomitant diseases, and detailed donor features were not available. However, some of these issues can be assumed to be in accordance with results from previously published data like an increased one-year GFR [8,29,30]. Ideally, comprehensive reporting of these parameters would allow for subgroup analyses and enable identification of distinct candidates with a maximum profit of RA kidneys and particularly suitable donor-recipient combinations.

Finally, a tool including all relevant and available parameters to predict the expected benefit of RA in every single case over continuation of dialysis would be useful. An outcome predictor might even accelerate decision making in case of an offered organ via SA and potentially antedate RA initiation which would reduce the CIT and therefore help to improve outcomes. Furthermore, comprehensive data on discarded organs could help to identify kidneys that were unnecessarily discarded. Unfortunately, these data cannot be generated



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

from the current ET database by now.

**Conclusions**

DDRTs of kidneys offered via RA should be expanded for both ETKAS- and ESP-listed recipients according to their excellent outcome in patient and graft survival, which is fully comparable to SA. The use of RA kidneys is an adequate extension of the donor pool and should be extended to increase transplant numbers and reduce waiting times. The acquiescence of longer CITs, less favorable HLA matching, and inferior histopathological renal parenchymal quality of RA kidneys is compensated by the weighty benefit of a significantly shorter waiting time. Although both ETKAS- and ESP-listed recipients profited from DDRT of RA grafts, we recommend to adhere to certain basic donor- and transplant-specific parameters such as careful consideration of proteinuria, hypertension, and diabetes of the donor and a limited donor-recipient age difference like previously recommended [8]. In CCOs for younger recipients, a patient with a favorable HLA match should be preferred over a candidate with an unfavorable match and even despite a potentially prolonged CIT in case of a young donor to further increase the outcome according to our data.

In ESP recipients, however, these considerations are secondary; the shortened waiting time in RA becomes even more attractive in the race against deterioration whilst waiting for SA, consecutively making RA a perfect supplement to the ESP.

This study clearly indicates that a mandatory joined register to collect all data on donors and recipients, including for example, concomitant diseases, is urgently needed to identify those candidates who do or do not profit from RA, enabling transplant physicians offered a RA kidney to separate the wheat from the chaff. Apart from these factors, our allocation procedures and organ logistics must become quicker and virtual crossmatching has to be implemented to reduce CITs and thus improve the quality of all grafts.

In the meantime, transplant centers should individually define or revise their center specific criteria for RA transplants, if not yet done.



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Acknowledgements:**

The authors thank all ET staff members for their support with sending the questionnaires and database analyses and the contributing centers for the data supply.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**References:**


1. Organ Procurement and Transplantation Network (OPTN), Policies, Policy 8: Allocation of Kidneys, available at https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf; accessed 01/12/2020. In.
2. Eurotransplant Manual–version 8.2; Chapter 4 - Kidney (ETKAS and ESP),available at https://my.eurotransplant.org/wp-content/uploads/2020/11/H4-Kidney-2020.3-November-2020.pdf, accessed 01/12/2020.
3. NHS Blood and Transplant (NHSBT) AP, Kidney Transplantation: Deceased Donor Organ Allocation, POL186/9, available at https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/16915/kidney-allocation-policy-pol186.pdf, accessed 01/12/2020.
4. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med.* 1999;341(23):1725-1730.
5. Eurotransplant Manual-version 8.2; Chapter 3 - Allocation General, available at https://my.eurotransplant.org/wp-content/uploads/2020/09/H3-Allocation-v2020.2-September-2020.pdf, accessed 01/12/2020.
6. Vinkers MT, Smits JM, Tieken IC, et al. Kidney donation and transplantation in Eurotransplant 2006-2007: minimizing discard rates by using a rescue allocation policy. *Prog Transplant.* 2009;19(4):365-370.
7. Farid S, Aldouri A, Fraser S, et al. Outcomes of kidney grafts refused by one or more centers and subsequently transplanted at a single United Kingdom center. *Transplant Proc.* 2009;41(5):1541-1546.




ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

8. Assfalg V, Misselwitz S, Renders L, et al. Kidney transplantation after rescue allocation-meticulous selection yields the chance for excellent outcome. *Nephrol Dial Transplant.* 2021. Doi:10.1093/ndt/gfaa286

9. Metzger RA, Delmonico FL, Feng S, et al. Expanded criteria donors for kidney transplantation. *Am J Transplant.* 2003;3 Suppl 4:114-125.

10. Querard AH, Le Borgne F, Dion A, et al. Propensity score-based comparison of the graft failure risk between kidney transplant recipients of standard and expanded criteria donor grafts: Toward increasing the pool of marginal donors. *Am J Transplant.* 2018;18(5):1151-1157.

11. Ko KJ, Kim YH, Kwon KH, et al. Kidney transplantation using expanded-criteria deceased donors: a comparison with ideal deceased donors and non-expanded-criteria deceased donors. *Transplant Proc.* 2018;50(10):3222-3227.

12. Merion RM, Ashby VB, Wolfe RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA.* 2005;294(21):2726-2733.

13. Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. *Transplantation.* 2002;74(10):1377-1381.

14. Assfalg V, Huser N, van Meel M, et al. High-urgency kidney transplantation in the Eurotransplant Kidney Allocation System: success or waste of organs? The Eurotransplant 15-year all-centre survey. *Nephrol Dial Transplant.* 2016;31(9):1515-1522.

15. Assfalg V, Selig K, Tolksdorf J, et al. Repeated kidney re-transplantation-the Eurotransplant experience: a retrospective multicenter outcome analysis. *Transpl Int.* 2020;33(6):617-631.



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

16. Hughes RA, Heron J, Sterne JAC, et al. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epidemiol.* 2019;48(4):1294-1304.

17. Ranganathan P, Pramesh CS. Censoring in survival analysis: Potential for bias. *Perspect Clin Res.* 2012;3(1):40.

18. Terry M. Therneau PMG. *Modeling Survival Data: Extending the Cox Model.* New York: Springer; 2000.

19. Scheike TH, Sun Y, Zhang MJ, et al. A semiparametric random effects model for multivariate competing risks data. *Biometrika.* 2010;97(1):133-145.

20. Scheike TH, Zhang MJ. Flexible competing risks regression modelling and goodness of fit. *Lifetime Data Anal*. 2008;14:464-83.

21. Scheike TH, Zhang MJ. Analyzing competing risk data using the R timereg package. *J Stat Softw.* 2011;38(2).

22. Heinze G, Dunkler D. Five myths about variable selection. *Transpl Int.* 2017;30(1):6-10.

23. Yacoub R, Nadkarni GN, Cravedi P, et al. Analysis of OPTN/UNOS registry suggests the number of HLA matches and not mismatches is a stronger independent predictor of kidney transplant survival. *Kidney Int.* 2018;93(2):482-490.

24. Debout A, Foucher Y, Trebern-Launay K, et al. Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation. *Kidney Int.* 2015;87(2):343-349.

25. Postalcioglu M, Kaze AD, Byun BC, et al. Association of cold ischemia time with acute renal transplant rejection. *Transplantation.* 2018;102(7):1188-1194.

26. Revanur VK, Jardine AG, Kingsmore DB, et al. Influence of diabetes mellitus on patient and graft survival in recipients of kidney transplantation. *Clin Transplant.* 2001;15(2):89-94.



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

27. Opelz G, Dohler B. Association of HLA mismatch with death with a functioning graft after kidney transplantation: a collaborative transplant study report. *Am J Transplant.* 2012;12(11):3031-3038.

28. Therneau TM, Lumley T (2015): A Package for Survival Analysis in S. version 2.38. 2015. Available at https://CRAN.R-project.org/package=survival.

29. Wahba R, Teschner S, Stippel DL. Results of kidney transplantation after rescue allocation. *Transpl Int.* 2011;24(6):e46-47.

30. Wahba R, Suwelack B, Arns W, et al. Rescue allocation and recipient oriented extended allocation in kidney transplantation-influence of the EUROTRANSPLANT allocation system on recipient selection and graft survival for initially nonaccepted organs. *Transpl Int.* 2017;30(12):1226-1233.

31. Haugen CE, Chu NM, Ying H, et al. Frailty and access to kidney transplantation. *Clin J Am Soc Nephrol.* 2019;14(4):576-582.

32. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis. *J Am Geriatr Soc.* 2013;61(6):896-901.

33. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant.* 2013;13(8):2091-2095.

34. McAdams-DeMarco MA, Law A, King E, et al. Frailty and mortality in kidney transplant recipients. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons.* 2015;15(1):149-154.

35. Pelletier RP, Pesavento TE, Rajab A, Henry ML. High mortality in diabetic recipients of high KDPI deceased donor kidneys. *Clin Transplant.* 2016;30(8):940-945.



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

36. Mehdorn AS, Reuter S, Suwelack B, et al. Comparison of kidney allograft survival in the Eurotransplant senior program after changing the allocation criteria in 2010-A single center experience. *PLoS One.* 2020;15(7):e0235680.

37. Brice Ozenne, Anne Lyngholm Sorensen, Thomas Scheike, et al. riskRegression: predicting the risk of an event using cox regression models. *The R Journal*. 2017;9(2):440-460.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Legends to figures and tables**

**Figure 1:** Flowchart of selection process of transplants analyzed in this study. Counts refer to number of transplants. ETKAS: Eurotransplant Kidney Allocation System; ESP: Eurotransplant Senior Program; AM: Acceptable Mismatch Program.

**Figure 2: (A)** Recipient age and **(B)** amount of transplants between 2006 and 2018 with respect to allocation type. Percentages show the fraction of the respective period.

**Figure 3:** Cumulative incidence curves for ETKAS patients with respect to death (A), death with functioning graft (B), and graft loss (C) according to allocation.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Table 1:** Characteristics of transplants according to allocation.

| **Characteristics of ETKAS and ESP transplants** | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | **Standard allocation** | | | **Rescue allocation** | | |
| | Value | N (25475) | Group % | Allocation % | N (2421) | Group % | Allocation % | p-value |
| Recipient sex | Female | 9161 | 36.0 | 90.7 | 935 | 38.6 | 9.3 | 0.010 |
| | Male | 16314 | 64.0 | 91.7 | 1486 | 61.4 | 8.3 | |
| Disease group | Glomerulo-nephritis | 5891 | 23.1 | 91.3 | 558 | 23.0 | 8.7 | <0.001 |
| | Cystic disease | 3429 | 13.5 | 89.8 | 390 | 16.1 | 10.2 | |
| | Diabetes | 2160 | 8.5 | 90.6 | 225 | 9.3 | 9.4 | |
| | Other | 13995 | 54.9 | 91.8 | 1248 | 51.5 | 8.2 | |
| Donor sex | Female | 12057 | 47.3 | 91.7 | 1088 | 44.9 | 8.3 | 0.026 |
| | Male | 13418 | 52.7 | 91.0 | 1333 | 55.1 | 9.0 | |
| Allocation program | ETKAS | 19516 | 76.6 | 89.6 | 2257 | 93.2 | 10.4 | <0.001 |
| | ESP | 5959 | 23.4 | 97.3 | 164 | 6.8 | 2.7 | |
| Organ | Left kidney | 12381 | 48.6 | 91.8 | 1100 | 45.4 | 8.2 | 0.003 |
| | Right kidney | 13094 | 51.4 | 90.8 | 1321 | 54.6 | 9.2 | |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Transplant count | 1 | 23547 | 92.4 | 91.4 | 2224 | 91.9 | 8.6 | 0.266 |
| | 2 | 1807 | 7.1 | 90.5 | 189 | 7.8 | 9.5 | |
| | ≥3 | 121 | 0.5 | 93.8 | 8 | 0.3 | 6.2 | |
| Country | Germany | 15060 | 59.1 | 89.1 | 1836 | 75.8 | 10.9 | <0.001 |
| | Austria | 3066 | 12.0 | 92.5 | 247 | 10.2 | 7.5 | |
| | Belgium | 2920 | 11.5 | 97.8 | 65 | 2.7 | 2.2 | |
| | Netherlands | 1972 | 7.7 | 94.3 | 119 | 4.9 | 5.7 | |
| | Croatia | 1764 | 6.9 | 96.0 | 74 | 3.1 | 4.0 | |
| | Slovenia | 498 | 2.0 | 95.0 | 26 | 1.1 | 5.0 | |
| | Hungary | 171 | 0.7 | 76.0 | 54 | 2.2 | 24.0 | |
| | Luxembourg | 24 | 0.1 | 100.0 | 0 | 0.0 | 0.0 | |
| Sum of HLA matches | 0 | 271 | 1.3 | 70.9 | 111 | 5.4 | 29.1 | <0.001 |
| | 1 | 1022 | 4.8 | 75.1 | 338 | 16.3 | 24.9 | |
| | 2 | 3130 | 14.7 | 83.1 | 638 | 30.8 | 16.9 | |
| | 3 | 7148 | 33.5 | 92.3 | 596 | 28.8 | 7.7 | |
| | 4 | 5087 | 23.8 | 94.3 | 307 | 14.8 | 5.7 | |
| | 5 | 1308 | 6.1 | 95.1 | 67 | 3.2 | 4.9 | |
| | 6 | 3389 | 15.9 | 99.6 | 13 | 0.6 | 0.4 | |
| | Missing | 4120 | | 92.1 | 351 | | 7.9 | |
| HLA match grouping | favorable | 18365 | 86.0 | 93.3 | 1310 | 63.3 | 6.7 | <0.001 |
| | non-favorable | 2990 | 14.0 | 79.7 | 760 | 36.7 | 20.3 | |
| | Missing | 4120 | | 92.1 | 351 | | 7.9 | |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Dead | No | 19681 | 77.3 | 91.1 | 1923 | 79.4 | 8.9 | 0.016 |
| | Yes | 5794 | 22.7 | 92.1 | 498 | 20.6 | 7.9 | |
| Failure | No | 23417 | 91.9 | 91.4 | 2207 | 91.2 | 8.6 | 0.204 |
| | Yes | 2058 | 8.1 | 90.6 | 214 | 8.8 | 9.4 | |
| DwFG | No | 20109 | 78.9 | 91.1 | 1964 | 81.1 | 8.9 | 0.012 |
| | Yes | 5366 | 21.1 | 92.2 | 457 | 18.9 | 7.8 | |
| PNF | No | 25031 | 98.3 | 91.4 | 2368 | 97.8 | 8.6 | 0.132 |
| | Yes | 444 | 1.7 | 89.3 | 53 | 2.2 | 10.7 | |

**Characteristics of ETKAS transplants**

| | **Standard allocation** | | | **Rescue allocation** | | | |
|---|---|---|---|---|---|---|---|
| | Count (Missing) | Quartiles [range] | Mean ± SD | Count (Missing) | Quartiles [range] | Mean ± SD | p-value |
| Recipient age | 19516 (0) | 52 [43, 59] | 50.2 ± 11.9 | 2257 (0) | 58 [51, 64] | 56.6 ± 10.7 | <0.001 |
| Donor age | 19516 (0) | 50 [41, 58] | 47.6 ± 13.9 | 2257 (0) | 58 [48, 68] | 56.1 ± 17.1 | <0.001 |
| Cold ischemia time [min] | 16319 (3197) | 810 [612, 1020] | 832.5 ± 308 | 2058 (199) | 1002.5 [772.2, 1260] | 1032.3 ± 361.8 | <0.001 |
| Waiting time [days] | 19516 (0) | 1867 [1006, 2793] | 1989.9 ± 1211.5 | 2257 (0) | 1533 [823, 2416] | 1681.6 ± 1020.4 | <0.001 |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Characteristics of ESP transplants**

| | Standard allocation | | | Rescue allocation | | | |
|---|---|---|---|---|---|---|---|
| | Count (Missing) | Quartiles [range] | Mean ± SD | Count (Missing) | Quartiles [range] | Mean ± SD | p-value |
| Recipient age | 5959 (0) | 68 [66, 71] | 68.7 ± 3.4 | 164 (0) | 69 [67, 72] | 69.3 ± 3.3 | 0.007 |
| Donor age | 5959 (0) | 71 [67, 74] | 71.3 ± 4.8 | 164 (0) | 76 [71, 81] | 76.3 ± 6.8 | <0.001 |
| Cold ischemia time [min] | 5369 (590) | 635 [468, 822] | 665.1 ± 259.9 | 145 (19) | 880 [669, 1080] | 897.1 ± 285.3 | <0.001 |
| Waiting time [days] | 5959 (0) | 1258 [809.5,1813] | 1368.5 ± 736.6 | 164 (0) | 815 [528.2, 1409] | 1058.1 ± 726.2 | <0.001 |

ETKAS (Eurotransplant Kidney Allocation System), ESP (Eurotransplant Senior Program), DwFG (death with functioning graft), PNF (primary non-function).

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Table 2:** Comparison of HLA matching between allocation types limited to ETKAS data

| | | **Standard allocation** | | **Rescue allocation** | | |
|---|---|---|---|---|---|---|
| | Value | N | % | N | % | p-value |
| HLA-A matches | 0 | 1904 | 9.8 | 436 | 19.3 | <0.001 |
| | 1 | 9522 | 48.8 | 1188 | 52.6 | |
| | 2 | 8085 | 41.4 | 380 | 16.8 | |
| | Missing | 5 | 0.0 | 253 | 11.2 | |
| | Mean | | 1.3 | | 1.0 | |
| HLA-B matches | 0 | 3540 | 18.1 | 878 | 38.9 | <0.001 |
| | 1 | 10511 | 53.9 | 977 | 43.3 | |
| | 2 | 5460 | 28.0 | 149 | 6.6 | |
| | Missing | 5 | 0.0 | 253 | 11.2 | |
| | Mean | | 1.1 | | 0.6 | |
| HLA-DR matches | 0 | 1635 | 8.4 | 604 | 26.8 | <0.001 |
| | 1 | 10742 | 55.0 | 1100 | 48.7 | |
| | 2 | 7134 | 36.6 | 300 | 13.3 | |
| | Missing | 5 | 0.0 | 253 | 11.2 | |
| | Mean | | 1.3 | | 0.8 | |
| Sum of HLA matches | 0 | 82 | 0.4 | 102 | 4.5 | <0.001 |
| | 1 | 530 | 2.7 | 317 | 14.0 | |
| | 2 | 2625 | 13.5 | 613 | 27.2 | |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | |
|---|---|---|---|---|---|---|
| | 3 | 6757 | 34.6 | 594 | 26.3 | |
| | 4 | 4884 | 25.0 | 304 | 13.5 | |
| | 5 | 1252 | 6.4 | 62 | 2.7 | |
| | 6 | 3381 | 17.3 | 12 | 0.5 | |
| | Missing | 5 | 0.0 | 253 | 11.2 | |
| | Mean | | 3.7 | | 2.5 | |
| HLA match grouping | favorable | 17518 | 89.8 | 1287 | 57.0 | <0.001 |
| | non-favorable | 1993 | 10.2 | 717 | 31.8 | |
| | Missing | 5 | 0.0 | 253 | 11.2 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Table 3:** Univariate analysis of factors regarding survival and competing risk between DwFG (death with functioning graft) and graft loss of ETKAS transplants. For patient survival, Cox proportional hazards models and, for DwFG and graft loss, the Fine Gray proportional regression models were used. P-values show the significance of hazard ratios in the case of survival and of subdistributional hazard ratios in the case of DwFG and graft loss for pairwise comparisons of values (dotted line: p<0.05, dashed line: p<0.01, solid line: p<0.001)

| Univariate outcome analysis | | Availability survival | | Survival estimate | | | | Availability DwFG/graft loss | | Cumulative incidence of DwFG | | | | Cumulative incidence of graft loss | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Pat. | Compl. | 1y | 5y | 10y | p-value. | Pat. | Compl. | 1y | 5y | 10y | p-value. | 1y | 5y | 10y | p-value. |
| | | N | % | N | % | % ± SE | % ± SE | % ± SE | | N | % | % ± SE | % ± SE | % ± SE | | % ± SE | % ± SE | % ± SE | |
| Allocation type | | | | | | | | | | | | | | | | | |
| | Standard | 23688 | 90.3 | 19516 | 82.4 | 96.3 ± 0.1 | 86.9 ± 0.3 | 72.0 ± 0.5 | ┆ | 19181 | 81.0 | 3.7 ± 0.1 | 12.5 ± 0.3 | 25.7 ± 0.5 | ┆ | 1.4 ± 0.1 | 5.1 ± 0.2 | 12.0 ± 0.4 | |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rescue | 2553 | 9.7 | 2257 | 88.4 | 95.1 ± 0.5 | 80.6 ± 1.0 | 62.3 ± 1.9 | 2209 | 86.5 | 4.8 ± 0.5 | 18.3 ± 1.0 | 34.7 ± 1.8 | 2.0 ± 0.3 | 7.6 ± 0.7 | 12.7 ± 1.1 | |
| Donor sex | | | | | | | | | | | | | | | | | |
| | Female | 11797 | 45.0 | 9867 | 83.6 | 95.9 ± 0.2 | 85.9 ± 0.4 | 70.1 ± 0.7 | 9670 | 82.0 | 4.1 ± 0.2 | 13.4 ± 0.4 | 27.4 ± 0.7 | 1.6 ± 0.1 | 5.6 ± 0.3 | 12.9 ± 0.5 | |
| | Male | 14444 | 55.0 | 11906 | 82.4 | 96.4 ± 0.2 | 86.6 ± 0.4 | 72.1 ± 0.7 | 11720 | 81.1 | 3.5 ± 0.2 | 12.8 ± 0.4 | 25.6 ± 0.6 | 1.4 ± 0.1 | 5.1 ± 0.2 | 11.5 ± 0.5 | |
| Recipient sex | | | | | | | | | | | | | | | | | |
| | Female | 9933 | 37.9 | 8199 | 82.5 | 96.3 ± 0.2 | 87.6 ± 0.4 | 72.9 ± 0.8 | 8042 | 81.0 | 3.6 ± 0.2 | 11.6 ± 0.4 | 24.5 ± 0.7 | 1.4 ± 0.1 | 5.6 ± 0.3 | 12.9 ± 0.6 | |
| | Male | 16308 | 62.1 | 13574 | 83.2 | 96.1 ± 0.2 | 85.5 ± 0.4 | 70.1 ± 0.6 | 13348 | 81.8 | 3.9 ± 0.2 | 14.0 ± 0.3 | 27.7 ± 0.6 | 1.5 ± 0.1 | 5.2 ± 0.2 | 11.6 ± 0.4 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Organ | | | | | | | | | | | | | | | | | | | |
| | Left kidney | 12556 | 47.8 | 10380 | 82.7 | 96.3 ± 0.2 | 86.6 ± 0.4 | 71.7 ± 0.7 | | 10209 | 81.3 | 3.7 ± 0.2 | 12.9 ± 0.4 | 25.8 ± 0.7 | | 1.5 ± 0.1 | 5.3 ± 0.3 | 12.2 ± 0.5 | |
| | Right kidney | 13685 | 52.2 | 11393 | 83.3 | 96.1 ± 0.2 | 86.1 ± 0.4 | 70.7 ± 0.7 | | 11181 | 81.7 | 3.9 ± 0.2 | 13.2 ± 0.4 | 27.0 ± 0.7 | | 1.5 ± 0.1 | 5.3 ± 0.2 | 12.1 ± 0.5 | |
| Disease group | | | | | | | | | | | | | | | | | | | |
| | Glomerulo-nephritis | 6160 | 23.5 | 5175 | 84.0 | 96.7 ± 0.3 | 87.8 ± 0.5 | 74.4 ± 1.0 | | 5073 | 82.4 | 3.3 ± 0.3 | 11.4 ± 0.5 | 23.1 ± 0.9 | | 1.5 ± 0.2 | 6.0 ± 0.4 | 13.7 ± 0.8 | |
| | Cystic disease | 3741 | 14.3 | 3060 | 81.8 | 97.1 ± 0.3 | 89.8 ± 0.6 | 76.0 ± 1.2 | | 3012 | 80.5 | 2.9 ± 0.3 | 9.8 ± 0.6 | 22.6 ± 1.2 | | 1.5 ± 0.2 | 4.2 ± 0.4 | 10.0 ± 0.9 | |
| | Diabetes | 1836 | 7.0 | 1530 | 83.3 | 92.2 ± 0.7 | 70.3 ± 1.4 | 40.6 ± 2.3 | | 1501 | 81.8 | 7.8 ± 0.7 | 28.6 ± 1.4 | 56.6 ± 2.3 | | 1.4 ± 0.3 | 2.9 ± 0.5 | 4.5 ± 0.8 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Other | 14504 | 55.3 | 12008 | 82.8 | 96.3 ± 0.2 | 86.7 ± 0.4 | 72.1 ± 0.7 | | 11804 | 81.4 | 3.7 ± 0.2 | 12.7 ± 0.4 | 25.4 ± 0.6 | | 1.5 ± 0.1 | 5.6 ± 0.2 | 12.9 ± 0.5 | |
| Favourability | | | | | | | | | | | | | | | | | | | |
| | favorable | 22734 | 86.6 | 18805 | 82.7 | 96.4 ± 0.1 | 87.0 ± 0.3 | 72.1 ± 0.5 | | 18488 | 81.3 | 3.6 ± 0.1 | 12.4 ± 0.3 | 25.6 ± 0.5 | | 1.4 ± 0.1 | 5.0 ± 0.2 | 11.7 ± 0.4 | |
| | non-favorable | 3220 | 12.3 | 2710 | 84.2 | 95.7 ± 0.4 | 83.2 ± 0.8 | 66.9 ± 1.5 | | 2648 | 82.2 | 4.3 ± 0.4 | 15.9 ± 0.8 | 30.3 ± 1.5 | | 2.3 ± 0.3 | 7.3 ± 0.6 | 15.8 ± 1.2 | |
| | Missing | 287 | 1.1 | 258 | 89.9 | 89.2 ± 2.0 | 61.5 ± 3.8 | 42.2 ± 6.5 | | 254 | 88.5 | 11.0 ± 2.0 | 37.4 ± 3.8 | 53.3 ± 6.2 | | 0.8 ± 0.6 | 4.3 ± 1.6 | 7.8 ± 2.5 | |
| Transplantation period | 2006-2009 | 9188 | 35.0 | 8261 | 89.9 | 95.8 ± 0.2 | 86.8 ± 0.4 | 72.4 ± 0.6 | | 8120 | 88.4 | 4.2 ± 0.2 | 12.5 ± 0.4 | 25.5 ± 0.6 | | 1.4 ± 0.1 | 4.9 ± 0.3 | 10.8 ± 0.4 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2010-2013 | 8174 | 31.1 | 7354 | 90.0 | 96.4 ± 0.2 | 87.3 ± 0.4 | 69.4 ± 1.5 | | 7222 | 88.4 | 3.6 ± 0.2 | 12.2 ± 0.4 | 28.1 ± 1.4 | | 1.3 ± 0.1 | 4.6 ± 0.3 | 15.9 ± 1.3 |
| | 2014-2018 | 8879 | 33.8 | 6158 | 69.4 | 96.5 ± 0.2 | 80.3 ± 1.0 | | | 6048 | 68.1 | 3.5 ± 0.2 | 18.9 ± 1.0 | | | 1.8 ± 0.2 | 8.9 ± 0.7 | |
| Transplant count | 1 | 24185 | 92.2 | 20001 | 82.7 | 96.3 ± 0.1 | 86.6 ± 0.3 | 71.6 ± 0.5 | | 19649 | 81.2 | 3.7 ± 0.1 | 12.8 ± 0.3 | 26.1 ± 0.5 | | 1.5 ± 0.1 | 5.1 ± 0.2 | 11.7 ± 0.4 |
| | 2 | 1919 | 7.3 | 1654 | 86.2 | 95.4 ± 0.5 | 83.2 ± 1.1 | 66.3 ± 2.0 | | 1627 | 84.8 | 4.7 ± 0.5 | 16.4 ± 1.1 | 31.1 ± 1.9 | | 1.4 ± 0.3 | 8.0 ± 0.8 | 16.7 ± 1.5 |
| | ≥3 | 137 | 0.5 | 118 | 86.1 | 96.3 ± 1.8 | 83.3 ± 4.0 | 68.1 ± 7.4 | | 114 | 83.2 | 2.9 ± 1.6 | 15.2 ± 4.0 | 28.6 ± 7.2 | | 1.0 ± 1.0 | 5.9 ± 2.6 | 26.0 ± 8.4 |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Waiting-time | | | | | | | | | | | | | | | | | | |
| | 0-11 months | 1205 | 4.6 | 1034 | 85.8 | 98.1 ± 0.4 | 89.9 ± 1.1 | 77.1 ± 2.1 | | 1014 | 84.1 | 1.9 ± 0.4 | 9.7 ± 1.1 | 20.6 ± 2.0 | | 1.4 ± 0.4 | 7.0 ± 0.9 | 13.1 ± 1.6 |
| | 12-23 months | 2908 | 11.1 | 2440 | 83.9 | 98.0 ± 0.3 | 88.6 ± 0.7 | 70.7 ± 1.6 | | 2412 | 82.9 | 2.0 ± 0.3 | 10.7 ± 0.7 | 26.5 ± 1.5 | | 1.4 ± 0.2 | 5.0 ± 0.5 | 10.1 ± 0.9 |
| | ≥24 months | 22128 | 84.3 | 18299 | 82.7 | 95.9 ± 0.2 | 85.8 ± 0.3 | 70.9 ± 0.5 | | 17964 | 81.2 | 4.1 ± 0.2 | 13.6 ± 0.3 | 26.8 ± 0.5 | | 1.5 ± 0.1 | 5.3 ± 0.2 | 12.3 ± 0.4 |
| Age period | | | | | | | | | | | | | | | | | | |
| | 16-55 years | 15779 | 60.1 | 13077 | 82.9 | 97.7 ± 0.1 | 91.3 ± 0.3 | 81.8 ± 0.5 | | 12831 | 81.3 | 2.3 ± 0.1 | 8.3 ± 0.3 | 15.8 ± 0.5 | | 1.7 ± 0.1 | 6.5 ± 0.2 | 16.0 ± 0.5 |
| | 56-64 years | 8002 | 30.5 | 6650 | 83.1 | 94.8 ± 0.3 | 81.5 ± 0.6 | 58.0 ± 1.1 | | 6539 | 81.7 | 5.2 ± 0.3 | 17.7 ± 0.5 | 39.5 ± 1.0 | | 1.2 ± 0.1 | 3.7 ± 0.3 | 6.4 ± 0.4 |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ≥65 years | 2460 | 9.4 | 2046 | 83.2 | 91.5 ± 0.6 | 68.7 ± 1.2 | 37.2 ± 2.0 | | 2020 | 82.1 | 8.5 ± 0.6 | 30.0 ± 1.2 | 60.7 ± 2.0 | | 1.1 ± 0.2 | 2.7 ± 0.4 | 3.1 ± 0.5 | |
| Age period donor | 0-15 years | 529 | 2.0 | 496 | 93.8 | 97.1 ± 0.8 | 89.9 ± 1.5 | 81.5 ± 2.3 | | 489 | 92.4 | 2.8 ± 0.8 | 8.9 ± 1.4 | 16.7 ± 2.2 | | 1.3 ± 0.5 | 3.8 ± 1.0 | 9.2 ± 1.9 | |
| | 16-55 years | 16681 | 63.6 | 13737 | 82.4 | 96.9 ± 0.2 | 88.0 ± 0.3 | 73.3 ± 0.6 | | 13547 | 81.2 | 3.0 ± 0.2 | 11.5 ± 0.3 | 24.7 ± 0.6 | | 1.1 ± 0.1 | 4.6 ± 0.2 | 10.8 ± 0.4 | |
| | 56-64 years | 7296 | 27.8 | 6051 | 82.9 | 95.2 ± 0.3 | 84.1 ± 0.5 | 68.2 ± 1.0 | | 5912 | 81.0 | 4.9 ± 0.3 | 15.4 ± 0.5 | 29.0 ± 0.9 | | 1.9 ± 0.2 | 6.3 ± 0.4 | 15.0 ± 0.7 | |
| | ≥65 years | 1735 | 6.6 | 1489 | 85.8 | 93.2 ± 0.7 | 77.1 ± 1.3 | 57.2 ± 2.3 | | 1442 | 83.1 | 6.7 ± 0.7 | 20.9 ± 1.3 | 38.0 ± 2.2 | | 2.8 ± 0.5 | 9.5 ± 1.0 | 14.3 ± 1.3 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cold ischemia period | <10h | 4540 | 17.3 | 3975 | 87.6 | 96.6 ± 0.3 | 87.9 ± 0.6 | 74.6 ± 1.2 | | 3916 | 86.3 | 3.4 ± 0.3 | 11.4 ± 0.6 | 22.6 ± 1.1 | | 1.0 ± 0.2 | 3.9 ± 0.4 | 11.2 ± 0.9 | |
| | 10-18h | 11338 | 43.2 | 10296 | 90.8 | 96.4 ± 0.2 | 86.9 ± 0.4 | 71.8 ± 0.7 | | 10124 | 89.3 | 3.6 ± 0.2 | 12.8 ± 0.4 | 26.1 ± 0.7 | | 1.4 ± 0.1 | 4.8 ± 0.2 | 11.2 ± 0.5 | |
| | ≥18h | 4398 | 16.8 | 4106 | 93.4 | 96.0 ± 0.3 | 85.5 ± 0.6 | 69.3 ± 1.1 | | 4036 | 91.8 | 4.0 ± 0.3 | 13.7 ± 0.6 | 28.5 ± 1.0 | | 1.7 ± 0.2 | 5.7 ± 0.4 | 11.1 ± 0.7 | |
| | Missing | 5965 | 22.7 | 3396 | 56.9 | 95.4 ± 0.4 | 83.3 ± 0.8 | 67.8 ± 1.5 | | 3314 | 55.6 | 4.6 ± 0.4 | 15.5 ± 0.8 | 28.8 ± 1.4 | | 1.8 ± 0.2 | 8.4 ± 0.6 | 19.1 ± 1.2 | |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Table 4:** Univariate analysis of continuous variables regarding survival and competing risks between DwFG and graft loss for ETKAS patients **(A)** and multivariate analysis restricted to ETKAS **(B)** and ESP **(C)**. HR: Hazard ratio; subdist. HR: subdistribution hazard ratio; Concerning the categorical confounders of the multivariate analysis, the reported HRs and subdist. HRs refer to the second characteristic as compared to the characteristic named first.

| **A. Univariate analyses of variables in ETKAS data** | | | | | | |
|---|---|---|---|---|---|---|
| | **Mortality** | | **DwFG** | | **Graft loss** | |
| | Hazard ratio (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value |
| Donor age [years] | 1.02 (1.01 - 1.02) | <0.001 | 1.01 (1.01 - 1.02) | <0.001 | 1.02 (1.01 - 1.02) | <0.001 |
| Recipient age [years] | 1.07 (1.06 - 1.07) | <0.001 | 1.06 (1.06 - 1.07) | <0.001 | 0.96 (0.96 - 0.97) | <0.001 |
| Cold ischemia time [hours] | 1.01 (1.00 - 1.02) | 0.001 | 1.02 (1.01 - 1.03) | <0.001 | 1.02 (1.01 - 1.03) | 0.001 |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | |
|---|---|---|---|---|---|---|
| Waiting-time [years] | | 1.02 (1.01 - 1.03) | <0.001 | 1.01 (1.00 - 1.03) | 0.024 | 0.98 (0.96 - 1.00) | 0.024 |
| **B. Multivariate analysis ETKAS** | | | | | | | |
| | | **Mortality** | | **DwFG** | | **Graft loss** | |
| | | Hazard ratio (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value |
| Allocation type | standard vs. rescue | 0.89 (0.78 - 1.02) | 0.090 | 0.70 (0.60 - 0.81) | <0.001 | 0.98 (0.77 - 1.25) | 0.885 |
| Recipient sex | female vs. male | 1.10 (1.02 - 1.19) | 0.015 | 1.10 (1.00 - 1.21) | 0.039 | 0.83 (0.72 - 0.95) | 0.009 |
| HLA-match | favorable vs. non-favorable | 1.15 (1.03 - 1.29) | 0.011 | 1.18 (1.03 - 1.34) | 0.014 | 1.33 (1.09 - 1.62) | 0.005 |
| Donor age | (continuous) | 1.01 (1.01 - 1.01) | <0.001 | 1.00 (1.00 - 1.01) | 0.003 | 1.03 (1.02 - 1.03) | <0.001 |
| Recipient age | (continuous) | 1.06 (1.06 - 1.07) | <0.001 | 1.07 (1.06 - 1.07) | <0.001 | 0.95 (0.95 - 0.96) | <0.001 |
| Cold ischemia | (continuous) | 1.01 (1.00 - 1.02) | 0.017 | 1.02 (1.01 - 1.03) | <0.001 | 1.02 (1.01 - 1.03) | 0.004 |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| time [hours] | | | | | | | |
| Waiting time [years] | (continuous) | 1.06 (1.05 - 1.07) | <0.001 | 1.05 (1.03 - 1.06) | <0.001 | 0.98 (0.96 - 1.00) | 0.063 |
| Diabetes | non-diabetic vs. diabetic | 1.97 (1.76 - 2.20) | <0.001 | 1.77 (1.55 - 2.02) | <0.001 | 0.60 (0.40 - 0.91) | 0.017 |
| Transplant count | 1 vs. ≥ 2 | 1.56 (1.38 - 1.77) | <0.001 | 1.39 (1.19 - 1.61) | <0.001 | 1.32 (1.06 - 1.65) | 0.014 |

**C. Multivariate analysis ESP**

| | | **Mortality** | | **DwFG** | | **Graft loss** | |
|---|---|---|---|---|---|---|---|
| | | Hazard ratio (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value | Subdist. HR (95% Conf. int.) | p-value |
| Allocation type | standard vs. rescue | 0.61 (0.37 - 1.01) | 0.056 | 0.72 (0.41 - 1.26) | 0.246 | 0.30 (0.04 - 2.48) | 0.260 |
| Recipient sex | female vs. male | 1.27 (1.06 - 1.52) | 0.009 | 1.24 (1.01 - 1.52) | 0.036 | 1.28 (0.57 - 2.86) | 0.545 |
| HLA-match | favorable vs. non-favorable | 1.08 (0.92 - 1.26) | 0.343 | 1.09 (0.91 - 1.30) | 0.362 | 0.64 (0.35 - 1.19) | 0.160 |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Donor age | (continuous) | 1.01 (0.99 - 1.02) | 0.418 | 0.99 (0.97 - 1.01) | 0.457 | 1.09 (1.04 - 1.14) | <0.001 |
| Recipient age | (continuous) | 1.06 (1.04 - 1.09) | <0.001 | 1.08 (1.05 - 1.10) | <0.001 | 0.92 (0.84 - 1.02) | 0.126 |
| Cold ischemia time [hours] | (continuous) | 1.02 (1.00 - 1.04) | 0.070 | 1.02 (1.00 - 1.04) | 0.091 | 1.04 (0.98 - 1.10) | 0.217 |
| Waiting time [years] | (continuous) | 1.07 (1.03 - 1.12) | <0.001 | 1.08 (1.03 - 1.13) | <0.001 | 0.95 (0.80 - 1.12) | 0.512 |
| Diabetes | non-diabetic vs. diabetic | 1.66 (1.35 - 2.03) | <0.001 | 1.49 (1.18 - 1.87) | <0.001 | 1.46 (0.69 - 3.10) | 0.322 |
| Transplant count | 1 vs. ≥ 2 | 1.18 (0.87 - 1.59) | 0.284 | 1.30 (0.93 - 1.80) | 0.123 | 0.42 (0.12 - 1.49) | 0.179 |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Table 5:** The cumulative hazard function for survival predicted by the Cox proportional hazards model and the cumulative incidence predictions [33] for DwFG and graft loss from the competing risk model in percent for the timepoint of 5 years. For the other covariates we assumed the following values: female recipient, favorable match, recipient age of 55, waiting time of 5 years, non-diabetic, and first transplant. The models are equivalent to the ones in Table 4 but based on data from both ETKAS and ESP.

| | | **Survival** | | | | | **DwFG** | | | | | **Graft loss** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **CIT [hours]:** | 5 | 10 | 15 | 20 | 25 | 5 | 10 | 15 | 20 | 25 | 5 | 10 | 15 | 20 | 25 |
| **Allocation** | **Donor age [years]:** | | | | | | | | | | | | | | | |
| **Standard** | 10 | 7.6 | 8.0 | 8.4 | 8.8 | 9.2 | 7.4 | 8.2 | 9.1 | 10.0 | 11.1 | 1.0 | 1.1 | 1.2 | 1.3 | 1.4 |
| | 20 | 8.3 | 8.7 | 9.2 | 9.6 | 10.1 | 7.8 | 8.6 | 9.5 | 10.6 | 11.7 | 1.3 | 1.4 | 1.5 | 1.7 | 1.8 |
| | 30 | 9.1 | 9.5 | 10.0 | 10.5 | 11.0 | 8.2 | 9.1 | 10.0 | 11.1 | 12.3 | 1.6 | 1.8 | 2.0 | 2.2 | 2.4 |
| | 40 | 9.9 | 10.4 | 10.9 | 11.5 | 12.0 | 8.6 | 9.5 | 10.6 | 11.7 | 12.9 | 2.1 | 2.3 | 2.6 | 2.8 | 3.1 |
| | 50 | 10.9 | 11.4 | 11.9 | 12.5 | 13.1 | 9.1 | 10.0 | 11.1 | 12.3 | 13.5 | 2.8 | 3.0 | 3.3 | 3.7 | 4.0 |



ACCEPTED

Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 60 | 11.9 | 12.4 | 13.0 | 13.7 | 14.3 | 9.5 | 10.6 | 11.7 | 12.9 | 14.2 | 3.6 | 4.0 | 4.3 | 4.8 | 5.2 |
| | 70 | 13.0 | 13.6 | 14.2 | 14.9 | 15.7 | 10.0 | 11.1 | 12.3 | 13.5 | 14.9 | 4.7 | 5.1 | 5.6 | 6.2 | 6.8 |
| | 80 | 14.1 | 14.8 | 15.6 | 16.3 | 17.1 | 10.5 | 11.7 | 12.9 | 14.2 | 15.7 | 6.0 | 6.6 | 7.3 | 8.0 | 8.7 |
| **Rescue** | 10 | 6.7 | 7.0 | 7.4 | 7.7 | 8.1 | 5.1 | 5.7 | 6.3 | 7.0 | 7.7 | 1.0 | 1.1 | 1.2 | 1.3 | 1.4 |
| | 20 | 7.3 | 7.7 | 8.1 | 8.4 | 8.9 | 5.4 | 6.0 | 6.6 | 7.3 | 8.1 | 1.3 | 1.4 | 1.5 | 1.7 | 1.8 |
| | 30 | 8.0 | 8.4 | 8.8 | 9.2 | 9.7 | 5.7 | 6.3 | 7.0 | 7.7 | 8.6 | 1.6 | 1.8 | 2.0 | 2.2 | 2.4 |
| | 40 | 8.7 | 9.2 | 9.6 | 10.1 | 10.6 | 6.0 | 6.6 | 7.3 | 8.1 | 9.0 | 2.1 | 2.3 | 2.6 | 2.8 | 3.1 |
| | 50 | 9.5 | 10.0 | 10.5 | 11.0 | 11.5 | 6.3 | 7.0 | 7.7 | 8.6 | 9.5 | 2.8 | 3.0 | 3.3 | 3.7 | 4.0 |
| | 60 | 10.4 | 10.9 | 11.5 | 12.0 | 12.6 | 6.6 | 7.3 | 8.1 | 9.0 | 10.0 | 3.6 | 3.9 | 4.3 | 4.8 | 5.2 |
| | 70 | 11.4 | 11.9 | 12.5 | 13.1 | 13.8 | 7.0 | 7.7 | 8.6 | 9.5 | 10.5 | 4.6 | 5.1 | 5.6 | 6.1 | 6.7 |
| | 80 | 12.4 | 13.0 | 13.7 | 14.3 | 15.0 | 7.3 | 8.1 | 9.0 | 10.0 | 11.0 | 6.0 | 6.6 | 7.2 | 7.9 | 8.7 |

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Figure 1:**

Flowchart of selection process of transplants analyzed in this study

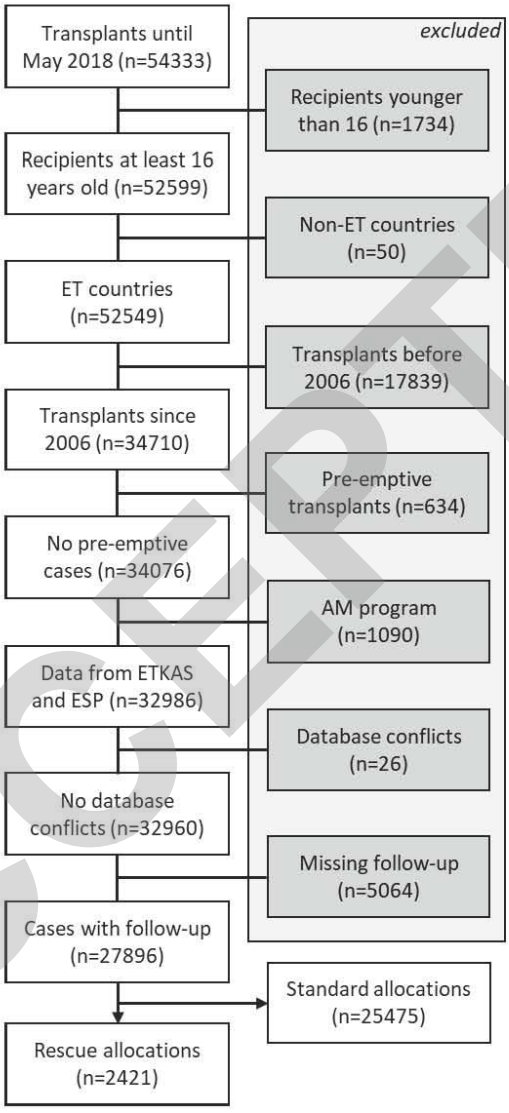


**Figure 1:** Flowchart of selection process of transplants analyzed in this study.

Counts refer to number of transplants. ETKAS: Eurotransplant Kidney Allocation System; ESP: Eurotransplant Senior Program; AM: Acceptable Mismatch Program.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Figure 2:**

Recipient age and transplant numbers for SA and RA

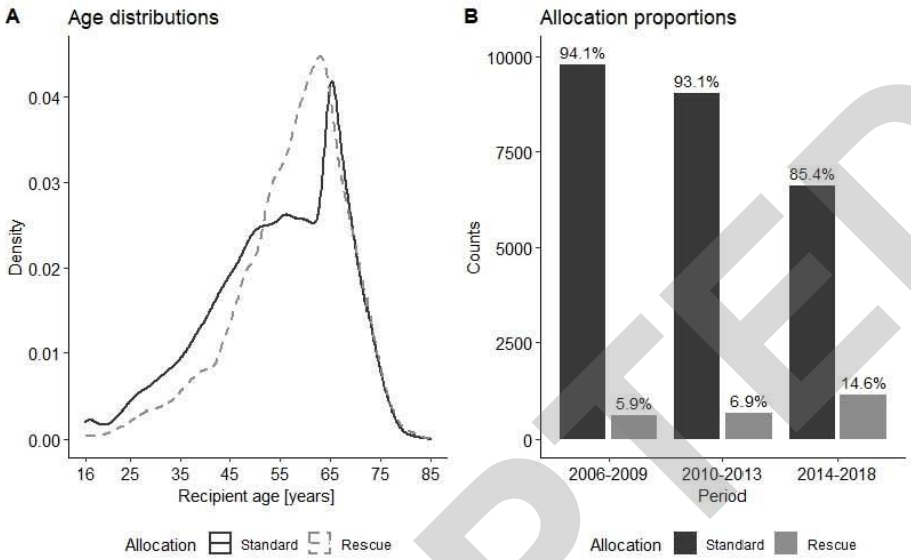


**Figure 2: (A)** Recipient age and **(B)** number of transplants between 2006 and 2018 with respect to allocation type. Percentages show the fraction of the respective period.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited

**Figure 3:**

Cumulative incidence curves of kidney transplantation outcome after RA vs. SA

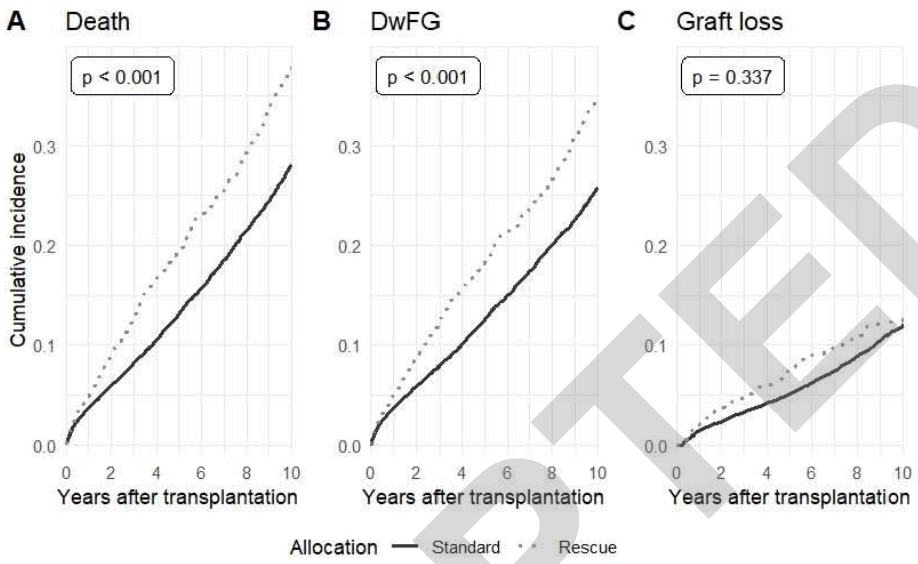


**Figure 3:** Cumulative incidence curves for ETKAS patients with respect to death (A), death with functioning graft (B), and graft loss (C) according to allocation.

ACCEPTED



Copyright © 2021 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited