

ORIGINAL ARTICLE

Outcome of kidney transplantation from very senior donors in Switzerland – a national cohort study

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SUMMARY

Kidney transplantation from older and marginal donors is effective to confront organ shortage. However, limitations after transplantation of kidneys from very marginal kidney donors remain unclear. We compared patient and graft outcome, achieved allograft function and quality of life of renal transplantations from Very Senior Donors (VSD, defined as donors aged 70 years and older) with Senior Donors (SD, aged 60–70 years) and Regular Donors (RD, aged younger than 60 years) in Switzerland. We evaluated the outcome of 1554 adult recipients of deceased donor kidney transplantations from 05/2008 to 12/2019; median follow-up was 4.7 years. Failure-free survival (freedom from graft loss or death), glomerular filtration rate (eGFR), and quality of life at 12 months were analyzed for RD (reference group, $n = 940$), SD ($n = 404$), and VSD ($n = 210$). Failure-free survival decreased with increasing donor age, mainly attributable to premature graft loss. Still, overall 5-year failure-free survival reached 83.1%, 81.0%, and 64.0% in the RD, SD, and VSD subgroups, respectively. eGFR 12 months post-transplantation was significantly higher in RD compared with SD and VSD. The acceptance rate of donor candidates for kidney TPL was 78% for the entire cohort (87% for RD, 79% for SD, and 56% for VSD). Deceased donor kidney transplantation from donors aged 70 years or older is associated with an inferior, yet acceptable failure-free outcome, with sustained quality of life.

Transplant International 2021; 34: 689–699

Key words

deceased donor transplantation, kidney transplantation, marginal donor

Received: 20 November 2020; Revision requested: 18 December 2020; Accepted: 29 January 2021; Published online: 5 March 2021

Introduction

Kidney transplantation (TPL) is an effective treatment for advanced and dialysis-dependent kidney insufficiency and provides a better quality of life (QoL) compared with long-term dialysis [1,2]. Various donor-derived factors are associated with graft survival after deceased donor TPL, such as increased age, impaired kidney function or acute kidney injury, history of hypertension, diabetes mellitus, and cerebrovascular event as the cause of death [3,4].

Discrepancies between patients on the waiting list and the number and quality of available donor organs have led to strategies to extend the donor pool, e.g., living donor TPL, ABO-incompatible TPL, donation after cardiac death (DCD), and expanding age limitation for deceased kidney donors [5,6]. There is convincing evidence that transplanting allografts of marginal donors (generally defined as donors older than 60 years or 50–60 years with comorbidities) are superior to maintaining dialysis in terms of a survival benefit [7,8]. However, only little research has been performed on very old kidney donors, e.g., 70 years of age or more.

Previous studies have shown a high risk of graft loss and patient death in TPLs from septua- and octogenarian donors, especially if transplanted into recipients of 60 years or younger [9]. Meanwhile, recent publications support TPLs of older and marginal donor organs to selected recipients, since five-year TPL outcome is acceptable and accompanied by limited morbidity and good QoL in the majority of recipients [10–12]. Furthermore, such organs show a survival benefit for elderly recipients when compared with remaining on dialysis [13]. Recently, Ruggenenti *et al.* [14] published a small multicenter cohort study on kidney donors aged 80 years or older. Depending on histopathological findings in preimplantation biopsies, recipients received single or dual kidney TPLs. Short-term outcome with median follow-up of two years was good and comparable to a matched cohort of recipients receiving organs from donors aged 60 years and younger.

These findings support the notion that deceased-donor kidney TPL from septua- and octogenarian donors is feasible after thorough selection of suitable donors and recipients. Indeed, various allograft-survival risk calculators have been created in an effort to improve upon the dichotomy of standard criteria donors versus extended criteria donors and allowing for prediction of short- and long-term outcomes. For example, the Kidney Donor Profile Index (KDPI) summarizes various donor-derived factors onto a

cumulative percentage scale, predicting the allograft outcome for all kidneys recovered in the US during the previous year [15]. However, donor age is a leading determinant for KDPI ranking, and donors aged 70 years and older are all within the highest quartile of the KDPI, which makes this tool virtually inapplicable for VSD. Furthermore, KDPI is calculated from the UNOS (United Network for Organ Sharing) cohort which prioritizes particularities specific to the US donors and therefore cannot be adapted to other countries without critical appraisal [16]. Meanwhile, KDPI scores have been validated for European cohorts, although it is still questionable if its predictive value is equivalent to the US recipients [17,18].

To date, outcome of TPL from septua- and octogenarian kidney donors is unclear although such candidates could provide a valuable source of deceased donor organs and help coping with organ scarcity. In this study, we employed data from the Swiss Transplant Cohort Study [19] (STCS, www.stcs.ch) to compare patient and allograft survival, estimated glomerular filtration rate (eGFR), and QoL of deceased donor kidney TPL from donors older than 70 years compared with donors aged 60 years and younger.

Materials and methods

Description of the cohort

The STCS prospectively enrolls all solid organ TPLs at all six Swiss TPL centers since May 2008. Data are collected at time of TPL, at 6 and 12 months and yearly thereafter, and comprise medical data as well as self-reported questionnaires exploring psychosocial and behavioral factors, including a self-assessment of health-related QoL. The study was approved by Swisstransplant and the Medical Ethics Committee of the study centers were involved, and informed consent was obtained from all the participants at enrollment in the study.

Parameters analyzed

Recipient characteristics and outcome were collected from the STCS database; donor-derived factors were retrieved from the SOAS database (Swiss Organ Allocating System). Baseline values: Recipient age, sex, BMI at time of TPL, history of kidney TPL, dialysis status and time, cold ischemia time, serum creatinine and eGFR, as well as QoL, were extracted from the STCS database. From the SOAS database, donor age, sex, further values to calculate KDPI, and cause of donor death were

extracted. From here, we also extracted data regarding nonutilized organs and organ conversion rate. Study outcomes: Recipient death and graft outcomes. We estimated renal allograft function at 12 months by using the CKD-EPI formula [20]. In case of graft failure without patient's death within 12 months post-TPL, the eGFR was set to 0 ml/min/1.73 m². We further determined QoL using the EuroQuol (EQ-5D) questionnaires for self-assessment of health-related QoL [19]. The SOAS identifier (ST-code) served as unique identifier to merge data from the two sources on the recipient level. Donor age was considered in two ways: once as a continuous variable transformed via restricted cubic spline transformation with knots placed at the 5th, 25th, 50th, 75th, and 95th percentiles of donor age [21], and also categorically grouped into Regular Donors (RD, age <60 years), Senior Donors (SD, 60–70 years), and Very Senior Donors (VSD, >70 years). KDPI was calculated according to the guide to calculating and interpreting KDPI [22].

Statistical analysis

Baseline recipient and donor characteristics were presented by donor age group. The TPL activity with allografts from the different donor groups was illustrated from 2008 to 2019. Average age of recipient and donor were presented over calendar time with cubic splines. Patient and graft survival was assessed as the time from TPL until patient death, allograft failure, or censoring. The relationship between donor age and survival was assessed with a Cox proportional hazard model with donor age as a continuous variable transformed with restricted cubic splines. Kaplan–Meier curves were used to compare failure-free survival between each donor age group. In order to investigate the etiology of the relationship between donor age and patient survival, cause-specific Cox proportional hazard models were fit for allograft failure and death, correcting for known predictors and taking into account that two recipients may have a renal allograft from the same donor by inclusion of donor identification as a cluster term in our models. Cumulative incidence curves for allograft failure and death were calculated for each donor age group using the cumulative incidence function (CIF) approach for competing risks [23]. Allograft function at 12 months was compared across donor ages with cubic splines and violin plots. The R version 3.6.1 was used for statistical analysis and visualization [24], R packages from the

“Tidyverse” were used for data manipulation [25] and R package “Survival” was used for time-to-event analyses [26].

Results

Baseline characteristics of recipients and donors in transplantations from regular donors, senior donors, and very senior donors

For the study population, we evaluated 3594 patients who received kidney TPLs and were thus enrolled in the STCS between May 1, 2008, and December 31, 2019. From this cohort, we excluded patients who met at least one of the following criteria: recipients with functioning graft but less than 90 days of follow-up, aged less than 18 years at time of TPL, with living donor or multi-organ TPL, with declined or withdrawn informed consent or with re-TPL (Fig. S1). To compare eGFR and QoL at 12 months, only patients who reached this study visit were included. Finally, 1554 adult recipients of deceased donor kidney TPLs from 983 donors remained for the analysis. Median follow-up for the final study population was 4.7 years (max: 12.1 years).

We compared donor and recipient characteristics at baseline between the three groups (Table 1). Recipients of VSD organs were older (65 years) than recipients from SD (58 years) and RD (55 years). Preemptive TPL was rare, and median time on dialysis was 3.8 years and comparable among all groups. Meanwhile, donors providing VSD organs had a higher incidence of cerebrovascular death [43.6% (RD), 68.2% (SD), and 74.4% (VSD)]. Median cold ischemia time was short for all groups investigated and below 12 h in 1139/1554 cases (73.3%). Overall, RD represented the majority of kidney donors with 62% of the entire donor cohort, while SD and VSD comprised 24% and 14%, respectively (Fig. 1a). Median age for donors and recipients at time of TPL increased throughout the observation period (Fig. 1b).

Donor age is an important determinant for KDPI calculation. KDPI was significantly distinct among the three donor categories investigated in our cohort, with a median KDPI of 40%, 82%, and 96% for RD, SD, and VSD organs, respectively (Fig. 1c–e). KDPI values of 95% or above were found in 0.3%, 6.2%, and 58.5% of TPLs involving RD, SD, and VSD, respectively. Median KDPI remained stable for the respective groups during the observational period from 2008–2019.

Table 1. Recipient and donor baseline values.

Recipients	All donors N = 1554	RD (donor <60 years) N = 940	SD (donor 60–70 years) N = 404	VSD (donor >70 years) N = 210
Age, median [IQR]	57.00 [48.00, 65.00]	55.00 [44.00, 63.00]	58.00 [51.00, 65.00]	65.00 [59.00, 69.00]
Sex = male, n (%)	981 (63.1)	588 (62.6)	253 (62.6)	140 (66.7)
BMI, median [IQR]	25.80 [22.70, 29.20]	25.70 [22.60, 29.30]	25.80 [22.80, 28.70]	26.40 [23.40, 29.30]
Earlier TPL, n (%)	256 (16.5)	179 (19.0)	61 (15.1)	16 (7.6)
Dialysis, n (%)	1482 (95.4)	899 (95.6)	385 (95.3)	198 (94.3)
Dialysis time, median [IQR]	3.78 [2.40, 5.64]	3.87 [2.41, 5.93]	3.79 [2.41, 5.49]	3.46 [2.22, 5.00]
Cold ischemia time, median [IQR]	9.23 [7.15, 12.16]	9.25 [7.03, 12.49]	9.31 [7.38, 11.78]	8.76 [7.10, 11.86]

Donors	All donors N = 983	RD (donor <60 years) N = 617	SD (donor 60–70 years) N = 233	VSD (donor >70 years) N = 133
Age, median [IQR]	54.50 [41.40, 64.80]	46.40 [32.00, 53.30]	64.70 [62.40, 67.00]	74.70 [72.60, 77.90]
Sex = male, n (%)	550 (56.0)	364 (59.0)	122 (52.4)	64 (48.1)
KDPI, median [IQR]	0.60 [0.35, 0.84]	0.40 [0.22, 0.56]	0.82 [0.74, 0.89]	0.96 [0.92, 0.98]
DCD, n (%)	103 (10.5)	61 (9.9)	35 (15.0)	7 (5.3)
Cardiovascular death, n (%)	527 (53.6)	269 (43.6)	159 (68.2)	99 (74.4)

Transplantations from very senior donors lead to inferior, yet acceptable outcome

A Cox proportional hazards model with restricted cubic spline showed that the risk for graft loss or death sharply increased with donor age, with a 12.5% increase in hazard for donors aged 65 years and a 98% increase in hazard for donors aged 75 years, compared with a reference donor age of 45 years. Meanwhile, the risk for death or graft loss modestly declined in TPLs for donors younger than 45 years (Fig. 2). Indeed, failure-free survival was significantly distinct across groupings (log-rank $P < 0.001$, Fig. 3a).

Multivariable cause-specific Cox proportional hazards models for death-free survival and allograft failure-free survival (Fig. 3c,e and Table S1) provided no evidence for a relationship between donor age group and patient death [VSD vs. RD: HR = 1.0, 95%-CI: (0.65, 1.54)]. The HR for the comparison between VSD and RD patients is highest in the model assessing allograft failure-free survival [HR = 2.92, 95%-CI: (1.89, 4.52)]. For the allograft failure-specific model, we found little evidence for Senior Donors having increased hazard compared with Regular Donors [HR = 1.45, 95%-CI: (1.01, 2.08)]. These findings are underlined by cumulative incidences estimated for allograft failure and death in all donor age groups: graft loss was highest in the VSD group, while death events did not differ among the donor age groups (Fig. 3b,e).

Primary immunosuppression and donor-specific antibody development did not differ between the groups (Table S2). 65.8% patients received an induction therapy with interleukin-2 receptor antibody (basiliximab) and 30.0% with anti-thymocyte globulin (ATG). The vast majority of patients were started on a calcineurin inhibitor (CNI)-containing regimen, i.e., 78% on tacrolimus and 21% on ciclosporin A. Steroid withdrawal was attempted in 32% of patients. Either Class I or Class II donor-specific antibodies (DSA) were reported in 8.9% of patients within the first 18 months of TPL. We have recently published a study covering immunosuppression in kidney TPL recipients within the STCS [27].

Lower graft function with intact quality of life in recipients of very senior donor organs

Estimated glomerular filtration rate estimates at 12 months were only available for patients who had more than 12 months of follow-up. Ultimately, 1315 (84.6%) patients contributed eGFR values to this analysis. Median allograft function was 56.4, 43.4, and 32.4 ml/min/1.73 m² for RD, SD, and VSD at 12 months after TPL (Fig. 4a,b). Chronic kidney disease (CKD) stage 4T or higher (eGFR < 30 ml/min/1.73 m²) was found in 10.3% (RD), 21.6% (SD), and 43.1% (VSD) of patients. eGFR at 12 months postoperatively was stable for kidney recipients from donors

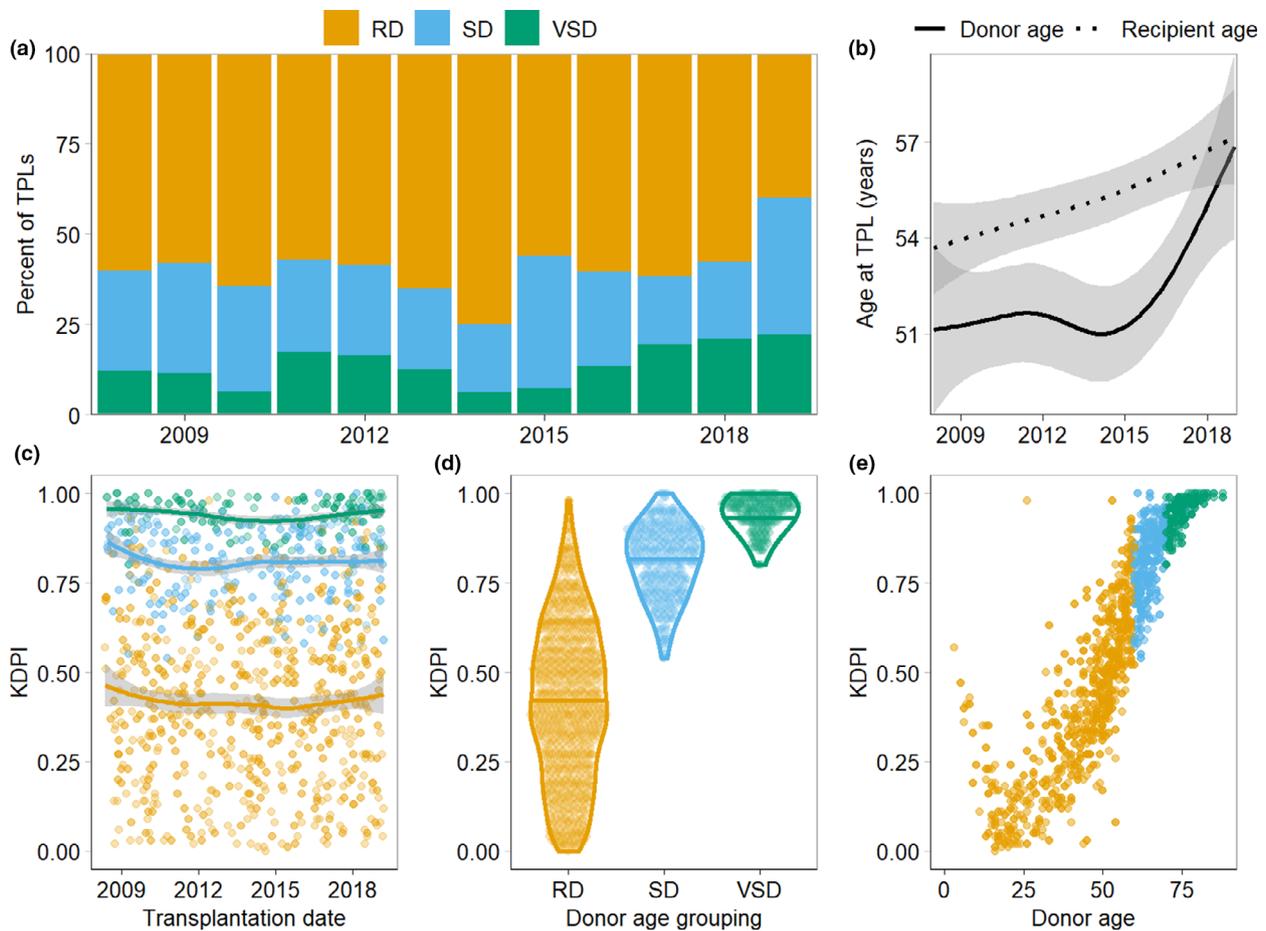


Figure 1 Evolution of age categories and KDPI for transplantations (TPLs) involving Regular Donors (RD), Senior Donors (SD), and Very Senior Donors (VSD) from 2008 to 2019. (a) Percentage of TPLs involving RD, SD, and VSD across the years 2008–2019. (b) Cubic-splines smoothing of recipient and donor ages across the years 2008–2019. Dotted line: Mean age of recipients. Solid line: Mean age of donors. Shaded ribbons: 95% CI for the cubic splines. (c–e) KDPI of donors leading to RD, SD, and VSD TPLs across the years 2008–2019 (c), across donor categories (d), and dependent on donor age (e).

younger than 35 years and subsequently deteriorated with an average decline of 6.7 ml/min/1.73 m² per decade of donor age.

Patient-reported QoL was available for 742 patients, reflecting 46.4% of the study population [$n = 463$ (RD), 176 (SD) and 103 (VSD)]. Median QoL was similar and between 68% and 72% at 12 months for the different age groups. The proportion of patients with a functioning graft who filled in a QoL questionnaire was indifferent, namely, 98.9%, 99.3%, and 96.5% for RD, SD, and VSD, respectively.

Selection of donor candidates for organ donation and deceased donor kidney transplantation

In Switzerland, potential organ donors are recruited in different procurement centers and reported to Swiss Transplant, which then coordinates organ allocation to

waitlisted patients enrolled in a nationwide waiting list by one of the six TPL centers. During the observation period, we evaluated 1545 deceased donor candidates for which consent for organ donation was given, either by the patient prior to death or by the next of kin (Table 2). In 37 cases (2.4%), organ procurement was interrupted either since brain-death was not confirmed or because of absolute contraindications for donation, e.g., risk of transmission of infection or tumor, or hemodynamic instability (Category 1). In 23 cases (1.5%), only nonrenal organs were offered for TPL (Category 2). Here, the majority of candidates suffered from advanced cardiovascular and/or kidney diseases. In 321 patients (20.8%), kidneys were offered, but organs were refused by all TPL centers because of medical reasons (Category 3). In the remaining 1164 donor candidates (75.3%), at least one kidney TPL was performed (Category 4). In comparison, candidates in Category 3

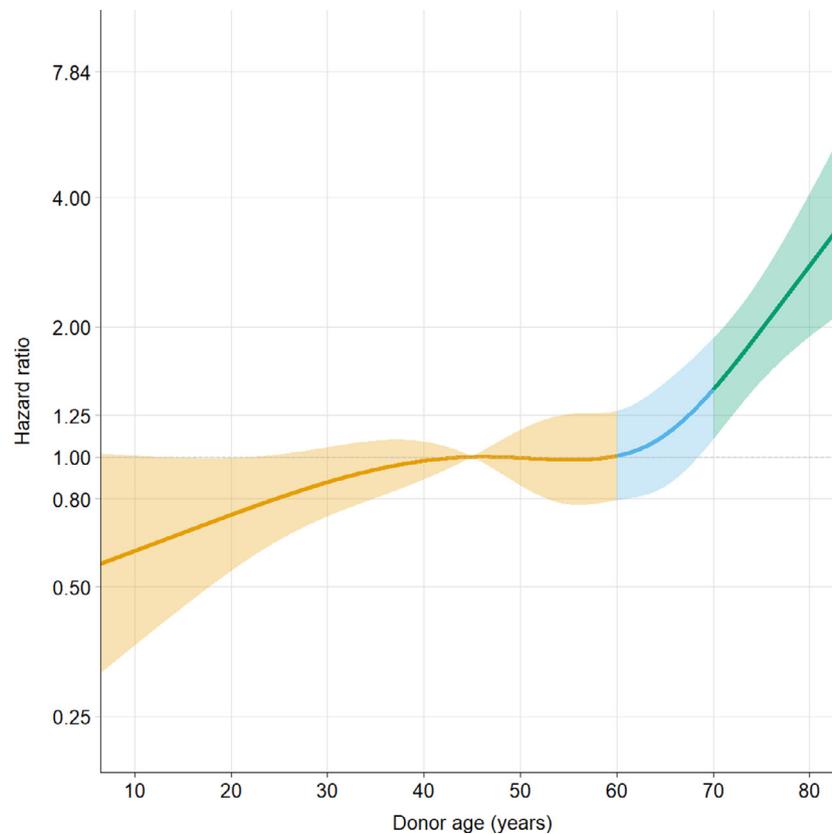


Figure 2 Donor age independently predicts failure-free survival after deceased donor transplantations: Hazard ratio (HR) for graft loss or patient death in relation to donor age, compared with a Regular Donor of 45 years of age. Derived from a single-variable Cox proportional hazards model relating failure to donor age, with donor age encoded as a restricted cubic spline with knots at 16, 45, 56, 64, and 76 years of donor age (5th, 25th, 50th, 75th, and 95th quantiles). Solid line: Estimated HR at each age, with the reference donor age being 45 years. Shaded ribbon: 95% CI for the estimated HRs. Yellow: Donor age ≤ 60 . Blue: Donor age ≤ 70 and > 60 . Green: Donor age > 70 .

were older, showed a higher prevalence of DCD procurement, heart disease, hypertension, diabetes mellitus, acute kidney injury (AKI), and pre-existing kidney disease compared to Category 4 candidates. The acceptance rate of donor candidates for kidney TPL was 78% for the entire cohort (87% for RD, 79% for SD, and 56% for VSD).

Discussion

This study represents the analysis of a large comprehensive and prospectively followed cohort of deceased donor TPLs from septua- and octogenarian donors. As presumed, allograft outcome decreases with donor age with a sharp and exponential risk for treatment failure in donors aged 70 years and older. We show that TPLs from VSD, i.e., donors aged above 70 years, harbors an independent, 2.92-fold increased risk for premature graft loss or death when compared with donors younger than 60 years. This difference was predominantly driven

by premature graft loss. Nevertheless, absolute outcome is acceptable even for this subgroup with 1-, 3-, and 5-year failure-free survival of 83%, 81%, and 64%, respectively. These findings are in strong alliance with earlier reports, which demonstrate an increased risk for graft loss in TPLs from older donors, yet acceptable absolute mid- and long-term results [10–12]. The results must be seen in the context of alternative treatment options for end-stage kidney disease (ESKD) patients, notably long-term dialysis, which comprises an annual death rate of 23% for older and multimorbid recipients [1].

Furthermore, we demonstrate a strong relationship between donor age and achieved eGFR at 12 months post-TPL. In recent years, lower eGFR at 1-year post-TPL has been associated with inferior long-term outcome [15,28,29], a notion that is supported by our study. Allograft function with eGFR below 30 ml/min/1.73 m² commonly requires supportive therapy to cope with hypertension, metabolic acidosis, hypervolemia, and mineral and bone disorders similar to patients with

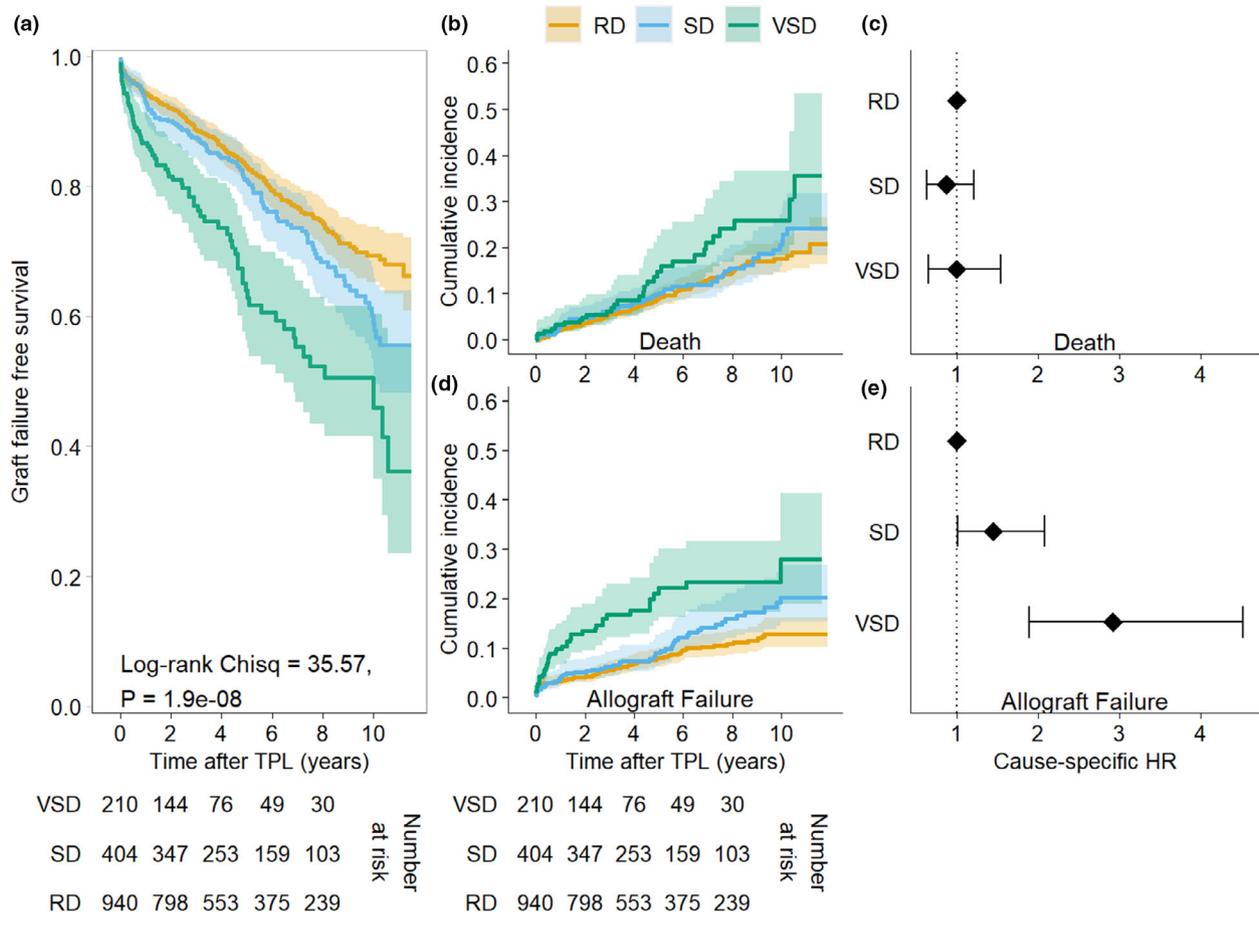


Figure 3 Increased risk for graft loss in transplantations (TPLs) from Very Senior Donors (VSD): (a) Kaplan–Meier curves showing failure-free survival (absence of graft loss and death). Green line: Recipients of VSD organs. Blue line: Recipients of Senior Donor (SD) organs. Yellow line: Recipients of Regular Donor (RD) organs. Shaded ribbons: 95% CI for the estimated survival. Number of patients at risk (without allograft failure, death, or censored status) at the start of each one-year interval. (b,d) Cumulative incidence curves for death and graft loss as competing risks. Yellow: Cumulative incidence curves for RD recipients. Blue: Cumulative incidence curves for SD recipients. Green: Cumulative incidence curves for VSD recipients. Shaded ribbons: 95% CI for cumulative incidence curves. Lower table: Number of patients at risk (without graft loss, death, or censored status) at the start of each one-year interval. (c,e) Cause-specific Cox proportional hazard models. Ratios comparing SD and VSD groups against RD for death and graft loss. Models include recipient age, recipient sex, recipient dialysis time, year of TPL, and account for clustering based on shared donor. Black diamonds: HR estimate for each group. Error bars: 95% CI for each HR.

CKD Stage 4 and higher [30]. Indeed, after 1 year, 43.1% of the VSD group had an eGFR below 30 ml/min/1.73 m² with reduced renal reserve and increased risk of graft loss. Strategies to support patients with a prior marginal allograft function need to be developed and evaluated. Among other factors, CNI-based immunosuppression is associated with progressive kidney insufficiency [31,32]. Therefore, recipients of VSD organs may profit from CNI-sparing regimens including belatacept, either de novo or as secondary conversion. The Benefit-EXT trial demonstrated excellent long-term outcome in TPLs from extended criteria donors [33–35]. To our knowledge, there is no ongoing randomized study investigating the value of CNI-sparing

regimens specifically in deceased donor TPL from septua- and octogenarian donors.

As an additional important endpoint, we investigated self-reported QoL after the first year of TPL. A large body of literature underscores a survival benefit of TPL in ESKD compared with long-term dialysis [1]. The largest benefit is attributed to children, adolescents, and younger adults, while recipients above 60 years tend to gain less life-time with successful TPL [12]. Meanwhile, improvement of QoL has been shown to be substantial among all age groups of kidney TPL recipients [36]. In our study, QoL was very high in the whole cohort. Neither donor age nor allograft function significantly influenced QoL at one-year post-TPL. This illustrates that

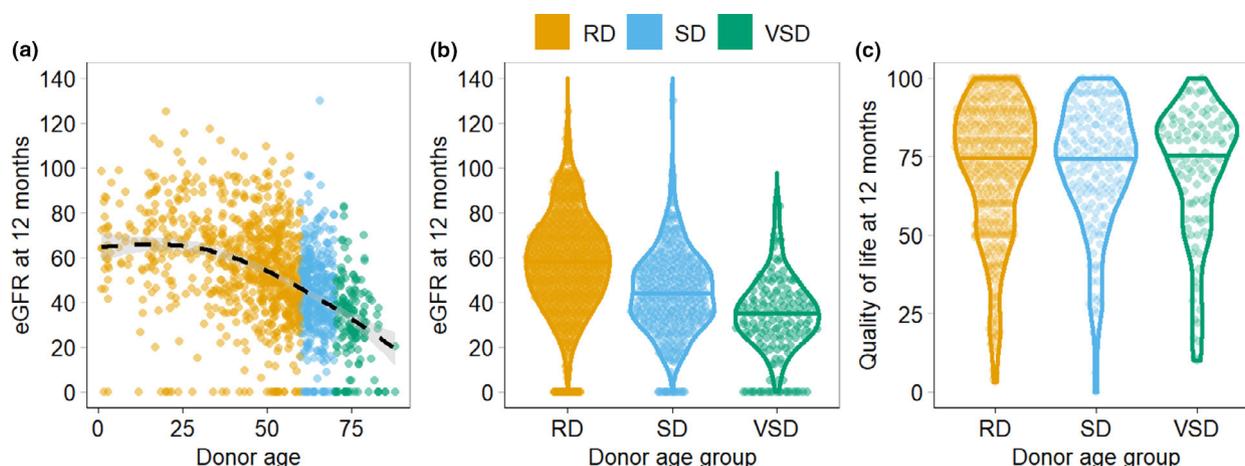


Figure 4 Recipients from Senior Donor (SD) and Very Senior Donor (VSD) kidneys achieve lower eGFR at 12 months with intact quality of life (QoL): (a): Scatter plot of eGFR at 12 months post-TPL and donor age with cubic spline smoothing line. (b) Violin plots showing eGFR 12 months after TPL grouped into Regular Donor (RD), SD, and VSD. In case of graft loss prior to 12 months, the eGFR was set to 0 ml/min/1.73 m². (c) Violin plots showing reported QoL 12 months after TPL as assessed by the PSQ questionnaire, split by donor age grouping.

patients do not necessarily perceive donor characteristics or medical parameters, and do profit from successful and lasting TPL. This QoL analysis clearly has limitations. Primarily, reporting was not compulsory and incomplete and certain biases cannot be excluded, notably underreporting of patients with low QoL. Secondarily, QoL in chronically ill patients, including TPL recipients, depends on biographic and socioeconomic factors including age, gender, educational status, income, and co-morbidity burden. Such factors were not included in detail in our analysis and may be unequally distributed among the groups investigated.

TPLs from VSD seems feasible in the presented context with acceptable mid- and long-term outcome. It is though clear that the outcomes described in the study are the result of a rigorous elimination process of VSD candidates with selection of the most suitable donors.

This is clearly reflected by the Swiss allocation practice, as demonstrated above. Indeed, kidneys were offered to the TPL centers in 96.1% of eligible organ donors. From here, a thorough selection process is evident based on age, medical history, kidney function, and other parameters. Nonetheless, the Swiss TPL community has accepted more than three-quarters of kidney donor candidates for deceased donor TPL, which led to 2177 deceased donor TPL in the period investigated (including pediatric, multiorgan, and repeated TPL). Among all 338 VSD candidates, 178 (56%) were accepted. From these donors, one kidney was transplanted in 19%, a dual TPL performed in 18%, and both kidneys transplanted to separate recipients in 63%. This underscores the notion that not every VSD candidate is a suitable donor for kidney TPL. It is up to debate, if selection should be based on clinical features only or also include

Table 2. Baseline characteristics of deceased donor candidates.

	Category 1 (consented, but no organs offered) N = 37 (2.4%)	Category 2 (organs offered, but no kidneys) N = 23 (1.5%)	Category 3 (kidneys offered, but no kidney TPL) N = 321 (20.8%)	Category 4 (kidneys offered, at least 1 kidney TPL) N = 1164 (75.3%)
Age, median [IQR]	59.3 [36.4, 71.4]	68 [51.1, 76.7]	68.1 [55.4, 75.8]	54.7 [41.7, 65.2]
DCD planned %	5.4%	26.1%	29%	12.2%
Heart disease %	36.8%	65.2%	45.4%	19.9%
Hypertension %	42.9%	60.9%	62.5%	29.8%
Diabetes mellitus %	20%	68.2%	17.8%	2.7%
AKI III %	8.1%	47.8%	17.8%	2.2%
Reanimation %	58.8%	34.8%	35.1%	30.3%
Kidney disease %	5%	39.1%	24.4%	5.9%

histopathology, gene expression, and/or hemodynamics of the explanted organ.

Various research groups have evaluated the impact of preimplantation biopsies or backtable wedge resections in donor evaluation, some in a specific context of marginal donor TPL [37–39,40]. For this purpose, several scoring systems have been established and evaluated, but none of these seem to predict TPL outcome with high precision (reviewed in Ref. [41]). Notably, selection and weighing of histological lesions, type of biopsy, and interobserver variation significantly influence biopsy findings and therefore donor selection. Furthermore, glomerulosclerosis and interstitial fibrosis underlie a significant sampling bias, and a recent publication demonstrated frequent such findings among healthy living kidney donors [42]). In our cohort, only 61/210 (29%) of VSD kidneys had implantation biopsies with a major center bias. Furthermore, only Banff scores were collected, but no other validated parameters to assess organ quality (e.g., Remuzzi score [39]). Notably, the histology data were collected retrospectively and thus not available for allocation decisions. Overall, we speculate that results from preimplantation biopsies do not significantly support decision-making during an allocation process in VSD, yet jeopardizes a short cold ischemia time. Likely, surrogate markers associated with structural nephropathies, i.e., donor hypertension, subnormal donor kidney function, cerebro- or cardiovascular disease, and smoking history may have equal or superior predictive value compared with histological findings.

Previously, large TPL consortia have established specific old-for-old TPL programs, where older donors are allocated to senior waitlisted candidates in the vicinity of the procurement center [43,44]. While such an approach is feasible for large consortia, it is not efficient for smaller programs such as Swisstransplant. Indeed, dividing a donor pool into unshared subgroups may decrease the likelihood for TPL, notably for recipients with blood group B and AB and recipients with high cPRA values [45].

In conclusion, our data demonstrate that deceased donor kidney TPL from donors 70 years and older is associated with an inferior, yet acceptable, failure-free

outcome with excellent QoL. Further studies to identify and validate donor-derived factors predictive for premature graft loss in this specific donor population are mandatory.

Authorship

CK: designed study, performed research, analyzed data and wrote the paper. BML: performed research, analyzed data and wrote the paper. SL and SS: analyzed data and wrote the paper. AK: analyzed data and performed research. IB, GB, DG, KH, TM, SS and FI: provided data and discussed the results. MK: provided data, designed study, analyzed data and wrote the paper. DS: designed study, provided data, performed research, analyzed data and wrote the paper.

Funding

Institutional funds of the primary investigator (DS) STCS project fund to DS.

Conflict of interest

All authors deny any conflict of interest that might bias their work.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Flowchart of selection and grouping of kidney transplantation recipients within the STCS cohort.

Table S1. HR for outcomes (death, loss) with regular donor (RD) organ recipients as the reference group and donor age included as the three-level grouping.

Table S2. Induction therapy, primary immunosuppression, and incidence of reported donor-specific antibodies at 12–18 months after TPL in SD, RD, and VRD.

REFERENCES

1. 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**: 1725.
2. Salek MS. Quality of life in patients with end-stage renal disease. *J Appl Ther Res* 1999; **2**: 163.
3. Port FK, Bragg-Gresham JL, Metzger RA, *et al.* Donor characteristics associated with reduced graft survival: an approach to expanding the pool of

- kidney donors. *Transplantation* 2002; **74**: 1281.
4. Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. *Transplantation* 2009; **88**: 231.
 5. Cohen B, Smits JM, Haase B, Persijn G, Vanrenterghem Y, Frei U. Expanding the donor pool to increase renal transplantation. *Nephrol Dial Transplant* 2005; **20**: 34.
 6. Rao PS, Ojo A. The alphabet soup of kidney transplantation: SCD, DCD, ECD—fundamentals for the practicing nephrologist. *Clin J Am Soc Nephrol* 2009; **4**: 1827.
 7. Merion RM, Ashby VB, Wolfe RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. *J Am Med Assoc* 2005; **294**: 2726.
 8. Ojo AO, Hanson JA, Meier-Kriesche HU, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; **12**: 589.
 9. Chavalitdhamrong D, Gill J, Takemoto S, et al. Patient and graft outcomes from deceased kidney donors age 70 years and older: an analysis of the organ procurement transplant network/United network of organ sharing database. *Transplantation* 2008; **85**: 1573.
 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**: 1151.
 11. Pippias M, Jager KJ, Caskey F, et al. Kidney transplant outcomes from older deceased donors: a paired kidney analysis by the European Renal Association-European Dialysis and Transplant Association Registry. *Transpl Int* 2018; **31**: 708.
 12. Peters-Sengers H, Berger SP, Heemskerck MBA, et al. Stretching the limits of renal transplantation in elderly recipients of grafts from elderly deceased donors. *J Am Soc Nephrol* 2017; **28**: 621.
 13. Arcos E, José Pérez-Sáez M, Comas J, Lloveras J, Tort J, Pascual J. Assessing the limits in kidney transplantation: use of extremely elderly donors and outcomes in elderly recipients. *Transplantation* 2020; **104**: 176.
 14. Ruggenti P, Silvestre C, Boschiero L, et al. Long-term outcome of renal transplantation from octogenarian donors: a multicenter controlled study. *Am J Transplant* 2017; **17**: 3159.
 15. Israni AK, Salkowski N, Gustafson S, et al. New national allocation policy for deceased donor kidneys in the United States and possible effect on patient outcomes. *J Am Soc Nephrol* 2014; **25**: 1842.
 16. Rose C, Sun Y, Ferre E, Gill J, Landsberg D, Gill J. An examination of the application of the kidney donor risk index in British Columbia. *Can J Kidney Heal Dis* 2018; **5**: 1–10.
 17. del Moral Martín RMG, Retamero Díaz JA, Cava Molina M, et al. Validation of KDRI/KDPI for the selection of expanded criteria kidney donors. *Nefrologia* 2018; **38**: 297.
 18. Dahmen M, Becker F, Pavenstädt H, Suwelack B, Schütte-Nütgen K, Reuter S. Validation of the Kidney Donor Profile Index (KDPI) to assess a deceased donor's kidneys' outcome in a European cohort. *Sci Rep* 2019; **9**: 11234.
 19. Koller MT, Van Delden C, Müller NJ, et al. Design and methodology of the Swiss Transplant Cohort Study (STCS): a comprehensive prospective nationwide long-term follow-up cohort. *Eur J Epidemiol* 2013; **28**: 347.
 20. Michels WM, Grootendorst DC, Verduijn M, Elliott EG, Dekker FW, Krediet RT. Performance of the Cockcroft-Gault, MDRD, and new CKD-EPI formulas in relation to GFR, age, and body size. *Clin J Am Soc Nephrol* 2010; **5**: 1003.
 21. Steyerberg EW, Harrell FE Jr. Regression modeling strategies: with applications, to linear models, logistic and ordinal regression, and survival analysis, 2nd ed. Heidelberg: Springer. *Biometrics* 2016; **72**: 1006.
 22. OPTN. A Guide to Calculating and Interpreting the Kidney Donor Profile Index (KDPI) [Internet], 2020. Available from: https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf.
 23. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat* 1988; **16**: 1141.
 24. R CT. R Core Team (2014). *R: A Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing.
 25. Wickham H, Averick M, Bryan J, et al. Welcome to the Tidyverse. *J Open Source Softw* 2019; **4**: 1686.
 26. Hourihan F. The influencer. *J Ir Dent Assoc* 2008; **54**: 256.
 27. Krisl A, Stampf S, Hauri D, et al. Immunosuppression management in renal transplant recipients with normal-immunological risk: 10-year results from the Swiss Transplant Cohort Study. *Swiss Med Wkly* 2020; **150**: w20354.
 28. Salvadori M, Rosati A, Bock A, et al. Estimated one-year glomerular filtration rate is the best predictor of long-term graft function following renal transplant. *Transplantation* 2006; **81**: 202.
 29. Kasiske BL, Israni AK, Snyder JJ, Skeans MA. The relationship between kidney function and long-term graft survival after kidney transplant. *Am J Kidney Dis* 2011; **57**: 466.
 30. Davison SN, Levin A, Moss AH, et al. Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care. *Kidney Int* 2015; **88**: 447.
 31. Nankivell BJ, Borrows RJ, Fung CL-S, O'Connell PJ, Allen RDM, Chapman JR. The natural history of chronic allograft nephropathy. *N Engl J Med* 2003; **349**: 2326.
 32. Stegall MD, Cornell LD, Park WD, Smith BH, Cosio FG. Renal allograft histology at 10 years after transplantation in the tacrolimus era: evidence of pervasive chronic injury. *Am J Transplant* 2018; **18**: 180.
 33. Vincenti F, Charpentier B, Vanrenterghem Y, et al. A phase III study of belatacept-based immunosuppression regimens versus cyclosporine in renal transplant recipients (BENEFIT Study). *Am J Transplant* 2010; **10**: 535.
 34. Vincenti F, Rostaing L, Grinyo J, et al. Belatacept and long-term outcomes in kidney transplantation. *N Engl J Med* 2016; **374**: 333.
 35. Larsen CP, Grinyó J, Medina-Pestana J, et al. Belatacept-based regimens versus a cyclosporine a-based regimen in kidney transplant recipients: 2-year results from the benefit and benefit-EXT studies. *Transplantation* 2010; **90**: 1528.
 36. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant* 2011; **11**: 2093.
 37. Husain SA, King KL, Batal I, et al. Reproducibility of deceased donor kidney procurement biopsies. *Clin J Am Soc Nephrol* 2020; **15**: 257.
 38. Girolami I, Gambaro G, Ghimenton C, et al. Pre-implantation kidney biopsy: value of the expertise in determining histological score and comparison with the whole organ on a series of discarded kidneys. *J Nephrol* 2020; **33**: 167.

39. Remuzzi G, Cravedi P, Perna A, *et al.* Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; **354**: 343.
40. Hopfer H, Kemény E. Assessment of donor biopsies. *Curr Opin Organ Transplant* 2013; **18**: 306.
41. Naesens M. Zero-time renal transplant biopsies: a comprehensive review. *Transplantation* 2016; **100**: 1425.
42. Bar Y, Barregard L, Sallsten G, Wallin M, Mölne J. Quantitative and semi-quantitative histopathological examination of renal biopsies in healthy individuals, and associations with kidney function. *Apmis* 2016; **124**: 393.
43. Fritsche L, Hörstrup J, Budde K, *et al.* Old-for-old kidney allocation allows successful expansion of the donor and recipient pool. *Am J Transplant* 2003; **3**: 1434.
44. Moers C, Kornmann NSS, Leuvenink HGD, Ploeg RJ. The influence of deceased donor age and old-for-old allocation on kidney transplant outcome. *Transplantation* 2009; **88**: 542.
45. Davis A, Mehrotra S, Friedewald J, *et al.* Predictors of kidney transplantation waiting time inequity across the United States. *Am J Transplant* 2013; **13**: 73.