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Benchmark Outcomes in Deceased Donor Kidney Transplantation: A Multicenter Analysis of 80 996 Transplants From 126 Centers

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Background. We defined clinically relevant benchmark values in deceased donor kidney transplantation (KT), to assess the best achievable results in low-risk patient cohorts from experienced centers. **Methods.** We identified the "ideal" cases from the United Network for Organ Sharing Standard Transplant Analysis and Research files from centers performing ≥50 KT per year between 2010 and 2018. Cases have been selected based on the kidney donor profile index values (<35%), a cold ischemia time (CIT) ≤18 h, a HLA mismatch ≤4, and excluding blood group (ABO) incompatible, dual and combined transplants. The outcomes of the benchmark cohort have been compared with a group of patients excluded from the benchmark cohort because but not meeting 1 or more of the abovementioned criteria. **Results.** The 171 424 KT patients in the United Network for Organ Sharing Standard Transplant Analysis and Research files were screened and 8694 benchmark cases of a total of 80 996 KT (10.7%) from 126 centers meeting the selection criteria were identified. The benchmarks for 1-, 3-, and 5-y patient survival are ≥97%, ≥92.5%, and ≥86.7%, and ≥95.4%, ≥87.8%, and ≥79.6% for graft survival. Benchmark cutoff for hospital length of stay is ≤5 d, ≤23.6% for delayed graft function, and ≤7.5% and ≤9.1% for 6-mo and 1-y incidence of acute rejection. Overall 1-, 3-, and 5-y actuarial graft survivals were 96.6%, 91.1%, and 84.2% versus 93.5%, 85.4%, and 75.5% in the benchmark and comparison groups, respectively ($P < 0.001$). Overall 1-, 3-, and 5-y actuarial patient survivals were 98.1%, 94.8%, and 90.0% versus 96.6%, 91.1%, and 83.0% in the benchmark and comparison groups, respectively ($P < 0.001$). **Conclusions.** For the first time, we quantified the best achievable postoperative results in an ideal scenario in deceased donor KT, aimed at improving the clinical practice guided by the comparison of center performances with the ideal outcomes defined.

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Ever since Merrill et al[1] performed the first successful kidney transplantation (KT) in humans between 2 monozygotic twins in 1954, this procedure has become the most frequent solid organ transplantation performed worldwide, with >24 000 yearly transplants in the United States to address the demand of approximately 90 000 patients on the waiting list.[2,3] Thanks to major breakthroughs such as the introduction of safer and more effective immunosuppressive regimens in the late 1970s[4,5] and the progressive improvements in medical and surgical management and techniques, KT has become the treatment of choice for patients with end-stage renal disease, providing a significant survival advantage over dialysis.[6] This has translated into the number of KT performed in the United States rising from 45 008 between 1996 and 1999 to 76 885 between 2016 and 2019, a 70.8% increase (78.8% and 56.4% for deceased and living donor KT, respectively).[7] Along with the increased volume, there have been constant improvements in the average graft survival, from 87.7% and 65.9% at 1 and 5 y, in the late 1990, to 94.3% and 78.1%, 2 decades later, respectively.[8]

Despite average 1-y patient and graft survival exceeding 95% and 90%, respectively, for both living and deceased donor recipients, it is often challenging to accurately evaluate the results of KT, because of the lack of reliable comparison groups.[3] National or international reports are generally derived from heterogeneous aggregate data, which do not allow a significant and meaningful comparison. International and specialist societies' guidelines promote "best practice" principles,[9,10] globally disseminating the necessary knowledge and tools to perform the highest level of care possible.

In the last few years, the concept of benchmarking has been introduced in medical and surgical fields to assess the best achievable results in low-risk patient cohorts from experienced centers. These analyses have been conducted in several surgical specialties[11-14] and in liver transplantation.[15,16]

This study aims to define the most clinically relevant benchmark cutoffs in deceased donor KT, from a multicentric, low-risk cohort of KT recipients from the United States.

MATERIALS AND METHODS

Cases and Centers Selection

Donor, recipient, transplant, and outcome data were retrieved from the United Network for Organ Sharing (UNOS) Standard Transplant Analysis and Research (STAR) files for cases from 2010 to 2018. Because of the retrospective and observational structure of the study, and the anonymous origin of the data, no consent or further approval was required. Centers performing ≥50 deceased donor KT per year in the study period were selected to be included in the analysis.

Study Population

To identify the "ideal" cases in every center, we selected patients based on donor, recipient, and transplant variables expected to be correlated with the best posttransplant outcomes. We therefore included patients receiving a first KT from a deceased donor, with recipients between 18 and 60 y of age. We also selected cases based on the kidney donor profile index (KDPI) values, which is the percentage representation of the kidney donor risk index, that indicates the estimate of the relative risk of graft failure, calculated from 10 donor characteristics (age, history of diabetes, height, cause of death, weight, serum creatinine, ethnicity, hepatitis C virus status from serological or nucleic acid testing, history of hypertension, and donation after circulatory death status) and compared with a reference donor.[17,18] We included transplants performed with donors from the lower KDPI tier (<35%), and only cases with a cold ischemia time (CIT) of ≤18 h. We also excluded KT performed with HLA mismatch >4.

To further select only the "best cases," we excluded blood group (ABO) incompatible transplants, dual KT, and KT combined with heart, liver, or pancreas.

Benchmark Values

Benchmark metrics were determined for the following outcome indicators: 1-, 3-, and 5-y patient survival, 1-, 3- and 5-y graft survival, delayed graft function (DGF), defined as acute kidney injury with the subsequent need for dialysis within 7 d of the transplant,[19,20] incidence of rejection at 6 and 12 mo, and hospital stay (from day of transplantation until hospital discharge). The benchmark cutoffs were obtained after calculating separately for each participating center the median value for each continuous indicator and the proportion for each binary parameter. Then, the 25th and 75th percentiles of each center-specific value for every outcome parameter were calculated, representing the benchmark cutoff values as previously reported.[21] Benchmark cutoffs indicating optimal outcomes were set at the 75th percentile and below for DGF, hospital stay, and rejection, and values at the 25th percentile and above for graft and patient survivals.

Comparison Group

The outcomes of the benchmark cohort have been compared with a higher risk cohort including adult patients receiving a kidney-only, first, deceased donor, and ABO compatible transplant during the same timeframe at the same centers and excluded from the benchmark cohort because of meeting 1 or more of the following criteria: age >60 y, KDPI ≥35%, CIT >18 h, and >4 HLA mismatch.

Statistical Analysis

Categorical variables were presented as frequency and percentages and compared using the χ^2 test with Yates correction or Fisher exact test, whichever was most appropriate. Normally distributed continuous data were reported as mean ± SD and compared using the 2-sided Student *t*-test. Nonnormally distributed continuous data were reported as median and interquartile range (IQR) and compared using the Mann-Whitney test. Patient survival was evaluated using the Kaplan–Meier method and compared using the log-rank test. A P value of <0.05 was used to determine statistical significance. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY).

RESULTS

All 171 424 KT patients in the UNOS STAR files transplanted between January 1, 2010, and December 31, 2018, were screened. The final study cohort consisted of 80 996 patients from 126 transplant centers following the selection as per the mentioned criteria and reported in Figure 1.

The 126 centers provided 8694 KT benchmark cases during the analyzed period, representing 10.7% of the study population. Each center contributed a median of 57 benchmark cases (range 9–254). Recipient, donor, and transplant characteristics of the benchmark, comparison, and the whole population groups are reported in Table 1. All demographic, donor, and transplant variables differed significantly between the benchmark and comparison groups. Overall 1-, 3-, and 5-y actuarial graft survival were 96.6%, 91.1%, and 84.2% versus 93.5%, 85.4%, and 75.5% in the benchmark and comparison groups, respectively ($P < 0.001$). Overall 1-, 3-, and 5-y actuarial patient survival were 98.1%, 94.8%, and 90.0% versus 96.6%, 91.1%, and 83.0% in the benchmark and comparison groups, respectively ($P < 0.001$), as shown in Figure 2.

Benchmark Values

The benchmark cutoffs, representing the best achievable results for each outcome parameter, have been calculated as the 75th or 25th percentile for each center and are reported in Table 2 and Figure 3A–D. The benchmarks for 1-, 3-, and 5-y patient survival are ≥97%, ≥92.5%, and ≥86.7%, respectively, and ≥95.4%, ≥87.8%, and ≥79.6% for graft survival. Benchmark cutoff for hospital length of stay is ≤5 d, ≤23.6% for DGF development, and ≤7.5% and ≤9.1% for 6-mo and 1-y incidence of acute rejection, respectively. Compared with the benchmark group, the comparison group showed similar

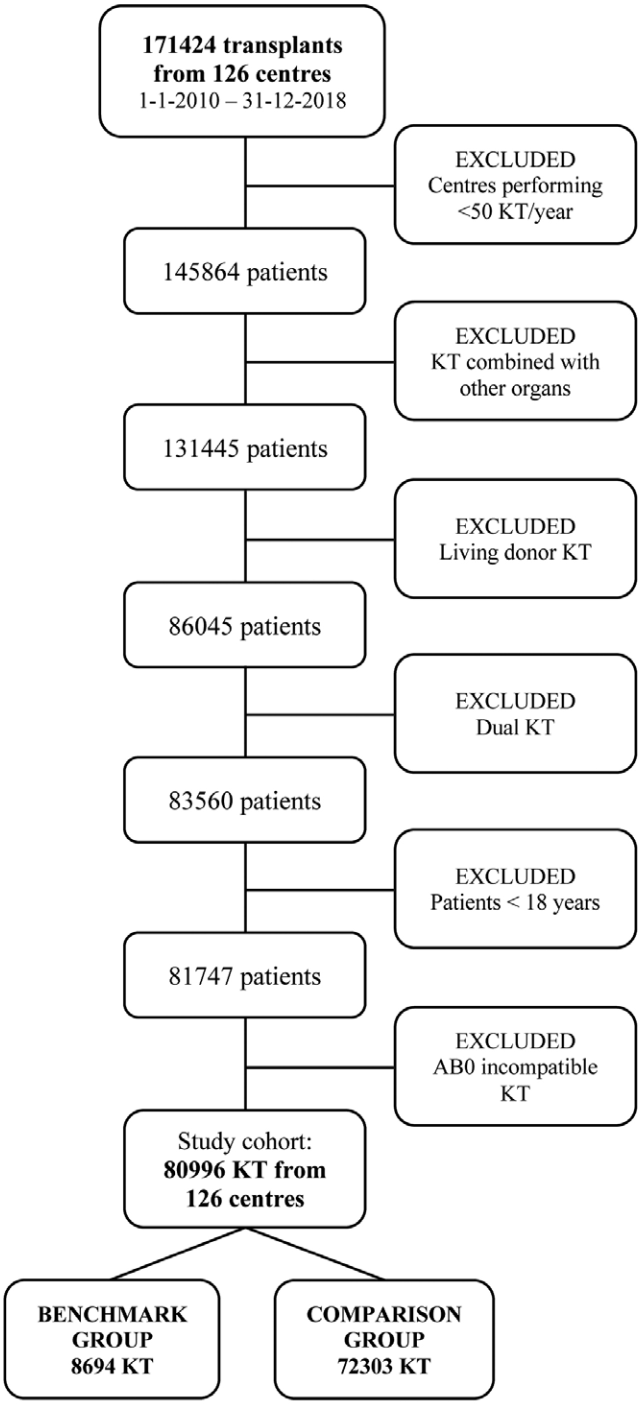

FIGURE 1. Study population selection flowchart. KT, kidney transplant.

length of stay (median 5 d, IQR 4–6), higher median DGF rate (28.0%, IQR 19.4–35.4), and higher 6-mo and 1-y median incidence of acute rejection (6.3%, IQR 3.5–9.2 and 7.7%, IQR 4.9–11.7, respectively).

DISCUSSION

This is the first study addressing the best achievable "benchmark" results after deceased donor KT, assuming as a sample population a large multicenter patient cohort. As the lack of a consistent reference population represents a remarkable limiting factor for a reliable assessment of deceased donor KT outcomes, the value of our analysis is essential to the evaluation and comparison of performances among different transplant centers.

The introduction of the benchmark concept in healthcare outcome analysis is recent but has rapidly gained an increasing role and popularity. Adopted initially in economics, the benchmarking tool has more recently been demonstrated to be effective for the appraisal of the quality of outcomes in medicine. The process of benchmarking has been defined as "a comparative assessment of high-level performances."[22] It represents a suitable analysis tool to assess the ideal results in the best conceivable scenario, that is, low-risk patient cohorts from experienced centers holding prospective databases, providing high-quality data. Notably, these analyses have already been successfully conducted in several surgical specialties, including liver transplantation performed in diverse settings, such as redo transplants, or transplant performed utilizing grafts from donation after circulatory death donors or for perihilar cholangiocarcinoma.[11-14,16,23,24] The benchmarking analyses, differently from to textbook outcome analyses, are not necessarily restricted to an extremely short timeframe that may bias the results because patients dying or losing the graft just a few months after KT can still be judged reaching the "textbook outcomes," whereas these results would ubiquitously be considered unsatisfactory.[25,26] Moreover, benchmarking shares with the "best practice" guidelines the aim of promoting the best level of care possible and through the achievement of the best possible results but provides evidence-based data originated in a rigorous, systematic manner, which serves as a reference for all transplant centers and professionals.

Our study population was selected based on pretransplant recipient characteristics, donor, and transplant factors ahead of data collection to identify patients expected to be correlated with better outcomes, yielding the "benchmark cohort" of deceased donor kidney transplants. Benchmark cases were screened via a systematic selection process. First, we selected patients in the UNOS STAR files who received deceased donor KT from January 1, 2010, to December 31, 2018. Because better posttransplant results have proven to be associated with higher volume centers compared with very low-, low-, and medium-volume centers,[27] only data from centers performing ≥50 KT per year were used for benchmark cases. Regarding deceased donor graft quality, we only included transplants performed from donors with a low KDPI, as high KDPI correlates negatively with graft survival.[28-30] Furthermore, only cases with a CIT ≤18 h were chosen because longer times have a detrimental impact on graft outcomes.[31] KT performed with an HLA mismatch >4 was excluded because 5 and 6 donor-recipient HLA mismatch have a kidney graft failure hazard ratio ≥1.5.[32,33] Elderly recipients (>60 y) have been shown to have significantly shorter graft and patient survivals.[34] Intuitively, the selection of "best cases" was restricted to ABO blood group compatible transplants, with a single KT (also cases of KT combined simultaneously with heart, liver, and pancreas transplants were excluded). Compared with the comparison group, the benchmark group generated outstanding patient and graft survival at 5 y (90.0% versus 83.0%, $P < 0.001$; 84.2% versus 75.5% $P < 0.001$, respectively), confirming the validity of the adopted a priori selection criteria. The 2 cohorts had statistically different baseline patient, donor, transplant, and scoring characteristics both because of the selection process and the large sample size that highlights

TABLE 1.

Recipient and donor characteristics in the benchmark group, comparison group, and the whole population

Variables	Whole population, N = 80 996	Benchmark group, N = 8694	Comparison group, N = 72 302	P^a
Age (y)	55 (44–63)	49 (39–59)	55 (45–63)	<0.001
Recipient gender (F/M)	32 887 (40.6%)/ 48 109 (59.4%)	3744 (43.1%)/ 4950 (56.9%)	29 143 (40.3%)/ 43 159 (59.7%)	<0.001
Recipient BMI (kg/m^2)	27.9 (24.2–32.1)	28.3 (24.3–32.5)	27.9 (24.2–32.0)	<0.001
Recipient blood group (0-A-B-AB)	37 201 (45.9%)/ 29 239 (36.1%)/ 10 286 (12.7%)/ 4270 (5.3%)	3873 (44.5%)/ 3345 (38.5%)/ 977 (11.2%)/ 499 (5.7%)	33 328 (46.1%)/ 25 894 (35.8%)/ 9309 (12.9%)/ 3771 (5.2%)	<0.001
Dialysis status (pre-emptive/dialysis)	14 191 (17.9%)/ 66 505 (82.1%)	1740 (20%)/ 6954 (80%)	12 751 (17.6%)/ 59 551 (82.4%)	<0.001
Donor age (y)	40 (26–51)	27 (21–34)	42 (28–52)	<0.001
Donor gender (F/M)	31 777 (39.2%)/ 49 219 (60.8%)	2635 (30.3%)/ 6059 (69.7%)	29 142 (40.3%)/ 43 160 (59.7%)	<0.001
Donor BMI (kg/m^2)	26.9 (23.2–31.5)	26.1 (22.1–30.25)	27.0 (23.3–31.7)	<0.001
Donor eGFR (mL/min/1.73 m^2)	88.0 (50.5–112.6)	105.0 (74.9–124.0)	86.1 (56.8–110.7)	<0.001
Donor cause of death (anoxia/cerebrovascular/ head trauma/CNS tumor/other)	28 820 (35.6%)/ 23 183 (28.6%)/ 26 463 (32.7%)/ 353 (0.4%)/ 2176 (2.7%)	3323 (38.2%)/ 763 (8.8%)/ 4314 (49.6%)/ 48 (0.6%)/ 245 (2.8%)	25 497 (35.3%)/ 22 420 (31.0%)/ 22 149 (30.6%)/ 305 (0.4%)/ 2176 (2.7%)	<0.001
Donor type (DBD/DCD)	65 594 (80.9%)/ 15 447 (19.1%)	7414 (85.3%)/ 1280 (14.7%)	58 135 (80.4%)/ 14 167 (19.6%)	<0.001
Kidney side (right/left)	38 515 (47.6%)/ 42 481 (52.4%)	4027 (46.3%)/ 4667 (53.7%)	37 814 (52.3%)/ 34 488 (47.7%)	<0.001
HLA mismatch (0/1/2-3/4-5/6)	10 481 (12.9%)/ 33 391 (41.2%)/ 37 124 (45.8%)	1749 (20.1%)/ 6945 (79.9%)/ 0 (0%)	8732 (12.1%)/ 26 446 (36.6%)/ 37 124 (51.3%)	<0.001
CIT (h)	16.8 (11.4–22.9)	11.8 (8.3–15)	17.9 (12–23.6)	<0.001
Graft preservation (SCS/MP)	55 535 (68.6%)/ 25 461 (31.4%)	6985 (80.3%)/ 1709 (19.7%)	48 551 (67.2%)/ 23 751 (32.8%)	<0.001
PRA	0 (0–54)	0 (0–42)	0 (0–55)	<0.001
KDPI	0.42 (0.21–0.63)	0.16 (0.09–0.25)	0.46 (0.25–0.66)	<0.001
EPTS	0.49 (0.21–0.77)	0.20 (0.1–0.56)	0.52 (0.25–0.79)	<0.001
KDRI	1.18 (0.96–1.46)	0.92 (0.83–1.00)	1.23 (1.00–1.50)	<0.001

[a]Analysis performed between benchmark group and comparison group.
BMI, body mass index; CIT, cold ischemia time; CNS, central nervous system; DBD, donation after brain death; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; EPTS, estimated posttransplant survival; KDPI, kidney donor profile index; KDRI, kidney donor risk index; MP, machine perfusion; PRA, panel-reactive antibody; SCS, static cold storage.

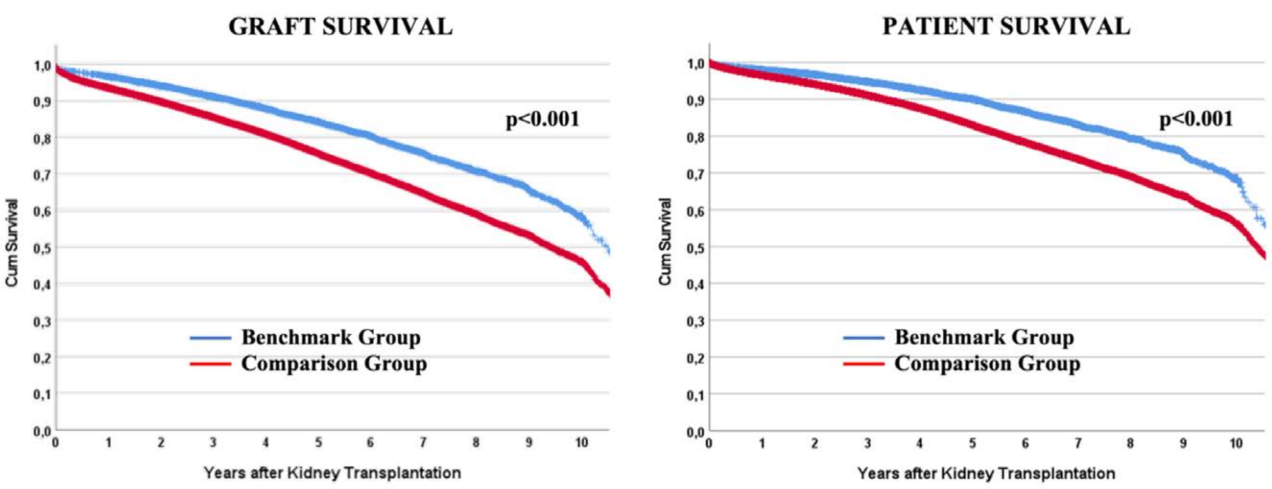

FIGURE 2. Graft and patient survival for the benchmark (8694 patients) and comparison (72 302 patients) groups.

TABLE 2.

Benchmark cutoffs in kidney transplantation

Hospital length of stay		**≤5 d**		
Delayed graft function		**≤23.6%**		
	6 mo, %	**1 y, %**	**3 y, %**	**5 y, %**
Rejection	≤7.5	≤9.1	—	—
Graft survival	—	≥95.4	≥87.8	≥79.6
Patient survival	—	≥97.0	≥92.5	≥86.7

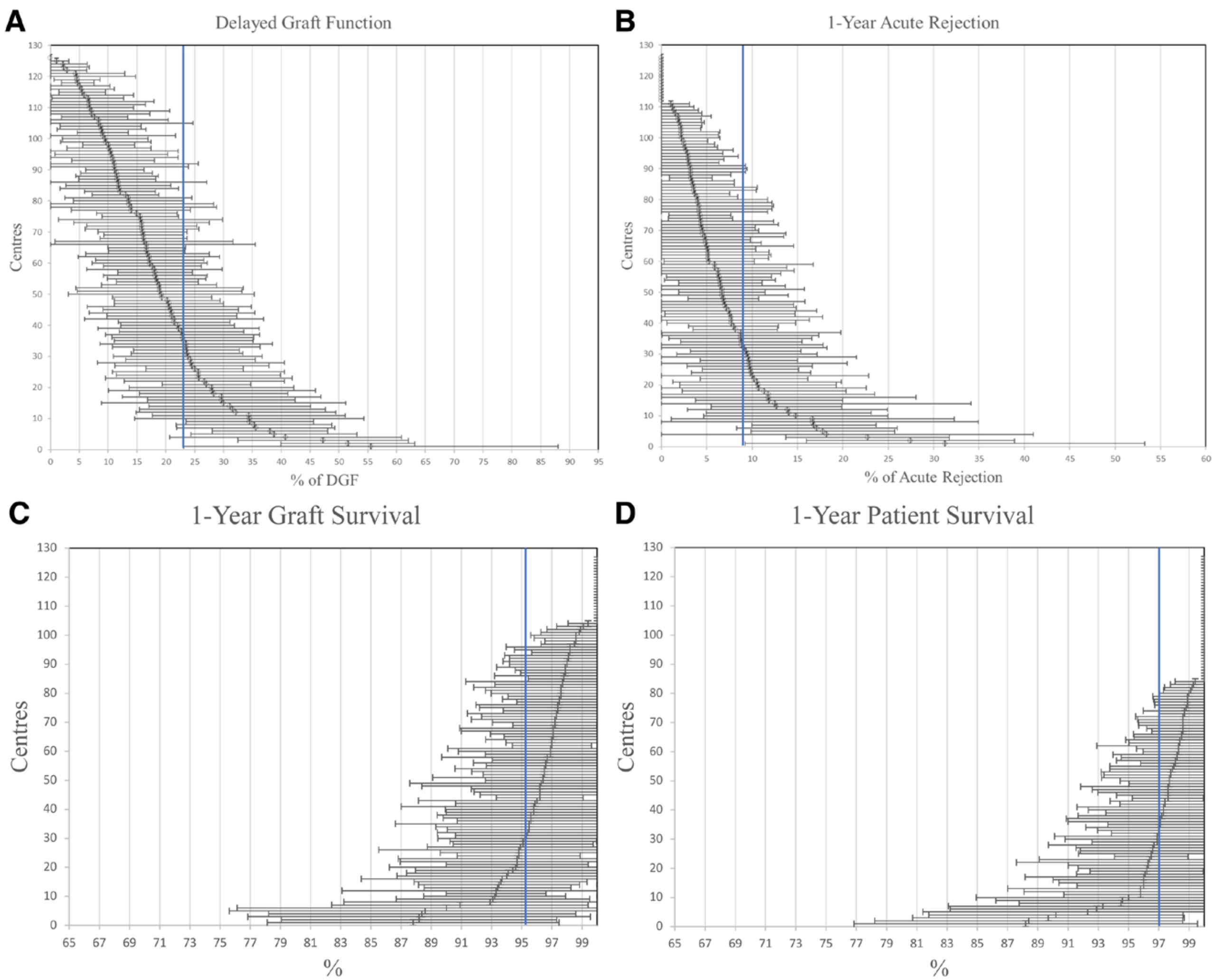

FIGURE 3. Caterpillar plots of benchmark outcomes. Caterpillar plots representing the incidence and confidence intervals of delayed graft function (A), 1-y acute rejection (B), 1-y graft survival (C), and 1-y patient survival (D) in the 126 included centers. The vertical blue lines represent the benchmark cutoffs. DGF, delayed graft function.

differences even when small and clinically not relevant. From the "ideal" population (8694 of 80 996 cases from 126 centers), we established benchmark metrics for 8 clinically relevant outcome indicators: postoperative hospital length of stay, incidence of DGF, 6- and 12-mo incidence of acute rejection and 1- and 3-y overall recipient and graft survival. In this setting, for each benchmark metric, cutoffs were set at the 25th or 75th percentile to exclude the 25% of cases with the worst outcomes or results. According to our results, the benchmark values all centers performing deceased donor KT transplants should aim for to strive for excellence are ≤5 d for the postoperative length of stay; ≤23.6% for the incidence of DGF; ≤7.5% and ≤9.1% for the incidence of graft rejection at 6- and 12-mo, respectively; ≥95.4%, ≥87.8%, and ≥79.6% for 1-, 3-, and 5-y graft survival, respectively, and ≥97.0%, ≥92.5%, and ≥86.7% for 1-, 3-, and 5-y patient survival, respectively (Table 2). As mentioned earlier, these results were obtained from a highly selected population of patients and can serve as a reference for optimal outcomes, instead of average-quality results extrapolated from highly heterogeneous populations, and therefore not representing an adequate comparator.[7,8,35] The Benchmark graft and patient survival results observed are similar or superior to the ones reported in the literature following deceased donor first KT derived from both the US and European cohorts, with 1- and 5-y graft survival values of 93.4% and 72.4% in the United States and 90.7% and 77.8% in Europe, respectively (1- and 5-y benchmark graft survival of ≥95.4% and ≥79.6%), and 1- and 5-y patient survival values of 97.0% and 86.1% in the United States and 96.0% and 87.1% in Europe, respectively (1- and 5-y benchmark patient survival of ≥97.0% and ≥86.7%).[35]

Of note, although our benchmark analysis displays the ideal achievable results from deceased donor KT, the purpose is not to penalize centers not achieving performances at least equaling the reference metrics but to help identify and quantify areas of improvement to the effort of continuously striving for high-quality results and patient outcomes. Indeed, not all individual cases can be appropriately compared with the benchmark values, individual donor and recipient characteristics should be taken into consideration, with high-risk, complex patients expected to achieve nonideal results but still being able to provide patient survival or quality of life benefit.[21] In fact, in our analysis, approximately only 1 transplant of 10 was identified as a "Benchmark case." The described results should not represent an indication to restrict access to KT only to the lowest risk patients, but nevertheless each center performing deceased donor KT should aspire to fill the gap between its performances and benchmark outcomes, which could be considered as the theoretical potential to improve. As already reported in the setting of economics, the benchmarking process promotes a continuous virtuous cycle because defining the best helps to compare with the best, learn from the best, and identify the areas with room for improvement.

Limitations of the present analysis are the lack of detailed data on postoperative complications, and the inclusions of patients transplanted only in the United States. Future studies with data from worldwide KT centers will provide a valuable comparator for all centers.

This study provides for the first time the quantification of the best achievable postoperative results in deceased donor KT, calculated in an ideal scenario and representing a valuable comparator for all centers. It sets the ground for future analyses aimed at improving clinical practice guided by the comparison of center performances with the ideal available outcomes.

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