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Elderly Ages in Liver Transplantation: Are Older Donors Really Higher Risk?

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Background. There is currently a supply and demand mismatch in liver transplantation, with more patients needing transplants than grafts available. The use of older donors is one potential way of expanding access to viable grafts. No national study has yet reported on outcomes of liver transplants with donors ≥70 y. **Methods.** The US Scientific Registry of Transplant Recipients registry was queried for deceased donor LT (1988–2021). Balance-of-risk (BAR) score was calculated for each patient. The primary outcome was graft survival. Cubic spline curves were used to evaluate the full spectrum of donor ages. **Results.** A total of 148 960 livers met inclusion criteria: 5414 (3.6%) from donors ≥70 y and 4291 (2.9%) recipients ≥70 y. Within the overall cohort, graft survival decreased with increased donor and recipient age. Median graft survival within donors ≥70 y improved over time from 2.2 y (interquartile range [IQR] 0.2–9.8 y) in 1987–1999 to 9.6 y (IQR 3.2–11.6 y) in 2010–2019 ($P < 0.0001$). Elderly donors had equivalent outcomes to donors <70 y when transplanted in elderly recipients (≥70 y). Outcomes for young recipients that received grafts from elderly donor improved with time, with median survival of 10.1 y (IQR 3.9–11.5 y) in 2010–2019. BAR and survival outcomes following liver transplant (SOFT) scores predicted improved graft survival on time-to-event analysis in all donors aged >70 y. In low-risk recipients, evidenced by preallocation SOFT score <5, elderly donors had comparable outcomes to young (<40 y) and middle-aged donors (40–69 y). Increasing donor age was not associated with worse graft survival in transplants performed between 2010 and 2019. **Conclusions.** Donors aged ≥70 y may be more comfortably considered for deceased donor liver transplantation, especially within low-risk recipients. The BAR and SOFT scores may be a useful guide for safely expanding the use of these theoretically riskier liver grafts.

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End-stage liver disease is increasingly prevalent.[1-3] The increase in numbers of annual transplants is accompanied by a disproportionate increase in patients awaiting transplant,[4] and there remains a serious supply and demand mismatch between donors and recipients awaiting LT.[5] Although the utilization of more living donors may help address this issue, cultural, ethical, and logistical limitations dictate that increasing the use of deceased donor liver grafts will be necessary. As such, there has been increased efforts to utilize extended criteria liver grafts with high-risk features such as micro/macrovesicular steatosis, donation after circulatory death (DCD) grafts, and grafts from older donors.[6-8]

Several studies have associated poor posttransplant outcomes with use of older donor grafts.[9] Increased donor age has also been identified as a significant predictor for poor transplant outcomes and utilized in several scoring systems for donor-recipient risk such as donor risk index,[10] balance-of-risk score (BAR),[11] and survival outcomes following liver transplant score (SOFT).[12] Although the use of grafts from older donors has been increasing with improvement in outcomes over time,[13] there remains hesitancy in utilization of these grafts as evidenced by high regional variability and discard rates.[14] Recipient age has also increased over time, and like older donors, older recipient age has been associated with worse long-term outcomes.[15]

To address concerns regarding elderly ages within transplant, we sought to provide evidence on the outcomes of transplantation with grafts from donors ≥70 y.

MATERIALS AND METHODS

Data were queried from the Scientific Registry of Transplant Recipients (SRTR) database. The study included patients of all ages who underwent deceased donor liver transplantation (LT) from 1987 to 2022. Patients with complete data on donor age, recipient age, and graft survival were included. Living donor LT, combined organ transplantation, domino transplant, and recipients who were lost to follow-up were excluded from analysis.

The primary outcome was actuarial 1-, 3-, and 5-y graft survival as well as median graft survival. Median graft survival was calculated through Kaplan–Meier analysis and defined as the time point at which probability of survival was 50%. Secondary comparisons included in-group predictors of graft survival in the respective cohorts of age ≥70 y. This study is exempted from institutional review board approval because it is a national database using only publicly available data. Principles of the Declaration of Helsinki were followed in the conduct of this research. No patients or public personnel were included in this research. All work has been reported in concordance with the strengthening the reporting of cohort studies in surgery criteria for reporting of retrospective cohort studies.[16]

Patient information was collected from the SRTR database included donor, transplant and recipient information. Donor factors included age, sex, race, body mass index (BMI), and diabetes. Recipient characteristics included age, sex, race, BMI, underlying liver disease (indication for transplant), model for end-stage liver disease (MELD) score, and history of tobacco or drug abuse. Holistic graft risk was assessed using the balance-of-risk (BAR) score, survival outcomes following liver transplant (SOFT) score, and MELD score.[11,12,17] BAR and SOFT were chosen as they include both recipient and graft risks, which we felt was critical when assessing risk tolerance in potentially higher-risk cohort. Preallocation SOFT (PSOFT) was also calculated to determine recipient risk. As allocation status (national, regional, or local) of the graft was not available, all grafts were assigned as local allocation. Transplant information included cold ischemia time (CIT), warm ischemia time and date of transplantation. Cumulative liver age is calculated as previously described as the sum of donor age + recipient graft survival.[18]

Statistical Analysis

Continuous variables are reported as median with interquartile range (IQR) and categorical variables are presented as frequencies (n) and percentages. Kaplan–Meier analysis was used to construct survival curves using time-to-event analysis. Median graft survival for cohorts was calculated from Kaplan–Meier analysis and was defined as the time point at which probability of survival was 50%. IQR was defined as the associated time points with probability of survival of 75% and 25%. Cox proportional hazards regression model was conducted to evaluate the association between predictor variables and graft survival. Hazard ratios along with 95% confidence intervals were estimated. Cubic spline curves were generated assessing increasing donor age of all ages versus the outcome of graft survival treated as a continuous variable and as a binary outcome (graft survival at 3 y post-LT). Color-based binning was applied to demonstrate the frequency of attained graft survival by donor age. All statistical analyses were conducted using SPSS version 28 (IBM Corp., Armonk, NY), R program (version 4.4.1, Vienna, Austria), and GraphPad Prism (Boston, MA), and a P value of <0.05 was considered statistically significant.

RESULTS

Cohort Overview

A total of 148 960 livers met inclusion criteria (**Figure S1, SDC,** http://links.lww.com/TXD/A753). Of these, 141 452 (95%) were from donation after brain death donors and 7508 (5%) from donation after circulatory death (DCD) (Table 1). The overall median graft survival in all comers was 10.8 (2.5–21.4) y. In total, 5414 (3.6%) transplants originated from donors aged ≥70 y and 4291 (2.9%) recipients were aged ≥70 y (Table 1). Of the 5414 transplants from donors aged ≥70 y, 5004 were performed in recipients aged <70 y and 410 transplant were in recipients aged ≥70 y (Table 2). Table 1 contains information on all included patients as well as the 2 groups of interest. Elderly donors (≥70 y of age) were distributed into the following age groups: 70–74 y of age (n = 3099, 57.2%), 75–79 y of age (n = 1710, 31.6%), 80–84 of age (n = 499, 9.2%), and ≥85 y of age (n = 106, 2.0%) (Table 2). Of the grafts utilized from elderly donors, 10.3% occurred from 1987 to 1999, 40.6% occurred from 2000 to 2009, 39.2% from 2010 to 2019, and 10% from 2020 to 2022 (Figure 1A). Most grafts from elderly donors were allocated to recipients 60–69 y of age (2179, 40.2%), with 410 (7.6%) grafts allocated to recipients ≥70 y of age (Figure 1B). Utilization of elderly grafts in elderly recipients was highest from 2010 to 2019, where 178 grafts (43%) from donors ≥70 y of age were transplanted in recipients ≥70 y of age (Figure 1B). DCD grafts were utilized in only 209 (0.04%) transplants with elderly grafts, with use increasing over the decades with the majority (61.7%) being performed after 2010 (Table 2).

Most elderly recipients (≥70 y) were aged 70–74 y (n = 3945, 91.9%), with 7.8% (n = 335) aged 75–79 y and only 11 recipients aged ≥80 y (0.3%) (Figure 1C). As with elderly donors, transplants with elderly recipients increased over time with 51% of transplants occurring between 2010 and 2019 and 21% occurring after 2020 (Figure 1C). Most elderly recipients received grafts from donors <50 y of age, with 10% receiving grafts from elderly donors (Figure 1D). DCD grafts were utilized in 221 (5%) transplants with elderly recipients, with only 15 (7%) of these grafts coming from elderly donors (Table 2).

Graft Survival in Older Donors and Recipients

We first examined graft survival for older donors and recipients across all decades. Median graft survival in all donors aged ≥70 y of age was lower at 7.3 (IQR 1.5–15.8 y) compared with 11.0 (IQR 2.6–21.7 y) in donors <70 y of age on time-to-event analysis ($P < 0.0001$) (Figure 1E). Similarly, median graft survival in all recipients aged ≥70 y of age was 7.9 (IQR 2.4–13.9 y) compared with recipients <70 y, where median survival was 10.9 (2.5–21.7) y ($P < 0.0001$) (Figure 1F). Grafts from older donors (≥70 y of age) had lower median survival when transplanted in younger recipients (<70 y) ($P < 0.0001$) and older recipients (≥70 y) ($P = 0.02$) (**Figure**

TABLE 1.

Donor, recipient, and preservation data for all included patients

Parameter	Total (n = 148 960)	Donor age ≥ 70 y (n = 5414)	Recipients age ≥ 70 y (n = 4291)	Donor age ≥ 70 and recipient age < 70 y (n = 5004)	Donor age ≥ 70 and recipient age ≥ 70 y (n = 410)
Decade, n (%)					
1987–1989	3393 (2.3)	2 (0.0)	6 (0.1)	2 (0.0)	0 (0.0)
1990–1999	28 155 (18.9)	554 (10.2)	266 (6.2)	530 (10.6)	24 (5.9)
2000–2010	44 285 (29.7)	2197 (40.6)	952 (22.2)	2058 (41.1)	139 (33.9)
2010–2019	57 525 (38.6)	2120 (39.2)	2179 (50.8)	1942 (38.8)	178 (43.4)
2020–2022	15 602 (10.5)	541 (10.0)	888 (20.7)	472 (9.4)	69 (16.8)
Donor information					
Donor type, n (%)					
DBD	141 452 (95.0)	5205 (96.1)	4070 (94.8)	4820 (96.3)	395 (96.3)
DCD	7508 (5.0)	209 (3.9)	221 (5.2)	194 (3.9%)	15 (3.7)
Donor age, y	38 (23–52)	74 (72–77)	46 (30–59.5)	74 (72–77)	74 (72–78)
Male sex	89 521 (60.1)	2456 (45.4)	2516 (58.6)	2278 (45.5)	178 (43.4)
Race and ethnicity, n (%)					
White	120 219 (80.7)	4571 (84.4)	3379 (78.7)	4227 (84.5)	344 (83.9)
Black	24 154 (16.2)	655 (12.1)	775 (18.1)	595 (11.9)	60 (14.6)
Asian/Pacific Islander	3522 (2.4)	171 (3.2)	108 (2.5)	166 (3.3)	5 (1.2)
Native American	618 (0.4)	11 (0.2)	18 (0.4)	11 (0.2)	0 (0.0)
Other/unknown/multiracial	447 (0.3)	6 (0.1)	11 (0.3)	5 (0.1)	1 (0.2)
Donor BMI (kg/m^2)	25.6 (22.2–29.8)	26.1 (23.1–29.6)	26.6 (23.1–31.0)	26.1 (23.2–29.6)	26.3 (22.7–30.2)
Recipient information					
Indication for transplant, n (%)					
ETOH	31 617 (21.2)	1183 (21.9)	468 (10.9)	1136 (22.7)	47 (11.5)
SLD-cirrhosis	11 025 (7.4)	613 (11.3)	770 (17.9)	547 (10.9)	66 (16.1)
Viral cirrhosis	31 331 (21.0)	938 (17.3)	608 (14.2)	887 (17.7)	51 (12.4)
Hepatocellular carcinoma	17739 (11.9)	956 (17.7)	1231 (28.7)	833 (16.6)	123 (30.0)
Other malignancy	2284 (1.5)	92 (1.7)	36 (0.8)	89 (1.8)	3 (0.7)
PBC/PSC/autoimmune	19 534 (13.1)	673 (12.4)	497 (11.6)	615 (12.3)	58 (14.1)
Other	35 430 (23.8)	959 (17.7)	681 (15.9)	897 (17.9)	62 (15.1)
Recipient age, y	54 (44–61)	59 (52–65)	71 (70–73)	58 (51–64)	71 (70–73)
Male sex, n (%)	94 286 (63.3)	3310 (61.1)	2724 (63.5)	3070 (61.4)	240 (58.5)
Race and ethnicity, n (%)					
White	126 903 (85.2)	4752 (87.8)	3774 (88.0)	4384 (87.6)	368 (89.8)
African	13 835 (9.3)	344 (6.4)	207 (4.8)	324 (6.5)	20 (4.9)
Asian/Pacific Islander	6467 (4.3)	269 (5.0)	287 (6.7)	248 (5.0)	21 (5.1)
Native American	1059 (0.7)	37 (0.7)	15 (0.3)	36 (0.7)	1 (0.2)
Other/unknown/multiracial	696 (0.5)	12 (0.2)	8 (0.2)	12 (0.2)	0 (0.0)
Recipient BMI (kg/m^2)	26.9 (23.2–31.3)	27.4 (24.1–31.7)	27.0 (24.1–30.5)	27.5 (24.2–31.8)	26.9 (24.0–30.2)
History of diabetes, n (%)	22 558 (15.1)	1173 (21.7)	1287 (30.0)	1052 (21.0)	121 (29.5)
Laboratory MELD score (points)					
<15	38 863 (26.1)	2041 (37.7)	1905 (44.4)	1831 (36.6)	210 (51.2)
>15–25	36 393 (24.4)	1836 (33.9)	1200 (28.0)	1697 (33.9)	139 (33.9)
>25–35	21 816 (14.6)	535 (9.9)	498 (11.6)	515 (10.3)	20 (4.9)
>35	14 875 (10.0)	237 (4.4)	339 (7.9)	231 (4.6)	6 (1.5)
Laboratory MELD ≥ 40 (n)	8445 (5.7)	142 (2.6)	158 (3.7)	139 (2.8)	3 (0.7)
Transplant information					
Donor WIT, min	17 (12–22)	16 (14–30)	18 (12–23)	16 (13–18.5)	75 (52.5–97.5)
Recipient WIT, min	43 (33–56)	40 (31–50)	39 (30–50)	40 (31–50)	37 (29–45)
Cold ischemia time, h	6.63 (5.0–8.8)	6.2 (5.0–8.0)	6.0 (4.9–7.8)	6.2 (5.0–8.0)	6.0 (4.8–7.8)

Recipient WIT is implantation time (liver out of ice to reperfusion).

BAR score, balance of risk score; BMI, body mass index; CIT, cold ischemia time; DBD, donation after brain death; DCD, donation after circulatory death; donor WIT, functional WIT, from SBP < 60 mm Hg or SpO2 < 80%; ETOH, alcohol use disorder; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; SLD-cirrhosis, steatotic liver disease, formerly known as NASH; WIT, warm ischemia time.

S2A and Table S1, SDC, http://links.lww.com/TXD/A753). Older DCD donors also had worse median survival than donors <70 y of age ($P < 0.0001$) (**Figure S2B, SDC,** http://links.lww.com/TXD/A753).

However, outcomes for older donors have improved over the years. From 1987 to 1999, transplants with older donor grafts had a median graft survival of 2.2 (IQR 0.2–9.8 y) with 1- and 5-y survival of 59.5% and 38.3%, respectively (Figure 2A). Between the years 2010 and 2019, graft survival drastically improved to 9.6 (IQR 3.2–11.6 y) with 87% and 71.9% 1- and 5-y survival, respectively (Figure 2B). Similarly older recipient survival also improved from median survival

TABLE 2.

Breakdown of donor and recipient ages in the SRTR database

	Recipient age, y					
Donor age, y	**<50 (n = 55 933)**	**50–59 (n = 50 251)**	**60–69 (n = 38 485)**	**70–74 (n = 3945)**	**75–79 (n = 335)**	**≥80 (n = 11)**
<50 (n = 103 946)	44 122 (2045)	33 450 (1787)	23 996 (1372)	2180 (115)	190 (9)	8 (1)
50–59 (n = 25 127)	7290 (294)	9674 (545)	7323 (410)	779 (50)	59 (3)	2 (0)
60–69 (n = 14 473)	3512 (135)	5311 (249)	4987 (256)	612 (26)	51 (2)	0 (0)
70–74 (n = 3099)	598 (18)	1068 (36)	1222 (66)	197 (9)	13 (0)	1 (0)
75–79 (n = 1710)	322 (12)	577 (17)	686 (29)	111 (4)	14 (1)	0 (0)
80–84 (n = 499)	72 (0)	139 (4)	231 (10)	51 (1)	6 (0)	0 (0)
≥85 (n = 106)	17 (1)	32 (1)	40 (0)	15 (0)	2 (0)	0 (0)

Cases in brackets are DCD livers.
DCD, donation after circulatory death.

of 4.2 (IQR 0.45–10.9) to 8.4 (IQR 3.3–11.4) from 1987–1999 to 2010–2019, respectively.

As graft survival for elderly donors and recipients has improved over the years, actuarial and median graft survival was examined for grafts from donors ≥70 y of age in transplants performed between 2010 and 2019 (n = 2120). As recipients past 2020 had only up to 1-y follow-up, they were excluded from this cohort. Donors ≥70 y of age had a median survival of 10.1 (IQR 3.8–11.5) y compared with those <70 y of age (n = 55 405), where median survival was 11.8 (IQR 5.6–NA) y ($P < 0.0001$). The 75th percentile for median survival was unable to calculate for those <70 y of age, as percentage survival does not fall <25% in the duration of follow-up. Actuarial graft survival for donors ≥70 y of age was 87%, 75%, and 62% at 1, 3, and 5 y, respectively, compared with donors <70 y of age where survival was 89.5% ($P = 0.0006$), 80% ($P < 0.0001$), and 69% ($P < 0.0001$) (Table 3). Although there was a statistically significant difference in actuarial survival, the <10% difference in survival may not be clinically significant. Elderly donors (n = 2120) were then subdivided into age groups of 70–74 (n = 1234 58.2%), 75–79 (n = 678, 32%), and 80+ (n = 208, 9.8%) y of age, with no significant difference in median survival of 10.9 (4.3–11.5), 9.4 (3.6–11.5), and 8.9 (2.4–11.6) y, respectively ($P = 0.08$). There was no statistical difference in actuarial graft survival at 1, 3, and 5 y for the subcohorts 75–79 and 80+ compared with 70–74-y-old donors. Median donor age among elderly donors was 74 (IQR 71–77) y with associated median cumulative liver age of 78.5 (75.3–82.0) y. There remained a significant difference in median graft survival DCD grafts from elderly donors compared with donors <70 y of age in this time period ($P = 0.02$), although there was no statistical significance in actuarial 1-, 3-, and 5-y graft survival (**Figure S2B, SDC,** http://links.lww.com/TXD/A753; Table 3).

The impact of using grafts from elderly donors were examined in younger (<70 y) and older (≥70 y) recipient. Among the 55 346 transplants performed in recipients <70 y of age, 1942 (3.5%) were performed with grafts from elderly donors. Median graft survival within this cohort was 10.1 (3.9–11.5) y compared with 11.9 (5.7–NA) y in recipients <70 y of age who received grafts from donors <70 y of age ($P < 0.0001$) (Figure 2C). Although there was a significant difference in actuarial graft survival, there was <10% difference in survival. Among elderly recipients (n = 2179), 8.2% (n = 178) received grafts from elderly donors. Within this cohort of elderly recipients, there was no significant difference in median graft survival of 9.1 (IQR 3.4–10.2) y with older grafts compared with 8.7 (3.7–11.4) y with grafts from donors <70 y of age ($P = 0.94$) (Figure 2C). Similarly, there was no significant difference in actuarial graft survival at 1, 3, and 5 y (Table 3).

Impact of Donor Age on Posttransplant Outcomes Stratified by Risk Models

The efficacy of risk assessment models was examined the whole cohort of elderly donors (n = 5414). Pretransplant laboratory MELD was not measured in 765 recipients. Because of laboratory MELD and other missing variables, BAR score was not calculated in 913 cases and PSOFT/SOFT in 1000 cases. The UK-DCD score was unable to be calculated in 116 (55.5%) cases and so was not included in the analysis. Laboratory MELD provided poor distinction in graft survival among the elderly donor cohort, with MELD >35 showing slight worse survival ($P = 0.03$) (Figure 2D). Meanwhile, BAR and SOFT showed clear difference in graft survival for 10 y ($P < 0.0001$) (Figure 2E and F). On Cox-regression analysis, increasing donor age was predictive of impaired graft survival (hazard ratio = 1.02, 95% CI, 1.01-1.03, $P = 0.003$) within the entire cohort of all elderly donors (**Table S2, SDC,** http://links.lww.com/TXD/A753). Increasing SOFT score, MELD, and CIT were associated with decreased graft survival. The year of transplant also had a significant association with more graft loss in the earlier years of transplant. Increasing MELD was the only risk factor that retained association with poor graft survival on Cox regression analysis for transplants between 2010 and 2019.

The preallocation SOFT (PSOFT) was developed in 2008 and categorizes recipients into risk groups based on 12 risk factors.[13] Recipients from 2010 to 2019 were divided into low- (0–5), moderate- (6–35), and high-risk groups (>35) based on the PSOFT score. Actuarial graft survival at 1, 3, and 5 y was examined within these groups with use of grafts from young (<40 y), middle aged (40–69 y), and elderly donor (≥70 y). Elderly donors had worse outcomes as recipient risk increased ($P < 0.0001$) (Figure 2F). Among the PSOFT-based low-risk cohorts, elderly donors had an actuarial 1-y graft survival of 92%, which was not significantly different when compared with 91% and 94% for donors 40–69 y of age and donors <40, respectively. Actuarial graft survival at 3 y (78% versus 82%, $P = 0.03$) and 5 y (67% and 71%, $P = 0.12$) was similar in elderly donors and middle-aged donors (Table 4), although graft survival was significant better with young donors (Figure 3A; Table 4). A similar trend was observed

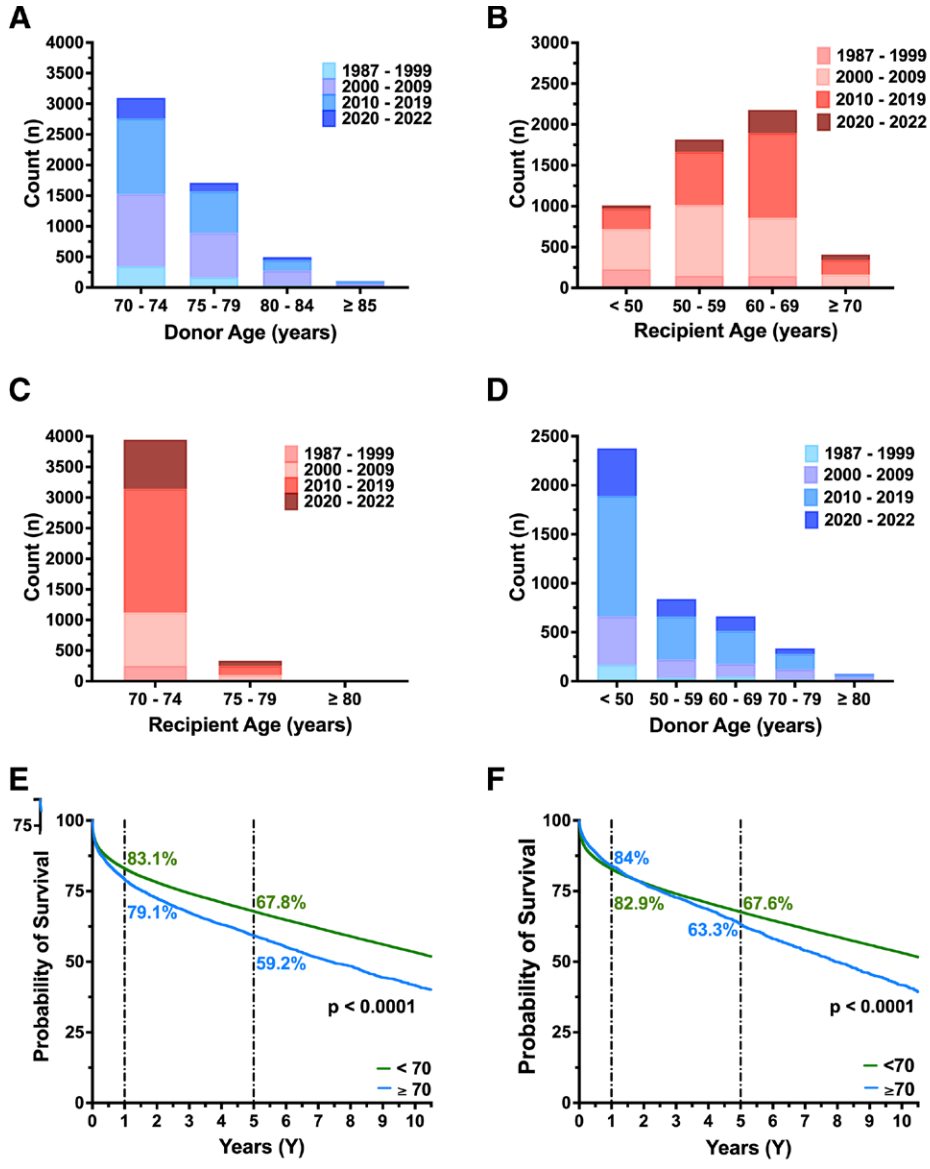

FIGURE 1. Donor and recipient ages and graft survival in older populations. A, Distribution of donors ≥70 y or age by decade during which transplant occurred. B, Distribution of recipients' age using grafts from elderly donors (≥70 y) by decade during which transplant occurred. C, Distribution of recipients ≥70 y of age by decade during which transplant occurred. D, Distribution of donors' age in transplants in elderly recipients (≥70 y) by decade during which transplant occurred. E, Graft survival in elderly donors (≥70 y) compared with younger donor (<70 y) with 1- and 5-y percentage graft survival. F, Graft survival in elderly recipients (≥70 y) compared with younger recipients (<70 y) with 1- and 5-y percentage graft survival.

with the moderate-risk recipient group (Figure 3B; Table 4). Only 6 grafts were allocated from elderly donors to recipients in the highest risk group, with low 1-, 3-, and 5-y actuarial graft survival when grafts from young and middle-aged donors were used (Figure 3C; Table 4).

Finally, the outcome of graft survival was assessed against the full spectrum of donor ages using cubic spline curves in transplants from 2010 to 2019. Such analysis demonstrated a reduction in 3 y and overall (Figure 3D) graft survival for the donor ages >80 y.

DISCUSSION

This study provides evidence supporting the use of older donors in LT. Outcomes from elderly donor grafts have significantly improved over time, including when used in low-risk and younger recipients. This provides some evidence that we may more comfortably consider the use of selected older donors in younger patients. We find that the already well-validated BAR and SOFT scores[11,12,17,19-21] might serve as a helpful guide for programs because they seek to expand the donor pool. The population of older donors undoubtedly represents a biased cohort, in that only a highly selected proportion of otherwise ideal grafts are likely to be used at this age. This work is not intended to suggest that outcomes are equivalent with older grafts, but rather that a cautious expansion of donor age might be appropriate in such highly selected cases.

Liver aging is different than other organs, and it has been shown that some livers are more resistant to age-based insult than others. However, older hepatocytes have been shown

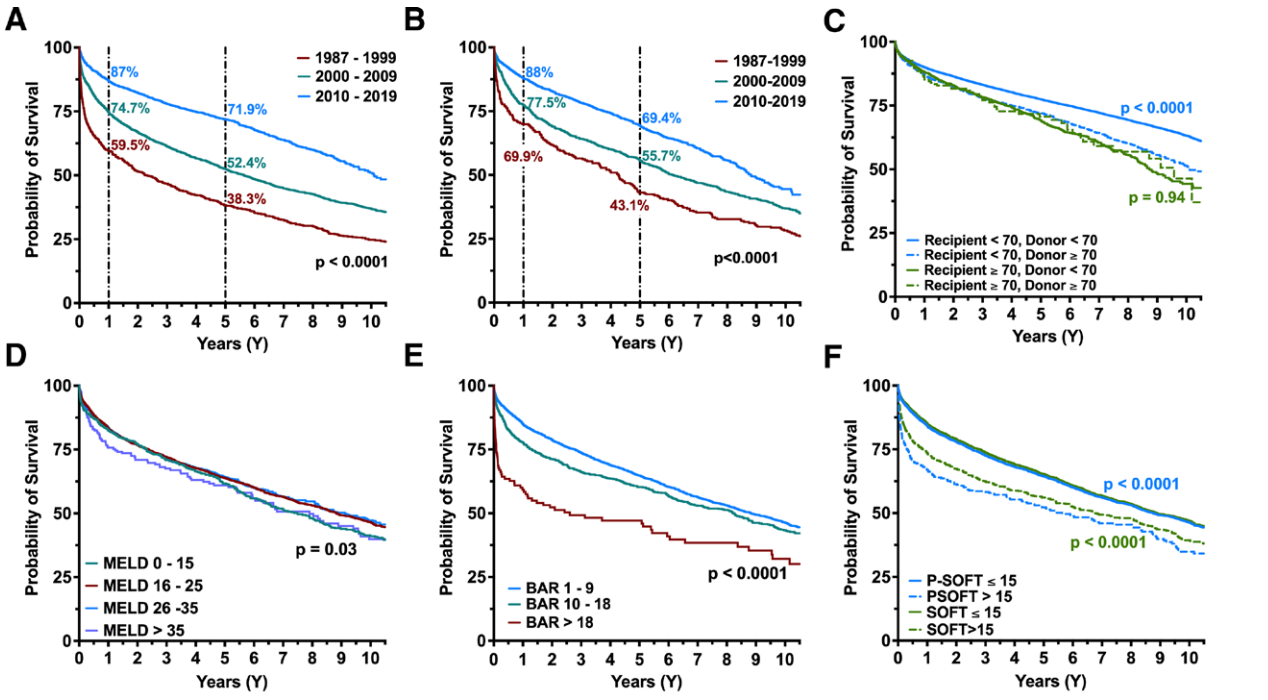

FIGURE 2. Graft survival stratified by decade transplant was performed and risk assessment score. A, Graft survival in donors ≥70 y of age by decade during which transplant was performed. B, Recipients ≥70 y of age by decade during which transplant was performed. C, Elderly donors (≥70 y) compared with younger (<70 y) donors within elderly (≥70 y) and younger recipient groups (<70 y). Graft survival in donors >70 y by risk score. D, Laboratory MELD. E, Balance-of-risk score.[11,17] F, PSOFT and SOFT scores.[12] BAR, balance of risk score; MELD, model for end-stage liver disease; PSOFT, preallocation survival outcomes following liver transplant; SOFT, survival outcomes following liver transplant.

as more susceptible to damage by reactive oxygen species produced during the ischemia–reperfusion injury in context of transplantation.[13,22,23] Furthermore, older liver cells demonstrate decreased synthetic function and reduced metabolic activity, which have caused concerns about implantation of such grafts.[24] These works also sparked concerns about subsequent graft longevity using livers that have already lived longer at time of transplantation, resulting in a general caution with use of "older" liver grafts. However, there have also been increasing reports of use of older liver grafts, even those up to 100 y at time of donation.[25-27] Additional work has shown that older liver grafts may be more resistant to transplant injury than previously thought, demonstrating that "changing the house" was not as detrimental to the ultimate lifespan of the graft as previously thought.[18] Unfortunately, research has shown that, despite select cases using older grafts, graft discard rates remained quite high in older donors.[28] One notable study on the topic concluded that "broader use of liver grafts from older donors might be reasonable," yet this has not fully borne out in practice.[28]

Our study adds to the growing body of literature supporting the expansion in use of elderly donors. Gilbo et al[29] reported in 2019 in a single-institution study of 849 patients that donors ≥70 y of age did not demonstrate reduced survival versus their younger counterparts. Multiple studies have highlighted the impact of recipient risk in survival outcomes with elderly grafts. Haugen et al[30] showed similar rates of graft loss in donors ≥70 y compared with young donors when utilized in low risk or "preferred" recipients. Preferred recipients were described as first-time, nonstatus 1 recipients older than 45 y with BMI <35 kg/m^2, non-hepatitis C virus-based indication and graft CIT of <8 h.[30,31] Shimada et al[32] developed a new recipient risk stratification system based on retransplant status, functional status measured through the Karnofksy score, need for mechanical ventilation, serum sodium, and presence of portal vein thrombosis. Elderly donors had similar outcomes as middle aged and young donors in low recipient risk groups. Our national analysis supplements these findings, as evidenced by worsening outcomes with increasing PSOFT score. Bittermann and Goldberg[33] highlighted that elderly donor grafts perform best in elderly recipients, and this is observed in the allocation of elderly grafts within our study, where most grafts were allocated to recipients ≥50 y of age. Our study finds similar results especially in the most recent transplants performed between 2010 and 2019. However, outcomes with use of elderly grafts in recipients <70 y has also improved with time.[34] Predominant use of elderly grafts in elderly recipients may contribute to the discrepancy in graft survival in elderly donors. Utilization of elderly grafts in nonaged recipients may be more feasible that previously though, especially as graft selection and posttransplant standard of care continues to improve. Furthermore, a recent meta-analysis found similar rates of posttransplant complications, such as primary nonfunction and vascular complications, in recipients receiving grafts from donors ≥80 y of age,[35] although these recipients experienced greater rates of biliary complications. Careful donor-recipient matching can circumvent these results, as donor hemodynamic instability, diabetes history, and use of octogenarian grafts in recipients with higher MELD have been identified as risk factors associated with development of biliary complications.[36]

These findings highlight the importance of the metabolic state of the liver, rather than the age of the graft alone. This fits with previous works showing that markers of mitochondrial

TABLE 3.

Median and actuarial 1-, 3-, and 5-y graft survival in donors aged >70 y stratified by recipient and donor age groups in transplants performed between 2010 and 2019

Outcomes	All included patients (57 525)	Donor <70 (55405)	Donor ≥70 (2120)	*P*	Donor subcohorts 70–74 (1234)	75–79 (678)	≥80 (208)	Donor <70, recipient <70 (n = 53 404)	Donor ≥70, recipient <70 (n = 1942)	*P*	Donor < 70, recipient ≥ 70 (n = 2001)	Donor ≥ 70, recipient > 70 (n = 178)	*P*	DCD < 70 (3968)	DCD ≥ 70 (105)	*P*
Median graft survival	11.9 (5.7–NA)	11.8 (5.6–NA)	10.1 (3.8–11.5)	**<0.0001**	10.9 (4.3–11.5)	9.4 (3.6–11.5)	8.9 (2.4–11.6)	11.9 (5.7–NA)	10.1 (3.9–11.5)	**<0.0001**	8.73 (3.71–11.4)	9.1 (3.4–10.2)	0.94	11.6 (6.1–NA)	10.1 (4.2–11.5)	**0.02**
Actuarial 1-y graft survival	89% (n = 51 192/ 57 256)	89% (n = 49 357/ 55 149)	87% (n = 1835/ 2107)	**0.0006**	88% (n = 1076/ 1226)	86% (n = 583/ 674)	85% (n = 176/ 207)	90% (n = 47 610/ 53163)	87% (n = 1684/ 1931)	**0.0013**	88% (n = 1747/ 1986)	86% (n = 151/ 176)	0.40	90% (n = 3556/ 3950)	84% (n = 88/ 105)	0.05
Actuarial 3-y graft survival	80% (n = 39 583/ 49470)	80% (n = 38 208/ 47639)	75% (n = 1375/ 1831)	**<0.0001**	77% (n = 815/ 1063)	74% (n = 430/ 582)	70% (n = 130/ 186)	80% (n = 37 010/ 46020)	75% (n = 1273/ 1690)	**<0.0001**	74% (n = 1198/ 1619)	72% (n = 102/ 141)	0.69	81% (n = 2831/ 3484)	74% (n = 69/93)	0.11
Actuarial 5-y graft survival	68% (n = 26 482/ 38 679)	69% (n = 25 588/ 37 239)	62% (n = 894/ 1440)	**<0.0001**	63% (n = 519/ 822)	61% (n = 285/ 467)	60% (n = 90/ 151)	69% (n = 24 922/ 36 050)	62% (n = 827/ 1327)	**<0.0001**	56% (n = 666/ 1189)	59% (n = 67/ 113)	0.55	71% (n = 2011/ 2829)	64% (n = 48/75)	0.20

Bold values indicate statistical significant with *P* value <0.05.DCD, donation after circulatory death.

TABLE 4.

Actuarial 1-, 3-, and 5-y graft survival in young (0–39 y), middle age (40–69 y), and elderly (≥70 y) donors stratified by recipient risk based on PSOFT score

Donor age	PSOFT low risk (0–5) 0–39 y (n = 8680)	40–69 y (n = 8009)	≥ 70 y (n = 694)	*P* (≥70 vs 40–69)	*P* (≥70 vs <40)	PSOFT moderate risk (6–35) 0–39 y (n = 18 451)	40–69 y (n = 18 324)	≥70 y (n = 1397)	*P* (≥ 70 vs 40–69)	*P* (≥ 70 vs <40)	PSOFT high risk (>35) 0–39 y (n = 213)	40–69 y (n = 128)	≥70 y (n = 6)	*P* (≥70 vs 40–69)	*P* (≥70 vs <40)
Actuarial 1-y graft survival	94% (n = 8092/ 8645)	91% (n = 7290/ 7972)	92% (n = 633/ 691)	0.94	0.05	89% (n = 16 328/ 18 362)	88% (n = 16 024/ 18 235)	85% (n = 1180/ 1387)	**0.003**	**<0.0001**	69% (n = 148/213)	57% (n = 73/128)	50% (n = 3/6)	>0.99	0.3775
Actuarial 3-y graft survival	86% (n = 6441/ 7496)	82% (n = 5677/ 6911)	78% (n = 466/ 594)	**0.03**	**< 0.0001**	80% (n = 12 611/ 15 750)	77% (n = 12 127/ 15715)	74% (n = 897/ 1213)	**0.012**	**<0.0001**	61% (n = 120/197)	47% (n = 55/118)	20% (n = 1/5)	0.35	0.16
Actuarial 5-y graft survival	77% (n = 4475/ 5816)	71% (n = 3908/ 5543)	67% (n = 327/ 487)	0.120	**<0.0001**	69% (n = 8295/ 12 097)	64% (n = 7841/ 12 238)	60% (n = 555/ 929)	**0.009**	**<0.0001**	44% (n = 71/160)	31% (n = 30/97)	20% (n = 1/5)	>0.99	0.39

Bold values indicate statistical significant with *P* value <0.05.PSOFT, preallocation survival outcomes following liver transplant.

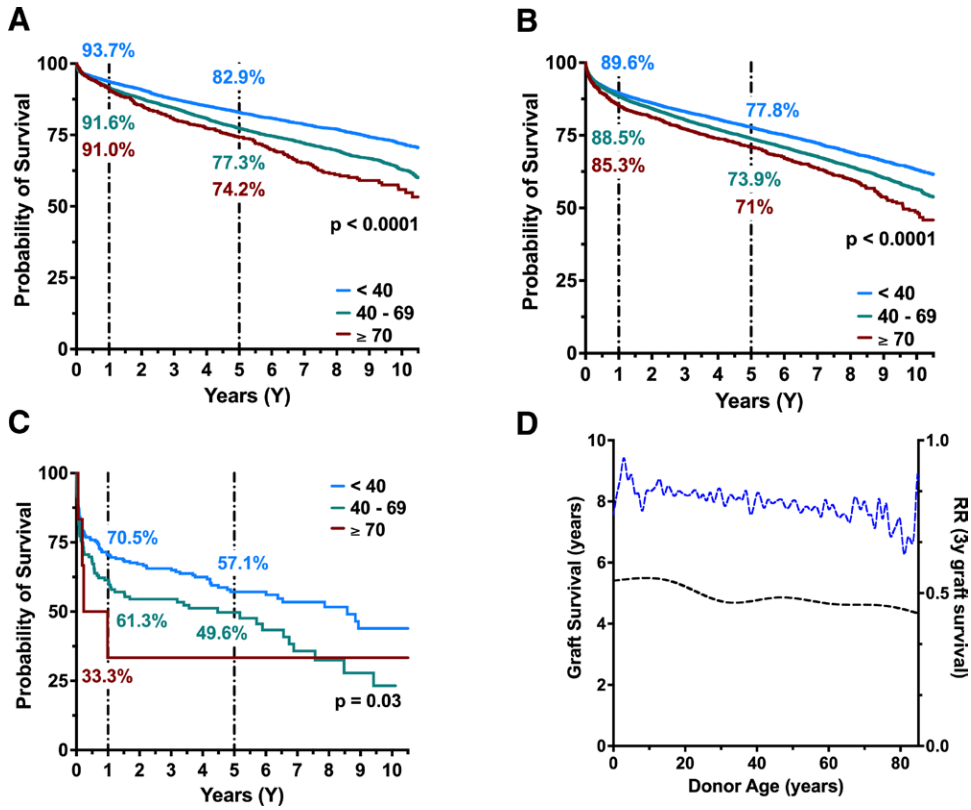

FIGURE 3. Graft survival by donor age based on recipient risk at time of transplant. A, Low PSOFT (0–5) recipient cohort with 1- and 5-y graft survival by donor age. B, Moderate PSOFT (6–35) recipient cohort with 1- and 5-y graft survival by donor age. C, High PSOFT (>35) recipient cohort with 1- and 5-y graft survival by donor age. D, Spline curves for overall (black) and 3-y actuarial (blue) graft survival by donor age. PSOFT, preallocation survival outcomes following liver transplant; RR, relative risk; SOFT, survival outcomes following liver transplant.

dysfunction, which report on the metabolic activity of the liver, predict graft outcomes.[37-40] Machine perfusion is being increasingly utilized within LT and can significantly expand the use of elderly grafts through metabolic reprogramming and viability assessment.[38] Several studies have highlighted the use of hypothermic oxygenated machine perfusion in improving survival and posttransplant complication rates in elderly donors.[41,42] Similarly, studies have shown safe transplantation of elderly grafts and extended criteria grafts with normothermic machine perfusion treatment.[43-45] Torri et al[46] performed a randomized control trial in elderly DCD donors exposed to hypothermic oxygenated machine perfusion or normothermic machine perfusion following normothermic regional perfusion. No significant difference was found in posttransplant complications and survival between the 2 perfusion groups, although the cohort size was small.[46] Sequential hypothermic and normothermic perfusion have also been shown to improve outcomes in elderly donors, with a recent study highlighting decreased incidence of nonanastomotic strictures with ex situ perfusion compared with static cold storage.[47]

Finally, we find that previously validated scores such as the BAR or SOFT scores might serve as a helpful guide in this cautious expansion. The BAR score (https://www.assessurgery.com/bar-score/bar-score-calculator/) is a simple, 6-item risk score first described in 2011 by the Zurich group.[11,17] This score was unique when described due to its' inclusion of donor (donor age), recipient (MELD score, retransplantation, life-support, age), and transplant factors (CIT) into 1 comprehensive score. It is interesting that the primary contributors to the BAR score (4 of 6 items) are recipient risk factors. The SOFT score utilizes a total of 18 recipient and donor risk factors to predict posttransplant outcomes, making it more difficult to calculate before transplant. Risk characterization by PSOFT score, based entirely on pretransplant recipient risk factors, significantly impacted graft survival in elderly donors within our cohort. Thus, these scores plus on-pump markers of graft viability, particularly markers of metabolic/mitochondrial function, might synergistically help us utilize these older grafts in a safe way.[37-40]

This study has limitations. Most notably, there is a clear likelihood that donors aged ≥70 y are vulnerable to significant selection bias. Surgeons are likely to accept only the best-quality livers in very old donors, where they might accept fattier or more damaged grafts that are younger in age. As such, this study only serves as a preliminary indication that older grafts may be considered, and cannot replace careful assessment of donor, recipient and transplant factors in each case. Our analysis found that the older cohorts are not extremely different with respect to traditional risk factors versus the general population, but this is only a very rough estimation of other un-recorded risk factors. As with all database studies, this is limited by the quality of the national data, and the primary outcome is vulnerable to reporting issues, particularly if graft loss is underreported, or patients are lost to follow-up. It would be ideal to have information on metabolic parameters (steatosis, markers of mitochondrial dysfunction, additional donor risk factors),

though these are not recorded in the SRTR database. Finally, we cannot determine why older grafts were accepted in some cases, which means that we cannot ascertain the degree of selection bias present.

CONCLUSIONS

Liver grafts from donors >70 y of age do not seem as detrimental as previously thought in our analysis of this large US database, including when employed in slightly younger recipients. The BAR and SOFT scores might serve as a useful guide for the cautious increase in the use of these grafts. Future work should further study which of these older grafts can be used safely in addition to recipient risk profiles that would benefit most from these grafts.

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