Liver Transplantation in Elderly Patients: A Systematic Review and First Meta-Analysis

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ABSTRACT

Background and Aims

Elderly recipients are frequently discussed by the scientific community but objective indication for this parameter has been provided.

Aim

Synthesize the available evidence on liver transplantation for elderly patients to assess graft and patient survival.

Methods

A literature search of the Medline, EMBASE, and Scopus databases was carried out from January 2000 to August 2018. Clinical studies comparing the outcomes of liver transplantation in adult younger (< 65 years) and elderly (> 65 years) populations were analyzed. The primary outcomes were patient mortality and graft loss rates. This review was registered (Number CRD42017058261) as required in the international prospective register for systematic review protocols (PROSPERO).

Results

Twenty-two studies were included involving a total of 242,487 patients (elderly: 23,660 and young: 218,827) were included in this study. In the meta-analysis, the elderly group had patient mortality (hazard ratio [HR]: 1.26; 95% confidence interval [CI]: 0.97-1.63; P = 0.09; I^2 = 48%) and graft (HR: 1.09; 95% CI: 0.81-1.47; P = 0.59; I^2 = 12%) loss rates comparable to those in the young group.

Conclusions

Elderly patients have similar long-term survival and graft loss rates as young patients. Liver transplantation is an acceptable and safe curative option for elderly transplant candidates.

Keywords: liver transplantation, outcomes, cirrhosis.

INTRODUCTION

The proportion of the global population older than 60 years will increase to 2 billion in 2050.[1] The health of this group is also improving: life expectancy at ages 65 and 75 increased from 16.4 years and 10.4 years in 1980 to 19.1 years and 12.1 years in 2010, respectively.[2,3] Therefore, surgeons are performing surgical procedures on an increasing number of elderly patients,[4] including organ transplantations.[5,6] The demand for grafts for the elderly is increasing in the field of liver transplantation (LT); based on data from the United Network for Organ Sharing (UNOS), the proportion of registrants and recipients aged ≥ 65 or ≥ 70 years doubled from 8.1% to 17% and from 1.4% to 3.1% between 2002 and 2014, respectively.[7] The same trend is present in the European Liver Transplant Registry; between 2000 and 2015, the proportion of recipients aged ≥ 65 or ≥ 70 years increased from 5% to 13% and from 0.3% to 1.3%, respectively (European Liver Transplant Registry, http://www.eltr.org accessed on March 13, 2017). This increased demand for LT in the elderly is not only due to the aging of the general population but also specifically to the aging of patients infected with HCV and the overall increasing proportion of patients with nonalcoholic fatty liver disease (NASH) or hepatocellular carcinoma (HCC), both of which tend to affect older individuals.[8]

In the early years of LT, the upper age limit for its indication was 45-55 years.[9] Since the 1993 consensus on LT, the chronological age has been used as a dichotomized value, with the cut-off limit shifted to the physiological age.[10-13]

Although analyses of registries in the model for end-stage liver disease (MELD) era consistently show reductions in post-transplantation survival with increasing age, single center studies examining the impact of age on post-transplantation survival provide conflicting conclusions. A systematic review or meta-analysis comparing post-liver transplantation survival in older versus younger patients has not been performed. This knowledge gap was the impetus for the present systematic review of the available literature and the first meta-analysis

comparing post-liver transplantation survival rates in older and younger patients. Our secondary objective were to assess graft survival in elderly patients and to compare to young patients who underwent elective liver transplantation.

METHODS

Literature search

The systematic review and meta-analysis were performed in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement[14] using identified published articles comparing short-and long-term outcomes following LT between young and elderly patients.

This review was registered (Number CRD42017058261) as required in the international prospective register for systematic review protocols (PROSPERO, www.crd.york.ac.uk/prospero/).

Study selection

By applying the PICO (Population, Intervention, Comparison, Outcome)[15,16] framework, the study selection criteria for the meta-analysis were: (i) Participants: adults who underwent liver transplantation, (ii) Interventions: adult liver transplant obtained from a cadaveric donor, (iii) Comparisons: liver transplantation in elderly patients vs. young patients, and (iv) Outcome measures: the primary outcomes were one- and five-year patient and graft survival rates.

Outcome measures

The primary outcomes assessed were patient mortality and graft loss rates. The secondary outcomes were perioperative morbidity and 90-day mortality.

Data extraction and quality assessment

An electronic search was formulated in collaboration with a medical librarian. The literature analysis was restricted to articles published between 2000 and 2018 and was not limited by publication language. The literature search was performed through the online databases MEDLINE (through PubMed), EMBASE, Scopus, Google Scholar, Cochrane Hepatobiliary Group Specialized Register, and ProQuest Dissertations and Thesis Database. To increase the probability of identifying relevant articles, a specific search strategy was formulated for each database using the following keywords and/or MeSH terms with equivalent free text: liver transplantation, orthotopic liver transplantation, liver transplant, elderly, advanced age, and/or recipient age.

In addition, reference lists from eligible studies and relevant review articles (not included in the systematic review) were crosschecked to identify additional studies. The literature review was carried out in articles published from January 2000 to April 2018 because after 2000 publications about liver transplantation in elderly patients increased. Two reviewers (FE and CG) independently screened the titles and abstracts of the retrieved studies for relevance. Records were removed only if both reviewers excluded the record at the title screening level. All disagreements were resolved by discussion with a third reviewer (DA). Subsequently, both reviewers performed a full-text review of the selected articles. The Grading of Recommendations Assessment Development and Evaluation (GRADE) system[17] was used to enable consistent judgment of the "body of evidence" (rated as high, moderate, low, and very low) of the studies included in the systematic review and meta-analysis. Additionally, when

researchers from the same center published more than one study, information from the different papers was retrieved according to the variable(s) analyzed.

Data from the studies included in the systematic review and meta-analysis were processed for qualitative and possibly quantitative analyses. Outcome measures (mean values, standard deviations, ranges and p-values) were extracted for each variable.

Data synthesis and analysis

Data from included studies were pooled, the quality was classified according to the GRADE system and after meta-analysis was performed. Statistical analyses were performed using Review Manager 5.3 software (Cochrane collaboration, Oxford, England).

The hazard ratio (HR) was used as a summary statistic for patient mortality and graft loss rates. An HR of less than 1 represented a survival benefit favoring elderly patients, whereas P values < 0.05 and 95% confidence intervals (CIs) lacking a value of 1 supported the statistical significance of the HR.

The fixed-effect model was first used to pool the results. Heterogeneity was assessed using the I^2 statistic. When the data were heterogeneous, a meta-analysis was performed using the random-effects model.[18,19] An I^2 value ranging from 0 to 40% was defined as acceptable heterogeneity, a value ranging from 30 to 60% was defined as moderate heterogeneity, a value ranging from 50 to 90% was defined as substantial heterogeneity, and a value ranging from 75 to 100% was defined as considerable heterogeneity, according to Cochrane Handbook Guidelines.

A meta-analysis was not performed for secondary endpoints (i.e., perioperative morbidity and mortality) in the present study due to the heterogeneity of the selected studies.

Publication bias was not investigated because of the low sensitivity of the qualitative and quantitative tests when the number of studies is lower than ten[20].

The statistical methodology used here was performed under the guidance of an expert in systematic reviews and meta-analyses (KG).

RESULTS

Literature search

Of the 822 initially identified articles, 22 articles[7,21-41] met the inclusion criteria and were selected for the present study. **Figure 1** shows the forest plot of study identification and the inclusion/exclusion process. All selected reports were published in English.

Study characteristics

The selected studies were performed in ten countries. Eight studies used data from registries,[7,22,24,26,27,29,32,37] two were comparative series,[30,41] and the remaining 12 were all single-center retrospective reviews of a cohort of adult deceased-donor LT[25,31,33-36,38-40] or living donor LT[21,23,28] in elderly versus younger recipients. The overall number of transplanted patients was 242,487, i.e., 218,827 patients (90.2%) in the young group, and 23,660 patients (9.7%) in the elderly group. Only data from patients included in single-center series were included in the meta-analysis to obviate the redundant inclusion of patients reported both in single center series and in registry series.

Study quality assessment

Obviously, no controlled studies were identified. The studies were epidemiological studies, case control studies, and case series with various methods and aims. A meta-analysis is not currently available. According to the GRADE system, 17 (77.3%) studies[7,21-29,31-33,37-40] were considered low quality, and the remaining 5 studies[30,34-36,41] had a very low quality of evidence.

Systematic review

Definition of elderly

Elderly was defined as a recipient age > 63 years in one study,[35] > 65 years in thirteen studies,[7,21,22,24,25,27,28,31,33,34,37,38,40] > 70 years in seven studies,[23,26,29,32,36,39,41] and > 75 years in one study[30] (**Table 1**). The oldest reported recipient was 80 years old[30] .

Young recipients were defined as < 70 years in six studies,[23,26,29,32,39,41] < 65 years in thirteen studies,[7,21,22,24,25,27,28,31,33,34,37,38,40] < 60 years in two studies,[30,36] and < 40 years in one study[35].

Comorbidities

Cardiovascular diseases were present in 4.1% to 50% of the elderly recipients and in 2.5% to 15% of the young recipients (**Table 1**). Two studies[26,33] reported a statistically significant higher prevalence of these comorbidities in the elderly, whereas 3 studies[21,36,38] did not report any evidence of difference in the comorbidities between age groups. This comparison was not performed in the remaining studies[7,22-25,27-32,34,35,37,39-41] .

Diabetes mellitus was present in 8.7% to 78% of the elderly recipients and in 11.7% to 68% of the young recipients. Two studies[7,27] reported a significantly higher prevalence of diabetes in the elderly group, whereas six studies[21,26,28,33,36,38] did not report any difference in the prevalence of diabetes mellitus. This comparison was not reported in the remaining studies[22-25,29-32,34,35,37,39-41].

Chronic hemodialysis was needed at the time of LT, with no evidence of a difference in prevalence in five studies,[21,26,33,36,38] and a significantly higher prevalence of chronic hemodialysis in the young recipients in another study[7]. The comparison was not reported in the remaining studies[22-25,27-32,34,35,37,39-41].

Indications for transplantation

Twenty studies reported the indications for LT[7,21-31,34-41] (**Table 2**).

Hepatocellular carcinoma was the most common indication for LT in the elderly in 4 studies[7,26,28,38] and was significantly more frequently observed in elderly patients than in young patients in these studies. Three studies[21,34,40] showed no significant difference in the incidence of hepatocellular carcinoma between the 2 groups.

Chronic viral hepatitis was the most common cause of LT in young patients in 5 studies[7,26,27,29,40] and was significantly more frequently observed in young patients than in elderly patients in these 5 studies. Two studies[28,38] showed a higher frequency of viral hepatitis in the elderly group. Three studies[21,25,34] did not report a significant difference in the incidence of viral hepatitis between the 2 groups.

Alcohol-related liver disease was more frequently observed in the young group (ranging from 3.1% to 31%) than in the elderly group (ranging from 6.5% to 19%). Four studies[7,24,26,38] reported a significantly higher incidence of alcohol-related liver disease in younger patients. Three studies[25,34,40] did not show a significant difference in the incidence of alcohol-related liver diseases between the 2 groups.

MELD score

The MELD scores for candidates for LT were reported in 17 studies[7,21-25,27-31,33-36,39,40] (**Table 2**).

In 5 studies,[7,27,28,39,40] the elderly group displayed a significantly lower MELD score, but a difference was not observed in 6 studies[21,32,25,31,33,34]. This comparison was not reported in the remaining studies[22,24,26,29,30,32,35-38,41].

Waitlist outcomes

Only two studies reported waitlist outcomes,[7,34] including dropout and death. Su et al.[7] reported a significantly higher risk of dropout from the waiting list and subsequent death before LT in

the older candidate group. Montalti et al.[34] reported a significantly higher risk of exclusion during the screening phase in the elderly group but no statistically significant differences in terms of dropout from the waiting list or death while on the waiting list or after LT between groups.

Donor characteristics

Ten studies[7,23,28,30,33,34,36,38-40] compared the donor age between the two groups. Only one study[7] showed a significantly higher donor age in the elderly group; the remaining 9 did not show any significant difference[23,28,30,33,34,36,38-40] (**Table 1**).

Other variables, such as the donor risk index, were not available for analysis.

Short-term outcomes

Perioperative deaths were reported in 5 studies;[23,33,38,40,41] in 3,[23,33,40] a significant difference was not detected between the two groups, and in the remaining studies, mortality was reported in only one of the groups[38,41]. Therefore, we were not able to determine whether there was a potential difference in perioperative mortality between groups (**Table 3**).

Six studies reported postoperative morbidity[21,28,33,34,36,38] (**Table 3**). Significant differences in the rates of technical complications or major infections were not observed between the 2 groups. Two studies[28,38] reported a significantly lower rate of acute rejection in the elderly group, whereas a significant difference in this variable was not identified in seven studies[21,31,33-36,40].

Three studies[28,34,38] reported neuropsychiatric postoperative complications. Only one[28] reported a significantly higher rate of neurological complications in the elderly group. The remaining two studies did not report any difference between the two groups [34,38].

Meta-analysis

Patient mortality

Seven studies compared patient survival using 65 years as the age cut-off[25,27,28,40] .

According to the results of the meta-analysis, patient mortality was not significantly different between the groups at the maximum follow-up interval (HR: 1.26; 95% CI: 0.97-1.63; P = 0.09; I^2 = 48%). Other studies[20,28,33,34] used different cut-off values and did not show differences **(Figure 2)**.

Graft loss

Three studies compared graft survival in patients < 65 years old with that in patients ≥ 65 years old[28,37,40]. None clearly defined how graft survival was calculated. In the meta-analysis, graft loss was not significantly different between groups at the maximum follow-up interval (HR: 1.09; 95% CI: 0.81-1.47; P = 0.59; I^2 = 12%). Other studies with different cut-off values did not show any difference in graft survival **(Figure 3)**.

DISCUSSION

The present systematic review and first meta-analysis of LT in the elderly yielded several main key points: *i)* The number of liver transplantations for the elderly increased exponentially during recent decades. *ii)* The cut-off age limit for recipients of LT increased from 50 to ~65 years, despite all successive consensus since 1993 and guideline reports that regularly stated

that the chronological age *per se* should not be used as a contraindication and that physiological age should be favored over chronological age. *iii)* LT in elderly and young patients achieves similar short-term outcomes. *iv)* Long-term outcomes of LT in the elderly were not different from those in younger recipients in the meta-analysis, whereas increases in the survival rate might be comparable (however, because confidence intervals were large, the lack of evidence cannot be considered equivalent to the absence of a difference). *v)* The level of evidence in the studied setting is poor and the limited data available hampered the meta-analysis of several important variables.

We were not able to clarify the selection of older candidates for LT. However, several studies stressed the importance of a preoperative evaluation of cardiovascular comorbidities,[42-44] because cardiovascular events, which occur in up to 41% of LT recipients,[45] remain the most common cause of death following liver transplantation in the elderly, with the highest rates occurring within 6 months of transplantation. A recently reported first meta-analysis of cardiovascular events following LT showed[45] that these events *i)* remain to be clearly defined, *ii)* have an increased incidence with incremental increases in age (effect size 1.02-1.17 per year) and the presence of an underlying cardiac disease (effect size 1.8-7.7), *iii)* are predicted with variable accuracy by dobutamine stress echography, and *iv)* are not accurately predicted by any of the models proposed to date.

The same poor level of evidence and confusion pertains to respiratory[46,47] and neurological complications[48].

We suspect that the significantly higher rate of exclusion during the screening phase before listing patients ≥ 65 years compared to patients < 65 years, as reported by Montalti et al.[34], is frequent.

The elderly group presented a significantly lower MELD score in half of the studies reporting this variable, reflecting the probable conservative selection of older patients. As a result of the

MELD score allocation system, a program of "old to old", such as the one developed for kidney transplantation by the European Senior program, does not exist in the field of LT[49].

Perioperative death, technical complication and major infection rates were not different between younger and elderly groups. Again, a conservative selection bias of elderly recipients might be responsible for this counterintuitive result. None of the studies analyzed here provided a prediction model for postoperative death (futile transplantation).

Only 2/7 studies analyzing the incidence of acute rejection showed a significantly lower incidence in the elderly group,[28,38] whereas 5 did not[21,31,33-36,40]. In the United Network for Organ Sharing database, Tullius and Milford[50] observed a steady decrease in acute rejection with increasing recipient age. Due to immunosenescence effects it has been hypothesized that rejection rates appear less frequent in older recipients. The aging process imposes a threat to diversity, because thymic function deteriorates and it appears to play a critical role for compromised adaptive immune responses, although precise mechanisms remain unclear[51,52].

The only conclusion of the meta-analysis was that patient and graft survival rates were not significantly different between elderly and younger recipients. Further studies are needed to confirm these *a priori* counterintuitive results.

Strengths and limitations

To the authors' knowledge, this study represents the first meta-analysis comparing survival following LT between elderly and young transplant recipients. This review was performed by two observers who independently selected studies and extracted data using a formal systematic review methodology according to the PRISMA guidelines.

This study has inherent limitations. First, selection bias may explain the results of this meta-analysis. In particular, a lower MELD score was observed for elderly patients than younger patients, which appeared to compensate for the increased incidence of comorbidities and

diabetes. Second, some publication bias may exist. Some studies indicating clearly lower survival rates in elderly patients may not have been submitted for publication. Third, a standardized definition of graft loss is not available. In particular, were people who died with a functioning graft considered to have graft loss? Fourth, we acknowledge that the present meta-analysis is based on a limited number of studies with some ambiguity in the definition of elderly patients. In addition, the limited availability of data for the elderly population hampered the meta-analysis of several important variables, such as waitlist outcomes and post-LT morbidity and mortality.

Future research

The following issues remain to be addressed in the field of LT in the elderly: the prognostic value of frailty[53], methods to improve the acknowledged failure-to-rescue[54], the specific refinements of available expert guidance for long-term survivors[55], specifically in terms of cardiovascular events, immunosuppression in the setting of frequent polypharmacy[56], functional[57] and cognitive impairment[58], and, obviously, quality of life[59]. Additionally, the concept of a cure, i.e., when the mortality of patients treated for a specific disease returns to the same level as the general population[60] , remains to be applied to this subset of patients.

CONCLUSIONS

In conclusion, although some articles reported a worse long-term survival rate in elderly patients, the present meta-analysis does not confirm this finding. Advanced age alone should not exclude a patient from LT. Careful preoperative screening, particularly for cardiovascular disease, and meticulous and adapted follow-up monitoring are mandatory.

Supporting information

Figure legends

S1 Fig. Flow chart of study search, selection, and inclusion. Search strategy for PubMed: (((Liver transplantation [Title/Abstract]) OR orthotopic liver transplantation [Title/Abstract]) OR Liver transplant [Title/Abstract]) AND Humans [Mesh] AND English [lang] AND adult [MeSH]) AND elderly [Title/Abstract]) OR elderly patient [Title/Abstract]) OR older [Title/Abstract]) OR older patient [Title/Abstract]) OR advanced age [Title/Abstract]) OR patients aged [Title/Abstract]) OR recipient age [Title/Abstract]).

S2 Fig. Forest plots describing the result of the meta-analysis comparing patient survival in elderly and young transplant recipients.

S3 Fig. Forest plots describing the result of the meta-analysis comparing graft survival in elderly and young transplant recipients.

Tables Legends

S1 Table. Baseline characteristics in Young and Elderly groups

S2 Table. Indications for transplantation in Young and Elderly groups

S3 Table. Postoperative complications in Young and Elderly groups

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PRISMA 2009 Forest Plot

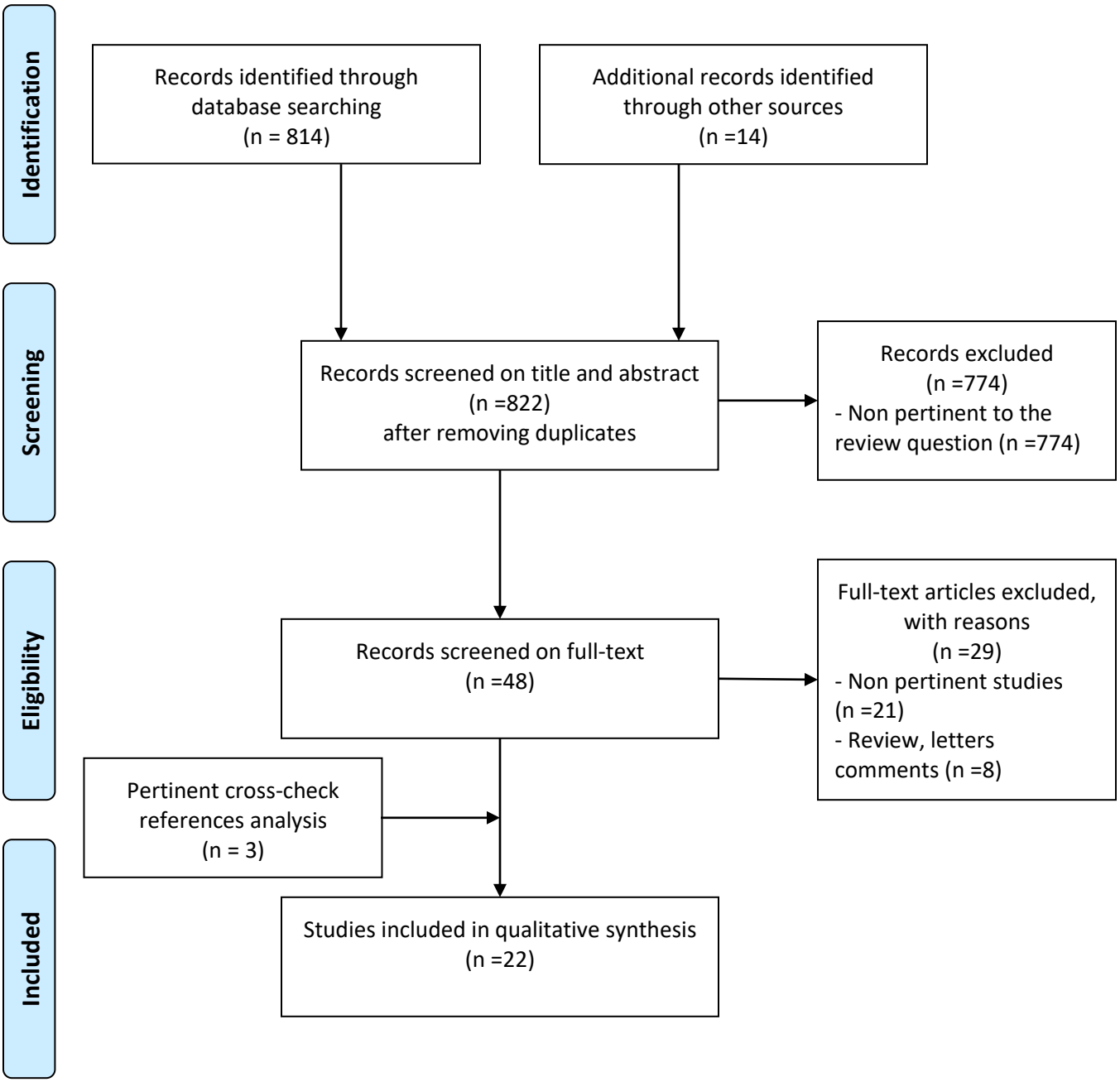

Table 1: Baseline characteristics in Young and Elderly groups

Year	1st author, Country	Age (yr)			Male sex (%)			Co-morbidities: 1. Diabetes Mellitus 2. Cardiovascular disease 3. Kidney disease			Donor Age		
		Younger Group	Elderly group	P value	Younger Group	Elderly group	P value	Younger Group	Elderly group	P value	Younger Group	Elderly group	P value
2016	Su F, UNOS[7,22,24,26,27,29,30,32,36,37,39,41*]	18-64	>65	nr	63-71%	74-77%	nr	1. 14-32% 2. nr 3. 11-12%	1. 32-34% 2. nr 3. 7-10%	s ns s	39.4±16.4 42.3 ±17.2	43.7±17.8 46.3±18.6	s
2015	Abdelfattah MR, Egypt[21]	60-64	>65	nr	70%	80%	ns	1. 53.3% 2. 3.4% 3. 16.7%	1. 60% 2. 0% 3. 24%	ns ns ns	nr	nr	ns
2015	Oezcelik A, Turkey[23]	45-58	>70	s	nr	50%	nr	nr	nr	nr	33 (26-40)	40 (31-44)	nr
2014	Felga G, Brazil[25]	55.1 ± 6.7	68.5 ± 2.9	s	83.7%	67.6%	s	nr	nr	nr	nr	nr	nr
2014	Ikegami T, Japan[28]	49.8 ±11.2	67.0 ±2.2	s	48.5%	32.6%	s	1. 17.3% 2. nr 3. nr	1. 21.7% 2. nr 3. nr	ns nr nr	38.0 ± 4.7	36.3 ±11.8	nr
2012	Slattery E,Ireland[31]	18-≤65	>65	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr
2010	Audet M, France[33]	48 (18-65)	67.8 (66-72)	ns	71.9%	61.7%	ns	1. 15.6% 2. 12% 3. 9.1%	1. 11.7% 2. 50% 3. 11.7%	ns s ns	44 ± 13	52.5 ±16.7	ns
2010	Montalti R, ITA[34]	53.5 ± 6.9	65.8 ± 1.2	s	90.3%	83.9%	ns	nr	nr	nr	56 ± 18.4	57 ± 18.4	ns

2009	Adani GL, ITA[35]	37 (18-40)	65 (63-70)	nr	65.6%	73.8%	nr	nr	nr	nr	nr	nr	nr
2008	Bilbao I, SPA[38]	≤65	>65	nr	67%	67%	ns	1. 22% 2. 15% 3. 20%	1. 25% 2. 19% 3. 17%	ns ns ns	47 ± 18	44 ± 18	ns
2007	Cross TJS, GB[40**]	18-64	≥65	nr	54%-58%	67%	ns	nr	nr	nr	43 ± 15.1 44 ± 14.2	45 ± 15.3	ns

- Abbreviations: nr= not reported; s= significant (p-value < 0.05); ns= not significant (p-value > 0.05).
* Patients were *grouped* by *recipient age*: 18 to 49, 50 to 59, 60 to 64, 65 to 69 and ≥ 70 years.
** Patients were *grouped* by *recipient age*: 18 to 59, 60 to 64 and > 65 years.

Table 2: Indications for transplantation in Young and Elderly groups

Year	1st author, Country	Liver disease: 1. HCC 2. Viral hepatitis 3. Alcohol related			MELD Score		
		Younger Group	Elderly group	P value	Younger Group	Elderly group	P value
2016	Su F, UNOS[7,22,24,26,27,29,30,32,36,37,39,41*]	1. 14-40% 2. 41-58% 3. 13-15%	1. 42-51% 2. 35% 3. 13-15%	s s s	20.3±10- 23.9±10.7	18.4±9.6 19.8 ±10	s
2015	Abdelfattah MR, Egypt[21]	1. 49% 2. 70% 3. nr	1. 48% 2. 76% 3. nr	ns ns nr	14.8 ±5.6	14.1 ± 6.9	ns
2015	Oezcelik A, Turkey[23]	1. nr 2. 57% 3. 14%	1. nr 2. 58% 3. 8%	nr nr nr	16(12-20)	13(11-17)	ns
2014	Felga G, Brazil[25]	1. 100% 2. 80.1% 3. 12.1%	1. 100% 2. 70.2% 3. 16.2%	ns ns ns	13.1 ± 4.6	12.1 ± 5.4	ns
2014	Ikegami T, Japan[28]	1. 37.8% 2. 37% 3. nr	1. 76.1% 2. 71.7% 3. nr	s s nr	17.5 ±7.2	14.8 ± 4.9	s
2012	Slattery E,Ireland[31]	1. 13.9% 2. 13.9% 3. 18.6%	1. 17.5% 2. 2.5% 3. 12.5%	nr nr nr	15	14	nr
2010	Audet M, France[33]	nr	nr	nr	18.1 (12-32)	14.9 (12-29)	ns
2010	Montalti R, ITA[34]	1. 51.6% 2. 80.6% 3. 6.5%	1. 51.6% 2. 80.6% 3. 6.5%	ns ns ns	17.9 ± 8.1	17.1 ± 7.3	ns
2009	Adani GL, ITA[35]	1. 21.8% 2. 31.2% 3. 3.1%	1. 33.3% 2. 35.7% 3. 19%	nr nr nr	12 (5-36)	12 (6-29)	nr
2008	Bilbao I, SPA[38]	1. 33% 2. 49% 3. 31%	1. 55% 2. 72% 3. 17%	s s s	nr	nr	nr
2007	Cross TJS, GB[40**]	1. 7-11% 2. 18-22% 3. 13-15%	1. 26% 2. 7% 3. 12%	ns s ns	15.79±7.2 16.49±7.6	12.2 ± 5.1	s

- Abbreviations: nr= not reported; s= significant (p-value < 0.05); ns= not significant (p-value > 0.05).
* Patients were *grouped* by *recipient age*: 18 to 49, 50 to 59, 60 to 64, 65 to 69 and ≥ 70 years.
** Patients were *grouped* by *recipient age*: 18 to 59, 60 to 64 and > 65 years.

Table 3: Postoperative complications in Young and Elderly groups

Year	1st author, Country	Vascular 1. Hepatic artery thrombosis 2. Portal vein thrombosis 3. Total			Biliary 1. Anastomotic leak 2. Anastomotic stricture 3. Total			Major infection		
		Younger Group	Elderly group	P value	Younger Group	Elderly group	P value	Younger Group	Elderly group	P value
2016	Su F, UNOS[7,22,24,26,27,29,30,32,36,37,39,41*]	nr	nr	nr	nr	nr	nr	nr	nr	nr
2015	Abdelfattah MR, Egypt[21]	1. 3.3% 2. 6.7% 3. 16.7%	1. 8% 2. 0% 3. 8%	ns ns ns	1. 0% 2. 18.5% 3. nr	1. 4.3% 2. 17.4% 3. nr	ns ns nr	20%	20%	ns
2015	Oezcelik A, Turkey[23]	nr	nr	nr	nr	nr	nr	nr	16%	nr
2014	Felga G, Brazil[25]	nr	nr	nr	nr	nr	nr	nr	nr	nr
2014	Ikegami T, Japan[28]	1. 1.9% 2. 2.2% 3. nr	1. 0% 2. 0% 3. nr	ns ns nr	1. nr 2. 18.9% 3. nr	1. nr 2. 28.3% 3. nr	nr ns nr	13.4%	4.3%	s
2012	Slattery E,Ireland[31]	nr	nr	nr	nr	nr	nr	nr	nr	nr
2010	Audet M, France[33]	1. 6.1% 2. 2.7% 3. nr	1. 8.8 2. 5.8% 3. nr	ns ns nr	1. 2.7% 2. 5.5% 3. nr	1. 5.8% 2. 5.8% 3. nr	ns ns nr	8.3%	8.8%	ns
2010	Montalti R, ITA[34]	1. 0% 2. nr 3. nr	1. 6.5 2. nr 3. nr	ns nr nr	1. 0% 2. 22% 3. nr	1. 6% 2. 25% 3. nr	ns ns nr	16.1%	9.7%	ns

2009	Adani GL, ITA[35]		nr		nr		nr		nr		nr		nr	nr	nr	nr
2008	Bilbao I, SPA[38]	1. 2. 3.	2% 1% nr	1. 2. 3.	0% 4% nr		ns ns ns	1. 2. 3.	nr nr 7%	1. 2. 3.	nr nr 6%		nr nr nr	25%	15%	ns
2007	Cross TJS, GB[40**]		nr		nr		nr		nr		nr		nr	43 ± 15.1 44 ± 14.2	45 ± 15.3	ns

- Abbreviations: nr= not reported; s= significant (p-value < 0.05); ns= not significant (p-value > 0.05).
* Patients were *grouped* by *recipient age*: 18 to 49, 50 to 59, 60 to 64, 65 to 69 and ≥ 70 years.
** Patients were *grouped* by *recipient age*: 18 to 59, 60 to 64 and > 65 years.