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REVIEW ARTICLE

Recipient donor sex combinations in solid organ transplantation and impact on clinical outcome: A scoping review

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Abstract

Introduction: Solid organ transplantation (SOT) is a lifesaving treatment for end-stage organ failure. Although many factors affect the success of organ transplantation, recipient and donor sex are important biological factors influencing transplant outcome. However, the impact of the four possible recipient and donor sex combinations (RDSC) on transplant outcome remains largely unclear.

Methods: A scoping review was carried out focusing on studies examining the association between RDSC and outcomes (mortality, graft rejection, and infection) after heart, lung, liver, and kidney transplantation. All studies up to February 2023 were included.

Results: Multiple studies published between 1998 and 2022 show that RDSC is an important factor affecting the outcome after organ transplantation. Male recipients of SOT have a higher risk of mortality and graft failure than female recipients. Differences regarding the causes of death are observed. Female recipients on the other hand are more susceptible to infections after SOT.

Conclusion: Differences in underlying illnesses as well as age, immunosuppressive therapy and underlying biological mechanisms among male and female SOT recipients affect the post-transplant outcome. However, the precise mechanisms influencing the interaction between RDSC and post-transplant outcome remain largely unclear. A better understanding of how to identify and modulate these factors may improve outcome, which is particularly important in light of the worldwide organ shortage. An analysis for differences of etiology and causes of graft loss or mortality, respectively, is warranted across the RDSC groups.

KEYWORDS
donor-recipient matching, graft dysfunction, infection, mortality, recipient donor sex combination (RDSC), solid organ transplantation

Practitioner points

- Recipient and donor sex combinations affect outcome after solid organ transplantation.
- While female recipients are more susceptible to infections after solid organ transplantation, they have higher overall survival following SOT, with causes of death differing from male recipients.
- Sex-differences should be taken into account in the post-transplant management.

1 | INTRODUCTION

In the field of solid organ transplantation (SOT), a recent meta-analysis incorporating data from 2016 to 2021 with 1 045 380 patients has shown that female recipients (FR) have a lower mortality post SOT compared to male recipients (MR), (OR .87; 95% CI, .83–.92).[1] However, sexual dimorphism in human diseases is a still poorly studied field.[2] Some organs, such as the liver are sexually dimorphic, with over 1000 genes differentially expressed in men and women.[3] Recipient donor sex combinations (RDSC) results in four different possible combinations (Table 1) and may be grouped in either congruent (male donor to male recipient [MDMR] and female donor female recipient [FDFR]) or incongruent (female donor to male recipient [FDMR] and male donor female recipient [MDFR]).

Sex-related differences of immune responses have been observed (e.g., female patients exhibit more pronounced immune responses to influenza).[4–7] Previous reviews have shown that males are more prone to experience severe infections, whilst females tend to have stronger innate and adaptive immune responses.[8–10] Underlying different genetic mechanisms on a cellular level, sex hormones and their interaction with environmental conditions (including microbiome modulation) are largely seen as the reasons for the observed differences between male and female innate and adaptive immune responses.[9–11] Furthermore, sex differences in pharmacokinetics and pharmacodynamics of immunosuppressive medication, which are particularly relevant in SOT recipients, have been described.[12–17]

The extent of the impact of RDSC on clinical endpoints such as mortality, rejection or infections in organ specific analyses is insufficiently understood. To our knowledge, there currently is no synopsis discussing the reported effect of RDSC with its detailed phenotyping on outcome after SOT. In the following review, we summarize the current literature on the relevance of RDSC in solid organ transplantation for heart- (HT), kidney- (KT), liver- (LiT) and lung transplantation (LuT).

2 | METHODS

A scoping literature search was conducted to identify relevant studies. The electronic database of pubmed.gov was searched using different combinations of Medical Subject Headings (MeSH terms; e.g., aging/immunology*, epidemiologic factors, female, graft rejection, heart transplantation*, hospitalization, humans, immune system, immunity*, immunosuppressive agents, infections*, kidney transplantation*, liver transplantation*, lung transplantation*, male, mortality, organ transplantation*, postoperative complications, risk factors, sex characteristics, sex, tissue donors*, transplant recipients). Any studies from inception of the database up to February 2023 were included. Potentially relevant articles were selected and included based on their title and abstract. If an article contained relevant information, related articles suggested by pubmed.gov and other publications cited in the article were also considered for further investigation. Outcome focusing on mortality, graft rejection, and infection were extracted with publication dates ranging from 1998 to 2022. No statistical analysis was performed for this review.

3 | RESULTS

3.1 | Heart transplantation

3.1.1 | Highlights

- Mortality: female recipients have decreased mortality (OR .91) and FDMR has a 15% 1-year mortality rate (70.4%, respectively 29.6% 15-year overall survival).
- Rejection: conflicting data, female recipients tend to have lower risk.
- Infection: no significant differences shown until now, data are sparse.

3.1.2 | Mortality

A total of 10 studies were identified assessing mortality after HT (Table 2). An International Society of Heart and Lung Transplantation (ISHLT) registry study with 60 584 HT recipients found significantly differing overall survival (OS) and death censored allograft survival, with congruent RDSC HT showing superior OS compared to incongruent transplantations (for male recipients (MR): female donors (FD) vs. male donors (MD) adjusted hazard ratio (HR) 1.10; 95% CI, 1.04–1.17; $p < .001$).[18] In a meta-analysis with 76 175 patients, 1-year OS was significantly improved in congruent compared to incongruent RDSC HT (odds ratio (OR) 1.30; 95% CI, 1.25–1.35; $p < .001$); however, data

TABLE 1 Possible constellations of recipient sex and donor sex combinations (RDSC).

	Female donor	Male donor
Female recipient (FR)	FDFR	MDFR
Male recipient (MR)	FDMR	MDMR

Abbreviations: FDFR, female donor female recipient; FDMR, female donor male recipient; FR, female recipient; MDFR, male donor female recipient; MDMR, male donor male recipient; MR, male recipient.

quality for in-depth analysis of female recipients was considered too low as only 21% of all recipients were female.[19] In a large cohort 1-year OS for RDSC was best for MDMR (83.74%), followed by MDFR (82.94%), FDFR (81.92%), with worst survival seen in FDMR (78.95%).[20] Worst short- (1-year OS)[21] and long-term survival for FDMR in HT was also confirmed by other studies,[18] whereas MDMR proved to be the group with the best survival after 5 years (70.75%; $p < .001$).[20,22] In contrast, the higher risk for all-cause mortality, as well as elevated 1-year mortality and higher incidence of graft failure in FDMR compared to MDMR did not remain significant after risk factor adjustment in another study.[23] In a cohort of 347 HT recipients, RDSC did not significantly differ in death rates, survival time and incidence of infection and cardiac allograft vasculopathy (CAV) in the first year following HT.[24] In a 3-year follow-up, MDFR in HT showed higher mortality rates (MDFR: 41.2% vs. FDMR: 22.5%, $p = .023$) compared to the congruent RDSC group (17.9%, $p = .002$).[25]

When congruent and incongruent RDSC were compared, 1-year OS rates significantly differed with incongruent RDSC transplantation resulting in an 18% decreased 1-year OS ($p = .003$).[21] However, these results are most likely affected by a representative bias as male recipients ($n = 135$) overpowered female recipients ($n = 39$) in this cohort.[21] In a review by Previato et al. the outcomes of HT were largely determined by RDSC rather than recipient or donor sex individually.[26] The most frequent causes of death included infection and acute rejection following HT at the 1- and 3-year follow up analysis.[24,25] Major confounding factors for differences of RDSC on survival in HT are likely to be donor and recipient age as well as organ size mismatch, as it is possible that a female donor heart might not meet the cardiac demands in the FDMR constellation.[19] Donor under-sizing (weight ratio <70% recipient weight) occurs in 88.2% of FDMR which is associated with an increased all-cause mortality (adjusted HR 1.33; 95% CI, 1.17–1.52), with a higher HR than size-matching (predicted lean body mass ratios).[27]

3.1.3 | Rejection and graft failure

Five studies assessed RDSC for rejection or graft failure after HT (Table 2). Re-hospitalization within the first year following HT occurred most frequently due to acute rejection, infection, cardiovascular, and gastrointestinal complications.[28] Treated acute rejection, female recipients, and incongruent RDSC were identified as some of the significant predictors of re-hospitalization within the first year after HT.[28] A non-significant trend towards acute rejection was observed with incongruent RDSC, while female recipients tended to experience more infections than male recipients.[28] Similarly, other studies found that HT with incongruent RDSC presented with a higher number of rejections within the first year after HT,[21] mainly represented by highest number of rejection episodes in MDFR HT.[21,24] However, another study found a similar impact of donor sex on acute rejection and CAV in female recipients and male recipients alike, suggesting that such complications were not accountable for the observed differing survival rates.[18] The lack of observed differences may, however, be due to poor data quality confounding their results.[18]

3.1.4 | Infection

A non-significant trend towards the development of post-transplant infections was observed with incongruent RDSC, and female recipients tended to experience more infections than male recipients.[28] Infections proved to be one of the leading causes for readmission within the first 3 years following HT.[25]

3.2 | Kidney transplantation

3.2.1 | Highlights

- Mortality: Female recipients have decreased risk of mortality.
- Rejection: MDFR are at highest risk.
- Infection: Female recipients are at increased risk with variable odds ratio.

3.2.2 | Mortality

Female recipients have decreased risk of morality after KT (OR .82; 95% CI, .76–.89), but heterogeneity amongst available publications was high ($I^2 = 72\%$)[1] (Table 3). Early re-hospitalization appeared to be associated with increased mortality especially in younger KT recipients (age 18 to <65 years; adjusted HR 1.52; 95% CI, 1.47–1.57; $p < .001$).[29] A recent meta-analysis including 466 892 patients assessed in age stratified groups the impact of RDSC and found a higher excess mortality risk in female recipients, prominent in the MDFR group.[30]

3.2.3 | Rejection and graft failure

Incongruent RDSC was not a risk factor for graft failure, when analyzed separately.[31] In every RDSC, kidney transplant recipients with body weight-mismatch (recipient weight > donor weight), presented with an increased risk of graft failure or death with a functioning graft.[31,32] The highest risk for graft failure was observed in incongruent RDSC with recipients weighing ≥10 kg more than the donor

TABLE 2 Studies assessing sex differences for outcomes after heart transplantation.

	Recipient sex		RDSC										
			Congruent		Incongruent								
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Mortality	76.3%	79.5%	84.8%		66.7%		.003	1y survival	174	US single center	Lowest 1y OS in FDMR	1998	Prendergast[21]
	5y OS 73.7%	5y OS 70.1%	HR 1.06 95%CI .92, 1.23	Reference	HR 1.15 95%CI 1.02, 1.30	HR 1.25 95%CI 1.07, 1.43	.002	Mortality	18240	UNOS	Sex incongruence highly significant	2009	Weiss[22]
	–	–	–	Reference	aHR 1.10 95%CI 1.04–1.17	–	<.001	Overall survival	60584	ISHLT	–	2012	Khush[18]
	–	–	81.92% 95%CI 81.02, 82.82	83.74% 95%CI 83.38, 84.11	78.95% 95%CI 78.24, 79.65	82.94% 95%CI 82.00, 83.89	–	1y survival	67855	ISHLT	–	2013	Kaczmarek[20]
	–	–	68.83% 95%CI 67.68, 69.99	67.18% 95CI 66.68, 67.69	62.49% 95%CI 65.04, 66.76	68.94% 95%CI 67.72, 70.16	–	5y survival					
	–	–	37.05% 95%CI 35.19, 38.9	33.19% 95%CI 32.45, 33.94	29.63% 95%CI 28.42, 30.84	35.37% 95%CI 33.52, 37.21	–	15y survival					
	–	–	17.90%		22.50%	41.20%	.002	3y mortality	347	Bi-centric prospective 10y study	Mismatched groups $n = 40$ and $n = 34$, respectively	2017	Jalowiec[25]
	17.7%	18.4%	18.6%	16.6%	21.2%	18.2%	–	1y mortality	76175	Meta-analysis including 10 studies	Low quality data for 21% FR, most patients from study by Kaczmarek et al. 2013	2019	Ayesta[19]
			OR 1.30 95%CI 1.25, 1.35		Reference		<.001	1y survival					
	Reference	OR .91 95%CI .60, 1.39	–	–	–	–	.280	Mortality	34528	Meta-analysis	–	2022	Tejada[1]
	–	–	–	Reference	HR 1.23 95%CI .90, 1.67	–	.188	Mortality	19805	UNOS	Adjusted analysis not significant	2022	Doulamis[23]

(Continues)

TABLE 2 (Continued)

	Recipient sex		RDSC									
			Congruent		Incongruent							
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Rejection or graft failure	2.1 ± .3	2.5 ± .4	1.8 ± .2		2.6 ± .5		.040	1y number rejection episodes	174	US single center	Highest rejection numbers in MDFR	1998	Prendergast[21]
	–	–	–	Reference	OR 1.21 95%CI 1.05–1.39	–	.250	Acute rejection	8380	ISHLT	Tendency of higher incidence in FR, not statistically assessed	2012	Khush[18]
	–	–	3 ± 3		3 ± 4	5 ± 4	.008	3y acute rejection number episodes	347	US bi-centric	Mismatched groups $n = 40$ and $n = 34$, respectively	2017	Jalowiec[25]
	–	–	12.10%		12.50%	32.40%	.002	3y cardiac allograft vasculopathy					
	Reference	HR .54 95%CI .17, .9	–	Reference	–	HR .35 95%CI -.08, .78	.108	Treatment for rejection	19805	UNOS	Recipient sex significant difference, no other difference in RDSC found	2022	Doulamis[23]
Infection	–	–	2 ± 3		2 ± 3	2 ± 3	.984	3y number iv treated infections	347	US bi-centric	–	2017	Jalowiec[25]

Abbreviations: BE, Belgium; CAN, Canada; CN, China; DE; Germany; ELTR, European Liver Transplant Registry; ES, Spain; FDFR, female donor female recipient; FDMR, female donor male recipient; FR, female recipient; FRE, France; HR, hazard ratio; IL, Israel; ISHLT, International Society for Heart and Lung Transplantation; JP; Japan; MDFR male donor, female recipient; MDMR male donor male recipient; MR, male recipient; mult., multivariate; (a)OR, (adjusted) odds ratio; OS, overall survival; UNOS, United Network for Organ Sharing; RDSC, recipient donor sex combination; RETH, Registro Español de Trasplante Hepático; UK, United Kingdom; US, United states; TR, Turkey

TABLE 3 Studies assessing sex differences for outcomes after kidney transplantation.

	Recipient sex		RDSC									
			Congruent		Incongruent							
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Mortality	23.1%	20.2%	–	–	–	–	–	Mortality	159417	US Scientific Registry of Transplant Recipients database	–	2017	Lepeytre[88]
	–	–	#2: HR 1.06 95%CI .95, 1.19	Reference #1	#1: HR .94 95%CI .87, 1.03	Reference #2	#1 .174 #2 .302	Survival	25140	UK Transplant Registry	–	2020	Morgan[89]
	Reference	OR .82 95%CI .76, .89	–	–	–	–	.060	Mortality	193132	Meta-analysis		2022	Tejada [1]
Rejection or graft failure	–	–	aHR 1.08 95%CI 1.02, 11.14	Reference	aHR 1.10 95%CI 1.05, 1.15	aHR 1.08 95%CI 1.03, 1.13	–	Death-censored graft loss	115124	US Scientific Registry of Transplant Recipients	highest risk in MDFR with weight difference >30kg D<R	2017	Miller[32]
	–	–	#2: aHR .92 95%CI .68,1.2	Reference #1	Reference #2	#1: aHR 1.51 95%CI 1.19, 1.90	–	Death-censored graft failure rates	159417	US Scientific Registry of Transplant Recipients database	Age-dependent significant difference only in male donors	2017	Lepeytre[88]
	–	–	Reference		aHR 1.15 95%CI .83–1.60		.402	Graft loss	826	DE single center	significance was found for weight-difference ≥10kg	2019	Tillmann[31]
	–	–	86.0%	86.5%	85.3%	88.1%	.009	Zero episodes of rejection at 12 months	25140	UK Transplant Registry	–	2020	Morgan[89]
	–	–	#2 HR 1.08 95%CI .99, 1.118	Reference #1	#1 HR 1.01 95%CI .94, 1.09	Reference #2	.096	Graft survival					

(Continues)

TABLE 3 (Continued)

Outcome	Recipient sex		RDSC				*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
			Congruent		Incongruent								
	MR	FR	FDFR	MDMR	FDMR	MDFR							
Infection	Reference	aOR 5.8 95%CI 3.79, 8.89	–	–	–	–	–	UTI	500	US bi-centric	–	2005	Chuang[39]
	Reference	mult. OR 1.74 95%CI 1.42, 2.13	–	–	–	–	.001	UTI	2174	Multi-center, prospective cohort study (RESITRA cohort) of the Spanish Network for Research in Infectious Diseases (REIPI)	Kidney and kidney-pancreas transplant	2012	Vidal[37]
	Reference	pooled OR 3.11 95%CI 2.10, 4.13	–	–	–	–	.002	UTI	3364	Meta-analysis	13 studies included	2016	Wu[35]
	Reference	aIRR 2.04 95%CI 1.59, 2.61	–	–	–	–	<.001	Incidence of hospitalization for pyelonephritis	2656	Danish Nephrology Registry database	Incidence rate-ratio calculated with a population controls cohort	2016	Graversen[33]

(Continues)

TABLE 3 (Continued)

	Recipient sex		RDSC									
			Congruent		Incongruent							
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Infection	Reference	mult. HR 1.323 95%CI 1.103, 1.587	mult. HR 1.192 95%CI .992, 1.433	Reference	mult. HR 1.192 95%CI .992, 1.433	Reference	.003	Post-transplant infectious complications with hospitalization < 6 months	3738	Korean Organ Transplantation Registry (KOTRY) database	–	2020	Kim[36]
	Reference	OR 1.89 95%CI 1.01, 3.55	–	–	–	–	.047	Infection and infection hospitalization	207	US Single center retrospective	Selection: at least one episode of rejection within 1 year of transplant combined KT and simultaneous LiT/KT	2022	Gupta[38]
	27.0%	32.6%	–	–	–	–	.318	Incidence of bacterial infection during the perioperative period	295	CN single center retrospective	Median time of occurrence 6 days after KT	2022	Cheng[40]

Abbreviations: BE, Belgium; CAN, Canada; CN, China; DE; Germany; ELTR, European Liver Transplant Registry; ES, Spain; FDFR, female donor female recipient; FDMR, female donor male recipient; FR, female recipient; FRE, France; HR, hazard ratio; IL, Israel; ISHLT, International Society for Heart and Lung Transplantation; JP; Japan; MDFR male donor, female recipient; MDMR male donor male recipient; MR, male recipient; mult., multivariate; (a)OR, (adjusted) odds ratio; OS, overall survival; UNOS, United Network for Organ Sharing; RDSC, recipient donor sex combination; RETH, Registro Español de Trasplante Hepático; UK, United Kingdom; US, United states; TR, Turkey

compared to congruent RDSC with <10 kg (multivariate HR 2.00; 95% CI, 1.15–3.48; $p = .014$).[31] Similarly, incongruent RDSC with a weight mismatch >30 kg was identified to have the highest risk of graft failure (MDFR: adjusted HR 1.50; 95% CI, 1.32–1.70 and FDMR: adjusted HR 1.35; 95% CI, 1.25–1.45).[32] In this cohort, MDFR, FDFR, and FDMR combinations tended to have an increased risk of graft failure, compared to the MDMR combination,[32] possibly being confounded by the size-mismatch.

Overall, the combined risk of graft loss and death was 22%–45%, whereas the latter was observed in recipients who required hospitalization for pyelonephritis (IRR 1.22; 95% CI, 1.01–1.48; $p = .043$) in a median follow-up of 4.3 years.[33] ABO-incompatible versus ABO-compatible KT recipients necessitated more frequent treatment for rejection.[34]

3.2.4 | Infection

Female recipients have been reported to be at increased risk for developing a urinary tract infection (UTI) following KT (pooled OR 3.11; 95% CI, 2.10–4.13; $p < .01$).[33,35–39] Independent risk factors for bacterial UTI in recipients of kidney and kidney-pancreas transplants were age (multivariate OR per decade 1.10; 95% CI, 1.02–1.17; $p = .001$), female sex (multivariate OR 1.74; 95% CI, 1.42–2.13; $p = .001$) and the need for immediate post-transplant dialysis (multivariate OR 1.63; 95% CI, 1.29–2.05; $p = .001$).[37] Graversen et al. showed that risk factors for first-time hospitalization for pyelonephritis included female sex (aIRR 2.04; 95% CI, 1.59–2.61; $p < .001$).[33] In younger KT patients, female recipients exhibited a slightly increased risk for early hospital readmission (aRR 1.05; 95% CI, 1.02–1.07; $p < .001$), whereas older male recipients and older female recipients had a similar risk (aRR .96; 95% CI, .92–1.00; $p = .07$).[29] Moreover, female recipient was an independent risk factor for post-transplant infection within the first 6 months following KT for the elderly (≥60 year-old: multivariate HR 1.398; 95% CI, 1.199–1.631, $p < .001$) and the younger recipient (<60 year-old: multivariate HR 1.323; 95% CI, 1.103–1.587, $p = .003$) group alike.[36] Similarly, female recipient (multivariate OR 1.89; 95% CI, 1.01–3.55; $p = .047$) was one of the identified predictors of infectious complications in a cohort of simultaneous KT-LiT recipients undergoing rejection therapy.[38] No relationship was observed between infection and recipient and donor sex in a study population, in which pulmonary infections (45.9%) were most frequent, followed by intra-abdominal infections (21.2%) and a relatively low rate of UTI (17.6%).[40] However, there was no separate analysis of the four RDSC.

Overall, infections are the predominant cause for hospital readmission within the first year following KT (49%, $n = 202/296$).[41] Bacterial infections are most frequent after KT, followed by viral infections, with fungal and parasitic infections being much rarer.[34,36,42,43] UTI after KT are the most common infectious complication, albeit with decreasing prevalence since the 1990s.[34,42,44,45] In a meta-analysis of 13 studies ($n = 3\,364$), the pooled prevalence of UTIs in KT recipients was 38.0% (95% CI, 29%–47%; $p < .01$).[35] In a multivariable analysis, higher plasma creatinine concentration at the end of the first year after KT, end stage kidney disease due to diabetes, longer duration of pretransplant dialysis and low plasma albumin remained risk factors for infection-related death.[45] Similar infection rates, range of causing pathogens and involved anatomical sites (e.g., UTI, respiratory tract) were reported for patients receiving an ABO incompatible and ABO compatible renal transplant.[34]

3.3 | Liver transplantation

3.3.1 | Highlights

- Mortality: conflicting data – whilst some authors found female recipients to have a lower mortality, others found the opposite to be true.
- Rejection: Male recipients are at an increased risk for rejection with FDMR constellation showing rates of up to 51% at 15 years.
- Infection: Inconclusive overlapping results. Studies are warranted.

3.3.2 | Mortality

Six studies were identified in which recipient sex after LiT was evaluated; however, none specifically evaluated RDSC (Table 4). While four studies showed a worse survival in male recipients,[1,46–48] two studies showed identical results in female recipients.[49,50] Serrano and colleagues reported an increased mortality in female LiT recipients during the first 48-months post-transplant (e.g., male recipient to female recipient 1-month mortality HR .82; 95% CI, .70–.97; $p = .019$ and 1-year mortality HR .88; 95% CI, .80–.98; $p = .014$), but no significant differences were observed with regard to 5-year OS (HR .97; 95% CI, .90–1.05, $p = .445$).[49] They identified infections to be the most common cause of death, accounting for 18.4% (684/3 723 in 11 914 recipients) of deaths in male recipient vs. 22.7% (282/1 241 in 4 069 recipients) in FR.[49] In 317 patients (65.3% male) male recipient was protective for long-term 14-year mortality (multivariate HR .52; 95% CI, .34–.80; $p = .003$) with the 5-year OS 66.5% (95% CI, 61%–72%) and 10-year OS 58% (95% CI, 52%–65%).[50] A meta-analysis found female recipient sex to be protective with regard to mortality (multivariate OR .89; 95% CI, .86–.92).[1] An analysis of the European Liver Transplant Registry (ELTR) with 46 334 patients from 2002 to 2012 has shown male recipients to have a lower 10-year OS (59% vs. 66%, $p < .001$), with multivariate analysis indicating male recipient sex as a risk factor (HR 1.11; 95% CI, 1.07–1.15; $p < .001$) as well as incongruent RDSC (HR 1.09; 95% CI, 1.03–1.15; $p = .001$).[46] Causes of death exhibited significant sex-specific differences for primary non function (female vs. male recipient, 3.6% vs. 2.7%; $p = .03$), tumor recurrence (10.1% vs. 14.4%; $p < .001$) or de novo tumor (5.1% vs. 7.7%; $p < .001$).[46]

3.3.3 | Rejection and graft failure

In a meta-analysis, incongruent RDSC in LiT was associated with a significantly increased occurrence of graft loss (OR 1.30; 95% CI, 1.13–1.50; $p < .001$) when compared to congruent RDSC, with FDMR

TABLE 4 Studies assessing sex differences for outcomes after liver transplantation.

	Recipient sex		RDSC Congruent		RDSC Incongruent								
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Mortality	83% 59%	84% 66%	- -	- -	- -	- -	- <.001	1y survival 10y survival	46334	ELTR	significant clinical differences between sex groups not adjusted for RDSC incongruency significant in multivariate analysis in both sexes	2020	Germani[46]
	mult. HR 1.115 95%CI .955, 1.302	Reference	–	–	–	–	.170	Survival	6463	ELTR	Selection: LiT for PSC	2021	Berenguer[47]
	mult. HR .52 95%CI .34, .80	Reference	–	–	–	–	.003	Mortality	317	IL single center retrospective	*n* = 340 were excluded	2021	Leibovici-Weissman[50]
	Reference	OR .89 95%CI .86, .92	–	–	–	–	.640	Mortality	93053	Meta-analysis		2022	Tejada[1]
	72.8%	86.3%	–	–	–	–	.004	1y survival	240	IL single center retrospective	significant difference only in autoimmune and viral hepatitis	2022	Gabbay[48]
	HR .884 95%CI .802, .975	Reference	–	–	–	–	.014	1y survival	15998	RETH	Short-term survival higher in males, overall and long-term survival higher in females; mean follow-up 4 years	2022	Serrano[49]
	HR 1.065 95%CI 1.000, 1.137	Reference	–	–	–	–	.050	Overall survival					
Rejection or graft failure	–	–	22.6%	21.6%	31.1%	26.1%	<.001	Graft failure	1042	CAN single center study	–	2013	Croome[52]
	–	–	–	–	HR 2.09 95%CI 1.27, 3.46	–	.013						
	–	–	83.4%	85.0%	79.6%	84.0%	.003	1y graft survival	2144	DE single center	de novo malignancy, HCC recurrence and infection most common reasons	2016	Schoening[53]
	–	–	75.7%	71.9%	65.6%	76.3%		5y graft survival					
	–	–	64.1%	63.0%	55.6%	67.7%		10y graft survival					
	–	–	55.6%	53.3%	48.6%	61.1%		15y graft survival					
	–	–	Reference		OR 1.30 95%CI 1.13, 1.50		<.001	Graft survival	3935	Meta-analysis	FDMR strongest correlation	2018	Giovanardi[51]
	mult. HR 1.11 95%CI 1.07, 1.15	Reference	Reference		HR 1.09 95%CI 1.03, 1.15		.001	Death or graft loss	46334	ELTR	composite outcome	2020	Germani[46]
	mult. HR 1.185 95%CI 1.041, 1.349	Reference	–	–	–	–	.010	Graft survival	6463	ELTR	Selection: LiT for PSC	2021	Berenguer[47]

(Continues)

TABLE 4 (Continued)

			RDSC										
	Recipient sex		Congruent		Incongruent								
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Infection	Reference	OR 1.13 95%CI .55, 2.32	–	–	–	–	>.05	Cholangitis	501	Finnish national LT registry	–	2011	Åberg[55]
	Reference	OR .75 95%CI .50, 1.11	–	–	–	–	>.05	Other infections					
	Reference	OR 1.33 95%CI .635, 2.833	–	–	–	–	.446	Recurrent cholangitis	310	JP single center study	–	2018	Yao[58]
	Reference	mult. OR 1.80 95%CI 1.09, 2.97	–	–	–	–	.029	CMV infection	530	DE single center	–	2018	Busch[59]
	35.7%	54.9%	–	–	–	–	–	–	107	TR single center	–	2020	Yamazhan[57]
	Reference	OR 1.87 95%CI .91, 3.85	–	–	–	–	.086	Infection and infection hospitalisation	50	US single center	Selection: at least one episode of rejection within 1 year of transplant	2022	Gupta[38]

Abbreviations: BE, Belgium; CAN, Canada; CN, China; DE; Germany; ELTR, European Liver Transplant Registry; ES, Spain; FDFR, female donor female recipient; FDMR, female donor male recipient; FR, female recipient; FRE, France; HR, hazard ratio; IL, Israel; ISHLT, International Society for Heart and Lung Transplantation; JP; Japan; MDFR male donor, female recipient; MDMR male donor male recipient; MR, male recipient; mult., multivariate; (a)OR, (adjusted) odds ratio; OS, overall survival; UNOS, United Network for Organ Sharing; RDSC, recipient donor sex combination; RETH, Registro Español de Trasplante Hepático; UK, United Kingdom; US, United states; TR, Turkey

representing the highest risk (OR 1.83; 95% CI, 1.20–2.80; $p = .005$). This correlation was not statistically significant for MDFR.[51] In 1042 patients with LiT, improved graft survival was observed in congruent RDSC compared to incongruent RDSC ($p = .047$), with FDMR experiencing the worst graft survival among all RDSC (multivariate HR 2.09; 95% CI, 1.27–3.46; $p = .004$).[52] These findings are in line with the 15-year survival rates by Schoening and colleagues.[53] Primary nonfunction, vascular thrombosis, and recurrent hepatitis C virus (HCV), which are known risk factors for graft failure, occurred more frequently in FDMR transplantations.[52] Additionally, if stratified according to RDSC, graft loss after LiT due to infections differed relevantly (MDFR 17.2%; FDMR 14.4%; MDMR 14.1%; FDFR 12.6%).[53] Interestingly, whilst female donor sex is a risk factor for graft loss from hepatic artery thrombosis (multivariate RR 1.63; 95% CI, 1.42–1.87; $p < .001$) female recipient sex is protective for the latter complication (multivariate RR .81; 95% CI, .70–.94; $p = .004$).[54]

3.3.4 | Infection

Infectious complications pose a major challenge after LiT, occurring in 45% of all patients (143/317) during the first 6 months.[50] Of these, 24.8% (59/238) developed bacteremia and 16.4% (39/238) septic shock.[50] Abdominal infections (e.g., cholangitis and peritonitis) (37.4%, 89/238) were observed to be most frequent, followed by pneumonia (15.1%, 36/238), surgical site infections (13.8%, 33/238), viral infections (6.7%, 16/238), UTI (6.3%, 15/238), fungal infections (4.2%, 10/238) and line infections (3.8%, 9/238).[50] One year after transplantation, cholangitis (19.7%, 51/259) was the leading type of infectious complication, followed by pneumonia (19.3%, 50/259) and sepsis (14.3%, 37/259).[55]

One study reported pre-transplant infection (multivariate OR 1.23; 95% CI, 1.00–1.50; $p = .05$) and extended post-operative intubation (multivariate OR 1.34; 95% CI, 1.13–1.59; $p < .01$) to be the only risk factors for early (within first 30 days) post-transplant bacterial infections, while no association with other characteristics, such as age and sex, were observed in this cohort.[56] Higher rates of bacterial and fungal infections within first year following LiT were observed in living donors (53.9%, 34/63) compared to deceased donors (33.3%, 15/45).[57] This was true for bacteremia ($p = .006$), respiratory tract infections ($p = .009$) and intraabdominal infections ($p < .001$).[57] In this cohort too, recipient sex was not a risk factor for infection.[57] Furthermore, donor age ≥ 45 y (OR 2.47; 95% CI, 1.217–5.232; $p = .012$), choledochojejunostomy (OR 5.41; 95% CI, 2.540–11.758; $p < .001$) and post-LiT portal hypertension (OR 2.74; 95% CI, 1.155–6.329; $p = .023$) were identified to be independent risk factors for development of bacterial cholangitis, but no differences were observed regarding sex of the recipient or donor.[58] Moreover, age, sex and CMV status did not alter occurrence of late infections.[55]

In contrast, viral infections (e.g., CMV, herpes simplex virus [HSV] and varicella zoster virus) were more common in female recipients compared to male recipients within first 3 months after LiT (54.7% vs. 45.3%, $p = .004$; 51.6% vs. 48.4%, $p = .005$; 54.5% vs. 45.5%, $p = .027$, respectively) and risk factors determined in multivariate analysis included female recipient for infections with CMV (OR 1.80; 95% CI, 1.09–2.97; $p = .029$) and HSV-1 (OR 2.36; 95% CI, 1.14–4.90; $p = .021$).[59]

3.3.5 | Other

Sex-related differences are also observed with regard to indications for LiT.[52,53,60] For instance, in male recipients major indications for LiT include alcohol-induced cirrhosis and hepatocellular carcinoma, whereas female recipients are more often listed for cholestatic and autoimmune diseases.[52,53,60] In the pre-transplant period, female recipients suffering from cirrhosis are more often hospitalized for acute bacterial infections (34.9% vs. 28.2% in male patients; $p < .001$; with a marked difference in UTI incidence).[61] However, some infectious complications, including spontaneous bacterial peritonitis (3.2% in female vs. 3.9% in male patients; $p < .001$) as well as cellulitis and abscesses were more frequently found in male patients (6.4% in male vs. 5.4% in female patients; $p < .001$).[61] In a recent ELTR study by Germani et al., hepatocellular carcinoma recurrence was responsible for the death of 10.1% ($n = 13\,678$) in female recipients and 14.4% ($n = 32\,656$) in male recipients ($p < .001$).[46] However, the RDSC subgroups have shown different clinical characteristics, possibly resulting in confounded/biased results.

Regarding biliary anastomotic stricture, FDMR was identified as a significant risk factor in univariate analysis ($p = .020$).[62] In line are findings by Karakoyun et al., where male recipient sex was a risk factor in the univariate analysis ($p = .008$), but did not persist in the multivariate analysis (HR 1.78; 95% CI, .95–3.33; $p = .072$).[63] However, this non-significant trend in the multivariate analysis might be affected by underpowering (observed biliary strictures females 12.8% [17/133], male 24.0% [67/279]).

3.4 | Lung transplantation

3.4.1 | Highlights

- Mortality: female recipients are at an increased risk for mortality.
- Rejection & Infection: inconclusive or no data available.

3.4.2 | Mortality

Ten LuT studies were identified assessing the impact of recipient sex and RDSC on mortality (Table 5). Incongruent versus congruent RDSC resulted in equal outcomes when looking at early graft function, short-term mortality and long-term survival.[64] There was nevertheless, a trend towards improved long-term survival in FR, irrespective of donor sex, albeit non-significant.[64] Similarly, other studies found no differences in 30-day mortality[65] and long-term survival[66,67] between the RDSC groups. In contrast, in another cohort of 461 LuT recipients,

TABLE 5 Studies assessing sex differences for outcomes after lung transplantation.

	Recipient Sex		RDSC										
			Congruent		Incongruent								
Outcome	MR	FR	FDFR	MDMR	FDMR	MDFR	*p*-value	Outcome variable	*n*=	Design	Comment	Year	Study
Mortality	–	–	OR .73 95%CI .56, .96	Reference	OR 1.52 95%CI 1.04, 2.21	OR 1.04 95%CI .73, 1.48	.023	90d mortality	9651	ISHLT	Adjusted for recipient diagnosis, lung capacity, age, body mass, blood type, procedure. FDMR survival curve separated from other RDSC within 90 days	2006	Sato[69]
	–	–	OR 2.96 95%CI .94, 9.30	Reference	OR 1.22 95%CI .43, 3.53	OR .74 95%CI .09, 6.42	–	30d mortality	152	ES single center	59% of patients in reference RDSC, remaining $n = 62$ for comparison	2008	Miñambres[65]
	Reference	HR 1.08	–	–	–	–	.003	5-year survival	18072	ISHLT	–	2010	Gries[66]
	–	–	–	–	–	–	.146	20y survival	249	FRE single center	Trend to lower survival in incongruent RDSC, not significant, only graphs shown	2011	Fessart[67]
	–	–	19% 95%CI 9, 29	16% 95%CI 9, 23	22% 95%CI 12, 32	13% 95%CI 3, 23	.665	30d mortality	256	ES single center	–	2013	Alvarez[64]
	–	–	Reference		HR 1.8 95%CI 1.1–2.8		.010	10y survival	461	BE single center	proportion of incongruent matches 11.5%	2015	Demir[68]
	52.3%	70.0%	71.3%	53.7%	37.8%	75.0%	<.001						
	HR 1.059 95%CI .961, 1.167	Reference	–	–	–	–	.245	10y mortality	6677	UNOS	Idiopathic pulmonary fibrosis only; statistical model including age identified sex as significant	2017	Sheikh[90]
	HR .999 95%CI .783, 1.274	Reference	–	–	–	–	.993	10y mortality	652	US single center	–	2018	Mabilangan[79]
	Reference	HR .40 95%CI .22, .72	–	–	–	–	.002	Mortality	87	UNOS	Pulmonary Langerhans cell histiocytosis only	2020	Wajda[91]
Rejection or graft failure	–	–	.39 ± .80	.26 ± .62	.48 ± .59	.40 ± .50	.431	Acute rejection episodes > 3 months	256	ES single center	–	2013	Alvarez[64]
	24.6%	21.0%	–	–	–	–	.670	Primary graft dysfunction grade 3 at day 72	203	US single center	Different incidences between sexes in detailed spatial analysis	2021	Chacon-Alberty[72]
	9.8%	7.4%	–	–	–	–	.731	Acute rejection					

Abbreviations: BE, Belgium; CAN, Canada; CN, China; DE; Germany; ELTR, European Liver Transplant Registry; ES, Spain; FDFR, female donor female recipient; FDMR, female donor male recipient; FR, female recipient; FRE, France; HR, hazard ratio; IL, Israel; ISHLT, International Society for Heart and Lung Transplantation; JP; Japan; MDFR male donor, female recipient; MDMR male donor male recipient; MR, male recipient; mult., multivariate; (a)OR, (adjusted) odds ratio; OS, overall survival; UNOS, United Network for Organ Sharing; RDSC, recipient donor sex combination; RETH, Registro Español de Trasplante Hepático; UK, United Kingdom; US, United states; TR, Turkey

female recipient had lower mortality rates (multivariate HR .5; 95% CI, .3–.9; $p = .023$).[68] When evaluating 5-year OS, highest rates were seen in FDFR (80%), followed by MDFR (72%) and MDMR (63%), with a significant reduction observed in FDMR (47%) ($p = .0001$).[68] Incongruent RDSC was reported to be the only risk factor for mortality in multivariate analysis (HR 1.8; 95% CI, 1.1–2.8; $p = .01$).[68] Furthermore, a previous analysis of 9651 patients from the ISHLT registry confirmed better OS in FDFR (HR .92; 95% CI, .87–.98; $p < .05$) and decreased OS in FDMR (HR 1.12; 95% CI, 1.01–1.23; $p < .05$).[69]

3.4.3 | Rejection and graft failure

The incidence of acute rejection ranges between 4% and 28%,[70] with chronic lung allograft dysfunction seen in up to 40% of LuT recipients.[71] No differences were found in rejection rates among male and female recipients in a cohort of 203 patients.[72]

3.4.4 | Infection

Readmissions within the first year after LuT were commonly due to infectious events.[73–76] Bacterial infections are the most frequent complication after intensive care unit (ICU) discharge and bacterial pneumonia are the most common cause of ICU readmission (36.6%, 56/153).[77] Patients who suffered from pneumonia during their ICU readmission showed an increased mortality (aOR 2.5; 95% CI, 1.0–7.1; $p < .05$) and pneumonia was the prevailing cause of death.[77] In a study assessing cytomegalovirus (CMV), infected (defined as published by Ljungman et al.[78]) recipients had an increased 10-year mortality after lung transplantation (adjusted HR 1.39; 95% CI, 1.03–1.87; $p = .033$) but no association was observed between recipient sex and outcome,[79] whilst no in depth analysis of RDSC were performed.

3.4.5 | Other

Mollberg et al. found no association between recipient sex and hospital readmission after LuT.[73] In contrast, Lushaj and colleagues identified in their cohort male recipients to be a risk factor for readmission (HR 1.82; 95% CI, 1.06–3.11; $p = .032$).[75] In the latter study the five most common causes for readmission were diagnosed as respiratory infections, respiratory adverse events, rejection, gastrointestinal events and renal.[75]

4 | DISCUSSION

Present data suggest that female recipient sex is associated with better survival following SOT. However, these data are mainly based on relatively small numbers, as female recipients are underrepresented in the studied cohorts.[1] Recipient sex appears to play a major role, but donor sex should not be disregarded, as currently available evidence suggests that both characteristics have an influence. Female and male SOT recipients are affected by different preconditions (e.g., main pathology indicating the need for transplantation, associated co-morbidities), which might lead to different short and long-term outcomes after solid organ transplantation. From a clinician's point of view, the term 'recipient donor sex combination', appears to better suit clinical application rather than the temporal/spatial sequenced term 'donor recipient sex combination', as the recipient's sex status is stronger associated with outcome measures than the donor's sex. This further highlights the importance of incorporating RDSC-stratified outcome analyses after SOT. RDSC is likely to have a relevant impact on outcome after SOT, not only influencing organ acceptance but also affecting post-transplant management alike, as certain risks such as allograft rejection[21,24,28,31,32,51,52] and occurrence of infections[28,33,35–39] may vary fundamentally.

While many studies mention recipient sex and its influence on SOT outcome, stratification according to RDSC is often neglected and missing. This may in part be associated with national legal restrictions on data protection of donor characteristics.

Furthermore, the impact of other donor characteristics and mismatch-problems with the recipient such as age[29] and body weight[31,32] (as a surrogate for donor organ size/weight) has been primarily evaluated in KT and HT. It is possible, that the impact of these characteristics may be distinctly different within the RDSC constellations. Additionally, studies evaluating ethnical (e.g., through metabolomics differences[80–82]) socio-cultural disparities[83] and their impact on outcome after SOT are warranted. These biological characteristics (e.g., sex, age, bodyweight and underlying preconditions) need to be adjusted for by case-matching or propensity-score matching analysis. However, the relevance of RDSC is possibly fundamentally different depending on the type of SOT as, for example, in the sexually dimorphic liver, estrogen promotes bile duct growth in the early post-LiT period[84] and has been argued as a promotor of liver regeneration.[85]

However, as most countries experience donor organ shortage,[86,87] it is unlikely that an incongruent RDSC will result in refusal of an offered organ. Incorporating the knowledge of the possible challenging combination of RDSC on SOT outcome and incorporating this awareness in the postoperative patient care will allow for a more individualized, patient-tailored approach within the peri- and post-transplant setting in SOT recipients. Establishing algorithms to integrate such risk factors–in the nearby future probably with the help of machine learning–will allow us to provide true precision medicine in the field of transplantation.

To summarize, the combination of donor and recipient sex impacts the outcome after solid organ transplantation, not only influencing organ acceptance but also affecting post-transplant management alike, as mortality, allograft rejection and occurrence of infections vary greatly depending on donor and recipient sex. Currently, in the vast majority of the studies, the impact of RDSC in SOT often remains underreported, and where present, there is often a lack of consistency how this value is reported. To our knowledge, no study was designed to evaluate sex-related differences of infectious complications

throughout all SOT patients. Additionally, an analysis for differences of etiology and causes of graft loss or mortality, respectively, across the RDSC groups is warranted.

AUTHOR CONTRIBUTIONS

Christian Tibor Josef Magyar: design; literature review; data collection; data interpretation; writing. **Charlene Pierrine Gretener**: literature review; data collection; writing. **Patricia Baldi**: data interpretation; critical revision. **Federico Storni**: data interpretation; critical revision. **Corina Kim-Fuchs**: data interpretation; critical revision. **Daniel Candinas**: data interpretation; critical revision. **Annalisa Berzigotti**: data interpretation; critical revision. **Matthias Knecht**: data interpretation; critical revision. **Guido Beldi**: data interpretation; critical revision. **Cédric Hirzel**: data interpretation; critical revision. **Daniel Sidler**: data interpretation; critical revision. **David Reineke**: data interpretation; critical revision. **Vanessa Banz**: design; data interpretation; writing; critical revision

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support these findings of this study are available in PubMed. This is a review article.

SOCIAL MEDIA/TWEET

Male recipients have a higher risk of mortality and graft failure while female are more susceptible to infections. Sex, illnesses, age, immunosuppression and distinct biological mechanisms interact.

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REFERENCES

1. Tejada S, Martinez-Reviejo R, Nogueira TA, et al. The effect of sex inequality on solid organ transplantation: a systematic review and meta-analysis. *Eur J Intern Med*. 2023:109:58-67.
2. Reddy KD, Oliver BGG. Sexual dimorphism in chronic respiratory diseases. *Cell Biosci*. 2023;13(1):1-16.
3. Lefebvre P, Staels B. Hepatic sexual dimorphism — implications for non-alcoholic fatty liver disease. *Nat Rev Endocrinol*. 2021;17(11):662-670.
4. Klein SL, Jedlicka A, Pekosz A. The Xs and Y of immune responses to viral vaccines. *Lancet Infect Dis*. 2010;10(5):338-349.
5. Engler RJM, Nelson MR, Klote MM, et al. Half- vs full-dose trivalent inactivated influenza vaccine (2004-2005): age, dose, and sex effects on immune responses. *Arch Intern Med*. 2008;168(22):2405-2414.
6. Falsey AR, Treanor JJ, Tornieporth N, Capellan J, Gorse GJ. Randomized, double-blind controlled phase 3 trial comparing the immunogenicity of high-dose and standard-dose influenza vaccine in adults 65 years of age and older. *J Infect Dis*. 2009;200(2):172-180.
7. Furman D, Hejblum BP, Simon N, et al. Systems analysis of sex differences reveals an immunosuppressive role for testosterone in the response to influenza vaccination. *Proc Natl Acad Sci USA*. 2014;111(2):869-874.
8. Bupp MRG, Potluri T, Fink AL, Klein SL. The confluence of sex hormones and aging on immunity. *Front Immunol*. 2018;9:1269.
9. vom Steeg LG, Klein SL. SeXX matters in infectious disease pathogenesis. *PLoS Pathog*. 2016;12(2):e1005374.
10. Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol*. 2016;16(10):626-638.
11. Markle JGM, Frank DN, Mortin-Toth S, et al. Sex differences in the gut microbiome drive hormone-dependent regulation of autoimmunity. *Science (80-)*. 2013;339(6123):1084-1088.
12. Katz-Greenberg G, Shah S. Sex and gender differences in kidney transplantation. *Semin Nephrol*. 2022;42(2):219-229.
13. Momper JD, Misel ML, McKay DB. Sex differences in transplantation. *Transplant Rev (Orlando)*. 2017;31(3):145-150.
14. Tornatore KM, Meaney CJ, Wilding GE, et al. Influence of sex and race on mycophenolic acid pharmacokinetics in stable African American and Caucasian renal transplant recipients. *Clin Pharmacokinet*. 2015;54(4):423-434.
15. Van Hest RM, Van Gelder T, Vulto AG, Mathot RAA. Population pharmacokinetics of mycophenolic acid in renal transplant recipients. *Clin Pharmacokinet*. 2005;44(10):1083-1096.
16. Zimmerman JJ. Exposure-response relationships and drug interactions of sirolimus. *AAPS J*. 2004;6(4):e28.
17. Velickovi-Radovanovi R, Mikov M, Paunovi G, et al. Gender differences in pharmacokinetics of tacrolimus and their clinical significance in kidney transplant recipients. *Gend Med*. 2011;8(1):23-31.
18. Khush KK, Kubo JT, Desai M. Influence of donor and recipient sex mismatch on heart transplant outcomes: analysis of the International Society for Heart and Lung Transplantation Registry. *J Hear Lung Transplant*. 2012;31(5):459-466.
19. Ayesta A, Urrútia G, Madrid E, Vernooij RWM, Vicent L, Martínez-Sellés M. Sex-mismatch influence on survival after heart transplanta-

tion: a systematic review and meta-analysis of observational studies. *Clin Transplant*. 2019;33(12):e13737.
20. Kaczmarek I, Meiser B, Beiras-Fernandez A, et al. Gender does matter: gender-specific outcome analysis of 67,855 heart transplants. *Thorac Cardiovasc Surg*. 2013;61(1):29-36.
21. Prendergast TW, Furukawa S, Beyer AJ, Browne BJ, Eisen HJ, Jeevanandam V. The role of gender in heart transplantation. *Ann Thorac Surg*. 1998;65(1):88-94.
22. Weiss ES, Allen JG, Patel ND, et al. The impact of donor-recipient sex matching on survival after orthotopic heart transplantation: analysis of 18 000 transplants in the modern era. *Circ Heart Fail*. 2009;2(5):401-408.
23. Doulamis IP, Tzani A, Kourek C, et al. Sex mismatch following heart transplantation in the United States: characteristics and impact on outcomes. *Clin Transplant*. 2022;36(12):e14804.
24. Jalowiec A, Grady KL, White-Williams C. First-year clinical outcomes in gender-mismatched heart transplant recipients. *J Cardiovasc Nurs*. 2012;27(6):519.
25. Jalowiec A, Grady KL, White-Williams C. Mortality, rehospitalization, and post-transplant complications in gender-mismatched heart transplant recipients. *Hear Lung J Acute Crit Care*. 2017;46(4):265-272.
26. Previato M, Osto E, Kerkhof PLM, Parry G, Tona F. Heart transplantation survival and sex-related differences. *Adv Exp Med Biol*. 2018;1065:379-388.
27. Miller RJH, Hedman K, Amsallem M, et al. Donor and recipient size matching in heart transplantation with predicted heart and lean body mass. *Semin Thorac Cardiovasc Surg*. 2022;34(1):158-167.
28. Jalowiec A, Grady KL, White-Williams C. Predictors of rehospitalization time during the first year after heart transplant. *Hear Lung J Acute Crit Care*. 2008;37(5):344-355.
29. Haugen CE, King EA, Bae S, et al. Early hospital readmission in older and younger kidney transplant recipients. *Am J Nephrol*. 2018;48:235-241.
30. Vinson AJ, Zhang X, Dahhou M, et al. A multinational cohort study uncovered sex differences in excess mortality after kidney transplant. *Kidney Int*. 2023;103(6):1131-1143.
31. Tillmann FP, Quack I, Woznowski M, Rump LC. Effect of recipient-donor sex and weight mismatch on graft survival after deceased donor renal transplantation. *PLoS ONE*. 2019;14(3):e0214048.
32. Miller AJ, Kiberd BA, Alwayn IP, Odutayo A, Tennankore KK. Donor-recipient weight and sex mismatch and the risk of graft loss in renal transplantation. *Clin J Am Soc Nephrol*. 2017;12(4):669-676.
33. Graversen ME, Dalgaard LS, Jensen-Fangel S, Jespersen B, Østergaard L, Søgaard OS. Risk and outcome of pyelonephritis among renal transplant recipients. *BMC Infect Dis*. 2016;16(1):264.
34. Hirzel C, Projer L, Atkinson A, et al. Infection risk in the first year after ABO-incompatible kidney transplantation: a nationwide prospective cohort study. *Transplantation*. 2022;106(9):1875-1883.
35. Wu X, Dong Y, Liu Y, et al. The prevalence and predictive factors of urinary tract infection in patients undergoing renal transplantation: a meta-analysis. *Am J Infect Control*. 2016;44(11):1261-1268.
36. Kim JS, Jeong KH, Lee DW, et al. Epidemiology, risk factors, and clinical impact of early post-transplant infection in older kidney transplant recipients: the Korean organ transplantation registry study. *BMC Geriatr*. 2020;20(1):519.
37. Vidal E, Torre-Cisneros J, Blanes M, et al. Bacterial urinary tract infection after solid organ transplantation in the RESITRA cohort. *Transpl Infect Dis*. 2012;14(6):595-603.
38. Gupta S, Gea-Banacloche J, Me H, et al. Infections following rejection therapies in kidney and liver transplant recipients. *Transpl Infect Dis*. 2022;24(6):e13981.
39. Chuang P, Parikh CR, Langone A. Urinary tract infections after renal transplantation: a retrospective review at two US transplant centers. *Clin Transplant*. 2005;19(2):230-235.
40. Cheng F, Li Q, Wang J, Wang Z, Zeng F, Zhang Y. Retrospective analysis of the risk factors of perioperative bacterial infection and correlation with clinical prognosis in kidney transplant recipients. *Infect Drug Resist*. 2022;15:2271-2286.
41. Boubaker K, Harzallah A, Ounissi M, et al. Rehospitalization after kidney transplantation during the first year: length, causes and relationship with long-term patient and graft survival. *Transplant Proc*. 2011;43(5):1742-1746.
42. Matej V, Karol G, Monika B, Juraj M, Ivana D. Age and sex disparity in infectious complications after kidney transplantation. *Bratislava Med J*. 2022;123(7):463-469.
43. Abou-Jaoudé M, El Hage S, Akiki D, Araman R. Effect of donor-to-recipient HLA matching in low-immunological risk kidney transplant recipients without induction therapy on acute rejection, graft survival, infections, and surgical complications at 3 years: the road towards new recommendations. *Transpl Immunol*. 2021;69:101490.
44. Alangaden GJ, Thyagarajan R, Gruber SA, et al. Infectious complications after kidney transplantation: current epidemiology and associated risk factors. *Clin Transplant*. 2006;20(4):401-409.
45. Kinnunen S, Karhapää P, Juutilainen A, Finne P, Helanterä I. Secular trends in infection-related mortality after kidney transplantation. *Clin J Am Soc Nephrol*. 2018;13(5):755-762.
46. Germani G, Zeni N, Zanetto A, et al. Influence of donor and recipient gender on liver transplantation outcomes in Europe. *Liver Int*. 2020;40(8):1961-1971.
47. Berenguer M, Di Maira T, Baumann U, et al. Characteristics, trends, and outcomes of liver transplantation for primary sclerosing cholangitis in female versus male patients: an analysis from the European Liver Transplant Registry. *Transplantation*. 2021;105(10):2255-2262.
48. Gabbay U, Issachar A, Cohen-Naftaly M, Brown M, Nesher E. Gender specific survival rates after deceased donor liver transplantation: a retrospective cohort. *Ann Med Surg*. 2022;79:103933.
49. Serrano MT, Sabroso S, Esteban LM, et al. Mortality and causes of death after liver transplantation: analysis of sex differences in a large nationwide cohort. *Transpl Int*. 2022;35:1.
50. Leibovici-Weissman Y, Anchel N, Nesher E, Leshno M, Shlomai A. Early post-liver transplantation infections and their effect on long-term survival. *Transpl Infect Dis*. 2021;23(4):e13673.
51. Giovanardi F, Melandro F, Laureiro ZL, et al. Donor-to-recipient gender match in liver transplantation: a systematic review and meta-analysis. *World J Gastroenterol*. 2018;24(20):2203-2210.
52. Croome KP, Segal D, Hernandez-Alejandro R, Adams PC, Thomson A, Chandok N. Female donor to male recipient gender discordance results in inferior graft survival: a prospective study of 1,042 liver transplants. *J Hepatobiliary Pancreat Sci*. 2014;21(4):269-274.
53. Schoening WN, Helbig M, Buescher N, et al. Gender matches in liver transplant allocation: matched and mismatched male-female donor-recipient combinations; long-term follow-up of more than 2000 patients at a single center. *Exp Clin Transplant*. 2016;14(2):184-190.
54. Stewart ZA, Locke JE, Segev DL, et al. Increased risk of graft loss from hepatic artery thrombosis after liver transplantation with older donors. *Liver Transplant*. 2009;15(12):1688-1695.
55. Åberg F, Mäkisalo H, Höckerstedt K, Isoniemi H. Infectious complications more than 1 year after liver transplantation: a 3-decade nationwide experience. *Am J Transplant*. 2011;11(2):287-295.
56. Heldman MR, Ngo S, Dorschner PB, Helfrich M, Ison MG. Pre- and post-transplant bacterial infections in liver transplant recipients. *Transpl Infect Dis*. 2019;21(5):e13152.
57. Yamazhan T, Avsar CB, Zeytunlu M, et al. Infections developing in patients undergoing liver transplantation: recipients of living donors may be more prone to bacterial/fungal infections. *Turkish J Gastroenterol*. 2020;31(12):894.
58. Yao S, Yagi S, Nagao M, et al. Etiologies, risk factors, and outcomes of bacterial cholangitis after living donor liver transplantation. *Eur J Clin Microbiol Infect Dis*. 2018;37(10):1973-1982.

59. Busch CJ, Siegler BH, Werle H, et al. Risk factors for early viral infections after liver transplantation. *Langenbeck's Arch Surg*. 2018;403(4):509-519.
60. Cullaro G, Sarkar M, Lai JC. Sex-based disparities in delisting for being "too sick" for liver transplantation. *Am J Transplant*. 2018;18(5):1214-1219.
61. Rubin JB, Sundaram V, Lai JC. Gender differences among patients hospitalized with cirrhosis in the United States. *J Clin Gastroenterol*. 2020;54(1):83.
62. Verdonk RC, Buis CI, Porte RJ, et al. Anastomotic biliary strictures after liver transplantation: causes and consequences. *Liver Transplant*. 2006;12(5):726-735.
63. Karakoyun R, Ericzon BG, Kar I, Nowak G. Risk factors for development of biliary stricture after liver transplant in adult patients: a single-center retrospective study. *Transplant Proc*. 2021;53(10):3007-3015.
64. Alvarez A, Moreno P, Illana J, et al. Influence of donor-recipient gender mismatch on graft function and survival following lung transplantation. *Interact Cardiovasc Thorac Surg*. 2013;16(4):426-435.
65. Miñambres E, Llorca J, Subrviola B, Ballesteros MA, Ortiz-Melón F, González-Castro A. Influence of donor-recipient gender mismatch in early outcome after lung transplantation. *Transplant Proc*. 2008;40(9):3076-3078.
66. Gries CJ, Rue TC, Heagerty PJ, Edelman JD, Mulligan MS, Goss CH. Development of a predictive model for long-term survival after lung transplantation and implications for the lung allocation score. *J Heart Lung Transplant*. 2010;29(7):731-738.
67. Fessart D, Dromer C, Thumerel M, Jougon J, Delom F. Influence of gender donor-recipient combinations on survival after human lung transplantation. *Transplant Proc*. 2011;43(10):3899-3902.
68. Demir A, Coosemans W, Decaluwé H, et al. Donor-recipient matching in lung transplantation: which variables are important?†. *Eur J Cardiothorac Surg*. 2015;47(6):974-983.
69. Sato M, Gutierrez C, Kaneda H, Liu M, Waddell TK, Keshavjee S. The effect of gender combinations on outcome in human lung transplantation: the International Society of Heart and Lung Transplantation Registry experience. *J Heart Lung Transplant*. 2006;25(6):634-637.
70. Zhou J, Chen B, Liao H, et al. The comparable efficacy of lung donation after circulatory death and brain death: a systematic review and meta-analysis. *Transplantation*. 2019;103(12):2624-2633.
71. Van Herck A, Verleden SE, Sacreas A, et al. Validation of a post-transplant chronic lung allograft dysfunction classification system. *J Hear Lung Transplant*. 2019;38(2):166-173.
72. Chacon-Alberty L, Ye S, Daoud D, et al. Analysis of sex-based differences in clinical and molecular responses to ischemia reperfusion after lung transplantation. *Respir Res*. 2021;22(1):1-12.
73. Mollberg NM, Howell E, Vanderhoff DI, Cheng A, Mulligan MS. Health care utilization and consequences of readmission in the first year after lung transplantation. *J Heart Lung Transplant*. 2017;36(4):443-450.
74. Alrawashdeh M, Zomak R, Dew MA, et al. Pattern and predictors of hospital readmission during the first year after lung transplantation. *Am J Transplant*. 2017;17(5):1325-1333.
75. Lushaj E, Julliard W, Akhter S, et al. Timing and frequency of unplanned readmissions after lung transplantation impact long-term survival. *Ann Thorac Surg*. 2016;102(2):378-384.
76. Osho AA, Castleberry AW, Yerokun BA, et al. Clinical predictors and outcome implications of early readmission in lung transplant recipients. *J Heart Lung Transplant*. 2017;36(5):546-553.
77. Mazo C, Pont T, Ballesteros MA, et al. Pneumonia versus graft dysfunction as the cause of acute respiratory failure after lung transplant: a 4-year multicentre prospective study in 153 adults requiring intensive care admission. *Eur Respir J*. 2019;54(3):1801512.
78. Ljungman P, Boeckh M, Hirsch HH, et al. Definitions of cytomegalovirus infection and disease in transplant patients for use in clinical trials. *Clin Infect Dis*. 2017;64(1):87-91.
79. Mabilangan C, Preiksaitis J, Cervera C, et al. Impact of donor and recipient cytomegalovirus serology on long-term survival of lung transplant recipients. *Transpl Infect Dis*. 2018;20(5):e12964.
80. Noren Hooten N, Pacheco NL, Smith JT, Evans MK. The accelerated aging phenotype: the role of race and social determinants of health on aging. *Ageing Res Rev*. 2022;73:101536.
81. Patel MJ, Batch BC, Svetkey LP, et al. Race and sex differences in small-molecule metabolites and metabolic hormones in overweight and obese adults. *OMICS*. 2013;17(12):627.
82. Vasishta S, Ganesh K, Umakanth S, Joshi MB. Ethnic disparities attributed to the manifestation in and response to type 2 diabetes: insights from metabolomics. *Metabolomics 2022 187*. 2022;18(7):1-21.
83. Kute VB, Chauhan S, Navadiya VV, et al. India: gender disparities in organ donation and transplantation. *Transplantation*. 2022;106(7):1293-1297.
84. Alvaro D, Mancino MG, Onori P, et al. Estrogens and the pathophysiology of the biliary tree. *World J Gastroenterol*. 2006;12(22):3537-3545.
85. Birrer DL, Linecker M, López-López V, et al. Sex disparities in outcomes following major liver surgery new powers of estrogen? *Ann Surg*. 2022;276(5):875-881.
86. Hanaway MJ, MacLennan PA, Locke JE. Exacerbating racial disparities in kidney transplant: the consequences of geographic redistribution. *JAMA Surg*. 2020;155(8):679-681.
87. Shafran D, Kodish E, Tzakis A. Organ shortage: the greatest challenge facing transplant medicine. *World J Surg*. 2014;38(7):1650-1657.
88. Lepeytre F, Dahhou M, Zhang X, et al. Association of sex with risk of kidney graft failure differs by age. *J Am Soc Nephrol*. 2017;28(10):3014-3023.
89. Morgan G, Goolam-Mahomed Z, Hodson J, Nath J, Sharif A. Donor-recipient sex differences do not affect survival outcomes after kidney transplantation: a population cohort study. *Transplantation*. 2020;104(5):1033-1040.
90. Sheikh SI, Hayes D, Kirkby SE, Tobias JD, Tumin D. Age-dependent gender disparities in post lung transplant survival among patients with idiopathic pulmonary fibrosis. *Ann Thorac Surg*. 2017;103(2):441-446.
91. Wajda N, Zhu Z, Jandarov R, Dilling DF, Gupta N. Clinical outcomes and survival following lung transplantation in patients with pulmonary Langerhans cell histiocytosis. *Respirology*. 2020;25(6):644-650.

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