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The impact of renal transplantation on sexual function in males with end-stage kidney disease: a systematic review and meta-analysis

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Abstract

Introduction Patients with end-stage kidney disease (ESKD) on dialysis have a special profile, including constant uremic status and frequent comorbidities, such as diabetes mellitus, arterial hypertension and coronary artery disease, as well as complications related to dialysis. All listed factors can influence or be the cause of sexual dysfunction in both men and women. There is a high incidence (70%) and prevalence (82%) of erectile dysfunction in men with CKD.

Purpose In this meta-analysis, we aimed to evaluate the impact of renal transplantation in patients with end-stage chronic kidney disease and erectile dysfunction, using the same study population before and after transplantation.

Data sources: we searched MEDLINE (PubMed**),** Embase, Scopus and Cochrane Library (Inception to August 2022) and clinicaltrials.gov (Inception to August 2022) without language restrictions.

Study selection: eligible studies evaluated the same patients with end-stage kidney disease before and after renal transplantation using IEEF questionnaire.

Data extraction: reviewers working independently and in duplicate extracted data and assessed the risk of bias.

Data synthesis: the final analysis included 28 cohort studies, comprising 2252 participants.

Results Our results showed improvement in erectile function after renal transplantation. Our study shows a 13% improvement in erectile dysfunction after renal transplantation.

Conclusions The results of this meta-analysis would suggest improvement in erectile dysfunction after renal transplantation.

Keywords Erectile dysfunction · Kidney transplantation/renal transplantation · Renal failure · Chronic kidney disease · End-stage renal disease · Meta-analysis · Dialysis

Introduction

Patients with end-stage kidney disease (ESKD) on dialysis have a special profile, including constant uremic status, frequent comorbidities, such as type 2 diabetes mellitus (T2DM), arterial hypertension, dyslipidaemia and coronary artery disease. Additionally, complications related to dialysis may occur, such as peritonitis in patients on continuous ambulatory peritoneal dialysis, access-related or hemodynamic in patients on haemodialysis. In addition, patients on dialysis have constant contact with the healthcare system, a lower quality of life, which can cause a range of neuropsychiatric disorders, such as depression, anxiety and distress. All these listed factors and the added comorbidities may influence or be the cause of sexual dysfunction in both men and women.

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Erectile dysfunction (ED) is known to have a negative impact on the quality of life. The first epidemiological survey of sexual dysfunction in patients with chronic kidney disease (CKD) was conducted in 1972 [1] and since then several studies confirmed that the prevalence of sexual dysfunction in haemodialysis patients is high [2].

Erectile and kidney dysfunction share common risk factors associated with conditions that involve endothelial impairment such as coronary artery disease, dyslipidaemia, diabetes mellitus, hypertension, smoking and obesity [3, 4]. Increasing evidence suggests that CKD is frequently associated with psychosocial factors, such as anxiety, depression, and health-related poor quality of life, all of which can result in sexual dysfunction [5]. There's a high incidence (70%) and prevalence (82%) of erectile dysfunction in men with CKD [2, 6].

Kidney transplant (KT) is recognized to be the best treatment for end-stage renal disease (ESRD), and the number of kidney transplants is increasing worldwide, with restoration of kidney function. Data regarding the state of erectile dysfunction after kidney transplantation is controversial: some studies show that erectile function improves after renal transplant (RT) [7–13] while other authors suggest that sexual parameters are not affected by renal transplantation [14–17]. Additionally, some studies have indicated that erectile dysfunction is worsened after kidney transplantation surgery [18–21].

In the twenty-first century, graft survival and survival of transplant recipients increased due to latest transplantation technology, as well as better evaluation of renal parameters and new immunosuppressive strategies that prevent graft rejection. In this new era of medicine, erectile function in the context of a better quality of life became an important concern for patients and doctors.

Aims

This review aims to evaluate the impact of renal transplantation on erectile dysfunction in men with end-stage chronic kidney disease.

Materials and methods

The updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were applied to standardize data search, collection, synthesis, and reporting [22]. For our meta-analysis, we used a protocol registered at OSF Registries (Registration https://doi.org/10.17605/OSF.IO/JV2MQ).

Data sources and search strategy

Potentially relevant studies were searched in the following databases, from the inception until August 2022: MELDINE (PubMed), SCOPUS, Embase and Cochrane library. No language filters were applied in the search process. In addition to aforementioned sources, ClinicalTrials.gov database was also screened for additional citations. References from representative studies were also searched to retrieve further studies for eligibility assessment. Hand search for relevant articles was also performed from textbooks. We used different combinations of keywords and controlled vocabulary to create a comprehensive search strategy: "renal transplant and erectile dysfunction", "CKD and erectile dysfunction", "erectile dysfunction after kidney transplant", "erectile dysfunction".

Study selection

We conducted a systematic review and meta-analysis including observational cohort studies and randomized controlled trials (RCTs) in men with ESRD that evaluated the role of renal transplant on the impact of erectile dysfunction in men. In this analysis, only ESRD who had undergone renal transplantation were included and the IIEF questionnaire was used. The same group of patients were analyzed using the same questionnaire after surgery. We considered studies that explored the prevalence and predictors of any form of sexual dysfunction in patients with CKD. Studies were eligible if they compared the same group of population before and after renal transplantation. Studies with a population of patients without CKD were excluded, as were studies that compared groups of patients on dialysis with different groups of patients with renal transplant.

Data extraction and synthesis

Data extracted included identifying information, aim of the study, details of the study protocol and demographic data. We extracted characteristics of each study including baseline IIEF score (IIEF—5), IIEF domain (IIEF – 15) (erectile function, intercourse satisfaction, orgasmic function, sexual desire, overall satisfaction), baseline clinical characteristics of the study population, known comorbidities, type of donor, type of anastomosis used during renal transplantation, type of study design, and total duration of follow-up.

Risk of bias

Two reviewers (AM and IN) evaluated the quality of the selected studies independently without blinding to

authorship or journal according to recommendations from the Cochrane Collaboration. For the observational studies, the quality was assessed using the Newcastle–Ottawa scale (NOS) [23] The scale used three categories to evaluate: selection of the study groups, the comparability of the groups and the assessment of outcome. Stars awarded for each quality item serve as a quick visual assessment. Stars are awarded such that the highest quality studies are awarded up to nine stars. Disagreements were resolved by consensus. Publication bias was assessed using the funnel plot technique[24].

Main outcomes and measures

The primary outcome of this analysis was to measure the impact of renal transplantation on sexual function using the International Index of Erectile Function (IEEF) score, sexual domains and also other questionaries. Secondary outcomes included: 1. establishing if mean IIEF-15 or IIEF-5 change from baseline in KTs, 2. Number of patients with improvement or worsening of ED on postoperative evaluation.

The International Index of Erectile Function (IIEF) is a widely used, multi-dimensional self-report instrument for the evaluation of male sexual function [25]. It has been recommended as a primary endpoint for clinical trials of ED and for diagnostic evaluation of ED severity [26], and it is now considered gold-standard for measurement of sexual function [27]. This questionnaire includes all aspects of male sexual functions (erection, orgasmic function, libido, and overall satisfaction) and can evaluate as objectively as possible sexual function in male patients [28].

Statistical analysis

We used a random-effects model for meta-analysis and expressed treatment effects as a risk ratio (RR) with 95% confidence intervals (CI). We used the I^2 statistic to assess for inconsistency across individual studies. An $I^2 > 50\%$ indicated large inconsistency across studies (heterogeneity) not explained by chance. We considered a p-value below 0.10 to indicate significant heterogeneity All statistical analyses were performed using Review Manager Version 5.2 (The Cochrane Collaboration 2012).

We conducted sensitivity analyses to explore the influence of the following factors on effect size: repeating the analysis excluding unpublished studies; repeating the analysis taking account of risk of bias; repeating the analysis excluding any very long or large studies to establish how much they dominate the results; repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, and country. A funnel plot was visually inspected. For all the analyses, a two-tailed p-value < 0.05 indicated statistical significance. We conducted the analyses in Review Manager (RevMan) Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

Possible source of heterogeneity was explored based on the type of anastomosis (end-to-side to external iliac artery, end-to-end to internal iliac artery or end-to-side to common iliac artery), risk of bias, type of transplantation and year of publication.

Results

The literature search using the specified databases retrieved 1703 articles. After removing duplicates, 943 articles were screened by title and abstract and 43 articles were read in full-text. We then removed articles where the inclusion criteria were not met, articles that included meta-analyses and articles where the study population was not the same before and after renal transplantation. Finally, a total of 28 articles were included in the present meta-analysis, comprising a total of 2252 participants (Fig. 1).

The articles included in this meta-analysis were observational conducted worldwide. The follow-up period varied between three and 282 months. 17 studies reported the type of renal replacement therapy before renal transplantation. The majority of patients underwent haemodialysis, while out of the same 17 studies, a total of 35 patients were on peritoneal dialysis and 34 patients had a pre-emptive transplantation. Dialysis time before RT was between 6 months to 7 years. 11 studies reported the type of donor involved in the process of RT. The follow-up between studies varied between three months to 72 months. The majority of studies used the IIEF-5 questionnaire as the main method to assess sexual function, while 5 studies used questionnaires developed by the authors. The characteristics of all included studies are included in Table 1.

Regarding the baseline characteristics of all included participants, few studies reported life-style risk factors such as smoking and alcohol [14, 17–19, 29–33] or the weight of included participants [17, 18, 30, 33]. Four studies [10, 13, 29, 34] excluded patients with diabetes mellitus. 12 studies reported data on immunosuppressive therapy, while five studies reported other chronic medications. 10 studies also reported the hormone panel before and after renal transplantation. The complete baseline characteristics of all included participants are summarized in Table 2.

Presence or absence of erectile dysfunction after renal transplantation

28 studies included (2252 patients) compared the rate of sexual dysfunction before and after renal transplantation. In dichotomic analysis with a comparison before and after renal

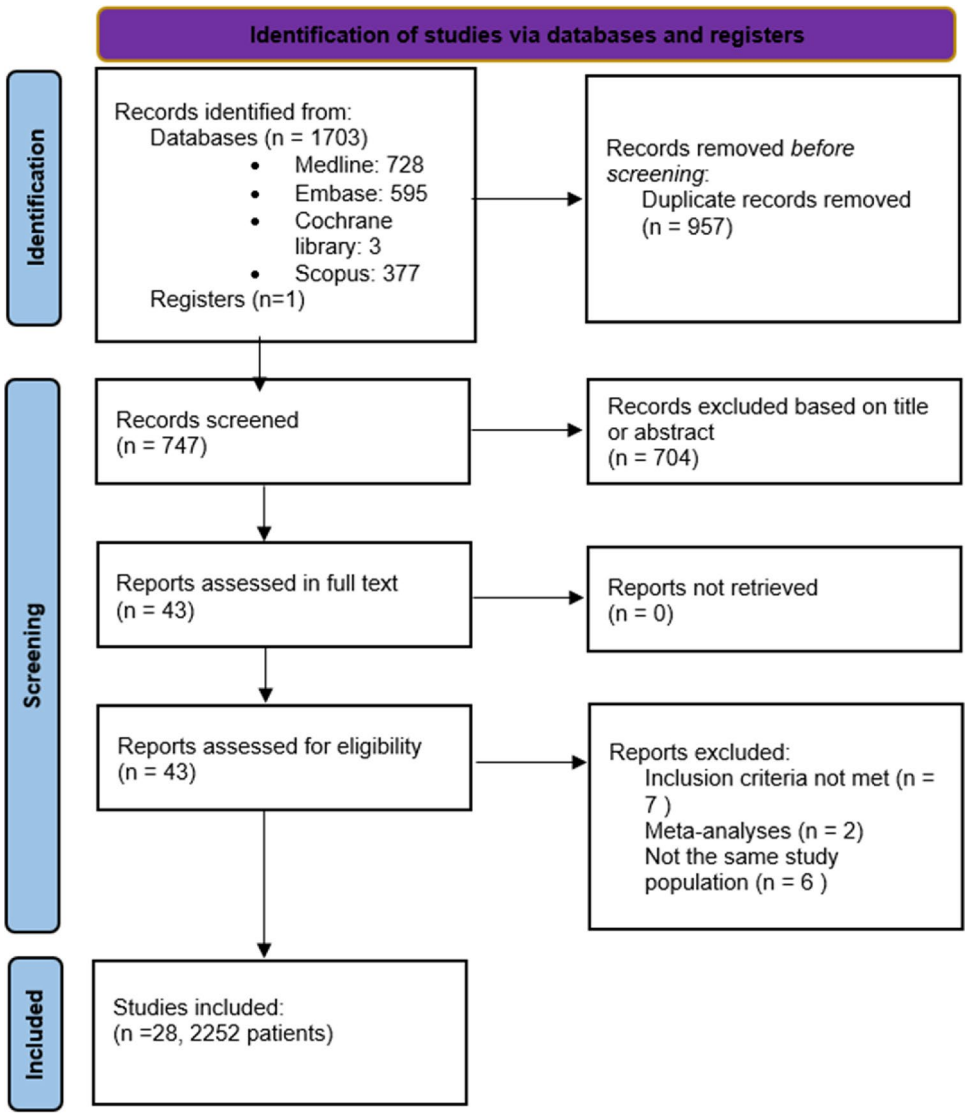

Fig. 1 Flow diagram of study selection process

transplantation, we found an improvement of 13% regarding sexual dysfunction after renal transplantation. (RR 0.87) (95% CI 0.76–1.00) (Fig. 2).

Improvement versus worsening of erectile dysfunction

We evaluated the impact of renal transplantation on sexual function in an analysis that included 19 studies comprising a total of 1613 participants. Our results show that post-renal transplantation, there was an improvement in erectile dysfunction with 234% (RR 2.3) (95% CI 1.36, 4.01) (Fig. 3).

Impact of renal transplantation on IEEF score

Data reported in six studies show an improvement of mean IEEF score with 3.92 points after KT: (MD 3.92) (CI 95% 3.26 to 4.58) (Fig. 4).

Subdomain analysis was not performed due to insufficient data. Three studies reported other components, such as erectile function, orgasmic function, intercourse satisfaction and overall satisfaction. However, there was not enough data to perform an analysis on these components, but the results generally suggest an improvement in sexual function after renal transplantation.

Type of anastomosis and impact on erectile function

14 studies included the type of anastomosis used during renal transplantation. *Gontero* et al. reported worsening erectile function with end-to side external iliac artery anastomosis and five studies reported good results using end-to-end or end-to-side internal iliac artery anastomosis. However, there was not enough data to perform an analysis.

Table 1 Characteristics of all included studies

Author, Year	Country	Period of study	No. Patients (*n*)	Mean age ± SD	Type of dialysis	Time on dialysis (months/years)	Second transplant	Type of donor	Follow-up time on RT (months)	ED evaluation tool
1.Ahmad, 2009	Pakistan	NR	30	39 ± 7.35	HD	NR	NR	NR	3 M, 6 M	IIEF- 5
2.Akbari, 2003	Iran	1999–2005	30	24–52	HD	> 6 M	NR	L	6 M	IIEF- 5
3. Buidak, 2003	Slovak Republic	NR	58	22–62 (mean 46.4)	HD	NR	NR	C	16 ± 2 M	IIEF- 5
4. Burgos, 1997	Spain	1991–1995	50	46 ± 6	NR	Mean 15 ± 6 M	5			Questinnaire developed by Burgos et al
5. El-Bahnasawy, 2004a	Egypt	NR	400	37 ± 10	NR	ED: 17.8 ± 15.5 M NO ED: 16.8 ± 17.6 M	14	L	ED: 87 ± 60.9 M NO ED: 54.6 ± 48.9 M	IIEF- 15 EF DOMAIN
6. El-Bahnasawy, 2004b	Egypt	Jan 2002–May 2003	50	35 ± 9	HD	19 ± 14/	NR	L	6 M	IIEF- 15 EF DOMAIN
7. Gontereo, 2011	Italy	2000–2003	22	50.62 ± 12.05	HD	6.25 ± 2.96 (range 21Y)	NR	NR	3 M	IIEF- 15 EF DOMAIN
8. Gou, 2010	China	Jan 2006–May 2009	87	21–50	HD 82 PD 5	Group 1: 11.27 ± 5.40 Group 2: 11.04 ± 5.53	NR	NR	6 M	IIEF- 5
9. Jabali, 2020	Irak	Jan 2018–March 2019	59	49.41 ± 7.12	HD	5.3 ± 7.2 M	NR	NR	NR	IIEF- 5
10. JI, 2010	China	NR	33	21–55Y	HD	NR	NR	NR	6 M	IIEF- 5
11. Jurgensen, 2008	Germany	NR	101	NR	NR	NR	NR	NR	NR	IIEF- 15 EF DOMAIN
12. Mirone, 2008	Italy	2001–2005	78	45.53	HD	53.9 M	5	C	12 M	IIEF- 15 EF DOMAIN
13. Mota, 2019	Portugal	May–August 2016	112	55.5 (SD = 11.4)	HD-88 PD-20 PRED- 4	HD 11.18 ± 7.395 Y DP 8.7 ± 6.165Y	NR	L-19 C- 84	< 36 M > 36 M	IIEF- 15 EF DOMAIN
14. Musone, 2003	Italy	NR	115	NR	NR	NR	NR	NR	NR	IIEF- 15 EF DOMAIN
15. Nanjappa, 2012	India	NR	127	NR	NR	NR	NR	NR	3 M	IIEF- 5
16. Nassir, 2009	Saudi Arabi	NR	16	49.2 ± 11.4	HD—6 PD—10	NR	NR	NR	20-36 M Mean 26 M	IIEF- 15 EF DOMAIN

Table 1 (continued)

Author, Year	Country	Period of study	No. Patients (*n*)	Mean age ± SD	Type of dialysis	Time on dialysis (months/years)	Second trans-plant	Type of donor	Follow-up time on RT (months)	ED evaluation tool
17. Nghiem, 1983	Virginia	NR	61	42.3 ± 10.9	NR	ED- 18.4 ± 17.86 M NO-ED 34..6 ± 36.32 M	20	NR	6–108 M	Questinnaire developed by Nghiem et al
18. Peng, 2007	China	NR	55	22–50 years	HD	NR	NR	NR	3 M, 6 M,9 M	IIEF- 5
19. PeskircioğL, 1998	Turkey	NR	65	42.5	HD	NR	4	NR	2–168 (mean 72 M)	Questinnaire developed by Peskircioğlu et al
20. Pourmand 2007	Iran	Sept. 2002-Nov 2005	64	42.3 ± 10.4	HD	16.8 ± 18.7 M	NR	L	6 M	IIEF- 5
21. Qiau, 2009	China	May 2001-Oct 2007	48	35.2 ± 10.2	NR	18.1 ± 9.6 M	NR	NR	41.8 ± 31.9 M	IIEF- 5
22. Salvatierra, 1975	San Francisco	NR	94	20–60	NR	14 m (4-36 m)	NR	C/L	Mean 36 M	Questinnaire developed by Salvatierra et al
23. Shamsa, 2005	Iran	March 2003- June 2004	15	35.26	NR	4.31Y	NR	L	NR	IIEF- 5
24. Soliman, 2017	Egypt	NR	30	NR	HD 48 Pred 30	NR	NR	NR	12 M	IIEF- 5
25. Spirito, 2020	Italy	Jan 2009- April 2019	95	47.20 SD = 8.68	NR	76.77 ± 45.13 M	NR	NR	6 M, 12 M	IIEF- 15 EF DOMAIN
26. Teng, 2010	China	NR	24	40.8 ± 7.1	HD	12.83 ± 20.5 (0.5–96 M)	NR	18-C 6-L	3–60 M (15.79 ± 8.1)	IIEF- 5
27. Tian,2007	China	NR	212	NR	NR	NR	NR	NR	NR	IIEF- 15 EF DOMAIN
28. Tsujimura, 2002	Japan	NR	121	44.7 ± 0.8	HD	42.3 ± 4 M	1	L-93(76.9%) C-29(23.1%)	107.9 ± 6.0 M (4-282 M)	Questinnaire developed by Tsujimura et al

NR- not reported, HD- haemodialysis, PD- peritoneal dialysis, L- living donor, C- cadaveric donor, ED- erectile dysfunction

Table 2 Baseline characteristics of all included studies

Author, year	Smoking/Alcohol	BMI/Weight	HTN	Diabetes	PAD/CAD	Treatment after RT	Type of renal anastomosis	Hormone panel (Testosterone, Prolactine, LH, FSH)		Renal Panel Hb levels (Cr-mg/dL, Hb g/dL)		Other medications
1.Ahmad, 2009	NR	NR	14	13	NR	NR	NR	6,33 ng/mL		Pre-RT Hb 8,48 ± 1,13	Post-RT Hb 12,9 ± 0,65	NR
2.Akbari, 2003	NR	NR	NR	Excluded	NR	Aza, Pred, CyA	NR	Pre-RT **T**- 3.92 (2.5) ng/mL **LH**: 8,6 mUI/mL **FSH**: 9,6 mUI/mL **PRL**: 16,6 ng/mL	Post-RT **T**: 4,5 (1,92) ng/mL **LH**: 7,04 mUI/mL **FSH**: 8,75 mUI/mL **PRL**: 10,52 ng/mL	NR		NR
3. Buidak, 2003	NR	NR	48	6	NR	NR	NR	NR		NR		NR
4. Burgos, 1997	NR	NR	Before ED: 46 After ED: 25	Excluded	NR	CyA + Pred: 32 Aza-Pred: 4 CyA-Aza-Pred: 14	End-to-side external iliac artery	Pre-RT **T:** 43.7 ± 22.3 nM/L **LH** 9.7 ± 9.5 mIU/mL **FSH** 10.1 ± 9.6 mIU/mL **PRL** 11 ± 3.2 ng/mL **ES** 28.4 ± 2.3 pM/L	Post-RT **T**: 298 ± 25 nM/L **LH**: 7 ± 7.7 mIU/mL **FSH:** 6.6 ± 4.8 mIU/mL **PRL**: 35.9 ± 8.7 ng/mL **ES**: 79.2 ± 12.9 pM/L	Pre-RT Hb: 10 ± 1.6	Post-RT Hb: 15.3 ± 1.8	NR
5. El-Bahnasawy, 2004a	86	NR	300	53	NR	CyA based: 215	End-to-end internal iliac artery 369 End-to-side external iliac artery21 End-to-side common iliac artery 10	**After RT** ED-143 **T**- 13 ± 17.1 **LH-** 6.6 ± 3.1 **FSH**- 6.4 ± 2.4 **PRL**-17.1 ± 13.6	NO ED – 257 **T**- 14.1 ± 19.6 **LH** – 6.4 ± 3.4 **FSH**- 5.5 ± 2.5 **PRL** – 14.9 ± 11.5	Cr ≤ 2: 329 Cr > 2: 171 Hb ≤ 11: 85 Hb > 11: 315		β-blockers: 36, Ca-blockers:-90, ACE inh: 13, α-blockers: 9, Angiotensin drugs: 15, Combined therapy: 137
6. El-Bahnasawy, 2004b	Before NO ED: 2 ED: 1 After No ED: 3 ED: 0	NR	Before- No ED: 21 ED: 11 After No ED: 10 ED:6	Excluded	Excluded	Pred + SRL + Tac or Tac/MMF: 41 Pred + Aza + CyA: 9	End to end internal iliac artery	NR		**After RT:** NO ED: Cr 1,3 ± 0,3 Hb:12,8 ± 1,7 ED Cr1,4 ± 0,7 Hb: 11,4 ± 2,2		NR
7. Gontereo, 2011	Smoking 13 (54.2%)	NR	19 (79.2%)	1 (4.2%)	2 (8.3)	Tac- Pred:2 Tac-Pred-MMF: 17 Tac-Pred- SLM: 2 CyA- Pred-MMF:1 SLM-Pred-MMF: 1 Pred-MMF: 1	End-to-side external iliac artey	Before RT **T**: 409.95 ± 181.87 **PRL**: 16.22 ± 35.04	Post-RT **T**: 419.04 ± 129.09 **PRL**: 10.54 ± 9	NR		NR
8. Gou, 2010	Smoking:48	Gr. I; 57.5 ± 11.6 kg Gr. II:.58.1 ± 10.9 KG	83	5	NR	Corticosteroid + Tac ± MMF	Internal iliac artery 84 External iliac artery 3	NR		Cr: Pre-op Gr. I: 996.1 ± 397.5 µmol/L Gr. II: 951.1 ± 345.5 µmol/L		NR

Table 2 (continued)

Author, year	Smoking/Alcohol	BMI/ Weight	HTN	Diabetes	PAD/ CAD	Treatment after RT	Type of renal anastomosis	Hormone panel (Testosterone, Prolactine, LH, FSH)		Renal Panel Hb levels (Cr-mg/dL, Hb g/dL)	Other medications
9. Jabali, 2020	NR	NR	10	21	NR	CyA, MMF, Tac: 32, Pred, MMF, Tac: 26 Everolimus, MMF, Tac: 1	NR	NR		NR	NR
10. JI, 2010	Nr	NR	NR	NR	NR	NR	End-to end internal iliac artery	NR		NR	NR
11. Jurgensen, 2008	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR
12. Mirone, 2008	Smocking:16 (20.51%) Alcohol: 12 (15.38%)	Mean 75.02 kg	69 (88.46%)	7 (8.97%)	13 (16.66%)	Combinations of: Aza: 8, MMF:18 Ly Ag:3 Methyl-Pred: 30 Pred:31, Everolimus: 5 Rapamycin: 2 SRL: 5 Tac: 10 CyA:57	End-to-side internal iliac artery	NR		Cr: 1.7 (0.8–4.0)	**HTN tt**- 69 (α-Blockers-28, Diuretics-5, β-blockers-34, Ca-blockers-38, ACE-inh-38 **Lipid-lowering drugs**-32
13. Mota, 2019	14	Obesity -7	105	22	10	NR	NR	NR		NR	α-blockers: 26 β- blockers: 54 Psychotropic: 31 5 **ALPHA REDD 8**
14. Musone, 2003	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR
15. Nanjappa, 2012	NR	NR	NR	39	NR	NR	Internal iliac:19.87 ± 4.52 External iliac: 19.26 ± 4.28	Pre-RT T: 8,05 ± 1,7	Post-RT T: 9,43 ± 2,16	NR	NR
16. Nassir, 2009	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR
17. Nghiem, 1983	NR	NR	29	19	NR	NR	End-to-end internal iliac artery 56 End-to-side iliac artery 5	NR		**Post-RT** Cr: <2: 42 2–4: 4 >4: 3 Dialysis: 12	<2 Anti – HTN: 22 >2 Anti -HTN: 7
18. Peng, 2007	Nr	NR	NR	NR	NR	NR	End-to end internal iliac artery: 39 End-to-side external iliac artery: 16	NR		NR	NR
19. PeskircioğL, 1998	NR	NR	NR	NR	NR	NR	NR	NR		NR	NR

Table 2 (continued)

Author, year	Smoking/Alcohol	BMI/Weight	HTN	Diabetes	PAD/CAD	Treatment after RT	Type of renal anastomosis	Hormone panel (Testosterone, Prolactine, LH, FSH)		Renal Panel Hb levels (Cr-mg/dL, Hb g/dL)		Other medications
20. Pourmand 2007	Excluded	NR	NR	None	None	Pred CyA MMF	Internal iliac artery: 45 External iliac artery: 11 Common iliac artery: 8	NR		NR		NR
21. Qiao, 2009	31	NR	37	NR	NR	NR	NR	NR		NR		NR
22. Salvatierra, 1975	NR	NR	NR	NR	NR	NR	NR	NR		Mean Cr 1.3		NR
23. Shamsa, 2005	11	NR	6	NR	NR	CICLO, AZA, MMF, PRED	Internal iliac artery	Pre-RT **T-** 633 ng/dL **PRL**: 22,96 ng/mL	Post-RT **T**: 387 ng/dL **PRL**: 14,6 ng/mL	Pre-RT Cr-7.17 ± 3.63 Hb -9.9 ± 1.97	Post-RT Cr 1.46 ± 0.35Hb 10.53 ± 1.38	NR
24. Soliman, 2017	NR	NR	NR	NR	NR	NR	NR	NR		NR		NR
25. Spirito, 2020	22	26.62 SD = 4.06	91	22	NR	NR	NR	T –380.20 NG/DL SD = 159.97		NR		Calcineurin-inh -91
26. Teng, 2010	NR	NR	Excluded	Excluded	Excluded	CyA + Pred + MMF: 7 Tac + Pred + MMF: 17	NR End-to end internal iliac artery-excluded	Before RT **T**: 3.07 ± 0.94 ng/mL **PRL**: 24,35 ± 11,62 ng/mL **FSH**: 6,34 ± 3,93 mIU/mL **LH**: 13,56 ± 10,43 mIU/L	After RT **T**: 6,54 ± 3,14 ng/mL **PRL**: 7,16 ng/mL **FSH**: 7,76 ± 4,89mIU/L **LH**: 7,39 ± 3,86mIU/L	NR		NR
27. Tian,2007	NR	NR	NR	NR	NR	NR	NR	NR		NR		NR
28. Tsujimura, 2002	NR	NR	NR	NR	NR	CyaA + Pred: 85 Aza + Pred: 23 Tac + Pred: 13	Internal iliac artery	Improvement in SF **T**: 369 ± 23,7 ng/dL **LH**: 5,1 ± 0,9mIU/mL **FSH**: 9,8 ± 1,9mIU/mL **PRL**: 5,7 ± 0,7mIU/mL	Wrosening SF **T**: 359 ± 31,9 ng/dL **LH**: 6,8 ± 1,2mIU/mL **FSH**: 8,4 ± 1,2mIu/mL **PRL**: 5,6 ± 0,8mIU/mL	Improv.SF Cr: 1,5 ± 0,1 Hb: 13,3 ± 0,3	Worse SF Cr:1,7 ± 0,3 Hb: 12 ± 0,4	

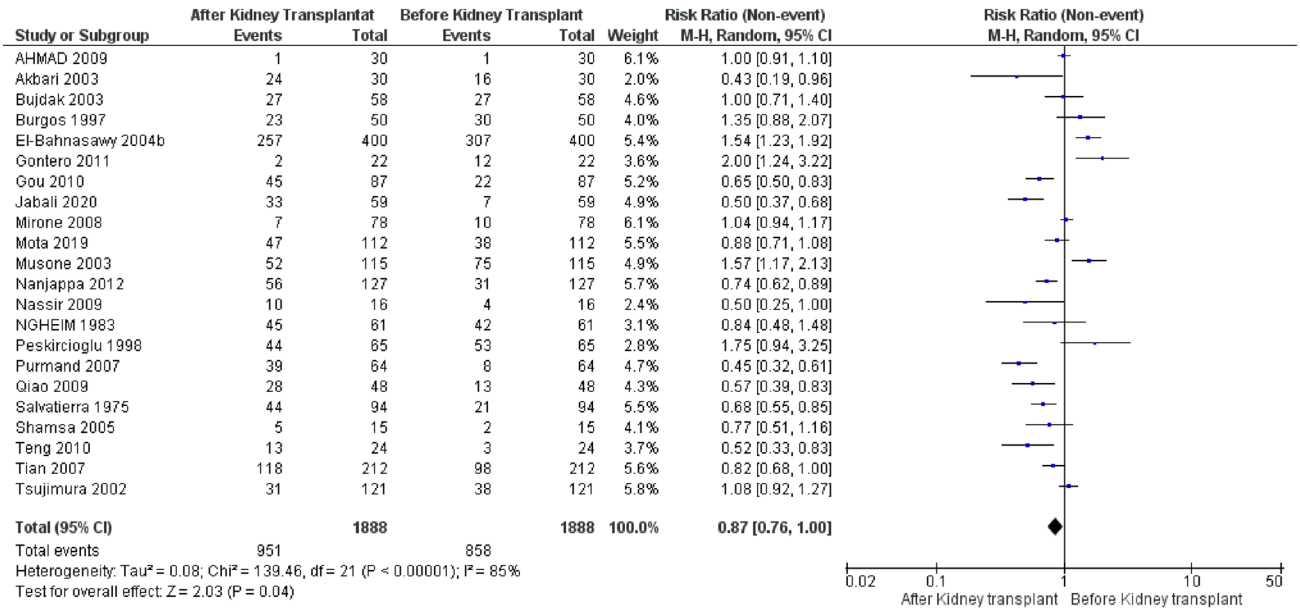

Fig. 2 Forest plot of the risk-ratio of patients with ED pretransplant compared to postoperative evaluation

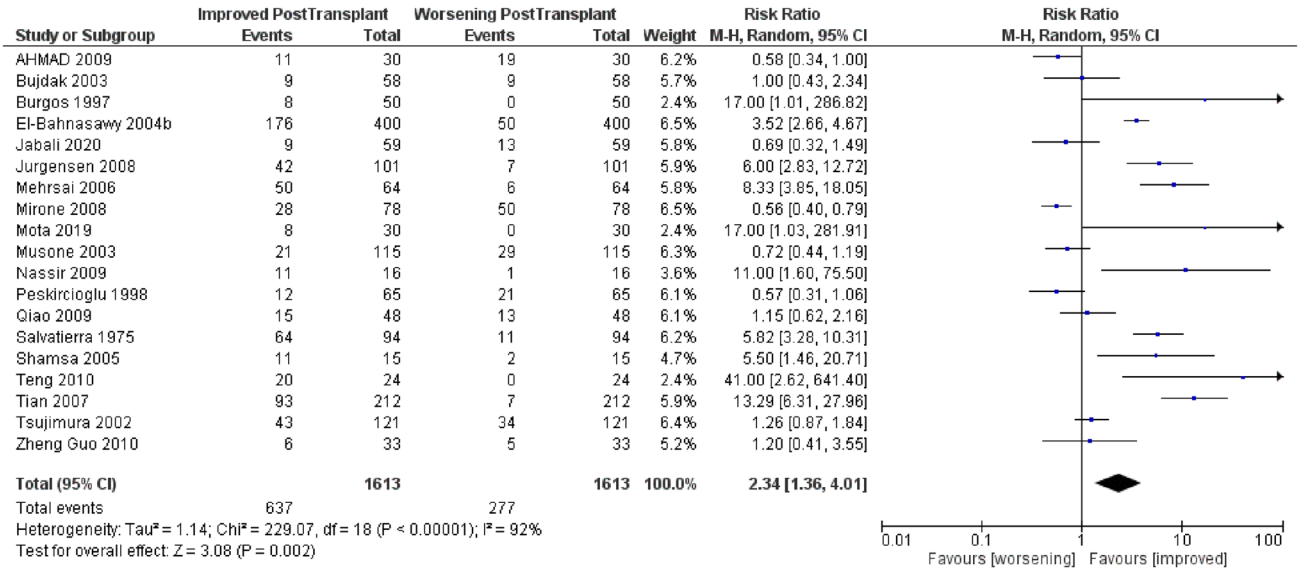

Fig. 3 Forest plot of the risk ratio of patients improved sexual function compared to patients with worsening sexual function at postoperative evaluation

Type of immunosuppression used after renal transplantation

13 Studies reported the current regimen of immunosuppression and five studies reported concurrent medications for comorbidities, but there was insufficient data, so that we could not perform a formal analysis based on these components.

Second transplantation and erectile function

Few studies in our analysis reported the number of included patients that had a second transplant. A total of 49 patients underwent a second kidney transplant, but there was insufficient data to perform an analysis.

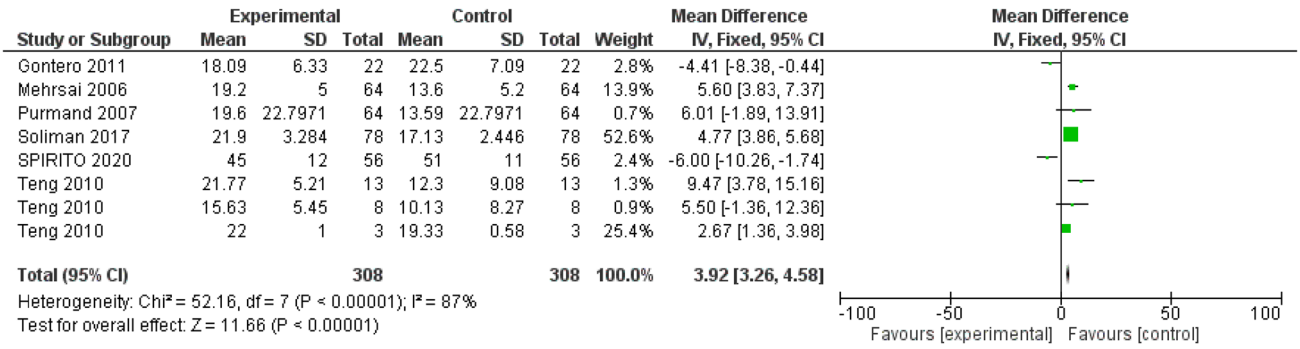

Fig. 4 Forest plot of mean difference in IEEF-15 or IEEF-5 score pre and postoperative evaluation

Risk of bias

We explored the publication bias and found an equal distribution of the included trials (Fig. 5).

The quality of the included studies was assessed using the Newcastle–Ottawa scale (NOS). Starts were awarded for each quality item investigated. Overall, the quality of studies was adequate, with only a few studies that had an average quality score under 7 points. The full assessment of the studies included and overall quality score of each study can be seen in Table 3.

Discussion

Sexual dysfunction is prevalent among individuals with chronic kidney disease. A meta-analysis of 50 studies comprising 8343 participants with CKD, both males and females, reported a high summary estimate of erectile dysfunction in men with CKD—70% [6]. The cause of erectile dysfunction in CKD could be related to the underlying disease (diabetes, arterial hypertension), but it can also be related to the uremic effects on the nervous system and the changes in the hormone panel, such as diminished testosterone production [35].

Our meta-analysis shows that renal transplantation improves erectile function in participants with end-stage renal disease. The majority of the participants included in our study were on renal replacement therapy (especially haemodialysis) before renal transplantation and only 34 had a pre-emptive transplant. Compared to pre-transplant evaluation, our study shows a 13% improvement in erectile dysfunction after renal transplantation. This improvement is also reflected in an analysis of six studies that shows a mean rise of 3.92 points in the IIEF score post-transplant.

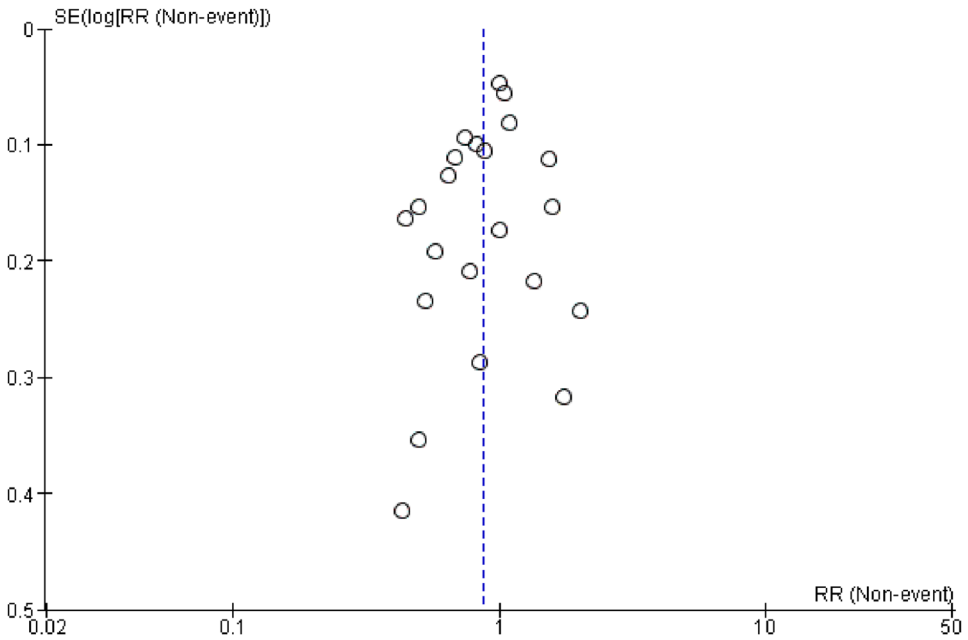

Fig. 5 Funnel-plot assessing publication bias

Table 3 Newcastle- Ottawa scale for assessment of quality of included studies (each asterisk represents if individual criterion within the subsection was fulfilled)

Quality assessment criteria	1)Representativeness of the Exposed Cohort	2)Selection of the non–exposed Cohort	3)Ascertainment of exposure	4)Demonstration that outcome of interest was not present at the start of study	5)Adequate control of most important cofounder?	6)Adequate control of any additional factor?	7)Assessment of outcome	8)Was follow-up long enough for outcome to occur?	9)Adequacy of follow-up cohorts	
Acceptable (*)	Representative of average adult in community (age/ sex/being at risk of disease)	Drawn from the same community as the exposed cohort	Secure record, structured interview				Independent/ Blind assessment		Complete follow–up or subjects lost to follow–up unlikely to introduce bias	Overall quality score (9)
1.Ahmad et al	*	*	*	*	–	*	–	*	*	7
2. Akbari et al	*	*	*	*	–	*	–	*	*	7
3. Bujdak et al	*	*	*	*	–	*	–	–	–	5
4. Burgos et al	*	*	*	*	–	*	–	*	*	7
5. El Bahnasawy et al. 2004a	*	*	*	*	–	*	–	*	*	7
6. El Bahnasawy et al. 2004b	*	*	*	*	–	*	–	*	*	7
7. Gontero et al	*	*	*	*	–	*	–	*	*	7
8. Gou et al	*	*	*	*	–	*	–	*	*	7
9. Jabali et al	*	*	*	*	–	*	–	*	*	7
10. Ji et al	*	*	*	*	–	*	–	*	*	7
11. Jurgensen et al	*	*	*	*	–	*	–	–	–	5
12. Mirone et al	*	*	*	*	–	*	–	*	*	7
13. Mota et al	*	*	*	*	–	*	–	*	*	7
14. Musone et al	*	*	*	*	–	*	–	–	–	3
15. Nanjappa et al	*	*	*	*	–	*	–	*	*	7
16. Nassir et al	*	*	*	*	–	*	–	*	*	7
17. Nghiem et al	*	*	*	*	–	*	–	*	*	7
18. Peng et al	*	*	*	*	–	*	–	*	*	7
19. Peskircioğl et al	*	*	*	*	–	*	–	*	*	7
20. Pourmand et al	*	*	*	*	–	*	–	*	*	7
21. Qiau et al	*	*	*	*	–	*	–	*	*	7
22. Salvatierra et al	*	*	*	*	–	*	–	*	*	7
23. Shamsa et al	*	*	*	*	–	*	–	–	*	6

Table 3 (continued)

Quality assessment criteria	1)Representativeness of the Exposed Cohort	2)Selection of the non–exposed Cohort	3)Ascertainment of exposure	4)Demonstration that outcome of interest was not present at the start of study	5)Adequate control of most important cofounder?	6)Adequate control of any additional factor?	7)Assessment of outcome	8)Was follow-up long enough for outcome to occur?	9)Adequacy of follow-up cohorts	
Acceptable (*)	Representative of average adult in community (age/sex/being at risk of disease)	Drawn from the same community as the exposed cohort	Secure record, structured interview				Independent/ Blind assessment		Complete follow–up or subjects lost to follow–up unlikely to introduce bias	Overall quality score (9)
24. Soliman et al	*	*	*	*	–	*	–	*	*	7
25. Spirito et al	*	*	*	*	–	*	–	*	*	7
26. Teng et al	*	*	*	*	–	*	–	*	*	7
27. Tian et al	*	*	*	*	–	*	–	–	*	6
28. Tsujimura et al	*	*	*	*	–	*	–	*	*	7

Payne et al. [36] conducted a literature review regarding the prevalence and treatment of erectile dysfunction in male solid organ transplant recipients and indicated that the prevalence of erectile dysfunction in male renal transplant recipients was between 54 and 66%. However, it did not evaluate the population pre-transplantation.

Our findings are in line with other meta-analyses that researched sexual function after renal transplantation in CKD patients or patients on renal replacement therapy. One meta-analysis published in 2020 by Kang et al. [37] that included 9 observational studies indicated that renal transplantation may improve erectile function in patients with end-stage kidney disease. They also showed improvement in the mean IIEF 5 and IIEF-15 scores. Compared to our meta-analysis, Kang et al. did not include the same study population before and after renal transplantation and the overall sample size was significantly smaller compared to our analysis. Another meta-analysis conducted by Pyrgidis et al. [38] included a total of 10,320 males with end-stage kidney disease and showed a high prevalence of erectile dysfunction in patients with chronic kidney disease: 79% in patients on haemodialysis, 71% in patients with peritoneal dialysis, 82% in patients starting dialysis. The lowest prevalence of erectile dysfunction was 59% in participants with renal transplantation. However, although Pyrgidis et al. showed that in renal transplantation there is a lower prevalence of erectile dysfunction, they did not evaluate the effect of renal transplantation on erectile function.

Our meta-analysis has a few strong points. First, it has a large population of males (2252 participants) with end-stage kidney disease that underwent renal transplantation. Another advantage is that we only included studies using the same study population before and after renal transplantation. This way, we could evaluate directly the impact of renal transplantation on erectile function. Additionally, the majority of the studies in our meta-analysis used the standardized IIEF to assess sexual function.

However, our study has some limitations, one of which being the observational nature of the studies included and the lack of RCTs conducted on this subject. Another limitation is that we cannot completely rule out overlapping study populations. For example, two of the articles included: *El-Bahnasawy* et al. A and *El-Bahnasawy* et al. B had an overlap of 50 patients. Other limitations include the inability to perform analyses regarding the effect of the type of anastomosis used and the effect on erectile function. We could not perform analyses on other factors that could affect erectile function, such as concurrent immunosuppressive regimens used after renal transplantation.

Abnormalities in the serum levels of testosterone, LH, FSH and prolactin have been reported in patients with ESKD. Specifically, testosterone levels tend to be suboptimal in patients on haemodialysis. Some of the studies

included in this meta-analysis reported the hormone levels before and after renal transplantation. For example, *Akbari* et al. *and Teng* et al. showed that the level of testosterone increased after renal transplantation, while levels of LH, FSH and prolactin decrease. Increase in testosterone levels seem to be consistent among the studies that reported hormone levels, but an analysis could not be performed on these components due to insufficient data.

The underlying pathological mechanisms involving ED and CKD are not completely understood, but various treatments are available, including phosphodiesterase type 5 inhibitors or testosterone therapy in patients with low levels of testosterone. It is important to study the effect of renal transplantation on erectile dysfunction, since erectile dysfunction further affects quality of life and could accentuate certain neuropsychiatric disorders, such as depression and anxiety.

Conclusions

In conclusion, the findings from our meta-analysis show improvement in erectile dysfunction after renal transplantation when compared to pre-transplant evaluation. Additionally, there is also improvement in mean IIEF score. However, further studies with a larger number of patients are needed to investigate the impact of renal transplantation on erectile dysfunction. Moreover, studies are needed to determine whether the type of anastomosis used has an effect on post-transplant sexual function.

Data availability Data analyzed in this study were a re-analysis of existing data, which are openly available at locations cited in the reference section.

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