REVIEW

Incidence and Severity of Erectile Dysfunction in Chronic Kidney Disease Patients Undergoing CAPD and Hemodialysis: A Systematic Review and Meta-analysis

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Summary

Background: Erectile dysfunction (ED) is an adverse effect of chronic kidney disease (CKD) treatment that can reduce patients' quality of life. Consequently, the purpose of this study is to assess the incidence and severity of ED in CKD patients who have undergone continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis. **Methods:** We performed a systematic search on several electronic reference databases (PubMed, ScienceDirect, Web of Science, and Cochrane). Inclusion criteria are articles published in English, full-text availability, and articles published between 2001 and 2023. The reviewed studies were observational studies. The studies analyzed either CAPD or hemodialysis. **Results:** A total of 15 studies were included. ED in patients with CKD who had undergone CAPD and hemodialysis varied, ranging from 51.84% to 80.5%and 56% to 89%, respectively. A pooled estimate showed that CKD patients who underwent hemodialysis had higher odds of developing ED (odds ratio [OR]=12.56; 95% confidence interval [CI]=6.37–24.77; $p<0.001$) compared with those who underwent CAPD (OR=8.02; 95%CI=1.64–39.15; $p=0.01$). Regarding the laboratory outcomes, no significant differences were found in creatinine serum (MD= −1.08; 95%CI= −3.21 to 1.06; $p=0.32$) and hemoglobin levels (MD= −0.38; 95%CI= −1.05 to 0.30; $p=0.27$) between CKD patients who underwent dialysis, either with or without ED. **Conclusion:** ED is prevalent among patients undergoing hemodialysis. In addition, hemodialyzed patients exhibited more severe levels of ED compared with CAPD patients. Therefore, we suggest CAPD for CKD patients with ED.

Keywords: Erectile dysfunction, Chronic kidney disease, CAPD, Hemodialysis, Peritoneal dialysis

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Introduction

About 8–16% of the world's population is diagnosed with chronic kidney disease (CKD), based on renal structure abnormalities and kidney dysfunction lasting longer than 3months (1,2). Untreated CKD can lead to a variety of complications, including renal failure and early cardiovascular disease, which can reduce patients' life expectancy (3). Hence, CKD patients are always

suggested to undergo treatments to improve their quality of life (QoL).

Treatments for patients with CKD, such as continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis, are essential to improve their conditions. However, these treatments and CKD patients have a close relationship with erectile dysfunction (ED), which is the persistent inability to attain and/or maintain an erection for satisfactory sexual activity (4). Sexual dysfunction is highly prevalent in patients with CKD, especially those receiving dialysis (5).In addition, ED and metabolic syndrome are highly related, ranging from 40% to 60% in peritoneal dialysis (6,7).

Many components of the endocrine system are affected in CKD patients. The disruption of the hypothalamic–pituitary–gonadal axis in men with CKD is associated with significant functional impairment and diminished QoL (8). Males with CKD have a high prevalence of ED, with 71% of people with estimated glomerular filtration rates (eGFR) below 60 mL/min per 1.73 m^2 affected (9).

Hypogonadism (low testosterone), defined as total testosterone below 300 ng/mL, is common in men with CKD, particularly those undergoing dialysis, and can contribute to decreased libido, ED, oligospermia, infertility, and anemia. Patients undergoing hemodialysis are reported to have an abnormal response to the Valsalva maneuver, impaired nocturnal penile tumescence, and bulbocavernous reflex, all of which are correlated with sexual dysfunction (4,5).

The treatment of EDshould begin with an assessment of the general condition, an evaluation of potential covariates, and the adoption of lifestyle modifications such as quitting smoking, reducing alcohol consumption, and engaging in regular physical activity. Regarding dialysis patients, clinicians should concentrate on optimizing dialysis delivery and ensuring adequate nutritional intake (4).

However, the treatments are closely related to and may induce ED directly or indirectly in CKD patients. In addition, considering the incidences of ED in CKD patients who have received treatment, there have always been concerns among CKD patients regarding clinical properties, which can directly diminish patients' QoL. Nevertheless, the incidence of ED differs considerably between populations and treatments (6). The purpose of this study is to determine the incidence and severity of ED in CAPD and hemodialysis patients.

Materials and Methods

Eligibility criteria

Inclusion criteria for these studies are as follows:

1. Published in English, and full-text was available.
2. Published between January 2001 and May 2023.
3. The studies were randomized controlled trials or observational studies.
4. The studies used CAPD or hemodialysis.
5. The studies assessed the outcome or complication of CAPD or hemodialysis in patients with CKDs.

Guidelines

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline to perform the reporting of this study. We can find 13 appropriate studies included in the review, as shown in the flow diagram in Figure 1.

Search strategy

Two investigators (I.P. and D.H.) independently conducted a literature search on May 9, 2023 for relevant articles available in several databases (PubMed, ScienceDirect, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) following PRISMA guidelines. The following keywords were used: ((sexual dysfunction) OR (erectile dysfunction)) AND ((chronic kidney disease) OR (chronic renal failure)) AND ((dialysis) OR (CAPD) OR (continuous ambulatory peritoneum dialysis)).A manual search was also conducted to obtain the relevant articles fulfilling the criteria mentioned. Any inconsistencies were resolved by consensus.

Data extraction and quality assessment

The key outcome measure was the post-treatment outcomes, the ED, assessed by the International Index of Erectile Function (IIEF) questionnaire, used to evaluate

the male sexual function, erectile function, sexual desire, intercourse satisfaction, orgasmic function, and overall satisfaction. The total scores ranged from 1 to 30, which can be classified as severe [1–6], moderate [7–12], mild to moderate [13–18], mild [19–24], and no dysfunction [25–30] (10).

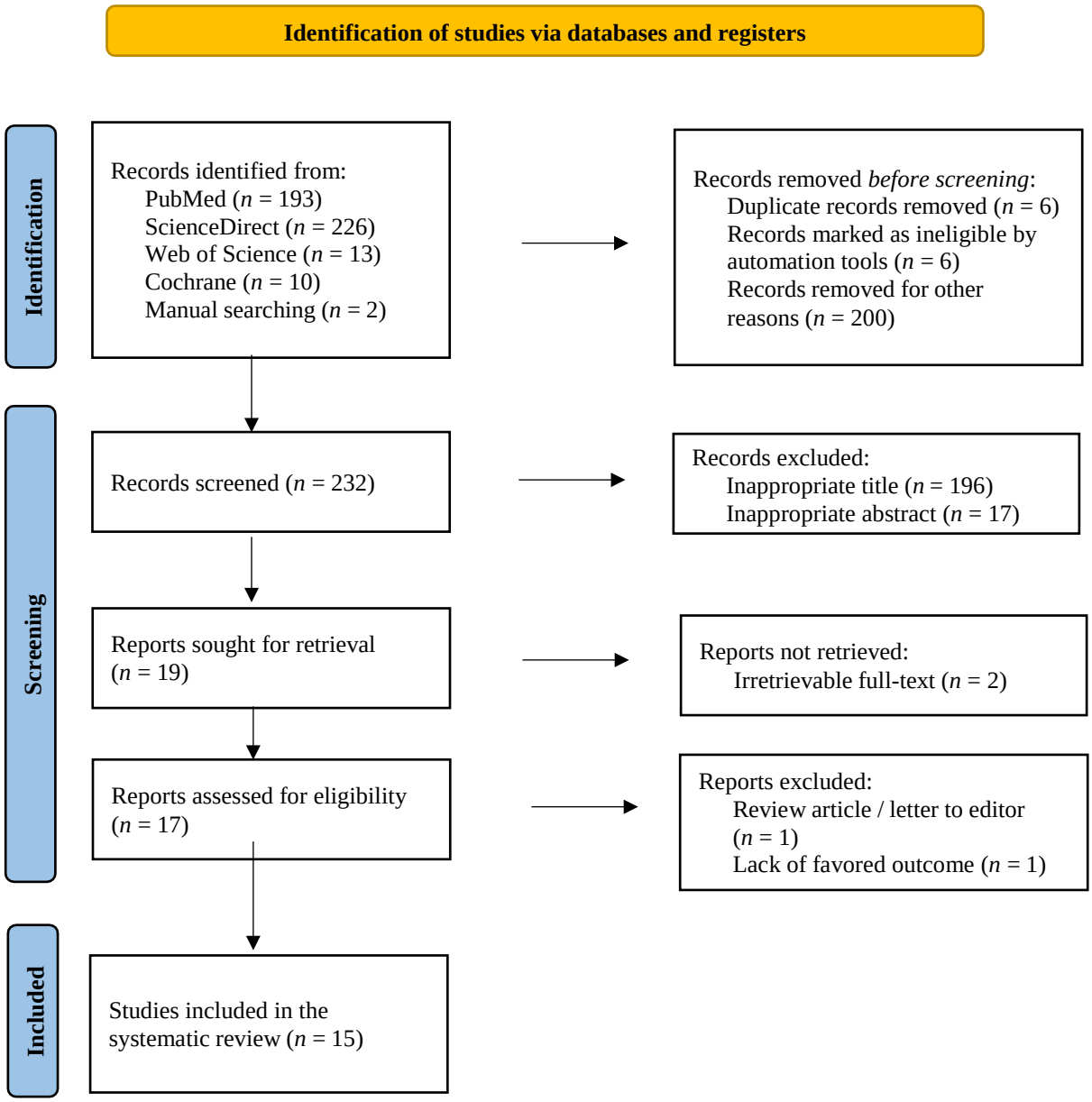

Figure 1. PRISMA flow diagram.

Results

Study characteristics

In this systematic review, we found a total of eight cross-sectional studies related to hemodialysis (11–18), one case–control study (19), one cohort study (20), and one prospective study (21), comparing ED in CKD patients undergoing hemodialysis (Table 1). To our knowledge,

there were only five studies related to CAPD in patients with CKD (18,22–25).

The IIEF Questionnaires assessed the ED in all those studies. The mean age of the patients was in the range of 35.26 to 59.5 ± 15.5 years.

Table 1. Characteristics of the included studies

Authors	Study design	Sample size	Mean age (mean ± SD), years	Type of dialysis	Incidence of ED *n* (%)
Messina et al. (11)	Cross-sectional	58	50.2 ± 14.6	Hemodialysis	35 (60.3)
Nishida et al. (12)	Cross-sectional	178	59.2 ± 10.7	Hemodialysis	161 (89)
Rosas et al. (13)	Cross-sectional	302	59.5 ± 15.5	Hemodialysis	234 (82)
Malekmakan et al. (14)	Cross-sectional	73	55.4 ± 16.1	Hemodialysis	64 (87.7)
Ali et al. (20)	Cohort	75	40.85 ± 8.94	Hemodialysis	62 (80)
Al Khallaf et al. (21)	Prospective	25	38.2 ± 6.6	Hemodialysis	14 (56)
Fernandes et al. (15)	Cross-sectional	275	48.6 ± 12.8	Hemodialysis	198 (72.3)
Makarem et al. (16)	Cross-sectional	59	54.73 ± 14.08	Hemodialysis	50 (84.74)
Antonucci et al. (19)	Case–control	44	49	Hemodialysis	31 (70)
Gorsane et al. (17)	Cross-sectional	30	49.1	Hemodialysis	24 (80)
Tekkarismaz A et al. (18)	Cross-sectional	31	48.5 ± 7.4	Hemodialysis	23 (74.19)
Tekkarismaz B et al. (18)	Cross-sectional	20	53.6 ± 10.8	CAPD	17 (85)
Ye et al.(22)	Cross-sectional	170	43.2 ± 9.6	CAPD	137 (80.5)
Lai et al.(23)	Prospective	54	48.8 ± 10.8	CAPD	28 (51.9)
Hassan et al.(24)	Cross-sectional	27	59.0 ± 7.1	CAPD	14 (51.84)
Krishnan et al. (25)	Cross-sectional	44	61.8 ± 13.9	CAPD	39 (88)

Abbreviation: ED,erectile dysfunction.

Incidence of ED

ED rates in the hemodialysis studies varied from 60.3%, 89%, 82%, 87.7%, 80%, 56%, 72.3%, 84.74%, 70%, 80%, and 74.19%. In CAPD studies, the ED rates were 85%, 80.5%, 51.9%, 51.84%, and 88%.

A pooled analysis of 16 studies involving 1465CKD patients revealed that those CKD patients who underwent dialysis had higher odds of developing ED (odds ratio [OR]=10.82; 95%confidence interval [CI]=5.82–20.11; p<0.001). Subsequently, subgroup

analysis was performed according to the type of dialysis, including hemodialysis (11–21) and CAPD (18,22–25). CKD patients who underwent both hemodialysis ((OR=12.56; 95%CI=6.37–24.77; p<0.001)) and CAPD (OR=8.02; 95%CI=1.64–39.15; p=0.01) had significantly higher odds of developing ED. (Figure 2). In terms of potential publication bias, Begg's funnel plots analysis was performed qualitatively by visual inspections, as documented in Figure 3.

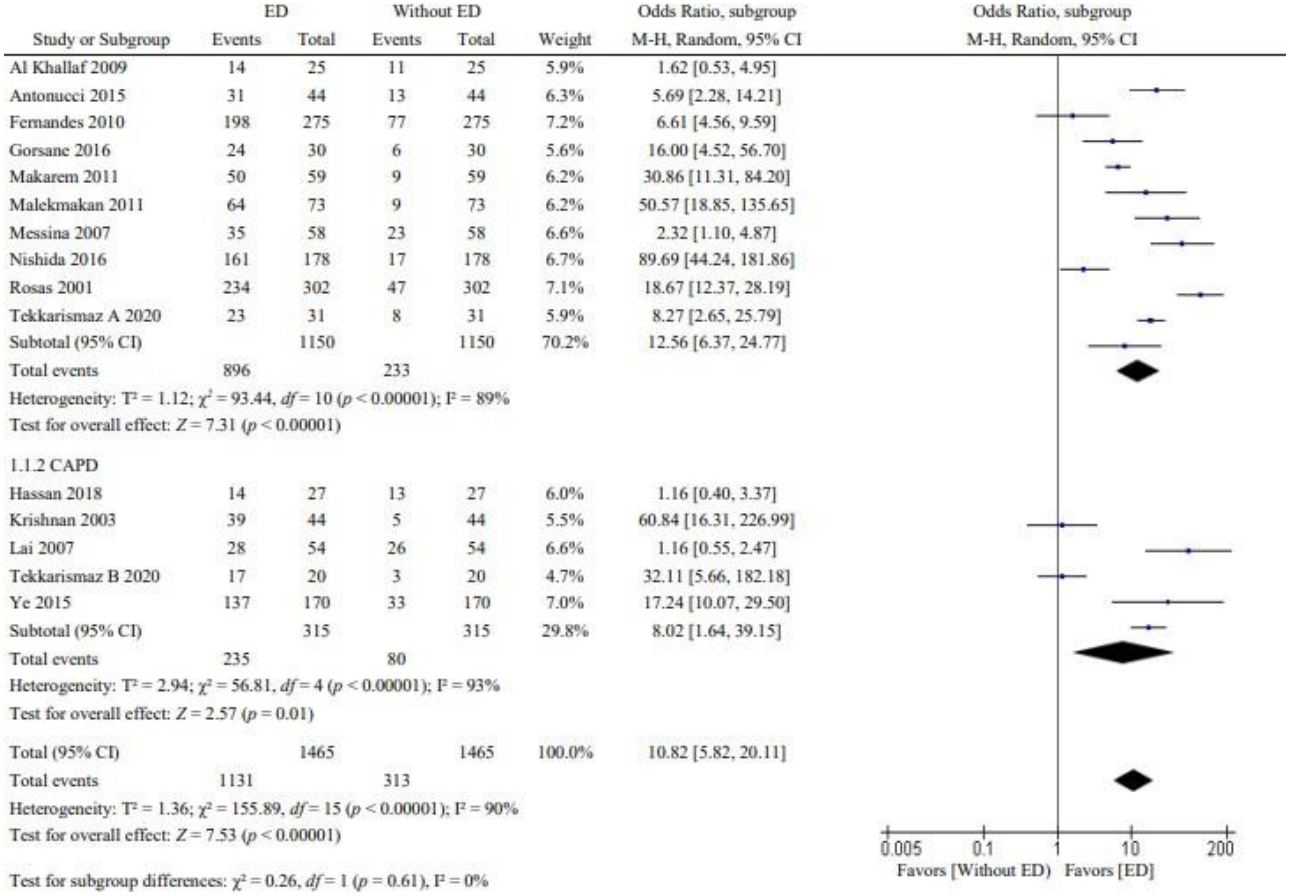

Figure 2. Forest plot of comparison of incidence of ED among CKD patients who underwent hemodialysis and CAPD. Individual studies are represented by a blue square and a horizontal line, which corresponds to the point estimate and 95% confidence interval of the odds ratio. The size of the black square reflects the weight of the study in the meta-analysis. The solid vertical line corresponds to "no effect" of treatment—an odds ratio of 1.0. When the confidence interval includes 1, it indicates that the result is not significant at conventional levels (p>0.05).

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; CI, confidence interval;CKD, chronic kidney disease; ED, erectile dysfunction.

Severity of ED

The severity of ED in hemodialysis studies has the most percentages in severe ED, ranging from 4% to 63%. Similarly, the patient distributions in CAPD studies also peak in the severe ED (35%) (Table 2).

Diabetes mellitus and ED

Messina et al. mentioned in their study that there was only 1patient among 15 CKD patients with diabetes mellitus (DM) who did not have ED, which indicated that there was a significant association between DM and ED (11).

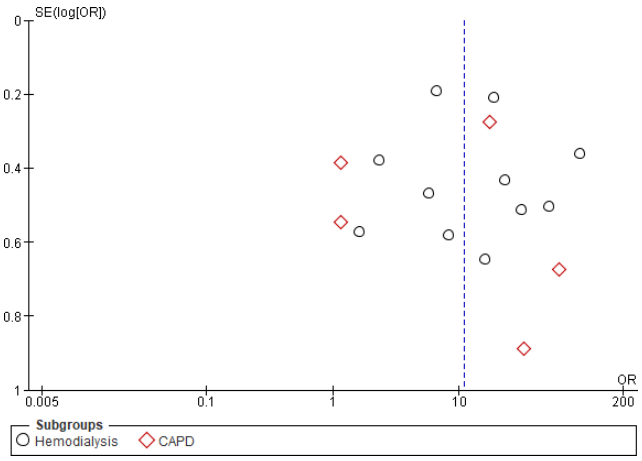

Figure 3. Funnel plot for comparison of studies reporting the incidence of ED among CKD patients who underwent hemodialysis and CAPD.
Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; ED, erectile dysfunction; OR, odds ratio; SE, standard error.

In addition, Al Khallaf et al. showed another evidence, which stated that fewer incidences of ED were found in non-diabetic CKD patients who underwent hemodialysis than in other patients in this systematic review, where diabetic patients were included (21).

In terms of laboratory outcomes, the pooled estimate of four studies (11,13, 14,22) comparing the mean of serum creatinine in CKD patients undergoing dialysis with or without ED revealed no statistically significant difference between both the groups (MD= −1.08; 95%CI= −3.21 to 1.06; *p*=0.32) (Figure 4).

Similarly, the pooled estimate of five studies (11,13, 14, 22,25) comparing hemoglobin levels also demonstrated no statistically significant difference (MD= −0.38; 95%CI= −1.05 to 0.30; *p*=0.27) between CKD patients undergoing dialysis either with or without ED (Figure 5).

Table 2. Severity of ED in CKD patients with hemodialysis

Authors	Severity of ED			
	Mild (%)	Mild–moderate (%)	Moderate (%)	Severe (%)
Messina et al. (11)	8.6	19	5.1	27.6
Nishida et al. (12)	9	13	16	52
Rosas et al. (13)	21	8	8	45
Malekmakan et al. (14)	6.8	N/A	17.8	63
Ali et al. (20)	32	16	12	20
Al Khallaf et al. (21)	8	28	16	4
Fernandes et al. (15)	26.3	12.8	8	8
Makarem et al. (16)	10.2	16.9	11.9	45.8
Antonucci et al. (19)	16	N/A	22	31.8
Tekkarismaz Aet al. (18)	16.1	25.8	22.6	9.7
Tekkarismaz Bet al. (18)	20	25	5	35

Abbreviations: CKD, chronic kidney disease; ED, erectile dysfunction.

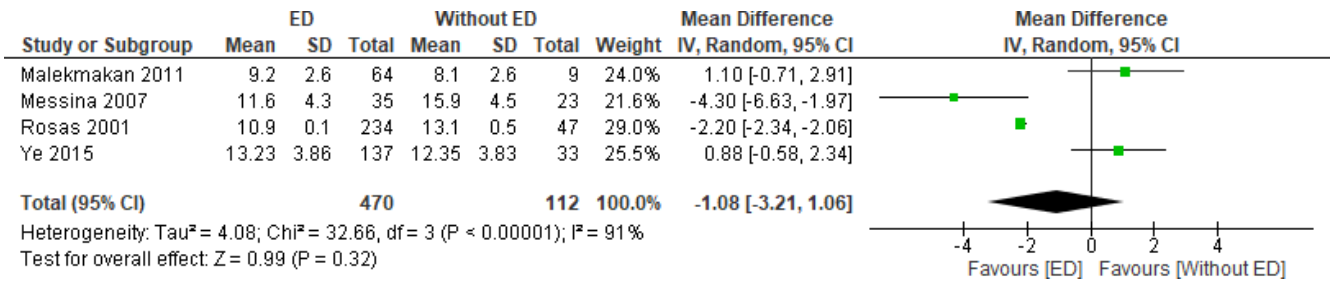

Figure 4. Forest plot of creatinine concentrations in CKD patients with or without ED undergoing hemodialysis.
Abbreviations: CKD, chronic kidney disease; ED, erectile dysfunction; SD, standard deviation.

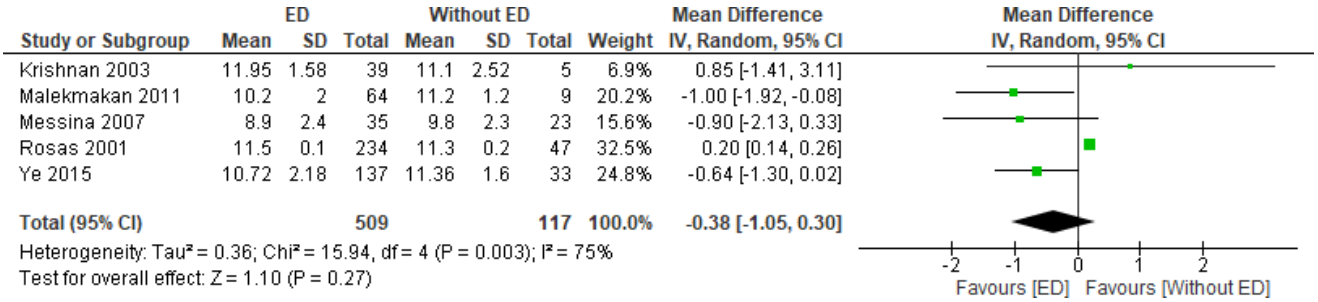

Figure 5. Forest plot comparison of Hb concentrations in CKD patients undergoing HD with or without ED.
Abbreviations: CI, confidence interval; ED, erectile dysfunction; Hb, hemoglobin; HD, hemodialysis; SD, standard deviation.

Discussion

In this systematic review including 13 studies, we found that the prevalence of ED in CKD is high, affecting more than 50% of the population included. This is in line with a previous meta-analysis of observational studies, indicating a prevalence of ED in CKD patients of 70% (26). First, even onlya moderate reduction in theglomerular filtration rate (GFR) is able to result in a disturbance of the pituitary–gonadal axis that rarely normalizes with dialysis, which could, however, generally be restored by a well-functioning kidney transplant (27).

In CKD, pituitary luteinizing hormone(LH) secretion maintains its pulsatile character, but the amplitude of the pulses is diminished (8). A defect in hormonal regulation of the Leydig and Sertoli cells results in gonadotropin deficiency or resistance. The baseline levels of LH are high, due in part to feedback from low testosterone levels and in part to reduced renal clearance. In particular, the total and free testosterone levels are reduced, while sex hormone-binding globulin is normal. In addition to these secretory changes, the normal signaling of LH is inhibited in CKD. This appears to occur in a proportionate degree of severity to the reduction in glomerular GFR. Consequently, the main clinical outcomes related to this are the loss of libido and ED, some regression of secondary sexual characteristics, fatigue, decrease of bone mineral density, and loss of muscle mass and strength (8, 14).

Disturbances in neurovascular control, abnormal hormone levels, or psychological factors are responsible for the vast majority of ED that is broadly classified as psychogenic (generalized, situational), organic (vasculogenic, neurogenic, anatomic, endocrinologic), or mixed (27).

According to our knowledge, this systematic review is one of the few studies that evaluates ED in different treatments such as hemodialysisand CAPD. Nevertheless, there are already a numberof studies that discuss these treatments separately and evaluate the incidence of ED in their studies.

Our systematic review found the fewest ED incidences in CAPD studies. In addition, a study by Tavallaii et al. declared that CAPD showed better outcomes in sexual function in CKD patients than in CKD patients who underwent hemodialysis (28).Unlike CAPD in several

studies, which showed an improvement in their subjects' sexual functions significantly, the work of Duarsa et al. stated that CKD patients who had undergone hemodialysis showed no significant differences in ED between pre- and post-hemodialysis (29–33).

In this review, we found that more ED incidence happened in patients who underwent hemodialysis than those who got CAPD. Whereas CKD patients who underwent hemodialysis is highly correlated with the incidence of ED, thisis inconvenient for the patients. Hence, CAPD can be suggested to those struggling with this problem, as it may lower the ED rate in CKD patients (30).In contrast, a study by Mirone et al. had different results, which showed worse erectile function in patients <45 years old and no progression in patients >45 years old (34). Therefore, this topic is still controversial, and future studies are needed to evaluate the ED level improvement in hemodialyzed patients.

Erectile and kidney dysfunction share common risk factors and are associated with diseases involving endothelial impairment such as DM, hypertension, dyslipidemia, coronary artery disease, smoking, and obesity (5).In CKD, various inflammatory pathways are induced by the use of glucose-based solutions in peritoneal dialysis or the extracorporeal circuit in hemodialysis, which results in the formation of oxidative stress (8).Also, metabolic disorders are known to worsen the ED level in CKD patients, such as diabetes, in similar pathogenesis(11,21),hence, lowering the sperm quality in CKD patients and resulting in ED (8).

Conclusion

ED is more prevalent in patients undergoing hemodialysis. It has also been discovered that the population of hemodialyzed patients contains more patients with more severe levels of ED than patients who have undergone CAPD. We recommended CAPD for CKD patients who encountered ED-related discomfort. To evaluate the ED and its progression in CKD patients, particularly those who have undergone hemodialysis and CAPD, it is recommended that additional topics be included in future works.

Author contributions

Both authors equally contributed to conceptualization, data curation, formal analysis, investigation, project administration, validation and in writing, reviewing and editing of the original draft.

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