

Impact of pre-transplant dialysis modality on kidney transplant outcomes: a systematic review and meta-analysis

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Abstract. – **OBJECTIVE:** For end-stage renal disease (ESRD), patients receiving kidney transplantation, peritoneal dialysis (PD) and hemodialysis (HD) are both appropriate modes of pre-transplant dialysis. The aim of this review is to assess the impact of pre-transplant PD compared to HD on kidney transplant outcomes in ESRD patients.

MATERIALS AND METHODS: A comprehensive search in digital databases, like PubMed, SCOPUS and EMBASE and a manual search were conducted to identify cohort studies comparing the kidney transplant outcomes of both pre-transplant dialysis modalities. The data were subjected to both qualitative and quantitative analysis. A meta-analysis was carried out to calculate the effect estimate for patient survival, graft survival and delayed graft function, death-censored graft survival, acute rejection-free graft survival, graft vessel thrombosis, urological complications, surgical complications, any infections, and onset of diabetes after transplantation. The qualities of the included studies were judged by the New-castle Ottawa scale.

RESULTS: The overall patient survival is shown to be better with patients who underwent pre-transplant PD compared to HD with OR 1.34 95% CI [1.11, 1.61], $p = 0.002$. Delayed graft function was found to be highly associated with HD compared to PD with OR 0.60 [0.52, 0.70], $p < 0.0001$ with moderate heterogeneity ($i^2 = 48\%$). However, no difference was observed in terms of graft survival, complications, infections, and new onset of diabetes mellitus compared to patients undergoing pre-transplant HD.

CONCLUSIONS: Within the limitations of the review, it can be concluded that ESRD patients undergoing pre-transplant PD were found to have better patient survival and lower incidence of delayed graft function.

Key Words:

End-stage renal disease, Kidney transplantation, Pre-transplant dialysis, Peritoneal dialysis, Hemo-dialysis, Systematic review, Meta-analysis.

Introduction

End stage renal disease (ESRD) is a stage of chronic kidney disease, where kidney function is severely reduced and fails to meet the body's needs. The global health burden of ESRD is rapidly increasing, with an estimated 2.6 million people affected worldwide¹. These patients are often advised to undergo routine dialysis prior to kidney transplantation. Pre-transplant dialysis is often recommended to delay the process of transplantation until the ESRD patients find a matching donor². The dialysis is performed either with help from an external filtration device, known as hemodialysis (HD), or by using the inside lining of your abdomen (the peritoneum) as the filter, rather than a machine, known as peritoneal dialysis (PD).

HD and PD are both acceptable modes of pre-transplant dialysis with their own benefits and limitations. PD has greater patient preference and satisfaction, as the procedure can be carried out at home and does not require any external device³. On the other hand, HD is performed in a hospital setting, with longer sessions every week. PD must be performed on a daily basis, while patients being treated with HD may have an advantage of treatment free days^{4,5}.

Many large cohort studies⁶⁻⁸ have evaluated the effect of PD in comparison to HD on kidney transplant outcomes, with conflicting results. Unfortunately, the conclusions drawn from these studies were difficult to interpret resulting in a number of systematic reviews and meta-analyses to provide pooled evidence. The conclusions from these studies⁶⁻⁸ suggest that PD is a better pre-transplant dialysis modality than HD. Further evidence from Tang et al⁹ 2016 and Joachim et al¹⁰ 2016, indicates that pre-transplant PD is associated with higher post-transplant survival than HD and that PD may be the preferable dialysis modality for patients awaiting a transplant. Both reviews considered patient survival, graft survival and delayed graft function as primary outcomes and did not take into account other important outcomes like death-censored graft survival, acute rejection-free graft survival graft vessel thrombosis, urological complications, surgical complications, any infections, onset of diabetes after transplantation due to lack of data.

With new evidence published in recent years, there is a need to update and analyze additional outcomes to strengthen the existing evidence. Therefore, we conducted a systematic literature search and meta-analysis comparing patient outcomes following PD vs. HD prior to kidney transplantation.

Materials and Methods

This systematic review and meta-analysis aimed to compare patient outcomes following PD vs. HD prior to kidney transplantation and was carried out in strict adherence to Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines¹¹. The protocol for this review was registered with International prospective registry for systematic reviews (PROSPERO) with registration number CRD42021267373.

Research Question

What is the impact of pre-transplant PD compared to pre-transplant HD on kidney transplant outcomes in ESRD patients?

The research question was framed according to the PICO criteria.

Population (P): Patients undergoing dialysis prior to kidney transplant; **Intervention (I):** Peritoneal dialysis (PD);

Comparison (C): Hemo-dialysis (HD);

Outcome (O): patient survival, graft survival and delayed graft function, death-censored graft survival, acute rejection-free graft survival graft vessel thrombosis, urological complications, surgical complications, any infections, onset of diabetes after transplantation.

Search Strategy

A comprehensive search strategy was framed to search in both digital databases and issues of relevant journals. The electronic search was run on digital databases like PubMed *via* MEDLINE, SCOPUS and Experta Medical dataBASE (EMBASE) using relevant search keywords: “Pre-transplant dialysis”, “Peritoneal dialysis”, “Hemodialysis”, “End stage renal disease”, “Kidney transplant”. A manual search was also carried out to search the issues from start of publication year to till date of relevant peer-reviewed journals like Journal of dialysis, Peritoneal dialysis international journal, Hemodialysis international and Nephrology dialysis transplantation journal. The last search was completed on 30th June 2021. The search was also extended to screen the bibliography section of potentially eligible studies and previous systematic review and meta-analyses.

Study Selection

To eliminate duplication, the reports found through this comprehensive search were imported into citation management (ENDNOTE X7). The relevance of the title and abstract of the final set of retrieved reports was then checked. The papers that were potentially eligible were then subjected to a full text evaluation by two independent reviewers. The eligibility criteria were established to make the full text evaluation more efficient.

Eligibility Criteria

The studies comparing the kidney transplant related outcomes of patients under PD vs. HD prior to kidney transplantation were included. The studies assessing patient survival, graft survival and delayed graft function were considered primary outcomes.

Exclusion Criteria

1. studies recruiting patients who underwent transplantation prior to 1990;
2. Studies not reporting relevant outcomes;
3. Studies published other than in the English language.

Data Extraction

The data was retrieved from all included studies by two independent reviewers using an excel spreadsheet organized under the following domains: author information, study design, sample size, demographic characteristics, donor and recipient characteristics, interventional characteristics, outcomes like patient survival, graft survival and delayed graft function, death-censored graft survival, acute rejection-free graft survival graft vessel thrombosis, urological complications, surgical complications, any infections, onset of diabetes after transplantation.

Data Analysis

The retrieved data was subjected to both qualitative and quantitative analysis. The qualitative analysis was used for the demographic characteristics, as well as donor and recipients' characteristics and tabulated. The quantitative outcomes expressed as numbers, ratios and percentage were pooled using meta-analysis. The meta-analysis was attempted only if two or more studies with similar outcomes were available to sum-up the data and synthesis the evidence. The forest plot was constructed using RevMan 5.4v (Cochrane Collaboration, UK). The significance of the effect estimate was set at $p < 0.05$. The dichotomous outcomes like patient survival, graft survival, delayed graft function and other adverse events were expressed as odd's ratio (OR). Pooled OR was calculated to assess the effect estimate. A random effect model was used to pool the data of all included studies considering the heterogeneity of the studies. The heterogeneity between the studies was calculated using I^2 statistics. An I^2 value of less than 40% was considered as low heterogeneity, a value ranging between 40-70% was considered moderate, and a value more than 70% was considered high.

Quality of Included Studies

Two independent reviewers used the Newcastle-Ottawa Scale (NOS) to assess the methodological quality of the included studies. The NOS is made up of eight different components that are divided into three categories: selection, comparability, and outcome. The quality of the study under evaluation was graded using a star scale that ranged from zero to nine. Each included study was given one of three categorical scores: good (three or four scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain),

fair (two scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain), or poor (two scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain) (zero or one score in selection domain OR zero score in comparability domain OR zero or one score in outcome domain). Any disagreements between independent reviewers were solved by a third reviewer.

Results

This systematic review and meta-analysis included twenty studies^{6-8,12-28} comparing the kidney transplant outcomes in patients undergoing pre-transplant PD vs. HD. The comprehensive search retrieved a total of 819 reports, of which, when screened, twenty-two studies were found to be eligible. These eligible studies underwent a full text assessment, where one study was not retrieved, and another did not report relevant outcomes. Finally, twenty studies were included for both qualitative and quantitative analysis. The details of the study selection process are provided in Figure 1.

The included studies comprised eighteen retrospective cohort studies^{6-8,12-14,16-27} and only two prospective cohort studies^{15,28} comparing both pre-transplant dialysis procedures.

The included studies recruited a total of 362,056 ESRD patients undergoing pre-transplant dialysis with PD or HD alone. Out of which, 302,818 patients were undergoing HD and 59,238 patients were undergoing PD. The weighted mean age of the recipient and donor was found to be 48.45 yrs and 46.75 yrs respectively. The weighted mean height of the recipient and donor was calculated to be 171.16 cm and 172.75 cm, respectively and weighted mean weight was 72.54 kg and 76.99 kg, respectively. The mean BMI for recipient was 26.02 and for donor was 25.90. The gender distribution and type of donor used (living or cadaveric) are provided in Table I.

Meta-Analysis

Meta-analysis was performed on the quantitative data. Table II shows the data and factors for the outcomes studied. When two or more trials with similar results were available, a meta-analysis was undertaken.

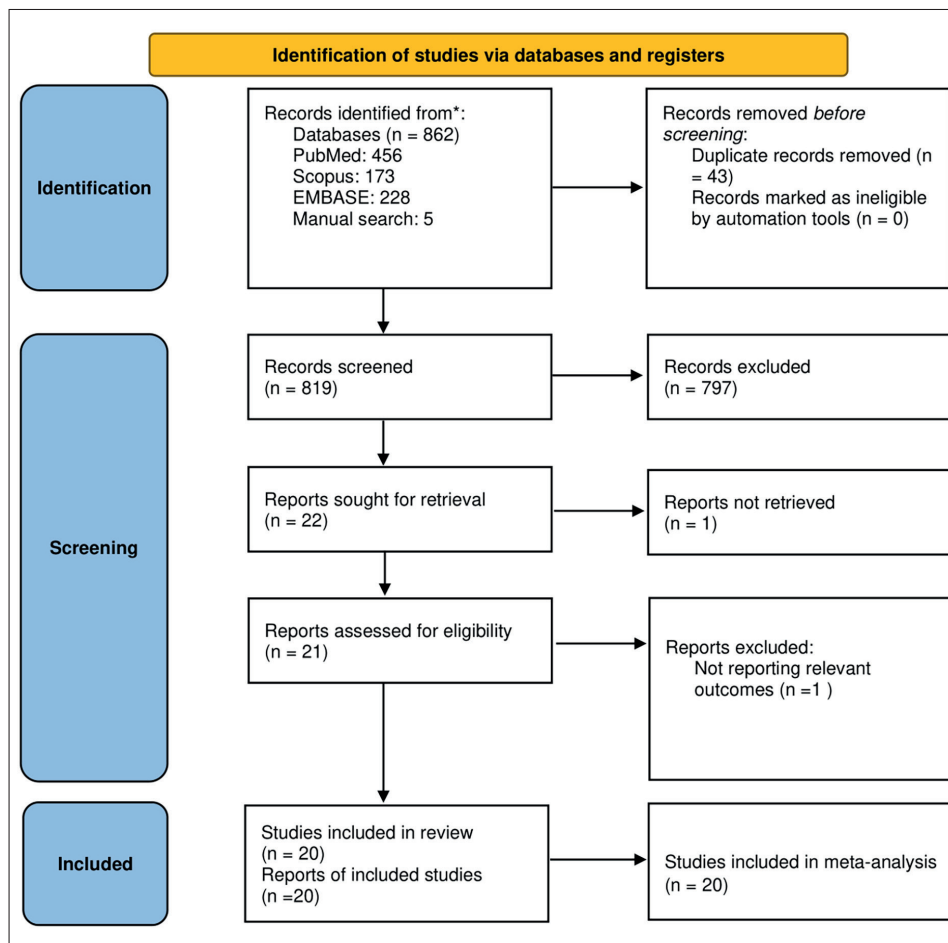


Figure 1. PRISMA flow chart depicting study selection process.

Overall- Patient Survival

The survival of a transplanted patient from the time of transplantation to death or the last follow-up is referred to as patient survival. Patients who had pre-transplant PD had a higher overall survival rate than those who had HD, with an OR of 1.34 95% CI [1.11, 1.61], $p = 0.002$. The heterogeneity among the included studies, however, was found to be substantial ($I^2 = 87\%$) (Figure 2). Patients undergoing pre-transplant PD showed a higher five-year patient survival rate than patients undergoing HD with a HR 0.87 95% CI [0.79, 0.95], $p=0.003$; $I^2= 79\%$ (Supplementary Figure 1). No significant difference was observed for all-cause patient death in patients undergoing pre-transplant PD vs. HD with HR 0.98 95% CI [0.88, 1.08], $p=0.64$, $I^2=76\%$.

Graft Survival

No significant difference was observed in non-censored graft survival between patients undergoing pre-transplant PD compared to HD

with OR 1.08 95% CI [0.93, 1.26], $p=0.31$ (Figure 3). No significant difference was observed in death-censored graft survival between patients undergoing pre-transplant PD compared to HD with OR 1.08 95% CI [0.89, 1.31], $p=0.42$. (Supplementary Figure 2). Similar results were shown with pooled HRs of death-censored graft loss between both modalities with HR 0.97 95% CI [0.91,1.04], $p=0.46$, $I^2=67\%$.

Acute Rejection-Free Graft Survival

No significant difference was observed in acute rejection-free graft survival among both the pre-transplant dialysis modalities with OR 1.14 95% CI [0.71, 1.83], $p=0.59$.

Delayed Graft Function (DGF)

DGF was found to be highly associated with HD compared to PD with OR 0.60 [0.52, 0.70], $p<0.0001$ with moderate heterogeneity ($i^2 = 48\%$).

Table I. Interventional characteristics of included studies.

Author & Year	Type of study	Total participants	Dialysis modality	Participants per group	Recipient Gender (%)		Height, cm (Mean ± SD)	Weight, kg (Mean ± SD)	Body mass index (BMI), kg/m ² (Mean ± SD)	Age, years (Mean ± SD)	Dialysis vintage / time prior to Tx, months (Mean ± SD)	Donor Donor Type (%)		Gender (%)		Height, cm (Mean ± SD)	Weight, kg (Mean ± SD)	BMI, kg/m ² (Mean ± SD)	Age, years (%)	
					Female	Male						Cadaveric	Living	Female	Male					
Balzer et al ¹³ 2020	Retrospective	2277	No RRT	136	54 (39.7)	82 (60.3)	173 ± 10	72.8 ± 14.8	24.3 ± 3.7	43.5 ± 16	3.7 ± 14.5	24 (17.6)	112 (82.4)	83 (61)	53 (39)	171 ± 9	73.8 ± 12.4	25.1 ± 3.5	50 ± 12.1	
			HD	1847	692 (37.5)	1155 (62.5)	172 ± 10	74.2 ± 14.7	25 ± 3.9	51.6 ± 13.1	65.5 ± 36.1	1580 (85.5)	267 (14.5)	924 (50)	923 (50)	173 ± 10	77.5 ± 15	25.9 ± 4.1	50.6 ± 16.2	
			PD	159	79 (49.7)	80 (50.3)	172 ± 10	73.3 ± 13.8	24.7 ± 3.8	46.4 ± 12.7	44 ± 30.8	113 (71.1)	46 (28.9)	87 (54.7)	72 (45.3)	172 ± 11	75.7 ± 16.7	25.5 ± 4.6	47.7 ± 15.7	
			HD + PD	135	71 (52.6)	64 (47.4)	171 ± 12	71.8 ± 15.2	24.3 ± 4.3	45.2 ± 13.1	73 ± 32.6	112 (83)	23 (17)	73 (54.1)	62 (45.9)	172 ± 9	74.8 ± 14.2	25.2 ± 3.8	49.3 ± 14.9	
Dębska-Ślizień et al ¹⁷ 2018	Retrospective	266	PD	133	68 (51.1)	65 (48.9)	NR	NR	NR	44.42 ± 15.1	20.35 ± 17	NR	NR	52	87	NR	NR	NR	43.3 ± 14	
			HD	133	47 (35.3)	86 (64.7)	NR	NR	NR	48.88 ± 15.5	33.55 ± 36	NR	NR	NR	NR	NR	NR	NR	NR	
Che et al ¹⁵ 2018	Prospective	202	HD	104	39 (37.5)	65 (62.5)	NR	NR	NR	21.2	42.4 ± 9.7	15.5	79 (100)	0 (0)	27 (34.2)	52 (65.8)	NR	NR	21.5	40.3 ± 13.7
			PD	98	42 (42.9)	56 (57.1)	NR	NR	NR	21.5	39.5 ± 11.6	24	83 (100)	0 (0)	21 (25.3)	62 (74.7)	NR	NR	21.2	37.7 ± 16.5
Lin et al ²² 2018	Retrospective	1812	HD	1209	530 (43.84)	679 (56.16)	NR	NR	NR	44.79 ± 11.57	NR	NR	NR	NR	NR	NR	NR	NR	NR	
			PD	603	293 (48.59)	310 (51.41)	NR	NR	NR	38.28 ± 13.45	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dipalma et al ¹⁸ 2016	Retrospective	160	HD	80	27 (33.8)	53 (66.2)	NR	NR	NR	24.8 ± 5.6	46.6 ± 15.1	25.5	80 (100)	0 (0)	21 (26.2)	59 (73.8)	NR	NR	NR	39.2 ± 18.1
			PD	80	26 (32.5)	54 (67.5)	NR	NR	NR	25.3 ± 5.4	43.2 ± 13.9	15	NR	NR	NR	NR	NR	NR	NR	
Song et al ²⁷ 2016	Retrospective	275	HD	178	67 (37.6)	111 (62.4)	165.5 ± 10.8	60.9 ± 7.9	22.1 ± 3.3	46.7 ± 10.4	81.2 ± 48.7	NR	NR	72 (40.4)	106 (59.6)	NR	NR	NR	42.7 ± 14.3	
			PD	97	48 (49.5)	49 (50.5)	161.8 ± 12.7	61.7 ± 12.8	23.4 ± 3.4	44.9 ± 11.2	74.5 ± 42.1	NR	NR	38 (39.2)	59 (60.8)	NR	NR	NR	NR	
López-Oliva et al ²³ 2014	Retrospective	236	PD	118	56 (47.5)	62 (52.5)	NR	NR	NR	25.5 ± 4.39	43.5 ± 12.4	27.9 ± 27.9	114 (96.6)	4 (3.4)	45 (38.1)	73 (61.9)	NR	NR	NR	45.8 ± 16.2
			HD	118	47 (39.8)	71 (60.2)	NR	NR	NR	23.8 ± 3.83	47.5 ± 13.1	50.7 ± 67.5	114 (96.6)	4 (3.4)	44 (37.3)	74 (62.7)	NR	NR	NR	44.7 ± 14.9
Kramer et al ²¹ 2012	Retrospective	29088	PD	10135	3993 (39.4)	6142 (60.6)	NR	NR	NR	46.7	2.1	8219 (81.1)	1916 (18.9)	NR	NR	NR	NR	NR	NR	
			HD	18953	6671 (35.2)	12282 (64.8)	NR	NR	NR	49.5	2.2	15921 (84)	3032 (16)	NR	NR	NR	NR	NR	NR	
Molnar et al ⁸ 2012	Retrospective	14508	HD	12416	4731 (38.1)	7685 (61.9)	NR	NR	NR	27 ± 6	49 ± 14	NR	NR	4097 (33)	NR	NR	NR	NR	39 ± 15	
			PD	2092	990 (47.3)	1102 (52.7)	NR	NR	NR	26 ± 6	44 ± 15	NR	NR	753 (36)	NR	NR	NR	NR	NR	
Sharma et al ¹⁶ 2012	Retrospective	401	HD	339	149 (44)	190 (56)	NR	NR	NR	47.6 ± 12.7	44 ± 39.2	241 (71.1)	98 (28.9)	172 (50.7)	167 (49.3)	NR	NR	NR	39.8 ± 14.7	
			PD	62	38 (61.3)	24 (38.7)	NR	NR	NR	44 ± 13.8	35.2 ± 32.8	46 (74.2)	16 (25.8)	24 (38.7)	38 (61.3)	NR	NR	NR	41.2 ± 16.9	
Ardalan et al ¹² 2011	Retrospective	143	PD	69	21 (30.4)	48 (69.6)	NR	NR	NR	35.3 ± 15.9	16.4 ± 10.3	0 (0)	69 (100)	14 (20.3)	55 (79.7)	NR	NR	NR	28.4 ± 4.4	
			HD	74	36 (48.7)	38 (51.3)	NR	NR	NR	40.7 ± 13.3	21.4 ± 11	0 (0)	74 (100)	28 (37.8)	46 (62.2)	NR	NR	NR	29.7 ± 5.6	
Freitas et al ¹⁹ 2011	Retrospective	306	HD	268	97 (36.2)	171 (63.8)	NR	NR	NR	45.8 ± 12.1	33 ± 49.6	233 (86.9)	35 (13.1)	NR	NR	NR	NR	NR	44.8 ± 14.2	
			PD	38	26 (68.4)	12 (31.6)	NR	NR	NR	38.2 ± 14.1	59.6 ± 57.3	26 (68.4)	12 (31.6)	NR	NR	NR	NR	NR	NR	
Schwenger et al ²⁴ 2011	Retrospective	60008	No RRT	1150	483 (42)	667 (58)	NR	NR	NR	47.6 ± 13.2	0	NR	NR	NR	NR	NR	NR	NR	41.2 ± 16.9	
			HD + PD	1543	630 (40.8)	913 (59.2)	NR	NR	NR	48.3 ± 13.3	3.9 ± 2.9	NR	NR	NR	NR	NR	NR	NR	NR	
			HD	45651	16389 (35.9)	29262 (64.1)	NR	NR	NR	50.2 ± 12.9	4.1 ± 3.3	NR	NR	NR	NR	NR	NR	NR	NR	
			PD	11664	4969 (42.6)	6695 (57.4)	NR	NR	NR	48.7 ± 12.6	3.1 ± 2.7	NR	NR	NR	NR	NR	NR	NR	NR	

Continued

Table I (Continued). Interventional characteristics of included studies.

Author & Year	Type of study	Total participants	Dialysis modality	Participants per group	Recipient Gender (%)		Height, cm (Mean ± SD)	Weight, kg (Mean ± SD)	Body mass index (BMI), kg/m ² (Mean ± SD)	Age, years (Mean ± SD)	Dialysis vintage / time prior to Tx, months (Mean ± SD)	Donor Donor Type (%)		Gender (%)		Height, cm (Mean ± SD)	Weight, kg (Mean ± SD)	BMI, kg/m ² (Mean ± SD)	Age, years (%)
					Female	Male						Cadaveric	Living	Female	Male				
Sezer et al ²⁵ 2011	Retrospective	250	HD	180	69 (38.3)	111 (61.7)	NR	NR	23.4 ± 10.2	30 ± 9	18.5 ± 11.6	50 (28)	130 (72)	115 (64)	65 (36)	NR	NR	NR	32
			PD	70	22 (31.4)	48 (68.6)	NR	NR	24.6 ± 11.4	29 ± 11	25.4 ± 10.1	22 (31)	48 (69)	43 (62)	27 (38)	NR	NR	NR	30
Courivaud et al ¹⁶ 2010	Retrospective	2010	No RRT	114	52 (45.6)	62 (54.4)	NR	NR	23 ± 4	44 ± 14	NR	NR	NR	NR	NR	NR	NR	NR	NR
			HD	1564	579 (37)	985 (63)	NR	NR	23 ± 4	47 ± 13	NR	NR	NR	NR	NR	NR	NR	NR	NR
Caliskan et al ¹⁴ 2009	Retrospective	88	PD	332	125 (37.7)	207 (62.3)	NR	NR	22.7 ± 3.8	44 ± 14	NR	NR	NR	NR	NR	NR	NR	NR	NR
			PD	44	18 (40.9)	26 (59.1)	NR	NR	21 ± 4	26 ± 9	26 ± 18.9	8 (18.2)	36 (81.8)	25 (56.8)	19 (43.2)	NR	NR	NR	41 ± 14
Yang et al ²⁸ 2009	Prospective	402	HD	44	18 (40.9)	26 (59.1)	NR	NR	20 ± 3	27 ± 11	25 ± 24.6	8 (18.2)	36 (81.8)	23 (52.3)	21 (47.7)	NR	NR	NR	41 ± 14
			PD	303	99 (32.7)	204 (68.3)	NR	NR	NR	41.59 ± 12.4	NR	303 (100)	0(0)	NR	NR	NR	NR	NR	NR
Goldfarb-Rumyantzev et al ⁷ 2005	Retrospective	92844	HD	99	38 (38.4)	61 (61.6)	NR	NR	NR	44.02 ± 13.72	NR	69819 (75.2)	23025 (24.8)	40666 (43.8)	52178 (56.2)	164.3 ± 21.9	72.8 ± 19	NR	34.72 ± 15.64
			PD	NR	NR	NR	NR	NR	41.1 ± 15.1	NR	NR	NR	NR	NR	NR	NR	NR	NR	33.81 ± 15.41
Joseph et al ²⁰ 2002	Retrospective	325	HD	117	46 (39.3)	71 (60.7)	NR	NR	NR	42.7 ± 14.6	34.5 ± 31.9	NR	NR	61 (52.6)	56 (47.4)	NR	NR	NR	39.7 ± 17.1
			PD	183	83 (45.4)	100 (54.6)	NR	NR	NR	41.5 ± 13.2	24 ± 19.7	NR	NR	NR	83 (46.1)	100 (53.9)	NR	NR	NR
Snyder et al ⁶ 2002	Retrospective	252402	HD + PD	25	8 (32)	17 (68)	NR	NR	NR	44.6 ± 13.7	50.68 ± 44.8	NR	NR	11 (44)	14 (56)	NR	NR	NR	36.9 ± 18.7
			HD	219240	103043 (47)	116197 (53)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
			PD	33162	15255 (46)	17907 (54)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

RRT – Renal Replacement Therapy, HD – Haemodialysis, PD – Peritoneal dialysis, NR – Not Reported.

Table II. Outcomes of pre-transplant dialysis in kidney transplant patients of included studies.

Author & Year	Dialysis modality	Participants per group	Outcomes												
			Patient survival (%)	Death - censored graft survival (%)	Graft survival (%)	Acute rejection (AR) - free graft survival (%)	Delayed graft function (DGF) (%)	Graft vessel thrombosis (%)	Urological complications (%)	Cytomegalovirus (CMV) infection (%)	Other infections (mostly urinary tract infection) (%)	Surgical complications (%)	New-onset diabetes after transplantation (%)		
Balzer et al ¹³ 2020	No RRT	136	123 (90.2)	89 (65.5)	NR	101 (73.9)	NR	NR	NR	NR	NR	NR	NR	NR	NR
	HD	1847	920 (49.8)	1167 (63.2)	NR	1178 (63.8)	NR	NR	NR	NR	NR	NR	NR	NR	NR
	PD	159	116 (73.1)	114 (71.5)	NR	117 (73.8)	NR	NR	NR	NR	NR	NR	NR	NR	NR
	HD + PD	135	70 (51.6)	105 (78.1)	NR	87 (64.4)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dębska-Ślizięń et al ¹⁷ 2018	PD	133	130 (98)	120 (90)	118 (89)	114 (85.72)	28 (21.05)	9 (6.7)	9 (6.8)	20 (15)	37 (27.8)	NR	NR	16 (12)	
	HD	133	128 (96)	124 (93)	120 (90)	90 (67.67)	57 (42.86)	4 (3)	7 (5.3)	13 (9.8)	33 (24.8)	NR	NR	13 (9.8)	
Che et al ¹⁵ 2018	HD	104	100 (96.2)	101 (97.1)	97 (93.3)	104 (100)	19 (18.3)	NR	7 (6.8)	21 (20.2)	60 (57.5)	11 (10.6)	NR	NR	
	PD	98	95 (96.9)	95 (96.9)	92 (93.9)	70 (71.4)	16 (16.3)	NR	5 (5.1)	20 (20.4)	57 (58.1)	9 (9.2)	NR	NR	
Lin et al ²² 2018	HD	1209	1071 (88.59)	NR	1020 (84.37)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	PD	603	549 (91.04)	NR	534 (88.56)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dipalma et al ¹⁸ 2016	HD	80	69 (86.2)	65 (81.2)	NR	71 (88.8)	32 (39.5)	4 (5)	13 (15.5)	30 (40)	NR	NR	NR	23 (29.9)	
	PD	80	69 (86.2)	67 (83.8)	NR	70 (87.5)	26 (32.4)	3 (4)	20 (26.2)	33 (44)	NR	NR	NR	14 (18.7)	
Song et al ¹⁷ 2016	HD	178	NR	NR	156 (87.7)	153 (85.6)	57 (32)	1 (0.5)	4 (2.1)	NR	NR	NR	NR	NR	
	PD	97	NR	NR	80 (82.3)	82 (84.2)	19 (19.6)	0 (0)	2 (2.1)	NR	NR	NR	NR	NR	
López-Oliva et al ²³ 2014	PD	118	101 (85.6)	NR	75 (63.6)	85 (71.8)	16 (13.9)	4 (3.4)	NR	8 (6.7)	NR	NR	NR	34 (29.3)	
	HD	118	88 (74.6)	NR	86 (72.9)	84 (70.9)	27 (23.1)	1 (0.8)	NR	7 (5.9)	NR	NR	NR	39 (33.1)	
Kramer et al ²¹ 2012	PD	10135	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	HD	18953	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Molnar et al ⁶ 2012	HD	12416	11505 (92.7)	NR	10970 (88.4)	NR	2478 (20)	NR	NR	NR	NR	NR	NR	NR	NR
	PD	2092	1987 (95)	NR	1887 (90.2)	NR	292 (14)	NR	NR	NR	NR	NR	NR	NR	NR
Sharma et al ²⁶ 2012	HD	339	285 (84.1)	NR	227 (67.1)	290 (85.5)	130 (38.8)	2 (0.59)	NR	119 (35.1)	NR	NR	NR	NR	
	PD	62	54 (87)	NR	45 (72.6)	58 (93.5)	11 (17.7)	0 (0)	NR	15 (27.4)	NR	NR	NR	NR	
Ardalan et al ¹² 2011	PD	69	66 (95)	NR	56 (81)	62 (89.9)	6 (8.7)	2 (2.9)	NR	2 (2.9)	NR	NR	NR	3 (4.3)	
	HD	74	53 (71)	NR	55 (74)	65 (87.8)	9 (12.2)	3 (4.1)	NR	6 (8.1)	NR	NR	NR	3 (4.1)	
Freitas et al ¹⁹ 2011	HD	268	242 (90.3)	NR	188 (70)	240 (89.6)	96 (35.8)	NR	NR	NR	NR	NR	NR	NR	
	PD	38	36 (93.7)	NR	31 (81.2)	36 (94.7)	5 (13.2)	NR	NR	NR	NR	NR	NR	NR	
Schwenger et al ²⁴ 2011	No RRT	1150	1061 (92.3)	1037 (90.2)	979 (85.1)	NR	NR	NR	NR	NR	NR	NR	NR	NR	
	HD + PD	1543	1336 (86.6)	1304 (84.5)	1173 (76)	NR	NR	NR	NR	NR	NR	NR	NR	NR	
	HD	45651	39625 (86.8)	38895 (85.2)	34740 (76.1)	NR	NR	NR	NR	NR	NR	NR	NR	NR	
	PD	11664	10451 (89.6)	10148 (87)	9285 (79.6)	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Sezer et al ²⁵ 2011	HD	180	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
	PD	70	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Courivaud et al ¹⁶ 2010	No RRT	114	NR	NR	NR	80 (70.2)	NR	NR	NR	23 (21.3)	NR	NR	NR	7 (5.2)	
	HD	1564	NR	NR	NR	1195 (76.4)	NR	NR	NR	269 (20.6)	NR	NR	NR	108 (78.8)	
	PD	332	NR	NR	NR	253 (76.2)	NR	NR	NR	65 (22)	NR	NR	NR	22 (16)	
Caliskan et al ¹⁴ 2009	PD	44	30 (91)	NR	26 (79.3)	41 (93)	4 (9)	NR	7 (15.9)	2 (4.5)	10 (22.7)	NR	NR	NR	
	HD	44	32 (96.7)	NR	31 (93.1)	40 (91)	2 (5)	NR	5 (11.4)	1 (2.3)	8 (18.2)	NR	NR	NR	
Yang et al ²⁸ 2009	HD	303	281 (92.8)	NR	269 (88.8)	241 (79.5)	14 (4.6)	NR	NR	127 (41.9)	61 (20.1)	NR	NR	NR	
	PD	99	89 (90)	NR	92 (92.9)	83 (83.8)	4 (4)	NR	NR	31 (31.3)	13 (13.1)	NR	NR	NR	
Goldfarb-Rumyantzev et al ⁷ 2005	HD	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
	PD	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Joseph et al ²⁰ 2002	HD	117	98 (83.8)	NR	87 (74.4)	94 (51.3)	58 (49.5)	NR	NR	NR	NR	NR	NR	NR	
	PD	183	140 (76.5)	NR	123 (67.2)	84 (45.9)	56 (30.6)	NR	NR	NR	NR	NR	NR	NR	
	HD + PD	25	18 (72)	NR	20 (80)	10 (40)	13 (53)	NR	NR	NR	NR	NR	NR	NR	
Snyder et al ⁶ 2002	HD	219240	186354 (85)	188546 (86)	164430 (75)	255 (73)	35078 (16)	106 (30)	7 (2)	34 (10)	11 (6)	NR	NR		
	PD	33162	28188 (85)	28188 (85)	24540 (74)	114 (73)	3979 (12)	64 (41)	3 (2)	12 (8)	3 (3)	NR	NR		

RRT – Renal Replacement Therapy, HD – Haemodialysis, PD – Peritoneal dialysis, NR – Not Reported.

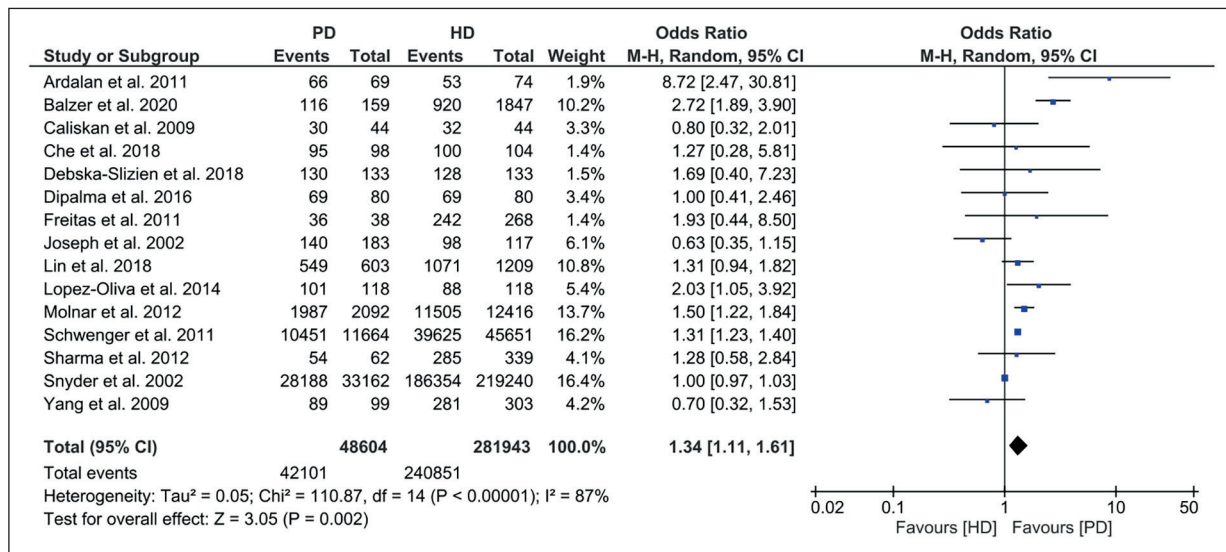


Figure 2. Forest plot showing pooled association of overall patient survival between patients undergoing pre-transplant PD vs. HD.

Graft Vessel Thrombosis

Kinking of the renal vein or stenosis of the venous anastomosis can cause renal vein thrombosis. It can also occur as a result of a hypercoagulable condition. Graft vascular thrombosis was considerably more common in patients receiving PD than in patients undergoing HD, with an OR of 2.04 95 percent CI [1.00, 4.14], $p=0.05$, and a i^2 of 40% (Figure 4).

Other Complications

No significant difference was observed in urological complications, cytomegalovirus infection,

post-transplant infections, surgical complications, and new-onset diabetes after transplantation among both the pre-transplant dialysis modalities (Supplementary Figure 3-7).

Publication Bias

The funnel plots among the included studies for various primary outcomes are provided in Supplementary Figure 6. No publication bias was found among the included studies assessing graft survival (both death-censored and non-censored), acute rejection free graft survival, delayed graft function or graft vessel thrombosis. Among

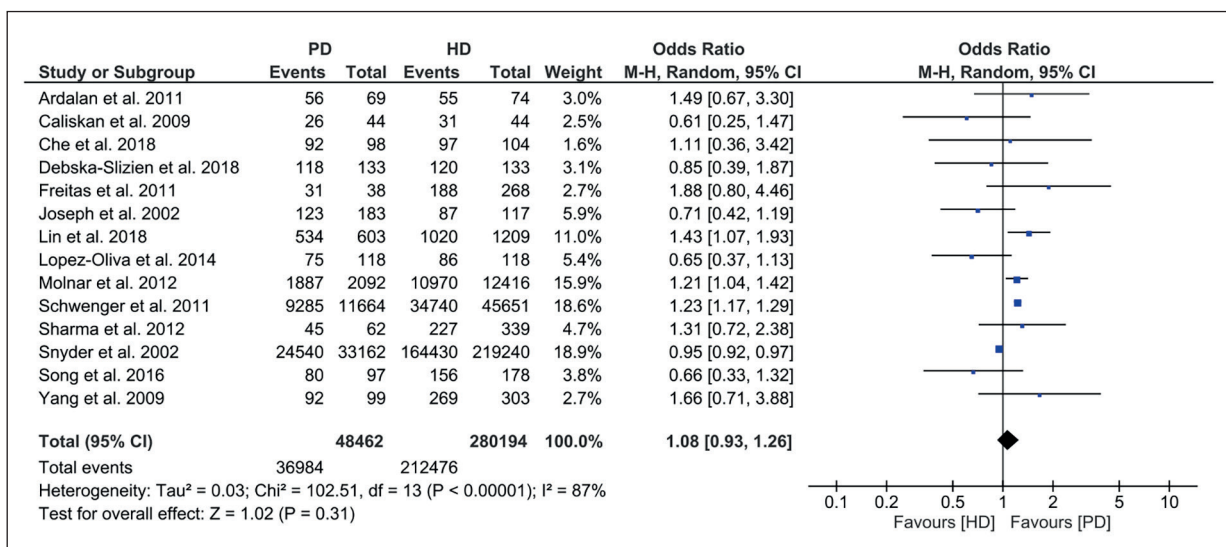


Figure 3. Forest plot showing pooled association of graft survival between patients undergoing pre-transplant PD vs. HD.

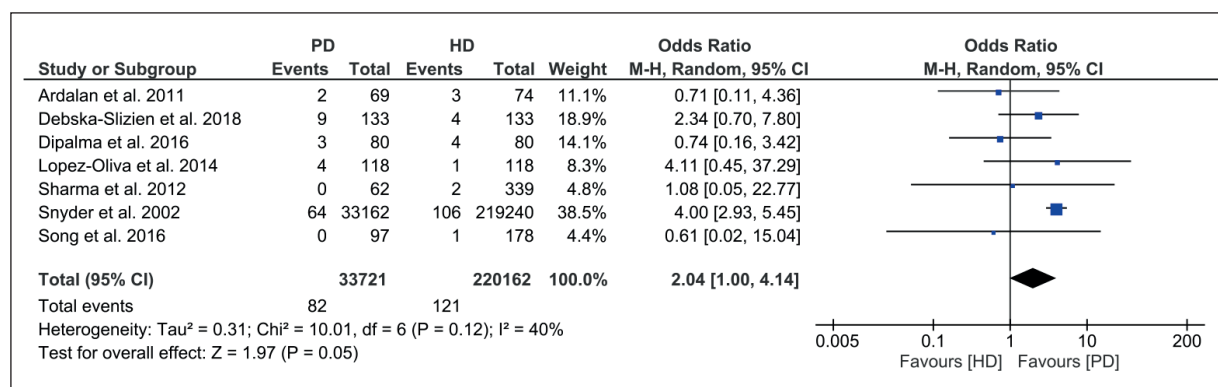


Figure 4. Forest plot showing pooled association of graft vessel thrombosis between patients undergoing pre-transplant PD vs. HD.

the included studies assessing patient survival, Ardalan et al¹² 2011 and Balzer et al¹³ 2020 were found to be outside the 95% CI limit. For acute rejection free graft survival, Che et al¹⁵ 2018 was found to be outside the funnel (**Supplementary Figure 8**).

Sensitivity Analysis

A sensitivity analysis was carried out within the included studies to assess patient survival. No difference in effect estimate was observed after removing the studies showing publication bias with OR lying outside the 95% CI limit.

Quality of Included Studies

The quality of included studies was assessed using NOS. All the studies were assessed to be of good quality (Table III).

Discussion

This systematic review and meta-analysis included twenty cohort studies which examined the kidney transplant outcomes in patients undergoing pre-transplant PD compared to HD. The results showed patients undergoing pre-transplant PD presented with better five year-patient survival and comparatively lower incidence of delayed graft function than patients undergoing pre-transplant HD. However, no difference was observed between both dialysis methods in terms of outcomes like graft survival (non-censored or censored for death), any complications or infections. Additionally, it was noticed that the incidence of graft vessel thrombosis was highly, and significantly, associated with renal transplant patients undergoing pre-transplant PD.

Patients with ESRD have a terminal illness and require daily dialysis to maintain kidney function²⁹. Renal transplantation improves the patient's quality of life and overall survival. Our meta-analysis examined both five-year patient survival and overall patient survival in patients undergoing pre-transplant PD. Our findings were in accordance with the previous systematic reviews^{9,10,30}. Patient survival (both five-year and overall) in ESRD patients undergoing renal transplantation showed high heterogeneity among the included studies due to the presence of numerous confounding factors, like baseline patient characteristics, residual renal function, frequency of dialysis, incidence of infections, and presence of co-morbidities. Similar adjustments could not be made to estimate the patient survival.

There was no difference in graft survival between the two pre-transplant dialysis methods in our meta-analysis. Graft survival is defined as the ability of a graft to function and was censored and uncensored for death³¹. Graft survival (not censored for death) is measured from the time of transplantation until the time of irreversible graft failure, which is defined as a return to long-term dialysis or retransplantation. Graft failure is the term used to describe mortality with graft function in this situation. Graft survival was computed from the date of transplantation to the date of irreversible graft failure, which is defined as returning to long-term dialysis or re-transplantation³¹. The follow-up period is censored at the date of death in event of death with functioning graft.

The included studies showed varied results in predicting patient and graft survival. Two of the analyzed studies^{6,24} with the largest cohort showed almost contradictory results, making the

Table III. Quality of included studies assessed by New-castle Ottawa Scale.

Author & Year	Selection		Comparability			Outcome		Total	
	Representativeness of the ex-posed cohort	Selection of the non-exposed cohort	Ascertainment of expo-sure	Demonstration of out-come of interest	Basis of the design or analysis	Assessment of outcome	Follow-up long enough for outcomes		Adequate follow up
Balzer et al ¹³ 2020	1	1	0	1	1	1	1	1	7
Dębska-Słizień et al ¹⁷ 2018	1	1	1	1	1	1	1	1	8
Che et al ¹⁵ 2018	1	1	1	1	1	1	1	1	8
Lin et al ²² 2018	1	1	1	1	1	1	1	1	8
Dipalma et al ¹⁸ 2016	1	1	1	1	1	1	1	1	8
Song et al ²⁷ 2016	1	1	1	1	2	1	1	1	9
López-Oliva et al ²³ 2014	1	1	1	1	1	1	1	1	8
Kramer et al ²¹ 2012	1	1	1	1	1	1	1	1	8
Molnar et al ⁸ 2012	1	1	1	1	2	1	1	1	9
Sharma et al ²⁶ 2012	1	1	1	1	1	1	1	1	8
Ardalan et al ¹² 2011	1	1	1	1	1	1	1	1	8
Freitas et al ¹⁹ 2011	1	1	1	1	1	1	1	1	8
Schwenger et al ²⁴ 2011	1	1	0	1	1	1	1	1	7
Sezer et al ²⁵ 2011	1	1	1	1	1	1	1	1	8
Courivaud et al ¹⁶ 2010	1	1	0	0	1	1	1	1	6
Caliskan et al ¹⁴ 2009	1	1	0	1	1	1	1	1	7
Yang et al ²⁸ 2009	1	1	1	1	1	1	1	1	8
Goldfarb-Rumyantzev et al ⁷ 2005	1	1	0	1	1	1	1	1	7
Joseph et al ²⁰ 2002	1	1	1	1	1	1	1	1	8
Snyder et al ⁶ 2002	1	1	1	1	2	1	1	1	9

effect estimate inconclusive due to high heterogeneity. Snyder et al⁶ 2002, with a sample size of 33,162 patients undergoing pre-transplant PD, did not show any significant differences in patient and graft survival, compared to HD. In contrast, Schwenger et al²⁴ 2011, with 11,614 patients undergoing pre-transplant PD, showed a 10% lower all-cause mortality, suggesting increased patient survival compared to HD. Additionally, Goldfarb-Rumyantzer et al⁷ 2005 found that pre-transplant PD predicted better graft and patient survival with HR 0.96 and 0.97 respectively, resulting in a better patient mortality (all-cause death).

DGF is described as the failure of a kidney transplant to function immediately, necessitating dialysis in the first week after the transplant³². When compared to HD, pre-transplant PD was linked to a reduced risk of DGF, with a pooled odds ratio of 0.60 (95% CI 0.52-0.70). A moderate heterogeneity of 48% was found in the meta-analysis. Among the analyzed studies for DGF, all but one study (Caliskan 2009¹⁴) showed a higher incidence of DGF with PD. Infection and inflammatory pathways may be triggered by utilizing a filtration device with an external dialysis membrane, resulting in an increase in circulating complement, phagocytic leukocyte activation, and free radical generation, leading to a persistent micro-inflammatory state³³. By activating complement components and phagocyte leukocytes, artificial membranes employed in HD might boost free radical generation even further³⁴. The increased delay in graft function with ESRD patients undergoing frequent HD could be due to the presence of the external membrane, in contrast to patients undergoing PD where the patient's own abdominal peritoneal membrane is used as the filtration device.

Higher incidence of graft vessel thrombosis was evident in our meta-analysis in patients undergoing pre-transplant PD. Kinking of the renal vein or stenosis of the venous anastomosis can cause renal vein thrombosis³⁵, and can be caused by a hypercoagulable state, resulting in a higher graft failure rate. However, the results from our meta-analysis, show the HR estimate of death censored graft loss to be non-significant among both the dialysis modalities.

Pre-transplant PD patients typically have better biochemical and hematological stability due to improved nutritional balance and increased social independence. These patients also see a prevention in metabolic and nutritional damage to the immune system, with a better immunologic state

contributing to a higher incidence of acute rejection compared to HD patients. The results presented here, contrast this explanation, and match with the results from Tang et al⁹ 2016, showing no significant difference in acute rejection free graft survival between dialysis modalities. The use of immune-suppressive and anti-microbial drugs to combat graft rejection and infections during the first few weeks of kidney transplantation could be the reason of similar incidence of acute rejection free graft survival, infections, cytomegalovirus infections, and other complications was found between dialysis modalities.

The potential benefit observed in patients undergoing PD when compared to HD in terms of patient survival, graft survival and reduced delayed graft function could be because PD is carried out continuously and allows the maintenance of residual kidney function. The success of the kidney transplantation is dependent on the residual kidney function. Infection also continues to be an important cause of mortality and morbidity among HD patients due to use of an external filtration device. Non-transplant patients treated with PD showed similar beneficial results. Korevaar et al³⁶ conducted a randomized clinical trial that found patients treated with PD compared to HD had a substantial improvement in survival throughout the first five years.

There were a couple of limitations associated with this review. The inability to control and adjust the confounding factors between the included studies, such as age, body mass index, geographical region, time of dialysis, frequency of dialysis, residual renal function, type of donor (living or cadaveric), incidence of infections, presence of co-morbidities and use of immunosuppressive drugs, may have limited the between study comparisons. Additionally, the HR estimates used to assess the all-cause death and death censored graft failure were unadjusted values, and it would have been interesting to see the results with adjusted outcomes. Another limitation of this review is that the sample size among the included studies was varied, and further research is needed to provide much stronger evidence.

Conclusions

Within the limitations of the review, it can be concluded that ESRD patients undergoing pre-transplant PD were found to have better patient survival and a lower incidence of delayed

graft function. However, no difference was observed in terms of graft survival, complications, infections, and new onset of diabetes mellitus compared to patients undergoing pre-transplant HD. The results from this review suggest that PD may be regarded as the better pre-transplant dialysis option for ESRD patients undergoing kidney transplantation due to the benefits observed on patient survival and overall patient acceptance.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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