Renal Replacement Therapy

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Comparison of peritoneal dialysis and hemodialysis as first renal replacement therapy in patients with end-stage renal disease and diabetes: a systematic review

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Abstract

Background: Diabetes has become the most common cause of end-stage renal disease (ESRD) requiring renal replacement therapy (RRT) in most countries around the world. Peritoneal dialysis (PD) is valuable for patients newly requiring RRT because of the preservation of residual renal function (RRF), higher quality of life, and hemodynamic stability in comparison with hemodialysis (HD). A previous systematic review produced conflicting results regarding patient survival. As several advances have been made in therapy for diabetic patients receiving PD, we conducted a systematic review of studies published after 2014 to determine whether incident PD or HD is advantageous for the survival of patients with diabetes.

Methods: For this systematic review, the MEDLINE, EMBASE, and CENTRAL databases were searched to identify articles published between February 2014 and August 2017. The quality of studies was assessed using the GRADE approach. Outcomes of interest were all-cause mortality; RRF; major morbid events, including cardiovascular disease (CVD) and infectious disease; and glycemic control. This review was performed using a predefined protocol published in PROSPERO (CRD42018104258).

Results: Sixteen studies were included in this review. All were retrospective observational studies, and the risk of bias, especially failure to adequately control confounding factors, was high. Among them, 15 studies investigated all-cause mortality in diabetic patients initiating PD and HD. Differences favoring HD were observed in nine studies, whereas those favoring PD were observed in two studies. Two studies investigated effects on CVD, and both demonstrated the superiority of incident HD. No study investigated the effect of any other outcome.

Conclusions: In the present systematic review, the risk of death tended to be higher among diabetic patients with ESRD newly initiating RRT with incident PD in comparison with incident HD. However, we could not obtain definitive results reflecting the superiority of PD or HD with regard to patient outcomes because of the severe risk of bias and the heterogeneity of management strategies for diabetic patients receiving dialysis. Further studies are needed to clarify the advantages of PD and HD as RRT for diabetic patients with ESRD.

Keywords: Cardiovascular disease, Diabetes, End-stage renal disease, Hemodialysis, Morbidity, Mortality, Peritoneal dialysis, Quality of life, Renal replacement therapy, Residual renal function

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Background

Diabetes has become the most common cause of end-stage renal disease (ESRD) treated by renal replacement therapy (RRT) in most countries around the world; it accounts for 45%, 23%, and 44% of incident cases of RRT requirement in North America [1], Europe [2], and Japan [3], respectively.

Peritoneal dialysis (PD) is valuable for patients newly requiring RRT due to the preservation of residual renal function (RRF), higher quality of life, and hemodynamic stability in comparison with hemodialysis (HD) [4]. Approximately 196,000 patients worldwide underwent PD in 2008, representing 11% of the dialysis population [5]. However, diabetic patients were less likely than non-diabetic patients to receive PD as first RRT in North America (9.0% vs. 10.1%, respectively) [1], Europe (14% vs. 15%, respectively) [2], and Japan (4.9% vs. 6.6%, respectively) [3]. Possible reasons for this therapeutic preference include anxiety regarding worsening of glycemic control, higher prevalence of PD-associated peritonitis, overhydration and rapid RRF decline due to proteinuria and inflammation, and technical problems due to visual disorders and peripheral neuropathy. Additionally, several factors including demographic, medical, social, pre-ESRD, and geographic factors are associated with the selection of dialysis modality [6].

Several reports have provided conflicting results regarding patient survival. Ideally, randomized controlled trials (RCTs) are needed to clarify the survival advantage of PD or HD. Although one such RCT has been conducted, the number of included patients was small and no analysis stratified by diabetes was performed [7]. Couchoud et al. [8] conducted a systematic review based on 25 observational studies published until February 2014, which included 821,783 diabetic patients receiving HD and 106,790 such patients receiving PD. Due to the heterogeneity of study designs and PD and HD practices, they could not provide an evidence-based argument in favor or against the use of either modality as the first dialysis treatment for diabetic patients.

As several advances have been made in therapy for diabetic patients undergoing PD, we conducted a systematic review based on studies published after February 2014 to examine whether incident PD or HD is advantageous with regard to patient survival and other clinical outcomes among patients with diabetes.

Methods

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [9] (Additional file 1). The review was performed using a predefined protocol published in PROSPERO (CRD42018104258). No ethical approval was required because this study did not involve the use of confidential personal data or patient interventions.

The MEDLINE, EMBASE, and CENTRAL databases were searched to identify articles published from February 2014 to August 2017 with no language, time, or methodological restriction using focused and highly sensitive search strategies (Additional file 2). We included any type of trial comparing any type of PD (i.e., automated PD or continuous ambulatory PD) with any type of HD (i.e., conventional HD, hemofiltration, hemodiafiltration, daily HD) as first RRT in diabetic patients with ESRD.

Outcomes of interest were all-cause mortality; urinary volume (RRF); major morbid events, including cardiovascular disease (CVD) and infectious disease; and glycemic control.

Studies were excluded (i) if outcomes were not reported separately for diabetic patients, (ii) if they did not provide longitudinal data on any of the abovementioned outcomes, or (iii) if they did not directly compare HD and PD. Case reports, reviews, editorials, and letters were also excluded, although they were screened as potential sources of additional references.

Four reviewers (YM, CH, HI, and KW) independently reviewed the title and abstract of each retrieved publication, and articles were selected for full-text review. The same four reviewers independently screened the reference lists of articles selected for full-text review. The inclusion of full-text articles was finalized after consultation with a fifth reviewer (HT). All disagreements were resolved by consensus.

We used forest plot for comparison of all-cause mortality in diabetic patients receiving incident PD and those receiving incident HD. For this analysis, only publications reporting hazard ratios (HRs) with 95% confidence interval (CIs) for all enrolled diabetic patients were included. We did not conduct a meta-analysis because of the high risk of bias in each study.

Quality assessment

We used the key criteria for limitations of observational studies developed by the GRADE working group (handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach, http://gdt.guidelinedevelopment.org/app/handbook/handbook.html#h.m9385o5z3li7). Two authors of this review independently assessed the items listed below. Disagreements regarding the risk of bias were resolved by consultation with other review authors:

1. Failure to develop and apply appropriate eligibility criteria (inclusion of a control population)
   - Under- or overmatching in case-control studies
   - Selection of exposed and unexposed groups from different populations in cohort studies

2. Flawed measurement of both exposure and outcome
   - Differences in the measurement of exposure (e.g., recall bias in case-control studies)
   - Differential surveillance for outcome in exposed and unexposed groups in cohort studies
3. Failure to adequately control confounding factors
   - Failure to accurately measure all known prognostic factors
   - Failure to match prognostic factors and/or adjust statistical analysis
4. Incomplete or inadequately short follow-up
   - Especially for prospective cohort studies, both groups should be followed for the same amount of time.

Results

Study selection

Figure 1 summarizes the search strategy that was used. The initial search yielded 766 articles, of which 620 articles were excluded after review of the titles and abstracts. A total of 146 articles underwent full-length review, and 16 studies were included in the qualitative analysis.

Characteristics of studies

The characteristics of the 16 studies are summarized in Table 1 [10–25]. All studies were observational and were conducted using registry or cohort databases. One study included only diabetic patients receiving incident PD [14]; the percentages of diabetic patients ranged from 10.3 [12] to 70.3% [16] in the other studies. The total numbers of diabetic patients included were 50,298 receiving PD and 71,532 receiving HD. Eight studies were from Asia [10, 11, 14, 16, 18, 19, 21, 23], three were from Australia and New Zealand [15, 20, 22], three were from Europe [17, 24, 25], one was from North America [13], and one was from South Africa [12]. Several studies were based on the same registry or cohort databases, such

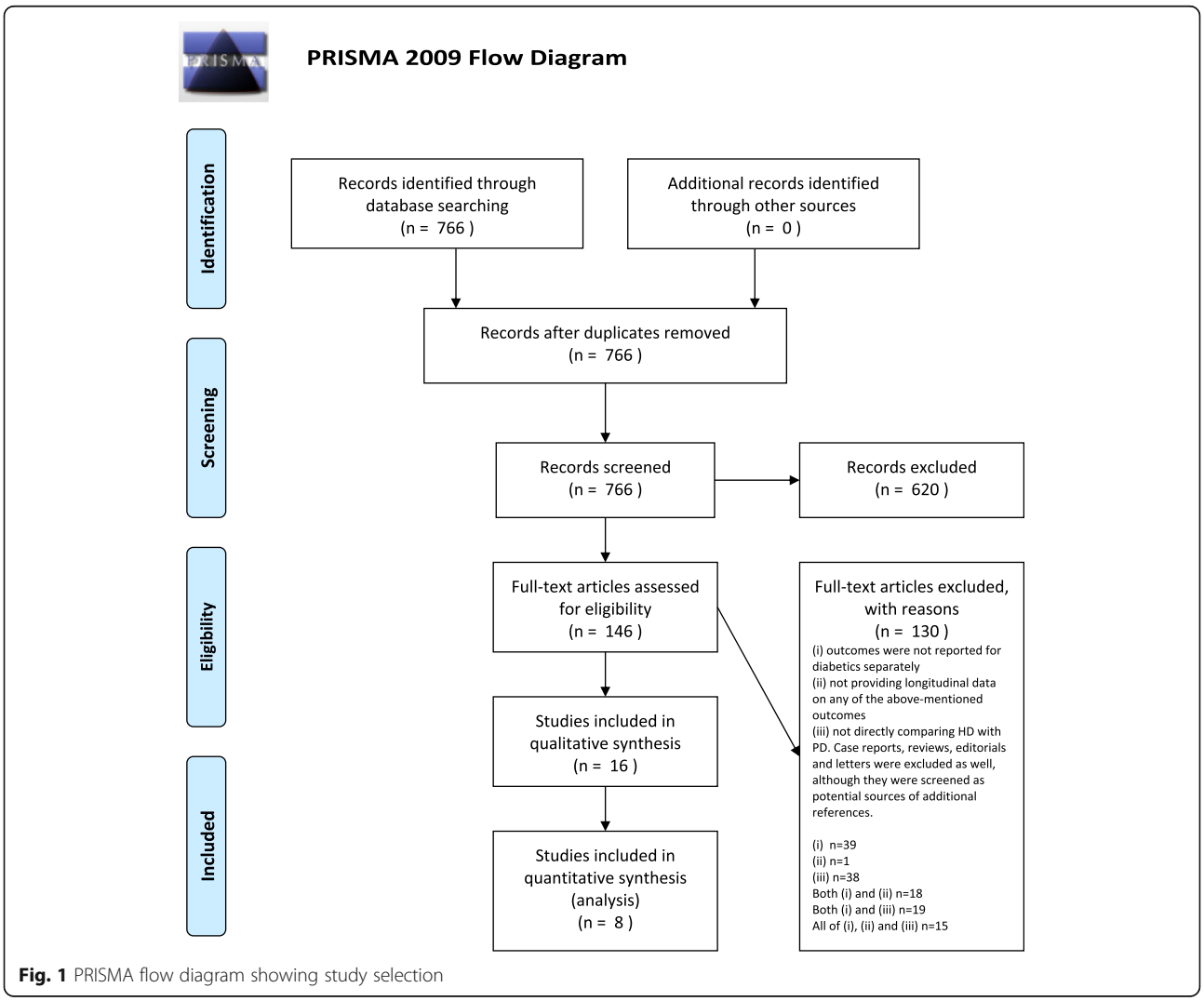

Fig. 1 PRISMA flow diagram showing study selection

Table 1 Characteristics of studies

Study/ year	Region	Type of data	Name of database	Period of patient recruitment	Inclusion criteria	Exclusion criteria	Sample size (% diabetes)	PD patients with diabetes	HD patients with diabetes	Outcome discussed in diabetic patients	Funding source	Potential COI
Kim 2017	Korea	Registry	Korean HIRA database	2005–2008	Patients initiating dialysis and remaining on chronic dialysis for at least 3 months	Younger than 18 years	32,280 (50.1)	3996	12,190	All-cause mortality	None	None
Shen 2016	Taiwan	Registry	LHID	2002–2003	Patients initiating HD or PD	Younger than 18 years or older than 85 years, history of malignancy, incomplete information on age and gender	15,947 (49.2)	359	7485	New-onset AF	Yes	None
Tamayo Isla 2016	South Africa	Cohort	The Pietersburg Provincial Hospital	2007–2014	Patients initiating dialysis and remaining on chronic dialysis for at least 3 months	N.A.	340 (10.3)	13	22	All-cause mortality	None	None
Nesrallah 2016	USA	Registry	USRDS	2004–2011	Patients initiating daily home HD or PD	Younger than 18 years	78,064 (31.6)	23,825	858	All-cause mortality	Yes	None
Lee 2016	Korea	Cohort	The CRC for ESRD	2008–2013	Diabetic ESRD patients initiating HD or PD	Younger than 18 years, history of kidney transplantation, underlying active malignancy or acute infection, expected to survive < 3 months	902 (100)	265	637	All-cause mortality	Yes	None
Marshall 2016	Australia and New Zealand	Registry	ANZDATA	1996–2012	Patients initiating dialysis	Younger than 18 years	57,738 (41.6)	7271	16,727	All-cause mortality	Yes	Yes
Wang 2016	Taiwan	Registry	NHIRD	2000–2010	Patients newly diagnosed with ESRD, undergoing dialysis for 3 months or longer and with a history of stroke prior to dialysis	Under 20 years, with renal transplantation before the index date or with incomplete demographic information	2857 (70.3)	648	1359	All-cause mortality	Yes	None
Waldum-Grevbo 2015	Norway	Registry	The Norwegian Renal Registry	2005–2012	Patients starting dialysis as initial RRT	Younger than 18 years	3089 (32.1)	200	792	All-cause mortality	None	None
Yang 2015	Singapore	Registry	National University Hospital	2005–2010	Patients initiating either HD or PD and surviving the first 90 days of dialysis	Younger than 18 years	871 (68.7)	172	426	All-cause mortality	None	Unclear
Kim 2015	Korea	Registry	Korean HIRA database	2005–2008	Patients initiating dialysis	Patients experiencing MACCE within < 90 days from the date of dialysis initiation, younger than 18 years	30,279 (48.9)	3658	11,154	All-cause mortality MACCE	Yes	None
Marshall 2015	Australia and New Zealand	Registry	ANZDATA	1998–2012	Patients initiating dialysis	Younger than 18 years	37,123 (43.8)	?	?	All-cause mortality	Yes	Yes
Ryu 2015	Korea	Registry	Korean HIRA database	2005–2008	Patients initiating dialysis	Younger than 18 years or surviving for < 90 days from the date of dialysis initiation	32,357 (50.1)	?	?	All-cause mortality	Yes	None

Table 1 Characteristics of studies *(Continued)*

Study/ year	Region	Type of data	Name of database	Period of patient recruitment	Inclusion criteria	Exclusion criteria	Sample size (% diabetes)	PD patients with diabetes	HD patients with diabetes	Outcome discussed in diabetic patients	Funding source	Potential COI
Marshall 2014	Australia and New Zealand	Registry	ANZDATA	1997–2011	Patients initiating dialysis	Younger than 18 years	18,441 (50.1)	4785	4624	All-cause mortality	Yes	Yes
Kim 2014	Korea	Registry	Korean HIRA database	2005–2008	Patients initiating dialysis	Patients who survived for < 90 days from the date of dialysis initiation, younger than 18 years	32,280 (50.1)	3996	12,190	All-cause mortality	Yes	None
Heaf 2014	Denmark	Registry	DNR, LPR	1990–2010	Patients initiating PD or HD, and the following data were extracted: patient age, sex, renal diagnosis, initial therapy (PD/HD), therapy at 90 days, and all changes of therapy	N.A.	12,095 (22.6)	916	1822	All-cause mortality	None	Yes
Mircescu 2014	Romania	Registry	RRR	2008–2011	Patients initiating dialysis	Younger than 18 years, patients who received pre-emptive transplantation or kidney transplantation during the first 90 days of RRT, and patients who had recovery of renal function or who were lost to follow-up during the first 90 days of RRT	9252 (15.5)	194	1246	All-cause mortality	Unclear	Unclear

Abbreviations: *COI* conflict of interest, *HD* hemodialysis, *PD* peritoneal dialysis, *HIRA* Health Insurance Review and Assessment Service, *LHID* Longitudinal Health Insurance Database, *USRDS* US Renal Data System, *CRC* Clinical Research Center, *ESRD* end-stage renal disease, *ANZDATA*, Australia and New Zealand Dialysis and Transplant Registry, *NHIRD* National Health Insurance Research Database, *DNR* Danish Nephrology Registry, *LPR* National Patient Registry, *RRR* Romanian Renal Registry, *AF* atrial fibrillation, *MACCE* major adverse cardiac and cerebrovascular events

as the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) [15, 20, 22], the Korean Health Insurance Review and Assessment Service (HIRA) database [10, 19, 21, 23], and the National Health Insurance Research Database (NHIRD) of Taiwan [11, 16].

Risk of bias

Table 2 shows the quality of the studies included in the analysis. As all were retrospective observational studies, the risk of bias, especially with regard to the failure to adequately control confounding factors, was high.

All-cause mortality

Fifteen studies [10, 12–25] investigated all-cause mortality among diabetic patients undergoing PD and HD (Table 3). Several studies investigated differences in survival between diabetic and non-diabetic patients in subgroup analyses. Figure 2 shows a forest plot comparing all-cause mortality between diabetic patients receiving incident PD and those receiving incident HD. For this analysis, only publications reporting HRs with 95% CIs for whole populations of enrolled diabetic patients were included. We did not conduct a meta-analysis of all-cause mortality data due to the high risk of bias in each study.

Differences in mortality favoring HD were observed in nine studies [10, 12, 13, 15, 16, 19, 21–23]. Marshall et al. [15] reported an HR of 1.17 (95% CI 1.11–1.25) for death among patients receiving incident PD relative to those receiving incident HD, based on ANZDATA data. Among patients receiving incident PD, they found that the risk of death was higher for elderly diabetic patients [22]. Wang et al. [16] reported an HR of 1.22 (95% CI 1.05–1.43) for patients receiving incident PD in a propensity score-matched cohort, based on NHIRD data. Based on HIRA data, Kim et al. [10] reported that the HR for death, calculated by multivariate Cox proportional hazards regression, among patients undergoing PD was 1.27 (95% CI 1.19–1.35), and Kim et al. [19] reported that the adjusted relative risk of death, calculated by multivariate Poisson regression, was 1.29 (95% CI 1.19–1.40). Ryu et al. [21] and Kim et al. [23] reported similar results, and they found that the risk of death among patients receiving incident PD was high for elderly diabetic patients. Tamayo Isla et al. [12] reported HRs for diabetic patients receiving PD and HD of 4.99 (95% CI 2.13–11.71) and 1.02 (95% CI 0.43–2.50), respectively, in comparison with non-diabetic patients receiving HD among 340 patients receiving incident dialysis, based on data from a South African single-center

Table 2 Quality assessment

Key	Failure to develop and apply appropriate eligibility criteria (inclusion of control population)	Flawed measurement of both exposure and outcome	Failure to adequately control confounding factors	Incomplete or inadequately short follow-up
Kim 2017	Low	Low	High	Unclear
Shen 2016	Low	Low	High	Unclear
Tamayo Isla 2016	Low	Low	High	High
Nesrallah 2016	High	Low	High	Unclear
Lee 2016	Low	Low	High	Low
Marshall 2016	Low	Low	High	Low
Wang 2016	Low	Low	High	Unclear
Waldum-Grevbo 2015	Low	Low	High	Low
Yang 2015	Low	Low	High	Unclear
Kim 2015	Low	High	High	Unclear
Marshall 2015	Low	Low	High	Unclear
Ryu 2015	Low	Low	High	Unclear
Marshall 2014	Low	Low	High	Unclear
Kim 2014	Low	Low	High	Unclear
Heaf 2014	Low	Low	High	Unclear
Mircescu 2014	Low	Low	High	Low

Table 3 Mortality of diabetic PD patients

Study/year	PD patients with diabetes	HD patients with diabetes	Confounding factors or factors used for calculating the propensity score	Analysis method	Effect measure	Results
Kim 2017	3996	12,190	Age, sex, NHI, comorbidity (MI, CHF, PAD, cerebrovascular disease, chronic pulmonary disease, peptic ulcer disease, and liver disease), and CCI	Cox proportional hazards model	Hazard ratio	All diabetic patients: 1.27 (1.19–1.35)
Tamayo Isla 2016	13	22	Age, albumin, cholesterol, and hemoglobin	Cox proportional hazards model	Hazard ratio	Diabetic PD patients: 4.99 (2.13–11.71) Diabetic HD patients: 1.02 (0.43–2.50) (Reference: non-diabetic HD patients)
Nesrallah 2016	768	768	Age, sex, race, smoking, alcohol, drugs, private coverage, ESRD start date, duration of ESRD, weight, prior transplant, comorbidities (cancer, hypertension, CHF, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, and diabetes), and laboratory values (albumin and hemoglobin)	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	All diabetic patients: 1.16 (0.99–1.39) (Reference: diabetic patients with home daily HD)
Lee 2016	265	637	Age, sex, modified CCI, comorbid disease (CAD, PAD, CVA, and CHF), smoker, SBP, DBP, BMI, HbA1c, white blood cells, hemoglobin, BUN, creatinine, albumin, calcium, phosphorous, hs-CRP, ESA, and RRF	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	All diabetic patients: 0.65 (0.47–0.90) HbA1c <8.0%: 0.59 (0.37–0.93) ($n = 398$) HbA1c ≥8.0%: 1.43 (0.47–2.81) ($n = 72$)
Marshall 2016	7271	14,309	Age, sex, ethnicity, primary kidney disease, eGFR calculated using MDRD study equation at dialysis therapy initiation, late referral for nephrology predialysis care, diabetes mellitus (none, type 1, and type 2), BMI, medical comorbid conditions (CAD, peripheral vascular disease, cerebrovascular disease, and chronic lung disease), current smoking, and country/state at dialysis therapy initiation	Cox proportional hazards model	Hazard ratio	All diabetic patients: 1.17 (1.11–1.25) (Reference: diabetic patients with conventional facility HD)
Wang 2016	648	647	Year of stroke diagnosis, year of dialysis initiation, age, sex, and comorbidities (CAD, CHF, cancer, hyperlipidemia, hypertension, diabetes, atrial fibrillation, stroke, chronic hepatitis, and COPD)	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	All diabetic patients: 1.22 (1.05–1.43)
Waldum-Grevbo 2015	200	209	Age, sex, county, primary cause of ESRD, comorbidities (diabetes mellitus, LVH, established heart disease, PAD, CVD, and previous malignancy), eGFR, hemoglobin, serum albumin, number of antihypertensive drugs, use of statins, ESA, vitamin D supplementation, candidate for future transplantation, and late referral (knowledge of patients < 4 months prior to start of dialysis)	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	2-year mortality (as-treated): 1.20 (0.76–1.91) 2-year mortality (intention-to-treat): 1.22 (0.80–1.86) 5-year mortality (as-treated): 0.99 (0.69–1.42) 5-year mortality (intention-to-treat): 0.90 (0.65–1.25)
Yang 2015	172	426	Not described	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	Not described
Kim 2015	3658	11,154	Age, sex, NHI (vs. Medical Aid), diabetes, comorbidities other than diabetes, including any CVD, MI, CHF, PAD, CVA, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, and cancer	Multivariate Poisson regression analysis	Adjusted relative risk	All diabetic patients: 1.29 (1.19–1.40)

Table 3 Mortality of diabetic PD patients *(Continued)*

Study/year	PD patients with diabetes	HD patients with diabetes	Confounding factors or factors used for calculating the propensity score	Analysis method	Effect measure	Results
Marshall 2015	?	?	Age, sex, ethnicity, primary kidney disease, eGFR calculated using MDRD Study equation at dialysis therapy initiation, late referral for nephrology predialysis care, diabetes mellitus (none, type 1, and type 2), BMI, medical comorbid conditions (CAD, peripheral vascular disease, cerebrovascular disease, and chronic lung disease), current smoking, and country/state at dialysis therapy initiation	Cox proportional hazards model	Hazard ratio	Not described
Ryu 2015	?	?	Age, sex, healthcare security system, dialysis modality, and modified CCI	Cox proportional hazards model	Hazard ratio	Age ≥ 65: 1.32 (1.11–1.54) Age < 65: 1.08 (0.90–1.28)
Marshall 2014	4381	4378	Not described	Cox proportional hazards model	Hazard ratio	All diabetic patients: 1.15 (1.03–1.29) Follow-up < 3 years: 0.95 (0.83–1.09) Follow-up > 3 years: 1.54 (1.30–1.82)
Kim 2014	3996	12,190	Age, sex, type of insurance (NHI versus Medical Aid), and the presence or absence of a variety of clinical and coexisting conditions (diabetes mellitus, MI, CHF, CVA, PAD, chronic pulmonary disease, liver disease, peptic ulcer disease, and cancer)	Cox proportional hazards model (propensity-matched analysis)	Hazard ratio	All diabetic patients: 1.27 (1.19–1.35) Age > 55: 1.35 (1.22–1.48) (n = 4467) Age ≤ 55: 0.97 (0.82–1.16) (n = 2820)
Heaf 2014	916	1822	First dialysis modality (PD, HD), cohort (according to date of dialysis initiation: 1990–1994, 1995–1999, 2000–2004, 2005–2010), patient age at date of dialysis initiation (categorized into 0-, 60-, 70-, and 80-), sex, renal diagnosis, CCI (categorized into 0, 1–2, ≥ 3), and type of ESRD initiation (early and routine, late and acute, other)	Cox proportional hazards model	Hazard ratio	Diabetes (1990–99): 0.97 (0.84–1.12) Diabetes (2000–10): 0.86 (0.75–0.97) Diabetes and ≥ 65 years (1990–1999): 1.00 (0.77–1.29) Diabetes and ≥ 65 years (2000–2010): 0.85 (0.71–1.01)
Mircescu 2014	194	1246	Age, sex, primary renal disease, and dialysis modality	Cox proportional hazards model	Hazard ratio	Age 18–60 years: 1.73 (1.14–2.62) Age > 60 years: 0.99 (0.66–1.49)

Abbreviations: *HD* hemodialysis, *PD* peritoneal dialysis, *NHI* National Health Insurance, *MI* myocardial infarction, *CHF* congestive heart failure, *PAD* peripheral artery disease, *CCI* Charlson comorbidity index, *ESRD* end-stage renal disease, *CAD* coronary artery disease, *CVA* cerebrovascular accident, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *BMI* body mass index, *HbA1c* hemoglobin A1c, *BUN* blood urea nitrogen, *hs-CRP* high sensitive C-reactive protein, *ESA* erythropoiesis-stimulating agent, *RRF* residual renal function, *eGFR* estimated glomerular filtration rate, *MDRD* Modification of Diet in Renal Disease, *COPD* chronic obstructive pulmonary disease, *CVD* cardiovascular disease

database. Nesrallah et al. [13] reported an unadjusted HR of 1.16 (95% CI 0.99–1.39), based on data for a propensity score-matched cohort of 5336 patients receiving incident dialysis extracted from the US Renal Data System.

Differences in mortality favoring PD were observed in two studies [14, 24]. Lee et al. [14] extracted data on 902 diabetic patients who started dialysis between 2008 and 2013 from a nationwide prospective cohort in Korea, and found that PD was associated with a lower risk of death than was HD, not only in the whole cohort (HR 0.65, 95% CI 0.47–0.90), but also in the group with available hemoglobin A1c (HbA1c) data (HR 0.64, 95% CI 0.46–0.91). In addition, they found that PD had a significant survival advantage over HD in patients with HbA1c < 8.0% (HR 0.59, 95% CI 0.37–0.94), but not in the poor glycemic control group (HbA1c ≥ 8.0%: HR 1.21, 95% CI 0.46–2.76). Heaf and Wehberg [24] extracted data on 12,095 diabetic patients who started dialysis between 1990 and 2010 from the Danish Nephrology Registry, and found that PD was associated with a lower risk of death compared with HD, with a more pronounced difference in recent years (1990–1999: HR 0.97, 95% CI 0.84–1.12; 2000–2010: HR 0.86, 95% CI 0.75–0.97).

Statistical analyses in all of the abovementioned studies were conducted using only an intention-to-treat

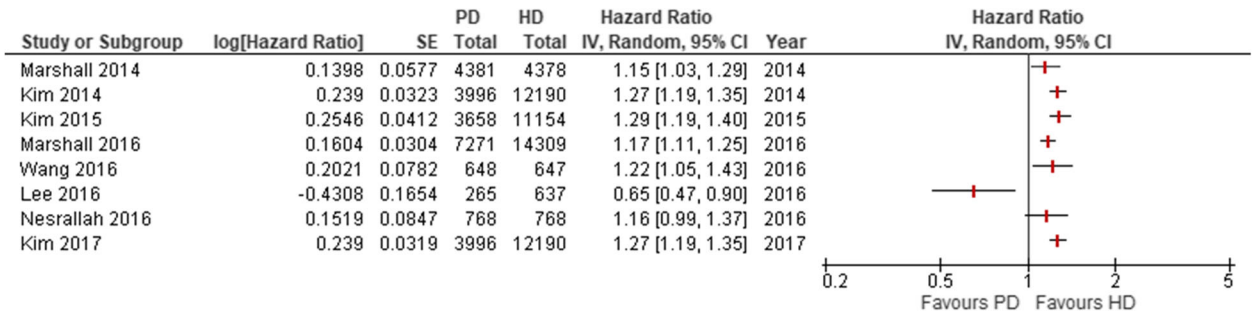

Fig. 2 Forest plot comparing all-cause mortality in diabetic patients receiving incident PD and those receiving incident HD. For this analysis, only publications reporting hazard ratios (HRs) with 95% confidence interval (CIs) for all enrolled diabetic patients were included. We did not conduct a meta-analysis because of the high risk of bias in each study. The Marshall 2014 and Marshall 2016 studies used the same database, i.e., the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). In Marshall 2014, diabetic patients were divided into those with type 1 and those with type 2 diabetes, and we extracted the HR and 95% CI from the type 2 diabetes group. The Kim 2014, Kim 2015, and Kim 2017 studies were conducted using the same database, i.e., the Korean Health Insurance Review and Assessment Service (HIRA) database. In Nesrallah 2016, the control patients received home HD rather than conventional HD

approach. However, Waldum-Grevbo et al. [17] examined survival using both intention-to-treat and as-treated analyses with data extracted from the Norwegian Renal Registry. They reported that the 2-year mortality rate tended to be higher (intention-to-treat analysis: HR 1.22, 95% CI 0.80–1.86; as-treated analysis: HR 1.20, 95% CI 0.76–1.91), whereas the 5-year mortality rate tended to be lower (intention-to-treat analysis: HR 0.90, 95% CI 0.65–1.25; as-treated analysis: HR 0.99, 95% CI 0.69–1.42) in diabetic patients receiving PD compared with those receiving HD.

Major morbid events, including cardiovascular disease and infectious disease

Two studies investigated the effects of dialysis modality on new-onset CVD among diabetic patients [11, 19]. Shen et al. [11] reported that the risk of new-onset atrial fibrillation was higher in the incident PD group (HR 1.76, 95% CI 1.13–2.75 vs. controls without ESRD) than in the incident HD group (HR 1.52, 95% CI 1.33–1.75vs. controls without ESRD) among 7844 patients with diabetes. Kim et al. [19] reported that the risk of developing major adverse cardiac and cerebrovascular events, including all-cause mortality, non-fatal acute myocardial infarction, target vessel revascularization including percutaneous coronary intervention and coronary artery bypass grafting, and non-fatal stroke, was higher in patients receiving incident PD than in those receiving incident HD among 14,812 patients with diabetes (HR 1.15, 95% CI 1.07–1.24).

None of the 16 studies investigated the effects of dialysis modality on urinary volume or RRF, infectious disease, or glycemic control among diabetic patients.

The findings are summarized in Table 4.

Discussion

The present systematic review was performed to examine whether PD or HD as the first RRT for diabetic patients with ESRD improved clinical outcomes. The chief findings were that differences in mortality favoring HD were observed in nine studies, whereas those favoring PD were observed in two studies. Although the risk of death tended to be higher among patients receiving incident PD than among those receiving incident HD, we could not confirm the superiority of PD or HD because of conflicting results and a high risk of bias in the included studies, especially with regard to the failure to adequately control confounding factors. These results are similar to those of a previous systematic review conducted by Couchoud et al. [8], which included 25 observational studies published until February 2014.

We conducted this systematic review on the assumption that improved outcomes were expected among patients with diabetes undergoing incident PD because of advances in the management of these patients, including the use of icodextrin-containing PD solutions and dipeptidyl peptidase-4 (DPP-4) inhibitors.

RRF is a strong predictor of patient survival [26, 27] and is preserved better among patients receiving PD than in those receiving HD [28]. Among patients undergoing PD, the rate of RRF loss is higher in diabetic than in non-diabetic patients [28, 29]. Interestingly, fluid overload and impaired RRF are closely linked. Udo et al. [30] reported that diabetic patients electively starting PD showed greater extracellular water retention 6–10 weeks after starting PD than did non-diabetic patients, despite similar peritoneal function, as determined by the peritoneal equilibration test. In addition, Kim et al. [31] reported that an increase in body weight during the first year and diabetes were associated independently with a

Table 4 Summary of findings

Peritoneal dialysis compared to hemodialysis for first renal replacement therapy in end-stage renal disease patients with diabetes

Patient or population: end-stage renal disease patients with diabetes considering renal replacement therapy
Setting: all settings
Intervention: peritoneal dialysis
Comparison: hemodialysis

Outcomes	Impact	No. of participants (studies)	Certainty of the evidence (GRADE)
New-onset cardiovascular disease	Two studies investigated new-onset cardiovascular disease among diabetic patients undergoing PD and HD. The differences in incidence favored HD in both studies.	22,656 (2 observational studies)	⊕◯◯◯ Very low[a,b]
New-onset infectious disease—not reported		–	–
Residual renal function—not reported		–	–
Glycemic control—not reported		–	–

*Risk in the intervention group (and 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and 95% CI).
CI: confidence interval

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

[a]Study limitations: failure to adequately control confounding factors and incomplete or inadequately short follow-up
[b]Substantial heterogeneity of results
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rapid decline of RRF. Icodextrin-containing solutions improve peritoneal ultrafiltration and mitigate uncontrolled fluid overload. Icodextrin became commercially available in 1997 in Europe, in 2001 in Korea, in 2002 in Australia and New Zealand, in 2003 in the USA and Japan, and in 2004 in Taiwan. In a recent systematic review, the use of icodextrin was shown to uniformly result in improved peritoneal ultrafiltration compared with glucose exchange, especially among patients with higher peritoneal transport characteristics, and to reduce reported episodes of uncontrolled fluid overload [32]. However, icodextrin had no appreciable impact on RRF, technical failure, or death [32].

Several advances have been made in the treatment of diabetes, including the development of DPP-4 inhibitors. These drugs, which were approved for clinical use in 2006, provide an effective therapeutic option without the drawback of inducing hypoglycemia and can be used safely in patients receiving dialysis. DPP-4 inhibitor use was found to significantly improve the HbA1c level and hyperglycemia in patients receiving PD [33, 34]. Glycemic control is known to influence clinical outcomes, including mortality, in patients with chronic kidney disease who are and are not receiving dialysis. Duong et al. [35] reported that poor glycemic control (HbA1c ≥ 8% or serum glucose ≥ 300 mg/dl) was associated with decreased survival in a population of 2798 diabetic patients receiving PD. Furthermore, Lee et al. [14] reported a significant survival advantage of PD in patients with HbA1c < 8.0%, but no significant difference in the survival rate according to dialysis modality (PD or HD) in the poor glycemic control group (HbA1c ≥ 8.0%). Unfortunately, the details of diabetes treatment were not provided in all cited studies.

In this systematic review, the results differed among studies due to the heterogeneity of dialysis practices; diabetes treatments; patient backgrounds, including educational and social insurance statuses; and the timing of referral to a nephrologist. Unfortunately, these factors

were not clarified in all of the included studies. In addition, no report from Japan was included. We recently reported that technical and patient survival did not differ between diabetic and non-diabetic patients receiving incident PD and that the presence of diabetes did not affect either survival measure in multivariate analyses [36].

Conclusions

In the present systematic review, the risk of death tended to be higher among diabetic patients with ESRD receiving incident PD as RRT than among those receiving incident HD. However, we could not determine definitively whether PD or HD was superior with regard to patient outcomes because of the high risk of bias and the diversity of management of diabetic patients undergoing dialysis. Further studies are needed to clarify the advantages of RRT with PD and HD in diabetic patients with ESRD.

Additional files

Additional file 1: PRISMA 2009 Checklist. (DOC 64 kb)
Additional file 2: Search strategy. (XLSX 11 kb)

Abbreviations

ANZDATA: Australia and New Zealand Dialysis and Transplant Registry; CI: Confidence interval; CVD: Cardiovascular disease; DPP-4: Dipeptidyl peptidase-4; ESRD: End-stage renal disease; HbA1c: Hemoglobin A1c; HD: Hemodialysis; HIRA: Health Insurance Review and Assessment Service; HR: Hazard ratio; NHIRD: National Health Insurance Research Database; PD: Peritoneal dialysis; RCT: Randomized controlled trial; RRF: Residual renal function; RRT: Renal replacement therapy

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Authors' contributions

YM drafted the manuscript. YM, CH, HI, KW, HT, YT, and HY contributed to the research concept and study design. YM, CH, HI, KW, HT, YT, and HY contributed to the data acquisition, risk of bias assessment, data analysis/interpretation, and statistical analysis. MR, YI, and NK contributed to the supervision or mentorship. Each author contributed important intellectual content during manuscript drafting or revision. All authors have read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

No ethical approval was required because this study did not involve the use of confidential personal data or patient interventions.

Consent for publication

Not applicable.

Competing interests

YM has received scholarship funds from Baxter International, Inc. and Terumo Corporation. YI belonged to a department endowed by Baxter International, Inc. The other authors declare that they have no competing interests.

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