Dialysis modality choice in diabetic patients with end-stage kidney disease: a systematic review of the available evidence

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ABSTRACT

Background. Diabetes is the leading cause of end-stage kidney disease (ESKD). Because of conflicting results in observational studies, it is still subject to debate whether in diabetic patients the dialysis modality selected as first treatment (haemodialysis or peritoneal dialysis) may have a major impact on outcomes. We therefore aimed at performing a systematic review of the available evidence.

Methods. MEDLINE, EMBASE and CENTRAL databases were searched until February 2014 for English-language articles without time or methodology restrictions by highly sensitive search strategies focused on diabetes, end-stage kidney disease and dialysis modality. Selection of relevant studies, data extraction and analysis were performed by two independent reviewers.

Results. Twenty-five observational studies (23 on incident and 2 on prevalent cohorts) were included in this review. Mortality was the only main outcome addressed in large cohorts. When considering patient survival, results were inconsistent and varied across study designs, follow-up period and subgroups. We therefore found no evidence-based arguments in favour or against a particular dialysis modality as first choice treatment in patients with diabetes and ESKD. However, peritoneal dialysis (PD) as first choice seems to convey a higher risk of death in elderly and frail patients.

Conclusions. The available evidence derived from observational studies is inconsistent. Therefore evidence-based arguments indicating that HD or PD as first treatment may improve patient-centred outcomes in diabetics with ESKD are lacking. In the absence of such evidence, modality selection should be governed by patient preference, after unbiased patient information.

Keywords: diabetes, epidemiology, haemodialysis, peritoneal dialysis, systematic review

INTRODUCTION

Diabetes has become the most common cause of end-stage kidney disease (ESKD) in most countries, with still increasing incidence, while incidence rates of ESKD from other causes seem to have stabilized [1, 2].

The question on optimal choice of dialysis modality, whether it be peritoneal dialysis (PD) or haemodialysis (HD), remains a matter of debate, especially in diabetic patients with ESKD [3–5]. Modality choice might have some peculiar aspects in diabetics with advanced chronic kidney disease (CKD). There is the fear that constant exposure to glucose in the dialysate may further worsen glycaemic control in diabetic patients when on peritoneal dialysis. On the contrary, PD therapy may be better tolerated than HD because of a more stable blood pressure in diabetic patients, e.g. with autonomic neuropathy. Also, creation of a good vascular access in the presence of advanced calcific atherosclerosis might be challenging [3].

Randomized controlled trials comparing PD and HD [6] have been proven to be very difficult due to recruitment problems. Because of conflicting results in observational studies [7–9], it is still unclear whether in diabetic CKD patients one dialysis modality should be preferred over another as a first line

approach because of a substantial difference in major outcomes. Currently, there is great heterogeneity in practice concerning the information given to the patients and the choice of first modality of treatment [10]. A US survey among nephrologists has shown that people with diabetes had half the odds of being recommended for PD [11]. On the other hand, a similar survey among Canadian, British Isles and American nephrologists showed that diabetes operates slightly to favour PD [12–14].

The European Renal Best Practice (ERBP) Diabetes guideline development group therefore aimed at performing a systematic review of the available evidence in order to establish whether in diabetic patients the choice of the first dialysis modality may impact on their clinical outcomes.

MATERIALS AND METHODS

Data source and search strategy

MEDLINE, EMBASE and CENTRAL databases were searched until February 2014 for English-language articles without time or methodology restrictions through focused and highly sensitive search strategies (Supplementary Table S1). Supplementary articles were added by manual search.

Study selection

We planned to include any randomized or non-randomized controlled trial, single-arm, prospective or retrospective observational study comparing any kind of peritoneal dialysis (automated peritoneal dialysis APD, continuous ambulatory peritoneal dialysis CAPD) to any kind of haemodialysis (conventional HD, haemofiltration HF, haemodiafiltration HDF, daily HD) as first renal replacement therapy in diabetic patients with ESKD. Studies were considered without follow-up duration restrictions. Diabetes (type I or II) was considered either as being the cause of ESKD or a superimposed condition. Studies where a well-defined part of the population fulfilled the above criteria were included in the review. Outcomes of interest were survival, quality of life, major morbid events (including but not limited to myocardial infarction, stroke, amputation and loss of vision), hospital admissions, deterioration of residual renal function when already on dialysis, minor morbid events (including but not limited to hypoglycaemia, delayed wound healing, infection, visual disturbances and pain), functional status, glycaemic control, access to transplantation and technique survival. Studies were excluded if: (i) outcomes were not reported for diabetics separately; (ii) not providing longitudinal data on any of the above mentioned outcomes; (iii) not directly comparing HD with PD. Case reports, reviews, editorials and letters were excluded as well, although they were screened as potential sources of additional references. Selection of relevant studies was independently performed by two authors (C.C. and D.B.). Discrepancies were solved collegially.

Quality assessment

We used the Newcastle–Ottawa Scale [15] to assess the study quality for observational studies. This scale considers a quality score calculated on the basis of three major issues: study participants (0–4 points), adjustment for confounding (0–2 points) or ascertainment of the exposure or outcome of interest (0–3 points) with a maximum score of 9 points which represents the highest methodological quality.

Data extraction and analysis

Data extraction and analysis were performed by two reviewers independently (C.C. and D.B.). In studies considering mixed populations, the subgroup of patients with documented diabetes was described only if corresponding data were available.

RESULTS

Search results and study selection

Four hundred and twenty-three records were identified through database searches. In addition, three more studies were found through additional sources. Among them, 76 full-text articles were assessed for eligibility. Fifty-one full-text articles were excluded: 19 because of an inappropriate study population, 15 because of the absence of the comparator or an inappropriate intervention and 17 for other causes, mainly because of a lack in reporting of outcomes for diabetic patients separately. Figure 1 provides a flow diagram of the study selection process.

Study characteristics

Among the 25 studies included, there were no randomized controlled trials, 23 were cohort studies in incident patients (registries, historical prospective cohorts, retrospective cohorts) and 2 studies in prevalent patients [16, 17]. Eight studies started inclusion before 1995 [7, 18–24], 7 studies between 1995 and 2000 [8, 25–31] and 7 after 2000 [32–38]. The details of the 23 studies that included incident patients are summarized in Table 1. The total number of patients included in the 23 incident cohort studies was 1 008 453, ranging from 181 [31] to 398 940 [27]. None included only diabetic patients; the percentage of diabetic patients ranged from 9 [26] to 61% [38]. The total number of diabetic patients included was 721 783 on HD and 106 790 on PD. In those studies, no treatment details were available allowing us to analyse the benefit from haemodiafiltration or automated PD for example. Eleven cohort studies reported on North American patients, 8 on European patients, 3 from Asia and 1 from South America. Three studies were based on the CMS form for ESKD patients in the USA with overlapping periods [27, 29, 30]. The two retrospective cohort studies that included United States Renal Data System (USRDS) prevalent patients ended their inclusion more than 15 years ago and did not give the number of diabetic patients according to their dialysis modality [16, 17].

Risk of bias

The overall study quality assessed by the Newcastle–Ottawa scale was moderate to high (range 5–9). The details are given in Table 2.

Because of their observational design, none of the included studies was free from selection bias. Furthermore, since none
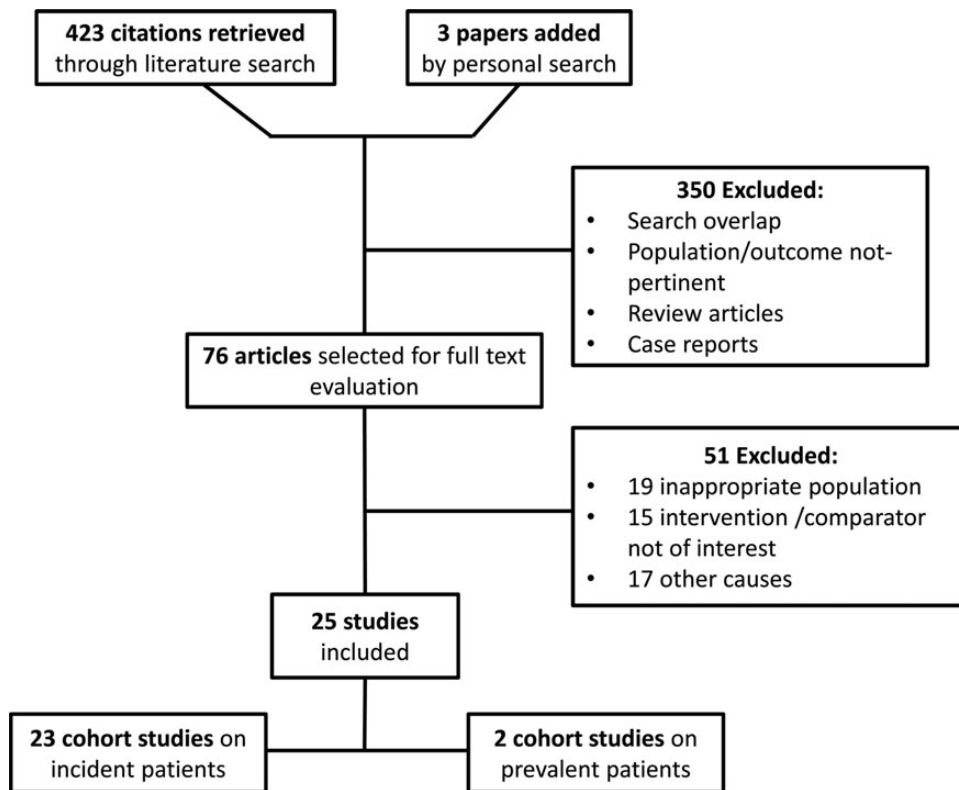
FIGURE 1: Flow chart of the study selection process.

included only diabetic patients, only few details were available, on for example the case mix of the diabetic patients according to their modality of treatment.

There was some heterogeneity in the length of follow-up among studies (from 1 to 8 years) which may hamper the generalizability of results. Because many studies have shown a non-proportional hazard, the risk over time was evaluated using various methods. Five studies used a Poisson regression model which allowed them to take into account person-time [21, 22, 24, 27, 31], eight used a non-proportional hazards (Cox) model stratified on time [19, 20, 22, 23, 25, 28–30] and one used a marginal structural model stratified on time [38].

Outcomes

None of the reviewed studies provided data on quality of life, patient satisfaction, major and minor morbid events, hospital admissions, deterioration of residual renal function, functional status, glycaemic control, access to transplantation or survival of the technique. Twenty-four cohort studies analysed the risk of death. Only one cohort study considered the risk of infectious complications [31].

First dialysis modality and mortality

Supplementary Table S2 shows the association of PD with mortality in incident diabetic patients within the 23 cohort studies.

In intention-to-treat analyses (i.e. patients are assigned to their initial treatment and not to the treatment eventually received), the results were as follows.

Statistically significant difference in favour of PD (highlighted in red in Supplementary Table S2) was observed in patients aged 40–50 years before 15 months after the start of dialysis [19], in patients aged 18–44 years without other comorbidities during the first 3 years [27], in patients under 60 years in the first 2 years [25], in the first 12 months [34], 9 months [38] or 6 months [23].

Statistically significant difference in favour of HD (highlighted in green in Supplementary Table S2) was observed in patients aged over 50 years after 15 months [19], in all the patients [39], in patients with or without CAD after 6 months [29, 30], in patients with congestive heart failure (CHF) [29], in patients without CHF after 6 months [29], in patients over 45 years [27], in patients over 67 years [22], in patients over 65 years after 6 months [20], in elderly women over 70 years [8], after 1 year when starting at Day 90, and in patients under 60 years [36], in patients aged 18–60 years [36], in all the subgroups over 45 years [24].

No statistically significant difference was observed in all patients [7, 18, 21, 26, 32, 35], in men or women under 70 years [8], in elderly patients over 75 [33], in patients under 40 years after 15 months or 60–70 years before 15 months [19], in patients 18–44 years with comorbidities [27], in all patients during the first 2 years [28], in patients <60 years or patients over 60 years in the first 2 years [25], in patients over 65 years before 6 months [20], in patients over 60 years [36], in all the patients after 6 months [23], in patients aged 18–44 years [24].

In as-treated analyses (i.e. patients are considered at risk as long they are treated in the modality), a statistical difference in favour of PD was observed in all patients [7], only in patients under 60 years during the first 2 years [25], patients under 65

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Table 1. Characteristics of the included studies

Author [ref]	Publication year	Study design	Location	Start of study (year)	End of study (year)	Type of data	Name of the database	Patient characteristics inclusion	Patient characteristics exclusion	Total number of patients included (with or without diabetes)	% patients with diabetes or diabetic nephropathy	Haemodialysis patients with diabetes	Peritoneal patients with diabetes
Data from of incident patients													
Aslam [31]	2006	Prospective cohort study	North America	1999	2005	Cohort	Oakland dialysis centre	All incident dialysis patients at a single centre		181	51%	119	62
Chang [37]	2013	Retrospective cohort study	Korea	2000	2009	Cohort	Gachon University Gil hospital	All incident adult dialysis patients at Day 90	Pre-emptive transplantation, missing data	836	54%	321	128
Choi [35]	2013	Prospective cohort study	Korea	2008	2011	Registry	CRC for ESRD	all incident patients over 20 years, with dialysis for more than 3 months	Kidney transplantation within the first 3 months	1060	48%	367	145
Collins [22]	2002	Prospective cohort study	USA	1989	1993	Registry	Medicare USRDS	All incident patients aged 67 years and over	Less than 60 days in one modality and missing data for gender, race, renal network of residence, primary cause of renal failure	89 193	41%	63 513	6695
Couchoud [33]	2007	Prospective cohort study	France	2002	2005	Registry	REIN	All incident dialysis patients aged 75 years and over		3512	36%	2880	632
Fenton [21]	1997	Prospective cohort study	Canada	1990	1994	Registry	CORR	All incident patients	Missing data on comorbidity	10 633	25%	1800	907
Ganesh [30]	2003	Prospective cohort study	USA	1995	1997	Registry	CMS ESRD	All new ESRD adult patients at Day 90	Age less than 18 and missing data on age, gender, race, indicators of CAD, no modality assignment at Day 90	107 922	44%	93 900	14 022
Heaf [7]	2002	Prospective cohort study	Danemark	1990	1999	Registry	DNR	All incident dialysis patients		4921	19%	4020	2208
Heaf [23]	2014	Prospective cohort study	Danemark	1990	2010	Registry	DNR	All incident dialysis patients	Pre-emptive transplantation	12 095	23%	1822	916
Jaar [28]	2005	Prospective cohort study	USA	1995	1998	Cohort	CHOICE	All incident English or Spanish speakers dialysis patients aged >17 years. Population of the CHOICE study.		1041	54%	764	274
Lee [18]	2009	Prospective cohort study	Taiwan	1991	2005	Cohort	Chang Gung Memorial hospital	All incident dialysis patients with dialysis for more than 3 months	Severe comorbidities: malignancy, COPD, decompensated cirrhosis, class IV heart failure, vegetative life.	1347	38%	1089	258
Liem [19]	2007	Prospective cohort study	Netherlands	1987	2002	Registry	RENINE	All incident dialysis patients	Age <18 years, dialysis vintage <30 days, death within first 90 days of RRT, transplantation (pre-emptive) or renal function recover, and centres with fewer than 20 patients or fewer than 5 PD patients	16 643	15%	10 841	5802
Lukowsky [38]	2013	Prospective cohort study	USA	2001	2006	Dialysis chain data base + registry	Da Vita USRDS	All incident dialysis patients at Day 90	No missing data	23,718	61%	13 885	740

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Table 1. Continued

Author [ref]	Publication year	Study design	Location	Start of study (year)	End of study (year)	Type of data	Name of the database	Patient characteristics inclusion	Patient characteristics exclusion	Total number of patients included (with or without diabetes)	% patients with diabetes or diabetic nephropathy	Haemodialysis patients with diabetes	Peritoneal patients with diabetes
Mircescu [26]	2006	Retrospective cohort study	Romania	1995	2002	Registry	RRR	All incident patients surviving at least 3 months after RRT initiation		2284	9%	1872	412
Mircescu [36]	2014	Prospective cohort study	Romania	2008	2011	Registry	RRR	All adult incident patients surviving at least 3 months after RRT initiation	Kidney transplantation or recovery of renal function within the first 3 months	9252	15%	1246	194
Sanabria [32]	2008	Retrospective cohort study	Colombia	2001	2005	Cohort	DOC	All incident patients who reached the 90th day of therapy, over 18 years	Missing data on comorbidity	923	41%	157	220
Stack [29]	2003	Prospective cohort study	USA	1995	1997	Registry	CMS ESRD	All incident patients age 18 years and older at Day 90	Renal transplant within 90 days, data missing for demographic, comorbid and laboratory variables and no treatment modality assignment at Day 90	158 685	44%	93 900	14 022
Termorshuizen [25]	2003	Prospective cohort study	Netherlands	?	2002	Cohort	NECOSAD	All incident dialysis patients, age 18 years and older, informed consent, survived the first 3 months		1222	15%	742	480
van de Luijtgaarden [8]	2011	Prospective cohort study	Europe	1998	2006	Registry	ERA EDTA	All incident patients aged ≥20 years, start with dialysis	Missing data on comorbidity	15 828	31%	12 731	3097
Vonesh [27]	2004	Prospective cohort study	USA	1995	2000	Registry	CMS ESRD	All incident patients who survived 90 days		398 940	45%	35 2706	46 234
Weinhandl [34]	2009	Retrospective cohort study	USA	2003	2006	Registry	CMS ESRD	All incident adult patients, over 18 years	Missing data on age, sex, race or ethnicity	98 875	46%	47 937	3190
Winkelmayer [20]	2002	Prospective cohort study	USA	1991	1996	Registry	CMS ESRD	All patients aged >65 years, active participants in Medicare or Medicaid programs for at least 12 months, >2 months of survival after dialysis start	Renal transplantation in the first month of dialysis	2503	49%	1966	537
Yeates [24]	2012	Prospective cohort study	North America	1991	2007	Registry	CORR	All incident patients over 17 years	Pre-emptive transplantation	46 839	40%	13 205	5615
Data from prevalent patients													
Bloembergen [16]	1995	Retrospective cohort study	North America	1987	1989	Registry	USRDS	Three national cohorts of prevalent patients receiving PD and centre HD, each with 365 days of follow-up.	Follow-up less than 3 months and switch between treatment modalities 60 days before	170 700 patients years	25%	?	?
Mattana [17]	1997	Retrospective cohort study	North America	1989	1991	Registry	USRDS	All prevalent dialysis patients		?	?	?	?

PD, peritoneal dialysis; RRT, renal replacement therapy; CMS, Centers for Medicare and Medicaid services; USRDS, United States Renal Data System; REIN, French Renal Epidemiology and Information Network; CRC for ESRD, Clinical Research Center for End Stage Renal Disease; CORR, Canadian Organ Replacement Register; ERA EDTA, European Renal Association – European Dialysis Transplantation Association; NECOSAD, The Netherlands Cooperative Study on Adequacy of Dialysis; DOC, Dialysis Outcomes in Colombia study; RRR, Romanian Renal Registry; Da Vita Inc, DaVita HealthCare Partners Inc. company; DNR, Danish Nephrology registry; CHOICE, Choices for Healthy Outcomes in Caring for ESRD study; RENINE, Dutch End-Stage Renal Disease Registry.

Table 2. Quality assessment of the included cohort studies

Author	Publication year	Newcastle–Ottawa scale			Potential financial interest	Methods	Comments
		Selection (up to 4)	Comparability (up to 2)	Outcome (up to 3)			
Bloembergen	1995	3	1	3	No	Adjusted death rates	Prevalent patients. Censoring at transplantation.
Aslam	2006	3	1	3	Yes	Multivariate Poisson regression	Low number of events. Censoring at treatment switch, at transplantation and at death.
Chang	2013	3	2	1	No	Multivariate Cox proportional hazards model.	Retrospective. Propensity score. Censoring at transplantation.
Choi	2013	4	2	3	No	Kaplan Meier curve on matched population	Propensity score. Stratification on age and gender.
Collins	2002	4	1	3	No	Multivariate Poisson regression	Stratification on time. Censoring at transplantation and at treatment switch. Some death rates per 1000 patients years >1000?
Couchoud	2007	4	2	3	No	Multivariate Cox proportional hazards model.	No stratification on time.
Fenton	1997	4	2	3	No	Multivariate Poisson regression + Multivariate Cox proportional hazards model	Various additional models
Ganesh	2003	4	2	2	Yes	Multivariate time-dependant Cox regression.	Censoring at transplantation. Additional as-treat analysis. Stratification on time and coronary artery disease.
Heaf	2002	4	0	3	No	Multivariate Cox proportional hazards model.	Adjustment on comorbidities not clear. No stratification on time, stratification on age. Censoring at transplantation. Additional as-treat analysis and censoring at treatment switch.
Heaf	2014	4	2	3	No	Multivariate Cox proportional hazards model.	Stratification on time, age and vintage. Censoring at transplantation.
Jaar	2005	4	1	2	Yes	Multivariate Cox proportional hazards model.	Propensity score. Stratification on time. Censoring at transplantation. Additional as-treat analysis and censoring at treatment switch or switch analysed as treatment failure.
Lee	2009	2	1	2	No	Multivariate Cox proportional hazards model.	Censoring at transplantation and at treatment switch. No stratification on time.
Liem	2007	4	1	3	Yes	Multivariate Cox proportional hazards model.	Stratification on time and age. Censoring at transplantation.
Lukowsky	2013	3	2	3	Unclear	Marginal structural model	Inverse probability of treatment weight and inverse probability on censoring weight. Stratification on time.
Mattana	1997	3	1	1	No	Multivariate Cox proportional hazards model.	Prevalent patients. Effect measure not provided. No details for other mortality causes (competing risks).
Mircescu	2006	3	1	3	Yes	Multivariate Cox proportional hazards model.	Retrospective. Low number of events. Adjustment unclear. No stratification on time, stratification on age. Censoring at transplantation.
Mircescu	2014	4	1	3	No	Multivariate Cox proportional hazards model.	Stratification on age. No adjustment on comorbidities.
Sanabria	2008	3	2	1	Yes	Multivariate Cox proportional hazards model.	Retrospective. No stratification on time, stratification on age. Censoring at transplantation.

Continued

Table 2. Continued

Author	Publication year	Newcastle–Ottawa scale			Potential financial interest	Methods	Comments
		Selection (up to 4)	Comparability (up to 2)	Outcome (up to 3)			
Stack	2003	4	2	3	No	Time-dependant Cox regression.	Stratification on time and congestive heart failure. Additional as-treat analysis.
Termorshuizen	2003	4	1	2	Unclear	Multivariate Cox proportional hazards model.	Stratification on time and age. Additional as-treat analysis. Censoring at transplantation. Low number of patients
van de Luijtgaarden	2011	4	2	2	Yes	Multivariate Cox proportional hazards model.	Propensity score. Censoring at transplantation. No stratification on time, stratification on age and gender.
Vonesh	2004	4	2	3	Yes	Multivariate Poisson regression	Additional as-treat analysis. Censoring at transplantation. Stratification on age, comorbidities.
Weinhandl	2010	4	2	3	Yes	Multivariate Cox proportional hazards model.	Propensity score. Additional as-treat analysis. Censoring at transplantation. Stratification on age, comorbidities.
Winkelmayer	2002	3	2	3	Yes	Multivariate Cox proportional hazards model.	Propensity score. Stratification on time. No quantitative results for diabetic patients. Censoring at transplantation
Yeates	2012	4	2	3	Yes	Multivariate Poisson regression	Additional as-treat analysis. Stratification on age, gender and vintage.

years [21], during the first year [34]. In patients aged over 44 years, Yeates *et al.* [24] showed a higher risk of death in diabetic patients on PD. Stack *et al.* [40] reported adjusted mortality to be higher for PD patients with CHF who remained on this therapy during the follow-up and for patients who switched compared with those who remained on HD. In the subgroup without CHF, the mortality was similar for patients who remained either on HD or PD but was higher for those who switched.

In the USRDS cohort that also included prevalent patients, PD was associated with higher mortality [16]. In another USRDS cohort, diabetic patients appeared to suffer from a substantially higher cerebrovascular death rate on PD versus HD with advancing age [17]. Of note, this study did not provide details on other mortality causes (competing risks).

Dialysis modality and infectious complications

In one small cohort study, higher infection rates (hospitalization or access-related infections) were observed in diabetic PD patients (1.28 versus 0.84/year, $P < 0.004$) but this difference lost its statistical significance after adjustment for albumin, age, race and gender (RR 1.13; 95% CI 0.76–1.67) [31].

DISCUSSION

When considering patient survival, in presence of conflicting results, we found no evidence-based arguments in favour or against a particular dialysis modality as first treatment in patients with diabetes and ESKD. According to subgroup analyses, some concerns may arise about choosing PD for elderly and frail patients since this technique was associated with a higher risk of death, particularly in the mid-short term.

Differences between studies can be explained by differences in PD and HD practices, and can thus be country or centre-specific. Mehrotra *et al.* [41], using the database of five large US dialysis providers, found that the propensity to start PD in a certain chain substantially influenced relative mortality risk in PD versus HD patients. Most studies compared all PD techniques with all HD modalities, blurring the interpretation of results for those separate techniques. The higher mortality on PD versus HD reported in the Australia and New Zealand Dialysis and Transplant (ANZDATA) cohort, for example, disappeared when home HD patients are excluded [42]. It has been well demonstrated that, in peritoneal dialysis, applying short dwells results in better survival in fast transporting patients, whereas long dwells result in better survival in slow transporting patients [43, 44]. Neglecting this type of (subtle) nuances in treatment practice might severely impact on the final interpretation of the data.

Unfortunately, most of the studies based on registry data did not take into account the renal function at dialysis start. The better survival associated with PD in the initial phase seen in some studies could be explained by a higher residual renal function in those patients who started earlier than their counterparts on HD, as observed in many registries [45, 46]. Early starters have an artificial survival advantage, since at baseline they are earlier in the course of their disease than late starters; this bias is usually referred to as 'lead-time bias'.

Another possible explanation of contradictory results may be due to the vascular access used in HD patients in the various countries. In fact, some studies have shown important influence of HD vascular access type on survival comparisons between incident HD and PD patients [47, 48]. In a study including 40 526 incident adult dialysis patients from the Canadian Organ Replacement Register between 2001 and 2008, patients starting HD using a central venous catheter had a higher risk of death in the first year compared with those who started PD (adjusted HR, 1.8; 95% CI, 1.6–1.9), whereas there was no difference in survival between HD patients with artero-venous fistula or graft and PD patients (adjusted HR, 0.9; 95% CI, 0.8–1.1) [47]. In a study including 152 patients in Portugal, the number of infection-free patients in two groups either PD or HD with tunnelled cuffed catheter was, respectively, 57 and 65% after 1 year of follow-up; both catheter-related bacteraemia and hospital admissions were significantly higher in the HD-tunnelled cuffed catheter group. Only one study analysed the association of dialysis modality and infection in diabetic patients [31]. Mainly because of lack of power, this study was inconclusive. In an ANZDATA cohort, PD was consistently associated with increased hazard of death from infection compared with HD after 6 months of treatment using a competing risks approach [49]. This increased risk of infectious death in PD patients was largely accounted for by an increased risk of death caused by bacterial or fungal peritonitis. Unfortunately, no subgroup analyses were performed in diabetic patients. In addition to the direct effects of central venous catheter use on morbidity and mortality, initiation of HD with a central venous catheter is a proxy for comorbid patient characteristics that are associated with reduced survival among dialysis patients. In diabetic patients, the difficulty to create a fistula due to advanced calcific atherosclerosis in peripheral vessels reflects probably also the poor vascular condition of vital organs. Also, emergency dialysis start is an additional risk factor associated to HD with a catheter. When PD was compared with unplanned HD, the risk of death at 2 years tended to be higher in elderly French patients starting dialysis after 75 years (HR: 1.3, 95% CI: 0.9–1.7) [33].

Discrepant results between studies may be due to the period of observation. One may argue that practice concerning adequate dialysis or timing of dialysis initiation may have changed over time and may have an impact on the relative benefit from one modality over another. A Danish study showed an overall benefit for PD in diabetic patients in the cohort 2000–2010 (HR 0.85, 95% CI 0.75–0.97) which is mainly due to the initial period of 6 months: HR 0.48 (95% CI 0.32–0.73). After 6 months, no statistical difference between the two modalities was observed [23]. In the cohort 1990–1999, survival was better on PD for the first 6 months (HR 0.34, 95% CI 0.2–0.56) but was better on HD after 48 months (HR 1.52, 95% CI 1.08–2.12). We found no association between the year of publication and the conclusions drawn from the included studies.

There might be differences in the outcomes between PD and HD based on variation in regional practices, and also over with changing practices over time. Whereas formal analysis of this aspect is difficult, it has been suggested that countries with higher PD prevalence tend to have better outcomes [7, 19, 21, 23, 25].

Because of the numerous methodological pitfalls in observational studies comparing PD and HD, utmost caution is required in the interpretation of results, as in all studies, selection bias may not be set aside.

First, the methodology of data management has an influence. In 13 studies, patients were included only if they had survived at least 90 days [18–20, 25–27, 29, 30, 32, 35–38]. As mortality risk is much higher in HD patients in the first 3 months, studies including prevalent patients, or including only patients who survived the first 90 days, have a selection bias in favour of HD (survival of the fittest bias). In a matched pair cohort study, Weinhandel et al. [34] demonstrated that PD was associated with improved survival when analysis included all patients from Day 0, but not if patients were only included after 90 days.

Second, differences in patient mix (age, gender, diabetes, cardiovascular disease, dropout rate for transplantation) of the cohorts may influence outcome. With the exception of three studies [26, 32, 33], PD patients were younger and had less comorbidity. All studies used adjustment on case-mix to overcome indication bias due to the fact that treatment was not allocated in a randomized way. The confounders included in the multivariate analysis were highly variable among studies and one cannot exclude residual confounding. Five used a propensity score [8,20, 28, 34, 35]. One study used a marginal structural model with an inverse probability of treatment weighting [38] to balance the known treatment-specific covariate distributions, a new approach for causal inference from observational data. This technique, however, still does not balance unknown confounders. None used an instrumental variable. Third, the type of performed statistical analyses could influence the results, as most patients transfer between modalities, and censoring may be informative [50]. Since most techniques are based on the hypothesis of a non-informative censoring at transplantation, this may result in overestimation of the cumulative risk of death. Seven intention-to-treat studies considered all deaths after the start of renal replacement therapy, regardless whether they occurred during dialysis or transplantation [21, 24, 29, 30, 33, 35, 36]. In fourteen other studies, patients were censored at the time of renal transplantation [7, 18–20, 22, 23, 25–28, 30, 37, 38], but only one study used an inverse probability of censoring weighting [38] to address informative censoring. In the technique of inverse probability of censoring weighting patients are weighted by the inverse of their probability of getting a transplant and this taking into account their specific covariates. None used transplantation as time-dependent variable to take into account a risk factor that is not present at start. None used competing risks analysis [51, 52] to estimate the survival probability in both groups as death during dialysis can only be observed if patients are not transplanted. However, the Cox model used in the majority of the studies allows to estimate the hazard ratio in a cause-specific approach [53].

More treatment switches have been observed for PD patients [7, 29, 38]. Therefore, the way those switches are analysed may result in selection bias. All studies used an intention-to-treat analysis. Some of them also performed additional analysis: as-treated [7, 21, 25, 27–30], censoring at switch [7, 18, 22, 28] or switch considered as treatment failure [21, 28].

Last, all studies performed numerous subgroup analyses which may result in low power and the risk of introducing selection bias. One has to find a good balance between taking into account details of differences between different variations of both haemodialysis and peritoneal dialysis, and still preserving sufficient statistical power. Careful planning of studies with *a priori* specification and power calculation of analyses to be performed should be recommended. Because of non-proportional hazards, with only one exception [18], all studies stratified their analysis: on time and age [19, 20, 22, 25], time and some comorbidities [29, 30], time alone [28], age alone [7, 21, 26, 32, 33], age and gender [8], age and comorbidities [27, 34].

In the absence of data concerning comparison of HD and PD in terms of quality of life in diabetic ESKD patients, it was not possible to explore this critically important outcome. Although diabetics have a lower quality of life than non-diabetic dialysis patients [54, 55], the influence of dialysis modality needs further exploration. Four systematic reviews on this topic, including ESKD patients with or without diabetes, did not find statistically significant differences in quality of life (QOL) or utility [55–58] between PD and HD patients even if PD patients tend to rate their quality of life higher than HD patients. Yet, HD patients may enjoy a relatively better QOL in the physical dimensions over time [56]. Mental health components are comparable between both dialysis populations. However, there is evidence that free modality choice is associated with more satisfaction of patients with their overall care (Van Biesen *et al.*, NDT, CEAPIR data under submission).

The question of whether peritoneal dialysis or haemodialysis should be the preferred modality to start renal replacement therapy has been posed since the very introduction of PD. Only one randomized controlled trial has been published, showing no difference in 3-year mortality [6]. This study was hampered by recruitment problems and, despite many efforts, only included 38 patients, probably pointing out that patients do not want to be randomized to a modality, but prefer to make their own choice.

Our review has some strengths and limitations that deserve mentioning. Strengths include a systematic search of medical databases, data extraction, analysis and study quality assessment by two independent reviewers. In contrast, this review is limited by the quality and the number of data available to address the question of modality selection in diabetic patients. Except mortality, no other outcomes have been addressed by large cohorts. Accordingly, a previous meta-analysis of outcome studies in ESKD patients was also unable to resolve the question of whether PD and HD provide equivalent outcomes because of the heterogeneity of the studies [59]. Due to the nature of our search question, our study was not intended to answer other important questions such as the place of transplantation, or of conservative care. Our conclusions consequently apply only to patients who, in view of their expected life expectancy [60, 61], decided to start renal replacement therapy, and have no access to a pre-emptive transplantation.

In conclusion, the available evidence derived from observational studies is inconsistent. Therefore evidence-based arguments indicating that HD or PD as first treatment may improve patient-centred outcomes in diabetics with ESKD are lacking. In the absence of such evidence modality selection should be governed by patient preference, after unbiased patient information.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxford-journals.org.

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DISCLAIMER

The present text is based upon the information available to the guideline development group at the time of the preparation of this publication. It has been designed to provide information and assist decision-making, but is not intended to define a standard of care or to improve an exclusive course of diagnosis, prevention or treatment. Variations in practice are inevitable when physicians take into account individual patient needs, available resources and limitations specific for a geographic area, country, institution or type of practice. In addition, evidence may change over time as new information becomes available, so that practice may be modified subsequently. Every practitioner using this text is responsible for its application to any particular clinical situation. The work group members involved in the development of the present text have disclosed all actual and potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest at the website of ERBP (www.european-renal-best-practice.org).

CONFLICT OF INTEREST STATEMENT

None declared.

(See related article by Combe *et al.* Evidence-based choice of dialysis technique in diabetics with end-stage kidney disease: half a loaf is better than no bread. *Nephrol Dial Transplant* 2015; 30: 160–162.)

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