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The Glomerular Filtration Rate (GFR) at Dialysis Initiation and Mortality in Chronic Kidney Disease (CKD) in East Asian Populations: A Meta-analysis

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Abstract

Objective The impact of dialysis initiation on survival is still somewhat controversial. Given that race or ethnicity has been observed to be a predictor of mortality and the rate of progression of chronic kidney disease, we conducted a meta-analysis to investigate the effect of early vs. late dialysis initiation on mortality in East Asian populations.

Methods All eligible cohort studies of target were selected from the MEDLINE (PubMed), EMBASE, The Cochrane Library and the Clinical Trials Registry databases from inception to October 2014. The data were extracted with all-cause mortality rates as the primary outcome, and pooled adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated.

Results Ten studies examined the association between early vs. late dialysis initiation and mortality. Compared to late dialysis initiation, patients who received early dialysis initiation had a higher overall mortality risk (adjusted HR, 1.36; 95% CI, 1.0-1.85; $p<0.05$) in East Asian populations. In a subgroup analysis, baseline characteristic differences (adjusted HR, 2.0; 95%CI, 1.56-2.57; $p<0.001$), initial dialysis modalities (adjusted HR, 2.12; 95% CI, 1.72-2.62; $p<0.001$) and follow up duration (adjusted HR, 1.59; 95% CI, 1.19-2.12; $p=0.002$), demonstrated that the association between early dialysis initiation and mortality were significant.

Conclusion A higher glomerular filtration rate (early) at the initiation of dialysis is associated with a higher all-cause mortality risk in East Asian populations.

Key words: chronic kidney disease (CKD), early dialysis initiation, late dialysis initiation, mortality, glomerular filtration rate (GFR)

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Introduction

End-stage renal disease (ESRD) is not only a devastating medical problem, but also a social and economic issue. The numbers of ESRD patients continue to increase worldwide, as well as in East Asia. According to the ESRD Registry Committee of the Korean Society of Nephrology (KSN), in 2009, the total number of patients with renal replacement therapy (RRT) in Korea was 56,396 and the rate of ESRD cases per million population reached 1,113.6 (1). In Japan, the number of new dialysis patients was 38,055 and the number of dialysis patients per million was 2,431.2 at the end of 2012 (2). The Chinese Society of Blood Purification (CSBP) also showed that in mainland China, at the end of 2008, a total of 102,683 ESRD patients on dialysis and the prevalence was 79.1 patients per million populations, with an annual increasing rate of 52.9% (3). China is not like many Western countries, the lower rate of dialysis patients is mainly due to the lack of sufficient financial and clinical resources, and inequalities in access to health care across regions and populations. In fact, the number of ESRD patients requiring dialysis in China is underestimated in the above figures.

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It is known that adequate dialysis therapy can relieve the burden of painful uremic symptoms and improve the overall survival. However, the optimal timing for ESRD patients to initiate dialysis remains uncertain. During the past decades, there had been a strong prevalent trend to initiate dialysis earlier in progressive chronic kidney disease (CKD) patients, with a traditional belief that starting dialysis at a relatively high glomerular filtration rate (GFR) might be beneficial in terms of mortality, employment opportunity and quality of life (4-6). However, recent studies showed that early dialysis initiation was associated with a poor survival (7-20), although, some also found no difference (21-26) or a survival benefit (27-29). The Initiating Dialysis Early and Late (IDEAL) study, the only randomized controlled trial performed to data, indicated that there was no survival benefit of early dialysis initiation (30). According to this trial, the Japanese Society for Dialysis Therapy (JSDT) guidelines (31), recommended that hemodialysis should be initiated prior to a GFR of 2 mL/min/1.73 m^2, even if there are no symptoms of renal failure; however, current guidelines on when to initiate dialysis are based more on the comprehensive assessment of renal failure symptoms, daily life activities, and nutritional status, suggesting that the GFR should not be the only factor to guide the timing of dialysis initiation (32-34).

Ethnicity has been observed to be a predictor of mortality and the rate of progression of CKD. The United States Renal Data System (USRDS) revealed that Asians were younger and had a lower body mass index (BMI) than Caucasians at the initiation of dialysis therapy (35). In addition, the primary causes of ESRD also differed between Asians and Caucasians: glomerulonephritis and diabetes were the main causes of ESRD in Asians, however, fewer Asian patients had ESRD due to cystic kidney disease and hypertension compared to Caucasians (35). Furthermore, several studies showed that there were significant differences in the clinical outcome, mortality rate and cardiovascular morbidity in dialysis patients according to the demographic characteristics of race or ethnicity (36-40). Hence, we herein performed a meta-analysis in East Asian populations (Chinese, Korean, and Japanese) to examine whether a higher GFR at the initiation of dialysis was associated with harmful clinical outcomes.

Materials and Methods

Search strategy

A search of the medical literature was conducted using the MEDLINE (PubMed), EMBASE, The Cochrane Library and the Clinical Trials Registry (http://clinicaltrials.gov/) databases from inception until October 2014 to identify randomized controlled trials and cohort studies that assessed the association between the GFR and mortality. Our search was based on four search themes using the Boolean operator "OR". The first Boolean heading employed terms describing CKD. The second Boolean search included terms describing the timing or initiation of therapy. The third heading included keyword/MeSH terms describing the GFR. The fourth search was mortality or the survival (attachment 1). These were combined using the set operator "AND". We restricted our search to human adult, articles published in the English language and excluded reviews, meta-analyses, case-reports, comments, guidelines and news.

Study selection

Two reviewers (X.L. and X.Z.Z.) independently performed an initial eligibility screen of all retrieved titles and abstracts (when available). Studies reporting original data that specifically mentioned the association between the timing of dialysis initiation (assessed by the GFR) and mortality were selected for further review. Full texts were independently assessed by the same two authors. No restrictions were placed on the sample size or study duration. Disagreements between the reviewers were resolved by a third reviewer or by discussion and a consensus.

Data extraction

All data were extracted independently by the two reviews (X.L. and X.Z.Z) to a predesigned form (Microsoft Office Excel 2007; Microsoft Corp, Redmond, WA, USA). All data extractions were then checked by a third reviewer (J.A.). The following data were extracted from each trial: first author and year, country of origin, study design, sample size, study period, initial dialysis modality [including hemodialysis (HD), peritoneal dialysis (PD), or both], follow-up duration, demographics and baseline characteristics (mean age, proportion of male patients, rate of diabetes, mean BMI, mean serum albumin level, mean hemoglobin), and estimated-GFR [calculated using the Modification of Diet in Renal Disease (MDRD) formula, the Cockcroft-Gault equation, or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation]. Outcomes of interest were all-cause mortality rates and cardio-cerebrovascular mortality, which were calculated as adjusted hazard ratios [HRs; with 95% confidence intervals (CIs)]. Some exact HRs were not directly stated in some studies, in which the results were presented as Kaplan-Meier survival curves, in this situation, we obtained the data from the curves using the Get Data Graph Digitizer2.25 software program and a consensus was achieve between the two reviewers. Five studies did not directly state the HRs of the GFR for cardio-cerebrovascular mortality, but provided the number of cardio-cerebrovascular deaths or the survival curves, from which we obtained the HRs through the curve or directly calculated them.

Assessment of methodological quality

We evaluated the quality of each study using the Newcastle-Ottawa Scale (NOS) (41). The NOS criteria are categorized into three sections: selection, comparability and outcome. Each study is designated a score for each section, based on some queries, with a total score of 9. Scores 0-3,

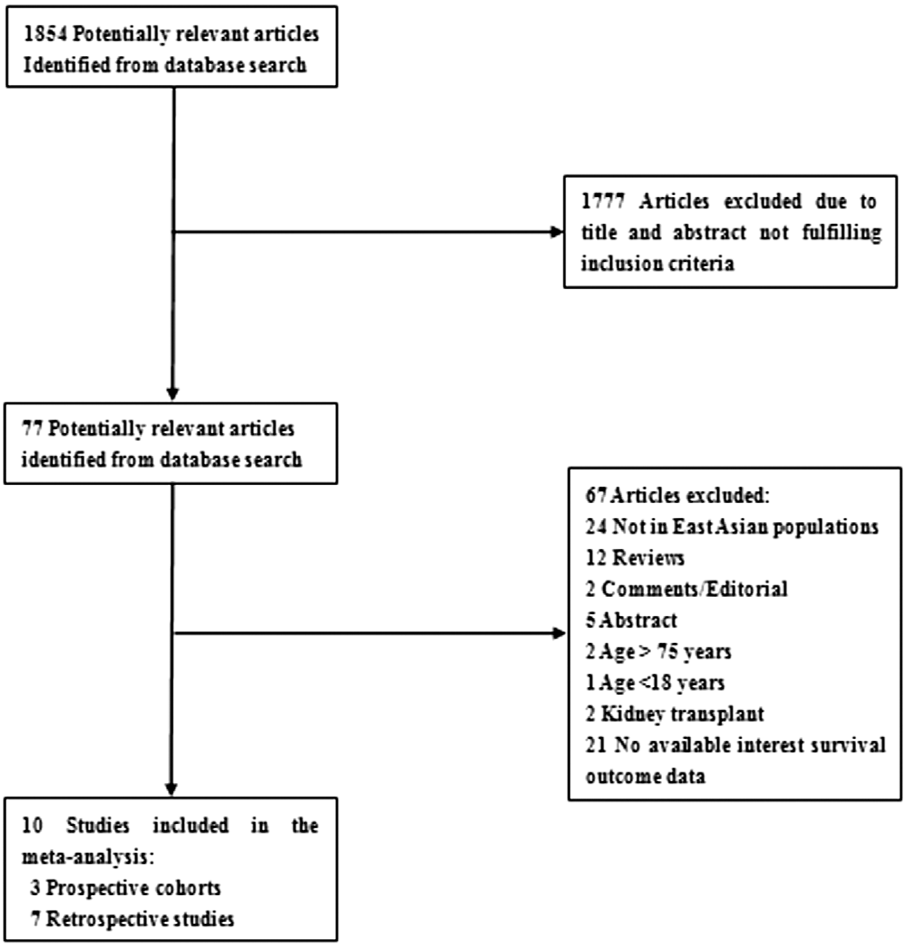

Figure 1. Study selection diagram.

4-6, and 7-9 indicate an overall study quality of poor, fair, and good, respectively. The quality of the studies was independently assessed by two authors (X.L. and X.Z.Z.). In cases of disagreement, a consensus was reached by discussion.

Statistical analysis

Data were analyzed using the STATA software program (version 12.0, StataCorp, College Station, TX, USA). We assessed and quantified statistical heterogeneity for each pooled summary estimate using Q statistic p value and the I^2 statistic, respectively. The random effects model was used to combine the data if significant heterogeneity existed ($p<0.1$; $I^2>50\%$). The adjusted HR was used as a measure of the association for all-cause or cardio-cerebrovascular mortality between early and late dialysis initiation. A meta-regression analysis was performed to assess the possible sources of heterogeneity. Publication bias was assessed using Egger's regression model (42).

Results

Literature search

The literature search yielded 1,854 articles, of which 76 were reviewed in full text (Fig. 1). After primary and secondary screening, 10 cohort studies fulfilled all criteria for final analysis (9 articles and 1 abstract); their study characteristics are listed in Table 1.

Trial characteristics

We identified 10 cohort studies (9, 13, 20-26, 28): three prospective cohort studies (25, 26, 28), and eight retrospective cohort studies (9, 13, 20-24, 27). Of these, 9 studies were published as journal articles (9, 13, 21-26, 28) and 1 study was published as an abstract only (20). The patients of the 10 cohort studies were of East Asian descent. These studies varied in sample size (210-23,551 patients), follow-up duration (1-15 years) and involved patients with various initiating dialysis modalities (HD, PD, or both). Five studies had more men (range 51-65%), with a mean age ranging from 46 to 67 years. The proportion of patients with diabetes varied from 19-59%. The GFR was calculated using different equations (the MDRD, CKD-EPI, Cockcroft-Gault equation or urea and creatinine clearance rates). A propensity score (PS) analysis was employed in three cohorts (22, 23, 26) to eliminate baseline differences between the early and late groups. In five cohorts (9, 13, 20, 21, 25), baseline characteristic differences were present between the early and late dialysis initiation groups (the early dialysis

Table 1. Characteristics of Studies Included in the Meta-analysis.

Study (first author+ year)	Country of origin	Study design	Sample size	Accrual period	Initial dialysis modality	Max follow-up duration (year)	Mean age (y)	Male (%)	DM (%)	Mean eGFR ($mL/min/1.73m^2$)	NOS scale
Tang et al. 2007 [28]	HK	PCS	233	2002-2004	PD	2	58	51	42	9.1	6
Shiao et al. 2008 [9]	TW	RCS	275	1997-2005	PD	6	51	45	19	4.8	3
Kim et al. 2009 [21]	Korea	RCS	210	2000-2005	HD+PD	7	50	33	47	5.8	4
Huang et al. 2010 [13]	TW	RCS	23,551	2001-2004	HD	1	62	48	50	4.7	4
Oh et al. 2012 [22]	Korea	RCS	491	2000-2010	PD	2[a]	49	61	34	8.2	5
Chang et al. 2012 [23]	Korea	RCS	450	2000-2009	HD+PD	11	54	54	59	8.6	5
Yamagata et al. 2012[24]	Japan	RCS	20,854	1989-1990	HD+PD	18	58	65	32	5.0	6
Lee et al. 2014 [26]	Korea	PCS	854	2008-2013	HD+PD	5	57	63	57	11.2	6
Liu et al. 2014 [20]	China	RCS	5,612	2007-2012	HD	6	--	--	--	--	--
Kim et al. 2014 [25]	Korea	PCS	495	2009-2013	PD	2	52	61	44	7.8	6

e-GFR: estimated glomerular filtration rate, DM: diabetes mellitus, HD: hemodialysis, HK: Hong Kong, NOS scale: Newcastle-Ottawa Quality Assessment Scale, NR: not reported, PCS: prospective cohort study, PD: peritoneal dialysis, RCS: retrospective cohort study, TW: Taiwan

[a] median follow up

Table 2. Baseline Characteristics and Outcomes in the Early- and Late Dialysis Initiation Groups in 10 Studies Included in the Meta-analysis.

Study	GFR category		Mean GFR ($mL/min/1.73m^2$)		Mean age (y)		Male (%)		DM (%)		ALB (g/dL)		All-cause mortality (early vs. late)
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late	
Tang et al. 2007 [28]*	Elective starter	Initial refusers	9.2 ± 0.9	8.9 ± 1.4	58 ±14	58 ± 11	50	54	40	46	NR	NR	0.33 (0.11-0.76)
Shiao et al. 2008 [9]	≥5	<5	6.8 ±2.1	3.5 ±0.9	56 ±19	48 ±16	65	32	38	12	3.4 ± 0.7	3.7 ± 0.6	1.81 (1.01-3.22)
Kim et al. 2009 [21]	≥5	<5	8.0 ± 3.0	3.4 ± 1.1	53 ± 15	48 ± 14	43	21	58	36	3.1 ± 0.7	3.1 ± 0.7	0.81 (0.39-1.69)
Huang et al. 2010 [13]	≥6.52	<3.29	7.7[c]	2.6[c]	65 ± 14	55 ± 14	62	39	69	25	NR	NR	2.44 (2.11-2.81)
Oh et al. 2012 [22]*	>7.7	<7.7	10.8 ± 2.5	5.5 ± 1.3	48 ±15	49 ± 13	37	61	37	31	3.5 ± 0.5	3.6 ± 0.6	0.47 (0.16-1.35)
Chang et al. 2012 [23]*	≥7.74	<7.74	11.1 ± 3.9	6.1 ±1.2	53 ± 14	54 ± 14	55	54	59	59	3.2 ± 0.6	3.3 ± 0.5	1.32 (0.87-1.99)
Yamagata et al. 2012[24]*	>10	4-6	NR	NR	63[b]	60[b]	67	65	54	30	NR	NR	0.965 (0.447-2.084)
Lee et al. 2014 [26]*	>7.372	<7.372	10.4 ± 4.9	5.5 ± 1.2	57 ± 14	58 ± 13	64	62	57	56	3.3 ± 0.6	3.3 ± 0.6	1.665 (0.958,2.849)
Liu et al. 2014 [20]	>10	2.5-5	--	--	--	--	--	--	--	--	--	--	2.29 (1.9-2.76)
Kim et al. 2014 [25]	13.1 ± 3.4	7.3 ± 1.4	13.1 ± 3.4	7.3 ± 1.4	55 ± 14	52 ± 13	73	58	56	48	3.2 ± 0.7	3.5 ± 0.6	1.5 (0.59-3.8)

ALB: serum albumin, DM: diabetes mellitus, NR: not reported, GFR: glomerular filtration rate, Plus-minus values indicated the means ± SD.

[b] Median age.

[c] Median GFR at the initiation of dialysis.

*No differences in the baseline characteristics between the early- and late dialysis initiation groups were observed in these studies (the early dialysis initiation group was older, had a higher incidence of diabetes, lower ALB and higher burden of comorbidities than the late dialysis initiation group).

initiation group was older, predominantly male, had a higher incidence of diabetes, lower serum ALB and higher burden of comorbidities than the late dialysis initiation group) (Table 2).

Mortality in the early vs. late dialysis initiation groups

Ten studies examined the association between early vs. late dialysis initiation and mortality. Compared to late dialysis initiation, patients who received early dialysis initiation had a higher overall mortality risk (adjusted HR, 1.36; 95% CI, 1.0-1.85; $p<0.05$) (Fig. 2). However, there was significant heterogeneity (I^2=79.5%; $p<0.001$).

A subgroup analysis was performed according to the differences in the baseline characteristic (including age, diabetes, the proportion of male patients and comorbidity, and serum albumin level), follow-up duration (>10 or <10 years), initial dialysis modalities (HD, PD, or both). In the five cohorts (9, 13, 20, 21, 25) that showed baseline characteristic differences between the groups, early dialysis initiation was associated with a higher mortality risk (adjusted HR, 2.0; 95% CI, 1.56-2.57; $p<0.001$). Compared with the other five cohorts (22-24, 26, 28) that showed no baseline characteristic differences between early dialysis initiation and mortality (adjusted HR, 0.92; 95% CI, 0.54-1.55; $p=0.752$). In four cohorts (13, 20, 23, 26) where HD therapy was initiated, the association between early dialysis initiation and mortality was significant (adjusted HR,2.12; 95% CI, 1.72-2.62; $p< 0.001$) in comparison to, the six cohorts restricted to PD (9, 21-23, 26, 28) therapy as the initial dialysis mortality, for which early dialysis initiation was not associated with mortality (adjusted HR, 1.37; 95% CI, 0.96-1.94; $p=0.08$). The cohorts (9, 13, 20-22, 25, 26, 28) that had a maximum follow-up of less 10 years showed, a significant association between early dialysis initiation and mortality (adjusted HR, 1.59; 95% CI, 1.19 to 2.12; $p=0.002$), whereas, the cohorts (23, 24) that had a maximum follow-up of 10 years or longer did not (adjusted HR, 1.23; 95% CI, 0.85 to 1.77; $p= 0.265$) (Table 3).

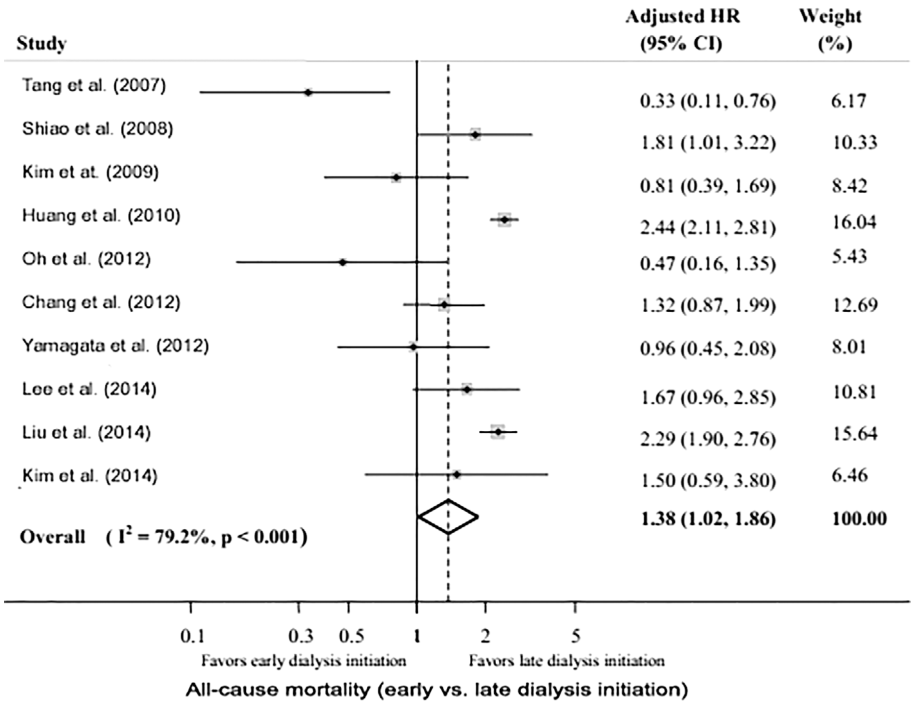

Figure 2. A forest plot shows the effect of early vs. late dialysis initiation on all-cause mortality. A meta-analysis was performed using a random-effects model. Data are presented as adjusted hazard ratios with 95% confidence intervals (CIs). Boxes are scaled to the weight of the studies in the overall meta-analysis. The test for heterogeneity is significant (I^2=79.2% and p<0.001 by Q test).

Table 3. Subgroup Meta-analysis.

Subgroup	Number of studies	Total patients	Hazard Ratios	95% Confidence Intervals	I-square	p for Heterogeneity
Baseline characteristic differences						
Yes	5	30,143	2.03	1.6 to 2.59	59.6%	0.042
No	5	22,882	0.92	0.54 to 1.55	65.1%	0.022
Dialysis modality						
Hemodialysis	4	30,467	2.12	1.72 to 2.62	55.6%	0.08
Peritoneal dialysis	6	1,887	1.06	0.62 to 1.83	60.1 %	0.028
Follow-up duration						
< 10 years	8	52,333	1.61	1.2 to 2.14	82%	<0.001
>10years	2	21,304	1.23	0.85 to 1.77	0	0.482

Baseline characteristic differences (Yes): in these 5 studies the early dialysis initiation group was older, had a greater incidence of diabetes, lower ALB and higher burden of comorbidities than the late dialysis initiation group.

Publication bias and sensitivity analysis

Publication bias was assessed using Egger's linear regression test and statistical evidence of bias was demonstrated (β=-1.50, 95% CI=-2.06 to -0.94, p<0.0001). When we conducted a sensitivity analysis, excluding 3 small sample size studies (9, 28, 21), the finding that early dialysis initiation was associated with mortality was maintained (adjusted HR, 1.65; 95% CI, 1.24-2.2; p=0.001; I^2=73.5%). In addition, a sensitivity analysis using the trim and fill method showed negligible differences between the corrected and uncorrected HRs, suggesting the result to be relatively reliable.

Discussion

This systemic review and meta-analysis of 10 unique studies compared early vs. late initiation of dialysis with mortality in East Asian populations and indicated that early dialysis initiation was associated with an increased mortality risk. A subsequent subgroup analysis showed that cohorts with baseline characteristic differences between early and late dialysis and HD therapy, demonstrated that early dialysis initiation resulted in a poor survival. Cardio-cerebrovascular events are the main cause of death in dialysis patients. Thus we also performed a subgroup analysis of five cohorts (21, 22, 25, 26, 28), which suggested that a higher GFR at dialysis initiation did not appeared to be associated with cardio-cerebrovascular mortality (HR, 0.54; 95% CI, 0.26-1.14; p=0.108). But three (22, 25, 28) of these five studies were PD patients and all five studies had small sample sizes (the total number of patients was 2,283).

During the past decades, there had been a worldwide trend toward early dialysis initiation. However, according to recent a report from the USRDS, the proportion of early dialysis initiation grew from 19% to 54% between 1996 and 2009, but remained stable between 2009 and 2011 in the United States (43). The decreasing trend of early initiation dialysis patients might be due to recent observational studies, which have consistently suggested that early dialysis initiation might be harmful (7-20). Additionally, the IDEAL study also suggested that early dialysis initiation had no significant benefit on the survival (30), which is the only randomized controlled trial to date to address the timing of chronic dialysis initiation. In this trial, a total of 828 ESRD patients were randomized to the early group (10-14 mL/min/1.73 m^2) and late group (5-7 mL/min/1.73 m^2) according to the eGFR (MDRD formula); after a median follow-up of 3.6 years, the results showed that there were no significant differences between the two groups regarding the survival, complications, or quality of life. However, we must note that the patients in the IDEAL study, were younger, better nourished, better prepared for ESRD, had fewer requirements for temporary dialysis catheter access, and a greater proportion were started on peritoneal dialysis compared with the typical European dialysis patients. Thus, it was difficult to generalize the results of the IDEAL study to all patients preparing for dialysis. In addition, two recent systemic reviews also indicated that a higher GFR at the initiation of dialysis was associated with an increased risk of death (44, 45). Reflecting the results of these investigations, recent guidelines have recommend delaying dialysis and emphasized the clinical symptoms or signs to guide the initiation of dialysis, rather than only considering the GFR (32-34). In addition, the follow-up times of previous studies may affect the judgment of dialysis initiation; however, a recent study in Japan, which included 25,804 patients (GFR>10 mL/min/1.73 m^2 as the early dialysis group and 4-6 mL/min/1.73 m^2 as the late dialysis group), showed that early dialysis initiation had an increased mortality risk in the short-term follow-up (1-5 years), but there was no survival differences between the early and late dialysis initiation groups after unadjusted and multivariable adjusted analyses from the long-term outcome (5-10 years or >10 years) (24). Our findings were similar to this result; when the follow-up duration was less than 10 years, early dialysis initiation indicated a poor prognosis, with a 61% increased mortality risk, but no significant differences were observed when the follow-up duration was more than 10 years.

The baseline characteristics, such as older age, lower ALB, higher incidence of diabetes and higher burden of comorbidities in dialysis initiation, could lead to a poor prognosis. Recently, several studies used the propensity score (PS) matching method to overcome the limitation of non-random allocation to the baseline differences, and the results suggested that before matching, early dialysis had a poor survival. However, after propensity score matching, patients with early and late initiation demonstrated no differences in the survival (23, 26). In line with these observations, a retrospective analysis of 11,685 patients in the French Renal Epidemiology and Information Network Registry showed that each 5 mL/min/1.73 m^2 increase in the GFR was associated with a 40% increase in the risk of mortality. However, after adjusting for age, ALB, diabetes, and comorbidities, the risk of mortality in early dialysis was greatly attenuated to 9%. This study indicated that age and comorbidity strongly determined the decision to start dialysis and might explain most of the paradoxical inverse associations observed between the GFR and survival (46). Our subgroup analysis was supportive of these findings, whereby early dialysis was associated with a higher mortality risk when restricted to five cohorts that showed baseline differences between the dialysis groups (early dialysis initiation group was older, had a higher incidence of diabetes, lower ALB and higher burden of comorbidities than the late dialysis initiation). However, there was no association between the GFR and mortality in five cohorts wherein no baseline differences were observed between the early and late dialysis initiation. Taken together, existing patient conditions might be more important predictors of the survival than the timing of dialysis initiation.

HD is the major dialysis modality in most East Asia countries (1, 47). Two recent systemic reviews suggested that early dialysis initiation was associated with a higher mortality in HD patients, but lower in PD patients (45, 48). In addition, a study based on the IDEAL trial showed that early- and late-start PD patients showed no differences in mortality (49). Our subgroup analysis was consistent with this result, for which a higher GFR in patients initiating HD therapy was associated with an increased risk of death, whereas in studies restricted to PD populations, the GFR was not associated with mortality. PD had a lower risk of mortality compared to HD, because although HD therapy might have increase central venous catheter exposure, HD could more easily promote transient myocardial ischemia, myocardial stunning, and ventricular arrhythmias (50). Furthermore, HD therapy was associated with an increased risk of residual kidney function loss, which was strongly related to a risk of mortality while receiving dialysis (51). Additionally, diabetes, age, and co-morbidity all significantly modify the effect of dialysis modality on the patient survival (52). Therefore, these factors must be considered when selecting the dialysis modality.

There are several limitations associated with our meta-analysis. The studies included were cohort studies, particularly retrospective cohort studies. This could inevitably lead to various biases, particularly survival bias, which could favor late dialysis initiation. On the other hand, the definitions of early and late dialysis were not standardized and only simply defined by the serum creatinine-based eGFR, for which seven of ten studies used the MDRD equation. A study found that patients initiated on dialysis therapy with a higher eGFR were found to represent a lower creatinine production rather than higher creatinine clearance, thus the assumptions of the MDRD for estimating the GFR were invalid in patients with advanced renal failure with high and low creatinine production (53). The 2011 European dialysis guidelines also showed that the MDRD equation should not be used to estimate renal function in patients with stage 5 CKD (54). Another potential limitation of any meta-analysis is the possibility of publication bias, due to the fact that studies obtaining optimistic results are more readily published than studies with unfavorable results. However, sensitivity analyses using the trim and fill method showed the results were reliable. Finally, there was substantial heterogeneity in the effect size estimates across studies. The dialysis modality, baseline characteristic differences and the duration of follow-up might be sources of the heterogeneity.

In conclusion, this meta-analysis suggested that early dialysis initiation for ESRD patients is associated with an increased mortality risk, a higher mortality risk in HD therapy and poor outcomes in the short-term follow-up. Moreover, this systemic review showed that baseline characteristics, such as older age, diabetes, lower ALB and comorbidity, strongly influenced the result of dialysis, suggesting that the decision to initiate dialysis should consider patient's clinical conditions rather than the GFR alone. Cardio-cerebrovascular mortality between the early and late dialysis initiation groups in this meta-analysis showed no survival differences, however, this could be due to the limited number of studies. This review was based on observational studies with significant heterogeneity, therefore, well designed randomized controlled trials are necessary to confirm these results.

The authors state that they have no Conflict of Interest (COI).

Xin Lin and Xiang-Zhen Zeng contributed equally to this work.

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