Risk factors for mortality in patients undergoing peritoneal dialysis: a systematic review and meta-analysis

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ABSTRACT

Aim: Inconsistent investigations of the risk factors for all-cause mortality in patients undergoing peritoneal dialysis (PD) were reported. The present meta-analysis aimed to assess the impact of some clinical characteristics on the risk of mortality in PD patients.

Methods: PubMed and Embase were systematically searched for studies evaluating the risk factors for all-cause mortality in PD patients. Hazard ratio (HR) and 95% confidence interval (CI) were derived using a random-effect or fixed-effect model considering the heterogeneity across studies.

Result: A total of 26 studies were included in this meta-analysis in accordance with the inclusion and exclusion criteria. Age, primary cardiovascular diseases, diabetes mellitus, and high level of alkaline phosphatase showed significant positive associations with elevated risk of all-cause and cardiovascular mortality in PD patients, while hemoglobin acted as a benefit factor. Furthermore, early onset of peritonitis, high peritoneal transport status, elevated body mass index and high-sensitivity C-reactive protein could also considerably increase the risk of all-cause mortality. The absolute serum level of magnesium, potassium, and uric acid required to improve survival in PD patients should be verified further.

Conclusions: Multiple factors could affect the risk of mortality in PD patients.

Introduction

Peritoneal dialysis (PD) is one of the major renal replacement therapies for patients with end-stage kidney disease (ESKD) [1]. The number of PD patients has been increasing in numerous developing countries. However, the long-term survival rate of PD patients remains low [2]. Additionally, cardiovascular disease (CVD) and death are highly prevalent in patients with ESKD [3,4]. These findings may be attributed to chronic inflammation, disturbed mineral metabolism, primary CVD, and other physical conditions. For instance, commonly accepted nutritional markers, such as serum albumin (ALB) level, serum creatinine (Cr) level, hemoglobin (Hb) level, and body mass index (BMI), might be used to assess prognosis of patients with chronic kidney disease (CKD) [5,6]. However, other studies reported a poor predictive value of serum ALB, serum Cr, and other characteristics of PD patients for all-cause mortality or cardiovascular outcomes [7,8]. Furthermore, the prognostic values of various physiological ions have not been well determined [9–12]. This meta-analysis aimed to identify the risk factors for mortality in PD patients to improve prognosis.

Materials and methods

Search strategy

This meta-analysis was conducted following the meta-analysis of observational studies in epidemiology (MOOSE) guidelines [13]. PubMed and Embase were searched for studies conducted from January 2000 to December 2020. Studies evaluating the risk factors for all-cause mortality or cardiovascular mortality in patients undergoing PD satisfied the inclusion criteria in the present meta-analysis. We used (((‘peritoneal dialysis’ OR ‘renal dialysis’ OR ‘renal replacement therapy’ OR ‘chronic kidney disease’ OR ‘end-stage kidney disease’ OR ‘ESKD’) AND (‘mortality’ OR ‘death’ OR ‘survival’) AND (‘potassium’ OR ‘magnesium’ OR ‘peritonitis’ OR ‘body mass index’ OR ‘albumin’ OR...))
hemoglobin) AND Clinical Trial[ptyp]) as the search terms. Moreover, the references of all the relevant original articles were manually reviewed to identify additional eligible studies.

Selection criteria
Respective study was assessed by two independent reviewers, and any disagreements between the two reviewers were resolved by another independent reviewer. The inclusion criteria were as follows: (1) studies including patients undergoing PD; (2) studies mentioning at least one of the risk factors, namely, age, Hb level, serum ALB level, BMI, diabetes mellitus (DM), serum potassium level, serum magnesium level, peritonitis, peritoneal transport characteristics, alkaline phosphatase (ALP) level, high-sensitivity C-reactive protein (hs-CRP) level, and uric acid (UA) level; (3) studies evaluating all-cause mortality; (4) studies reporting statistical data including hazard ratio (HR) and 95% confidence interval (CI). Studies without adjustment for specific potential confounders and non-English studies were excluded. Finally, a total of 26 studies were included.

Statistical analysis
All statistical analyses were conducted in Review Manager 5.3 software. HR adjusted for confounding variables and 95% CI were extracted from included studies. Each HR was transformed into a log HR, and the standard error was calculated based on the corresponding 95% CI. Statistical heterogeneity among studies was evaluated using the $I^2$ index. A random-effect model was adopted if the $I^2$ index was >50%, demonstrating substantial heterogeneity; otherwise, a fixed-effect model was employed. A $p$ value <0.05 was considered statistically significant. Furthermore, Egger’s tests were performed to assess potential publication bias, and a sensitivity analysis was conducted to determine the robustness of the conclusion by excluding each article from the meta-analysis.

Results

Literature search
A total of 4421 potentially relevant articles were retrieved from PubMed and Embase. After screening titles and abstracts, 112 duplicate studies and 4139 non-relevant studies were excluded. The remaining 170 studies were subjected to full-text assessment, and 144 trials were further removed based on the following criteria: (i) unavailable full-text, (ii) non-inclusion of PD patients, or (iii) unavailable desired outcomes. Finally, 26 papers were included in our systematic review. This meta-analysis had a good interreviewer agreement ($\kappa = 0.851$). A flowchart summarizing the selection process is presented in Figure 1.

Study characteristics
The baseline characteristics of included studies are shown in Table 1. Each study included 102-10,692 patients, and median follow-up duration ranged from 13.0 months to 52.8 months. Among these studies, 26 trials ascertained all-cause mortality, and 15 studies enrolled the outcomes of cardiovascular mortality. All

![Flow diagram of the trial selection process.](image)
| Study          | Country | Type     | Sample size | Mean age (year) | Percentage Male (%) | Percentage DM (%) | Follow-up duration (month) | Reported outcome                                                                 | Adjusted factors                                                                 |
|---------------|---------|----------|-------------|-----------------|---------------------|--------------------|--------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Ye H 2017 [15]| China   | Retrospec-tive | 1321        | 48.1 ± 15.3    | 58.7                | 23.5               | 34 (21–48)               | All-cause and cardiovas-cular mortality                                            | age, sex, DM, CVD, ALB, 24 h urine output, Hb, P DM, CVD, Ca, RRF, Hb, Cr, ALB, PTH, potassium, creatinine, P, fasting plasma glucose |
| Xiang S 2019 [16]| China   | Retrospec-tive | 9405        | 52.5 ± 14.6    | 54.9                | 12.2               | 34.5 ± 23.2              | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Xue Y 2019 [17]| China   | Retrospec-tive | 748          | 50.1            | 48                  | 34.6               | 36.4                     | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Hwang SD 2019 [18]| Korea  | Retrospec-tive | 6071        | 65.8 ± 13.7    | 57.5                | 36.1               | 90.96 ± 54.34            | All-cause mortality                                                              |                                                                                  |
| Lai KJ 2018 [19]| China   | Retrospec-tive | 492          | 53.5 ± 15.3    | 48                  | 34.6               | 36.0 ± 16.2              | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Jung HY 2018 [20]| Korea  | Prospective | 953          | 57.2 ± 12.8    | 58.6                | 45                 | 36.0 ± 16.2              | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Liu Y 2017 [21]| China   | Retrospec-tive | 667          | 42.9            | 24.7                | 32.64              | 36.4                     | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Rhee CM 2014 [22]| USA    | Retrospec-tive | 9244        | 54 ± 15        | 52                  | 32.4 (15.6–51.6)     | All-cause mortality                                                              |                                                                                  |
| Liu X 2014 [23]| China   | Retrospec-tive | 1021         | 47.4 ± 5.5     | 59.1                | 22.8               | 31 (19–45)               | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Li W 2017 [24]| China   | Retrospec-tive | 1228         | 46.96 ± 14.9   | 61.2                | 25.5               | 35 (18.7–52.3)           | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Lee S 2017 [25]| Korea   | Prospective | 1152         | 54 (45–64)     | 56.5                | 34.8               | 32.8 ± 20.4              | All-cause mortality                                                              |                                                                                  |
| Kim YK 2014 [26]| Korea  | Prospective  | 900          | 56 ± 12        | 57                  | 32                 | 24 (14 – 27)             | All-cause mortality                                                              |                                                                                  |
| Prasad N 2014 [27]| India | Prospective | 328          | 52.6 ± 12.6    | 73.8                | 53.7               | 20.0 ± 14.3              | All-cause mortality                                                              |                                                                                  |
| Tian Y 2016 [28]| China   | Retrospec-tive | 294          | 50.8 ± 14.0    | 62.2                | 14.3               | 33.3 (17.3–52.8)         | All-cause mortality                                                              |                                                                                  |
| Feng S 2016 [29]| China   | Retrospec-tive | 189          | 57.5 ± 15.9    | 56.1                | 51.3               | 35 (17–56)               | All-cause mortality                                                              |                                                                                  |
| Liu X 2016 [30]| China   | Retrospec-tive | 1778         | 47.4 ± 15.6    | 59.5                | 25.3               | 35 (17–56)               | All-cause and cardiovas-cular mortality                                            |                                                                                  |
| Yang X 2016 [31]| China   | Retrospec-tive | 10692        | 56 ± 16        | 55                  | 40                 | 13 (7–23)                | All-cause mortality                                                              |                                                                                  |
| Study          | Country | Type          | Sample size | Mean age (year) | Percentage Male (%) | Percentage DM (%) | Follow-up duration (month) | Reported outcome                                      | Adjusted factors                                                                                                                                                                                                 |
|---------------|---------|---------------|-------------|-----------------|---------------------|-------------------|--------------------------|-------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cai K 2016    | China   | Retrospective | 253         | 58 ± 16         | 55.3                | 22.9              | 29 (4–120)              | All-cause and cardiovascular mortality               | age, sex, DM, rGFR, MAP, urinary output, sodium, Cr clearance, malnutrition, bone disorder-related factors                                                                 |
| Wu X 2016     | China   | Retrospective | 1068        | 48.0 ± 15.4     | 58.8                | 23.1              | 21.7 ± 14.1             | All-cause mortality                                   | age, heart disease, DM, stroke, MAP, Hb, ALB, hs-CRP, time to first peritonitis                                                                                                                                  |
| Xiong L 2015  | China   | Retrospective | 1263        | 47.8 ± 15.0     | 58.6                | 24.1              | 25.3 (3.03–82.07)       | All-cause and cardiovascular mortality               | age, sex, BMI, DM, Hb, ALB, CVD, MAP, Hb, ALB, hs-CRP, TG, rGFR, Kt/Vurea, total cholesterol                                                                                                              |
| Xu Q 2014     | China   | Retrospective | 886         | 48.5 ± 15.4     | 57.1                | 23.9              | 31 (0.5–81.0)           | All-cause and cardiovascular mortality               | age, sex, RRF, ALB, Hb, P, CRP, CVD, DM, MAP, BMI, LDL                                                                                                                                                    |
| Dong J 2014   | China   | Retrospective | 2264        | 58.1 ± 15.5     | 49.1                | 37.7              | 26.5 (13.6–43.6)        | All-cause and cardiovascular mortality               | age, sex, BMI, DM, Hb, ALB, CCI, hs-CRP, age, smoking, BMI, Hb, primary insurance, CVD, cancer, ferritin, ALP, total iron binding capacity, WBC, ALB                                                                 |
| Torlén K 2012 | Sweden  | Retrospective | 10468       | 56 ± 16         | 53                  | 49                | 27                       | All-cause and cardiovascular mortality               | age, sex, DM, race, dialysis vintage, Hb, primary insurance, marital status, BMI, smoking, CVD, cancer, ferritin, ALP, WBC, ALB, Ca, P, PTH, total iron binding capacity |
| Angela        | China   | Prospective   | 246         | 55 ± 12         | 52                  | 31                | 24 (2–34)               | All-cause and cardiovascular mortality               | age, weight, height, BMI, CVD, DBP, LV mass index, LV end-diastolic diameter, LV ejection fraction, LV fractional shortening |
| Guan JC 2015  | China   | Retrospective | 102         | 57.8            | 22.6                |                  |                           | All-cause mortality                                   | age, ALB, Hb, glycated Hb A1c, clearance of Cr, RRF, PNA                                                                                                                                                    |
| Rumpf-Leid M  | Australia| Retrospective | 3702        | 59.4 ± 14.8     | 53.9                | 38.1              |                           | All-cause mortality                                   | age, sex, race, smoking, BMI, weekly Kt/V, RRF, vintage year, PD modality, hypertension, chronic lung disease, DM, coronary artery disease, peripheral vascular disease, cerebrovasculare disease |

Hb: hemoglobin; PTH: parathyroid hormone; DM: diabetes mellitus; RRF: residual renal function; ALB: albumin; hs-CRP: hypersensitive C-reactive protein; CVD: cardiovascular disease; TG: total triglyceride; WBC: white blood cell; LDL: low density lipoprotein; HDL: high density lipoprotein; BMI: body mass index; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; Ca: calcium; Cr: creatinine; eGFR: estimated glomerular filtration rate; rGFR: residual glomerular filtration rate; MAP: mean arterial pressure; SGA: subjective global assessment; PNA: protein equivalent of total nitrogen appearance; MCCI, modified Charlson comorbidity index.
studies reported HR adjusted for possible confounders, such as age, sex, BMI, DM, and laboratory indices.

**Risk factors for all-cause mortality in patients undergoing PD**

As shown in Table 2 and Figure 2, age (HR: 1.04, 95% CI: 1.04–1.05, \( p < 0.00001 \)), DM (HR: 1.58, 95% CI: 1.41–1.78, \( p < 0.00001 \)), primary CVD (HR: 1.72, 95% CI: 1.17–2.52, \( p = 0.006 \)), high BMI (HR: 1.15, 95% CI: 1.04–1.28, \( p = 0.005 \)), ALP level (HR: 2.11, 95% CI: 1.86–2.39, \( p < 0.00001 \)), early onset of peritonitis (HR: 1.83, 95% CI: 1.26–2.64, \( p = 0.001 \)), high hs-CRP level (HR: 1.39, 95% CI: 1.04–1.82, \( p = 0.03 \)), and high peritoneal transport status (HR: 1.39, 95% CI: 1.10–1.76, \( p = 0.006 \)) showed significant positive associations with all-cause mortality in PD patients. A fixed-effect model was applied to analyze variables because the \( I^2 \) index was <50%. Sensitivity analysis was conducted in CVD and hs-CRP, given the substantial heterogeneity, while the conclusion was not affected. Egger’s test revealed no significant publication bias for any abovementioned risk factors (\( p \) for age = 0.712, \( p \) for DM = 0.458, \( p \) for CVD = 0.801, \( p \) for high BMI = 0.738, \( p \) for hs-CRP = 0.113, and \( p \) for ALP = 0.221).

Furthermore, the pooled HR suggested a significant association between Hb level (HR: 0.87, 95% CI: 0.83–0.90, \( p < 0.00001 \)) and a low risk of all-cause mortality in PD patients. Egger’s test revealed no significant publication bias for Hb (\( p = 0.876 \)).

Meanwhile, this study identified no associations between serum ALB, low BMI, high UA level, high magnesium level, low potassium level, and the risk of all-cause mortality in PD patients.

**Risk factors for cardiovascular mortality in patients undergoing PD**

As shown in Figure 3, the pooled HR indicated that age (HR: 1.04, 95% CI: 1.03–1.050, \( p < 0.00001 \)), primary CVD (HR: 2.12, 95% CI: 1.39–3.23, \( p = 0.0005 \)), DM (HR: 1.60, 95% CI: 1.30–1.96, \( p < 0.00001 \)), and high ALP (HR: 2.39, 95% CI: 1.22–4.66, \( p = 0.01 \)) might elevate the risk of cardiovascular mortality in PD patients. Moreover, Hb level (HR: 0.87, 95% CI: 0.81–0.94, \( p = 0.0002 \)) acted as a protective factor for cardiovascular mortality. Egger’s test revealed no significant publication bias (\( p \) for age = 0.95, \( p \) for DM = 0.574, and \( p \) for CVD = 0.292). Serum ALB level, high UA level, and low potassium level did not significantly affect the risk of cardiovascular mortality (Table 3).

### Table 2. Factors influencing the risk of all-cause mortality in PD patients.

| Risk factors                        | HR (95% CI)       | \( p \) Value   | \( p \) Value for heterogeneity |
|-------------------------------------|-------------------|-----------------|---------------------------------|
| Age (per 1 year increase)           | 1.04 (1.04–1.05)  | \( p < 0.00001 \)*** | \( p = 0.30 \) \( I^2 = 17\% \) |
| CVD                                 | 1.72 (1.17–2.52)  | \( p = 0.006 \)** | \( p < 0.0001 \) \( I^2 = 87\% \) |
| DM                                  | 1.58 (1.41–1.78)  | \( p < 0.00001 \)*** | \( p = 0.09 \) \( I^2 = 46\% \) |
| Hs-CRP (mg/l)                       | 1.37 (1.04–1.82)  | \( p = 0.03 \)   | \( p < 0.00001 \) \( I^2 = 94\% \) |
| Hb (g/dl)                           | 0.87 (0.83–0.90)  | \( p < 0.00001 \)*** | \( p = 0.41 \) \( I^2 = 0\% \) |
| ALB (mg/dl)                         | 0.71 (0.42–1.21)  | \( p = 0.21 \)   | \( p < 0.00001 \) \( I^2 = 93\% \) |
| High BMI (kg/m\(^2\))               | 1.17 (1.04–1.31)  | \( p = 0.007 \)  | \( p = 0.40 \) \( I^2 = 0\% \) |
| Low BMI (kg/m\(^2\))                | 1.20 (0.83–1.73)  | \( p = 0.34 \)   | \( p = 0.009 \) \( I^2 = 71\% \) |
| ALP (U/l)                           | 2.11 (1.86–2.39)  | \( p < 0.00001 \)*** | \( p = 0.95 \) \( I^2 = 0\% \) |
| Magnesium (high vs low)             | 0.19 (0.02–2.22)  | \( p = 0.18 \)   | \( p = 0.03 \) \( I^2 = 73\% \) |
| Uric acid (high vs low)             | 0.93 (0.48–1.79)  | \( p = 0.83 \)   | \( p < 0.0001 \) \( I^2 = 91\% \) |
| Potassium (low vs high)             | 1.25 (0.97–1.60)  | \( p = 0.08 \)   | \( p = 0.10 \) \( I^2 = 56\% \) |
| Early on-set of peritonitis         | 1.83 (1.26–2.64)  | \( p = 0.001 \)*** | \( p = 0.41 \) \( I^2 = 0\% \) |
| Peritoneal transport status (high vs low) | 1.39 (1.10–1.76)  | \( p = 0.006 \) | \( p = 0.21 \) \( I^2 = 36\% \) |

HR: hazard ratio; CI: confidence interval; ALB: albumin; DM: diabetes mellitus; CVD: cardiovascular diseases; hs-CRP: hypersensitive C-reactive protein; Hb: hemoglobin; ALP: alkaline phosphatases; GFR: glomerular filtration rate; BMI: body mass index.

* \( p < 0.01 \)
** \( p < 0.001 \)
*** \( p < 0.0001 \)

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Discussion

The present meta-analysis of 26 studies, including a total of 66,735 patients, was considered as the first meta-analysis exploring the risk factors for all-cause and cardiovascular mortality in patients undergoing PD. It covered five prospective studies. Our results indicated that age, primary CVD, DM, and ALP level negatively affected the risk of all-cause and cardiovascular mortality. Furthermore, early onset of peritonitis, obesity, high hs-CRP level, and membrane transport status might elevate the risk of all-cause mortality. Hb level was found to have a beneficial impact on the risk of all-cause mortality, while serum ALB level had a slight beneficial impact.

Figure 2. Forest plots for the hazard risk (HR) between risk factors and all-cause mortality in PD patients (a) age (per 1 year increase); (b) cardiovascular disease; (c) diabetes mellitus; (d) hypersensitive-C reaction protein (mg/l); (e) hemoglobin (g/dl); (f) albumin (mg/dl); (g) high body mass index; (h) low body mass index; (i) alkaline phosphatases (U/l); (j) magnesium (high vs low); (k) uric acid (high vs low); (l) potassium (low vs high); (m) early on-set of peritonitis; (n) peritoneal transport status (high vs low).
In this meta-analysis, only articles with sufficient data to calculate HR and adjusted ones were included. In the existing study, functional status of patients undergoing PD might predict the risk of mortality, such as employment status and family education [37,38]. The use of medicine, such as angiotensin receptor blockers and oral active vitamin D, could also reduce the risk of major cardiovascular events and total mortality [39]. Notably, the associations between several clinical and laboratory characteristics of PD patients and all-cause mortality were still under debate.

In the present meta-analysis, age, primary CVD, DM, and high level of ALP were found to be the risk factors for both all-cause and cardiovascular mortality in patients undergoing PD. Additionally, patients with high BMI, high peritoneal transport status, high level of hs-CRP, and early onset of peritonitis also had an elevated risk of all-cause mortality. Primary DM and CVD might impair vascular endothelial cells and cause chronic inflammation, primarily leading to arterial stiffness; it might predict the risk of fatal cardiovascular events and all-cause mortality. Furthermore, poor

**Figure 3.** Forest plots for the hazard risk (HR) between risk factors and cardiovascular mortality in PD patients (a) age (per 1 year increase); (b) diabetes mellitus; (c) cardiovascular disease; (d) albumin (mg/dl); (e) hemoglobin (g/dl); (f) uric acid (high vs low); (g) potassium (low vs high); (h) alkaline phosphatases (U/l)).

**Table 3.** Factors influencing the risk of cardiovascular mortality in PD patients.

| Risk factors | HR (95% CI) | p Value | p Value for heterogeneity (p, I²) |
|--------------|-------------|---------|----------------------------------|
| Age (per 1 year increase) | 1.04 (1.03-1.05) | <0.00001 *** | p = 0.67 |
| DM | 1.60 (1.30-1.96) | <0.00001 *** | p = 0.50 |
| CVD | 2.12 (1.39-3.23) | 0.0005 *** | p = 0.01 |
| ALB (g/dl) | 0.79 (0.61-1.02) | 0.07 | I²=77% |
| Hb (g/dl) | 0.87 (0.68-1.09) | 0.83 | I²=0% |
| Uric acid (high vs low) | 0.74 (0.23-2.45) | 0.63 | p = 0.009 |
| Potassium (low vs high) | 1.46 (0.67-3.16) | 0.34 | I²=85% |
| ALP (U/l) | 2.39 (1.22-4.66) | 0.01** | I²=79% |

HR: hazard ratio; CI: confidence interval; ALB: albumin; Hb: hemoglobin; DM: diabetes mellitus; CVD: cardiovascular diseases; ALP: alkaline phosphatases.

***p < 0.01.

**p < 0.001.
hypokalemia may have more comorbidities. Miner...cific and osteomalacia. In this meta-analysis, high
level of ALP might be associated with vascular cal-
fication and osteomalacia. In this meta-analysis, high
peritoneal membrane transport, assessed by the peri-
toneal equilibration test, was also found to be a risk fac-
tor for mortality. An increased rate of peritoneal
membrane solute transport might enhance protein
losses through peritoneal membrane leading to a mal-
nutrition status. Guan et al. [35] reported that higher
peritoneal transport status was not an independent
predictor after adjusting for ALB level, Hb level, and
RRF. Large-scale randomized clinical trials are required
to verify this relationship. In addition, we showed that
early onset of peritonitis and elevated hs-CRP level
increased the risk of all-cause mortality significantly
although there was significant heterogeneity among
studies in terms of hs-CRP level. Two prospective and
one retrospective study were included for hs-CRP as a
categorical variable. Xu et al. [12] and Lee et al. [25]
reported a serum potassium level of <3 mEq/L or <4.5 mmol/L to be an independent
risk factor for all-cause mortality in PD patients.
However, the baseline values in another study did not
show this relationship [11]. The change or fluctuation in
serum potassium level during PD might be more reli-
able to predict death risk in PD patients and should be
investigated further. Magnesium, the fourth most abun-
dant cation in the body, plays a key role in various bio-
logical processes. Tubular injuries might cause renal
magnesium wasting. Serum magnesium level of
<1.8 mg/dL was reported to be a risk factor after
adjusting for baseline demographic characteristics and
comorbidities, but the risk was attenuated after further
adjustment for laboratory indices [9]. Furthermore, the
beneficial effect of a serum magnesium level of
>0.7 mmol/L might be different between male and
female individuals [10]. Considering that lower serum
magnesium is associated with a poor nutrition status
and increased inflammation, the independent relation-
ship between serum magnesium and mortality in PD
patients should be evaluated, and an appropriate treat-
ment to maintain the right serum magnesium level
needs to be determined. UA is the final product of
nucleotide metabolism, and it is primarily excreted
from the kidney by glomerular filtration. High level of
serum UA could be an endothelial toxin and aggra-
vated endothelial function by activating the inflama-
tory pathway [46]; it is also associated with RRF loss
[47]. However, we did not observe any significant asso-
ciation between hyperuricemia and mortality. Xiang
et al. [16] studied the impact of high serum UA level on
mortality in PD patients by divided them into five
groups according to their serum UA level. Patients with
UA > 7.28 mg/dL had a higher all-cause mortality com-
pared to those in the middle group. Furthermore, UA <
6.06 mg/dL was found to be a risk factor only in an
unadjusted model. The other two studies divided
patients into three groups according to their UA level.
However, Lai et al. [19] reported high serum UA level to
be a protective factor for mortality. Serum UA level
reflects patients' nutrition condition, and a low serum
UA level might lead to inflammation. Considering a
potential U-shaped association between UA and mortal-
ity, a proper range of serum UA and treatments to
lower serum UA level should be determined to improve
survival. However, these outcomes might not be feas-
ible because there are only few studies reporting such
indices. To confirm this association, more studies
were required.
Importantly, the present meta-analysis is the first one to explore the risk factors for all-cause mortality in PD patients. This study had a large enough sample size and HR adjusted for possible confounders. There was a debate about different risk factors in previous studies, and this meta-analysis might be more reliable to predict all-cause and cardiovascular mortality in PD patients.

This study has several limitations. First, individual studies adjusted for the different potential confounders, which might result in a high heterogeneity. Second, the present meta-analysis might have missed some unpublished articles without conference abstracts in line with the selection criteria. Third, although we observed a significant heterogeneity in the impact of CVD on mortality across studies, we did not perform a subgroup analysis according to race. Moreover, we applied a random-effect model in this meta-analysis. Fourth, this meta-analysis was not registered in PROSPERO, which might lead to a bias. However, importantly, this meta-analysis was conducted in accordance with the standards of systematic review. Furthermore, more data regarding the respective risk factors are recommended.

In conclusion, the present meta-analysis revealed that a considerable number of risk factors displayed significant associations with an elevated risk of all-cause and cardiovascular mortality in PD patients. A proper threshold for serum magnesium, potassium, and UA should be determined to improve the survival in PD patients. Since data on several indices were limited, more studies are required to confirm the findings of this meta-analysis.

Author contributions
Han Li and Shixiang Wang conceived and designed the experiment; Jialing Zhang searched the literature and acquired the data primarily, while Xiangxue Lu secondarily; Han Li settled any inconsistencies between these two authors; Han Li and Jialing Zhang analyzed and interpreted the data; Han Li, Jialing Zhang and Xiangxue Lu wrote the paper; Han Li obtained the funding. All authors read and approved the final manuscript.

Disclosure statement
No potential conflict of interest was reported by the author(s).

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Data availability statement
The data of this study are available from the corresponding author.

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