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Risk factors associated with mortality among patients on maintenance hemodialysis: The Thailand Renal Replacement Therapy registry

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Abstract

Introduction: End-stage kidney disease (ESKD) has been increasing in prevalence across the world, including Thailand, and patients with ESKD on hemodialysis have a high mortality risk.

Methods: A retrospective cohort study was performed across 855 hemodialysis centers in the Thailand Renal Replacement Therapy registry. The database and mortality data were analyzed.

Results: A total of 58 952 patients were included. The survival rates at 1, 3, and 5 years were 93.5%, 69.7%, and 41.2%, respectively. On multivariate analysis, factors such as aging, permanent catheter or arteriovenous graft, twice-weekly hemodialysis, low levels of urea reduction ratio, normalized protein catabolic rate, hemoglobin, transferrin saturation, serum albumin, LDL-cholesterol, intact-parathyroid hormone, uric acid, sodium, phosphate, and bicarbonate were significantly related to death.

Conclusion: Mortality is high in ESKD patients on hemodialysis. Age, type of vascular access, twice-weekly hemodialysis, inadequate dialysis, low protein intake, anemia, abnormal electrolytes, and bone mineral disorders are associated with all-cause mortality.

KEYWORDS

adequacy of dialysis, frequency of, hemodialysis, hemodialysis, mortality, survival

1 | INTRODUCTION

End-stage kidney disease (ESKD) represents a rapidly increasing global health and healthcare burden. According to the United States Renal Data System (USRDS) annual report for 2023, the average yearly increase in dialysis prevalence between 2011 and 2021 exceeded 50.0 per million population (pmp) in several Asian countries, including Thailand (124.2 pmp) [1]. Currently, Thailand ranks among the top eight countries in Asia with high incidence rates of treated ESKD at 179 pmp [1]. The elevated incidence rates of ESKD in Thailand raise significant national concerns regarding the sustainability of health financing and healthcare service delivery [2]. In response, Thailand has implemented a "PD-first" universal coverage policy, where all eligible patients are offered peritoneal dialysis (PD), reserving the more costly hemodialysis for patients with a clinical indication or private insurance coverage, leading to an expansion of ESKD care [3].

The mortality rate among maintenance hemodialysis (MHD) patients remains high. The USRDS reported a decrease in all-cause mortality among prevalent patients with ESRD from 2010 to 2019, but a sharp increase in mortality was observed in 2021 during the COVID-19 pandemic, reaching 187.7 per 1000 patient-years for those receiving dialysis [1]. Among individuals undergoing MHD with a known cause of death in 2021, COVID-19 emerged as the third-leading cause, accounting for 9.9% [1]. The improved survival rates in ESKD patients may be attributed to advancements in dialysis technology, new medication agents, and enhanced adherence to practice guidelines [4]. Additionally, factors associated with mortality in MHD patients include gender, age, diabetic nephropathy, low body mass index, residual renal clearance, adequacy of dialysis, type of vascular access and levels of serum calcium, phosphate, albumin, and hemoglobin [5–8]. Recent studies have indicated that employing higher-order clinical risk interaction analysis offers a viable strategy for detecting non-traditional risk factor interactions affecting overall mortality in maintenance hemodialysis patients [9]. However, most studies have been conducted on specific populations, leaving a gap in national-level evidence reflecting factors associated with mortality among MHD patients in Thailand. This study aims to analyze the factors associated with death in patients undergoing maintenance hemodialysis in Thailand.

2 | MATERIALS AND METHODS

We retrospectively reviewed national registry data collected by the Thailand Renal Replacement Therapy (TRT) regarding new patients on MHD in Thailand over a 5-year period, from January 2017 to December 2021. The new patients received hemodialysis treatment from 855 hemodialysis centers across 77 provinces in Thailand. The inclusion criteria were as follows: age ≥ 18 years old, new patients undergoing regular MHD for more than 3 months, and complete laboratory data including adequacy of dialysis, hemoglobin, serum electrolytes, serum albumin, serum calcium, and serum phosphate. Patients were excluded from the study if they (1) initiated hemodialysis before January 1, 2017, (2) transitioned to peritoneal dialysis or kidney transplantation, (3) had missing medical data, or (4) had duplicate identify data in the registration data. This study adhered to the Declaration of Helsinki.

Data on various demographic factors, primary diseases, complications, laboratory tests, and mortality were collected from electronic medical records for each patient at the onset of dialysis and continuously for 5 years until December 2021. Baseline characteristics at the commencement of MHD were also gathered, including age, gender, educational status, and medical history. Information specific to hemodialysis was captured, such as type of vascular access, dialysis frequency, and parameters related to dialysis adequacy, including single-pool Kt/V and urea reduction ratio (URR). Laboratory parameters encompassed hemoglobin, serum electrolytes, uric acid, calcium, phosphate, lipid profiles, iron studies, serum intact-parathyroid hormone (PTH), serum albumin, normalized protein catabolic rate (NPCR), and infectious serology status, including HIV, hepatitis B, and hepatitis C infections.

Statistical analysis was conducted using SPSS 23.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were

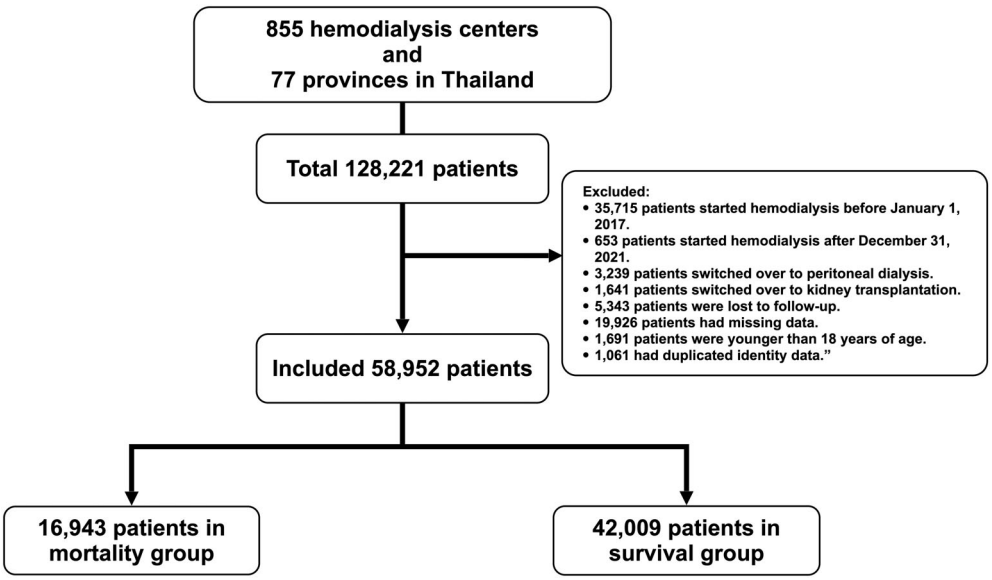

FIGURE 1 Flow chart of the study.

TABLE 1 Baseline characteristics and comparisons between mortality and survival groups.

Characteristics	All ($n = 58\,952$)	Mortality group ($n = 16\,943$)	Survival group ($n = 42\,009$)	*p*-Value
Male (*N*, %)	31 381 (53.2)	8920 (52.7)	22 461 (53.5)	<0.001
Median age (years)	59.0 [47.0–69.0]	66.0 [56.0–76.0]	56.0 [45.0–66.0]	<0.001
Education levels (*N*, %)				
Primary school or lower	19 944 (33.8)	4307 (25.4)	15 637 (37.2)	<0.001
Secondary school	10 877 (18.5)	4886 (28.8)	5991 (14.3)	
High school	6471 (11.0)	1452 (8.6)	5019 (12.0)	
Vocational/High vocational certificate	5185 (8.8)	1319 (7.8)	3866 (9.2)	
Bachelor degrees or higher	11 042 (18.7)	2748 (16.2)	8294 (19.7)	
Unknown	5433 (9.2)	2231 (13.2)	3202 (7.6)	
Expense within a dataset (*N*, %)				
Universal coverage	15 897 (27.0)	4068 (24.0)	11 829 (28.2)	<0.001
Social security scheme	12 316 (20.9)	2167 (12.8)	10 149 (24.2)	
Government/State enterprise officer	18 059 (30.6)	6292 (37.4)	11 767 (28.0)	
Self-payment	8361 (14.2)	2783 (16.4)	5578 (13.3)	
Others	504 (0.9)	107 (0.6)	397 (1.0)	
Unknown	3815 (6.5)	1526 (9.0)	2289 (5.5)	
Cause of ESKD (*N*, %)				
Diabetic nephropathy	21 644 (36.7)	6830 (40.3)	14 814 (35.3)	<0.001
Hypertensive nephropathy	913 (1.6)	116 (0.7)	797 (1.9)	
Glomerulonephritis	239 (0.4)	24 (0.1)	215 (0.5)	
Presumed glomerulonephritis	951 (1.6)	260 (1.5)	691 (1.7)	
Others	24 533 (41.6)	4990 (29.5)	19 543 (46.5)	
Unknown	10 662 (18.1)	4720 (27.9)	5942 (14.2)	
Type of vascular access (*N*, %)				
Arteriovenous fistula	18 546 (47.5)	2621 (39.8)	15 925 (49.1)	<0.001
Arteriovenous graft	2482 (6.4)	480 (7.3)	2002 (6.2)	
Permanent catheter	8723 (22.3)	1800 (27.3)	6923 (21.3)	
Nonpermanent catheter	7105 (18.2)	1344 (20.4)	5761 (17.8)	
Unknown	1599 (4.1)	242 (3.7)	1357 (4.2)	
Dialysis frequency (*N*, %)				
Twice weekly hemodialysis	14 632 (29.9)	3032 (35.1)	11 600 (28.7)	<0.001
Thrice weekly hemodialysis	21 555 (44.0)	3933 (45.5)	17 622 (43.7)	
Twice-weekly alternative to thrice-weekly hemodialysis	12 830 (26.2)	1686 (19.5)	11 144 (27.6)	

Note: Values are presented as *n* (%) and median [IQR].
Abbreviation: IQR, interquartile range.

presented as the mean ± standard deviation for continuous variables and as frequencies (percentages) for categorical variables. All clinical parameters were compared between the mortality and survival groups using the Mann–Whitney *U* test or the Kruskal-Wallis test for continuous variables and the Chi-square test for categorical variables. Both univariate and multivariate Cox regression analyses were employed to determine factors associated with all-cause mortality. Survival analysis for patients in this cohort study was performed using the Log-rank test. Statistical significance was defined as $p < 0.05$.

TABLE 2 Baseline laboratory data and comparisons between mortality and survival groups.

Parameters	All ($n = 58\,952$)	Mortality group ($n = 16\,943$)	Survival group ($n = 42\,009$)	p-Value
Hemoglobin (g/dL)	10.0 [8.9–10.9]	9.7 [8.7–10.7]	10.0 [9.0–10.9]	<0.001
Serum uric acid (mg/dL)	6.7 [5.5–7.9]	6.4 [5.2–7.6]	6.8 [5.6–8.0]	<0.001
Serum sodium (mEq/L)	137.4 [135.4–139.0]	136.7 [134.3–138.7]	137.5 [135.6–139.1]	<0.001
Serum potassium (mEq/L)	4.4 [4.1–4.8]	4.3 [4.0–4.7]	4.4 [4.1–4.8]	<0.001
Serum bicarbonate (mEq/L)	23.8 [22.0–25.5]	23.7 [22.0–25.5]	23.8 [22.0–25.5]	0.044
Serum calcium (mg/dL)	9.0 [8.5–9.5]	9.0 [8.5–9.5]	9.1 [8.6–9.5]	<0.001
Serum phosphate (mg/dL)	4.5 [3.6–5.5]	4.3 [3.4–5.3]	4.5 [3.7–5.6]	<0.001
Serum albumin (g/dL)	3.9 [3.6–4.2]	3.7 [3.3–4.0]	3.9 [3.7–4.2]	<0.001
Serum intact-PTH (pg/mL)	296.5 [149.0–534.8]	238.6 [110.9–479.1]	306.9 [157.3–543.0]	<0.001
Total cholesterol (mg/dL)	155.0 [131.8–182.5]	149.4 [125.0–179.0]	156.0 [133.0–183.0]	<0.001
LDL-cholesterol (mg/dL)	86.4 [67.5–109.0]	83.0 [63.8–107.0]	87.0 [68.1–109.5]	<0.001
Triglycerides (mg/dL)	109.0 [79.0–153.0]	106.0 [78.3–150.0]	109.8 [79.0–154.0]	0.004
Transferrin saturation (%)	27.0 [20.6–35.1]	26.1 [19.5–34.8]	27.2 [20.8–35.2]	<0.001
Ferritin (ng/mL)	399.2 [201.0–685.3]	426.6 [219.1–764.0]	395.3 [197.9–671.9]	<0.001
HIV status ($n = 47\,165$)				
Positive	486 (1.0)	77 (0.9)	409 (1.1)	0.389
Negative	46 679 (99.0)	8089 (99.1)	38 590 (98.9)	
HBsAg ($n = 47\,165$)				
Positive	2363 (5.0)	390 (4.8)	1973 (5.1)	0.286
Negative	44 802 (95.0)	7776 (95.2)	37 026 (94.9)	
Anti-HCV antibody ($n = 47\,165$)				
Positive	1699 (3.6)	315 (3.9)	1384 (3.6)	0.174
Negative	45 466 (96.4)	7851 (96.1)	37 615 (96.4)	
spKt/V	1.7 [1.5–1.9]	1.6 [1.4–1.8]	1.7 [1.5–1.9]	0.004
URR (%)	75.1 [70.2–79.5]	74.8 [69.5–79.5]	75.2 [70.4–79.6]	<0.001
NPCR	1.2 [1.0–1.3]	1.1 [0.9–1.3]	1.2 [1.0–1.3]	<0.001

Note: Values are presented as *n* (%) and median [IQR].

Abbreviations: IQR, Interquartile range; NPCR, normalized protein catabolic rate; PTH, parathyroid hormone; spKt/V, single-pool Kt/V; URR, urea reduction ratio.

3 | RESULTS

3.1 | Baseline characteristics

Initially, 128 221 patients were included. After applying the inclusion and exclusion criteria, a total population of 58 952 patients was included in the final statistical analysis (Figure 1). The mean age was 59.0 [IQR 47.0–69.0] years, and 16 943 (28.7%) patients had died. In terms of educational status, the majority of patients had completed primary school or less. The most common type of medical insurance among MHD patients in Thailand was universal coverage (UC) ($n = 15\,897$, 27%). The leading cause of ESKD was diabetic nephropathy ($n = 21\,644$, 36.7%). The three most common types of vascular access were arteriovenous fistula ($n = 18\,546$, 47.5%), permanent catheter ($n = 8723$, 22.3%), and nonpermanent catheter ($n = 7105$, 18.2%). Patients undergoing MHD were predominantly on thrice-weekly MHD ($n = 21\,555$, 44%) and twice-weekly MHD ($n = 14\,632$, 29.9%).

Baseline characteristics and comparisons between the mortality and survival groups are presented in Table 1. The mortality group exhibited a significantly higher median age (66.0 [IQR 56.0–76.0] vs. 56.0 [IQR 45.0–66.0] years, $p < 0.001$) and a lower proportion of males (52.7% vs. 53.5%, $p < 0.001$) compared to the survival group. Significant differences were also observed in educational levels, insurance coverage, cause of ESKD, type of vascular access, and frequency of dialysis between the two groups. The mortality group exhibited a significantly higher proportion of diabetic nephropathy (40.3% vs. 35.3%, $p < 0.001$) and a higher proportion of twice-weekly hemodialysis (35.1% vs. 28.7%, $p < 0.001$) compared to the survival group.

Baseline laboratory data and comparisons between the mortality and survival groups are detailed in Table 2. Relative to the survival group, the mortality group displayed lower levels of serum sodium, potassium, bicarbonate, uric acid, calcium, total cholesterol, LDL-cholesterol, triglycerides, transferrin saturation, NPCR, and URR. Especially, the mortality group displayed clinically significant lower levels of hemoglobin (9.7 [IQR 8.7–10.7] vs. 10.0 [9.0–10.9] g/dL, $p < 0.001$), phosphate (4.3 [IQR 3.4–5.3] vs. 4.5 [IQR 3.7–5.6] mg/dL, $p < 0.001$), albumin (3.7 [IQR 3.4–4.0] vs. 3.9 [IQR 3.7–4.2] g/dL, $P < 0.001$), intact-PTH (238.6 [IQR 110.9–479.1] vs. 306.9 [IQR 157.3–543.0] pg/mL, $p < 0.001$), and spKt/V (1.6 [IQR 1.4–1.8] vs. 1.7 [IQR 1.5–1.9], $p = 0.004$). Conversely, the mortality group exhibited higher levels of ferritin (426.6 [219.1–764.0] vs. 395.3 [IQR 197.9–671.9] ng/mL, $p < 0.001$).

3.2 | Survival analysis

Survival analysis was also conducted in this study. The results showed that survival rates at 1, 3, and 5 years were 93.5%, 69.7%, and 41.2%, respectively (Figure 2). Patients with diabetic nephropathy had the lowest 5-year survival rate (36.7%). Those on with a permanent catheter had the shortest 5-year survival rate (51.9%) compared to other groups (Figure 2).

3.3 | Factors associated with mortality

Multivariable-adjusted hazard ratios for mortality rates were significantly higher among patients aged >65 years, those who paid for dialysis out-of-pocket, individuals with catheters or arteriovenous grafts, patients on twice-weekly hemodialysis, and those exhibiting specific biochemical markers outside the defined ranges. These markers included hemoglobin <10 g/dL, serum uric acid <3.5 mg/dL, sodium <135 mEq/L, bicarbonate <22 mEq/L, calcium >10 mg/dL, phosphate levels outside the range of <2.7 mg/dL or >6.0 mg/dL, albumin <3.5 g/dL, intact-PTH <130 pg/mL, LDL-cholesterol <70 mg/dL, transferrin saturation < 30%, URR <65%, and nPCR <1.2 g/kg/day. Conversely, adjusted hazard ratios for mortality rates were significantly lower among patients aged 18–40 years and those on twice-weekly hemodialysis as an alternative to thrice-weekly (Table 3).

In the subgroup analysis of patients on thrice-weekly hemodialysis, the multivariable-adjusted hazard ratios for mortality aligned with the overall population findings and additional factors, including patients with spKt/V < 1.2. Mortality rates were notably elevated for specific

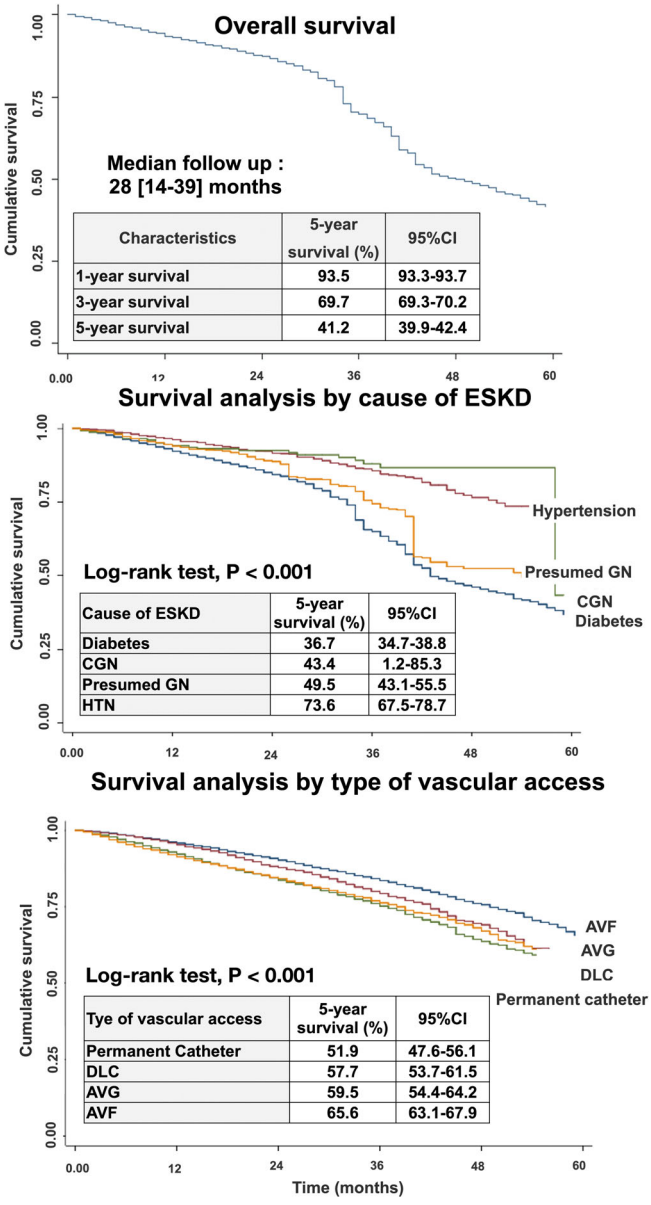

FIGURE 2 5-year survival of all patients and in subgroup analysis.

factors but lower only for patients aged 18–40 years (Table 4). For patients undergoing twice-weekly hemodialysis, the analysis identified similar factors associated with mortality and revealed additional factors, including serum calcium levels <8 or > 10 mg/dL, LDL-cholesterol >100 mg/dL, and nPCR <0.8 g/kg/day (Table 5).

4 | DISCUSSION

In this study, we utilized records from Thailand's national registration data, which represent the nationwide situation and information within the country. Limited research has been conducted on such a large

TABLE 3 Risk factors for mortality in the overall population.

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Sex						
Female	Reference					
Male	1.00	0.97–1.03	0.860			
Age (years)						
41–65	Reference			Reference		
18–40	0.53	0.49–0.57	<0.001	0.48	0.35–0.66	<0.001
>65	1.89	1.83–1.95	<0.001	1.64	1.41–1.90	<0.001
Education level						
Primary school or lower	Reference			Reference		
Secondary school	1.66	1.59–1.73	<0.001	1.21	0.99–1.46	0.052
High school	0.92	0.87–0.98	0.008	0.97	0.77–1.21	0.763
Vocational/High vocational certificate	1.01	0.94–1.07	0.866	0.83	0.61–1.14	0.247
Bachelor degrees or higher	1.00	0.96–1.06	0.859	1.03	0.85–1.25	0.762
Unknown	1.68	1.60–1.77	<0.001	1.38	1.08–1.75	0.009
Expense within a dataset						
Universal coverage (UC)	Reference			Reference		
Social security scheme	0.66	0.62–0.69	<0.001	1.01	0.80–1.28	0.933
Government/State enterprise officer	1.27	1.22–1.33	<0.001	1.05	0.88–1.26	0.587
Self-payment	1.37	1.3–1.44	<0.001	1.26	1.01–1.57	0.037
Others	0.90	0.74–1.10	0.326	0.73	0.3–1.78	0.490
Unknown	1.46	1.38–1.56	<0.001	1.22	0.9–1.65	0.203
Cause of ESKD						
Diabetic nephropathy	Reference			Reference		
Hypertensive nephropathy	0.37	0.31–0.45	<0.001	0.87	0.52–1.44	0.579
Glomerulonephritis	0.31	0.21–0.47	<0.001	0.25	0.04–1.81	0.171
Presumed glomerulonephritis	0.77	0.68–0.88	<0.001	0.93	0.51–1.70	0.810
Others	0.60	0.57–0.62	<0.001	0.76	0.65–0.88	<0.001
Unknown	1.24	1.19–1.29	<0.001	0.84	0.67–1.06	0.142
Type of vascular access						
Arteriovenous fistula	Reference			Reference		
Arteriovenous graft	1.29	1.17–1.43	<0.001	1.43	1.15–1.77	0.001
Permanent catheter	1.63	1.54–1.74	<0.001	1.37	1.16–1.61	<0.001
Nonpermanent catheter	1.57	1.47–1.68	<0.001	1.41	1.18–1.69	<0.001
Unknown	0.90	0.79–1.03	0.139	0.88	0.65–1.21	0.441
Dialysis frequency						
Thrice weekly hemodialysis	Reference			Reference		
Twice weekly hemodialysis	1.43	1.36–1.50	<0.001	1.34	1.14–1.59	0.001
Twice-weekly alternative to thrice-weekly hemodialysis	0.67	0.63–0.71	<0.001	0.65	0.56–0.76	<0.001

TABLE 3 (Continued)

Factors	Univariate			Multivariate		
	Crude HR	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Hemoglobin (g/dL)						
10–11.5	Reference			Reference		
<10	1.60	1.52–1.69	<0.001	1.60	1.39–1.85	<0.001
>11.5	0.97	0.88–1.06	0.516	1.25	1.00–1.57	0.046
Serum uric acid (mg/dL)						
3.5–7.5	Reference			Reference		
<3.5	1.31	1.09–1.58	0.004	1.68	1.13–2.49	0.010
>7.5	0.80	0.74–0.86	<0.001	0.87	0.75–1.02	0.085
Serum sodium (mEq/L)						
135–145	Reference			Reference		
<135	2.00	1.89–2.11	<0.001	1.24	1.07–1.45	0.005
>145	2.59	1.59–4.24	<0.001	4.25	0.58–30.99	0.153
Serum potassium (mEq/L)						
3.5–5.5	Reference			Reference		
<3.5	2.17	1.96–2.4	<0.001	1.04	0.74–1.48	0.807
>5.5	1.14	1.00–1.30	0.049	1.32	0.87–2.02	0.197
Serum bicarbonate (mEq/L)						
22–26	Reference			Reference		
<22	1.21	1.14–1.28	<0.001	1.34	1.14–1.57	<0.001
>26	1.08	1.01–1.15	0.029	1.06	0.87–1.28	0.566
Serum calcium (mg/dL)						
8–10	Reference			Reference		
<8	1.28	1.17–1.40	<0.001	1.02	0.80–1.29	0.903
>10	1.06	0.97–1.15	0.229	1.50	1.15–1.94	0.003
Serum phosphate (mg/dL)						
2.7–4.5	Reference			Reference		
<2.7	1.81	1.67–1.97	<0.001	1.42	1.19–1.70	<0.001
4.5–6.0	0.85	0.80–0.90	<0.001	1.10	0.97–1.25	0.125
>6.0	0.89	0.82–0.95	0.002	1.38	1.16–1.64	<0.001
Serum albumin (g/dL)						
≥3.5	Reference			Reference		
<3.5	3.18	3.02–3.36	<0.001	2.56	2.21–2.96	<0.001
Serum intact-PTH						
135–585	Reference			Reference		
<130	1.70	1.59–1.82	<0.001	1.33	1.14–1.54	<0.001
>585	0.90	0.83–0.97	0.009	0.94	0.77–1.14	0.522
Total cholesterol (mg/dL)						
<200	Reference			Reference		
200–240	0.88	0.78–0.98	0.019	0.90	0.69–1.16	0.401
>240	1.26	1.08–1.47	0.004	0.90	0.60–1.35	0.613

(Continues)

TABLE 3 (Continued)

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
LDL-cholesterol (mg/dL)						
70–100	Reference			Reference		
<70	1.36	1.26–1.46	<0.001	1.20	1.03–1.39	0.019
>100	0.98	0.91–1.06	0.663	1.14	0.96–1.36	0.145
Triglycerides (mg/dL)						
150–500	Reference					
<150	1.05	0.97–1.13	0.236	1.12	0.85–1.46	0.357
>500	0.97	0.63–1.48	0.878	0.94	0.49–2.16	0.460
Transferrin saturation (%)						
30–40	Reference			Reference		
<30	1.32	1.22–1.43	<0.001	1.29	1.09–1.52	0.002
>40	1.32	1.20–1.46	<0.001	1.17	0.95–1.45	0.146
Ferritin (ng/mL)						
200–500	Reference			Reference		
<200	0.96	0.89–1.04	0.292	1.11	0.93–1.32	0.261
>500	1.13	1.06–1.21	<0.001	1.01	0.87–1.17	0.884
spKt/V						
≥1.2	Reference			Reference		
<1.2	1.14	1.09–1.19	<0.001	1.15	0.99–1.32	0.053
URR (%)						
≥65	Reference			Reference		
<65	1.53	1.43–1.64	<0.001	1.45	1.15–1.83	0.002
NPCR						
≥1.2	Reference			Reference		
<1.2	2.59	2.42–2.76	<0.001	1.62	1.29–2.05	<0.001

Note: Statistically significant at *p*-value <0.05 determined by Cox regression. Covariates introduced into the multivariate model were gender, age, education level, expense within a dataset, cause of ESKD, type of vascular access, dialysis frequency, hemoglobin, serum uric acid, serum electrolytes, calcium, phosphate, albumin, intact-PTH, lipid profiles, transferrin saturation, ferritin, spKt/V, URR, and NPCR.

Abbreviations: CI, confidence interval; ESKD, end stage kidney disease; HR, hazard ratio; NPCR, normalized protein catabolic rate; PTH, parathyroid hormone; spKt/V, single-pool Kt/V; URR, urea reduction ratio.

population in Thailand. The survival percentages for MHD patients in Thailand at 1, 3, and 5 years were 93%, 69%, and 41%, respectively. The results indicated that factors such as aging, patients using catheters or arteriovenous grafts, twice-weekly hemodialysis, anemia with iron deficiency, hyponatremia, hypoalbuminemia, low LDL-cholesterol levels, low protein intake, reduced urea clearance, and abnormalities in mineral bone disease biomarkers particularly low intact-PTH, elevated calcium, and phosphate levels were associated with higher mortality rates. Furthermore, among patients undergoing twice-weekly hemodialysis, additional factors such as abnormal serum calcium levels, elevated LDL-cholesterol, and nPCR <0.8 g/kg/day were significantly associated with higher mortality.

In terms of ethnicity, mortality rates among hemodialysis patients vary greatly across regions. The 1-year mortality rates of hemodialysis patients were 15.6% in Europe and 21.7% in the United States from an observational study of the Dialysis Outcomes and Practice Patterns Study (DOPPS) [10]. Recently, in a survival analysis in Brazil and Iran patients undergoing hemodialysis, the overall survival rates at 1 year were only 82.3% and 72%, respectively [11, 12]. In comparison, studies from other Asian countries have shown varying survival rates for patients on maintenance hemodialysis. Japanese patients on dialysis enjoyed the longest survival with 1-year crude mortality rates of 6.6% [13]. Data from the Taiwan registry showed a first-year mortality of 15% and a 5-year

TABLE 4 Risk factors for mortality in patients undergoing thrice-weekly hemodialysis ($N = 21\ 555$).

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Sex						
Female	Reference					
Male	1.00	0.93–1.06	0.881			
Age (years)						
41–65	Reference			Reference		
18–40	0.50	0.45–0.56	<0.001	0.38	0.24–0.59	<0.001
>65	1.74	1.63–1.86	<0.001	1.52	1.22–1.90	<0.001
Education level						
Primary school or lower	Reference			Reference		
Secondary school	0.94	0.86–1.03	0.207	1.18	0.90–1.54	0.233
High school	0.73	0.65–0.81	<0.001	0.98	0.71–1.34	0.885
Vocational/High vocational certificate	0.62	0.55–0.71	<0.001	0.71	0.45–1.12	0.138
Bachelor degrees or higher	0.70	0.64–0.77	<0.001	1.00	0.76–1.32	0.981
Unknown	1.01	0.89–1.13	0.917	1.07	0.74–1.56	0.721
Expense within a dataset						
Universal coverage (UC)	Reference			Reference		
Social security scheme	0.70	0.64–0.77	<0.001	0.97	0.71–1.32	0.850
Government/State enterprise officer	1.14	1.06–1.23	0.001	0.97	0.75–1.24	0.788
Self-payment	1.53	1.36–1.72	<0.001	1.65	1.15–2.38	0.007
Others	1.04	0.74–1.46	0.835	0.75	0.18–3.09	0.689
Unknown	1.01	0.87–1.17	0.891	0.97	0.59–1.59	0.906
Cause of ESKD						
Diabetic nephropathy	Reference			Reference		
Hypertensive nephropathy	0.46	0.35–0.62	<0.001	0.66	0.29–1.52	0.332
Glomerulonephritis	0.35	0.18–0.71	0.003	-	-	-
Presumed glomerulonephritis	0.58	0.44–0.77	<0.001	0.82	0.30–2.24	0.699
Others	0.60	0.56–0.64	<0.001	0.77	0.62–0.95	0.017
Unknown	0.78	0.70–0.86	<0.001	0.86	0.61–1.21	0.395
Type of vascular access						
Arteriovenous fistula	Reference			Reference		
Arteriovenous graft	1.35	1.18–1.55	<0.001	1.52	1.12–2.04	0.006
Permanent catheter	1.51	1.38–1.65	<0.001	1.52	1.20–1.93	<0.001
Nonpermanent catheter	1.40	1.26–1.56	<0.001	1.40	1.07–1.83	0.013
Unknown	1.00	0.76–1.32	0.999	0.56	0.25–1.28	0.172
Hemoglobin (g/dL)						
10–11.5	Reference			Reference		
<10	1.50	1.38–1.62	<0.001	1.48	1.20–1.82	<0.001
>11.5	1.01	0.89–1.14	0.884	1.32	0.98–1.76	0.066
Serum uric acid (mg/dL)						
3.5–7.5	Reference			Reference		
<3.5	1.27	0.99–1.63	0.053	1.47	0.84–2.58	0.175
>7.5	0.75	0.66–0.85	<0.001	0.88	0.69–1.12	0.300

(Continues)

TABLE 4 (Continued)

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Serum sodium (mEq/L)						
135–145	Reference			Reference		
<135	1.97	1.81–2.14	<0.001	1.23	0.98–1.54	0.077
>145	2.47	1.23–4.95	0.011	-	-	-
Serum potassium (mEq/L)						
3.5–5.5	Reference			Reference		
<3.5	2.14	1.82–2.52	<0.001	1.08	0.63–1.82	0.787
>5.5	1.13	0.91–1.39	0.275	0.91	0.45–1.86	0.795
Serum bicarbonate (mEq/L)						
22–26	Reference			Reference		
<22	1.30	1.18–1.43	<0.001	1.34	1.06–1.71	0.016
>26	1.13	1.03–1.24	0.012	1.13	0.87–1.48	0.357
Serum calcium (mg/dL)						
8–10	Reference			Reference		
<8	1.12	0.97–1.29	0.129	1.04	0.73–1.49	0.816
>10	1.09	0.97–1.23	0.146	1.56	1.11–2.2	0.011
Serum phosphate (mg/dL)						
2.7–4.5	Reference			Reference		
<2.7	1.75	1.55–1.97	<0.001	1.19	0.90–1.56	0.216
4.5–6.0	0.83	0.76–0.91	<0.001	1.22	1.01–1.47	0.038
>6.0	0.85	0.76–0.96	0.006	1.50	1.15–1.95	0.003
Serum albumin (g/dL)						
≥3.5	Reference			Reference		
<3.5	3.06	2.82–3.33	<0.001	2.42	1.94–3.01	<0.001
Serum intact-PTH						
135–585	Reference			Reference		
<130	1.53	1.38–1.70	<0.001	1.29	1.03–1.61	0.027
>585	0.95	0.86–1.06	0.402	0.97	0.74–1.26	0.795
Total cholesterol (mg/dL)						
<200	Reference			Reference		
200–240	0.83	0.70–0.98	0.029	0.86	0.58–1.27	0.443
>240	1.00	0.78–1.29	0.978	0.91	0.48–1.71	0.767
LDL-cholesterol (mg/dL)						
70–100	Reference			Reference		
<70	1.45	1.29–1.62	<0.001	1.38	1.11–1.72	0.004
>100	0.94	0.84–1.06	0.321	1.13	0.87–1.47	0.353
Triglycerides (mg/dL)						
150–500	Reference					
<150	1.10	0.99–1.23	0.087	1.13	0.89–1.43	0.317
>500	1.23	0.71–2.14	0.454	0.96	0.29–3.15	0.940

TABLE 4 (Continued)

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Transferrin saturation (%)						
30–40	Reference			Reference		
<30	1.33	1.19–1.50	<0.001	1.42	1.11–1.80	0.004
>40	1.29	1.11–1.50	0.001	1.18	0.87–1.61	0.294
Ferritin (ng/mL)						
200–500	Reference			Reference		
<200	0.93	0.84–1.04	0.220	1.14	0.9–1.45	0.288
>500	1.09	0.98–1.20	0.109	1.00	0.8–1.25	0.990
spKt/V						
≥1.2	Reference			Reference		
<1.2	1.58	1.39–1.80	<0.001	1.77	1.03–3.05	0.038
URR (%)						
≥65	Reference			Reference		
<65	1.50	1.36–1.65	<0.001	1.40	0.96–2.05	0.083
NPCR						
≥1.2	Reference			Reference		
<1.2	1.34	1.25–1.44	<0.001	1.07	0.86–1.32	0.560

Note: Statistically significant at *p*-value <0.05 determined by Cox regression. Covariates introduced into the multivariate model were gender, age, education level, expense within a dataset, cause of ESKD, type of vascular access, dialysis frequency, hemoglobin, serum uric acid, serum electrolytes, calcium, phosphate, albumin, intact-PTH, lipid profiles, transferrin saturation, ferritin, spKt/V, URR, and NPCR.
Abbreviations: CI, confidence interval; ESKD, end stage kidney disease; HR, hazard ratio; NPCR, normalized protein catabolic rate; PTH, parathyroid hormone; spKt/V, single-pool Kt/V; URR, urea reduction ratio.

survival of 54% [13]. In a survival analysis and risk factors for death in MHD patients conducted in the northeast of Thailand, the regional data showed that the overall probability of survival after 1 year was 0.94 (95% CI; 0.92 to 0.96) [14]. The findings were similar to our Thailand's national registration data, which found a high patient survival rate at 1 year at 93%.

Optimal management of ESRD in MHD patients should be studied more because it is a serious risk factor for mortality and is considered an unquestionable global priority. Hemodialysis patients experience a wide variety of intermediate complications, including anemia, mineral bone disease, hypoalbuminemia, malnutrition, arrhythmias, and cardiac death. A large European cohort of dialysis patients reported that more stringent application of guideline targets was associated with lower mortality [15]. Additionally, a meta-analysis determined various patient characteristics on the risk of mortality in MHD patients and found that multiple factors, including aging, diabetes, anemia, iron study, body mass index, serum albumin, and cardiac biomarkers, influence the risk of mortality and cardiac death in MHD patients [16]. Additionally, low albumin levels, LDL-cholesterol levels, protein intake, and serum phosphate levels could be representations of protein-energy malnutrition in hemodialysis patients and have been linked to increased mortality risk [17]. These factors play a crucial role in assessing the nutritional status and overall health outcomes of individuals undergoing dialysis treatment. Our study attempts to highlight the importance of frequency of dialysis, adequate dialysis, vascular access, electrolyte abnormalities, and nutritional status with patient survival. This is in agreement with previous studies where all factors were an independent predictor of mortality [5–8, 18, 19].

Residual renal function is a powerful predictor of patient survival on dialysis, more so than dialysis clearance alone [20]. Twice-weekly MHD is considered for patients with residual renal urea clearance, and the recommendation for twice-weekly MHD was an extrapolation of urea kinetics in patients who were treated with thrice-weekly hemodialysis [21]. For twice-weekly dialysis, the recommended Kt/V values are different from those for thrice-weekly dialysis. In the United States, the guidelines suggest a minimum spKt/V of 1.2 without rebound and a target value of 1.4 for thrice-weekly dialysis sessions. However, for twice-weekly dialysis, the

TABLE 5 Risk factors for mortality in patients undergoing twice-weekly hemodialysis ($n = 14\,632$).

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Sex						
Female	Reference					
Male	1.09	1.01–1.17	0.025	1.19	0.87–1.62	0.280
Age (years)						
41–65	Reference			Reference		
18–40	0.56	0.48–0.66	<0.001	0.61	0.30–1.25	0.179
>65	1.64	1.52–1.77	<0.001	1.53	1.14–2.04	0.004
Education level						
Primary school or lower	Reference			Reference		
Secondary school	1.00	0.90–1.11	0.934	1.28	0.85–1.91	0.237
High school	0.75	0.66–0.86	<0.001	1.11	0.70–1.77	0.651
Vocational/High vocational certificate	0.64	0.53–0.76	<0.001	0.54	0.24–1.21	0.136
Bachelor degrees or higher	0.69	0.62–0.78	<0.001	0.80	0.50–1.26	0.331
Unknown	1.15	1.01–1.30	0.029	1.55	0.95–2.54	0.082
Expense within a dataset						
Universal coverage (UC)	Reference			Reference		
Social security scheme	0.50	0.44–0.57	<0.001	1.10	0.63–1.90	0.745
Government/State enterprise officer	0.92	0.84–1.01	0.096	1.41	0.96–2.07	0.083
Self-payment	0.88	0.80–0.98	0.015	1.09	0.74–1.62	0.655
Others	0.89	0.60–1.32	0.553	0.77	0.17–3.38	0.726
Unknown	1.03	0.88–1.21	0.683	1.75	0.98–3.12	0.060
Cause of ESKD						
Diabetic nephropathy	Reference			Reference		
Hypertensive nephropathy	0.59	0.42–0.84	0.003	0.72	0.26–2.02	0.533
Glomerulonephritis	0.41	0.20–0.82	0.011	0.37	0.05–2.94	0.349
Presumed glomerulonephritis	0.71	0.52–0.97	0.031	1.00	0.30–3.30	0.998
Others	0.67	0.62–0.72	<0.001	0.46	0.33–0.63	<0.001
Unknown	0.82	0.73–0.91	<0.001	0.70	0.45–1.09	0.110
Type of vascular access						
Arteriovenous fistula	Reference			Reference		
Arteriovenous graft	1.12	0.92–1.36	0.265	1.65	1.02–2.69	0.042
Permanent catheter	1.59	1.43–1.76	<0.001	1.08	0.76–1.54	0.656
Nonpermanent catheter	1.69	1.52–1.88	<0.001	1.62	1.15–2.28	0.005
Unknown	0.68	0.43–1.09	0.109	1.15	0.40–3.28	0.792
Hemoglobin (g/dL)						
10–11.5	Reference			Reference		
<10	1.69	1.53–1.86	<0.001	2.13	1.59–2.86	<0.001
>11.5	0.95	0.79–1.14	0.571	0.95	0.56–1.62	0.855
Serum uric acid (mg/dL)						
3.5–7.5	Reference			Reference		
<3.5	1.32	0.89–1.95	0.170	1.68	0.65–4.32	0.285
>7.5	0.74	0.65–0.84	<0.001	0.89	0.67–1.18	0.405

TABLE 5 (Continued)

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Serum sodium (mEq/L)						
135–145	Reference			Reference		
<135	1.83	1.66–2.02	<0.001	1.21	0.89–1.65	0.222
>145	3.05	1.37–6.81	0.006	-	-	-
Serum potassium (mEq/L)						
3.5–5.5	Reference			Reference		
<3.5	2.15	1.83–2.53	<0.001	0.94	0.48–1.85	0.861
>5.5	1.12	0.91–1.37	0.282	1.42	0.68–2.96	0.354
Serum bicarbonate (mEq/L)						
22–26	Reference			Reference		
<22	1.03	0.93–1.15	0.515	1.06	0.76–1.48	0.725
>26	1.09	0.97–1.24	0.157	0.81	0.55–1.21	0.310
Serum calcium (mg/dL)						
8–10	Reference			Reference		
<8	1.39	1.22–1.59	<0.001	1.56	1.03–2.37	0.036
>10	1.16	0.97–1.4	0.106	1.81	1.02–3.21	0.042
Serum phosphate (mg/dL)						
2.7–4.5	Reference			Reference		
<2.7	1.84	1.59–2.13	<0.001	1.98	1.44–2.74	<0.001
4.5–6.0	0.92	0.83–1.03	0.146	1.33	1.05–1.68	0.016
>6.0	0.97	0.85–1.10	0.601	1.53	1.13–2.06	0.005
Serum albumin (g/dL)						
≥3.5	Reference			Reference		
<3.5	3.20	2.91–3.51	<0.001	3.25	2.43–4.34	<0.001
Serum intact-PTH						
135–585	Reference			Reference		
<130	1.80	1.59–2.03	<0.001	1.44	1.06–1.96	0.019
>585	0.90	0.77–1.06	0.225	0.79	0.51–1.22	0.289
Total cholesterol (mg/dL)						
<200	Reference			Reference		
200–240	0.94	0.77–1.15	0.563	0.81	0.48–1.37	0.429
>240	1.27	0.96–1.68	0.089	0.81	0.37–1.77	0.594
LDL-cholesterol (mg/dL)						
70–100	Reference			Reference		
<70	1.16	1.01–1.33	0.041	0.98	0.72–1.35	0.916
>100	0.97	0.84–1.12	0.673	1.49	1.05–2.10	0.024
Triglycerides (mg/dL)						
150–500	Reference					
<150	0.98	0.86–1.12	0.747			
>500	0.57	0.18–1.78	0.336			

(Continues)

TABLE 5 (Continued)

	Univariate			Multivariate		
Factors	**Crude HR**	**95%CI**	***p*-Value**	**Adjusted HR**	**95%CI**	***p*-Value**
Transferrin saturation (%)						
30–40	Reference			Reference		
<30	1.16	1.01–1.33	0.036	0.93	0.67–1.29	0.675
>40	1.25	1.05–1.48	0.013	0.99	0.66–1.49	0.970
Ferritin (ng/mL)						
200–500	Reference			Reference		
<200	1.01	0.87–1.19	0.867	0.84	0.55–1.27	0.405
>500	1.16	1.03–1.31	0.014	0.87	0.65–1.18	0.380
spKt/V						
≥1.8	Reference			Reference		
<1.8	1.26	1.17–1.37	<0.001	0.96	0.71–1.30	0.806
URR (%)						
≥65	Reference			Reference		
<65	1.56	1.38–1.77	<0.001	0.97	0.52–1.80	0.928
NPCR						
≥0.8	Reference			Reference		
<0.8	2.89	2.56–3.26	<0.001	2.20	1.21–3.99	0.010

Note: Statistically significant at p-value <0.05 determined by Cox regression. Covariates introduced into the multivariate model were gender, age, education level, expense within a dataset, cause of ESKD, type of vascular access, dialysis frequency, hemoglobin, serum uric acid, serum electrolytes, calcium, phosphate, albumin, intact-PTH, lipid profiles, transferrin saturation, ferritin, spKt/V, URR, and NPCR.

Abbreviations: CI, confidence interval; ESKD, end stage kidney disease; HR, hazard ratio; NPCR, normalized protein catabolic rate; PTH, parathyroid hormone; spKt/V, single-pool Kt/V; URR, urea reduction ratio.

specific recommended Kt/V values may vary. In Thailand, the guidelines suggest a minimum spKt/V of 1.8 and a target value of 2.1 for twice-weekly dialysis sessions based on using the calculated equivalent renal urea clearance (EKR) values of >13 mL/min [22]. Several studies have demonstrated a comparable short-term survival rate between patients with twice- and thrice-weekly MHD [23, 24]. A recent study comparing the clinical outcomes of twice-weekly and thrice-weekly hemodialysis in patients with residual kidney function found that patients undergoing twice-weekly HD had non-inferior outcomes for mortality and cardiovascular event hospitalization [25]. Another two studies comparing practice patterns and outcomes of twice-weekly and thrice-weekly MHD patients found no significant difference in mortality rates between the two groups [26, 27]. However, these studies had limitations, including their retrospective nature, small sample size, short duration of follow-up, varying frequency of laboratory monitoring intervals, lack of detailed data on hospitalizations, and clear documentation of comorbidities. In contrast, our study attempts to highlight the importance of frequency of dialysis and indicates that twice-weekly hemodialysis is associated with higher mortality rates (HR 1.34; 95% 1.14–1.59) compared to thrice-weekly hemodialysis. However, our study utilizes registration data from Thailand, and the findings likely resulted from a selection bias due to patient selection, individualized treatment for dialysis patients based on clinical features and socioeconomic factors, and the lack of determination of residual kidney function, which could have affected patients' survival.

This is a large population-based study that reflects the overall status of MHD patients in Thailand and is the first large study derived from Thailand's national registration data on survival analysis. Several limitations associated with the present study warrant mention. First, our study was a retrospective study, and bias cannot be denied because the data were collected from medical records and not entirely reported in all cases. Second, we were not able to consider the cause of mortality because it was not available in the dataset. More variables which could have some impact on the survival. Inflammatory markers, which could modify the relationship of some of the variables with survival. Third, there are limitations on dynamic changes in all parameters of MHD patients.

More large prospective cohort studies may be required to emphasize and confirm the results of this study.

In summary, mortality rates of patients on MHD in Thailand's national registration data were high, and patients with diabetic nephropathy (36.7%), permanent catheter (51.9%), and twice-weekly MHD (49.2%) had the lowest 5-year survival rate. Factors such as age, vascular access, dialysis frequency, anemia with iron deficiency, inadequate dialysis, low protein intake, anemia, abnormal electrolytes, and bone mineral disorders were associated with all-cause mortality in hemodialysis patients in Thailand.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author upon request.

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