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ORIGINAL ARTICLE

Temporal changes and risk factors for death from early withdrawal within 12 months of dialysis initiation—a cohort study

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ABSTRACT

Background. Mortality risk is high soon after dialysis initiation in patients with kidney failure, and dialysis withdrawal is a major cause of early mortality, attributed to psychosocial or medical reasons. The temporal trends and risk factors associated with cause-specific early dialysis withdrawal within 12 months of dialysis initiation remain uncertain.

Methods. Using data from the Australia and New Zealand Dialysis and Transplant Registry, we examined the temporal trends and risk factors associated with mortality attributed to early psychosocial and medical withdrawals in incident adult dialysis patients in Australia between 2005 and 2018 using adjusted competing risk analyses.

Results. Of 32 274 incident dialysis patients, 3390 (11%) experienced death within 12 months post-dialysis initiation. Of these, 1225 (36%) were attributed to dialysis withdrawal, with 484 (14%) psychosocial withdrawals and 741 (22%) medical withdrawals. These patterns remained unchanged over the past two decades. Factors associated with increased risk of death from early psychosocial and medical withdrawals were older age, dialysis via central venous catheter, late referral and the presence of cerebrovascular disease; obesity and Asian ethnicity were associated with decreased risk. Risk factors associated with early psychosocial withdrawals were underweight and higher socioeconomic status. Presence of peripheral vascular disease, chronic lung disease and cancers were associated with early medical withdrawals.

Conclusions. Death from dialysis withdrawal accounted for >30% of early deaths in kidney failure patients initiated on dialysis and remained unchanged over the past two decades. Several shared risk factors were observed between mortality attributed to early psychosocial and medical withdrawals.

Keywords: dialysis, frailty, kidney supportive care, mortality, treatment withdrawal

INTRODUCTION

Withdrawal from kidney replacement therapy is a major cause of death in patients on dialysis. In Australia and New Zealand, the proportion of deaths in incident dialysis patients attributed to dialysis withdrawal increased by 2-fold between 1997 (15%) and 2017 (30%) [1–3]. A similar trend has been observed in the USA, Canada and the UK [4–7]. The reason for the upward

KEY LEARNING POINTS

What is already known about this subject?

- dialysis withdrawal is a major cause of death in patients with kidney failure, and international registry reports suggested temporal increase in withdrawal-related mortality; and
- risk factors associated with mortality from dialysis withdrawal were older age, Caucasian ethnicity, late nephrologist referral and haemodialysis as initial dialysis modality.

What this study adds?

- the proportion of early mortality from dialysis withdrawal has remained unchanged in Australia since 2005;
- the annual proportion of early mortality attributed to medical withdrawals consistently surpassed the proportion of psychosocial withdrawals; and
- early mortality attributed to psychosocial and medical withdrawals was associated with similar risk factors.

What impact this may have on practice or policy?

- recognizing the patient at risk of early mortality attributed to dialysis withdrawal may better inform the shared decision-making process, empower patient-focused treatment choices and facilitate advanced care planning.

trend is likely multifactorial including patient selection for dialysis initiation, cultural acceptance of dialysis withdrawal and accessibility of kidney supportive care [3, 8, 9].

Early mortality after dialysis initiation is known to be high [10–12]. A recent US Renal Data System (USRDS) registry study suggested that the risk factors associated with death from dialysis withdrawal were similar to other causes of death within 6-month post-initiation of haemodialysis (HD) [13]. Risk factors associated with death from cause-specific withdrawals have not been studied previously. A greater understanding of these risk factors will better inform shared decision-making, assist appropriate patient selection for dialysis initiation and facilitate institution of pertinent resources allocation.

The aims of this study were 2-fold. First, we examined the temporal trends of death attributed to dialysis withdrawal related to psychosocial and medical reasons in the first 12 months post-dialysis initiation. Secondly, we assessed the risk factors associated with death attributed to early dialysis withdrawal related to psychosocial and medical causes.

MATERIALS AND METHODS

Study cohort

Incident adult patients (aged ≥18 years) commencing maintenance dialysis for kidney failure in Australia between 2005 and 2018 were included using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) registry, censored on 31 December 2018. The study period was restricted to 2005–18 because ANZDATA expanded the pre-specified withdrawal-related causes of death in October 2003 [14], which was associated with a step-wise increase in deaths from withdrawal between 2004 and 2005. Patients who had commenced dialysis following failure of pre-emptive kidney transplant were also included. Patients who had recovered kidney function or had received a kidney transplant within 12 months after dialysis initiation were excluded (Figure 1). The conduct of this study was approved by the University of Western Australia Human Research Ethics Committee, Perth, Australia. The study was conducted in accordance with Strengthening the Reporting of

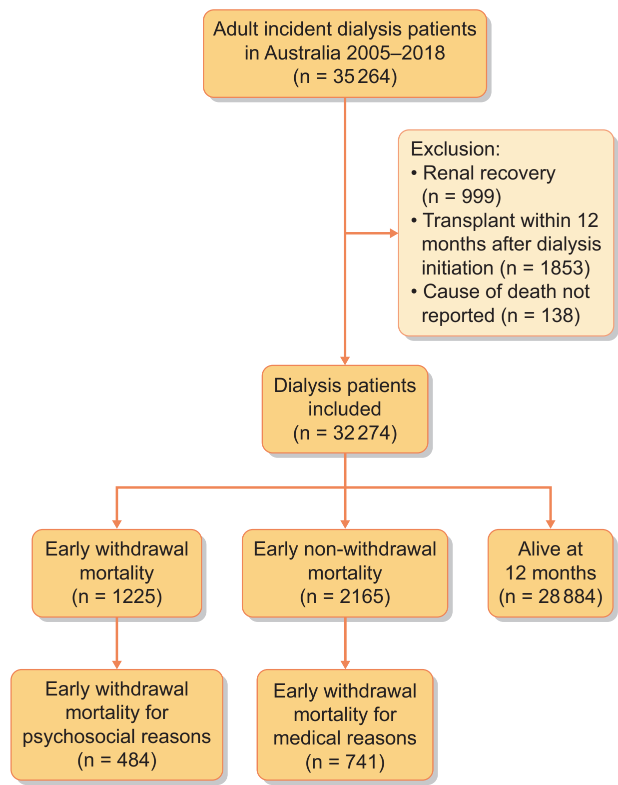

FIGURE 1: Patient flowchart for adult incident dialysis patients in Australia between 2005 and 2018.

Observational Studies in Epidemiology (STROBE) guidelines [15].

Data collection

Patient and treatment characteristics at time of dialysis initiation were extracted from the ANZDATA registry, including age, sex, ethnicity, body mass index (BMI), geographical location (urban, regional and remote), socioeconomic status (SES; measured by Index of Relative Socio-economic Advantage and Disadvantage using postcode and categorized into tertiles) [16], era (categorized as 2005–09, 2010–13 and 2014–18), initial dialysis modality, dialysis access [native arteriovenous fistula (AVF), central venous catheter (CVC), synthetic graft, peritoneal dialysis (PD) catheter], smoking status, comorbid medical conditions (presence or absence of chronic lung disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease, diabetes mellitus and prior cancer), late nephrologist referral (defined as <3 months before dialysis initiation), primary cause of kidney failure (diabetic nephropathy, glomerulonephritis, hypertensive nephrosclerosis, cystic kidney disease and other), state/territory at dialysis initiation and prior pre-emptive kidney transplantation. Dialysis modality was categorized as HD (both facility HD and home HD) and PD (both continuous ambulatory PD and automated PD). The categorization of the causes of kidney failure was reported to the ANZDATA registry by each treating centre and not verified by the registry. Baseline centre-level characteristics included centre size (calculated as the mean annual number of patients on incident HD, PD or either dialysis modality) and transplant centre. Centre size was divided into quartiles by patient number and grouped into three categories by combining the second and third quartiles. The dialysis centre was defined as the centre where dialysis was initiated, but did not consider the potential transfer to alternative dialysis centre(s) over time.

Clinical outcomes

The primary outcome was death from dialysis withdrawal attributed to psychosocial or medical reasons, separately, within 12 months after dialysis initiation. Death from dialysis withdrawal for psychosocial reasons included psychosocial withdrawal and treatment refusal. Death from dialysis withdrawal from medical reasons included comorbid medical conditions (cardiovascular disease, cerebrovascular disease, peripheral vascular disease or cancer), access difficulties or other reasons. The causes of death were pre-specified in the ANZDATA registry survey form [17].

Statistical analysis

The baseline data were expressed as numbers (proportion) for categorical data, mean [standard deviation (SD)] for normally distributed continuous data and median and interquartile range (IQR) for non-normally distributed continuous data. The annual trends of cause-specific early mortality and cause-specific early withdrawal-related mortality were examined and expressed as proportion of total early mortality and annual incidence rates. Time trends of the incidence rates were examined using Joinpoint regression [18]. Mann–Kendall test was used to assess the significance of temporal variations. The association between covariates and early deaths attributed to psychosocial or medical withdrawals was examined using adjusted Cox proportional hazard regressions followed by competing risk regression analyses using the method described by Fine and Gray [19], expressed as subdistribution hazard ratios (SHRs). Covariates included in the competing risk models were identical to those included in the Cox regression models. The starting time in all models was time of dialysis initiation. The proportional hazard assumptions of all models were checked graphically by plotting the Schoenfeld residuals. Collinearity between covariates was checked by correlation matrix of coefficients. Initial dialysis modality was not included in the models because of collinearity with initial dialysis access. For all models, causes of death other than the outcome were considered as competing events. Kidney transplantation was not considered as a competing event as patients who received kidney transplantation within 12 months after dialysis initiation were excluded. The centre-level risk factors associated with early mortality were examined using adjusted γ-distributed Cox shared frailty model, considering initial dialysis centre as the cluster. Covariates with $P < 0.1$ in the univariate models were included in the multivariable-adjusted models.

Sensitivity analysis restricted to incident patients on dialysis for ≥90 days was conducted because of potential ascertainment bias from underreporting of patients on dialysis for <90 days. Statistical evaluation was performed using SPSS version 27, STATA version IC 15.1 and Joinpoint version 4.8.0.1 statistical programmes. P-values <0.05 were considered statistically significant.

RESULTS

The study cohort comprised 32 274 incident patients who commenced dialysis between 2005 and 2018 in Australia, with 199 (0.6%) having commenced dialysis following pre-emptive kidney transplant failure. The overall follow-up period was 29 046 person-years. Among all incident patients, 3390 (11%) patients experienced early death within 12 months post-dialysis initiation. Of those, 484 (14%) died from early withdrawal for psychosocial reasons, and 741 (22%) for medical reasons (Figure 1). The mean ± SD age at dialysis initiation was 61.9 ± 14.8 years. Patients who experienced early withdrawal were more likely to be Caucasian and to have commenced HD as the initial dialysis modality, compared with patients who were alive at 12 months post-dialysis initiation (85% versus 66%, $P < 0.001$; 87% versus 74%, $P < 0.001$, respectively). The 32 274 incident patients received dialysis in 97 centres. Table 1 shows the baseline patient and centre characteristics of the study cohort.

Temporal trend in the causes of early mortality

The proportion of death from early withdrawal remained unchanged between 2005 and 2017 and accounted for 33–38% of all-cause early mortality. The annual proportions of early psychosocial and medical withdrawals also remained unchanged with the proportion of medical withdrawals consistently surpassing psychosocial withdrawals (Figure 2A). Linear trends were observed in Joinpoint regression for incidence rates of death from early withdrawal. The incidence rates of early

Table 1. Baseline characteristics of adult incident dialysis patients in Australia between 1998 and 2018

	Early death from psychosocial withdrawal	Early death from medical withdrawal	Early death from non-withdrawal causes	Overall
Patient-level characteristics				
Number of patients	484	741	2165	32 274
Age starting dialysis (mean ± SD), years	71.1 ± 12.5	70.9 ± 11.2	67.2 ± 13.3	61.9 ± 14.8
Men, *n* (%)	285 (59)	451 (61)	1367 (63)	20 001 (62)
Ethnicity, *n* (%)				
Caucasians	406 (84)	636 (86)	1634 (76)	21 752 (67)
Asians	17 (4)	22 (3)	133 (6)	3084 (10)
Indigenous[a]	39 (8)	46 (6)	228 (11)	3834 (12)
Others	22 (5)	37 (5)	170 (8)	3604 (11)
BMI (mean ± SD), kg/m^2	26.7 ± 6.7	26.8 ± 6.1	27.5 ± 7.0	28.5 ± 7.1
BMI categories, *n* (%)				
Underweight	27 (6)	30 (4)	100 (5)	895 (3)
Normal	172 (38)	276 (40)	748 (37)	9702 (31)
Overweight	148 (33)	219 (31)	619 (30)	10 061 (32)
Obese	105 (23)	173 (25)	579 (28)	10 980 (35)
Dialysis modality, *n* (%)				
PD	69 (14)	92 (12)	381 (18)	8210 (25)
HD	415 (86)	649 (88)	1784 (82)	24 064 (75)
Home HD	2 (0.4)	2 (0.3)	2 (0.1)	266 (0.8)
Dialysis access, *n* (%)				
Native AVF	85 (18)	138 (19)	398 (19)	9696 (30)
CVC	320 (67)	501 (68)	1347 (63)	13 673 (43)
Synthetic graft	6 (1)	8 (1)	29 (1)	455 (1)
PD catheter	101 (14)	92 (12)	381 (18)	8210 (26)
Smoking status, *n* (%)				
Non-smoker	205 (43)	304 (42)	887 (42)	14 671 (46)
Current smoker	58 (12)	78 (11)	268 (13)	4067 (13)
Ex-smoker	213 (45)	347 (48)	967 (46)	13 057 (41)
Comorbidities, *n* (%)				
Chronic lung disease	100 (21)	166 (23)	509 (24)	4229 (13)
Coronary artery disease	214 (45)	365 (49)	1161 (54)	11 265 (35)
Peripheral vascular disease	134 (28)	234 (32)	641 (30)	5979 (19)
Cerebrovascular disease	103 (21)	169 (23)	389 (18)	3783 (12)
Diabetes mellitus				
Type 1 diabetes mellitus	15 (3)	20 (3)	86 (4)	1370 (4)
Type 2 diabetes mellitus	237 (49)	354 (48)	1079 (50)	14 977 (47)
Cancer	51 (11)	223 (30)	335 (16)	3804 (12)
Late nephrologist referral	150 (31)	263 (36)	673 (32)	6571 (21)
Cause of kidney failure, *n* (%)				
Diabetic nephropathy	179 (37)	248 (34)	837 (39)	12 323 (38)
Glomerulonephritis	62 (13)	81 (11)	246 (11)	6168 (19)
Hypertension nephrosclerosis	94 (19)	133 (18)	388 (18)	4834 (15)
Cystic kidney disease	9 (2)	9 (1)	43 (2)	1786 (6)
Others	140 (29)	270 (36)	651 (30)	7163 (22)
Geographical location, *n* (%)				
Urban	326 (68)	481 (66)	1447 (67)	21 399 (67)
Regional	130 (27)	233 (32)	583 (27)	8541 (27)
Remote	27 (6)	20 (3)	117 (5)	2058 (6)
SES, *n* (%)				
Low	147 (30)	194 (27)	633 (30)	10 007 (31)
Mid	166 (34)	317 (43)	832 (39)	12 135 (38)
High	170 (35)	222 (30)	680 (32)	9842 (31)
State/territory at dialysis initiation, *n* (%)				
New South Wales	105 (22)	196 (27)	708 (33)	10 096 (31)
Queensland	107 (22)	168 (23)	437 (20)	6344 (20)
Victoria	121 (25)	180 (24)	463 (21)	7664 (24)
Australian Capital Territory	8 (2)	27 (4)	41 (2)	664 (2)
South Australia	48 (10)	58 (8)	132 (6)	2260 (7)
Western Australia	68 (14)	83 (11)	295 (14)	3408 (11)
Northern Territory	15 (3)	10 (1)	58 (3)	1237 (4)
Tasmania	12 (3)	19 (3)	31 (1)	601 (2)

Continued

Table 1. Continued

	Early death from psychosocial withdrawal	Early death from medical withdrawal	Early death from non-withdrawal causes	Overall
Era, *n* (%)				
2005–09	185 (38)	288 (39)	889 (41)	10 769 (33)
2010–13	149 (31)	220 (30)	599 (28)	8764 (27)
2014–18	150 (31)	233 (31)	677 (31)	12 741 (40)
Pre-emptive transplant, *n* (%)	1 (0.2)	0 (0)	9 (0.4)	199 (0.6)
Centre-level characteristics				
Number of centres	63	72	75	97
Transplant centre, *n* (%)	16 (28)	16 (24)	16 (24)	18 (21)
Centre size, median (IQR)				
Incidence dialysis patient/year	28 (11–51)	22 (9–46)	22 (8–45)	13 (2–40)
Incidence PD patient/year	6 (1–14)	5 (0–12)	5 (0–12)	2 (0–10)
Incidence HD patient/year	21 (10–38)	17 (6–36)	17 (6–36)	12 (2–31)
State/territory at dialysis initiation, *n* (%)				
New South Wales	20 (32)	24 (33)	26 (35)	32 (33)
Queensland	17 (27)	19 (26)	21 (28)	29 (30)
Victoria	13 (21)	15 (21)	15 (20)	21 (22)
Australian Capital Territory	1 (2)	2 (3)	1 (1)	2 (2)
South Australia	4 (6)	4 (6)	4 (5)	5 (5)
Western Australia	4 (6)	4 (6)	4 (5)	4 (4)
Northern Territory	2 (3)	2 (3)	2 (3)	2 (2)
Tasmania	2 (3)	2 (3)	2 (3)	2 (2)

[a]Indigenous—Aboriginal and Torres Strait Islander.

withdrawal-related mortality reduced from 5.3 deaths/100 person-years in 2006 to 3.1 deaths/100 person-years in 2018 ($\tau = -0.59$, $P = 0.06$), attributed to reduction of both psychosocial and medical withdrawals (Figure 2B). Figure 2C shows the annual proportions of cause-specific early mortality in Australia between 2005 and 2017, and Supplementary data, Figure S1 shows the mortality rates of early dialysis withdrawals stratified by months after dialysis initiation.

Risk factors associated with death attributed to dialysis withdrawal

The common risk factors associated with increased risk of early mortality attributed to psychosocial and medical withdrawals were older age, dialysis access via CVC, late referral and the presence of cerebrovascular disease. The common risk factors associated with decreased risk were obesity and Asian ethnicity. Underweight and high SES were associated with increased risk for early psychosocial withdrawal only. Presence of peripheral vascular disease, chronic lung disease and cancer at time of dialysis initiation were associated with increased risk for early medical withdrawal only (Figure 3 and Supplementary data, Table S1).

For every decade increment of age, the adjusted SHRs were 1.65 (95% confidence interval 1.50–1.82) for early psychosocial withdrawal and 1.51 (1.40–1.62) for early medical withdrawal. For Asian patients, the adjusted SHRs were 0.34 (0.21–0.56) for early psychosocial withdrawal and 0.36 (0.24–0.56) for early medical withdrawal, compared with Caucasian patients.

Compared with patients with normal weight, the adjusted SHRs for underweight patients were 1.86 (1.23–2.82) for early psychosocial withdrawal and 1.19 (0.80–1.76) for early medical withdrawal. In contrast, for obese patients, the adjusted SHRs were 0.59 (0.46–0.78) for early psychosocial withdrawal and 0.66 (0.54–0.81) for early medical withdrawal.

For late nephrologist referral, the adjusted SHRs were 1.33 (1.07–1.64) for early psychosocial withdrawal and 1.51 (1.28–1.79) for early medical withdrawal. Compared with patients who initiated dialysis via native AVF, the adjusted SHRs for patients who initiated dialysis via CVC were 2.43 (1.87–3.15) for psychosocial withdrawal and 1.99 (1.62–2.43) for medical withdrawal. No statistically significant association was observed between dialysis initiation via synthetic graft or PD catheter with early psychosocial or medical withdrawal.

The presence of vascular disease was associated with death from early withdrawal for psychosocial and medical reasons. Among patients with cerebrovascular disease, the adjusted SHRs were 1.51 (1.20–1.91) for early psychosocial withdrawal and 1.62 (1.34–1.92) for early medical withdrawal. For peripheral vascular disease, the adjusted SHRs were 1.25 (1.00–1.56) for early psychosocial withdrawal and 1.51 (1.27–1.80) for early medical withdrawal. For chronic lung disease, the adjusted SHRs were 1.25 (0.99–1.58) for early psychosocial withdrawal and 1.31 (1.09–1.58) for early medical withdrawal. The presence of cancer was associated with a decreased risk for early psychosocial withdrawal (SHR = 0.55, 0.40–0.75) but an increased risk for early medical withdrawal mortality (SHR = 2.05, 1.74–2.43).

Sex, era and geographical location were not associated with early death from psychosocial or medical withdrawal. Compared with middle SES, high SES was associated with increased risk for early psychosocial withdrawal (SHR = 1.33, 1.06–1.67), but no association was observed for low SES. Variability in the risk of early mortality from psychosocial or medical withdrawal was observed between different states and territories in Australia. The risk factors associated with early

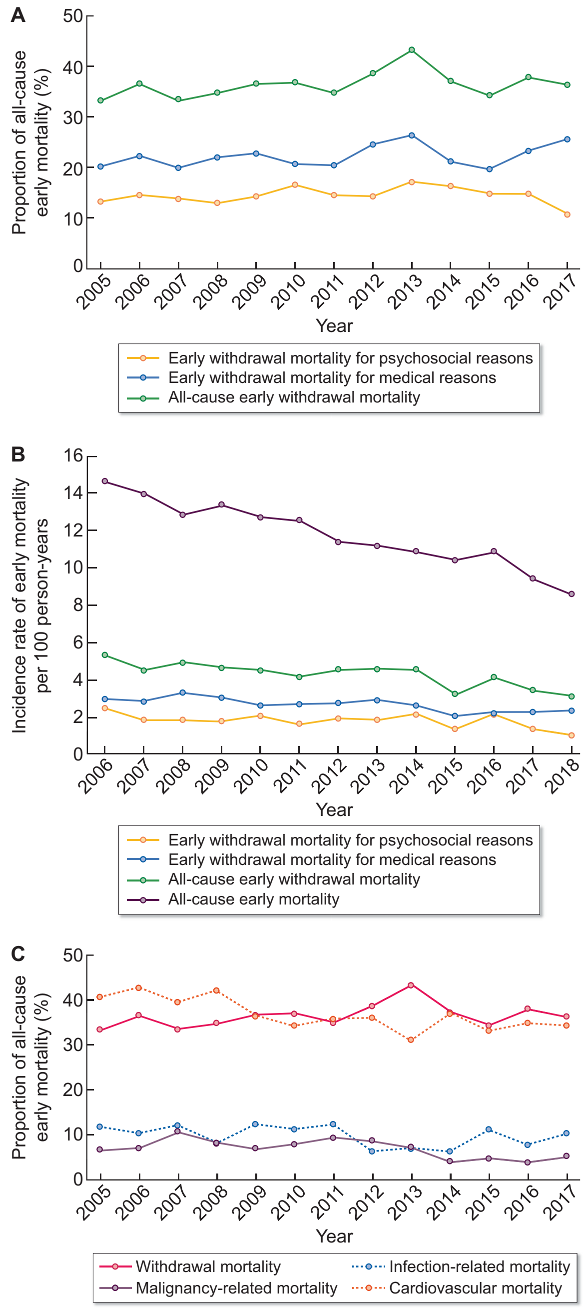

FIGURE 2: (**A**) Annual proportions of early mortality attributed to dialysis withdrawal, stratified by psychosocial and medical withdrawals, in Australia between 2005 and 2017. (**B**) Annual incidence rates of early mortality attributed to dialysis withdrawal, stratified by psychosocial and medical withdrawals, in Australia between 2006 and 2018 ($\tau = -0.33$, $P = 0.1$ for early psychosocial withdrawal, $\tau = -0.56$, $P = 0.009$ for early medical withdrawal and $\tau = -0.59$, $P = 0.006$ for all-cause early withdrawal). (**C**) Annual proportion of early mortality, stratified by causes of early mortality, in Australia between 2005 and 2017.

psychosocial and medical withdrawals within the 12 months post-dialysis initiation are shown in Supplementary data, Table S1. Cox regression analyses showed similar estimates of the same risk factors. Centre-level covariates including centre size and transplant centre were not associated with death from early withdrawal.

Sensitivity analysis

In the sensitivity analysis restricted to incident patients on dialysis for >90 days, similar estimates were observed for age, ethnicity, underweight, dialysis access and presence of co-morbid medical conditions. No association was observed between late referral and early psychosocial withdrawal. Low

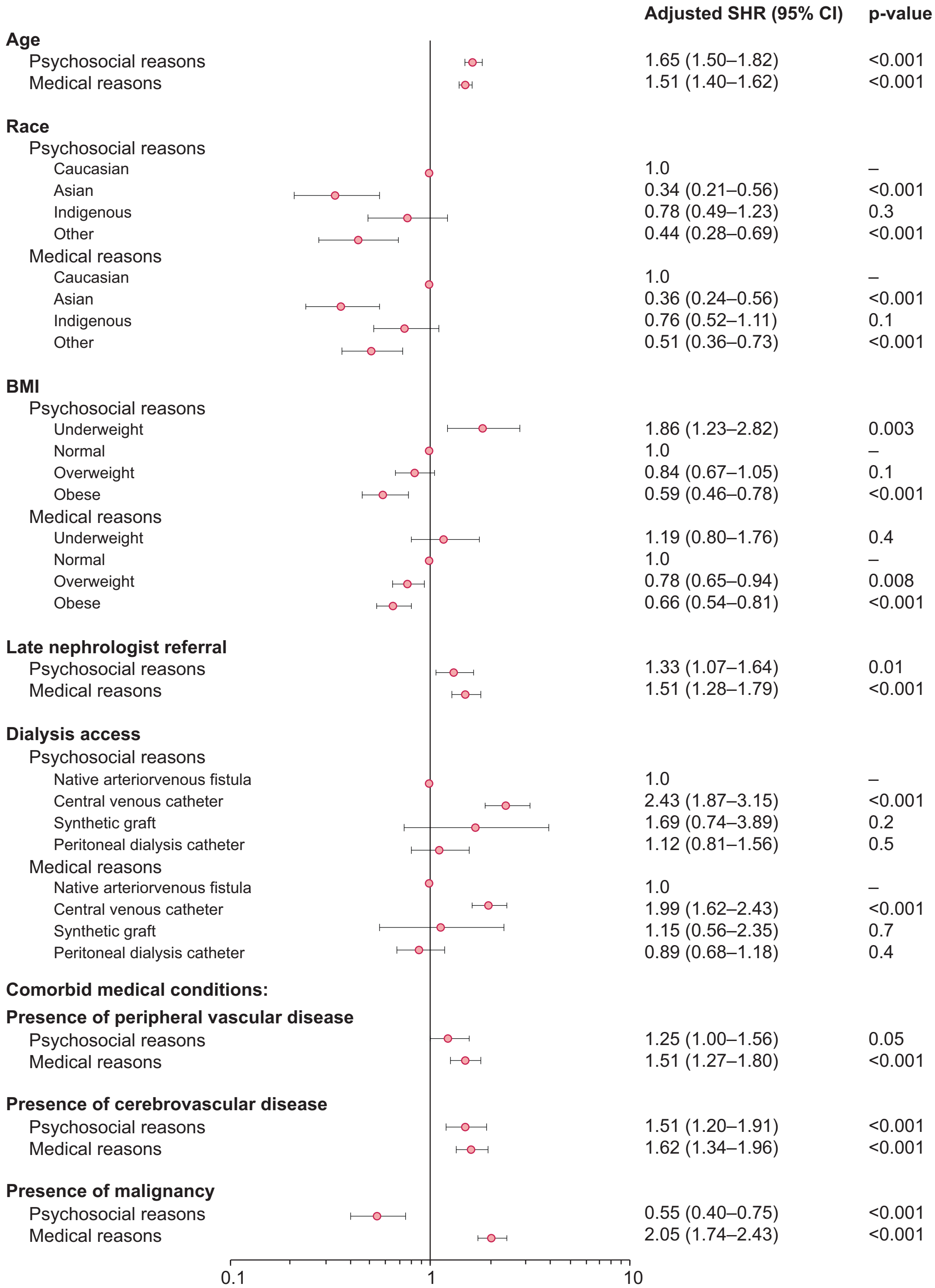

FIGURE 3: Competing risk analyses of factors associated with early mortality attributed to dialysis withdrawal for psychosocial and medical reasons.

SES was an additional risk factor for early psychosocial withdrawal (SHR = 1.39, 1.06–1.81) (Supplementary data, Table S2).

DISCUSSION

In this observational cohort study of incident dialysis patients in Australia, one in three deaths within the first 12 months post-dialysis initiation was attributed to early dialysis withdrawal, and the proportion remained unchanged over the last two decades. There were several common risk factors associated with both psychosocial and medical withdrawals including older age, Caucasian ethnicity and presence of prevalent comorbidities. These findings suggest that early identification and education relating to the risks and benefits of dialysis treatment may allow for a more informed shared decision-making process.

Our study showed early withdrawal had become the most common cause of early death after dialysis initiation in Australia, surpassing cardiovascular mortality in recent years, despite a reduction in the incidence rates of early dialysis withdrawal that was likely related to the advances in medical interventions and management strategies and the increased incidence of patients on a conservative, non-dialysis pathway [20, 21]. For patients who withdrew from dialysis, medical withdrawal consistently outnumbered psychosocial withdrawal annually. A Canadian study showed almost two in three patients with kidney failure regretted their decision to commence dialysis [22]. Although responses to questionnaires may not accurately reflect real-life decisions, the high proportion of early dialysis withdrawal highlighted in our study supports the likelihood of patients' preference for prioritizing a better quality of life (QoL) over survival. Providing adequate information forms an important part of a legally valid informed consent to dialysis [23]. Tailoring resource allocation to facilitate the transition from survival-oriented to patient-focused decision-making process and to promote the option of a conservative, non-dialysis pathway in selected patient groups may minimize early withdrawal and unnecessary morbidity related to dialysis treatment [8, 10].

Contrary to other studies, our study has shown that the proportion of patients who had experienced early dialysis withdrawal has remained unchanged over the last two decades [4–7, 24]. As our study focused on early mortality within 12 months post-dialysis initiation, our primary outcome might include patients on palliative dialysis for which early withdrawal was an expected outcome [25]. It is noteworthy that ANZDATA registry reporting was revised in October 2003, with reclassification of withdrawal-related deaths [14, 17]. Hence, the temporal increase in dialysis withdrawal observed in previous ANZDATA studies may be related to misclassification bias [14, 24]. Similarly, the definition of death from dialysis withdrawal had been revised several times in the USRDS [26]. When interpreting and comparing temporal and geographical variations in withdrawal-related mortality, it is important to recognize the differences in definition of dialysis withdrawal.

With advances in dialysis technology and treatments of life-threatening conditions, a greater number of older, frailer patients with kidney failure are being considered for dialysis [27]. However, dialysis initiation is known to be associated with significant decline in functional status [28]. In our study, older age, underweight and the presence of prevalent comorbidities were associated with increased risks for early withdrawals and were likely surrogate markers for frailty, although this domain of health is not collected by the ANZDATA registry [28–32]. Dialysis via CVC and late referral are known to be associated with significant disease and symptom burdens, which may result in higher prevalence of frailty [33–36]. Frailty is a geriatric syndrome that is closely associated with comorbidity and disability but also encompasses physiological decline. It is expected that frail patients are more likely to withdraw from dialysis due to poor health-related QoL and cognitive impairment [37–39]. Many studies are currently evaluating the best-fit frailty assessment tool for patients with kidney failure [27]. Incorporating frailty assessment into the decision-making process and treatment planning can potentially reduce the increasing burden of early dialysis withdrawal.

In our study, the risk of early medical withdrawals doubled in patients with prior cancer, compared with those without; however, the risk halved for early psychosocial withdrawals. The reason for this observation is unclear but may be related to the progressive nature of cancer in combination with delayed diagnosis and limited cancer treatment options in patients with kidney failure [40, 41]. Withdrawal of treatment in patients with prior cancer might consist of both dialysis withdrawal and withdrawal/withholding of anticancer therapy, and therefore was more likely to be considered as medical withdrawal instead of psychosocial withdrawal.

Caucasians have been reported to have a greater risk of dialysis withdrawal attributed to social supports and cultural acceptance of treatment withdrawal [24, 42]. Although our study showed similar findings, it is difficult to ascertain the correlation due to the high proportion (70%) of Caucasian dialysis patients in Australia, which was also observed in other dialysis withdrawal studies [6, 13, 24]. In many non-Western countries, dialysis initiation and withdrawal may not be based on patients' preferences, due to systemic differences in dialysis resources, palliative care access and ethico-legal regulations [43, 44]. Studies collating non-Caucasian dialysis patients in Western countries or those in non-Western countries where dialysis withdrawal is legally permitted may provide more insights into racial, religious and cultural differences in the acceptance of dialysis withdrawal.

A non-linear association between SES and early psychosocial withdrawal was observed in this study. This might reflect dissimilarities in health literacy, healthcare access and psychosocial supports between patients from different socioeconomic backgrounds. Previous studies have shown that patients with high SES were more likely to access palliative care and stay home as the place of death, suggesting a predominant emphasis on autonomy and QoL [45, 46]. In contrast, patients with low SES may lack access to community support, financial assistance and transportation to sustain long-term dialysis [47, 48]. More detailed studies focusing on specific socioeconomic determinants, including financial position, QoL and palliative care acceptance, may facilitate a greater understanding of the non-linear association between SES and early psychosocial withdrawal.

There are several limitations inherent with registry data. First, the ANZDATA registry does not collect information on patients who opt for a conservative pathway without ever initiating dialysis. Therefore, selection bias might take place. In addition, there may be ascertainment bias from underreporting of patients maintained on dialysis for $<$90 days, due to overlap between acute kidney injury and chronic kidney disease. Secondly, deaths from dialysis withdrawal were reported to the ANZDATA registry by the treating centres, and the registry does not verify the accuracy of these causes. Hence, misclassification bias of the cause of death is possible. Lastly, there are unmeasured and residual confounders that are likely to be dissimilar between patients who experienced death from withdrawal and those with other causes of death. Details on psychosocial factors, functional status, cognitive impairment, severity of comorbidities and mental health conditions were not collected by the ANZDATA registry. Furthermore, state-level and centre-level systemic differences, including the availability of kidney supportive care or palliative care and changes in dialysis access policies, were also not collected by the ANZDATA registry to provide a better understanding of the circumstances associated with early dialysis withdrawal.

In conclusion, early dialysis withdrawal accounted for >30% of early deaths with minimal temporal variation in the last two decades. Many of the risk factors were common between early psychosocial and medical withdrawals and may be related to surrogate measures of frailty. Detailed discussion outlining the medical and psychosocial risks and benefits of dialysis and non-dialysis pathways for high-risk patients approaching kidney failure may better inform the shared decision-making process, empower patient-focused treatment choices and facilitate informed consent and advanced care planning.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

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AUTHORS' CONTRIBUTIONS

All authors have contributed to this manuscript and approve of this submission. J.H.C.C. and W.H.L. participated in the design and analysis of this study. All authors participated in the interpretation of data and drafting/revising the paper. The results presented in this article have not been published previously in whole or part, except in abstract form.

CONFLICT OF INTEREST STATEMENT

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