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Research Article

A Retrospective Cohort Study of hemodialysis optimization in elderly renal patients with diabetic nephropathy

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Abstract

Background: Diabetic nephropathy is the leading cause of end-stage renal disease among elderly patients starting hemodialysis, and this subgroup carries a disproportionate burden of frailty, cardiovascular disease, and vascular access dysfunction.

Objective: To describe five-year survival among elderly hemodialysis patients with diabetic nephropathy and identify which components of dialysis adequacy, vascular access, glycemic control, and comorbidity burden are independently associated with mortality.

Methods: We retrospectively studied 412 patients aged 65 years or older who initiated in-center hemodialysis for diabetic nephropathy at our affiliated units between 2019 and 2020, followed through 2025. Survival was estimated by the Kaplan-Meier method and independent predictors of mortality were identified by multivariable Cox regression.

Results: Over a median follow-up of 4.1 years, 187 patients (45.4%) died. Five-year survival ranged from 38.9% in the lowest Kt/V tertile to 63.8% in the highest (log-rank $p < 0.001$). Catheter access at initiation, frailty, both the lowest and highest glycosylated hemoglobin categories, and low serum albumin were each independently associated with higher mortality after adjustment.

Conclusions: Dialysis adequacy, vascular access planning, individualized glycemic targets, frailty, and nutritional status each independently predicted survival in this population, supporting a bundled rather than single-parameter approach to hemodialysis optimization in elderly diabetic nephropathy patients.

Keywords: hemodialysis; diabetic nephropathy; elderly; dialysis adequacy; frailty

1. Introduction

Diabetic nephropathy is the leading cause of end-stage renal disease among patients entering maintenance hemodialysis, and the proportion of incident dialysis patients who are both elderly and diabetic has risen as populations age [1]. Once nephropathy is established, the trajectory toward end-stage disease is often more rapid than in non-diabetic kidney disease [2]. Renin-angiotensin blockade slows, but does not halt, this progression [3,4,5], and sodium-glucose cotransporter-2 inhibitors extend renoprotection further without eliminating the eventual need for dialysis in many patients [6,7].

Once on hemodialysis, elderly diabetic patients carry a disproportionate burden of cardiovascular disease, frailty, and functional decline, and a substantial minority lose independence within months of starting dialysis [8,9]. Frailty at initiation independently predicts mortality beyond comorbidity indices [10,11], and cognitive impairment complicates adherence to the regimens optimization depends on [12]. These patients also face elevated risk from vascular access dysfunction [13], intradialytic hypotension [14], vascular calcification [15], and cardiovascular mortality exceeding that of non-diabetic dialysis patients [16].

Several dialysis-prescription and metabolic parameters are, in principle, modifiable. Dialysis adequacy (Kt/V) has long been tied to survival, though the HEMO Study found no incremental benefit of raising dialysis dose beyond standard targets [17,18,19]. More frequent hemodialysis improved intermediate outcomes without a clear mortality signal in the Frequent Hemodialysis Network trial [20], residual native kidney function contributes independently to survival [21,22], and targeting a normal hematocrit with erythropoiesis-stimulating agents was associated with harm in cardiac patients [23,24]. Glycemic control in dialysis-dependent diabetes is its own unresolved question: several cohorts describe a "reverse

epidemiology" in which very low glycated hemoglobin is paradoxically associated with higher mortality [25,26].

Few single-institution cohorts have examined how these modifiable components jointly associate with survival specifically among elderly diabetic hemodialysis patients. We undertook a retrospective cohort study to describe baseline characteristics, quantify five-year mortality, and identify which components of dialysis adequacy, vascular access, glycemic and anemia management, and comorbidity burden were independently associated with survival, to inform a practical optimization strategy.

2. Methods

We retrospectively studied patients aged 65 years or older with end-stage renal disease attributed to diabetic nephropathy who initiated in-center hemodialysis at our affiliated units between January 2019 and December 2020, followed through December 2025 or death. Diabetic nephropathy was assigned using the treating nephrologist's coded diagnosis, consistent with registry convention [1]. Patients with fewer than 90 days on hemodialysis, early transition to peritoneal dialysis or transplantation, or incomplete baseline data were excluded, leaving 412 patients.

Baseline data included age, sex, body mass index, diabetes duration, vascular access type at initiation, a comorbidity index adapted from the Index of Coexistent Disease [11], and a frailty phenotype assessed as in prior dialysis cohorts [10]. Dialysis adequacy was quantified as single-pool Kt/V by the second-generation Daugirdas formula [19,17]. Residual renal function was estimated from interdialytic urine collections, as in NECOSAD [21]. Glycemic control was summarized as time-averaged HbA1c over the first year, and anemia management as time-averaged hemoglobin and erythropoiesis-stimulating agent dose. Depressive symptoms were screened given their established association with adverse dialysis outcomes [27], and quality of life was assessed with an instrument

comparable to that used in DOPPS [28].

Table 1: Baseline characteristics of the cohort (n=412) stratified by five-year survival status.			
Characteristic	Survivors (n=225)	Non-survivors (n=187)	p-value
Age at initiation, years (mean)	72.9	76.6	<0.001
Male sex, %	52.4	57.8	0.29
Duration of diabetes, years (median)	12	17	0.002
Catheter access at initiation, %	36.4	58.8	<0.001
Frailty phenotype present, %	31.6	52.9	<0.001
Mean Kt/V (first 3 months)	1.32	1.14	<0.001
Residual renal function present, %	35.6	19.8	<0.001
Time-averaged HbA1c, % (mean)	7.4	8.1	0.01
Serum albumin <3.5 g/dL, %	24.0	44.9	<0.001

The primary outcome was five-year all-cause mortality; secondary outcomes were cardiovascular mortality, hospitalization, and access-related intervention rate. Patients were stratified by Kt/V tertile, HbA1c category, and access type. Survival was estimated by the Kaplan-Meier method with log-rank comparison. Independent predictors were identified by multivariable Cox regression adjusting for age, sex, comorbidity index, frailty, access type, Kt/V tertile, residual renal function, HbA1c, hemoglobin, and albumin, informed by covariates known to affect dialysis survival [16,29,30]. The proportional-hazards assumption was assessed via scaled Schoenfeld residuals; two-sided p<0.05 was significant. The study was approved by our institutional ethics board with a waiver of individual consent given its retrospective, de-identified design.

3. Results

Mean age at initiation was 74.6 years (SD 6.1), 54.9% were men, and median diabetes duration was 14 years. A tunneled catheter was the access in use at initiation in 46.4% of patients, reflecting late or unplanned starts as

previously described [31], while 38.1% initiated with a fistula and 15.5% with a graft. A frailty phenotype was present in 41.0%, comparable to prior cohorts [10], and 27.7% screened positive for depressive symptoms [27].

Dialysis adequacy and mortality outcomes

Over a median follow-up of 4.1 years, 187 patients (45.4%) died, 61.5% of cardiovascular causes, consistent with the disproportionate cardiovascular mortality of diabetic hemodialysis populations [16,15]. Five-year survival differed across Kt/V tertiles: 63.8% in the highest tertile (mean Kt/V 1.42), 51.2% in the middle, and 38.9% in the lowest (mean Kt/V 1.05; log-rank p<0.001), broadly consistent with earlier dose-outcome observations even though the randomized HEMO trial found no incremental benefit of higher dose in an unselected population [18,17]. Residual renal function at one year, present in 28.4%, was independently associated with lower mortality, echoing NECOSAD [21,22].

Access type at initiation was strongly associated with mortality and infection. Catheter starters had 5-year mortality of 54.2% versus 34.7% for fistula starters, consistent with prior vascular-access literature [13]. Access-related hospitalizations occurred at 0.61 per patient-year with catheters versus 0.19 with fistulas.

Glycemic control and cardiovascular outcomes

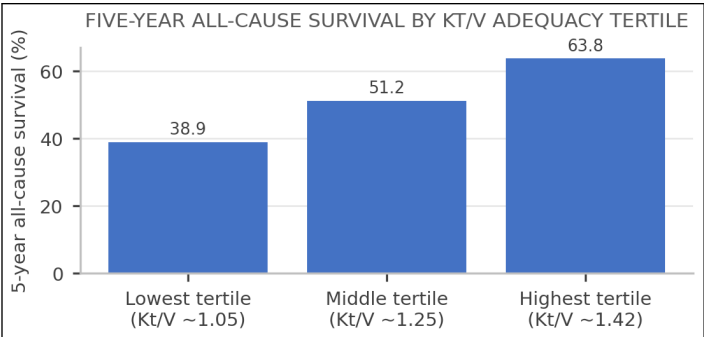


Figure 1: Five-year all-cause survival by single-pool Kt/V adequacy tertile, showing a stepwise gradient from 38.9% in the lowest tertile to 63.8% in the highest tertile (log-rank p<0.001), broadly consistent with earlier observational dose-outcome relationships even though the randomized HEMO Study found no incremental mortality benefit from raising dialysis dose beyond a conventional target [18,17].

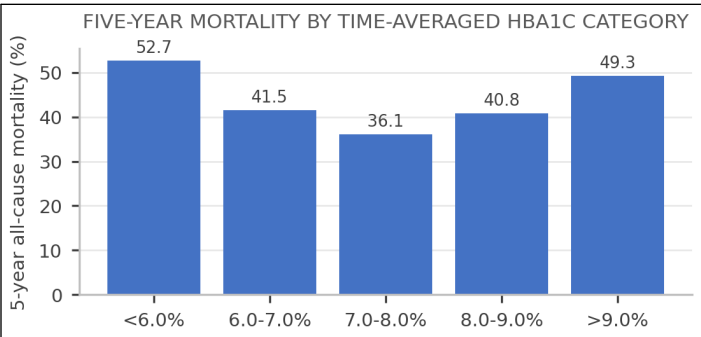


Figure 2: Five-year all-cause mortality by time-averaged glycated hemoglobin (HbA1c) category, showing a U-shaped relationship with the lowest mortality (36.1%) in the intermediate 7.0-8.0% band and higher mortality at both the lowest and highest HbA1c categories, consistent with the reverse-epidemiology pattern reported in larger multicenter diabetic hemodialysis cohorts [25,26].

Time-averaged HbA1c showed a U-shaped association with mortality: 52.7% for HbA1c below 6.0%, a nadir of 36.1% for 7.0-8.0%, and 49.3% above 9.0%, paralleling reverse-epidemiology findings in larger cohorts [25,26]. Intradialytic hypotension, occurring in 31.6% of patients on at least 10% of sessions, was more frequent with the lowest HbA1c and blood pressure, consistent with prior descriptions [14]. Hemoglobin and erythropoiesis-stimulating agent dose were not linearly associated with mortality; patients near-normal hematocrit showed no survival advantage, mirroring trials targeting higher hemoglobin in cardiac patients [23,24].

Table 1 summarizes baseline characteristics by survival status, and Table 2 the multivariable predictors of mortality. In the adjusted model, lowest-tertile Kt/V (HR 1.71, 95% CI 1.24-2.36), catheter access (HR 1.58, 1.16-2.15), frailty (HR 1.46, 1.07-1.99), and both HbA1c extremes relative to the intermediate band (HR 1.62 and 1.39) remained independent predictors. Albumin below 3.5 g/dL was independently associated with higher mortality (HR 1.55, 1.13-2.13), consistent with albumin's established prognostic value [18,29,30]. Lowest-quartile quality-of-life scores were also associated with excess mortality, as in DOPPS [28].

4. Discussion

In this cohort, dialysis adequacy, access type, glycemic

control, frailty, and nutritional status were each independently associated with five-year survival after adjustment for age and comorbidity. Outcomes appear determined less by any single target than by the joint burden of suboptimal dialysis delivery, unplanned access, metabolic derangement at either extreme, and frailty, consistent with calls for bundled rather than single-parameter risk reduction [16,1].

The association between lower Kt/V and mortality should be read against the HEMO Study, which found no mortality benefit from a higher dose target [17], and the Frequent Hemodialysis Network trial, which found functional but not clear survival benefit from more frequent dialysis [20]. Our gradient is more plausibly explained by adequacy marking overall session tolerance, access function, and residual clearance, each an independent predictor, rather than evidence that further intensifying dose in already-adequate patients would help [18,21,22]. This argues for correcting why a given patient fails to reach adequacy targets rather than simply escalating dialysis time once a threshold is met, consistent with current guidance [32].

Vascular access and comorbidity burden

The excess mortality and hospitalization with catheter access is consistent with prior literature describing catheters as a marker of, and plausible contributor to, adverse outcomes through bacteremia and interrupted sessions [13]. Because over 45% of our cohort began with a catheter, reflecting unplanned initiation after inadequate predialysis care, earlier nephrology referral, previously tied to reduced mortality [31], and preemptive fistula planning once nephropathy is recognized as advancing [2,4,5], appear to be tractable levers for this subgroup.

The U-shaped HbA1c-mortality relationship reproduces, in a cohort restricted to elderly diabetic hemodialysis patients, the reverse-epidemiology pattern seen in larger analyses [25,26]. Very low HbA1c in this population may reflect malnutrition and advanced comorbidity rather

than tight control, while very high HbA1c reflects poorly controlled diabetes with its own vascular consequences; both extremes may mark a sicker phenotype as much as a causal exposure. Rigid ambulatory HbA1c targets are unlikely to be appropriate here; an individualized target informed by nutrition, hypoglycemia risk, and life expectancy fits our findings better [14]. Likewise, the absence of survival benefit from higher hemoglobin or erythropoiesis-stimulating agent dose is consistent with trial evidence against normalizing hematocrit [23] and with darbepoetin increasing stroke risk without mortality benefit in diabetic chronic kidney disease [24], supporting conservative anemia management.

Table 2: Multivariable Cox proportional-hazards model of independent predictors of five-year all-cause mortality, adjusted for age, sex, and comorbidity index [11,16].			
Predictor	Hazard ratio	95% CI	p-value
Lowest Kt/V tertile (vs highest)	1.71	1.24-2.36	0.001
Catheter access at initiation (vs fistula)	1.58	1.16-2.15	0.004
Frailty phenotype present	1.46	1.07-1.99	0.02
HbA1c <6.0% (vs 7.0-8.0%)	1.62	1.14-2.30	0.007
HbA1c >9.0% (vs 7.0-8.0%)	1.39	1.01-1.91	0.04
Serum albumin <3.5 g/dL	1.55	1.13-2.13	0.007
Lowest quartile quality-of-life score	1.33	1.02-1.75	0.03

Frailty, cognitive status, and depression were common and each tracked with worse survival, consistent with frailty as an independent predictor distinct from age or comorbidity count [10,12,27]. Because many elderly patients lose independence within months of starting dialysis [8,9], and withdrawal from dialysis is a recognized outcome in frail patients with limited reserve [33], optimization cannot rest on laboratory targets alone; it requires attention to functional trajectory and quality of life, which itself predicts survival and hospitalization [28]. A dedicated statin trial in diabetic hemodialysis patients did not reduce cardiovascular events despite lowering LDL cholesterol, underscoring that general-population interventions do not automatically translate to this group

[34], and both very low and very high blood pressure have been linked to excess mortality in hemodialysis cohorts, a U-shape analogous to what we observed for glycemia [35].

Two comparative questions lie outside a single-modality cohort but bear on application. A randomized trial found no benefit to earlier dialysis initiation before symptoms developed [36], suggesting our catheter-associated excess mortality reflects unplanned, late referral rather than early initiation itself. Propensity-matched registry comparisons have also found similar or modestly better early survival with peritoneal dialysis in comparable patients, relevant when counseling newly diagnosed elderly diabetic patients on modality choice [37].

This study has limitations: it was retrospective and single-system, so residual confounding by indication cannot be excluded; frailty and depression instruments were adapted rather than identical to those in larger cohorts; and because the cohort required 90 days of survival, our findings describe optimization opportunities among patients past the highest-risk early period rather than early mortality itself, a distinct question addressed elsewhere in the dialysis-withdrawal literature [33].

5. Conclusion

Dialysis adequacy, access type, a U-shaped glycemic exposure, frailty, and nutritional status each independently predicted five-year survival among elderly hemodialysis patients with diabetic nephropathy. These findings support early nephrology referral and preemptive fistula planning to avoid catheter-dependent initiation [31,13], individualized rather than uniformly tight glycemic targets that account for reverse epidemiology at both HbA1c extremes [25,26], conservative anemia management consistent with trial evidence against normalizing hematocrit [23,24], and systematic attention to frailty, nutrition, and quality of life alongside adequacy targets [10,29,28]. Because none of these levers acted in isolation, a bundled approach to hemodialysis optimization is likely needed, and prospective multicenter

confirmation is a reasonable next step [1,32].

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