EARLY INITIATION OF DIALYSIS AND LATE IMPLANTATION OF CATHETERS ADVERSELY AFFECT OUTCOMES OF PATIENTS ON CHRONIC PERITONEAL DIALYSIS

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◆ **Objectives:** Predialysis nephrology care is thought to affect morbidity and mortality in hemodialysis patients. This study evaluated the impact of different patterns of predialysis care on outcomes of patients undergoing chronic peritoneal dialysis (PD).

◆ **Design:** Retrospective cohort.

◆ **Setting and Participants:** 275 patients enrolled from January 1997 to March 2005 in a medical center in North Taiwan who recently initiated dialysis were classified according to early or late referral to nephrologists (≥ 6 or < 6 months of dialysis), planned or late implantation of Tenckhoff catheters (absence or presence of preceding emergent hemodialysis), and early or late start of dialysis [glomerular filtration rate (GFR) ≥ 5 or < 5 mL/minute/1.73 m²].

◆ **Main Outcome Measures:** All-cause mortality and hospitalization.

◆ **Results:** During a median follow-up of 2.5 years, 41 deaths, 38 transfers to hemodialysis, and 26 renal transplantations occurred. Late start of dialysis was associated with a significant survival benefit (log rank, $p = 0.012$) and, along with planned implantation of catheters, exhibited a reduced risk for all-cause hospitalization (log rank, $p = 0.025$, 0.013). The predictors of overall mortality included baseline GFR [hazard ratio (HR) 1.18, $p = 0.023$], age (HR 1.07, $p < 0.001$), and diabetes (HR 3.64, $p = 0.001$); whereas the risk factors for all-cause hospitalization included age (HR 1.02, $p = 0.012$), late implantation of catheters (HR 1.78, $p = 0.011$), and diabetes (HR 1.92, $p = 0.005$). The timing of nephrology referral did not affect either death or hospitalization.

◆ **Conclusions:** Our data do not support earlier initiation of PD, but underscore the importance of planned

implantation of catheters before commencement of chronic PD.

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KEY WORDS: End-stage renal disease; hospitalization; mortality.

The incidence of treated end-stage renal disease (ESRD) in Taiwan is among the highest in the world (1). The resultant reimbursement for chronic dialysis therapy absorbs a large proportion of the nation's healthcare budget (2). More than 90% of ESRD patients choose hemodialysis (HD) as the modality of chronic renal replacement therapy, which is being looked at with concern by policymakers and healthcare providers. As a result, the government is promoting the implementation of chronic peritoneal dialysis (PD) for incident ESRD patients due mainly to its inexpensiveness relative to HD. However, while official detailed figures are lacking, only a small proportion of ESRD patients undergoing chronic PD had a planned start of dialysis, that is, without preceding acute HD through temporary HD catheters. This would greatly offset the economic advantage of PD, since any complications associated with the use of HD catheters could invariably lead to an increase in morbidity and mortality, let alone medical costs. The reasons for failure to initiate chronic PD in time are likely multifactorial but could be related, at least in part, to inadequate predialysis care.

Predialysis nephrology care has been shown to affect morbidity and mortality after patients begin chronic renal replacement therapy, particularly HD. For instance, delayed nephrology referral has been implicated in increased mortality and hospitalization after initiation of chronic HD (3,4), and timely referral allows

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implementation of multidisciplinary predialysis care, which can lead to improved patient survival after initiation of dialysis (5). Further, timely creation of a permanent vascular access before starting chronic HD is associated with a lowered risk of sepsis and death from the use of temporary HD catheters (6), and earlier creation allows the fistula to become mature before cannulation, thus providing long-term complication-free vascular access (3,7,8). Finally, recent studies suggest that earlier initiation of dialysis may not be linked with better patient outcomes (9,10), and could even cause a paradoxically increased risk for death (11). By contrast, information is limited regarding the impact of different predialysis care on outcomes of patients undergoing chronic PD. This study was performed to evaluate overall mortality and hospitalization in a retrospective cohort of incident PD patients stratified by different care patterns (early vs late nephrology referral, catheter implantation, and dialysis initiation) at a medical center in North Taiwan where ESRD is endemic.

METHODS

STUDY POPULATION

This study screened 310 ESRD patients started on PD at the National Taiwan University Hospital between 1 January 1997 and 31 March 2005. These patients were treated at the same unit by the same team of physicians and nurses. Patients were treated with continuous ambulatory PD or automated PD using conventional dialysates (Dianeal 1.5%, 2.5%, or 4.25% glucose; Baxter Healthcare, Deerfield, Illinois, USA). Other types of dialysates, such as Nutrineal (1.1%; Baxter) and Extraneal (7.5%; Baxter), were prescribed whenever needed for patients with significant hypoalbuminemia (serum albumin <3.5 g/dL measured by the bromocresol green assay) or poor ultrafiltration (<0.5 L/day despite the use of high osmolality solutions) respectively. Seventeen patients that discontinued PD treatment within 3 months of commencement were excluded at initial screening. The reasons for discontinuation included death (7 patients: 5 died from cardiovascular disease, 2 from infection), transfer to HD (3 patients: 2 due to catheter dysfunction or leakage, 1 due to lack of family support), renal transplantation (3 patients), transfer to other hospitals (3 patients), and recovery of renal function (1 patient). Another 18 patients were excluded for lack of initial biochemical data or peritoneal equilibration test (PET). Finally, a total of 275 persons (124 males, 151 females) were selected and followed until 30 June 2005. This study was approved by the National Taiwan

University Hospital's Research Ethics Committee (No. 9461700833).

OUTCOMES

The primary end point of the study was overall mortality; the secondary end point was all-cause hospitalization at termination of follow-up. The baseline demographic characteristics and laboratory data of each patient were documented by reviewing medical charts. The earliest (performed within 3 months after start of chronic PD) and the last available PET, including urine amount, total Kt/V, total weekly creatinine clearance (WCCr), peritoneal Kt/V, peritoneal WCCr, renal Kt/V, renal WCCr, and normalized protein catabolic rate (nPCR) were also recorded. The last PET data were unavailable in 16 patients due to insufficient follow-up period, that is, less than 6 months. All parameters were calculated according to standard formulas presented in the European best practice guidelines for PD (12).

COVARIATES

The patients were categorized according to the timing of nephrology referral, implantation of Tenckhoff catheters, or initiation of PD. Early referral was defined as referral to nephrologists at least 6 months before the initiation of chronic PD; late referral was defined as referral less than 6 months before commencement of chronic PD. The planned implantation category included patients that received implantation of Tenckhoff catheters before initiation of chronic PD, without preceding emergent HD; the late implantation category included patients that had undergone at least one session of emergent HD via temporary non-cuffed catheters, before implantation of Tenckhoff catheters. Early start was defined as initiation of chronic PD when glomerular filtration rate (GFR) was ≥ 5 mL/minute/1.73 m²; late start was defined as initiation of chronic PD with GFR <5 mL/minute/1.73 m². The cutoff level to define early and late start of dialysis has been used by Wilson *et al.* (13). The GFRs were estimated according to the Modification of Diet in Renal Disease equation: $\text{GFR (mL/min/1.73 m}^2\text{)} = 186 \times \text{sCr}^{-1.154} \times \text{age}^{-0.203} \times 1.212$ (if black) $\times 0.742$ (if female) (7).

STATISTICAL ANALYSES

Student's t-test and Wilcoxon signed rank test were performed to compare differences in continuous and non-normally distributed variables between subgroups. Chi-square test was used to compare the nominal vari-

ables between subgroups. Logistic regression analysis was used to determine the factors associated with planned implantation of catheters. Patient survival and event probability were evaluated using Kaplan–Meier survival analysis, with comparisons between survival curves made by the log-rank test. The backward stepwise model of the Cox proportional hazards method was applied to calculate hazard ratio (HR) and adjusted survival curves for time to event, adjusting for age, gender, level of education, occupational activity, nephrology referral, implantation of catheters, initiation of dialysis, comorbidities (diabetes, coronary artery disease, congestive heart failure), and laboratory data that had probability values less than 0.2 on univariate analysis or were considered to be important. Data were analyzed using the Scientific Package for Social Science (SPSS, version 12.0; SPSS Inc, Chicago, Illinois, USA) for Windows operating system (Microsoft Corp., Redmond, Washington, USA). Any probability values less than 0.05 were considered significant.

RESULTS

STUDY POPULATION

Baseline characteristics of the 275 patients enrolled in this study are shown in Table 1. The patients were mostly female (55%), middle-aged (mean age 51.3

years), occupationally active (67%), and had a higher educational level (62%). Among the participants, 43% of patients were referred early and 21% received planned implantation of catheters before the start of PD. Mean duration of PD treatment was 30.1 months. One hundred and ten patients dropped out due to various causes, including death, modality shift to HD, kidney transplantation, and transfer to other hospitals (Table 2). At initiation of chronic PD, mean serum creatinine level and GFR were 12.0 mg/dL and 4.8 mL/minute/1.73 m² respectively (Table 3).

TIMING OF INITIATION OF DIALYSIS AND PATIENT OUTCOMES AFTER START OF CHRONIC PD

Kaplan–Meier plots show that late start of dialysis was associated with a significant survival benefit (log rank, $p = 0.012$) and a reduced risk for all-cause hospitalization (log rank, $p = 0.025$) (Figure 1). Compared with the early start group, patients in the late start group were younger ($p < 0.001$), occupationally more active ($p < 0.001$), and had fewer comorbidities (for diabetes, $p < 0.001$; for congestive heart failure, $p = 0.017$) (Table 1). The late start group had higher serum albumin ($p = 0.005$) and calcium-phosphate product ($p = 0.001$), but lower hemoglobin ($p = 0.004$) and renal WCCr ($p = 0.001$) at study baseline (Table 3). They also had a lower rate of dropout due to death ($p = 0.023$) and a higher rate of

TABLE 1
Comparison of Baseline Demographic Characteristics of Patients with Different Patterns of Initiation of Dialysis and Implantation of Catheters

	Total (n=275)	Initiation of dialysis ^c			Implantation of catheters ^d		
		Early (n=110)	Late (n=165)	p Value	Planned (n=58)	Late (n=217)	p Value
Age (years)	51.3±17.2	56.1±18.5	48.1±15.5	<0.001	51.0±15.3	51.4±17.7	NS
Female gender	151 (55%)	39 (35%)	112 (68%)	<0.001	35 (60%)	116 (53%)	NS
Higher education level ^a	171 (62%)	67 (61%)	104 (63%)	NS	44 (76%)	127 (59%)	0.015
Occupationally active ^b	184 (67%)	57 (52%)	127 (77%)	<0.001	49 (85%)	135 (62%)	0.001
Referral time>6 months	119 (43%)	48 (44%)	71 (43%)	NS	47 (81%)	72 (33%)	<0.001
Planned implantation	58 (21%)	24 (22%)	34 (21%)	NS	—	—	—
Comorbidity							
Diabetes	53 (19%)	33 (30%)	20 (12%)	<0.001	7 (12%)	46 (21%)	NS
Hypertension	136 (49%)	56 (51%)	80 (48%)	NS	32 (55%)	104 (48%)	NS
CAD	15 (5.5%)	6 (5%)	9 (5%)	NS	0 (0%)	15 (7%)	0.046
CHF	18 (6.5%)	12 (11%)	6 (4%)	0.017	4 (7%)	14 (6.5%)	NS

CAD = coronary artery disease; CHF = congestive heart failure; NS = not significant.

^a Higher education level denotes junior high school and above.

^b Occupationally active is defined by being a student or having a job, including housekeeping.

^c Early or late start of dialysis means glomerular filtration rate ≥ 5 or < 5 mL/minute/1.73 m².

^d Planned or late implantation of Tenckhoff catheters means absence or presence of preceding emergent hemodialysis.

Values are presented as mean±SD or number (%) unless otherwise specified.

TABLE 2
Dropouts Among Patients with Different Patterns of Initiation of Dialysis and Implantation of Catheters

	Total (n=275)	Initiation of dialysis ^d			p Value	Implantation of catheters ^e		
		Early (n=110)	Late (n=165)			Planned (n=58)	Late (n=217)	p Value
Follow-up period (months) ^a	30.1±20.8	28.5±19.4	31.2±21.7	NS		32.0±20.7	29.7±20.9	NS
Dropout rate ^b	110 (40%)	49 (45%)	61 (37%)	NS		17 (29%)	93 (43%)	0.049
Causes of dropout ^c								
Death	41 (38%)	23 (47%)	18 (30%)	0.023		7 (41%)	34 (37%)	NS
Shift to hemodialysis	38 (35%)	21 (43%)	17 (28%)	0.039		6 (35%)	32 (34%)	NS
Transplant	26 (24%)	3 (6%)	23 (38%)	0.002		4 (24%)	22 (24%)	NS
Transfer to other hospital	5 (4.5%)	2 (4%)	3 (5%)	NS		0 (0%)	5 (5%)	NS

NS = not significant.

^a From the start of peritoneal dialysis to the end of follow-up.

^b Parentheses denote percentage among total participants.

^c Parentheses represent percentage among dropout patients.

^d Early or late start of dialysis means glomerular filtration rate ≥ 5 or < 5 mL/minute/1.73 m².

^e Planned or late implantation of Tenckhoff catheters means absence or presence of preceding emergent hemodialysis.

Values are presented as mean±SD or number (percentage) unless otherwise specified.

TABLE 3
Baseline Laboratory Data of Patients with Different Patterns of Initiation of Dialysis and Implantation of Catheters

	Total (n=275)	Initiation of dialysis ^a			p Value	Implantation of catheters ^b		
		Early (n=110)	Late (n=165)			Planned (n=58)	Late (n=217)	p Value
BUN (mg/dL)	115.5±41.4	99.3±28.1	126.3±45.2	<0.001		111.1±23.9	116.7±45.0	NS
Creatinine (mg/dL)	12.0±4.7	8.4±1.8	14.3±4.6	<0.001		11.1±3.5	12.2±5.0	0.048
GFR (mL/min/1.73 m ²)	4.8±2.2	6.8±2.1	3.5±0.9	<0.001		5.0±2.4	4.8±2.1	NS
Potassium (mmol/L)	4.7±1.2	4.6±0.8	4.8±1.4	NS		4.6±0.9	4.8±1.2	NS
Albumin (g/dL)	3.6±0.7	3.4±0.7	3.7±0.6	0.005		3.9±0.7	3.5±0.6	<0.001
Phosphate (mg/dL)	5.8±2.5	5.0±1.8	6.3±2.7	<0.001		6.3±2.0	5.6±2.6	NS
Ca×P	47.5±19.1	43.0±16.3	50.4±20.2	0.001		51.8±14.8	46.3±19.9	0.049
iPTH (pg/mL)	339.3±311.8	258.1±249.3	382.3±333.9	0.010		338.1±271.5	339.6±321.5	NS
Triglycerides (mg/dL)	145.4±90.7	131.8±64.1	155.7±105.6	NS		145.7±71.5	145.3±95.5	NS
Total cholesterol (mg/dL)	183.2±49.0	179.8±52.8	185.6±49.1	NS		180.7±42.7	183.8±50.7	NS
WBC ($\times 10^9$ /L)	6.9±2.3	7.3±2.8	6.6±1.8	0.026		6.1±1.7	7.1±2.4	0.001
Hemoglobin (g/dL)	8.0±2.1	8.5±1.6	7.7±2.4	0.004		8.5±2.1	7.9±2.1	NS
CRP (mg/L)	2.2±2.4	2.0±2.4	2.4±2.5	NS		1.7±3.2	2.1±3.5	NS
Urine amount (L/day)	0.63±0.55	0.63±0.58	0.62±0.54	NS		0.9±0.6	0.6±0.5	<0.001
Total Kt/V	2.4±1.3	2.3±0.6	2.4±1.6	NS		2.5±0.6	2.3±1.5	NS
Total WCCr (L/week)	63.0±20.2	66.9±24.6	60.3±16.2	0.014		70.5±21.6	61.0±19.4	0.001
Peritoneal Kt/V	1.8±0.4	1.7±0.4	1.8±0.5	0.011		1.7±0.6	1.8±0.4	NS
Peritoneal WCCr (L/week)	39.5±10.7	39.9±11.2	39.3±10.3	NS		38.7±13.5	39.7±9.8	NS
Renal Kt/V	0.6±0.9	0.7±0.8	0.5±0.9	NS		0.7±0.5	0.5±1.0	NS
Renal WCCr (L/week)	19.9±18.0	24.7±21.9	16.7±14.1	0.001		27.3±17.5	17.9±17.7	<0.001
nPCR (g/kg/day)	1.12±0.26	1.10±0.28	1.13±0.24	NS		1.19±0.26	1.10±0.25	0.010

BUN = blood urea nitrogen; GFR = glomerular filtration rate; Ca×P = product of calcium and phosphate; iPTH = intact parathyroid hormone; WBC = white blood cell count; CRP = C-reactive protein; Kt/V = urea clearance; WCCr = weekly creatinine clearance; nPCR = normalized protein catabolic rate; NS = not significant.

Values are presented as mean±SD unless otherwise stated.

^a Early or late start of dialysis means glomerular filtration rate ≥ 5 or < 5 mL/minute/1.73 m².

^b Planned or late implantation of Tenckhoff catheters means absence or presence of preceding emergent hemodialysis.

Figure 1 — Kaplan-Meier survival curves for overall mortality, as cumulative patient survival (A), and hospitalization, as cumulative hazards of hospitalization (B), in patients with different patterns of predialysis care.

renal transplantation ($p = 0.002$) during the period of observation (Table 2).

TIMING OF IMPLANTATION OF CATHETERS AND PATIENT OUTCOMES AFTER START OF CHRONIC PD

The timing of implantation of the PD catheter did not affect patient survival, but was associated with a reduced risk for all-cause hospitalization (log rank, $p = 0.013$) (Figure 1). This difference in hospitalization rate persisted throughout the period of observation. Compared with the late implantation group, patients in the planned implantation group had higher education levels ($p = 0.015$) and suffered less comorbidity of coronary heart disease ($p = 0.046$). They were referred to nephrologists earlier ($p < 0.001$) and were occupationally more active ($p = 0.001$) (Table 1). The planned implantation group had higher serum albumin ($p < 0.001$), nPCR ($p = 0.01$), calcium-phosphate product ($p = 0.049$), and renal WCCr ($p < 0.001$) and lower white blood cell count ($p = 0.001$) at study baseline (Table 3). They also had a marginally lower rate of dropout during the fol-

low-up although no apparent causes could be identified (Table 2).

TIMING OF NEPHROLOGY REFERRAL AND PATIENT OUTCOMES AFTER START OF CHRONIC PD

Unlike initiation of dialysis and implantation of catheters, the timing of referral to nephrologists did not have an appreciable impact on either patient survival or hospitalization rate (Figure 1). By contrast, early nephrology referral ($p < 0.001$) and higher occupational activity ($p = 0.009$), but not early initiation of dialysis, were significantly associated with planned catheter implantation (Table 4).

COX PROPORTIONAL HAZARDS MODEL FOR PREDICTORS OF PD PATIENT OUTCOME

The results of Cox regression analysis for overall mortality and hospitalization are shown in Tables 5 and 6 respectively. The tables show the results when variables were analyzed first in the univariate analysis and also in

the final backward stepwise model; $p < 0.2$ on univariate analysis was considered important. The predictors for overall mortality include baseline GFR (HR 1.18, $p = 0.023$), age (HR 1.07, $p < 0.001$), and diabetes (HR 3.64, $p = 0.001$). The independent factors associated with all-cause hospitalization include age (HR 1.02, $p = 0.012$),

late catheter implantation (HR 1.78, $p = 0.011$), and diabetes (HR 1.92, $p = 0.005$). Although baseline GFR was not statistically significant in the backward stepwise model: [HR 1.08, 95% confidence interval (CI) 0.999 – 1.160; $p = 0.054$], it was significant when using the single-step model (HR 1.09, 95% CI 1.001 – 1.181; $p = 0.048$) (data not shown).

TABLE 4

Factors Associated with Planned Implantation of Catheters (Logistic Regression Analysis)

Variable	B	SE	χ^2	p Value
Age at enrollment	-0.010	0.012	0.990	NS
Female gender	0.191	0.354	1.210	NS
Higher education level	0.651	0.376	1.918	NS
Occupationally active	1.285	0.490	3.615	0.009
Early nephrology referral	2.030	0.383	7.616	<0.001
Early dialysis start	0.618	0.358	1.856	NS
Diabetes	-0.004	0.556	0.996	NS
CAD	-19.079	9729.741	<0.001	NS

CAD = coronary artery disease; B = estimated coefficient; SE = standard error; NS = not significant.

DISCUSSION

This study demonstrates that early start of PD, together with diabetes and old age, are strong predictors for overall mortality after commencement of chronic PD. Additionally, late implantation of Tenckhoff catheters, diabetes, old age, and probably early start of PD are independent risk factors for all-cause hospitalization after initiation of chronic PD.

The timing of initiation of dialysis and its impact on patient outcomes has been a subject of debate. Earlier observations suggested that higher GFR at initiation of dialysis was associated with better patient outcomes, including hospitalization and patient survival (14). Sub-

TABLE 5

Independent Predictors for Overall Mortality Using Cox Proportional Hazards Model

Variable ^a (reference group)	HR	Univariate		p Value	Backward logistical regression		
		95% CI			HR	95% CI	p Value
Late implantation of catheter ^b (hazard for planned implantation=1.0)	1.643	0.689–3.915	NS	—	—	—	—
Late referral to nephrologist ^c (hazard for early referral=1.0)	1.901	0.949–3.809	NS	—	—	—	—
Male (hazard for female=1.0)	1.877	1.008–3.533	0.047	—	—	—	—
Diabetes (hazard for nondiabetic=1.0)	6.733	3.579–12.668	<0.001	3.644	1.697–7.825	0.001	—
CAD (hazard for non-CAD patient=1.0)	3.628	1.600–8.225	0.002	—	—	—	—
Age (per 1 year)	1.083	1.058–1.108	<0.001	1.072	1.043–1.095	<0.001	—
Albumin (per g/dL) ^d	0.471	0.286–0.776	0.003	—	—	—	—
GFR (per mL/minute/1.73 m ²) ^d	1.168	1.061–1.287	0.002	1.182	1.023–1.366	0.023	—
Hemoglobin (per g/dL) ^d	1.152	1.034–1.284	0.010	—	—	—	—
WBC (per 1×10 ⁹ /L) ^d	1.191	1.067–1.330	0.002	—	—	—	—
Total Kt/V (per 1 unit) ^e	0.426	0.260–0.697	0.001	—	—	—	—
Total WCCr (per L/week) ^e	0.977	0.960–0.994	0.007	—	—	—	—
Renal Kt/V (per 1 unit) ^e	0.312	0.119–0.819	0.018	—	—	—	—
Renal WCCr (per L/week) ^e	0.978	0.957–1.000	NS	—	—	—	—
nPCR (per g/kg/day) ^e	0.055	0.012–0.254	<0.001	—	—	—	—

CAD = coronary artery disease; GFR = glomerular filtration rate; WBC = white blood cell; Kt/V = urea clearance; WCCr = weekly creatinine clearance; nPCR = normalized protein catabolic rate; HR = hazard ratio; 95% CI = 95% confidence interval; NS = not significant.

^a The independent variables were selected for multivariate analysis if they had $p < 0.2$ on univariate analysis or because they were considered to be important.

^b Planned or late implantation of Tenckhoff catheters means absence or presence of preceding emergent hemodialysis.

^c Early or late referral to nephrologist means ≥ 6 or < 6 months of dialysis.

^d The last biochemical data before initiation of chronic peritoneal dialysis.

^e The earliest data of peritoneal equilibration tests after initiation of chronic peritoneal dialysis.

TABLE 6
Independent Predictors for All-Cause Hospitalization Using Cox Proportional Hazards Model

Variable ^a (reference group)	HR	Univariate	<i>p</i> Value	Backward logistical regression		
		95% CI		HR	95% CI	<i>p</i> Value
Late implantation of catheter ^b (hazard for planned implantation=1.0)	1.694	1.111–2.583	0.014	1.783	1.142–2.784	0.011
Late referral to nephrologist ^c (hazard for early referral=1.0)	1.294	0.939–1.784	NS	—	—	—
Male (hazard for female=1.0)	1.297	0.944–1.784	NS	—	—	—
Diabetes (hazard for nondiabetic=1.0)	2.654	1.832–3.844	<0.001	1.922	1.225–3.017	0.005
CAD (hazard for non-CAD patient=1.0)	1.065	0.560–2.023	NS	—	—	—
Age (per 1 year)	1.022	1.011–1.032	<0.001	1.015	1.003–1.028	0.012
Albumin (per g/dL) ^d	0.784	0.606–1.013	NS	—	—	—
GFR (per mL/minute/1.73 m ²) ^d	1.075	1.011–1.142	0.020	—	—	—
Hemoglobin (per g/dL) ^d	0.996	0.923–1.076	NS	—	—	—
WBC (per 1×10 ⁹ /L) ^d	1.102	1.032–1.176	0.004	—	—	—
Total Kt/V (per 1 unit) ^e	0.806	0.615–1.058	NS	—	—	—
Total WCCr (per L/week) ^e	0.995	0.987–1.003	NS	—	—	—
Renal Kt/V (per 1 unit) ^e	0.876	0.669–1.147	NS	—	—	—
Renal WCCr (per L/week) ^e	0.995	0.986–1.004	NS	—	—	—
nPCR (per g/kg/day) ^e	0.700	0.363–1.350	NS	—	—	—

CAD = coronary artery disease; GFR = glomerular filtration rate; WBC = white blood cell count; Kt/V = urea clearance; WCCr = weekly creatinine clearance; nPCR = normalized protein catabolic rate; HR = hazard ratio; CI = 95% confidence interval; NS = not significant.

^a The independent variables were selected for multivariate analysis if they had *p* < 0.2 on univariate analysis or because they were considered to be important.

^b Planned or late implantation of Tenckhoff catheters means absence or presence of preceding emergent hemodialysis.

^c Early or late referral to nephrologist means ≥6 or <6 months of dialysis.

^d The last biochemical data before initiation of chronic peritoneal dialysis.

^e The earliest data of peritoneal equilibration tests after initiation of chronic peritoneal dialysis.

sequent studies, however, argued that any survival benefit from early initiation of dialysis could be accounted for by lead-time bias, and they did not support initiating dialysis therapy for patients with significant residual renal function (9,10). In this report, the patients starting chronic PD at higher GFR levels (*i.e.*, earlier start of PD) exhibited a higher dropout rate and an increased risk of overall death. They also tended to have more hospitalization during the follow-up. A plausible explanation for this seeming paradox could be inferred from Tables 1, 2, and 3. Noticeably, patients in the early start group were older and occupationally less active, suffered more comorbidity (diabetes and congestive heart failure), and had poorer nutritional status (lower serum albumin and phosphate) at initiation of dialysis. Some of these factors, such as older age and diabetes, are well-known prognostic factors for death in patients on chronic PD (15). These features of the early-start patients also may be causally related to fewer dropouts from kidney transplantation in this group. Collectively, our results were consistent with the report by Beddhu *et al.* (11), which showed that patients initiating chronic dialysis with significant residual renal function were associated with

higher mortality, even when other confounders were taken into consideration. They suggested that low serum creatinine levels, as seen in those patients, could be a marker of reduced muscle mass and unhealthy nutritional status, which in turn might contribute to the poor survival. Future research should elucidate whether this phenomenon may represent a part of the “reverse epidemiology” in the dialysis population (16).

The present study shows for the first time that patients receiving planned implantation of Tenckhoff catheters, namely those that started chronic PD without preceding emergent HD, were associated with reduced risk of overall hospitalization after initiation of PD. Because emergent dialysis via temporary HD catheters has been linked with an increased risk of sepsis (6), one might argue that the lower hospitalization rate seen in the planned implantation group was due to the lack of emergent HD before the start of chronic PD. However, our cohort recruited patients that had been on PD for more than 3 months, at which point none still had a HD catheter in place. Further, the difference in hospitalization rates retained significance not only immediately but also months after the start of chronic PD (Figure 1). Thus, it

seems unlikely that complications associated with the use of HD catheters could explain the different hospitalization rates between patients with planned and patients with late catheter implantation. Our logistic regression analysis showed that early nephrology referral and higher occupational activity were the only two factors correlated significantly with planned implantation of catheters. Based on Table 1, patients in the planned implantation group had higher levels of education and suffered less comorbidity of coronary heart disease. These features could be associated with higher motivation for self-care and better compliance to dialysis prescriptions and nursing advice, which might contribute to fewer hospitalization events during the follow-up. Additionally, as shown in Table 3, the planned implantation group exhibited higher residual renal function (higher urine output and renal WCCr), better nutritional indices (higher albumin and nPCR), and reduced inflammatory status (lower baseline white cell count). These variables have all been implicated in better patient outcomes after initiation of chronic PD (17).

Early referral for patients with advanced chronic kidney disease has been associated with reduction of morbidity, mortality, and economic burden (18). The present study, however, failed to show such benefits of early nephrology referral. The retrospective nature of this study may account in part for the lack of such an association. Conversely, the association of timing of nephrology referral with patient outcomes remains controversial (19). In the current analysis, early referral was found to be the most important factor associated with planned implantation of catheters. Indeed, as shown in Table 1, more patients in the planned implantation group (81%), compared with the late implantation group (33%), were referred earlier (>6 months) to nephrologists. It is conceivable that early nephrology referral allowed patients multidisciplinary pre-ESRD care, including planned implantation of catheters, which then leads to reduced hospitalization after the start of chronic PD. Thus, planned implantation of catheters may represent the adequacy of predialysis care, which is more important than the timing of nephrology referral. Consistent with this notion, previous studies have shown that patients with chronic kidney disease that are referred earlier to nephrologists can receive more consistent pre-ESRD care, including earlier creation of vascular access and timely use of fistulas, which is associated with a reduced risk of sepsis and death by avoiding the use of HD catheters (5,6).

There are limitations to the present study. First, there exists potential selection bias since 35 patients were excluded from the study after initial screening. Among

those, 7 deaths were caused by cardiovascular or infectious diseases, which arguably might have affected the outcome. Nevertheless, even when these patients were taken into consideration, our findings as described in the earlier sections remain the same (data not shown). Second, this study was a single-center experience. Therefore, observations accrued here might not be extrapolated to PD patients elsewhere. Further multicenter prospective studies using a randomized clinical trial design [such as the ongoing IDEAL trial (20)] are needed to confirm our findings.

In summary, this study shows that early start of dialysis adversely affects patient outcomes, whereas planned implantation of catheters reduces hospitalization. Our data do not support earlier initiation of PD, but underscore the importance of planned implantation of catheters to reduce hospitalization after the start of chronic PD.

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