

# Predialysis Psychoeducational Intervention Extends Survival in CKD: A 20-Year Follow-Up

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● **Background:** Predialysis psychoeducational interventions increase patient knowledge about chronic kidney disease (CKD) and its treatment and extend time to dialysis therapy without compromising physical well-being in the short run. The present research examines long-term survival after predialysis psychoeducational intervention. In addition, we examined whether survival differed because of early (ie,  $\geq 3$  months) versus late referral to nephrology. **Methods:** We collected follow-up data for patients with CKD who participated in a multicenter randomized controlled trial of predialysis psychoeducational interventions in the mid-1980s. We gathered 20-year survival data from clinical records and databases. **Results:** Participants included 335 patients with CKD, including 172 patients randomly assigned to receive predialysis psychoeducational interventions (63.0% men; mean age, 50.8 years) and 163 patients assigned to usual care (62.1% men; mean age, 52.7 years). Two hundred forty-six patients (66.8%) died during the course of the study. Mean duration of follow-up was  $8.5 \pm 7.23$  (SD) years. Analyses were by intention to treat. Adjusting for age, general nonrenal health at inception, and time between identification and predialysis psychoeducational intervention or usual care, Cox proportional hazards multiple regression analyses indicated that median survival was 2.25 years longer after patients with CKD received predialysis psychoeducational interventions compared with usual care (chi-square-change [1] = 3.75;  $P = 0.053$ ; hazard ratio, 1.32; 95% confidence interval, 1.0 to 1.74). Predialysis psychoeducational intervention recipients survived a median of 8.0 months longer than usual-care patients after the initiation of dialysis therapy (chi-square-change [1] = 4.39;  $P = 0.036$ ; hazard ratio, 1.35; 95% confidence interval, 1.02 to 1.775). No significant survival advantage was evident for early referral to nephrology or the combination of early referral plus predialysis psychoeducational interventions. **Conclusion:** Predialysis psychoeducational intervention is a safe and useful intervention that contributes valuably to multidisciplinary predialysis care. *Am J Kidney Dis* 46:1088-1098.

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**INDEX WORDS:** Survival; early referral; patient education; psychology; chronic kidney disease (CKD); renal replacement therapy; multidisciplinary predialysis care.

**C**URRENT THINKING IN nephrology advocates 2 fundamental and complementary practices: (1) early referral (ER) and (2) patient education.<sup>1,2</sup> ER of patients with chronic kidney disease (CKD) at risk for end-stage renal disease (ESRD) makes it possible to implement conservative medical management and introduce renal replacement therapy (RRT) at a point in the disease trajectory that minimizes morbidity and improves prognosis. ER decreases complications at the initiation of hemodialysis therapy,<sup>3-7</sup> im-

proves survival,<sup>5-7</sup> and may even help retard the progression of renal failure<sup>8,9</sup> (although this remains controversial<sup>10</sup>).

Patient education has many goals, most directly to increase knowledge of disease and treatment. Predialysis psychoeducational interventions present information about normal functions of the kidneys, diseases of the kidneys, nutrition, medications, alternative modes of RRT, and lifestyle. In addition to providing needed information, an important goal of predialysis psychoedu-

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cational interventions is to socialize patients into a collaborative role in relating to service providers (eg, reporting problems in a timely manner, taking responsibility for component treatments to the extent that this is possible, and adhering to medical recommendations). The hope is that socializing patients into a collaborative role will assist them in extracting the maximum benefit from medical treatment and increase involvement in self-care.<sup>11,12</sup> Consistent with the emphasis on ER, one might speculate that predialysis psychoeducational interventions should be presented when it becomes probable that patients will progress to ESRD (eg, when a patient enters stage 3 CKD), but this is not always possible. In many cases, patients do not come to the attention of nephrologists until RRT is urgently required (hereafter referred to as "late" referral [LR]).<sup>13-15</sup>

A growing body of evidence substantiates the value of predialysis psychoeducational intervention in the management of patients with CKD. Predialysis psychoeducational intervention helps patients learn about CKD and its medical management and supports long-term knowledge retention.<sup>16,17</sup> Predialysis psychoeducational intervention facilitates vocational rehabilitation<sup>18</sup> and promotes quality of life.<sup>19</sup> We previously reported 2 independent multicenter randomized controlled trials in which predialysis psychoeducational interventions extended time to dialysis therapy by significant durations relative to usual care. In the first trial, time to dialysis therapy was extended by a median of 6 months<sup>20</sup>; in the second (when usual care in many of the participating centers approximated the predialysis psychoeducational intervention implemented in the earlier study), median delay of dialysis therapy was 2.8 months.<sup>21</sup> In both trials, time to dialysis therapy correlated significantly and uniquely with predialysis psychoeducational intervention-induced knowledge acquisition.

In as much as predialysis psychoeducational intervention provides medical and treatment information in a timely fashion and attempts to socialize patients into a role that emphasizes collaboration with health care providers, it seems reasonable to consider whether predialysis psychoeducational intervention also may contribute to improved physical well-being and survival. Psychosocial interventions can extend survival in patients with chronic life-threatening conditions,<sup>22-26</sup> including CKD.<sup>27</sup>

A second reason to examine the association between predialysis psychoeducational intervention and survival on RRT is to rule out the possibility of inadvertent adverse effects. Serious questions would arise if the predialysis psychoeducational intervention-induced delay of dialysis therapy were associated with negative consequences (eg, premature death).

In the present report, we return to our initial cohort to examine outcomes after 20 years.<sup>20</sup> Specifically, we want to determine whether ER and/or predialysis psychoeducational intervention influenced patient survival in addition to extending time to dialysis therapy. Because we previously established that predialysis psychoeducational intervention extends time to dialysis therapy, we examined survival in 2 complementary ways: (1) survival from the time of predialysis psychoeducational intervention (or usual care) and (2) survival from the date on which dialysis therapy commenced.

## METHODS

### *Participants*

The method relating to the first predialysis psychoeducational intervention cohort has been described previously.<sup>20</sup> Briefly, between August 1983 and January 1988, we attempted to identify all individuals at our participating hospitals in Montreal (Royal Victoria Hospital, Montreal General Hospital, Centre Hospitalier Cotes-des-Neiges, and St. Mary's Hospital) and Calgary, Canada (Foothills Hospital and its satellite centers in Lethbridge, Medicine Hat, and Vulcan, Alberta) with deteriorating CKD. No formal sample-size calculations were performed; we simply attempted to include all available prospective participants. We screened all nephrologists' appointments or consultations and all hospital lists indicating potential patients with CKD. We attempted to identify patients with CKD with a serious and progressive reduction in kidney function. Our operational criterion was a serum creatinine concentration of 3.96 mg/dL (350  $\mu$ mol/L) and increasing. We also included all patients for whom RRT initiation was required imminently. Because many prospective participants could not be identified well in advance of the point that RRT initiation was required, it was necessary to create 2 groups based on the timing of referral for RRT. The ER group includes patients with CKD referred for nephrological care 3 or more months before RRT initiation.<sup>6,7,28</sup> The LR group includes people referred less than 3 months before RRT initiation.

### *Materials*

Patients participated in structured interviews administered by trained interviewers. Interviews covered a very wide range of topics related to quality of life and psychosocial adaptation to chronic disease, measured by using standard questionnaires. In this report, we present information gathered by using the following instruments.

*Nonrenal health.* The average of 3 single-item health ratings represented general nonrenal health. Nephrologists, nurses closely affiliated with the patient, and patients themselves provided ratings for each participant. The average of these 3 ratings relates reliably and meaningfully to objective indicators of health in patients with CKD.<sup>29</sup>

*Survival.* We determined survival by reference to the patient's medical record at the participating center. We recorded dates of death when these occurred during the follow-up interval for the original experiment (1983 to 1994). We returned to the medical records (and/or attending nephrologists' databases) in winter 2002 to 2003 and summer 2004, documenting additional deaths that occurred in the interim. We did not validate survival data independently. We calculated the duration of survival in 2 ways. First, we calculated survival from the time of predialysis psychoeducational intervention treatment by subtracting the date of death from the date the participant participated in a psychosocial interview and received the predialysis psychoeducational intervention. This corresponded to the occasion on which usual-care patients participated in the psychosocial interview. Second, we calculated survival from the time patients started treatment by maintenance dialysis therapy. We examined survival from the time of dialysis therapy initiation because participants were enrolled in the cohort at very different stages of CKD. We reasoned that biomedical status would be comparatively standard across participants at the time nephrologists initiated dialysis therapy. This was the case. Routine clinical indicators (eg, serum creatinine, urea, inorganic phosphate, potassium, and hematocrit levels) did not differ significantly between groups at the time of randomization or the time they started dialysis therapy.<sup>20</sup> In the case of participants who received a kidney transplant or were lost to follow-up, we used the last date on which the participant interacted with research staff (as a hemodialysis patient) as the date on which to censor data. For patients still alive at the conclusion of follow-up, we used September 30, 2004, as the date to censor the case. Duration of survival is expressed in years.

### *Intervention*

*Predialysis psychoeducational intervention.* The predialysis psychoeducational intervention entailed a single one-on-one slide-lecture presentation that provided information about normal functions of the kidneys, diseases of the kidneys, dietary management of renal disease, and alternative modes of RRT, including maintenance hemodialysis, peritoneal dialysis, and renal transplantation. Pharmacological regimen and dietary and fluid-intake restrictions received limited coverage. Participants were given ample opportunity to ask questions and received a 22-page booklet summarizing the content for future reference. A bachelors-level health educator was trained specifically to deliver the predialysis psychoeducational intervention in a consistent and standard fashion. The predialysis psychoeducational intervention session required 60 to 75 minutes to complete. In an effort to encourage a collaborative patient role, the health educator encouraged patients to report problems directly to the nephrology treatment team whenever they raised questions about medical symptoms or indicated they were experiencing a problem related to their disease or treatment. Health

educators limited interactions with patient-participants to delivery of the predialysis psychoeducational intervention and data collection.

*Usual care.* None of the participating hospitals had a formal program that routinely provided predialysis education at the time patients were enrolled in this experiment (1983 to 1988). This is in contrast to the current situation, in which 96% of Canadian nephrologists report they have easy access to a multidisciplinary team-based predialysis clinic in which education is a primary focus.<sup>30</sup> Patients received relevant information from the attending physician in the form of written materials or by special referral to a nurse clinician. Patients in the usual-care condition thus received amounts and kinds of educational information that varied widely within and among hospitals.

### *Procedure*

Research ethics boards at all participating institutions approved the protocol. Participants were randomly assigned to predialysis psychoeducational intervention or usual care by using random-numbers tables. Randomization was undertaken as soon as possible after attending nephrologists confirmed an individual's eligibility for the trial. All participants completed an initial structured psychosocial interview that required an average of 2.5 hours to complete. Predialysis psychoeducational intervention group participants received the intervention midway through the interview at the initial wave of data collection. Interviews were repeated on a fixed schedule for all surviving patients who were willing and able to continue their participation (at 18 months after the initiation of maintenance dialysis therapy and annually thereafter until the person had been receiving RRT for a minimum of 5.5 years). On average, predialysis psychoeducational intervention patients started dialysis therapy 14.9 months (median, 12.0 months) after receiving the intervention; mean time to dialysis therapy was 10.3 months (median, 6.1 months) for usual-care patients.

Because health educators administered psychosocial questionnaires, they were not blind to patient group membership in the experiment. However, attending nephrologists were kept blind in this regard. The decision to initiate dialysis therapy was made by attending nephrologists without input from the research team (interested readers are referred to the original publications<sup>17,20</sup> for greater detail about the procedures).

### *Experimental Design*

This is a multicenter randomized controlled trial. The original hypotheses involved quality-of-life benefits of predialysis psychoeducational intervention. Patients with CKD were randomly assigned to either predialysis psychoeducational intervention or usual care according to random-numbers tables. It was not possible, of course, to assign participants randomly to ER versus LR. This categorization arose as a result of events independent of our experimental design and thus was studied retrospectively.

### *Statistical Treatment of Data*

Analyses were conducted according to intention to treat.<sup>31</sup> We calculated descriptive statistics (frequencies, means, medians, SDs) to characterize the sample by group member-

ship. We undertook survival analyses to investigate the effects of (1) ER versus LR and (2) predialysis psychoeducational intervention versus usual care. We used multiple regression analysis using a Cox proportional hazards model. Covariates included age, general nonrenal health at inception, and time from identification to predialysis psychoeducational intervention (or usual care). All analyses were undertaken using the Statistical Package for the Social Sciences (version 12.0.1; SPSS Inc, Chicago, IL).

## RESULTS

### *Description of Cohort*

We identified 588 prospective participants. This included 400 people (68%) who agreed to enter the cohort and 188 people (32%) who did not enter for a variety of reasons (most commonly because they were very seriously ill, moribund, or died shortly after being identified). Of those who entered the study, 32 patients (8.0% of the enrolled cohort) did not progress beyond the first data-collection point (eg, because of death, transfer, or loss to follow-up). Of the remainder, 172 patients (46.5%) were referred to nephrologists affiliated with the trial 3 or more months before the initiation of RRT, constituting the ER group; 163 patients (44.6%) required the initiation of RRT within less than 3 months, constituting the LR group. The remaining 33 patients (9.0%) were not eligible for predialysis psychoeducational intervention because their physicians considered it inappropriate (eg, because of severe illness or cognitive or emotional problems).

A number of participants ( $n = 39$ ) who had been randomly assigned to receive predialysis psychoeducational interventions refused it; however, we included these participants in the predialysis psychoeducational interventions group in all data analyses in concordance with the intention-to-treat principle. To rule out the possibility that intention-to-treat analyses may have produced spurious findings, we repeated all analyses including only patients who actually received the predialysis psychoeducational intervention (ie, analysis by treatment received). In each case, results paralleled those generated by intention-to-treat analyses. Final group sizes for intention-to-treat analyses are 163 patients for usual care and 172 patients for predialysis psychoeducational intervention. Table 1 lists descriptive statistics for study participants. Additional details about participants may be found in earlier publications.<sup>17,20</sup>

Two hundred forty-six patients (66.8% of the cohort) died during the course of the experiment and follow-up. Median survival from the point of predialysis psychoeducational interventions (or usual care) was 6.37 years. Median survival from initiation of dialysis therapy was 4.52 years.

This cohort was enrolled more than 20 years ago, when patients were younger and presented fewer comorbid conditions than is presently the case. Although they may no longer be representative of patients with CKD and ESRD, the demographics were typical for Canadian patients at the time.<sup>32</sup>

### *Group Differences in Nonrenal Health*

As might be expected, nonrenal health was significantly better in patients with CKD in the ER group (mean,  $6.7 \pm 1.33$  [SD]) compared with those identified at a point when RRT was required more immediately (LR; mean,  $5.7 \pm 1.53$ ;  $t_{320} = 5.49$ ;  $P < 0.0001$ ). Patients randomly assigned to receive predialysis psychoeducational intervention were healthier (mean,  $6.3 \pm 1.49$ ) than those who received usual care (mean,  $6.0 \pm 1.50$ ;  $t_{291} = -1.87$ ;  $P = 0.062$ ). The inclusion of age and general nonrenal health as covariates in survival analyses adjusted statistically for these inequalities.

### *Survival*

Separate survival analyses compared ER versus LR and predialysis psychoeducational intervention versus usual care. The 3 covariates were significantly associated with duration of survival from the time patients received the predialysis psychoeducational intervention (chi-square [3] = 104.86;  $P < 0.0001$ ); this appeared to be attributable more to the effects of age (relative risk, 1.04; 95% confidence interval [CI], 1.03 to 1.05;  $P < 0.0001$ ) and nonrenal health (relative risk, 0.90; 95% CI, 0.82 to 0.99;  $P = 0.034$ ) than time from identification to predialysis psychoeducational intervention or usual care (relative risk, 0.99; 95% CI, 0.74 to 1.34). Similarly, covariates significantly predicted survival from the time dialysis therapy was initiated (chi-square [3] = 98.54;  $P < 0.0001$ ); in this case, only age was uniquely and significantly related to survival (relative risk, 1.04; 95% CI, 1.03 to 1.06;  $P < 0.0001$ ).

**Table 1. Description of Sample at Inception to Cohort**

Variable	Group			
	ER		LR	
	Usual Care	Predialysis Psychoeducational Intervention	Usual Care	Predialysis Psychoeducational Intervention
No. of patients	78	93	85	79
Age* (y)	51.5 ± 16.8	47.4 ± 15.4	53.4 ± 15.8	53.9 ± 17.4
Sex† (% male)	67.9	66.7	58.8	62.0
Primary renal diagnosis‡ (%)				
Glomerulonephritis	20.8	25.8	24.7	21.8
Hypertension	11.7	9.7	9.4	6.4
Diabetic nephropathy	10.4	17.2	10.6	17.9
Health rating§	6.1 ± 1.5	6.8 ± 1.3	5.9 ± 1.5	5.8 ± 1.6
Education   (% postsecondary or beyond)	24.4	29.0	36.1	30.3
Employment¶ (% working for pay)	48.7	58.1	25.9	23.1
Marital status# (%)				
Never married	19.2	14.0	11.8	19.0
Married	66.7	73.1	71.8	60.8
Identification to predialysis psychoeducational intervention or usual care (mo)**	3.5 ± 6.4	3.3 ± 5.8	3.5 ± 4.7	3.1 ± 4.0
Identification to first dialysis (mo)††	17.2 ± 13.5	20.4 ± 12.0	1.5 ± 4.6	1.7 ± 4.7

NOTE. Values expressed as mean ± SD or percent.

\* $F_{3,331} = 2.88$ ;  $P = 0.036$ .

†Chi-square (3) = 1.9;  $P > 0.10$ .

‡Chi-square (15) = 24.0;  $P = 0.065$ .

§ $F_{3,287} = 7.78$ ;  $P < 0.0001$ .

||Chi-square (12) = 18.8;  $P = 0.094$ .

¶Chi-square (6) = 31.6;  $P < 0.0001$ .

#Chi-square (6) = 5.0;  $P > 0.10$ .

\*\* $F_{3,330} < 1.0$ .

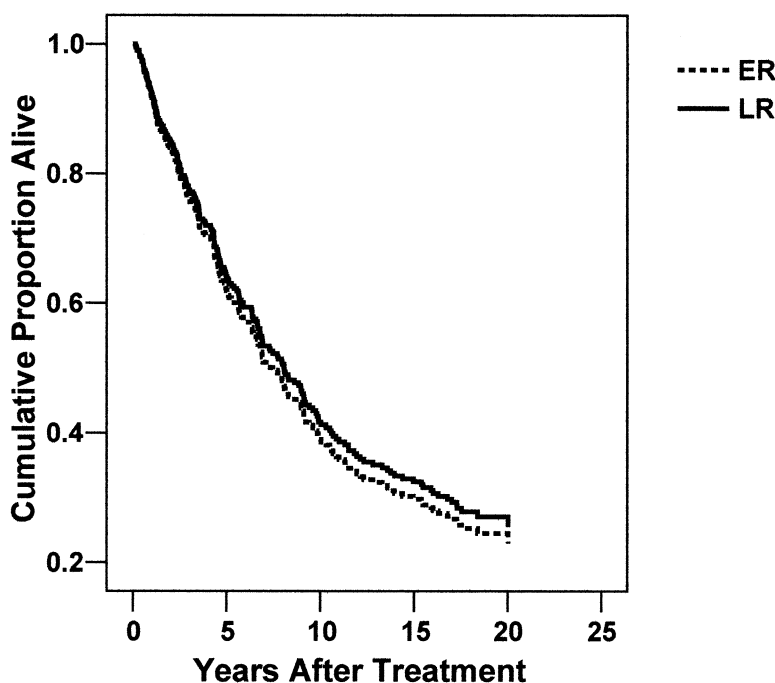
†† $F_{3,331} = 55.02$ ;  $P < 0.0001$ .

*Early referral.* Adjusting for age, general nonrenal health, and time from identification to predialysis psychoeducational intervention or usual care, duration of survival did not differ significantly across patients with CKD referred to nephrology early (ER) compared with late (LR). This was evident regardless of whether the duration of survival examined was from the time of predialysis psychoeducational intervention or from the time patients started dialysis therapy. For survival from predialysis psychoeducational intervention, chi-square-change (1) = 1.39; median survival was 7.96 years (mean, 9.93 years) for patients in the ER group and 5.59 years (mean, 7.95 years) for those in the LR group. For survival from dialysis therapy initiation, chi-square-change (1) = 1.67; median survival was 4.57 years (mean, 6.64 years) for patients in the ER group and 4.42 years (mean, 5.79 years) for those in the LR group. Figure 1 shows survival

curves for these groups (survival from predialysis psychoeducational intervention). Consistent with reported medians, the 2 curves are almost overlapping.

*Psychoeducation.* Adjusting for age, general nonrenal health at inception to the cohort, and time from identification to predialysis psychoeducational intervention or usual care, duration of survival was significantly longer for patients with CKD who received predialysis psychoeducational intervention compared with those in the usual-care group. This was true for both measures of survival. For survival from predialysis psychoeducational intervention, chi-square-change (1) = 3.75 ( $P = 0.053$ ; relative risk, 1.32; 95% CI, 1.00 to 1.74). Patients who received predialysis psychoeducational intervention survived longer (median, 7.84 years; mean, 9.36 years) than those who received usual care (median, 5.07 years; mean, 7.96 years). Simi-





**Fig 1.** Survival curves (years after predialysis psychoeducational intervention or usual care) for patients referred 3 or more months before starting maintenance dialysis therapy (ER) versus those referred less than 3 months before starting dialysis therapy (LR). Durations of survival did not differ significantly between groups.

larly, survival after initiation of dialysis therapy differed significantly between groups (chi-square-change (1) = 101.53;  $P = 0.036$ ; relative risk, 1.35; 95% CI, 1.02 to 1.78). Survival after initiation of dialysis therapy was significantly longer in predialysis psychoeducational intervention recipients (median, 4.57 years; mean, 6.52 years) compared with those who received usual care (median, 3.91 years; mean, 5.67 years). Curves for survival from predialysis psychoeducational intervention are plotted in Fig 2. Survival durations diverged between the 2 groups during the first few years of the experiment. Throughout the follow-up period, participants who received predialysis psychoeducational intervention continued to survive longer than patients in the usual-care group.

*Early intervention plus psychoeducation.* We examined whether benefits of predialysis psychoeducational intervention relative to usual care might be enhanced if delivered at the point of ER compared with an occasion closer in time to the initiation of maintenance dialysis therapy. We tested this hypothesis by comparing survival curves for the 4 groups formed by the factorial crossing of predialysis psychoeducational interventions versus usual care and ER versus LR. Results indicated no significant differences after

adjusting for age, general nonrenal health, and time between identification and predialysis psychoeducational intervention or usual care. Results were not statistically significant for either (1) survival from predialysis psychoeducational intervention (chi-square-change [3] = 4.32;  $P = 0.23$ ; Fig 3) or (2) survival from dialysis therapy initiation (chi-square-change [3] = 3.69;  $P = 0.30$ ).

#### DISCUSSION

Predialysis psychoeducational interventions increase relevant knowledge and extend time to dialysis therapy. In the present study, we observed a statistically significant survival advantage for predialysis psychoeducational intervention recipients after adjusting for age, general nonrenal health at inception, and time between identification and receipt of predialysis psychoeducational intervention or usual care. Predialysis psychoeducational intervention recipients survived a median of 2.25 years longer than usual-care patients from the time they received the intervention and a median of 8.0 months longer than usual-care patients after the initiation of maintenance dialysis therapy. In interpreting these results, it is important to recall that our trial is not designed to examine survival differences between predialy-

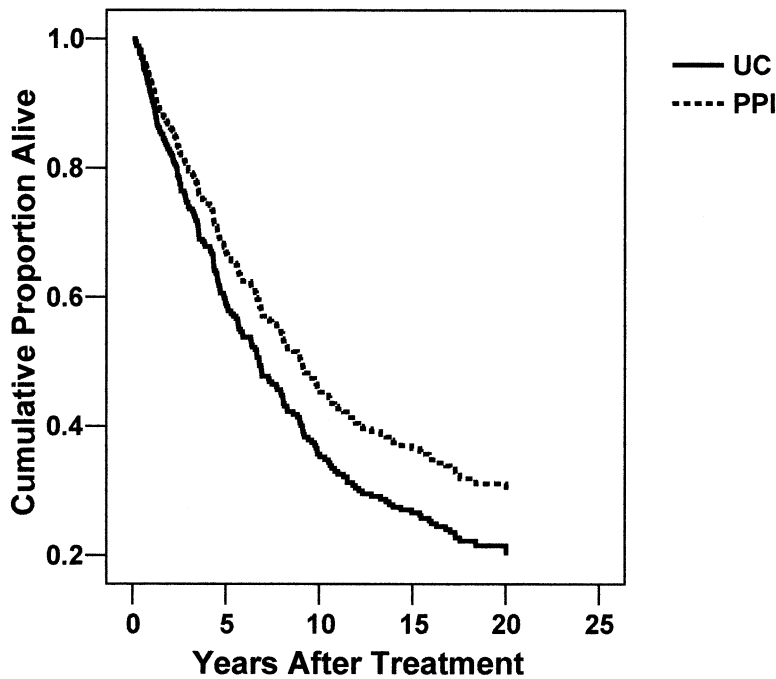


Fig 2. Survival curves (years after predialysis psychoeducational intervention [PPI] or usual care [UC]) for patients who received PPI versus UC. Patients who received PPI survived significantly longer than those in the UC group.

sis psychoeducational intervention and usual care. As a result, it likely is underpowered. The observation of a significant survival advantage thus is all the more compelling.

The present results calm concerns that the delay of dialysis therapy attributable to predialy-

sis psychoeducational intervention may be achieved at the cost of later negative effects. Moreover, findings are in keeping with a broader literature that documents beneficial effects when adjunctive psychosocial interventions complement medical management of chronic disease.

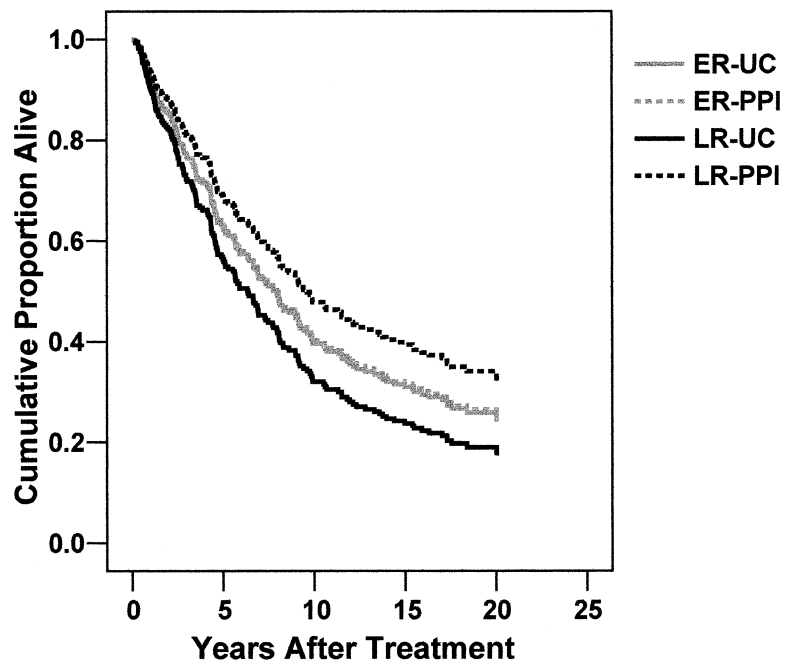


Fig 3. Survival curves (years after predialysis psychoeducational intervention [PPI] or usual care [UC]) for 4 groups of patients with CKD. Durations of survival did not differ significantly across groups.

Psychosocial interventions decrease disease activity in patients with rheumatoid arthritis and asthma,<sup>33</sup> ameliorate pain and disability in patients with osteoarthritis,<sup>34</sup> decrease the incidence of type 2 diabetes mellitus,<sup>35-37</sup> and, although observed serendipitously, appear to extend survival in patients with a number of conditions,<sup>22-26</sup> including CKD.<sup>27</sup> Unlike earlier findings in patients with CKD, the present results are based on a prospective randomized controlled trial. These features enhance confidence in the validity of our findings. Evidence concerning biomedical benefits of adjunctive psychosocial interventions has been reported most consistently in people with diabetes mellitus, for whom efforts have emphasized behavioral changes intrinsic to the biomedical regimen: lifestyle changes emphasizing weight loss and physical fitness.<sup>35-37</sup>

Current consensus in nephrology advocates ER of patients with CKD at high risk for ESRD and patient education in the context of multidisciplinary predialysis care to prepare them for life on maintenance dialysis therapy. Optimal pre-ESRD care involves early interventions aimed at delaying the progression of chronic renal failure, judicious management of uremic complications, treatment of comorbid diseases that accompany CKD, reduction of cardiovascular risk factors, timely placement of vascular access, timely initiation of RRT, and implementation of educational programs targeted at maximum rehabilitation.<sup>38</sup> Encouraging evidence is mounting to support the value of such an approach in producing superior clinical outcomes and decreasing morbidity and mortality.<sup>6,28,39</sup> A new model of care integrating adjunctive psychosocial and psychoeducational interventions into multidisciplinary predialysis care merits serious consideration. Adjunctive psychosocial interventions in patients with early CKD might cover a number of foci. One important component involves the presentation of factual information (eg, normal functions of the kidneys, diseases of the kidneys, alternative RRTs, and nature of the therapeutic regimen). It also might include training in relevant skills (eg, detection of complications, communication with service providers, maximizing adherence to therapeutic regimens, and integrating CKD and RRT into daily life). Predialysis psychoeducational intervention should include a

philosophical emphasis on collaboration with health care professionals (eg, increased participation in the treatment process, self-monitoring for complications, and timely reporting of problems and treatment seeking).<sup>11,40,41</sup>

Our results indicate that predialysis psychoeducational intervention extends time to dialysis therapy<sup>20</sup> and overall survival from both the point of predialysis psychoeducational intervention delivery and after the initiation of RRT. Survival from the initiation of dialysis therapy was extended significantly in predialysis psychoeducational intervention recipients, a finding that extends our earlier observations.<sup>20,21</sup> However, we have not examined the specific mechanism(s) responsible for these effects. A number of possibilities merit investigation, including the benefits of increased collaboration with service providers in the form of adaptive illness behavior (ie, increased participation in the treatment process and timely reporting of problems and treatment seeking), retarded progression of renal failure (eg, caused by improved adherence to recommended lifestyle and dietary changes), reduced stress and associated biomedical effects (eg, hypertension), or another as yet unspecified biopsychosocial process. Delineation of the mechanism by which predialysis psychoeducational intervention extends time to dialysis therapy represents an important next step for research. Of course, an independent demonstration of the hypothesized survival advantage associated with predialysis psychoeducational intervention is crucial, and we intend to undertake this in future.

Current consensus favors ER of patients with CKD to nephrologists, but our results did not indicate an associated survival advantage. Contrary to our hypotheses, there was no significant difference in 20-year survival between ER and LR conditions. The current emphasis in treatment philosophy is on ER to nephrology, but results have been inconsistent in terms of survival.<sup>38,42-46</sup> Although a growing body of evidence supports this perspective, methodological limitations raise doubts about the validity of findings. It is important, for example, to control for such established prognostic factors as age and general nonrenal health, as in the present research. A consistent and medically meaningful definition of ER and LR also is necessary; however, to date, this remains to be established.<sup>28</sup> In



the present study, we adopted the widely used criterion of 3 months to differentiate ER and LR to nephrology.<sup>6,28</sup> It also is important to standardize the component elements of predialysis care. A comprehensive multidisciplinary progressive renal disease clinic, as described by Goldstein et al<sup>6</sup> and Curtis et al,<sup>7</sup> would be desirable as the standard, but this has not been the case in all investigations.<sup>28</sup> Because evidence to date is based on retrospective analyses and naturalistic comparisons, it is not yet possible to conclude with confidence whether ER to nephrology is associated consistently with improved clinical outcomes and extended survival. It also is possible that predialysis care in the mid-1980s was less effective than it is at present, and it may be for this reason that we detected no difference in survival as a function of ER versus LR.

Albeit encouraging, the present findings are based on a single experiment and require definitive replication and extension. We did not validate dates of death documented in the medical record. Serious illness and death resulted in some attrition from our sample, and in a small proportion of cases, it was not possible to determine the duration of survival. Although predialysis psychoeducational intervention versus usual care was randomly assigned in our experiment, ER versus LR to nephrology was not: it was examined retrospectively. In addition, a sizeable proportion of ER patients assigned to the predialysis psychoeducational intervention excluded themselves from the intervention because they suspected it would be redundant with clinical teaching they had already received. A limitation of this study is that the research database is not designed to track initial or secondary dialysis-modality utilization. We cannot ascertain whether the PPI influenced modality decisions or whether the joint effects of PPI and modality choice may have influenced mortality.

The validity of our findings and of the conclusions based on them are supported by the following considerations: (1) the results are based on a rigorous multicenter randomized controlled trial comparing predialysis psychoeducational intervention versus usual care and (2) we adopted a conservative intention-to-treat approach to statistical analyses. Cox proportional hazards multiple regression analysis adjusted for age, general non-renal health at inception to the cohort, and time

between identification and receipt of predialysis psychoeducational intervention or usual care. The experiment was not designed with survival as a primary outcome and, as a result, may have been underpowered. Two additional considerations strengthen our confidence in the validity of the findings: Our original hypotheses did not include the possibility that predialysis psychoeducational intervention might be associated with improved survival, and participating nephrologists were blind with regard to their patients' group membership in the experiment. As noted, results were similar regardless of whether analyses involved only participants who actually received the predialysis psychoeducational intervention versus usual care or were based on the more conservative intention-to-treat approach.

We conclude that predialysis psychoeducational intervention is a safe and desirable adjunct to the medical management of patients with CKD at risk for ESRD and for whom RRT will soon become necessary. In addition to achieving a meaningful delay in the initiation of maintenance dialysis therapy, predialysis psychoeducational intervention is associated with a statistically significant survival advantage compared with usual care, both from the time it was initially delivered and from the point at which dialysis therapy was initiated. Future research should replicate these observations and delineate the mechanism(s).

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