Patient and Technique Survival among a Canadian Multicenter Nocturnal Home Hemodialysis Cohort

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Background and objectives: As a result of improved clinical and quality-of-life outcomes compared with conventional hemodialysis, interest in nocturnal home hemodialysis (NHD) has steadily increased in the past decade; however, little is known about the flow of patients through NHD programs or about patient-specific predictors of mortality or technique failure associated with this modality. This study addressed this gap in knowledge.

Design, setting, participants, & measurements: This study included 247 NHD patients of the Canadian Slow Long nightly ExtEnded dialysis Programs (CAN-SLEEP) cohort from 1994 through 2006 inclusive. The association between program- and patient-specific variables and risk for adverse outcomes was determined using uni- and multivariable Cox regression.

Results: A total of 14.6% of the cohort experienced death or technique failure. Unadjusted 1- and 5-year adverse event-free survival was 95.2 and 80.1%, respectively. Significant predictors of a composite of mortality and technique failure included advanced age ($P < 0.001$), diabetes ($P < 0.001$), central venous catheter use ($P = 0.01$), and inability to perform NHD independently ($P = 0.009$) and were adjusted for center effect. Weekly frequency of NHD was not predictive. Age and diabetes remained significant with multivariable analysis (hazard ratio 1.07 and 2.64, respectively). Unadjusted 1- and 5-year technique survival was 97.9 and 95.2%, respectively. Only age was a significant predictor of technique failure.

Conclusions: NHD is associated with excellent adverse event-free survival. This study underscores the importance of modality-specific predictors in the success of home hemodialysis, as well as favorable baseline characteristics such as younger age and the absence of diabetes.

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Nocturnal home hemodialysis (NHD) is a form of intensive renal replacement therapy whereby patients self-administer their dialysis on 4 to 6 nights per week, with each session lasting 6 to 8 hours. This approach affords considerable patient autonomy regarding treatment scheduling and individualization of therapy. Interest in this dialysis paradigm has surged in recent years with an increasing body of evidence documenting the clinical and quality-of-life advantages of this modality compared with conventional thrice-weekly hemodialysis (1–5). Investigators from Australia and New Zealand reported superior patient survival among their home hemodialysis population compared with both in-center hemodialysis and peritoneal dialysis, whereas recent studies from North America suggested that NHD survival is significantly better compared with conventional hemodialysis and may be similar to deceased-donor transplantation (6–8).

Increased uptake of NHD has prompted interest in evaluating patient suitability for this home-based therapy in an effort to offer this treatment to a broader range of patients with ESRD. Understanding patient and program characteristics that predict NHD success as well as technique failure is critical to developing protocols and procedures to identify patients who are appropriate for NHD and retain them once they have initiated this form of dialysis. Because NHD remains relatively novel, few dialysis programs have sufficient numbers of patients to examine adequately questions of patient and technique outcomes, leading us to establish the Canadian Slow Long nightly

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ExtEnded dialysis Programs (CAN-SLEEP) collaborative group (9). CAN-SLEEP is a multicenter Canadian NHD research network that brings together a larger cohort of NHD patients than would be possible for any individual program and collect data with granularity not typical of larger dialysis registries. Our study used this multicenter cohort to describe patient and technique survival for NHD and identify patient- and program-level characteristics that predict these outcomes. Addressing this gap in knowledge will help benchmark outcomes and is an important step in the evolution of NHD program development.

Materials and Methods

Study Cohort and Data Sources

The study cohort included all home NHD patients from Wellesley Hospital, Humber River Regional Hospital, Toronto General Hospital, and the Northern Alberta Renal Program between January 1, 1994, and December 31, 2006. Demographic and clinical data of NHD patients were obtained from our institutional paper and electronic records. These data included gender, patient self-reported race, underlying renal disease, body mass index (BMI) at the initiation of ESRD, and duration of ESRD before initiating NHD. Vascular access was defined by that access in use in December 2006 or the type of access in use at the time of program exit. Also recorded were the number of nightly dialysis runs per week, the number of hours per run, and whether the patient was living alone or cohabiting with someone who served as a helper for performing the dialysis procedure. With respect to their ability to perform NHD, patients were specifically categorized by their NHD primary care team as to their ability to perform all logistical aspects of NHD independently (*i.e.*, without any assistance from a helper), with minimal assistance (*e.g.*, a helper assisting with fistula cannulation, blood sample collection, or machine setup/take-down), or completely dependent on a helper to carry out all aspects of their treatment at home. Patient disposition from the study cohort was categorized as dead, transplantation, program exit for reasons unrelated to a physical or cognitive capacity to perform NHD (*e.g.*, relocation to a geographic region where NHD was not provided) or for reasons unrelated to ESRD management (*e.g.*, for employment), or technique failure. Technique failure was defined as the inability to carry out home NHD (either independently or with assistance from a caregiver) as a result of physical or cognitive incapacity as may be associated with conditions such as (but not limited to) stroke, debilitating arthritis, progressive dementia, and prohibitive deconditioning after hospitalization. This study was performed as part of our institutional quality assurance initiatives to evaluate the flow of patients through our NHD programs and received research ethics board approval at the appropriate institutions; individual patient informed consent was not obtained.

Statistical Analysis

Baseline patient demographic data as well as dialysis characteristics and patient disposition were tabulated and summarized using standard descriptive statistics. Kaplan-Meier survival estimates were used to assess the unadjusted patient retention to the NHD cohort at 1, 2, 5, and 10 years. Similar analyses were performed to estimate the probability of adverse event-free survival (whereby an adverse event was defined as a composite of death and technique failure) and technique survival (analysis censored for all program exits except technique failure). Cox proportional hazards models were used to identify patient or program characteristics that potentially were associated with adverse event–free and technique survival. When applicable, associations between variables and adverse outcomes were adjusted for the effect of the treating center. Predictor variables included age at NHD start, gender, duration of ESRD before commencing NHD, diabetes status, BMI, NHD and ESRD era (both defined as before 2001 *versus* 2001 and later; this cut point was chosen because it divided the follow-up time in half), number of previous transplants, vascular access type (arteriovenous fistula or graft *versus* tunneled cuffed central venous catheter [CVC]), ability to perform NHD independently (*versus* requiring minimal assistance or complete dependence on a caregiver), and nights per week of NHD. Patient or program characteristics for which center effect–adjusted analysis indicated $P < 0.2$ were entered into center effect–adjusted multivariable models and eliminated by sequential backward selection, yielding the most parsimonious models with maximum R^2 and $P < 0.05$ for all included variables. Statistical analysis was performed using Stata 10 (Stata Corp., College Station, TX).

Results

The study cohort consisted of 247 patients from three study sites in Canada (116 from Wellesley and Humber River Regional Hospitals, 98 from Toronto General Hospital, and 33 from the Northern Alberta Renal Program). The baseline characteristics of these patients are summarized in Table 1. The mean age of this cohort at the initiation of NHD was 45.7 years; 61.1% were male. The mean duration of ESRD before commencing NHD was 4.9 years; approximately one quarter of the patients had previously received a transplant. The patients received a median of 5 nights per week NHD with each session lasting an average of 7.2 hours (data on NHD session duration was available for 131 of the 247 patients). Two thirds of the patients used an arteriovenous fistula as their vascular access, and approximately 30% used a tunneled cuffed CVC; the remainder had an arteriovenous graft. Although only 12.1% of patients actually lived alone, 73.7% of patients performed their hemodialysis without any assistance from a caregiver or family member. The proportion of individuals who required minimal assistance was 17.8%, whereas 8.5% of patients were completely dependent on a caregiver to perform all aspects of their treatment.

Unadjusted Kaplan-Meier survival estimates are plotted in Figure 1 to show the overall NHD program retention over time censored only at the time of study termination; this reflects program exits from all causes. At 1 year, 90.1% of patients were retained in the NHD cohort and 51.1% at 5 years. Figure 2 outlines the disposition of the cohort at study termination. The majority (60.7%) of patients remained on NHD; 21.9% underwent transplantation, and 10.5% died. A small proportion (2.8%) of patients exited the NHD program because of relocation to a geographic region where NHD was not available or because of lifestyle reasons unrelated to a physical or cognitive capacity to perform NHD. Only 4.1% experienced technique failure as defined above.

Figure 3 shows patient survival from adverse outcomes (death and technique failure) with the analysis censored for transplantation and program exits unrelated to the ability to perform NHD. The analysis indicates that 95.2% of patients were retained in the cohort at 1 year and 80.1% at 5 years. Unadjusted survival for age-specific strata is shown in Figure 4.

Table 1. Baseline characteristics of the NHD cohort

Characteristic	Value
No. of patients	247
Age at NHD initiation (years; mean ± SD)[a]	45.7 ± 11.9
Duration of ESRD before NHD (years, median [range])	4.9 (0.0 to 27.1)
BMI at ESRD (kg/m^2; mean ± SD)[b]	26.2 ± 6.1
Male (*n* [%])	151 (61.1)
Race (*n* [%])	
white	180 (72.9)
black	25 (10.1)
Asian	22 (8.9)
other	20 (8.1)
Primary renal disease (*n* [%])	
diabetes	30 (12.1)
glomerulonephritis	94 (38.1)
renovascular disease	36 (14.6)
polycystic kidney disease	27 (10.9)
other	60 (24.3)
Patients with ≥1 previous renal transplant (*n* [%])	57 (23.1)
Duration of ESRD before NHD for patients with no previous renal transplant (years; mean ± SD)	2.5 ± 3.6
Nights per week of dialysis (median)	5
Hours per dialysis session (mean ± SD)[c]	7.2 ± 1.0
Type of vascular access (*n* [%])	
arteriovenous fistula	161 (65.2)
arteriovenous graft	13 (5.3)
Tunneled cuffed CVC	73 (29.6)
Patients living alone (*n* [%])	30 (12.1)
Capacity to perform NHD (*n* [%])	
completely independent	182 (73.7)
with minimal assistance	44 (17.8)
completely dependent	21 (8.5)

[a]Median age 45.8 years (range 19 to 78 years; interquartile range 37 to 54 years).
[b]$n = 173$.
[c]$n = 131$.

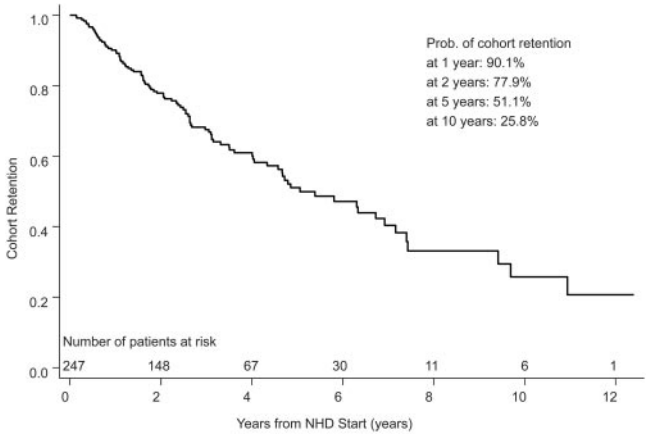

Figure 1. Overall NHD cohort retention censored only at time of study termination.

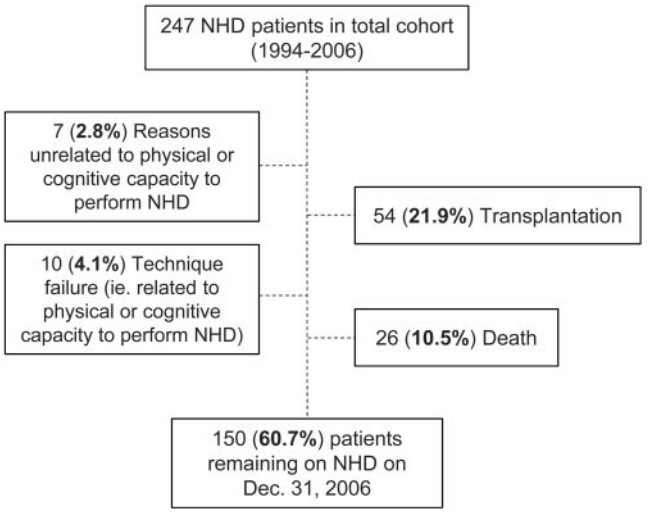

Figure 2. Patient disposition of the multicenter CAN-SLEEP NHD cohort from 1993 to year-end 2006.

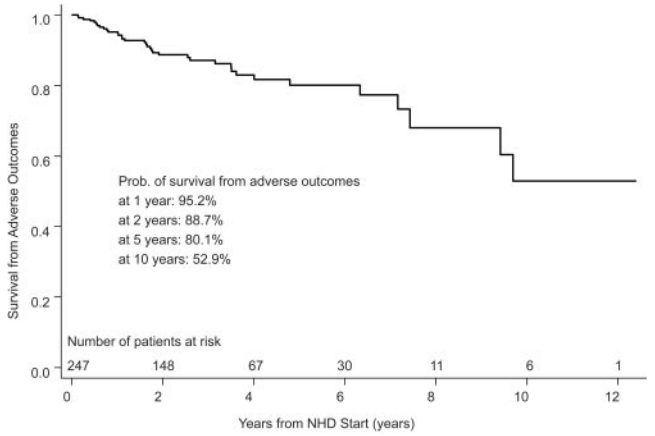

Figure 3. Event-free survival from adverse outcomes (composite of death and technique failure; $n = 36$ events) among the NHD cohort with analysis censored for transplantation and cohort dropout unrelated to technique failure.

Table 2 shows the hazards of adverse events according to NHD treatment center and demonstrates that a center effect exits. Table 3 summarizes the patient and program characteristics predictive of adverse events and are adjusted for the effect of the NHD treatment program. The strongest predictors (hazard ratio >2) of poor outcomes included diabetes, CVC use, and the inability to perform NHD independently or with minimal assistance. The most significant predictors of adverse events ($P < 0.05$) were age, diabetes, CVC use, and the complete dependence on a caregiver to perform NHD. BMI, NHD prescription, NHD or ESRD era, and the number of previous transplants were not found to be predictive. Only age and diabetes status remained significant in the multivariable model (also adjusted for the treatment center). Restricting the analysis to mortality (*i.e.*, adverse events limited to death, excluding technique failure) did not substantively alter these results.

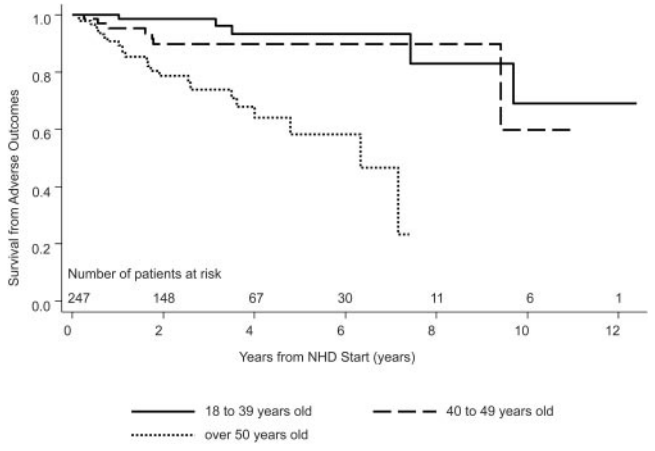

Figure 4. Survival from adverse events (composite of death and technique failure; $n = 36$ events) according to age strata 18 to 39 years ($n = 85$ individuals; 34%; solid line), 40 to 49 years ($n = 69$ individuals; 28%; dashed line), and >50 years ($n = 93$% individuals; 38%; dotted line).

Table 2. Adverse NHD program exits (death and technique failure; $n = 36$ events in 247 patients) according to center

Center	HR	95% CI	*P*
1	1.00	Reference	
2	2.49	1.07 to 5.79	0.03
3	1.06	0.22 to 5.10	0.95

CI, confidence interval; HR, hazard ratio.

The unadjusted Kaplan-Meier estimates for technique survival alone were 97.9, 96.0, 95.2, and 90.2% at 1, 2, 5, and 10 years, respectively. No center effect was found. Univariable predictors of technique survival (analysis censored for all program exits except technique failure) are shown in Table 4. Advanced age was the only significant predictor of technique failure in this analysis. Multivariable modeling was limited because of a small event rate ($n = 10$ episodes of technique failure).

Discussion

This study is novel in that it describes patient disposition from the largest NHD cohort assembled for this purpose. To our knowledge, this is also the first report of predictors of patient and technique survival that incorporates patient-level variables that are relevant for home hemodialysis, such as duration and frequency of dialysis, type of vascular access, and degree of patient independence for performing NHD. The results are encouraging with an overall mortality rate of approximately 10% over the 12 year since the cohort start date. Advanced age, diabetes status, CVC use, and dependence on others to perform the dialysis procedure are possible predictors of program exits as a result of adverse events. Technique failure, as defined by a physical or cognitive inability to perform NHD at home either alone or with assistance, is uncommon (<3% at 1 year and <5% at 5 years) and is best predicted by age alone. This study also demonstrated an important relationship between transplantation and NHD: almost one quarter of NHD patients had previously undergone transplantation, and a similar proportion exited NHD programs to undergo transplantation. This cohort also highlights that NHD patients are younger (mean age 45.7 years) and largely without diabetes (12.1% prevalence of diabetes). Our finding that the NHD treatment center significantly affected adverse events suggests that differences in clientele demographics, cultural background, socioeconomic status, education, and other such factors that may be different between the centers likely result in residual confounding. A center effect also highlights the need to examine practice patterns among NHD programs with eventual standardization of procedures and protocols to optimize outcomes.

This investigation builds on previous work by Komenda *et al.* (10) that outlined the home hemodialysis program outcomes in British Columbia, Canada, between 2004 and 2007. That cohort included 105 patients, approximately 70% of whom were performing NHD. Those authors described 19% program attrition as a result of all causes of program exit after 1 year (this study

Table 3. Predictor variables and multivariable model of adverse NHD program exits (death and technique failure; $n = 36$ events in 247 patients) adjusted for the effect of center (see Statistical Analysis section)

Variable	HR	95% CI	*P*
Predictor variables[a]			
age (per 1-year increase)	1.08	1.05 to 1.12	<0.001
diabetes	3.82	1.83 to 7.97	<0.001
BMI (per 1-kg/m^2 increase)	1.77	0.77 to 4.09	0.18
CVC (*versus* AVF/AVG)	2.34	1.20 to 4.55	0.01
completely dependent (*versus* completely independent with or without minimal assistance)	4.02	1.42 to 11.40	0.009
no. of previous transplants	0.33	0.07 to 1.64	0.18
Multivariable model			
age (years)	1.07	1.03 to 1.10	<0.001
diabetes	2.64	1.21 to 5.76	0.02

AVF, arteriovenous fistula; AVF, arteriovenous graft; CI, confidence interval; HR, hazard ratio.
[a]All variables for which $P < 0.2$ are shown.

Table 4. Univariable predictors of NHD program exits as a result of technique failure ($n = 10$ events in 247 patients)

Univariable Models	HR	95% CI	*P*
Age (per 1-year increase)	1.09	1.03 to 1.16	0.002
CVC (*versus* AVF/AVG)	2.38	0.69 to 8.25	0.17

AVF, arteriovenous fistula; AVF, arteriovenous graft; CI, confidence interval; HR, hazard ratio.

had a 1-year program attrition of approximately 10%). NHD survival from adverse program exits (death and all other program exits) censored for transplantation was 85% at 1 year, and 1-year technique survival was reported as 94% (97.9% in this study). Given the variable demographic makeup of these populations (*e.g.*, our cohort was 6 to 7 years younger than the British Columbia cohort) and the different rates of transplantation in these groups (12% in the British Columbia cohort *versus* 22% in our study), these unadjusted statistics are reasonably similar.

Whereas technique failure is explicitly defined in the peritoneal dialysis literature as an inability to continue that modality (usually because of peritonitis, ultrafiltration failure, or inability to perform peritoneal dialysis independently), necessitating a unidirectional modality change to hemodialysis, no consensus definition has yet emerged in the NHD literature. For the purpose of this investigation, we defined technique failure as a physical or cognitive inability to perform home NHD either independently or with assistance and censored our analysis of technique survival not only for death and transplantation but also for program exits unrelated to physical or cognitive functional decline. Given that many NHD patients are young, independent, and employed, the motivation for exiting the program includes reasons unrelated to ESRD management (*e.g.*, geographic relocation for the purpose of employment to a region where NHD is not offered) and would not truly represent a failure in a patient's ability to perform NHD. The highly selected nature of the NHD population precludes meaningful unadjusted comparisons with technique failure reported for other dialysis modalities.

Several important strengths and limitations of this study warrant consideration. Most notably, this study maximized the sample size of a large multicenter Canadian NHD cohort, including patient-level variables related to NHD frequency and duration, as well as vascular access type and the degree of (in)dependence with which NHD is performed at home. Indeed, this analysis suggests that hemodialysis-specific variables such as CVC use and the dependence on a caregiver to perform NHD may predict poor outcomes for these patients; however, we were unable to demonstrate an effect of dialysis duration or frequency on adverse events or technique survival. That these variables were not predictive in univariate analyses or were no longer predictive in multivariable models may be reflective of insufficient statistical power rather than an actual absence of association. In addition, because the event rate for adverse outcomes is low (26 deaths, 10 technique failures), the number of variables that can be incorporated into survival models is limited. Furthermore, this study lacks comorbidity data as well as data for patients who commenced NHD training but never graduated to perform NHD in their home setting. This latter deficit means that this study did not address issues concerning training failure (as distinct from technique failure), arguably an important outcome in the recruitment of patients to NHD. It must also be acknowledged that the mean duration of ESRD before commencing NHD was almost 5 years, so patients who self-administered this therapy were survivors of previous modalities, thereby contributing to the overall excellent survival observed in this cohort. Initiatives such as the International Quotidian Dialysis Registry may eventually be able to help address some of the aforementioned limitations (11).

Conclusions

We present patient disposition of a large multicenter NHD cohort and demonstrate relatively low adverse events (a com-

posite of death and technique failure) with excellent technique survival. Because of differences in baseline characteristics between this NHD cohort and the broader ESRD population, unadjusted comparisons between dialysis modalities cannot readily be made on the basis of these results. Larger prospective cohort studies will be required to confirm these predictors of patient and technique survival.

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Disclosures

None.

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