Technique Survival and Determinants of Technique Failure in In-Center Nocturnal Hemodialysis: A Retrospective Observational Study

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Abstract
Background: Long-duration (7-8 hours) hemodialysis provides benefits compared with conventional thrice-weekly, 4-hour sessions. Nurse-administered, in-center nocturnal hemodialysis (INHD) may expand the population to whom an intensive dialysis schedule can be offered.
Objective: The primary objective of this study was to determine predictors of INHD technique failure, disruptions, and technique survival.
Design: This study used retrospective chart and database review methodology.
Setting: This study was conducted at a single Canadian INHD program operating in Victoria, British Columbia, within a tertiary care hospital. Our program serves a catchment population of approximately 450,000 people.
Patients/Sample/Participants: Forty-three consecutive incident INHD patients took part in the INHD program of whom 42 provided informed consent to participate in this study.
Methods: We conducted a retrospective observational study including incident INHD patients from 2015 to 2017. The primary outcome was technique failure ≤6 months (TF ≤6). Secondary outcomes included technique survival and reasons for/predictors of INHD discontinuation or temporary disruption. Predictors of each outcome included demographics, comorbidities, and Clinical Frailty Scale (CFS) scoring.
Results: Among 42 patients, mean (SD) age, dialysis vintage, CFS score, and follow-up were 63 (16) years, 46 (55) months, 4 (1), and 11 (9) months, respectively. 52% were aged ≥65 years. TF ≤6 occurred in 12 (29%) patients. One-year technique survival censored for transplants and home dialysis transitions was 60%. Discontinuation related to insomnia (32%), medical status change (27%), and vascular access (23%). In unadjusted Cox survival analysis, 1-point increases in CFS score associated with a higher risk of technique failure (hazard ratio: 2.04, 95% confidence interval [CI]: 1.26-3.31). In an adjusted analysis, higher frailty severity also associated with temporary INHD disruptions (incidence rate ratio: 2.64, 95% CI: 1.55-4.50, comparing CFS of ≥4 to 1-3).
Limitations: The retrospective, observational design of this study resulted in limited ability to control for confounding factors. In addition, the relatively small number of events observed owing to a small sample size diminished statistical power to inform study conclusions. Use of a single physician to determine the clinical frailty score is another limitation. Finally, the use of a single center for this study limits generalizability to other programs and clinic settings.
Conclusions: INHD is a sustainable modality, even among older patients. Higher frailty associates with INHD technique failure and greater missed treatments. Inclusion of a CFS threshold of ≤4 into INHD inclusion criteria may help to identify individuals most likely to realize the long-term benefits of INHD.
Trial Registration: Due to the retrospective and observational design of this study, trial registration was not necessary.

Abrégé
Contexte: L’hémodialyse prolongée (7-8 heures) offre des avantages comparativement aux séances habituelles de quatre heures, administrées trois fois par semaine. L’hémodialyse nocturne en centre (HDNC), administrée par une infirmière, pourrait permettre de proposer un programme de dialyse prolongée à davantage de patients.
Objectif: L’étude visait principalement à déterminer les prédicateurs de l’échec, de l’interruption temporaire ou du succès de la modalité HDNC.
Introduction

Studies suggest that intensive dialysis beyond the conventional 4 hours, thrice-weekly schedule associates with improved outcomes.1-4 Advantages include better blood pressure,1 regression of left ventricular hypertrophy,3 improved anemia, phosphate,4 nutrition,4 quality of life,1,2 and possibly lower mortality.5-8 These benefits are most often noted with frequent (>3 times per week), long duration (>6 hours) dialysis using independent or helper-assisted nocturnal hemodialysis (NHD) performed in the patient’s home. However, barriers to adopting NHD remain. For example, fear of self-cannulation and reluctance to medicalize the home commonly limit NHD uptake.5,10 Moreover, at some centers, peritoneal dialysis (PD) and NHD serve distinct patient populations,11 whereas at others, these modalities may draw from overlapping patient pools. Despite concerted efforts it has been challenging to increase NHD utilization at our center, our older dialysis patients often decline NHD or are unable to complete training. Remoteness from training locations and our PD-assist program are additional factors, which may dissuade NHD candidates.12 In-center nocturnal hemodialysis (INHD) programs have been developed to broaden the population to which intensive hemodialysis can...
be offered. These programs offer prolonged dialysis (>6 hours) 3 nights per week. We initiated INHD in 2015 and rapidly grew to an 18-patient census. We hypothesized that INHD would be sustainable for our older dialysis population. The purpose of this study was to determine the proportion that experienced early technique failure; we also sought to document technique survival, the causes and determinants of technique failure, and the frequency of temporary interruptions to INHD.

Methods

Retrospective chart and database reviews were conducted including incident INHD patients at the Royal Jubilee Hospital following program inception February 27, 2015, until last follow-up August 22, 2017. Our renal program serves Greater Victoria with a catchment population of approximately 450,000 including ~300 dialysis patients. Study inclusion criteria were developed a priori and were applied in multidisciplinary rounds to select INHD patients (Supplemental Material 1). Research ethics boards at the University of Calgary and Vancouver Island Health Authority approved this study. Informed consent was obtained in June 2017 prior to retrospective data review.

Primary Outcome

The primary outcome was technique failure ≤6 months after INHD initiation. Technique failure was defined as permanent change to non-INHD dialysis not due to renal transplantation or transition to home dialysis. Although some published studies report 30-day technique failure, we chose a threshold of 6 months for the pragmatic reason that treatment beyond 6 months is enough time to accrue objective health benefits such as improved phosphate control and reduction in left ventricular hypertrophy. Six months was also sufficient from a programmatic perspective to justify the time investment required to support INHD patient transitions.

Secondary Outcomes

Prespecified secondary analyses evaluated unadjusted time to technique failure and prolonged technique survival greater than 12 months. “INHD modality disruptions” were defined as 3 consecutive, non-INHD treatments. Length of disruption was defined by the number of days spanning the first missed INHD run and the date of INHD resumption. Reasons for permanent discharge were determined by chart review and verbal confirmation with charge nurses when required.

Baseline Characteristics

Baseline characteristics were recorded at INHD initiation. Education level and home status (own/rent) were patient-reported. Distance from the renal unit was determined using mapping software (Google Maps, Mountain View, California). Dialysis vintage was defined as the time interval between INHD start and first-ever dialysis (HD or PD). Vascular access was defined as that used for the first INHD treatment. Patients who had a central venous catheter (CVC) as well as an arteriovenous fistula (AVF) or arteriovenous graft (AVG) were assigned to the CVC group to capture inherent risks associated with CVCs. Cause of end-stage renal disease (ESRD) was obtained from patient charts or patients’ primary nephrologist. Mode of transportation was defined as that most commonly used to commute to dialysis.

Frailty

Frailty was measured by a single investigator (M.E.S.) using the Canadian Study on Health and Aging Clinical Frailty Scale (CFS) (Supplemental Material 2). The Fried et al frailty phenotype and the CFS are 2 common tools that have been used to detect frailty among dialysis patients. The 5 frailty criteria of Fried are weight loss, exhaustion, low physical activity, slowness, and weakness. Scoring the sum of these 5 criteria allows a subject to be placed into 1 of 3 frailty categories: not frail (score 0), pre-frail (scores 1-2), and frail (scores 3-5). These criteria are often evaluated through patient self-reporting. Categorizing the frailty continuum by means of only 3 stages may lose some granularity in capturing degrees of frailty. The CFS allows an evaluator to place a patient into 1 of 9 frailty categories. This more incremental and subjective assessment may help to capture the gradual biologic continuum of frailty. It also allows the evaluator to subjectively weigh multiple layers of knowledge about the patient including medical, social, and physical observations. We therefore chose to record CFS scores in our INHD patients as a measure of frailty. In addition, the CFS has been validated in hemodialysis patients and is applicable at the bedside without additional cost and minimal training. A modified Charlson Comorbidity Index score for patients with ESRD was calculated for each patient at INHD initiation.

Dialysis Parameters

Dialysis duration was 7 to 8 hours. Dialysis was performed thrice weekly. Dialysate and blood flow rates were prescribed at 300 and 250 mL/min, respectively. Most of the patients ran on a dialysate prescription of 3 mmol/L potassium, 1.5 mmol/L calcium, 138 mmol/L sodium, and 35 mmol/L bicarbonate. Most patients used high-flux, steam-sterilized, single-use Fresenius hemodiafiltration membranes. All patients received bolus unfractionated heparin at the start of dialysis followed by heparin infusions, which were discontinued 60 to 120 minutes before dialysis completion for AVF/AVG accesses. Maximum ultrafiltration rates varied per nephrologists’ discretion.
Data Collection

Charted data were recorded per clinical guidelines by registered nurses. Data were obtained via chart review (M.J.S.) at start-up, 3 months, 6 months, and 1 year.

Statistical Analysis

Categorical variables are reported as numbers and percentages and continuous variables as means (SDs) for normally distributed data and medians (interquartile range [IQRs]) for data that were not normally distributed. To determine predictors of technique failure, univariable logistic regression was utilized. Multivariable modeling was avoided to avoid overfitting given anticipation of a small number of outcomes. Time to technique failure or death was assessed using the Kaplan-Meier Product Limit method. For the Kaplan-Meier analysis, follow-up was censored for INHD discontinuation due to (1) kidney transplantation, (2) home hemodialysis transition, and (3) end of study period, August 22, 2017. Univariable associations with time to technique failure were analyzed using a Cox survival analysis and reported using relative hazards with 95% confidence intervals (CIs).

For the secondary outcome, “INHD disruptions,” the unadjusted incidence rate ratio (IRR) (number of disruptions/follow-up time) for baseline variables was reported using the exact McNemar test. Significant univariable associations with disruptions were analyzed in an adjusted negative binomial regression model (to account for overdispersion), and IRRs and 95% CIs were reported. In all analyses, a 2-sided \( P \) value < .05 was considered statistically significant.

Results

From program start-up in February 2015 to May 2017, 43 patients commenced INHD. Forty-two patients were approached in June 2017 and provided consent. Consent was unattainable from one patient who had died. Thus, 42 patients were followed for a total 471 patient-months until the first of either permanent discharge from INHD or study completion. The mean length of follow-up was 11.2 (SD 9.3) months for all participants (n = 42) versus 16.6 (SD 9.7) months among those who did not require discharge during the course of follow-up (n = 20). Table 1 shows baseline demographic characteristics. Figure 1 shows the age distribution of the patients.

Technique Failure < 6 Months

Eighteen patients attended INHD for less than 6 months (Figure 2). Two of these 18 received a kidney transplant and 4 were enrolled late in the study period and remained on INHD at the end of study follow-up, August 22, 2017.

Table 1. Characteristics of Patients Who Participated in the In-Center Nocturnal Hemodialysis Program Between February 27, 2017 and August 22, 2017.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>63 (16)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>29 (69)</td>
</tr>
<tr>
<td>Education level, No. (%)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Elementary</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>16 (38)</td>
</tr>
<tr>
<td>University</td>
<td>24 (57)</td>
</tr>
<tr>
<td>Home status, No. (%) own</td>
<td>18 (43)</td>
</tr>
<tr>
<td>Mean distance from unit, km (SD)</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Mean dialysis vintage, mo (SD)</td>
<td>46 (55)</td>
</tr>
<tr>
<td>Prior HD setting hospital in-center unit, No. (%)</td>
<td>25 (60)</td>
</tr>
<tr>
<td>Vascular access, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Catheter</td>
<td>17 (40)</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td>19 (45)</td>
</tr>
<tr>
<td>Arteriovenous graft</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Cause of ESRD, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>21 (50)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (21)</td>
</tr>
<tr>
<td>Obstruction</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Interstitial nephritis</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Mode of transportation, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>26 (62)</td>
</tr>
<tr>
<td>Medical ride service</td>
<td>11 (26)</td>
</tr>
<tr>
<td>Family/friends</td>
<td>11 (26)</td>
</tr>
<tr>
<td>Taxi</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Mean Clinical Frailty Scale score (SD)</td>
<td>4.0 (1)</td>
</tr>
<tr>
<td>Diabetes, No. (%)</td>
<td>13 (31)</td>
</tr>
<tr>
<td>Previous home dialysis, No. (%)</td>
<td>15 (36)</td>
</tr>
<tr>
<td>Prior kidney transplant, No. (%)</td>
<td>10 (24)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index (median, IQR)</td>
<td>3 [1-6]</td>
</tr>
</tbody>
</table>

Note. ESRD = end-stage renal disease; HD = hemodialysis; IQR = interquartile range.

* Some patients had multiple modes of transportation; thus, the results have a sum greater than 100%.

Technique Failure at Any Time

Twenty-two of 42 INHD patients (52%) were permanently discharged at some point during the study. The reasons for discharge are outlined in Table 2. Four of 22 (18%) discharged patients discontinued INHD due to kidney transplantation and 1 (4.5%) due to a transition to home hemodialysis. Among the 17 (40%) patients permanently discharged for reasons other than kidney transplantation or transition to home dialysis, median technique survival was 5 months (IQR: 1.3-7.7). Sixteen of 42 (38%) patients remained on INHD greater than 12 months. Time to death or technique failure is shown in Figure 3.
Predictors of Technique Failure

In an unadjusted “time to event” Cox survival analysis, which was censored for positive outcomes (4 transplants and 1 home hemodialysis transition), there were a total of 17 permanent discharge events during the full follow-up period. Each 1-point increase in the CFS was associated with an increased risk of technique failure at any point during the study period (hazard ratio [HR]: 2.04, 95% CI: 1.26-3.31).

When treated categorically, a CFS score of ≥4 was associated with a 4.5-fold increase in the relative hazard for technique failure (HR: 4.51, 95% CI: 1.02-19.87). Other factors associated with technique failure in unadjusted analysis are noted in Table 3. Figure 4 shows that the percentage of patients with technique survival >6 months or renal transplant in each CFS category declined as CFS category rises.

Comparing those with prolonged technique survival of greater than 1 year (n = 16) to those who experienced technique failure in less than 6 months (n = 12; see Figure 1), the mean CFS score was significantly lower (3 ± 1 versus 5 ± 2) (2-tailed t test, P = .001) for who remained on INHD greater than 12 months. The mean ESRD modified Charlson Comorbidity Index was nonsignificantly lower (2.6 ± 2.2) for the patient group on INHD for more than 12 months versus 4.5 ± 4.3 for the patient group on INHD for less than 6 months (P = .06), respectively.

Sensitivity Analysis

We also calculated the odds of technique failure with increasing CFS score compared with a reference group combining CFS scores of 2 and 3. The CFS categories 2 and 3 were combined because there were no technique failure patients with a CFS score of 2. Compared with the reference group the odds of technique failure with CFS scores of 4, 5, and 6 were 1.3 (95% CI: 0.26-6.72), 5.5 (95% CI: 0.61-49.54), and 7.3 (95% CI: 0.48-111.19). The Cochran-Armitage trend test was statistically significant (P = .0056).

INHD Attendance

Twenty-two of 42 patients had at least 1 temporary INHD disruption (Table 4). The median number of days per disruption was 22 (IQR: 10-35). Nine of 22 patients had 2 or more disruptions. A total of 1286 INHD days were missed due to disruptions accounting for 9.0% of INHD time. The incidence rates of INHD modality disruptions for patients with a high (≥4) versus low1-3 The CFS scores were 1.42 per year and 0.61 per year, respectively (IRR: 2.30, 95% CI: 1.10-5.25, P = .02). Unadjusted IRRs (number of disruptions/ follow-up time) for baseline variables were as follows: CFS of 4 or greater, IRR 2.3 (95% CI: 1.10-5.25); Charlson Comorbidity Index score greater than 5, IRR 1.58 (95% CI: 0.8-2.0); home ownership, IRR 1.35 (95% CI: 0.7-2.6); medical transport service dependence, IRR 1.2 (95% CI: 0.5-2.56); age >65, IRR 0.77 (95% CI: 0.4-1.5); fistula dialysis access, IRR 0.72 (95% CI: 0.4-1.4); and dialysis vintage >1 year, IRR 0.65(95% CI: 0.3-1.4). In a multivariable adjusted model (including categories of age, Charlson Comorbidity Index, dialysis vintage, access, and medical transport service dependence), a higher frailty severity was the only factor associated with modality disruptions (IRR: 2.64, 95% CI: 1.55-4.50 comparing scores of ≥4 to 1-3).
This study considered 42 incident patients enrolled in a new INHD program. These individuals were older than those in prior case series. The mean age in our study was 63 years and 10 individuals were greater than 80. Among 20 INHD cohorts included in the 2017 review of Wong et al,7 mean age ranged from 35 to 57 years. This difference may relate to older demographics on Vancouver Island or to our inclusion criteria, which lacked age restrictions.12 Despite being older, we observed robust 1-year technique survival censored for transplants and home dialysis transitions of approximately 60%. This contemporary benchmark is similar to the only other report describing INHD technique survival of ~54% by Lacson et al,5 which included American patients within the Fresenius network. In contrast to the Lacson report, our study involved incident patients in the first-ever INHD cohort at our institution, among whom 29% experienced technique failure within 6 months. Therefore, it is possible that refinement of selection criteria using novel predictors of technique failure may increase the proportion of patients who realize benefits of sustained intensive dialysis and lessen those for whom early discontinuation results in unnecessary modality transitions and limited net benefit.

**Reasons for Permanent Discontinuation of INHD**

A better understanding of factors leading to INHD discontinuation may allow development of support measures intended to increase sustainability. For example, inability to sleep was the most common reason for discontinuation. The use of mechanical sleep aids (e.g., eye masks and earplugs), as well as pharmacological ones, was found to be beneficial. Sequestration of loud snorers in isolation rooms also helped facilitate a quieter environment. In addition, exploration of other causes of insomnia such as excess ultrafiltration leading to cramping may be helpful in select patients. Nonetheless, our findings signify that individuals with refractory insomnia are unlikely to become long-term adopters of INHD.

Another issue that arose was that of a disruptive patient with a prior diagnosis of a personality disorder. This programmatic experience led to amendment of our selection criteria. Half of the reasons for technique failure (change in medical status [27%] and vascular access issues [23%]) will likely occur at a fixed rate in INHD cohorts. However, the recognition that severe insomnia and inability to perform self-care activities are relative contraindications to INHD could attenuate the incidence of early technique failure.

It is also noteworthy that some patients discontinued INHD to pursue positive transitions; INHD functioned as a bridge to a beneficial modality in 5 of 42 patients (12%, 4 transplants, 1 home hemodialysis). This confirms that INHD may be successfully, and appropriately, employed as a transitional modality in some patients.
Predictors of Technique Failure

Our study used the Canadian Study of Health and Aging Clinical Frailty Scale to assess degree of frailty. This tool can be easily applied without extensive training. In addition, the CFS has been validated in hemodialysis patients both as a sensitive measure of frailty and as a factor predictive of mortality.\(^{15,17}\)

In our study, increasing frailty as measured by the CFS emerged as the strongest predictor of early technique failure. Each 1-point increment in CFS associated with a greater risk of technique failure. Among patients deemed to be only “mildly frail” (CFS category 5), just 40% were able to remain on the modality for more than 6 months, compared with 74% of CFS category 4 patients. A CFS designation of 5 suggests that an individual may move slowly and/or require assistance with finances, housework, or medication management.

Our findings also suggest that worsening frailty may be more predictive of early technique failure in INHD than advancing age. Similarly, Alfaadhel et al\(^ {15}\) found that the correlation with advancing frailty and mortality in dialysis patients persisted after adjustment for age. We observed 4 individuals who were above the age of 80 remain on INHD for more than 18 months. Thus, our findings do not support the use of “age” cut-offs for INHD program participation.

To our knowledge, no prior studies have described factors associated with technique failure in INHD. However, our findings align with previous studies of hemodialysis patients in which increasing frailty was found to predict other important adverse clinical endpoints including mortality and hospitalization.\(^ {18}\) Previous studies of home nocturnal dialysis patients have identified diabetes, use of rental housing, smoking, and drug or alcohol use as risk factors for discontinuing home hemodialysis.\(^ {19,20}\) However, these findings are not directly comparable with our study, given heterogeneous patient populations participating in self-care home dialysis versus nurse-dependent INHD.

INHD Attendance

Temporary disruptions occurred in approximately half of INHD patients (median duration: 3 weeks), and almost 10% of scheduled runs were missed. These missed runs represent an opportunity loss both for patients who fail to realize benefits related to intensive dialysis and program administrators wishing to maximize efficiency. Temporary disruptions were most commonly related to vascular access and medical complications, which are not typically preventable. However, higher CFS scores were found to associate with significantly greater absenteeism from INHD. Those with a CFS score of at least 4 (“Vulnerable”) were found to have more than double the incidence rate for modality disruption compared with those classed as CFS 1 to 3.

Study Limitations

This analysis is limited by its retrospective, single-center design, and small number of patients, which results in diminished statistical power to uncover other risk factors for technique failure. However, our study size is comparable with multiple previous reports.\(^ {21-24}\) Moreover, the use of predetermined INHD program admission criteria rather than accepting all-comers might have reduced the incidence of technique failure and thus diminished statistical power. The observational study design also limited the ability to control for factors, which could have influenced the results. Use of a single assessor to determine the clinical frailty score is another limitation. Given the small sample size, use of second
investigator for independent verification of CFS category could have improved data quality. In addition, important metrics such as patient satisfaction, and clinical and biochemical parameters, were outside the scope of this focused study and will be addressed in future studies.

Conclusions

Although limited by the retrospective design and small sample size, this study suggests that INHD is a sustainable modality choice, even in older patients. Increasing frailty was also found to be an important risk factor for technique failure as well as more frequent missed runs. Clinicians wishing their patients to access the benefits of INHD should consider whether they are likely to persist on the modality. The addition of a CFS score threshold of no greater than 4 into INHD selection criteria may increase the odds of identifying patients who will benefit from longer technique survival and lesser absenteeism.

Ethics Approval and Consent to Participate

This study was approved by research ethics boards at the University of Calgary and Vancouver Island Health Authority. Written informed consent was obtained in June 2017 prior to retrospective data review.

Consent for Publication

All authors have reviewed and approved this manuscript and consent to its publication.

Availability of Data and Materials

Data and materials may be made available upon reasonable request to the corresponding author.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

References


