Quality of Life and Hemodynamic Effects of Switching From Hemodialysis to Hemodiafiltration: A Canadian Controlled Cohort Study

Isabelle Ethier¹,², Immaculate Nevis³, and Rita S. Suri²,⁴

Abstract

Background: Recent randomized clinical trials have demonstrated beneficial effects of hemodiafiltration (HDF) compared with hemodialysis (HD) on mortality and hemodynamic stability. Data on quality of life in HDF compared with HD is limited.

Objective: This study aimed to determine whether patients receiving HD experience improvements in quality of life, hemodynamic and laboratory parameters after switching to HDF.

Design: Observational controlled cohort study.

Setting & Patients: Adult patients receiving maintenance dialysis were followed for 3 months both before and after transfer to a new unit, where they received HDF. Prior to transfer, control patients were already treated by HDF.

Methods: Quality of life at baseline and follow-up was measured using the validated minutes to recovery (MR) question. Dialysis data were collected for 3 consecutive sessions monthly; laboratory values were collected monthly. Wilcoxon signed rank test and repeated measures analysis of covariance were used to evaluate pre/post transfer changes and quantile regression to identify predictors of change in recovery time.

Results: Of 227 patients, 82 died, were transplanted, were hospitalized or did not transfer, leaving 123 subjects and 22 controls for analysis. MR did not improve with switching to HDF, although patients with MR > 60 min before transfer experienced a significant decrease in their MR, compared with controls. There was no improvement in intradialytic hypotension with HDF. There were no differences in laboratory values before vs after switch.

Limitations: Nonrandomized single-center study, including only small numbers of patients and covering a short follow-up period; hemodynamic values only evaluated over 1 week per month; residual kidney function not recorded.

Conclusions: In this Canadian experience of HDF, patients remained stable with respect to several laboratory and dialysis related parameters. Switch to HDF was associated with substantially reduced recovery time in patients with MR > 60 minutes at baseline.
Introduction

Patients treated with kidney replacement therapy have poorer quality of life and much higher cardiovascular morbidity and mortality risk than the general population. Dialysis has a negative impact on health-related quality of life (HRQOL), as reported by patients. Moreover, patients on dialysis seem to give more importance to HRQOL than survival. In recent years, online hemodiafiltration (HDF) utilization has emerged in North America. This treatment modality combines diffusive and convective clearance. There is growing evidence that HDF might be superior to hemodialysis on many levels: cardiovascular and all-cause mortality, cardiac structure and function, hemodynamic stability, better clearance of b2-microglobulin, and phosphorus and urea, as well as less anemia and better inflammation profile. However, comparison of HRQOL on HDF or hemodialysis (HD) is limited and whether quality of life improves with HDF compared with HD is still unknown. It has been hypothesized that the higher clearances of middle molecules, b2-microglobulin, and phosphorus; the cardiovascular stability; and the better anemia and inflammation profiles may play a role in HRQOL related to HDF compared with HD.

The Centre Hospitalier de l’Université de Montréal (CHUM), a large university center in Canada, opened a new outpatient dialysis center in 2016 with exclusive use of HDF. The current study was conducted to determine whether patients receiving maintenance dialysis experience improvements in quality of life, hemodynamic and laboratory parameters after switching to HDF.

Methods

Patients and Study Design

This observational cohort study was conducted at the CHUM after the opening of the new outpatient dialysis unit. The study was in accord with the ethical standards of the local committee on human experimentation. A waiver of consent was also obtained from the local ethics committee as this project was considered as a quality assurance study and the procedures were part of the regular patient follow-up. A few years ago, a new satellite dialysis unit was opened in our center, with exclusive use of HDF. This satellite center was planned to welcome all medically stable patients on maintenance dialysis from the CHUM. All patients previously treated at the CHUM a minimum of 3-hour sessions thrice weekly for at least 3 months before their transfer to the new outpatient center were included in the present study. The study period included the last 3 months of treatment of each patient at the CHUM before their transfer to the outpatient clinic and the 3-month period after transfer. Patients who were hospitalized in the 3-month period before transfer were excluded. However, patients who were hospitalized in the 3-month period following the transfer were still included in analysis. Prior to transfer, some patients were already treated on HDF at the hospital’s dialysis unit, in which part of the unit used this dialysis modality. There was no specific selection criteria for this group of patients treated on HDF at the hospital’s dialysis unit. This group of patients served as controls to evaluate if the changes observed were due to the transfer to the outpatient clinic or the switch from HD to HDF in the...
study group. In summary, all patients on maintenance dialysis from the CHUM deemed medically stable at the time of the opening of the new satellite unit were transferred: some were previously on HDF at the CHUM (control group), but most were on HD prior to their transfer (study group).

**Data**

Patient baseline characteristics and demographic data were obtained through patients’ electronic files. Dialysis data were obtained through software databases, NephroCare (Fresenius Medical Care, Richmond Hill, Canada; 2017) and Clinicalvision (Clinical Computing, Ipswich, United Kingdom; 2015). Laboratory data (hemoglobin, phosphate, calcium, parathyroid hormone [PTH], and albumin) at baseline and during follow-up were obtained through patients’ electronic files.

**Dialysis Systems**

At the hospital center, patients received low-flux HD with synthetic low-flux dialyzers (Optiflux 18NR, Fresenius Medical Care) with Integra (Gambro AB, Lund, Sweden) dialysis system. Online HDF was provided through 4008 or 5008 ONLINE (Fresenius Medical Care, Bad Homburg, Germany), with the Optiflux 200NR (Fresenius Medical Care) dialyzer membrane, in the postdilution mode, both at the hospital center (control group) and at the outpatient clinic (both groups).

**Primary End Point**

Primary end point was self-reported minutes to recovery (MR), expressed as the patient’s answer to the question “How long does it take you to recover from a dialysis session?,” as part of their dialysis follow-up. This question has been validated as having good correlation with HRQOL in previous studies.

**Secondary End Points**

Secondary end points were minimum systolic blood pressure (SBP) during treatment and maximum drop in blood pressure (measured as difference between predialysis SBP and minimum SBP during treatment). All SBP and diastolic blood pressure (DBP) values recorded pre-, during, and postdialysis sessions were obtained for 1 week of treatment (3 sessions) every month throughout the study period (6 months), for a total of 18 treatment sessions. Selected laboratory values were also evaluated through monthly blood sampling as per usual follow-up both at the hospital and outpatient center dialysis units.

**Statistical Analysis**

Continuous data are reported as mean ± standard deviation when normally distributed and as median (interquartile range [IQR]) when nonnormally distributed. Categorical data are expressed as frequency (percentage). Primary end point comparison included all patients. However, given the potential for “floor phenomenon” with minutes to recovery, we also conducted post hoc additional analyses in the subgroup of patients with MR >60 minutes at baseline, considering that patients reporting MR as “zero” could not experience any improvement upon modality switch. Comparison of intradialytic hypotension, minutes to recovery, and laboratory values over time was performed with Wilcoxon signed rank test and repeated measures analysis of covariance. Between-group mean difference in post- and pretransfer measurements was evaluated using a linear mixed effects model fitted to account for correlation due to repeated measures, within and between groups. To determine the predictors of change in recovery time, a fitted quantile regression (median regression) was used. All analyses were done using SAS version 9.4 (Cary, NC: SAS Institute Inc).

**Results**

Of the 227 evaluated patients receiving thrice-weekly outpatient dialysis, 82 were excluded from the study, due to death, hospitalization, transplant, or absence of transfer to the outpatient clinic, leaving a total of 145 patients (Figure 1). Of these, 123 received HD at the hospital center and transferred to HDF (study group) and 22 patients were undergoing HDF before and after transfer (control group). At baseline, patients’ characteristics were quite similar between groups, although patients in the control group were slightly older and in a larger proportion of men (Table 1). End-stage renal disease (ESRD) cause and comorbidities were similar to those expected from a Canadian dialysis cohort, except that 66% to 77% of patients had an arterio-venous fistula (AVF) as their primary vascular access. Both groups had median session duration of 4 hours, 3 times per week. High efficiency HDF was achieved for the whole duration of the study period. Median substitution volume was 28.9 (25.8-31.1) L/session in the control group before transfer and 27.3 (24.5-30.3) L/session after transfer; and 26.0 (23.0-28.8) L/session in the study group once on HDF.

**Minutes to Recovery**

Overall, there was no difference in minutes to recovery (MR) with the switch to HDF (Figure 2A). Predictors of the change in minutes to recovery from before to after transfer were identified through median regression: older age, longer duration of dialysis, and higher baseline MR were each significantly associated with better MR after transfer, whereas patients with hypertension were less likely to improve (Table 2). In the subgroup of patients who had a baseline recovery time >60 minutes (n = 53), the MR improved significantly more in the patients who switched from HD to HDF compared with controls—median
difference in MR = −120 [IQR: −630; 0] in the study group (n = 44) vs 0 [−180; 90] in the control group (n = 9); between-group difference $P < .001$; Figure 2B.

**Intradialytic Blood Pressure**

Transfer from HD to HDF was not associated with any improvement in intradialytic hypotension. First, intradialytic minimum systolic blood pressure was preserved in subjects, but went down in controls (Table 3, Figure 3A), with a statistically significant between-group median difference in pre-post values (5.0; $P < .0001$). Second, there was no statistically significant difference between groups in the maximum intradialytic drop in blood pressure with switching to HDF (Table 3, Figure 3B). We observed a significant widening of the predialysis pulse pressure in the study group compared with the control group: subjects who switched from HD to HDF had an increase in their predialysis SBP and a decrease in their DBP following transfer, whereas controls who remained on HDF experienced a decrease in both SBP and DBP after transfer to the new dialysis center (Table 3). The between-group median differences in changes of predialysis SBP and DBP values following transfer were of 9.0 and −8.0, respectively ($P < .0001$ for both; Table 3).

**Weight and Laboratory Data**

There was no observed difference between groups in the change in interdialytic weight gain before and after transfer. However, prescribed ideal weight increased in the study group, while remaining stable in controls (72.5 ± 20.1 kg to 73.4 ± 20.2 kg in the study group vs 71.2 ± 14.1 kg to 71.6 ± 14.4 kg in the control group; Table 3). There were no clinically significant differences between groups for hemoglobin, albumin, calcium, phosphate, and parathyroid hormone values (Table 3; Supplemental Figure 1).

**Discussion**

In this Canadian dialysis population experiencing the transfer of a complete dialysis unit to a new HDF exclusive center, transfer was well tolerated among patients and staff. This observational study did not show a difference in the primary end point of patient-reported minutes to recovery after

![Figure 1. Patient flow.](image-url)

*Note. HD = hemodialysis; HDF = hemodiafiltration; MR = minutes to recovery.*
transfer from HD to HDF. However, the effect of switch from HD to HDF appeared to be diluted by patients with low minutes to recovery at baseline, as patients with higher MR at baseline benefited the most from the transfer to HDF. In addition, transfer from HD to HDF was not associated with any improvement in intradialytic hypotension or any significant change in laboratory values.

The assessment of time to recovery through the minutes to recovery question used in the present study has been validated in previous studies as a good surrogate to evaluate quality of life and as being associated with mortality. Lindsay et al showed a highly significant test-retest correlation of this question over 3-month intervals demonstrating stability over time, but also a sensitivity to change. In our study, the question was asked at two different time points, at an approximately 3-month interval (before and after transfer), making it a valid method of evaluating quality of life changes with the modality transfer. Nevertheless, this measure is subjective and at risk for information bias (reporting and recall). However, since the question was asked by nurses as part of the routine assessment of patients, it should be non-differential between the groups.

The impact of HDF on quality of life is still controversial, and HRQOL data are limited in randomized control trials comparing HDF with HD. The CONvective TRAnsport STudy (CONTRAST) study did not find a significant difference between the two treatment modalities through the Kidney Disease Quality of Life 36-item short form survey (KDQoL SF-36) questionnaire. Small cross-over studies comparing HD to HDF have shown various results: some did not find any significant difference in quality of life between groups, whereas others found HDF to be beneficial in regard to “bodily pain” and “role limitations due to emotional functioning” and to be associated with better score on KDQoL SF-36 compared with HD. More recently, Smith et al, in a randomized, single-blind, cross-over study comparing high-flux HD with HDF, reported similar recovery time and quality of life scores, through KDQoL SF between groups. Median MR values were 47.5 and 30 minutes in HDF and HD in this study, in which, interestingly, HDF was associated with an increased rate of symptomatic hypotension compared with high-flux HD. Our results are in line with this last study in regard to recovery time. However, those MR values are significantly lower than the ones reported by the DOPPS in 2014 in a random sample of 6040 patients on hemodialysis in 12 countries: in this study, 32% of patients had MR < 120 minutes, whereas median MR values in our study were between 35 and 120 minutes. Moreover, in our study, in patients with baseline MR of more than an hour, switch to HDF was associated with significant improvement compared with control patients who received HDF before and after transfer (between-group median difference of a 2-hour improvement in MR). It seems reasonable that patients with higher baseline recovery time have more important decreases in their MR after switching to HDF, since patients who already tolerate dialysis well do not have much more to gain with regard to quality of life in terms of recovery time with a transfer from HD to HDF.

Contrary to previous studies showing a lower incidence of intradialytic hypotension in HDF compared with HD, our study did not demonstrate switching from HD to HDF to result in any decrease in intradialytic hypotension incidence, measured as both minimal systolic blood pressure during treatment and maximum drop in systolic blood pressure during dialysis from pretreatment value. In the present study, predialysis systolic BP increased in the study group (142 ± 17 to 148 ± 20) but decreased in controls after their transfer to the new dialysis center (153 ± 18 to 148 ± 14). Moreover, predialysis diastolic values showed the opposite changes before and after transfer in the study group (77 ± 11 to 71 ± 13), resulting in a widening of the pulse pressure. Those changes in blood pressure will need more investigating to better understand the factors involved in those variations.

### Table 1. Baseline Characteristics of the Patients.

| Variables                  | Study group (n = 123) | Control group (n = 22) |
|----------------------------|-----------------------|------------------------|
| **Body mass index (kg/m²)**| 26.5 ± 6.4            | 26.5 ± 4.6             |
| **Comorbidities**          |                       |                        |
| Coronary artery disease    | 43 (35%)              | 4 (18%)                |
| Diabetes mellitus          | 52 (42%)              | 8 (36%)                |
| Hypertension               | 93 (76%)              | 19 (86%)               |
| Peripheral artery disease  | 18 (15%)              | 5 (23%)                |
| Atrial fibrillation        | 22 (18%)              | 2 (9%)                 |
| Stroke                     | 12 (10%)              | 0 (0%)                 |
| Cancer                     | 24 (17%)              | 5 (23%)                |
| **Vascular access**        |                       |                        |
| Arterio-venous fistula     | 81 (66%)              | 17 (77%)               |
| Arterio-venous graft       | 2 (2%)                | 0 (0%)                 |
| Catheter                  | 40 (33%)              | 5 (23%)                |

Note. Values are expressed as mean ± SD or numbers (percentages).

HD = hemodialysis; HDF = hemodialfiltration; ESKD = end-stage kidney disease; FSGS = focal and segmental glomerulosclerosis.

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The between-group difference in the change in minimal systolic blood pressure showed statistically significant results: controls (on HDF pre and post transfer) seemed to have lower minimal systolic blood pressure following transfer to the new center. No difference between groups was shown in the interdialytic weight gain before and after transfer, although prescribed ideal weight seemed to increase in the study group compared with the control group. These changes in blood pressure in the control group, while interdialytic weight gain remained stable, might be due to differences in process of care at the time of transfer. We may hypothesize that medical staff might have paid closer attention to patients switching from HD to HDF while prescribing the new treatment modality at the time of transfer and made more prompt adjustments to dialysis prescriptions in the study group, while controls remained on their usual HDF prescription upon transfer to the new unit, without adjustment of their ideal weight.

Multivariate median regression analysis showed longer duration of treatment, older age, and higher baseline MR, as illustrated above, to be associated with an improvement in MR after switch to HDF, whereas hypertensive patients appeared to be less likely to improve with HDF. Smith et al found an association between longer recovery time and older age. In our study, older age and higher baseline MR were both independently associated with a greater change in MR after switch to HDF, suggesting that HDF could benefit more to older patients through better improvement in recovery time. Our study identified hypertension and shorter duration of treatment as predictors of less improvement in MR. It could be hypothesized that hypertensive patients and those undergoing shorter dialysis sessions might experience more intradialytic hypotension, higher ultrafiltration rate and worse global tolerance to treatment with more symptoms. In those patients, switching to HDF itself might not have such a beneficial effect on recovery times owing to these other implications. In this regard, it is our opinion that HDF is only one tool to improve quality of life and intradialytic hypotension, but overall follow-up and treatment of patients has to be adequate (ie, duration of sessions, blood pressure control, fluid intake restriction, etc).

Our study has some important strengths. First, our study included all patients from a dialysis center who transferred to a large HDF center in Canada with a cohort resembling that of the Canadian dialysis population, except that AVF were largely used as primary vascular access. Prior utilization of HDF in a subgroup of patients at the previous hospital center

**Table 2. Median Regression of Factors Associated With Change in Minutes to Recovery After Transfer.**

|                      | Median difference ± standard error | P value |
|----------------------|-----------------------------------|---------|
| Age                  | –2.0 ± 0.8                        | .01     |
| Male sex             | –30.1 ± 22.5                      | .18     |
| Dialysis vintage     | 1.9 ± 1.5                         | .20     |
| Diabetes             | –19.9 ± 20.5                      | .33     |
| Coronary artery disease | 5.9 ± 23.0                      | .80     |
| Peripheral vascular disease | 36.4 ± 27.9               | .20     |
| Hypertension         | 49.0 ± 22.0                       | .03     |
| Treatment duration   | –1.5 ± 0.6                        | .01     |
| Minutes to recovery at baseline | 0.41 ± 0.0                      | <.0001    |

**Figure 2.** Change in minutes to recovery pre/post transfer (all patients) (A) and change in minutes to recovery in the patients with minutes to recovery >60 minutes at baseline (n = 53) (B).

Note. HD = hemodialysis; HDF = hemodiafiltration; IQR = interquartile range; MR = minutes to recovery.
permitted to mitigate the impact of the transfer to a new dialysis unit by allowing the comparison to a control group. Moreover, a well-validated patient-centered outcome was used in the study; and many other physiological and laboratory parameters were also evaluated. Furthermore, we achieved high convection volumes upon switch to HDF, which was also maintained in controls throughout the duration of study. This might represent an important aspect of HDF treatment in our center, based on previous literature attributing greater benefits of HDF over HD when high convection volumes are obtained.

This study also has some limitations. This single-center study was not randomized, included only small numbers of patients and covered a short follow-up period. Moreover, hemodynamic values were only evaluated over 1 week per month, instead of assessing the values of all dialysis sessions over the study period. Unfortunately, residual kidney function was not recorded in this study and could have influenced the results obtained. It should also be noted that the high rate of AVF use, the medically stable population evaluated in a satellite center, and the use of low flux dialyzers in HD prior to transfer in the study group might limit the generalizability of the results to different populations.

Conclusions

In conclusion, in this first large-scale Canadian experience of HDF, patients remained stable with respect to several dialysis-related and laboratory parameters. HDF did not significantly improve minutes to recovery, although it was associated with substantially reduced recovery time from the dialysis procedure in the subgroup of patients with minutes to recovery higher than 60 minutes at baseline, compared with controls. This study also failed to demonstrate a decrease in intradialytic hypotension incidence, but proved to be a safe treatment modality in a large representative Canadian dialysis cohort.

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| Study group | Control group | Between-group difference in post-pre [delta] | P value |
|-------------|---------------|---------------------------------------------|--------|
| HD → HDF    | HDF → HDF     | value                                       |        |
| (n = 123)   | (n = 22)      |                                             |        |
| Pre transfer| Pre transfer  | Post transfer                               |        |
| Intradialytic minimum SBP (mmHg) | 118 ± 15 | 120 ± 17 | 128 ± 18 | 119 ± 18 | 5.0 | <.0001 |
| Maximum drop BP (mmHg) | 24 ± 15 | 28 ± 17 | 24 ± 12 | 29 ± 14 | 2.0 | .11   |
| Predialysis SBP (mmHg) | 142 ± 17 | 148 ± 20 | 153 ± 18 | 148 ± 14 | 9.0 | <.0001 |
| Predialysis DBP (mmHg) | 77 ± 11 | 71 ± 13 | 67 ± 13 | 65 ± 10 | –8.0 | <.0001 |
| Prescribed ideal weight (kg) | 72.5 ± 20.1 | 73.4 ± 20.2 | 71.2 ± 14.1 | 71.6 ± 14.4 | 2.4 | .004 |
| Interdialytic weight gain (kg) | 1.9 ± 1.0 | 1.7 ± 0.9 | 1.6 ± 0.7 | 1.9 ± 0.7 | 0.0 | 1.00 |
| Hemoglobin (g/L) | 110 ± 11 | 109 ± 11 | 113 ± 11 | 108 ± 12 | 2.0 | .07   |
| Albumin (g/L) | 35.5 ± 3.5 | 33.7 ± 3.7 | 34.5 ± 3.3 | 33.1 ± 3.2 | 0.0 | 1.00 |
| Calcium (mmol/L) | 2.32 ± 0.17 | 2.32 ± 0.14 | 2.28 ± 0.13 | 2.26 ± 0.15 | –0.06 | <.0001 |
| Phosphate (mmol/L) | 1.99 ± 0.54 | 1.52 ± 0.41 | 1.39 ± 0.26 | 1.47 ± 0.33 | –0.10 | .002 |
| Parathyroid hormone (ng/L) | 48 ± 41 | 46 ± 35 | 52 ± 29 | 49 ± 25 | 1.6 | .75   |

Note. Values are shown as mean ± SD. HD = hemodialysis; HDF = hemodiafiltration; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Figure 3. Mean intradialytic minimal blood pressure (A) and mean intradialytic drop in blood pressure (B) at each recorded time point during follow-up.

Note. Values were recorded at each dialysis session for a week each month for 3 months before (time points 1-3, 4-6, and 7-9) and after (time points 10-12, 13-15, and 16-18) transfer. The dotted lines represent the transfer to the new dialysis center.
Ethics Approval and Consent to Participate
The study was in accord with the ethical standards of the local committee on human experimentation. A waiver of consent was also obtained from the local ethics committee as this project was considered as a quality assurance study and the procedures were part of the regular patient follow-up.

Consent for Publication
The local ethics committee provided consent for publication of the findings of this quality assurance study.

Availability of Data and Materials
The data underlying this article will be shared on reasonable request to the corresponding author.

Declaration of Conflicting Interests
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ORCID iDs
Isabelle Ethier https://orcid.org/0000-0003-4909-0417
Rita S. Suri https://orcid.org/0000-0002-0519-3927

Supplemental Material
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