Improving the Quality of Hemodialysis Treatment
A Community-Based Randomized Controlled Trial to Overcome Patient-Specific Barriers

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Context  Mortality rates among US hemodialysis patients are the highest in the industrialized world at 23% per year. Measures of dialysis dose (Kt/V) correspond strongly with survival and are inadequate in one sixth of patients. Inadequate dialysis is also associated with increased hospitalizations and high inpatient costs. Our previous work identified 3 barriers to adequate hemodialysis: dialysis underprescription, catheter use, and shortened treatment time.

Objective  To determine the effect of a tailored intervention on adequacy of hemodialysis.

Design and Setting  Community-based randomized controlled trial with recruitment from April 1999 to June 2000 at 29 hemodialysis facilities in northeast Ohio.

Participants  Forty-four nephrologists and their 169 randomly selected adult patients receiving inadequate hemodialysis.

Intervention  Nephrologists were randomly assigned to an intervention (n=21) or control (n=23) group. For patients in the intervention group (n=85), depending on the barrier(s) present, a study coordinator gave nephrologists recommendations about optimizing dialysis prescriptions, expedited conversion of catheters to surgically created grafts or fistulas, and educated patients about the importance of compliance with treatment time. Patients in the control group (n=84) continued to receive usual care.

Main Outcome Measures  Changes in Kt/V and specific barriers after 6 months.

Results  At baseline, intervention and control patients had similar Kt/V measurements, specific barriers, and demographic and medical characteristics. After 6 months, intervention patients had 2-fold larger increases in Kt/V compared with control patients (+0.20 vs +0.10; P<.001) and were more likely to achieve their facility Kt/V goal (62% vs 42%; P=.01). Intervention patients also had nearly 3-fold larger increases in dialysis prescription (+0.16 vs +0.06; P<.001) and were 4 times more likely to change from use of catheters to use of fistulas/grafts (28% vs 7%; P=.04).

Conclusions  An intervention tailored to patient-specific barriers resulted in increased hemodialysis dose. Extending this approach to the 33 000 persons in the United States receiving inadequate hemodialysis may substantially enhance patient survival, diminish hospitalizations, and decrease inpatient expenditures.

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sent by Kt/V measurements less than 1.20 are widely considered inadequate. Below this level, each 0.10 decrease in Kt/V is estimated to increase the relative risk of death by 7%. Recent work suggests that even higher Kt/Vs are beneficial, and many providers accept values as high as 1.40.9

We reasoned that efforts to improve the quality of hemodialysis treatment should be informed by an understanding of patient-specific barriers. In fact, efforts toward quality improvement in any area typically begin with literature review and brainstorming sessions to identify potential barriers to optimal outcomes. However, the number of potential barriers identified by such methods is often very large, and it is difficult to know which barriers should be the focus of initial intervention. In this case, potential barriers to adequate hemodialysis include hypertension, comorbid conditions, non-compliance, poor vascular access, underprescription, reuse of dialyzers, and clotting.11

We also reasoned that promising barriers for intervention should have 4 features. First, a promising barrier should be independently associated with a poor outcome. Second, a promising barrier should be frequently present since uncommon barriers may be less fruitful areas for initial intervention. Third, a promising barrier should have a large effect on the outcome of interest. Fourth, a promising barrier should be modifiable.12 In a previous investigation of 721 randomly selected patients, we identified 3 potential barriers with all 4 features: underprescription of dialysis by the nephrologist, use of catheters for vascular access (as opposed to surgically created fistulas or grafts), and shortening of treatment time for the patient. For example, 11% of patients had a catheter, catheter use was independently associated with a 0.17 decrement in Kt/V, and catheters often can be replaced by fistulas or grafts.11

Based on these findings, we hypothesized that overcoming the 3 barriers would result in an increased dialysis dose. To test this hypothesis, we designed a community-based randomized controlled trial targeting patients receiving inadequate dialysis and their nephrologists.

METHODS

Subjects and Facilities
We first invited 31 hemodialysis facilities in northeast Ohio to participate, with 29 facilities agreeing. We then invited all 54 nephrologists practicing at these facilities to participate, with 53 nephrologists agreeing. We used a random-number generator to assign these nephrologists to an intervention or control group (FIGURE 1), assigning nephrologists rather than patients to prevent the possibility that a given nephrologist may care for both intervention and control patients. This randomization did not involve blocking or stratification.13 To limit the burden on individual nephrologists and facilities, a study coordinator also used a random-number generator to select a maximum of 10 eligible patients per physician and a maximum of 10% of the patients at each facility.

To determine eligibility, we identified patients receiving inadequate dialysis by abstracting medical records to identify patients whose most recent Kt/V and whose mean Kt/V for the previous 3 months were both less than the monthly goal for their facility (calculated by applying a standard formula to results of predialysis and postdialysis BUN determinations14). This ensured that only patients with persistently low Kt/V values were identified. Additional patient eligibility criteria were age 18 years or older and receiving dialysis for at least 6 months. We excluded new patients because the first several months of dialysis treatment often is a time of multiple changes in dialysis prescription and vascular access. Subjects who declined to participate, did not speak English, or were mentally impaired also were excluded. We obtained informed consent from eligible patients, and they were each given $10 at the beginning and again at the end of the trial to thank them for their participation. This study was approved by the institutional review board of MetroHealth Medical Center, Cleveland, Ohio.

Identification of Barriers
We abstracted medical records of consenting patients to determine the presence of 3 specific barriers to adequate dialysis: low prescription, catheter use, and shortened treatment time.

Low Prescription. While Kt/V (also called “delivered” Kt/V) is a measure of the amount of dialysis actually received by a patient, it is also possible to calculate the amount of dialysis prescribed for a patient (sometimes called “prescribed” Kt/V).15 We calculated the prescribed Kt/V based on manufacturer’s specifications for the prescribed dialyzer at the prescribed blood and dialysate flows, the prescribed treatment
time, and patient anthropometric volume.7,11,15-17 Because the in vivo performance of dialyzers is somewhat less than manufacturers’ in vitro specifications, delivered Kt/V is, on average, 0.10 to 0.20 lower than the prescribed Kt/V.6,7,11 Therefore, we subtracted 0.20 from the prescribed Kt/V and classified patients as having a low prescription when this value was lower than the facility goal for delivered Kt/V. Since a patient’s body size is reflected in the calculation of V, this method explicitly accounts for differences in the urea distribution volume of large vs small patients.

Catheter Use and Shortened Treatment Time. We noted whether the most recent treatment involved use of a catheter as opposed to a fistula or graft; we also noted prescribed vs actual treatment time for all treatments that were accompanied by Kt/V measurements over the previous 3 months. Patients who missed more than 5% of their prescribed treatment time were classified as having a shortened treatment-time barrier.11

Intervention Group

A study coordinator (J.B.L.) educated all intervention patients about the meaning and importance of adequate dialysis dose. She then provided feedback and recommendations to intervention patients (during a dialysis treatment) and to nephrologists (in their offices). The information provided was based on the specific barrier(s) present.

Low Prescription. The study coordinator explained why the current prescription was too low and how it could be optimized. If a low-efficiency dialyzer or submaximal flows of blood or dialysate were being used, she recommended a higher-efficiency dialyzer or higher flows of blood or dialysate. Otherwise, she recommended an increased treatment duration. Prescribed Kt/V was calculated for the recommended prescription changes to ensure that the new prescription was at least 0.20 above the facility goal for delivered Kt/V.

Catheter Use. The study coordinator interviewed patients and nephrologists to ascertain the reason for catheter use (eg, lack of vascular sites, frequent clotting, patient unwillingness to undergo surgery to receive a fistula or graft, no referral to vascular surgeon). If patients were unwilling to undergo surgery, she educated patients about the negative impact of catheter use on dialysis dose. If the patient had not been referred to a vascular surgeon, she encouraged the nephrologist to do so. Otherwise, she recommended an increased dialysis prescription.

Shortened Treatment Time. The study coordinator interviewed patients to ascertain reasons for shortened treatment time (eg, dialysis-associated symptoms, transportation problems, time conflicts related to work or family). She enlisted the aid of the nephrologist to address patient symptoms and the facility’s social worker to address transportation problems and time conflicts.

During the 6-month duration of the trial, the study coordinator communicated on a monthly basis with patients and nephrologists to reinforce the above recommendations, monitor progress, and answer questions. If specific barriers persisted, she noted whether this was due to a medical limitation, patient refusal, physician refusal, or a facility-related impediment. The study coordinator also assessed patient quality of life at the beginning and again at the end of the trial using 7 subscales (general health, energy/fatigue, emotional well-being, burden of kidney disease, dialysis-associated symptoms, sleep, satisfaction with care) of the Kidney Disease Quality of Life instrument.18 Because the study coordinator carried out the intervention, it was not possible for her to be blinded to subjects’ assignment to intervention vs control groups. There were no adverse events or side effects associated with the intervention.

Control Group

Control patients underwent quality-of-life assessments at the beginning and again at the end of the trial. Otherwise, they continued to receive usual care from their nephrologists. Neither control patients nor their nephrologists received any feedback from study personnel.

Follow-up Procedures

All patients were recruited between April 1999 and June 2000 and followed up for 6 months, or until they died or moved. During this interval, medical records of intervention and control patients were abstracted on a monthly basis to obtain data on Kt/V and specific barriers.

Outcomes

Primary outcomes were change in Kt/V and achievement of facility Kt/V goal. To increase the precision of the estimates, the “final” Kt/V of each patient was defined as the mean of all Kt/V measurements during months 4 through 6 of the trial while the “baseline” Kt/V was the mean of all Kt/V measurements during the 3 months prior to subject enrollment.19 Change in Kt/V was calculated as the final Kt/V minus the baseline Kt/V. The final Kt/V was used to determine if patients achieved their facility goal. Because we expected it would take about 3 months for our intervention to have an effect, patients who died or moved during months 1 through 3 of the trial were not included in the main analyses. Secondary outcomes were (1) changes in prescription, catheter use, and treatment time among patients who had these barriers at baseline and (2) changes in quality of life among all patients.

Statistical Analysis

Because nephrologists comprised the unit of randomization, our main analyses account for the clustering of patients by nephrologist. Specifically, we compared change in Kt/V for intervention patients vs control patients using an adjusted t test that reflects the clustering of patients by nephrologist.20 Similarly, we used an adjusted χ² test that reflects the clustering of patients by nephrologist to compare the proportion of patients in each group that achieved the facility Kt/V goal.21-23 Changes in specific barriers and quality of life were examined using the χ² test for dichotomous variables or the
Mann-Whitney rank-sum test for continuous variables.

We calculated the sample size required to detect a 25% difference in our dichotomous primary outcome (ie, 25% of control vs 50% of intervention patients achieving the facility Kt/V goal). To detect this difference with a power of 80% and an α of .05 requires 120 total subjects, or 2 to 3 patients per nephrologist.23 We then inflated this estimate to account for possible nonindependence of subjects clustered by nephrologist. We conservatively assumed that up to 75% of nephrologists would have concordant results (ie, at the end of the trial, all of their patients either will or will not have achieved the facility goal). This gives an inflation factor of 1.33 and a final sample size requirement of 160 subjects.24 JMP v3.2 (SAS Institute Inc, Cary, NC) was used for all analyses.

RESULTS

Subject and Facility Characteristics

Of 29 participating hemodialysis facilities, 23 (79%) were free standing (vs hospital based) and 21 (72%) were for profit. Of 53 participating nephrologists, 83% were men, 55% were white, and their mean age was 48 years.

Figure 1 illustrates the flow of participants through the trial. A total of 169 patients completed the trial. Eighty eligible patients did not complete the trial, either because they declined to participate, were unable to participate because they were mentally impaired or did not speak English, or died or moved prior to reaching the final evaluation phase. The 80 nonparticipants were older than the 169 participants (65 years vs 55 years, P < .001), but did not differ in sex, race, cause of renal failure, years receiving dialysis, or baseline Kt/V. Nine of the 53 nephrologists did not have any eligible patients.

Intervention and control patients had similar demographic and medical characteristics, baseline Kt/V and facility Kt/V goals, and specific barriers to adequate hemodialysis (Table 1). The most common barrier was low prescription, present in 68% of intervention patients and 75% of control patients (P = .33).

Changes in Dialysis Dose

As seen in Table 2, intervention patients had 2-fold larger increases in Kt/V compared with control patients (+0.20 vs +0.10; 95% confidence interval for difference, 0.05-0.15; P < .001). Intervention patients were also more likely to achieve their facility Kt/V goal compared with 31% of patients in both the middle and highest tertile (P = .04). Among intervention patients, there was no relationship between body size and likelihood of achieving the facility Kt/V goal. Sixty-two percent of control patients in the lowest tertile of body weight achieved the facility Kt/V goal compared with 31% of patients in both the middle and highest tertile (P = .04). Among intervention patients, there was no relationship between body size and likelihood of achieving the facility goal (61%, 69%, and 57% of patients in the lowest, middle, and highest tertile, respectively, achieved the facility goal, P = .64).

Changes in Barriers

Among the 121 subjects with low prescribed Kt/V at baseline (Table 2), in-
The 57 subjects with catheters at baseline, intervention patients were 4 times more likely to have catheters changed to fistulas or grafts compared with control patients (28% vs 7%, P = .04). Among the 39 subjects with shortened treatment time at baseline, both intervention and control patients had similar increases in treatment time (+13 minutes vs +13 minutes, P = .94).

The number of barriers remaining at the end of the trial correlated strongly with achieving the facility Kt/V goal among both intervention and control patients (FIGURE 2). Eighty-two percent of patients with no barriers remaining achieved the Kt/V goal, while only 13% of patients with 3 barriers remaining achieved the Kt/V goal.

**Reasons for Failing to Overcome Barriers**

Even though our intervention was an overall success, specific barriers persisted among some intervention patients. The reasons for failing to overcome barriers are listed in FIGURE 2.

The 4 possible ways to increase dialysis prescription are listed separately. Twenty intervention patients did not receive higher-efficiency dialyzers. In 1 case, the patient had a history of an allergic reaction to the higher-efficiency dialyzer; in 4 cases, the nephrologist refused to prescribe a higher-efficiency dialyzer; and in 15 cases, the facility did not use higher-efficiency dialyzers. Ten patients did not have blood flow increased, due to medical limitations (eg, poor function of fistula or graft) or patient refusal. Five patients did not have dialysate flow increased because their facility used older equipment that could not accommodate higher flows. Twenty-two patients did not have treatment time increased because of patient refusal, physician refusal, or a tight facility schedule that prevented increased treatment time.

Twenty-one patients did not have catheters changed to fistulas or grafts.

In 11 cases, patients had medical limitations such as lack of vascular sites or frequent clotting; in 6 cases patients refused; and in 4 cases, the physicians refused.

**Quality of Life**

There was no difference between intervention and control patients in baseline or final assessments of any of the 7 quality-of-life subscales examined (results not shown). In addition, there was no relationship between change in treatment time and items related to burden of kidney disease or specific dialysis-associated symptoms including cramping, nausea/vomiting, dizziness, and feeling washed out.

**COMMENT**

This is the first randomized controlled trial of an intervention that targets specific barriers to adequate hemodialysis. We demonstrated that addressing 3 common and easily identifiable patient-specific barriers resulted in 2-fold larger increases in dialysis dose compared with usual care. Only 18% of patients who overcame all their barriers still had inadequate dialysis doses (Figure 2). This suggests that other, as-yet unidentified barriers are unlikely to be important impediments to adequate dialysis. The finding of statistically significant and clinically important effects despite a modest sample size and relatively brief 6-month follow-up provides further evidence of the intervention’s effectiveness. By enrolling subjects receiving the lowest dialysis doses, we improved adequacy of dialysis among patients at the highest risk of mortality, morbidity, and increased health care costs. While some patients may view dialysis treatment time as burdensome, we found that increasing dialysis dose did not adversely affect patient quality of life.

By engaging the participation of virtually all dialysis facilities and nephrologists in a large geographic area, we enhanced the generalizability of our findings. With the exception of sex and race (TABLE 1), patient characteristics and facility characteristics are comparable to national data. As expected, men and black patients were overrepresented among those receiving inadequate hemodialysis. This appears to be due to

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[Table 3: Reasons for Failure of Intervention Patients to Overcome Specific Barriers]

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Medical Limitation</th>
<th>Patient Refusal</th>
<th>Physician Refusal</th>
<th>Facility-Related</th>
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<td>Low prescription</td>
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<td>Higher-efficiency dialyzer not used</td>
<td>10</td>
<td>6</td>
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<td>0</td>
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<tr>
<td>Blood flow not increased</td>
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<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Dialysate flow not increased</td>
<td>22</td>
<td>0</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Treatment time not increased</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter use</td>
<td>21</td>
<td>11</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Not changed to fistula or graft</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shortened treatment time</td>
<td>14</td>
<td>5</td>
<td>9</td>
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</tr>
</tbody>
</table>

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a larger body size and more frequent shortening of treatment time by men and black patients.\textsuperscript{16,26-28} Despite a larger urea distribution volume, large patients in the intervention group improved as much as smaller patients. By contrast, large patients did not do as well as smaller patients in the control group.

Our results have important implications for patients, providers, and health policy makers. Patients can improve dialysis adequacy by allowing increased prescriptions, expediting conversion of catheters to fistulas or grafts when possible, and minimizing shortening of treatments. Because symptoms such as cramping tend to occur near the end of a dialysis treatment, some patients are reluctant to increase treatment time.\textsuperscript{6,29} Such patients may be reassuring to know that a longer treatment time was not associated with an increase in symptoms or in perceived burden of kidney disease among study participants. Providers can improve dialysis adequacy by routinely monitoring not only Kt/V but also the 3 specific barriers to adequate dialysis. In particular, we found that nephrologists were unaware of low prescriptions because they do not explicitly calculate prescribed Kt/V as we did for this trial. In addition, it is imperative to identify and eliminate provider-related impediments such as a lack of higher-efficiency dialyzers or use of old machines. Policy makers can improve dialysis adequacy by reimbursing facilities more for longer treatments and for using higher-efficiency dialyzers (as opposed to the current fixed payment per treatment). Because inadequate dialysis is independently associated with more frequent hospitalizations, an increased reimbursement to outpatient dialysis facilities may be offset by savings in inpatient expenditures. In a previous investigation, we estimated that a 0.10 increase in Kt/V is independently associated with an $1880 per patient decrease in annual inpatient expenditures.\textsuperscript{3} Thus, applying our intervention to all 33,000 patients receiving inadequate dialysis may result in a $62 million savings in inpatient expenditures.

The randomized trial design allows us to differentiate the effect of our intervention from the usual care provided by nephrologists. Inadequate hemodialysis has been the focus of intense scrutiny and quality improvement efforts at the national, regional, and facility levels for the last several years.\textsuperscript{5-7} The improvements in Kt/V among control patients suggest that these efforts may indeed help to improve dialysis dose, although not as effectively as our targeted approach.\textsuperscript{30,31} Recruitment of both intervention and control patients from the same geographic area further diminishes the possibility that some external influence differentially affected the 2 groups. The favorable change in both the end point (Kt/V) and the intermediate variables (patient-specific barriers) strengthens the causal link between our intervention and increased dialysis dose. Two other possible contributors to the observed improvement in the control group are worth mentioning. First, control patients may have improved in part because they and their physicians were being observed (the Hawthorne effect).\textsuperscript{32} Second, it is possible that control patients were influenced by intervention patients if they were at the same facility (contamination). However, both of these effects would tend to decrease the difference between control and intervention patients, and therefore the measured effect size of 0.10 may underestimate the value of our intervention.

While our intervention was an overall success, many intervention patients failed to overcome specific barriers (Table 3). In addition, our intervention was no more effective than usual care for addressing the shortened treatment time barrier. Further refinements of our approach may be needed to increase its potency.

In conclusion, we recommend that nephrologists, individual hemodialysis facilities, dialysis chains, and regulatory agencies monitor and address 3 specific barriers to adequate dialysis: underprescription, catheter use, and shortening of treatment time. Although our modest sample size and brief follow-up period are insufficient to demonstrate an impact on patient mortality and morbidity, several large observational studies have demonstrated a link between Kt/V and these patient outcomes.\textsuperscript{3,33-35} Thus, overcoming patient-specific barriers has the potential to enhance survival and decrease both hospitalizations and inpatient expenditures. Our approach of first identifying promising barriers in observational studies and then testing interventions to overcome these barriers in randomized controlled trials may also be applicable to quality improvement efforts in other medical settings.

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REFERENCES


Author Contributions: Study concept and design: Sehgal, Leon, Siminoff, Singer, Cebul. Acquisition of data: Sehgal, Leon, Bunosky. Analysis and interpretation of data: Sehgal, Leon, Siminoff, Singer, Cebul. Drafting of the manuscript: Sehgal, Leon, Siminoff, Cebul. Critical revision of the manuscript for important intellectual content: Sehgal, Leon, Siminoff, Singer, Bunosky, Cebul. Statistical expertise: Sehgal, Siminoff, Singer, Cebul. Obtained funding: Sehgal, Siminoff, Cebul. Administrative, technical, or material support: Sehgal, Leon, Bunosky, Cebul. Study supervision: Sehgal, Leon, Cebul.

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Nothing is constant but change! All existence is a perpetual flux of “being and becoming”! That is the broad lesson of the evolution of the world.
—Ernst Heinrich Haeckel (1834-1919)