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Effect of Center- *Versus* Patient-Specific Factors on Variations in Dialysis Adequacy

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Abstract. Efforts to improve the delivery of hemodialysis have focused mostly on identifying patient-related factors that lead to inadequate dialysis. Less consideration has been given to the impact of the dialysis center on adequacy. This study evaluated whether the dialysis facility or individual-level factors were the primary influence on variations in dialysis adequacy. This was a retrospective analysis of 4971 hemodialysis patients in 189 centers with urea reduction ratio (URR) values obtained in the final quarter of 1997. The *between-center* variation and the *within-center* correlation in URR values were quantified to determine the contribution of a center effect on variations in adequacy; furthermore, the proportion of variance attributable to the centers' effect and individual-level dialysis covariates were compared. There was a wider between-center variation in mean URR values (SD, 4.8%) than expected if there were no center effect (SD, 2.5%). There was a strong within-center correlation in URR values, measured by the parameter ρ, which was only minimally diminished after adjusting for individual-level covariates (adjusted ρ, 0.14; $P < 0.0001$). The variation in URR attributable to the center effect, quantified by R^2, was greater than that related to individual-level dialysis factors (facility- and individual-level dialysis covariates R^2, 23.6 and 11.3%, respectively). Initiatives to improve the delivery of dialysis in patients with end-stage renal disease should be directed at facility policies governing dialysis care, along with patient-specific problems, because center effects have a major influence on dialysis adequacy.

A majority of patients who develop end-stage renal disease (ESRD) are placed on hemodialysis for renal replacement; however, many of these people do not receive adequate dialysis. This has been a major concern in the nephrology community and the emphasis of several studies of how to improve care in this population. The focus of both descriptive and prescriptive studies of inadequate dialysis has been on patient-specific causes rather than on factors at the facility level, or so-called center effects, which might play an important role in dialysis delivery. Center effects confer an exposure on all individuals within a center, which results in those individuals' behaving more alike than if they were from different centers (1,2). A previous study of ESRD patients who were receiving hemodialysis in Network 5 demonstrated that there was likely to be a significant center effect on dialysis adequacy as measured by the urea reduction ratio (URR) (3). There was no information available in that study, however, on individual dialysis characteristics, which are likely to have a major influence on variations in URR measurements. In the present study, we set out to confirm the presence of a center effect on dialysis adequacy in a sample of hemodialysis patients in whom there was information on dialysis delivery. We then compared the importance of the center effect relative to individual dialysis factors in determining hemodialysis adequacy in a regional population of ESRD patients.

Materials and Methods

Study Sample

This was a retrospective analysis of hemodialysis patients in Network 5 (the geographical region including Virginia, Maryland, West Virginia, and the District of Columbia) during October of 1997. In that year, the network requested that all facilities in the region collect the dialysis flow sheets of every patient on the day of their final quarterly measured URR in October and send them to the network office. In addition, the network office requested that each unit submit its policy on time of blood urea nitrogen (BUN) sampling after dialysis. The flow sheets of 12,330 patients were received with 1673 excluded from the study because they had no BUN data, or the calculated URR was ≤30% or ≥90%. Individual URR values were calculated with the following formula:

$$\text{URR} = (\text{predialysis BUN} - \text{postdialysis BUN}) \div \text{predialysis BUN}$$

using the predialysis and postdialysis BUN values obtained for each patient. The 10,657 patients who had adequate flow sheets were divided into quintiles on the basis of their URR values. Approximately

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1000 patients were randomly sampled from each quintile for detailed abstraction of the associated dialysis flow sheets. A total of 5023 patients initially were selected for the study; however, included were only 4971 patients who received dialysis at centers with at least 5 individuals in the sample.

The information recorded, along with URR and dialysis facility, included several other variables that were designated as either case-mix factors or dialysis-specific factors. The case-mix factors included age, race, gender, and presence of diabetes. The dialysis factors included access type, blood flow, time on dialysis, dialyzer urea clearance, and the predialysis BUN value. Access type was categorized into those who had an in-dwelling venous catheter, autologous arteriovenous fistula, or polytetrafluoroethylene arteriovenous graft. The manufacturer's estimate of urea clearance at a blood flow of 200 ml/min was used for all of the dialyzers in the study. The multivariate analyses used a reduced sample ($n = 3162$) that included only patients who had complete information on all covariates and dialyzed in units with at least 4 other patients who also were included in the reduced sample.

The study sample was contrasted to a data set designed to simulate the null hypothesis, which stated that patients are not influenced by a center effect in dialysis adequacy. The simulated data set included the same patients but replaced their actual URR values with random URR values. Each random URR value was drawn from a normal distribution with a mean and SD derived from the actual data and then was assigned to every patient who had no change in his or her actual facility identifier. All of the random URR values were independent from one another, and in the random sample a selected patient was no more likely to have a value similar to a neighbor at his or her facility than to any other patient in the population.

Analysis

The presence and significance of a center effect on dialysis adequacy was determined by (*1*) using the within-center correlation in URR values across all facilities, quantified with the parameter ρ, and (*2*) measuring the extent of the between-center variation in facility mean URR values, which is related to ρ (see the Statistical Analyses section). The implication of the null hypothesis was that there was no within-center correlation in URR values, with $\rho = 0$, and a minimal between-center variation in facility means around the overall network mean URR. To demonstrate the significance of within-center correlation and between-center variation in URR values, the ρ calculations and between-center variation for the actual URR values were compared with the same parameters calculated from the random data sample. The ρ estimated across all centers in the sample were also adjusted for patient-specific case-mix and dialysis factors to determine to what extent the within-center correlation in URR values was confounded by these covariates. Finally, because a portion of the within-center correlation may have been related to facility policies on postdialysis BUN sampling, units were grouped by timing of postdialysis BUN sampling and ρ estimates were made within each stratum.

The relative strength of the center effect *versus* case-mix and dialysis-specific factors as predictors of URR values was compared. The proportion of total variance in URR explained by each set of covariates was determined using R^2 estimates. The R^2 parameter was derived from a multivariate linear model and provided an estimate of that fraction of total variance that was attributable to the covariates included in the model.

Statistical Analyses

The details of the statistical model have been reported elsewhere but are outlined briefly here (3). A large sample of URR values approximates the distribution of all URR values with an overall (grand) mean designated by $\mu_{ij} = Y_{ij}/n$. Y_{ij} is observation j in center i, and the *naive* variance is σ^2/n, where n is the number of observations in the sample. The *naive* variance, which does not account for the within-center correlation, can be broken down into its components:

$$\sigma^2 = \sigma_b{}^2 + \sigma_e{}^2$$

where $\sigma_b{}^2$ is the between-center variance and $\sigma_e{}^2$ is the within-center variance. These terms can be used to calculate the average intraclass or within-center correlation of observations among dialysis centers in the sample:

$$\rho = (\sigma_b{}^2) \div (\sigma_b{}^2 + \sigma_e{}^2)$$

When patients within dialysis centers are independent and noncorrelated, observations from a center are equivalent to one in a series of random samples from the total population and each mean should approximate the grand mean of the entire population. In this scenario, $\sigma_b{}^2$ is small and ρ approaches 0. However, if patients within dialysis centers are highly correlated, then the observations from each center no longer represent a random sample of the population; therefore, the mean of each dialysis center differs from the grand mean, the variance $\sigma_b{}^2$ is large, and ρ approaches 1 (2).

A one-way ANOVA table can be used to decompose the elements of variation for a sample of URR values (Table 1) (4). The ANOVA table components can then be used to estimate the mean ρ (4,5):

$$\rho = (\text{MSbetween cluster} - \text{MSwithin cluster}) \div (\text{MSbetween cluster} + [m - 1]\text{MSwithin cluster})$$

where m = the average number of observations in all clusters.

The SAS PROC GLM procedure was used for this analysis (Statistical Analysis Software, Cary, NC). Estimates for ρ were also made using random effect models and the method of restricted maximum likelihood found in the PROC MIXED procedure of SAS (6). Because the results from PROC MIXED were not significantly different from

Table 1. One-way ANOVA

Source of Variation	Sum of Square	Degrees of Freedom	Mean Square (MS)	Parameter Estimated
Total	$\Sigma_i\Sigma_j(Y_{ij} - \ddot{Y}_{ij})^2$	$n - 1$		
Between clusters	$\Sigma_i\Sigma_j(u_i - \ddot{Y}_{ij})^2$	$i - 1$	$\frac{\Sigma_i\Sigma_j(u_i - \ddot{Y}_{ij})^2}{i - 1}$	$i\sigma_\mu{}^2 + \sigma_e{}^2$
Within cluster	$\Sigma_i\Sigma_j(Y_{ij} - u_i)^2$	$i(j - 1)$	$\frac{\Sigma_i\Sigma_j(Y_{ij} - u_j)^2}{i(j - 1)}$	$\sigma_e{}^2$

those derived with PROC GLM, only the latter are reported in the results.

Results

There were 4971 patients in 189 centers with at least 5 patients included in the study and 3162 patients in 149 centers included in the reduced sample. The demographic characteristics of the patients are shown in Table 2. The characteristics of the total and reduced data set were similar. The average number of patients per center included in the sample were 21.2 ± 1.3 (range, 5 to 73). The mean of the 4971 URR values in the total sample was 67.8 ± 0.1% (SD, 10%). The distribution of random URR values had a similar mean of 67.5 ± 0.1% (SD, 10%). Figure 1 demonstrates the between-center variation in achieved adequacy by plotting the distribution of facility means using actual URR values relative to the center means with random URR values. There was a wider spread in facility mean values using the actual URR values *versus* the random URR values; the characteristics of both distributions are shown in Table 3.

Table 4 provides ρ estimates of the within-center correlation in URR values and the proportion of variation, R^2, in URR explained by each set of variables. There was a strong within-center correlation across all centers in both the reduced and the total samples, which was in contrast to the null ρ estimate obtained for the individuals with random URR values. Adjusting for case-mix or dialysis-specific factors only minimally diminished the ρ estimate across centers. The strength of the within-center correlation, as estimated by ρ, was not diminished within groups of facilities with common policies for sampling of postdialysis BUN levels. In the analysis of the reduced sample, the proportion of variance in URR attributable to facilities was 23.6% and greater than that related to either the case-mix or dialysis covariates alone (unadjusted R^2, 12.3 and 11.3%, respectively). Inclusion of all covariates, in addition to centers in the final multivariate model, accounted for 37.8% of the total variance in URR values found in the sample.

Discussion

In this study, we demonstrated that there was a center effect on dialysis adequacy within a regional network. The evidence for the center effect included a wide between-center variation and strong within-center correlation in dialysis adequacy. Facilities tended to have a broader range in aggregate URR results than expected if there had been no center effect, and individuals within a dialysis unit were more likely to have similar URR values than individuals who received dialysis at different units. The extent of correlation in URR values within dialysis units was only minimally diminished after adjusting for several patient-specific factors that could have accounted for the observed correlation. Factors that were presumed to vary across facilities, such as dialyzer type and clearance as well as timing of postdialysis BUN sampling, had little effect

Table 2. Demographic characteristics of patients in Network 5 Study of dialysis adequacy[a]

Characteristics	Total Data Set	Reduced Data Set[b]
N	4971	3162
Age (yr)	59.97 ± 0.21	60.15 ± 0.27
Gender		
male	2511 (50.5%)	1653 (52.3%)
female	2460 (49.5%)	1509 (47.7%)
Race		
black	3060 (61.6%)	1894 (59.9%)
white	1678 (33.8%)	1106 (35.0%)
other	233 (4.7%)	162 (5.1%)
Diagnosis		
DM	1721 (34.6%)	1094 (34.6%)
other	3250 (65.4%)	2068 (65.4%)
Access		
PTFE graft	2301 (46.3%)	1936 (61.2%)
venous catheter	697 (14.0%)	543 (17.2%)
arteriovenous fistula	772 (15.5%)	683 (21.6%)
missing	1201 (24.2%)	—
Urea clearance at Qb 200 ml/min (ml/min)	189.7 ± 4.5	189.7 ± 4.6
Blood flow (ml/min)	400.34 ± 1.89	400.31 ± 1.25
Time on dialysis (min)	204.05 ± 0.69	205.22 ± 0.56
Predialysis BUN (mg/dl)	59.3 ± 0.3	58.5 ± 0.3
URR (%)	67.8 ± 1	67.7 ± 0.1

[a] DM, diabetes mellitus; PTFE, polytetrafluoroethylene; BUN, blood urea nitrogen; URR, urea reduction ratio.
[b] Reduced data set includes all patients from total data set with complete information for all covariates and dialyzed at centers with at least four other patients in reduced data set.

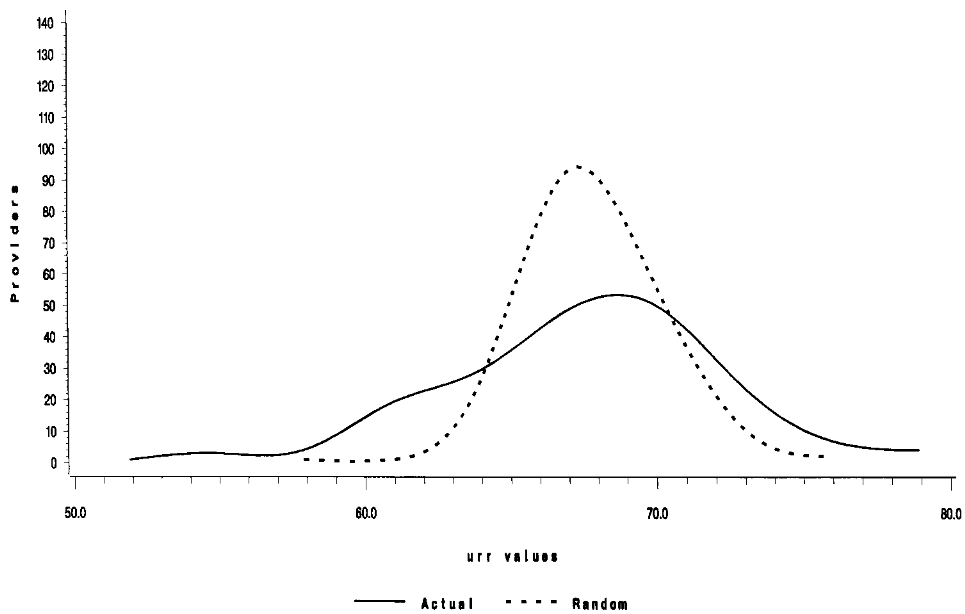

Figure 1. Distribution of facility means of individual urea reduction ratio values from Network 5 study of dialysis adequacy (n = 189 centers). ——, center means with actual data (mean, 67.2%; SD, 4.8%); -----, center means with random data (mean, 67.7%; SD, 2.5%).

Table 3. Distribution characteristics of Network 5 facility means with actual *versus* random URR values (N = 189 facilities)[a]

Characteristics	Actual Data	Random Data
Mean of facility URR values	67.5	67.8
Standard deviation of facility mean URR values	4.8	2.4
Range in facility mean URR values	27	17.3
Maximum facility mean URR value	79.3	76.0
Minimum facility mean URR value	52.3	58.7
Number of facilities (%) with mean URR ≤64%	40 (21.2)	9 (4.8)
Number of facilities (%) with mean URR ≥72%	34 (17.9)	10 (5.2)

[a] URR is urea reduction ratio × 100.

on the magnitude of ρ. Furthermore, adjusting for predialysis BUN, which is likely to be influenced by the frequency of dialysis sessions per week, had little effect on the within-center correlation. The facilities as a set of independent variables accounted for a larger proportion of variation in URR than either the case-mix or individual-level dialysis factors.

As physicians and policy makers devise strategies to improve overall dialysis adequacy in patients with ESRD, they need to choose interventions that have the greatest effectiveness because of finite resources. The results of this study suggest that variations in the adequacy of a hemodialysis population may be more attributable to policies and procedures that are unique to the dialysis facility than to individual variations in dialysis factors; therefore, initiatives to improve efficacy may be better directed to the facility. Although centers were found to be significant predictors of variations in URR, as indicated by the within-center correlation and between-center variation in adequacy, it is worth noting that these were characteristics of a network rather than of individuals. Hence, even units with superior aggregate results for adequacy were likely to have a significant fraction of individuals who did not meet the minimum criteria for adequate dialysis. These patients, despite the performance of their unit, probably required modification of those individual factors that accounted for their poor adequacy.

Several studies have examined the most common patient-specific factors that impede the delivery of adequate dialysis (7–10). Few studies have acknowledged the role of facilities in the outcomes of patients with ESRD. McClellan *et al.* (11) demonstrated that when the facility was treated as the unit of analysis, there was a broad between-center variation in both dialysis adequacy and mortality rates (12,13). In a report that used data from the U.S. Renal Data System, there was a higher mortality rate found for patients who received dialysis at for-profit dialysis units compared with similar individuals who received dialysis at not-for-profit dialysis units (14). A previous study by Fink *et al.* (15) showed that a significant factor that accounted for regional variations in dialysis adequacy

Table 4. The extent of within-center correlation (ρ) and proportion of variation, R^2, in dialysis adequacy explained by facility- and individual-level factors in Network 5 Study

	ρ	95% CI	R^2
Unadjusted			
facilities in total data set ($n = 189$)	0.16	(0.13, 0.19)[a]	18.9%[a]
facilities in reduced data set ($n = 149$)	0.20	(0.15, 0.23)[a]	23.6%[a]
facilities in reduced data set with random data	0.00	(0.00, 0.00)	0%
Covariates			
case-mix covariates	—	—	12.3%[a]
dialysis-specific covariates	—	—	11.3%[a]
Adjusted for case-mix and dialysis covariates			
all facilities in reduced data set	0.14	(0.11, 0.18)[a]	37.8%[a]
facilities by method and time of post-BUN measurement			
sampling with slow flow method ($n = 61$)	0.13	(0.08, 0.20)[a]	40.5%[a]
sampling $<$1 min postdialysis ($n = 31$)	0.10	(0.04, 0.18)[a]	34.1%[a]
sampling $>$1 min postdialysis ($n = 38$)	0.18	(0.11, 0.28)[a]	39.7%[a]
unknown postdialysis sampling time ($n = 19$)	0.08	(0.03, 0.18)[a]	30.8%[a]

[a] $P < 0.001$.

within a network was the difference in achieved adequacy attributable to dialysis centers in the region.

The present study was a unique effort that addressed problems of dialysis adequacy in two ways. First, the study quantified the degree of within-center correlation after adjusting for several individual-level dialysis characteristics that were not available in previous studies of center effects in dialysis patients. Second, the analysis compared the relative influence of center- *versus* individual-level characteristics within one large sample of patients with ESRD. These findings lend support to the notion that quality improvement efforts should be directed at the center and their associated practice patterns along with attention to individual patient problems that affect adequacy. In fact, there is growing evidence that quality improvement initiatives directed at facilities have a positive impact on the overall performance of a network in dialysis adequacy (16).

Studies that are based on retrospective data analyses such as this have several limitations that should be considered when interpreting the results. It is possible that the method of sampling may have introduced a bias that led to similarities in URR values within centers that could not have been adjusted for in the analysis. This study, however, confirmed that there was a strong within-center correlation in dialysis adequacy on an independent sample of patients with ESRD with a distinct sampling strategy from that used in the previous study of within-center correlations (3), thus minimizing the likelihood of a sampling bias. The final model derived in the study accounted for only one third of the total variance in URR values found in the Network 5 sample. This suggests that there probably were other important predictors of dialysis adequacy that as of yet have not been identified; however, it is not likely that there was a single unmeasured covariate that could have explained a predominant proportion of the residual variance in URR values. There may be explanations for the strong within-center correlation and between-center variation in dialysis adequacy other than the center effect. These include the possibility that there was an affinity among patients with similar characteristics for certain centers and interactions between individuals that could have led to similar outcome measurements. It would be difficult, however, to theorize a causal connection between such group behavior patterns and URR measurements that are a function of the efficacy of a given dialysis session.

The conclusion of this study was that there are likely to be center effects on hemodialysis adequacy that should be considered in efforts to improve delivery of adequate dialysis within a region. It remains to be determined whether the center effect that led to the measured within-center correlation and between-center variation in URR measurements were the same across all centers. It is probable that the characteristics that distinguish some centers as superior performers are different from those properties that lead others to have inferior results, and these characteristics should be identified. Because there are clear national standards for dialysis adequacy, strong within-center correlations and between-center variations in URR values drawn from a population of dialysis patients are likely to be an undesirable property for a network. Further work needs to be conducted to evaluate whether quality improvement efforts directed at center practice patterns can use changes in center effects as a gauge of the efficacy of those efforts.

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