

Differences in Dialysis Center Practices in Determining Hemodialysis Patient Postdialysis Target Weight and Patient Survival and Hospitalizations

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In this issue of the *Clinical Journal of the American Society of Nephrology*, Dasgupta *et al.* (1) report on responses to a questionnaire sent to medical directors of dialysis centers in phase 4 of the Dialysis Outcomes Practice Patterns Study (DOPPS). These responses were linked to patient outcome data. Patient survival, in particular overall and cardiovascular mortality, was lower in those centers reporting that patient “dry weight” was reassessed by a protocol specifying the frequency of assessments.

Survival of patients on hemodialysis varies both between and within countries. The DOPPS was designed to investigate how variation in clinical practice affected patient outcomes and to investigate which practices benefitted patients and conversely, those with adverse consequences. The DOPPS recruited a broad spectrum of dialysis centers to be representative of clinical practice within a country, ranging from university hospital dialysis centers to free-standing commercial dialysis units. A number of patients in a selected center were then recruited into the observational DOPPS and followed, with demographic data and comorbidity recorded at enrollment along with BP determined by three separate measurements and urine output arbitrability defined as <200 or >200 ml/d. The number of patients in any one center is then kept constant, and therefore, new patients coming into the center are recruited to replace patients leaving the center, maintaining the allotted number of study participants. Thus, in countries with low mortality and transplantation rates, the patient cohort remains relatively stable on follow-up, whereas in countries with higher mortality or transplantation rates, then there will be greater patient turnover. This turnover of patients accounts for the marked variation in follow-up time for the 3-year 2009–2012 DOPPS-4, with only a median follow-up of 1.4 years (interquartile range, 0.7–2.5) for all-cause mortality, a median follow-up of 1.2 (interquartile range, 0.5–2.2) years for cardiovascular events, and a median follow-up of 0.62 (interquartile range, 0.3–1.4) years for hospitalizations. Data from 10,898 patients were available: 52% from Europe, 22% from North America, and 21% from Japan, with the remainder from Australia and New Zealand. Depending on missing

data, between 10,086 and 10,250 patient datasets were analyzed. To try and overcome the problem of missing data, the authors used multiple imputation but did not perform sensitivity analyses (2).

Medical directors of 273 dialysis centers (44% European, 30% North American, and 21% Japanese) were sent a questionnaire on volume management of patients on hemodialysis, and the responses to ten (35%) of the 29 questions were analyzed. The answers to five of the ten questions, including “Does your unit have a policy that limits fluid removal during a dialysis session?,” “Does your unit perform isolated ultrafiltration?,” “Does your unit use online volume indicator when assessing dry weight?,” “Does your unit use on bioimpedance when assessing dry weight?,” and “Is there a standing protocol for management of patients who develop hypotension during a hemodialysis treatment?,” had no association with the risk of overall or cardiovascular mortality, cardiovascular events, or overall or cardiovascular hospitalizations. A positive response to “Is there a protocol in your unit that specified how often to assess dry weight?” was associated with 22% and 28% lower risks of overall and cardiovascular mortality, respectively, but it was not associated with cardiovascular events or overall or cardiovascular hospitalization. However, patients from centers that replied positively to “For patients prone to intradialytic hypotension, is sodium modeling/profiling used to limit or prevent intradialytic hypotension?” had higher risks of overall mortality (36%), cardiovascular events (21%), and mortality (34%) but no excessive risk of overall or cardiovascular hospitalization. Patients from centers that supported “For patients prone to intradialytic hypotension, is lower dialysate temperature used to limit or prevent intradialytic hypotension?” had a 24% lower risk of cardiovascular mortality, but there was no effect on overall mortality, cardiovascular events, or overall or cardiovascular hospitalizations. Centers that gave an affirmative response to “Does your unit use orthostatic BP measurement when assessing dry weight?” were associated with a 15% lower risk of cardiovascular events, but there was no effect on overall or cardiovascular mortality or all-cause or cardiovascular hospitalizations (the 95% confidence intervals for

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cardiovascular hospitalization cross 1.0). There was a 19% higher risk of all-cause hospitalization for patients dialyzing in centers replying that they used online volume indicators when assessing dry weight, but there was no higher risk in overall or cardiovascular mortality, cardiovascular events, or hospitalizations.

One has to sometimes be cautious when interpreting self-reported questionnaires, because without external validation, answers may be aspirational rather than accurate reflections of routine clinical practice. Similarly, without knowing the frequency of dry weight assessments, how low the dialysate temperature was set, or how dialysate sodium was adjusted during the dialysis session, it is unclear whether these apparent differences in center practices had an actual effect on outcomes. As with any observational report, the authors can propose associations but not causality. At first glance, it would seem logical that dialysis centers with protocols for assessing target postdialysis weight should have better patient outcomes, because numerous observational studies have shown a strong link between extracellular water excess and mortality (3,4). As such, one would have expected that those centers with protocols for assessing postdialysis weight would also have fewer cardiovascular events and cardiovascular hospitalizations. However, this study did not show lower cardiovascular events or cardiovascular hospitalizations. To investigate this apparent paradox, they analyzed whether there were differences in medical and nursing staffing and patient assessment between centers with and without a protocol for assessing postdialysis weight, whether centers were commercially run, and center protocols for managing intradialytic hypotension, and they found no differences. Unfortunately, the authors did not analyze the replies from two other questions in their questionnaire: "For a typical patient in your unit, how often is dry weight usually assessed?" and "For patients with excessive weight gain, who typically determines the ultrafiltration target?" There was one key missing question in their questionnaire about the frequency of review in the dialysis unit by the nephrologist. Patient review varies between countries from almost every time that the patient attends for dialysis in Japan, Spain, Italy, France, and Germany to weekly in Sweden to monthly in New Zealand and the United Kingdom to two or three times per month in Australia and the United States. Thus, whether a center has a formal protocol or not and whether this is likely to have an effect on patient outcomes will also potentially depend on the frequency and thoroughness of patient review by the supervising nephrologist. Unfortunately, these key differences in clinical practice were not addressed in this study.

Although the responses to the questionnaire were analyzed individually, many practices overlap. For example, Japanese centers gave the highest affirmative response to having protocols to regularly assess dry weight, whereas those from the United States had the lowest response rate. Conversely, Japanese centers were least likely to use dialysate sodium modeling, whereas North American centers reported the greatest use. Orthostatic measurement of BP is time consuming, requiring patients to be supine for 5–10 minutes and then stand for 2–3 minutes. Because more Japanese patients dialyze lying down in beds compared with the increasing use of dialysis chairs in North America and Europe and because Japanese centers tend to have two

rather than three dialysis shifts, it is surprising that more Japanese center directors did not report using orthostatic BP measurements. Nationally, Japan has lower overall and cardiovascular mortality for both the general and hemodialysis populations compared with those in the United States and Europe. The latter may be confounded by younger healthier patients in North America and Europe being transplanted. The replacement of enrolled patients who have been transplanted or died with "new" patients adds further confounding to interpretation of the results of this DOPPS.

Patients dialyzing in centers reporting use of sodium modeling for those prone to intradialytic hypotension had an higher overall mortality risk. If sodium modeling led to an increase in sodium tissue stores and greater interdialytic weight gains (5), then one might have expected an association not only with cardiovascular events, and cardiovascular mortality, but also with cardiovascular hospitalizations. However, no such higher risk with cardiovascular hospitalizations was observed. This may reflect differences in the application of sodium modeling and patient review between countries and centers, but there are many other confounders ranging from centers failing to calibrate dialysis machines and not checking the quality of delivered dialysate (6,7) to the frequency of use in centers and patient comorbidity. This is because dialysate sodium modeling is more frequently used for patients with greater cardiac dysfunction who tend to start dialysis with a lower BP, which increases as excess extracellular water is removed (8).

Although of interest, this analysis of ten of the 29 questions administered to dialysis center directors raises more questions than it provides answers. Answers to some of the subsidiary questions remain to be analyzed, and the responses analyzed so far open up further avenues that require greater exploration. However, one has to be cautious, because previous attempts, for example, to introduce BP targets led to an increase in intradialytic hypotension (9). As such, rather than targeting one particular aspect of clinical practice, just like reducing catheter-associated infections, a bundle approach (10) reviewing both frequency and thoroughness of clinical assessments and incorporating biomarkers and technological advances may well be needed to improve patient outcomes.

Disclosures

None.

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- See related article, “Associations between Hemodialysis Facility Practices to Manage Fluid Volume and Intradialytic Hypotension and Patient Outcomes,” on pages 385–393.