The New KDOQI Guidelines in PD
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Despite the significant improvements in dialysis technology renal replacement therapy (RRT) was still accompanied by a high morbidity and mortality, while there had been no comprehensive effort to standardize dialysis practice. Thus on March of 1995, the National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) was established, and its primary objective was to improve dialysis patients’ outcomes and survival by providing recommendations for optimal clinical practices.

In 1997 the Work Groups by subjecting the available literature on pertinent clinical issues to structure review published a total of 114 evidence-based clinical practice guidelines [1] in the selected main areas of hemodialysis (HD) adequacy, peritoneal dialysis (PD) adequacy, anemia management, and vascular access care.

The issue of “PD adequacy” elected as a topic for which guidelines would likely have the greatest impact on PD patient outcomes. Thus the PD Work Group developed 32 guidelines most of which had been labelled “opinion” while four cases labelled “evidence” since all components of their rational were based on the published evidence. The original guidelines included in eight subgroups referring to the following issues: I. Initiation of Dialysis, II. Measures of PD Dose, III. Measurement of PD Dose, IV. Assessment of Nutritional Status as it Relates to PD, V. Adequate Dose of PD, VI. Strategies for Increasing the Likelihood of Achieving the Prescribed Dose of PD, VII. Clinical Outcome Goals for Adequate PD, VIII. Suitable Patients for PD.

Among these guidelines three of the evidence-based ones were principally related to the assessment of residual renal function and to the adequate PD dose that must be delivered to the PD patients in order to prevent any possible complication related to underdialysis [1].

The success of the NKF DOQI guidelines, led to the initiation of a new and broader effort, the Kidney Disease Outcomes Quality Initiative, which will examine kidney disease at all stages. In 2000 an update process by the same Work Groups tried to subject new articles published since 1997, to make any changes needed to each of the areas covered by the original guidelines [2]. However in the area of PD adequacy, two major changes were made: (1) Nutritional indications for initiation of renal replacement therapy and (2) Dialysis dose targets and transport status.

Regarding nutritional statement the new guidelines represent a compromise between those who are proponents of low protein diets before initiating dialysis and those who are not, and emphasize the importance of appropriate early action. The suggested modification was in guideline 2 related to the initiation of dialysis, that instead of nPNA (normalised protein nitrogen appearance) criterion, one reads: initiation of maintenance dialysis or a renal transplant is recommended in patients with chronic kidney failure, if protein-energy malnutrition develops or persists despite vigorous attempts to optimize protein and energy intake and there is no apparent cause for malnutrition other than low nutrient intake.

Concerning the small solute clearances the targets that the new DOQI committee recommended (Guideline 15) was a weekly Kt/V urea of 2 and a weekly creatinine clearance (Ccr) of 60 L/1.73m² for high and high-average transporters, while a Kt/V urea of 2 and a Ccr of 50 for low and low-average transporters patients on continuous ambulatory peritoneal dialysis (CAPD). This difference based upon data that even after controlling for delivered dose, low and low-average transporters have better patient and technique survival than do high and high-average transporters [3]. Low and low-average transporters in the absence of adequate residual kidney function, may not be able to achieve a Ccr of 60 L/wk/1.73 m² on any reasonable dialysis prescription, while these patients can achieve a weekly Kt/V of 2.0, as urea clearance is less affected than creatinine clearance by transport status, low and low-average transporters Therefore, it seems reasonable to lower the Ccr target in low and low-average transporters without fear of jeopardizing patient outcome. These patients must be observed closely for evidence of inadequate dialysis. For continuous cyclic PD and nocturnal intermittent PD higher values have been recommended (Kt/V urea of 2.1 and 2.2, Ccr of 63 and 66 L/1.73m² respectively).

The evidence came mainly from three studies from France [4], Italy [5], and North America [6]. The French group found better survival among patients with an initial weekly Kt/V urea >1.7 than those with lower values, but did not evaluate changes the effect of changes in adequacy over time due to loss of residual kidney function (RRF), nor did they attempt to evaluate any association of higher weekly Kt/V urea or Ccr with survival. The Italian study evaluated 68 prevalent CAPD patients with minimal RRF (GFR was 1.73 ml/min on entrance), and showed improved patient survival was observed with a weekly Kt/V urea >1.96, while no further benefit was observed with a Kt/V urea higher than 1.96. The CANUSA study of 680 incident CAPD patients with base-
line GFR of 3.8 ml/min, reported a 5% decrease in patient survival in association with every 0.1 decrease in total weekly $Kt/V_{urea}$ for values between 1.5 and 2.3, and a decrease of 5 L/1.73 m²/week in $C_{cr}$ was associated with a 7% increase in the risk of death. In that study showed that over the range of solute clearances that were studied, the predicted 2-year survival increased throughout the whole range, without the plateau that found the Italian group. The predicted 2-year survival associated with a constant total $Kt/V_{urea}$ of 2.1 and 2.3 was 78% and 81% respectively. However the major assumptions of this study were: a) the peritoneal clearance, that one unit of peritoneal equals one unit of residual renal, which has not proven and b) that there was no change in clearance over time, which is incorrect as the clearances did change over time.

Analysing all that data DOQI committee assuming that the renal and peritoneal $Kt/V_{urea}$ are equivalent, recommended the use of one target for the entire range of experience for patients on PD, whether they it was the timing of dialysis initiation, whether they were incident or prevalent patients, or they were anuric.

However conversely to the increasing body of evidence [7, 5, 8] suggested that $K_t/V_{urea}$ is a reliable predictor of outcome in PD and that weekly values in the range of 2.0 provide adequate therapy, there is now data that indicates that once a certain minimal amount of small solute clearance is reached there does not appear to be any benefit from further incremental changes or increases in small solute clearance with our standard therapies.

More recent ADEMEX study [9], a randomized, prospective interventional study aimed at assessing whether survival improves with higher $Kt/V$. In this study there was a statistically significant difference in solute clearances maintained throughout the study in the control group ($K_t/V$ peritoneal of 1.62) and in the intervention group ($K_t/V$ peritoneal of 2.1), while there was no difference in outcomes between these two groups, that means that PD patients don’t need a $K_t/V$ as high as 2.1 to do well. Similarly in the HEMO study [10], there was no difference in survival between patients with standard dose and patients on high-flux hemodialysis, which may indicate that above some minimal targets of small solute clearances, outcomes may be more influenced by other variables (middle molecule solutes, blood pressure, phosphorus and volume control). Thus the currently used parameters ($K_t/V_{urea}$, $C_{cr}$) that do not represent equally all solutes, are just a surrogate for clearance (removal rate), which certainly correlates with short-term uremic symptoms and may not accurately predicts outcome. Besides, toxicity is not related to clearance, but to serum and tissue levels.

Although there is no doubt that dialysis treatment should provide adequate solute and fluid removal in order achieve good clinical outcome, it is still not clear what should be the targets for adequate PD [11]. Furthermore except for the issues related to small solute clearance, until recently the exact role of fluid removal in adequacy has largely been neglected, and consequently there was no guideline given as there was no any data on ultrafiltration and outcomes at the time the original guidelines were published. Actually, there are now data suggesting that sodium removal and volume control have an impact on survival [12], which means that not only solute clearance but also volume removal (ultrafiltration) need to be optimized. Besides USRDS data continue to show the high prevalence of hypertension and cardiovascular related death in dialysis population [13]. Another important issue that has to be addressed in the guidelines is the gradual decline of the RRF and its impact to the PD patient’s outcome. There are several studies reported that the amount of residual renal function the patient has is what predicts outcome, not the peritoneal clearance [5, 8, 14, 15]. Conversely by increasing the peritoneal portion of PD dose as RRF declines one could usually prevent the development of underdialysis symptoms in long-term PD patients, which is indirect evidence that PD does improve outcome.

Obviously there are some limitations in the original and new KDOQI guidelines, while as evidence becomes available KDOQI guidelines are likely to change. However, regardless of revision problem areas for PD solute clearance predictive importance, not all the patients below KDOQI recommended targets need a prescription change if they are doing well, since we always need to manage the patient though, not a number.

References


