I. NKF-K/DOQI CLINICAL PRACTICE GUIDELINES FOR HEMODIALYSIS ADEQUACY: UPDATE 2000

NOTE: The citation for these guidelines should read as follows: National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy, 2000. Am J Kidney Dis 37:S7-S64, 2001 (suppl 1)

Acronyms and Abbreviations

Abbreviation	Term
AAMI	Association for the Advancement of Medical Instrumentation
BUN	blood urea nitrogen
CKD	chronic kidney disease
EDW	estimated dry weight
ESRD	end-stage renal disease
GFR	glomerular filtration rate
HCFA	Health Care Financing Administration
HD	hemodialysis
HEMO	HEMOdialysis Study
NCDS	National Cooperative Dialysis Study
NPCR	normalized protein catabolic rate
PRU	percent reduction of urea
QALE	quality-adjusted life expectancy
RPA	Renal Physicians Association
TCV	total cell volume
TMP	transmembrane pressure
UFR	ultrafiltration rate
UKM	urea kinetic modeling
URR	urea reduction ratio
USRDS	United States Renal Data System

Introduction

APPROXIMATELY 284,000 Americans suffered from end-stage renal disease (ESRD) in 1996,[1] of whom 62% were treated by maintenance hemodialysis (HD).[2] Despite a longer life expectancy for the general population of the United States in comparison to that of most other industrialized nations, several analyses have reported that the gross and adjusted annual mortality of Americans with ESRD greatly exceeds the analogous rates observed in other countries.[3-8] Several explanations have been proposed for these differences in ESRD patient outcome, including:

1. The acceptance of patients for maintenance dialysis in the United States who are relatively older and/or have more comorbidity than dialysis patients in other countries.[9,10]
2. Genetic differences between the prevalent patient populations in the United States and abroad that confer differing risks for comorbid conditions such as cardiovascular disease.[11]
3. The prevalent practice in the United States of dialyzer reuse (81% of dialysis centers in 1996) that may expose hemodialysis patients to toxic chemicals, increased risk of infection, and/or less effective dialysis due to compromised dialyzer function.[12-17]
4. The lower tendency in the United States to adequately meet the nutritional needs of hemodialysis patients.[18-21]
5. The incomplete and/or inaccurate reporting of relevant patient comorbidity and outcomes by non-US ESRD registries.[7,22-25]
6. The lower tendency to deliver an adequate dose of hemodialysis to patients in the United States.[14,18,19,26-32]

Regardless of the precise reasons for the apparent difference in outcome between Americans with ESRD and patients from other industrialized nations, it is indisputable that the delivered dose of hemodialysis is a significant predictor of patient outcome[19,33-42] and that the dose of hemodialysis provided to many American patients can and should be increased.[19,27,29-31,43] This assertion is based on several premises, including:

1. The dose of hemodialysis can be measured precisely, reproducibly, and routinely in the clinical setting.[19,34,42-50]
2. A scientific consensus exists on what constitutes an adequate dose of hemodialysis.[51,52]
3. Many patients do not receive that dose of hemodialysis.[19,31,43,53-57]
4. Reasons for deficiencies in the delivered dose of dialysis can be identified and redressed.[35,51,53-55,58-61]

The Renal Physicians Association's (RPA) 1993 *Clinical Practice Guideline on Adequacy of Hemodialysis** describes acceptable methods for measuring hemodialysis adequacy and defines a minimum acceptable delivered dose of hemodialysis for adults (>18 years old) with ESRD who have negligible residual kidney function and are receiving outpatient hemodialysis three times per week. Specifically, the RPA recommended that the variable volume, single-pool model of urea kinetic modeling (Kt/V_d) should be measured monthly to assure the adequacy of hemodialysis (HD), such that patients receive the full benefit of HD for ESRD. The recommended Kt/V_d should be at least 1.2 (urea reduction ratio $\geq$65%). When the Kt/V_d falls below this level, corrective action should be undertaken.[51]

The NKF-K/DOQI HD Adequacy Work Group identified several topics pertinent to implementing and maintaining adequate hemodialysis that had received limited attention in the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*. As a result, the NKF-K/DOQI Work Group summarized data and developed recommendations that supplement the RPA guideline in the following areas:

1. Optimum hemodialysis dose.
2. Adequacy of hemodialysis for pediatric patients.
3. Blood sampling to measure the hemodialysis dose.
4. Reuse of hemodialyzers.
5. Patient comfort and adherence.

* To obtain a copy of the RPA guideline, see ordering information in Appendix A.

0272-6386/01/3701-0102$3.00/0
doi:10.1053/ajkd.2001.20777

Optimum Hemodialysis Dose

The RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* described a minimum delivered dose of hemodialysis for adults with no residual kidney function who were receiving hemodialysis three times per week. In this respect, the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* did not describe a dose of hemodialysis that maximizes the survival, health, and quality of life of ESRD patients. In the absence of financial constraints, a dose of dialysis that maximizes patient outcomes is the optimal dose of hemodialysis and is a more appropriate target for prescribed dialysis therapy than a minimum adequate dialysis dose. The HD Adequacy Work Group examined peer-reviewed literature published since the release of the RPA guideline in an attempt to define an optimal delivered dose of hemodialysis. Because of changes in the demographics of the ESRD population, eg, an aging ESRD population, an increasing prevalence of patients with diabetes mellitus,[1] the HD Adequacy Work Group considered what constitutes a minimum adequate dose for different subpopulations. Selected patient subsets (blacks and diabetics) were examined to determine if the minimum hemodialysis dose for them should differ from that for the rest of the dialysis population.

Because of inappropriate timing of acquisition of the postdialysis blood urea nitrogen (BUN) sample in many patients, some of the apparent improvement in hemodialysis adequacy that has been reported may be spurious.[62-64] Therefore, significant opportunities for improvement still exist. The HD Adequacy Work Group developed an algorithm that details recommended procedures for identifying and correcting deficiencies in the delivered dose of dialysis. The intent of the algorithm is to help dialysis care teams:

1. recognize deficiencies in the delivered dose of hemodialysis.
2. identify the cause(s) of inadequate delivered dose of hemodialysis.
3. correct the cause(s) of inadequate delivered dose of hemodialysis.

Adequacy of Hemodialysis for Pediatric Patients

Pediatric patients comprise less than 1% of the total hemodialysis patient population, even in industrialized countries with established pediatric ESRD treatment capabilities. In the United States, the point prevalence of ESRD patients less than 20 years of age was 4,777 per million in 1994-1996. Eighteen percent of ESRD patients less than 20 years old received maintenance hemodialysis.[1,65] There are two predominant reasons for the small number of pediatric as compared with adult patients. First, ESRD is not a common pediatric disorder. Its incidence in pediatric patients is just over 15 new patients per million per year. In contrast, incidence rates are 122/million/yr for people 20 to 44 years of age.[1,65] Second, most children spend a relatively short time on dialysis, typically only the time awaiting kidney transplantation. As a result, even the largest pediatric hemodialysis programs are quite small by adult program standards and rarely exceed 10 to 15 patients per facility.

There are few reports in the medical literature of studies involving pediatric hemodialysis patients and no data on outcomes as a function of hemodialysis dose in children. Previous efforts to develop guidelines for hemodialysis, including the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*, did not address pediatric patients. The HD Adequacy Work Group recognized the paucity of data on adequacy of hemodialysis in pediatric patients, and decided that it was desirable and possible to extend the guideline development process to children. All available pediatric hemodialysis literature was reviewed; where pediatric data were lacking, the Work Group extrapolated from adult patient data. Thus, the NKF-K/DOQI *Clinical Practice Guidelines for Hemodialysis Adequacy* addresses children as well as adults.

Blood Sampling Procedure

Considerable variability in sampling procedures exists in dialysis practice in the United States. For example, 33% of the hemodialysis units represented by members of the Medical Review Board of the ESRD Network of New England (ESRD Network 1) reported that the samples for testing postdialysis BUN were drawn immediately before the hemodialysis treatment was terminated, 25% obtained samples immediately after the end of the dialysis treatment, and 42% drew the sample 5 minutes after all blood was reinfused into the patient.[62] Similar proce-

dural inconsistency has been observed in ESRD Network 16. Data for all hemodialysis patients in Network 16 suggest that postdialysis BUN samples were drawn immediately upon the completion of dialysis at 21% of the dialysis facilities, after an interval of 1 to 2 minutes at 52% of the facilities, 2 to 10 minutes after the completion of dialysis at 15% of the facilities, and more than 10 minutes after completion of dialysis at 13% of facilities.[43] During 1993, the United States Renal Data System (USRDS) reported that, in the dialysis facilities surveyed, the postdialysis BUN sample was drawn immediately at the end of hemodialysis without changes in the blood flow at 15% of facilities, immediately upon ending hemodialysis with a slowing or stopping of the blood pump at 48% of facilities, 20 to 60 seconds after the end of dialysis at 9% of facilities, 1 to 2 minutes after the end of dialysis at 12% of facilities, 3 to 15 minutes after the end of dialysis at 15% of facilities, and more than 15 minutes after the completion of dialysis at 1% of facilities.[66] Because of inappropriate timing of the acquisition of postdialysis blood samples, the actual delivered dose of hemodialysis may be overestimated.[47,58,67,68] A 1995 survey of 195 dialysis units in the United States found that 5% and 42% of the centers used predialysis and postdialysis blood drawing procedures, respectively, that were judged to be erroneous.[64] Erroneous blood drawing techniques and needless procedural variability compromise the ability to compare the dose of hemodialysis delivered by different dialysis units, even when the same formulae for calculating Kt/V are used. More precise specification of appropriate procedural technique will increase the accuracy and comparability of measured hemodialysis doses. To address this problem, the HD Adequacy Work Group developed supplemental procedural guidelines for predialysis and postdialysis BUN sampling.

Reuse of Dialyzers

Predominantly for economic reasons, reuse of hemodialyzers is a prevalent practice in the United States.[16,17,69-71] In 1993, approximately 79% of adult hemodialysis patients used reprocessed dialyzers. Data describing the prevalence of dialyzer reuse among pediatric hemodialysis patients are not available. Because the essential function of a hemodialyzer is to permit the mass transfer of solutes from the patient's blood into the dialysate and vice versa, the solute transport capacity or clearance of a hemodialyzer is a critical variable in writing and delivering an adequate hemodialysis prescription. Reuse of a hemodialyzer can change its solute transport capacity.[72,73] For this reason, clinicians need an accurate assessment of the solute clearance of the hemodialyzer. In the absence of direct measures of change in solute clearance with reuse, change in the total cell volume (TCV), also described as the fiber bundle volume, has been the conventional surrogate used to monitor changes in solute transport characteristics for hollow fiber dialyzers.[74,75] Several factors prompted the HD Adequacy Work Group to evaluate the use of TCV as a measure of clearance, including:

- The TCV is an indirect measure of solute clearance.
- Reprocessing techniques have evolved.

The HD Adequacy Work Group examined the peer-reviewed literature and the *Association for the Advancement of Medical Instrumentation Standards and Recommended Practices for Reuse of Hemodialyzers*.[76]

Patient Comfort and Adherence

The HD Adequacy Work Group recognizes that a major barrier to providing adequate hemodialysis is patient nonadherence with the hemodialysis prescription. Patients may confound the health care teams' attempts to provide an otherwise adequate treatment by missing hemodialysis sessions, arriving late for treatments, temporarily interrupting the treatment, or discontinuing the hemodialysis session prematurely.[32,53,77,78] The RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* focused on the processes of patient care necessary to provide an adequate dose of hemodialysis, but did not offer clinical strategies and interventions to enhance patient acceptance of the hemodialysis prescription. The HD Adequacy Work Group examined the peer-reviewed literature to identify strategies that minimize patient discomfort during and immediately after hemodialysis treatments. Complications, such as hypotension and cramps, that would compromise patient acceptance of hemodialysis, were a major focus.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.