Ten Years of Collaboration: DOPPS Research

The European Dialysis Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA), Arbor Research Collaborative for Health, and the Dialysis Outcomes and Practice Patterns Study (DOPPS)

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20 YEARS

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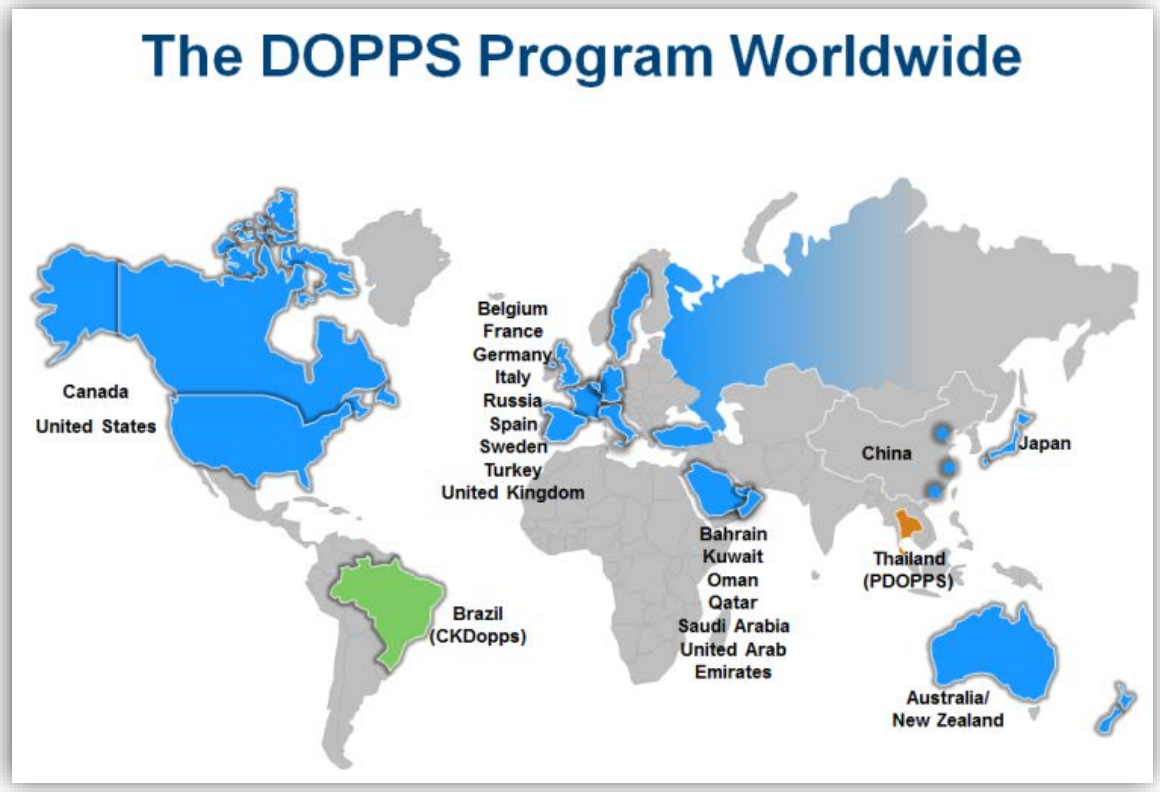
The DOPPS: A Review of the Study Design and 20 Years of Research

by Michelle Maxim

INTRODUCTION

The Dialysis Outcomes and Practice Patterns Study (DOPPS) began as a hemodialysis study in 1996 in the United States and over the past 20 years has evolved into a series of prospective studies in over 20 countries known collectively as the DOPPS Program. The DOPPS Program includes the DOPPS (in-center hemodialysis), the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps), and the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS). Designed to identify best clinical practices for treating patients with kidney disease, the DOPPS Program tracks internationally over 70,000 patients receiving hemodialysis, peritoneal dialysis (PD), and with advanced chronic kidney disease (CKD). By observing patients over time and correlating practices and outcomes in different medical settings around the world, the DOPPS Program helps researchers identify modifiable practices that improve patient lives and impact clinical outcomes.



Over the last two decades, the DOPPS Program has made landmark contributions in improving hemodialysis care and informing the nephrology community through its many scientific publications, presentations, and evidence impacting clinical practice guidelines and policy. Expanding on the success of the hemodialysis DOPPS two additional studies, the CKDopps and PDOPPS, were established and share the same goals and design as the DOPPS. CKDopps studies patients with advanced CKD (estimated glomerular filtration rate (eGFR) <45 ml/min/1.73m2). Patients are followed at nephrology clinics and data collection is currently occurring in Brazil, France, Germany, Japan, and the United States. PDOPPS is designed to identify predictors of technique survival in patients receiving PD, and is ongoing in Canada, Japan, Thailand, the United Kingdom, and the United States.

The DOPPS Program is coordinated in the United States by Arbor Research Collaborative for Health, a not-for- profit research organization based in Ann Arbor, MI USA since 1996. In 2005, after large study expansion within Europe, Arbor Research Collaborative for Health contracted with the European Dialysis and Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA) to support the participating study sites. EDTNA/ERCA Clinical Research Associates (CRAs) provide support in Germany, Italy, Spain, Sweden, Belgium, Turkey, and the United Kingdom. The CRAs liaison with the Country Investigators, Arbor Research, and the supporting staff at the study sites. The EDTNA/ERCA has been instrumental in the success of the DOPPS within Europe.

History

The DOPPS was launched in 1996 in the United States by a group of researchers from the University of Michigan with full support provided by Amgen. The researchers included Drs. Phillip Held, Friedrich Port, Robert Wolfe, and Eric W. Young. In 1998, after two successful years in the United States, the study expanded to include France, Germany, Italy, Spain, and the United Kingdom. In 1999, Kyowa Hakko Kirin (formerly Kirin) joined as a sponsor and Japan was added to the collective DOPPS countries. In 2002 the second phase of the DOPPS launched and Australia, Belgium, Canada, New Zealand, and Sweden joined for a total of 12 countries. The third phase launched in 2005 and continued through 2008 with the same 12 countries. DOPPS 4 launched in 2009 with new funders joining Amgen and Kyowa Hakko Kirin in the consortium as more organizations identified the value of the DOPPS data. DOPPS 5 launched in 2012 and added China and the Gulf Cooperation Countries (GCC), including Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates (UAE) for a total of over 20 countries. Most recently the sixth phase began in 2015. The fifth and sixth phase have seen the largest increase in collaborators and distinct projects, including the introduction of the DOPPS Practice Monitor (DPM) in 2010 in the United States.

Participation in DOPPS

Study Phase	Years	Countries	Facilities	Patients
DOPPS 1	1996-2001	7	308	17,034
DOPPS 2	2002-2004	12	322	12,839
DOPPS 3	2005-2008	12	300	11,170
DOPPS 4	2009-2011	12	380	15,528
DOPPS 5	2012-2015	21	580	36,743
DOPPS 6	2015-2017	19	~560	~30,000

DOPPS 1: France, Germany, Italy, Japan, Spain, UK, and US

DOPPS 2-4: DOPPS 1 countries plus Australia/New Zealand, Belgium, Canada, Sweden

DOPPS 5: DOPPS 4 countries plus China, GCC-6 (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates), Russia, Turkey

DOPPS 6: DOPPS 5 countries except Australia/New Zealand

OVERVIEW OF THE DOPPS PROJECT STUDY DESIGN

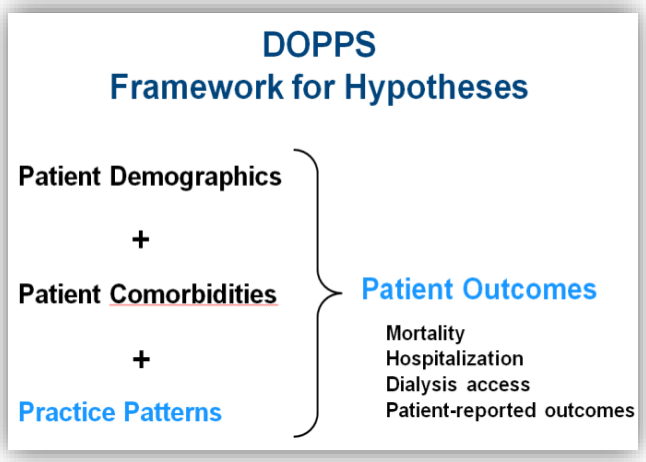
The DOPPS Project is a prospective cohort study of hemodialysis practices based on the collection of observational longitudinal data for a random sample of patients from dialysis facilities in a representative and random sample of units in more than 20 countries.

The samples of patients in each facility, and sample of facilities in each country, are designed to provide a reliable picture of practices and outcomes in each facility, and in each geographic area. Differences in patient outcomes of mortality and morbidity by country and by dialysis unit, helps DOPPS researchers:

- Describe differences in practice patterns that correlate with differences in outcomes
- Understand factors associated with patient outcomes that may lead to improved patient care and lower mortality and morbidity

Practice patterns

'Practice patterns' refers to the general range of treatment options faced by hemodialysis centers. Examples of practice patterns that may be related to outcomes include: staffing ratios and composition, size of unit, vascular access creation and salvage policies, dialysis prescription, and methods of delivering dialysis.



Outcomes

'Outcomes' refers to a variety of patient events that are associated with human and economic consequences. Important outcomes assessed in the DOPPS include: mortality, hospital admission, vascular access failure, quality of life, and development of new medical conditions.

The DOPPS is overseen by the DOPPS Steering Committee and investigators representing each of the DOPPS countries, which together, help guide research, support questionnaire development, and identify funding opportunities.

The study design and study instruments (questionnaires) are shared across all countries with minor local modifications as necessary. Facilities in the DOPPS are randomly selected in each country from a complete list of hemodialysis facilities treating at least 20 hemodialysis patients; facilities are stratified by geographic region and unit type. A random sample of subjects, averaging between 20 and 30 patients per study site, are drawn from each participating facility census. Detailed information on selected patients, facility practices, and physician practices are obtained by questionnaires that are completed at various points throughout the study. These data are analyzed at both the subject- and facility-levels, thereby providing the opportunity to monitor practice and policy changes and their effects on clinical outcomes such as mortality, hospitalization, and quality of life.

HOW DATA ARE COLLECTED

Once a study site has agreed to participate in the DOPPS, the Medical Director will select one (possibly two) staff member to serve as the main contact for the DOPPS, referred to as the Study Coordinator. The Study Coordinator is the staff member at each participating dialysis facility responsible for ensuring that patients are enrolled and forms are completed. DOPPS 6 is designed to randomly select a sample of hemodialysis patients for detailed capture of clinical and treatment data. All study participants, in order to be eligible for inclusion in the study, must be at least 18 years of age and receiving in-center hemodialysis for the treatment of chronic kidney failure, i.e., end-stage renal disease (ESRD). The hemodialysis patient sample is randomly selected among all in-center chronic hemodialysis patients receiving treatment at the facility at study start.

OVERVIEW OF STUDY DESIGNS USED IN THE DOPPS

Two study designs are used for study participation, DOPPS Plus and DOPPS Core. Both are designed to achieve key study hypotheses and objectives of the DOPPS. Such features as random, representative sampling of hemodialysis facilities and patients, as well as uniform data collection instruments and longitudinal data capture, remain consistent. The decision to utilize DOPPS Plus or DOPPS Core study designs is determined by the funding level achieved within a country or region. Details of the DOPPS Plus and DOPPS Core study designs are shown in the table below. Each phase lasts three years (we are currently partway through the sixth phase, 2015-2018).

Study Feature	DOPPS *Plus*	DOPPS *Core*
Countries	Canada, Japan, United States	Belgium, China, France, GCC, Germany, Italy, Russia, Spain, Sweden, Turkey, United Kingdom
Patient Sampling		
Patient Enrollment	• A sample averaging 20-30 patients per facility, replenished every 4 months	
Data Collection Frequency		
Baseline, Study Start	• Initial facility census (listing of all currently chronically dialyzing hemodialysis patients over the age of 18) • Enroll cross-sectional study sample • Baseline medical questionnaire, lab data, medications, vascular access information, hospitalizations, etc. and a patient questionnaire are completed for all enrolled patients[1]	
Every Four Months	• Update facility census for mortality and departures • Replenish cross-sectional study sample • Baseline medical questionnaire, lab data, medications, vascular access information, etc. and a patient questionnaire for newly enrolled patients[1] • Longitudinal measures for continuing patients[1] • Hospitalizations events and procedures • Update list of renal medications per patient • Provide additional information for departed patients (including cause of death, if applicable)	
Annually, Anniversary of Study Start	• Follow-up patient questionnaire for all continuing patients • Facility-level practices and preferences via the Medical Director Survey up to three times annually	

[1] IS longitudinal measures are collected for all four past months in the DOPPS Plus study design and for the most recent month for the DOPPS Core study design. GCC= Gulf Cooperation Council

Additionally, the DOPPS Program expanded to include two additional projects that launched in 2012 and 2013 respectively - the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps) and the Peritoneal Dialysis and Outcomes Practice Patterns Study (PDOPPS). The projects include similar data collection as described above for the DOPPS with specific questions and data collection schedules designed for the target patient population.

Data entry and management

Each participating facility received credentials to utilize DOPPSLink, the secure web-based application for data collection built by the staff at Arbor Research. DOPPSLink provides more timely data collection compared to paper-based data entry and increases the utility of DOPPS data. Patient Questionnaires are offered to patients on paper and can often be completed electronically. When possible the DOPPS utilizes electronic data downloads that do not require additional manual data entry. DOPPSLink is available in all participating countries and is localized to the regional language and dialect.

Burden to participants (patients)

As part of the study, at least one time per year the Study Coordinator will ask each selected subject to complete a Patient Questionnaire. However, a subject can still be part of the DOPPS even if they decide not to complete the questionnaire or to skip parts of it and allow only their clinical data to be provided in support of the study.

DOPPS COLLABORATORS

The accomplishments of the DOPPS would not be possible without the collaborators that contribute to the project. These collaborators are imperative to ensuring successful continuation of data collection, funding organizations, clinical research organizations and associates, leading nephrologists within the regions (country investigators), researchers, and above all the participating study sites and patients. Specifically, the nursing community has been vital for the success of the DOPPS – both the CRAs that support the participating study sites and the Study Coordinators at each participating study site that work to submit the data, consent patients, etc.

WHAT'S BEEN ACHIEVED IN 20 YEARS?

Over the past 20 years, results from the hemodialysis DOPPS have provided much needed support for optimal practice in hemodialysis. Specific examples are reported in detail in this issue. The DOPPS has been a leader in studying experiences of dialysis patients, collecting information directly from study participants.

NEW INITIATIVES

The DOPPS Practice Monitor (DPM)

The DOPPS Practice Monitor (DPM) was launched in December 2010 to track data on hemodialysis practices in the United States. The DPM reports representative data in the form of more than 1,500 regularly updated charts, figures, and data tables, based on a sample of over 11,000 patients in more than 200 hemodialysis facilities in the United States. It provides comparisons and trends over time, using weighting techniques. Data are also provided by race and facility types.

In July and December 2015, the DPM expanded to share data from hemodialysis facilities in Canada and Germany, respectively. These DPM initiatives are available publicly via websites and provide timely reports, aggregating data from representative hemodialysis facilities to describe trends in many different clinical aspects of hemodialysis practice across the participating countries.

The DPM fills an important need, providing a source of contemporaneous, representative data, while tracking the effects of policy changes. Findings from the DPM can serve as an early warning system for possible adverse effects on clinical care and as a basis for patient and dialysis community outreach, editorial comment, and informed advocacy.

EURODOPPS

EURODOPPS is a joint venture of the DOPPS and the European Renal Association, European Dialysis and Transplant Association (ERA-EDTA) to collect and analyze data to address questions of specific interest to the European community. Since its start in 2014, EURODOPPS has flourished in a fruitful collaboration among investigators on both sides of the ocean. The enthusiasm and number of European researchers applying to use EURODOPPS data to address specific research projects demonstrates the interest of the community in this endeavor. To date, six investigators were awarded this opportunity, including one project that was announced at the 2016 ERA-EDTA congress in Vienna.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

Over the past 20 years, the DOPPS has been successful in its mission to disseminate important findings that contribute to improving patients' lives. This success is owed to the patients and participating study site staff members who continue to dedicate their time to completing DOPPS surveys, ensuring a robust DOPPS database to complete important analyses.

Anemia Management
A Review of Findings from the DOPPS

By Jennie King and Karen Chalmers

Anemia management in renal care is challenging and has seen a transformation in treatment options over the past thirty years - from the only treatment being a blood transfusion to the complex drug therapy now available. Anaemic 'renal patients' back in 1980 were recognizable by their grey and sallow complexion with typical traits of little or no energy. In this article we consider five papers on the topic that have been published using data from the Dialysis Outcomes and Practice Patterns Study (DOPPS). The DOPPS is a prospective observational study of nationally representative samples of randomly selected hemodialysis (HD) facilities and patients. Since its inception in 1996 when data was collected only in the United States, today it collects data in 23 different countries thus allowing for a wealth of practice patterns to be followed.

Anemia management in patients with end-stage renal disease has improved considerably due to the introduction of erythropoietin-stimulating agents (ESAs) in the mid 1980s. Locatelli et al[1,2] reported on anemia in patients receiving HD in five European countries and its association with morbidity and mortality using results from the DOPPS. They found that patients with hemoglobin (Hb) <10 g/dl were 29% more likely to be hospitalized than patients with Hb 11-12 g/dl. They concluded that lower Hb concentrations were associated with higher morbidity and mortality in European HD patients, and suggested that efforts must continue to achieve the European Best Practice Guidelines (EBPG) target of Hb concentration equivalent or higher than 11g/dl in 85% of patients.

Locatelli et al[1,2] reported the findings from the DOPPS of anemia management for patients receiving HD in relation to the Kidney Disease Outcomes Quality Initiative (K/DOQI) Guidelines in the American Journal of Kidney Diseases. Acknowledging that by the time this paper was published, the management of renal anemia had been revolutionized over the past 15 years with the introduction of recombinant human erythropoietin (rHuEpo), which had replaced blood transfusions as the mainstay treatment for this complication, it also became evident that wide variations in anemia management were observed amongst different countries. The authors concluded that greater efforts are required to allow a larger proportion of patients to reach the recommended Hb concentrations. Significantly improved outcomes for patients in terms of morbidity, mortality, and quality of life may be expected by a more widespread achievement of recommended Hb levels. Monitoring of results by the DOPPS was instrumental in reporting the findings that countries were not easily able to meet the clinical guidelines set. This finding perhaps lead to the introduction of the extended role of the anemia nurse in many countries.

Moving on to 2013, Bailie et al[3] published a paper reviewing the variations in intravenous iron use internationally and over time using findings from the DOPPS. They reviewed results from more than 30,000 patients receiving HD across twelve countries participating in the DOPPS between 1999-2011. Adjusted associations of IV iron dose with serum ferritin and transferrin saturation (TSAT) values were also studied. They found that the use of iron increased from an administration level in 50% of patients in 1999 to 71% patients during 2009-2011, with most countries also increasing their use of IV iron. The DOPPS data results included detailed information of mean monthly dosing levels and the iron substances used with variation reported in interval administration of iron amount, and product administered. Ferritin values rose in most countries. They concluded that during this study period, IV iron prescription patterns had varied between countries and usage, and dosage had increased in most countries. Ferritin levels had also increased but not TSAT levels.

Anemia management is challenging. It has become clear that IV iron is required for optimal management of anemia in the majority of patients being treated with HD. While usage of iron has steadily increased over the twenty years of using ESAs, policies and funding have changed and a publication by Bailie et al[4] reviewed data from the DOPPS to validate an association between high IV iron doses and mortality. This study reported on the usage and dosage of IV iron in the twelve DOPPS countries between 2002-2011, drawing attention to the fact that IV iron use requires a careful balance between intended clinical effect and uncertain risks of toxicity. Bailie et al[4] concluded that hospitalization risk was elevated among patients receiving 300 mg/month or more IV iron compared to those having 100-199 mg/month and recommended a well-powered clinical trial to evaluate safety of different IV iron-dosing strategies in this patient cohort. In response, the United Kingdom is currently researching PIVOTAL - Proactive IV Iron Therapy in HD Patients – a 4-year clinical trial involving more than 2000 participants to investigate the optimum amount of IV iron that can be given to patients receiving dialysis to treat anemia effectively and safely.

Changes to the reimbursement system and other policy may have a significant impact in the delivery of high quality care. A new bundled payment system was introduced in the United States in 2011 and was reported in a paper by Karaboyas et al[5] which reviewed anemia management in respect of these changes to ESA reimbursement. The paper aimed to understand better the recent and sustained increases seen in ferritin levels in US dialysis patients. Data was examined from nearly 10,000 patients from 91 facilities participating in the DOPPS study between 2009 and 2013 to evaluate anemia management practice. Results, as expected, showed that mean ESA dose and Hb levels declined during the study while mean IV iron dose increased initially and then stabilized to around 200mg per month. Mean ferritin levels were seen to be increasing prior to the introduction of the bundle payment from 601 ng/ml in 2009 to 887 ng/ml by 2012. Models suggest that higher IV iron administration may have attributed to this but that lower ESA doses were likely to be the reason thereafter that ferritin levels remained high. Contrary to expectations, the rise in IV iron administration was not seen after 2011. However, the sustained increase in ferritin

levels in US dialysis patients after the introduction of the funding changes in 2011 has persisted with average levels being in excess of 800 ng/ml. Concern has been raised that high ferritin levels reflect excessive iron stores which some studies have shown lead to increased morbidity and mortality.[5] National guidelines are changing and now recommend that ferritin levels are kept below 500 ng/ml and evaluated on a case by case basis when levels exceed this target. It is clear that the long-term effects of a consistently raised ferritin level may have unfavorable effects on health and this is an area that requires further investigation.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

Based upon review of the anemia papers discussed above, professor Stefan H. Jacobson an expert renal physician, agrees that evaluation and treatment of renal anaemia is complex. He proposes that anaemia related to end-stage renal disease may be due to iron deficiency, blood loss in connection with hemodialysis, subclinical or overt inflammation, chronic infection, ESA resistance, secondary hyperparathyroidism, inappropriate production of EPO and more. Optimal Hb level in hemodialysis is still debated, though mostly recommended to be between 10-12 g/dl. However, many patients have Hb >12 g/dl with no need for ESA, while others have very low ESA doses with Hb around 12-13 g/dl (above guideline target). Many believe that it is not primarily the higher Hb levels that are harmful to patients causing cardiovascular disease and more, but rather the high ESA doses that are prescribed and recommended by doctors and nurses to achieve a Hb over 10 g/dl, to reach the guideline target. Patients who need very low doses of ESA to reach a Hb of 10-12 will not have a high risk of sometimes having a Hb of 12-14 g/dl, while those patients stressed with high doses of ESA and also often high doses of IV iron to reach a Hb of 10 g/dl are at the highest risk. Controversially the latter group most likely would benefit from a Hb of 8-10 g/dl since they are ESA resistant and likely have inflammation and more. These patients also show Hb variability and increased risk of mortality as been demostrated by the DOPPS.[6] Thus indeed, the management of renal anaemia is complex and complicated.

Renal nursing colleagues are encouraged to make themselves familiar with current clinical guidelines for anemia management and conduct audits to ensure the standard is being met. The renal nurse can share results of blood tests such as Hb levels and iron counts and correlate them with drug therapy in order to educate and empower their patients and junior colleagues.

Changes over the years has caused the anemia nurse role to also evolve. The anemia nurse specialist has become more autonomous, taking over more of the junior doctor role, demanding updated knowledge of anemia practices and keeping current with changing targets and guidelines. The anemia nurse specialist has evolved into an extensive role where the nurse interprets and analyses blood results and implements treatment changes. Many of these specialist nurses have become primarily responsible for anemia management to

ensure that treatment changes are made in a timely manner. Working with this group of patients, the anemia nurse specialist establishes a good patient/nurse relationship that promotes patient-centred care.

DOPPS research allows nurses to look at practices internationally and compare practices and outcomes, and to further reflect on their own practices to consider what changes can be made for improvements in patient care and outcomes. Anemia nurse specialists are a key focal point for the multi-disciplinary team to coordinate and advise on specialist knowledge. The anemia nurse specialist also participates in staff education providing staff with knowledge and evidence for Continuous Professional Development essential for revalidation for practice.

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Dialysis Prescription and Dialysis Dose: Patient Outcomes and Nurse Implications

A Review of Findings from the DOPPS

by Anna Marti i Monros

INTRODUCTION

Urea kinetic modeling introduced a measure of objectivity into the assessment of dialysis delivery in the 1980s following the landmark National Cooperative Dialysis Study (NCDS). Analyses based on the NCDS provided the impetus for routine quantification of delivered dialysis dose in hemodialysis (HD) practice throughout the world, by suggesting minimum targets for small solute (urea) clearance. Despite many technological advances in dialysis delivery, morbidity and mortality in dialysis populations remain high.

Since the Dialysis Outcomes and Practice Patterns Study's (DOPPS) inception in 1996, the DOPPS has published several papers in peer-reviewed journals addressing not only the topic of the right dialysis dose, how to measure it, and how to deliver it, but the effects of patient adherence as well.

In this article, we summarize DOPPS papers with special attention to the nursing role on dialysis dose prescription and delivery target.

DIALYSIS DOSE

According to Saran et al, "the current paradigm of thrice-weekly HD as renal replacement therapy is a poor imitation of the native kidney´s continuous high-quality blood purification…despite impressive advances in dialysis technology, overall prevalent mortality rates for dialysis patients in the United States have improved only marginally (10%) since 1988, according to the 2003 annual data report of the United States Renal Data System".[1]

Over the next two decades, data emerging from a number of observational studies showed that a higher dose of HD was associated with a lower mortality risk. Since 1990, a trend toward a higher dose of dialysis and use of high-flux dialyzers was reported. This steady increase in dialysis dose may have been responsible, at least in part, for the reduction in mortality observed during the 1990s.

Hence, the National Kidney Foundation's (NKF's) Kidney Disease Outcomes Quality Initiative (KDOQI) HD Adequacy Guideline 5: Prescribed Dose of Hemodialysis states, "to prevent the delivered dose of HD from falling below the recommended minimum dose, the prescribed dose of HD should be spKt/V 1.3. A Kt/V of 1.3 corresponds to an average urea reduction ratio (URR) of 70%, but the URR corresponding to a spKt/V of 1.3 can vary substantially as a function of ultrafiltration." The KDOQI guidelines are based predominantly on evidence from national registry data and expert opinion; these sources suggest that a higher dose of dialysis would result in better outcomes.

Moreover, results of observational studies could be biased in favor of healthier patients having superior outcomes, especially if they were able to receive a higher dose of dialysis, or if those less healthy could not receive the higher dose for reasons such as a poorly functioning vascular access. Thus, with equipoise and a firm focus on need to study interventions aimed at reducing the persistently high mortality rate among HD patients in the United States, the Hemodialysis (HEMO) Study, a randomized clinical trial sponsored by the National Institutes of Health, was undertaken. Higher than average dose was shown to be associated with a trend toward reduction in relative risk (RR) of mortality for women, but not men; this was found to be not significant after applying the Bonferroni correction for multiple comparisons. Unfortunately, the HEMO Study could not evaluate low dose of HD because of ethical considerations of exposing patients to an inadequate dose of dialysis.

Results from the international DOPPS are consistent with prior observational studies, insofar as the relationship between dialysis dose and mortality outcomes is concerned. The RR of mortality for spKt/V <1.2 was 1.16 (*P*=0.025). Furthermore, recent analyses of DOPPS data and the Centers for Medicare and Medicaid Services database have revealed that the benefit of eKt/V above 1.2 was seen for women, but not for men, despite adjustment for body size.

ULTRAFILTRATION

Ultrafiltration rate (UFR) during dialysis varies substantially among patients and, depending on patient tolerance for large swings in intravascular volume, may be responsible in large part for intradialytic hypotension (IDH) and the resultant unstable treatments requiring extra attention from staff. That UFR may be an independent predictor of mortality and hospitalization outcome has only recently come to light, based on an analysis of DOPPS data. Closely linked to UFR is the key issue of treatment time (TT) that has not yet received the attention it deserves in HD-related clinical trials. The NCDS suggested there was a trend for benefit of the longer TT, but this was borderline statistically significant. However, the data are supportive of the paradigm of longer dialysis time and need to be examined further. Preliminary data from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) indicate that dialysis duration of >4.5 hours may be associated with a lower RR of mortality and duration <3.5 hours associated with higher mortality risk. Recent evidence based on an analysis of European DOPPS data also suggests that hemodiafiltration is associated with a lower RR of mortality compared with conventional HD (RR=0.77, *P*=0.02).

TREATMENT TIME

Dose of dialysis is a crucial element in the overall management of patients with end-stage renal disease (ESRD). The NCDS provided the first evidence that monitoring small solute clearance was an effective means of quantification of dialysis dose. Subsequently, the duration of dialysis sessions was not given the importance it deserved and has not yet received scrutiny in randomized controlled clinical trials. There is some preliminary evidence from the DOPPS and ANZDATA that TT may be independently associated with outcomes among dialysis patients.

Saran et al described the associations between longer TT and slower UFR with reduced mortality; their analysis included 22,000 HD patients from seven countries in the DOPPS.[2]

The NCDS suggested a survival advantage with longer TTs. This clinically important trend failed to capture the attention of the nephrology community. The recently completed HEMO Study focused on dialysis dose as measured by urea kinetics (Kt/V) and membrane flux, rather than the length of dialysis treatments, but excessive interdialytic weight gain (IDWG) has been shown to be an independent predictor of mortality in a number of observational studies.

Patients with excessive IDWG tend to receive a higher UFR, potentially resulting in increased frequency of IDH. IDH, in turn, could result in altered sensorium, myocardial ischemia and infarction, blindness, and even stroke.

This article examined the relationship between TT and UFR with patient outcomes in the DOPPS. Average facility TT was normally distributed across the DOPPS regions with the mean and median at 228 and 229 min, respectively. Approximately half the patients were receiving a TT of 211-240 min (3.5-4 h), whereas 27.1% had TT >240 min and 22.2% had TT <211 min.

Mean TTs for Japan and Europe were significantly longer than those in the United States after accounting for facility clustering effects. TT in the United States increased significantly between DOPPS 1 and DOPPS 2 (from 211 to 221 min), whereas there was no significant change in mean TT in the other DOPPS regions.

Overall, the mean UFR was 8.9ml/h/kg, whereas the median value was 9.0 ml/h/kg. In DOPPS 1, the average UFR was significantly lower in Japan and Europe than in the United States. In Japan, this rate increased significantly ($P<0.05$), from 8.2 in DOPPS 1 to 9.9 ± 3.6 in DOPPS 2.

Using TT >240 min as the referent category, the RR of mortality for TT <211 min was 1.34 ($P<0.0001$), and the RR of mortality for TT of 211-240 min was 1.19 ($P=0.01$).

The main findings from this study are that, in the setting of conventional thrice-weekly HD: (1) longer HD session duration is independently associated with lower mortality; (2) a higher Kt/V and a longer TT were independently associated with mortality; and (3) a faster rate of fluid removal at dialysis, as measured by UFR >10 ml/h/kg body weight, is associated with higher risk of mortality and increased odds of IDH. The study also confirms prior reports from observational studies that lower Kt/V is a significant and independent predictor of higher mortality, both with and without adjustment for TT.

This study demonstrates that longer duration of HD session is independently associated with a lower mortality risk after extensive adjustment for case-mix, dialysis dose (Kt/V), body size measures, and indicators of nonadherence. The observed synergistic interaction between Kt/V and TT toward mortality risk reduction implies that delivering a high Kt/V over longer TT may be of greater value than delivering the same Kt/V over shorter TT (with implications for practice modification). Furthermore, the study finds that UFR >10ml/h/kg body weight is independently associated with higher risk of both IDH and mortality.

The issue of association between longer dialysis and intermediate outcomes was also analysed by Tentori et al.[3]

The morbidity and mortality rate of patients receiving three times per week HD remain unacceptably high. Compared with “standard” dialysis, daily in-center and long nightly home dialysis have been associated with better outcomes and quality of life in small cohorts of selected patients. In the recent

Frequent Hemodialysis Network trial, six times per week dialysis was associated with favorable outcomes compared with the standard regimen. While extended dialysis schedules may lead to better clinical outcomes, logistical, financial, and other impediments remain for their use for the majority of HD patients.

Most HD patients worldwide receive conventional three times per week dialysis with a duration of <5 h. Even in this setting, shorter dialysis session length (TT) has been associated with worse survival. While the association of TT with survival is independent of dialysis dose, most prior studies did not provide a mechanistic insight through assessment of the association of TT with clinical markers (e.g., hemoglobin, serum phosphorus, blood pressure), which may contribute to morbidity and mortality in this population.

The present study is an extension of the earlier DOPPS investigation;[2] it highlights international differences in TT, presents associations of TT with intermediate measures, and applies an instrumental variable approach to account, in part, for unmeasured confounders that may bias the associations of TT with clinical outcomes.

This study examined a large cohort of patients receiving in-center, three times per week maintenance HD at 930 facilities in 12 countries participating in the DOPPS (1996-2008). The study included 37,414 patients receiving three HD treatments per week with prescribed TT from 120-420 min at study enrollment; 15,442 patients were from 308 facilities in DOPPS 1, 11,553 patients were from 322 facilities in DOPPS 2, and 10,419 patients were from 300 facilities in DOPPS 3. The mean follow-up was 19 months. During the study period, 8961 patients died (mortality rate: 0.15/year).

Large differences in facility mean TT (FMTT) were observed across countries (P<0.001), with the longest average FMTT (256±23 min) in Australia-New Zealand (ANZ) and the shortest in the United States (214±17 min). Overall, FMTT increased over time from DOPPS 1 to DOPPS 3 (P<0.001). A significant increase in FMTT over time was found in ANZ, Belgium, Germany, Spain, Sweden, and the United States (P<0.05), and a significant decrease was found in Japan (P=0.01).

Patients with longer TT were younger, more likely male, had longer ESRD duration, and higher body weight (P<0.001 for all). The prevalence of comorbidities within each TT category varied across DOPPS regions. In all regions, patients with longer TT had higher hemoglobin and serum albumin levels, were less likely to use a catheter as vascular access, had higher blood flow rates, and were more likely to be treated with high-flux dialyzers (P≤0.01 for all).

TT prescription varied across countries, with the longest average TT in ANZ (255±41 min) and the shortest in the United States (212±32 min). These large differences must be interpreted along with consideration of other clinical practices, such as the use of high-flux dialyzers and delivered dialysis dose (which were both higher in North America).

In the present study, patients with longer TT had lower risk of all-cause and cardiovascular (CVD) mortality. A new interesting finding is the strong association between longer TT and lower risk of sudden death, which remained after adjusting for patient comorbidities that are risk factors for sudden death (i.e., diabetes and atrial fibrillation). It is likely that the smaller plasma to dialysate electrolyte gradients, less rapid volume shifts, and less sympathetic hyperactivity during longer dialysis sessions may contribute to the lower risk of sudden death.

The limitations of the study are related to its observational design. Despite extensive adjustments and use of an instrumental variable approach, the potential for residual confounders remain, and the results do not prove a causal effect between longer TT and better clinical outcomes.

Facilities delivering longer dialysis sessions may face higher costs, and shortening dialysis treatments may be associated with cost savings in certain payment environments.

In the absence of randomized controlled clinical trials, health care providers should take into account findings from observational studies as well as supportive principles of dialysis when making decisions regarding the duration of dialysis sessions. Similarly, policymakers and developers of quality measures worldwide may consider current evidence about the duration of dialysis session when creating policies or guidelines that may affect TT.

In summary, this study confirms generally favorable clinical outcomes with longer TT and demonstrates associations of longer TT with better anemia, phosphorus, and blood pressure control, indicating possible mechanisms for improved clinical outcomes. These findings support longer TT prescription in the setting of three times per week HD.

NONADHERENCE

Saran et al have described HD as a vital lifesaving but complex therapy.[4] The definition of nonadherence and its assessment have both been controversial. Nonadherence can relate to the HD schedule and to other aspects of care (e.g., dietary restrictions, phosphate binders). By compromising the delivery of dialysis, nonadherence can affect both patient morbidity and mortality. A detailed examination of practice patterns was undertaken in the DOPPS. In addition to practice patterns, patient behavior and adherence to prescribed treatment may be other determinants of outcomes.

The present study was based on the hypothesis that patients treated at facilities with lower nonadherence rates are likely to manifest lower mortality and fewer hospitalizations. Additionally, it provided an international perspective on the magnitude, distribution, and predictors of nonadherence (both at patient and facility level).

Patients were considered nonadherent if they skipped one or more HD sessions per month, shortened one or more sessions by more than 10 minutes per month, had a serum potassium level of >6.0 mEq/L, a serum phosphate level of >7.5 mg/dL (>2.4 mmol/L), or IDWG >5.7% of body weight. Predictors of nonadherence were identified using logistic regression. Survival analysis used the Cox proportional hazards model adjusting for case-mix.

Skipping treatment was associated with increased mortality (RR=1.30, *P*=0.01), as were excessive IDWG (RR=1.12, *P*=0.047) and high phosphate levels (RR=1.17, *P*=0.001). Skipping was also associated with increased hospitalization (RR=1.13, *P*=0.04), as were high phosphate levels (RR=1.07, *P*=0.05). Larger facility size (per 10 patients) was associated with higher odds ratios (OR) of skipping (OR=1.03, *P*=0.06), shortening (OR=1.03, *P*=0.05), and IDWG (OR=1.02, *P*=0.07). An increased percentage of hours for highly trained staff was associated with lower OR of skipping (OR=0.84 per 10%, *P*=0.02); presence of a dietitian was associated with lower OR of excessive IDWG (OR=0.75, *P*=0.08).

These findings show the importance of implementing educational strategies to support patients' adherence to therapies and self-care.

DAY-OF-WEEK MORTALITY

According to Zhang et al, the risk of death for HD patients is thought to be highest on the days following the longest interval without dialysis (usually Mondays and Tuesdays); however, prior results were inconclusive. To clarify this, data of 22,163 HD patients from the DOPPS (United States, Europe, and Japan) were analyzed.[5]

The study focused on the association between dialysis schedule and day of the week of all-cause, CVD, and non-CVD mortality, with day-of- week coded as a time-dependent covariate. The models were adjusted for dialysis schedule, age, country, DOPPS phase 1 or 2, and other demographic and clinical covariates, and compared mortality on each day to the 7-day average.

European patients tended to be older than US patients, whereas Japanese patients were on average younger than US patients. Each of these significant differences was accounted for in subsequent models, constructed from prevalent (cross-sectional) and incident patients.

In total, 4395 deaths were reported during the study period. Of the deaths, 2663 were among US patients, 1391 among European patients, and 341 among Japanese patients. In addition, 1744 out of 4395 (40%) deaths were caused by CVD. A total of 2489 out of 4395 (57%) deaths were among patients on Monday/Wednesday/Friday (MWF) schedules, whereas 1906 (43%) were among those on Tuesday/Thursday/Saturday (TTS) schedules.

Despite its proven value as a life-saving therapy, in-center HD remains an intermittent intervention, most typically administered three times a week. Harmful waste products and fluid accumulated over the extended weekend interval may therefore put patients at a higher risk of death than on other days of the week. Our results from the DOPPS in US, European, and Japanese patients indicate that, in all three regions, HD patients have a higher risk of all-cause death on Mondays if they are on MWF schedules, or Tuesdays if they are on TTS schedules. Thus, findings from prior reports are corroborated and expanded upon here. This day-of-week effect tends to be stronger for CVD than non-CVD death overall.

The European and Japanese data tend to confirm the association, which was quite evident in the US data, of increased mortality on the day of the first dialysis session in the week. On the other hand, there are unique features to the results in Europe and Japan, such as high mortality on Saturdays in the TTS schedule, which may be due to practice patterns unique to those countries/regions. One may speculate that continued aggressive/usual ultrafiltration and dialysis on Fridays or Saturdays (the last dialysis session of the week) – in order to allow for the anticipated longer weekend gap in dialysis – may contribute to this finding.

Patients on MWF schedules had elevated all-cause mortality on Mondays, and those on TTS schedules had increased risk of mortality on Tuesdays in all three regions. The association between day-of-week mortality and schedule was generally stronger for CVD than non-CVD mortality, and was most pronounced in the United States. Unexpectedly, Japanese patients on MWF schedules had a

higher risk of non-CVD mortality on Fridays, and European patients on TTS schedules experienced an elevated CVD mortality on Saturdays.

The day following dialysis showed lower RRs for mortality compared with dialysis days, perhaps because dialysis itself increases the risk of mortality. For HD patients, very large amounts of fluids and toxins are removed in a relatively short time period, particularly if the time elapsed since the last dialysis is long. This increases the potential for occurrence of IDH, which has previously been found to be a risk factor for mortality among HD patients. Rapid reduction in postdialysis potassium may also be a contributory factor, as hypokalemia can enhance the risk for cardiac arrhythmia and sudden death, and this is more likely to occur on a dialysis day as opposed to the day preceding dialysis.

Nonadherence with dialysis sessions ('shortening' or 'skipping' sessions) has been associated with higher mortality, as detailed in a previous DOPPS paper,[4] and would be expected to raise overall mortality rates. Unfortunately, there is insufficient information to the time of death or a direct effect of noncompliance in DOPPS data. Finally, a substantial proportion (66%) of patients died in the hospital. Often, patients who are hospitalized would no longer follow their regular dialysis schedule. In this case, one would expect the observed day-of-week effect in this study to be somewhat attenuated. Further study that considered the potential confounding effect of hospitalization would be valuable.

Our results imply that there may be an advantage to a more frequent dialysis schedule, such as every other day. This is supported by the relatively low rates of mortality for patients receiving "daily dialysis" based on various reports.

Thus, future studies may consider factors that could modulate this day of week observation.

INTERDIALYTIC WEIGHT GAIN

According to Hecking et al, for patients with ESRD undergoing HD, the importance of sodium removal by ultrafiltration to control extracellular volume expansion has been stressed since the earliest reports. Additional sodium can also be removed by diffusive transport if the dialysate sodium (DNa) level is set below the predialysis serum sodium (SNa) concentration. Vice versa, higher DNa levels translate into higher dialysate to SNa gradients, which are associated with thirst, IDWG, and hypertension.[6]

Using a patient's predialysis SNa as a reference to prescribe individualized or tailored DNa has thus been considered rational, and various prospective interventional trials have found a significant decrease in IDWG by reducing DNa. As a result of previous guidelines and recommendations and recent observational studies and commentaries, DNa tailoring may become routine clinical practice.[7]

Data from the DOPPS and a simultaneous report from the HEMO Study have demonstrated that predialysis SNa concentrations are inversely associated with mortality. Prior DOPPS analyses were restricted to patients with multiple SNa measurements and intriguingly suggested that, for patients with low mean SNa levels, higher DNa prescriptions are associated with lower mortality risk. The current study expanded the study population using "baseline" data obtained at entry of patients into the DOPPS and determined the following within various strata of SNa: (1) associations between

IDWG and DNa; (2) associations between DNa and outcomes; and (3) the influence of IDWG on outcomes.

In this study, nationally representative samples of dialysis facilities from 12 different countries were enrolled with random samples of HD patients from each participating facility based on four study phases (DOPPS 1-4). DOPPS 1 started in the United States in 1996. Follow-up information is obtained every 4 months and includes laboratory measurements and dates of and diagnoses associated with patient hospitalization and death.

In total, 29,593 patients from DOPPS phases 1-4 were eligible for and were included in the present analysis. Median follow-up time was 16.5 (interquartile range, 8.6-24.0) months. Mean (±SD) baseline SNa was 138.2±3.5 mEq/L in the study population and was unequally distributed throughout the DOPPS countries; levels were highest in Japan (139.0±3.2 mEq/L) and lowest in France (137.4±3.5 mEq/L), as previously observed for mean SNa.

We confirmed in the present study population that predialysis SNa was associated inversely with all-cause mortality (low SNa correlated with high mortality). Because higher IDWG has been associated with a higher mortality risk, it might be hypothesized that higher DNa also would be associated with higher mortality. However, higher DNa concentrations were not associated with higher mortality across all subgroups of baseline SNa. Instead, the fully adjusted overall mortality HR (also adjusted for predialysis SNa) was lower with higher DNa (HR, 0.98 per 2 mEq/L higher DNa). This association was stronger and statistically significant in an analysis restricted to dialysis facilities that prescribed a uniform DNa to virtually all patients, not by any specific indication. In this group of facilities, the association of higher DNa with lower mortality independent of SNa became very clear. Of note, additional adjustments for IDWG and predialysis SBP did not systematically affect the overall higher mortality risk (and hospitalization risk) associated with lower DNa prescriptions.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

Daily practice and analysis of the related literature in the above sections show evidence of the paramount implications (roles) of nursing practice and dose prescription-related outcomes. In conclusion, important aspects of nursing implications regarding dialysis delivery are:

- **Blood sample drawn.** Unless blood extraction for Kt/V and other dose indicators is done correctly, adjustments won't be done correctly and may have negative impact, not only on patient outcomes, but in cost and staff ratios. We recommend following the NKF KDOQI Guidelines, Clinical Practice Recommendations.
- **Vascular access performance.** Any single aspect related to vascular access performance, like proper needling, complication prevention, and infection control, is of paramount importance for dose prescription and adequate dose delivery; as it´s generally accepted, vascular access is a "nursing issue".
- **Practice patterns.** How nurses perform daily practice has a great impact on delivery dose, and these performances range from the quantity and quality of data recorded to any single aspect of nurses' work.
- **UFR.** All the summarized papers have described the importance of adjusting UFR to patient

tolerance. UFR is related to some negative patient outcomes and is even a cause of mortality. Nurses are the professionals responsible not only of adjusting UFR, but of informing physicians beforehand of high IDWG and patient tolerance to high UFR.

- **Patient counselling.** This is one of the most important nursing roles in any aspect of care, but some could say it is most significant when caring for chronic patients. Nurses can teach patients how to avoid extra IDWG, the risks of session-skipping, nonadherence, and related short- and long-term problems.
- **Helping patients choose.** Some countries have regulated by law the right for patients to choose among the different treatment options. Even when it´s not legally regulated, nurses have the professional and moral obligation of helping patients choose.
- **Patient advocate.** The nurse protects the client's human and legal rights and provides assistance in asserting those rights if the need arises. Advocacy may include, for example, providing additional information for a patient who is trying to decide whether or not to accept a treatment. Or, the nurse may defend a patient's rights in a general way by speaking out against policies or action that might endanger their well-being or conflict with their rights.

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Impact of Dialysis on Patients' Lives
A Review of Findings from the DOPPS

by Elena Cavero

INTRODUCTION

Patients undergoing hemodialysis (HD) see their lives significantly affected by treatment. There are many factors that determine the effects of the disease on the patient's life. Here, we examine several of those factors, which have been studied in the Dialysis Outcomes and Practice Patterns Study (DOPPS) since 1996. The areas studied will serve to establish future interventions to improve the quality of life (QOL) for renal patients and factors influencing the evolution of the disease.

SEVEN HEALTH FACTORS AFFECTING DIALYSIS PATIENTS

1. PHYSICAL ACTIVITY

Physical activity has been associated with better health status in the general population, and may be encouraged in HD patients by their health care teams.

Levels of physical activity among HD patients are typically low. Increasing physical activity in this population is associated with better health, QOL, and survival. The DOPPS has provided an international description of the patterns of exercise frequency and its association with exercise programs and clinical outcomes among study participants.

Data from a representative sample of 20,920 DOPPS participants in 12 countries between 1996 and 2004 were analyzed.[1]

Regular exercise was positively associated with improved sleep quality (SQ), less severe bodily pain, increased appetite, a patient's ability to walk, and lower body mass index (BMI). Exercise was inversely associated with advanced age and multiple comorbidities.

Due to the cross-sectional nature of the data, these results cannot establish a causal relationship; however, the results are generally consistent with previous clinical trials in HD, indicating exercise can reduce physical pain and increase healthy intake of calories and protein.

Mortality risk was lower for participants who reported exercising once a week, compared with patients exercising less than once a week or never.[2]

The results indicate that regular exercise is associated with better outcomes in this population; in addition, patients in facilities that offer exercise programs are more likely to exercise.

2. SLEEP QUALITY

Poor SQ is common among patients on HD and may be associated with QOL and clinical outcomes.

Data on SQ were obtained from 11,351 patients in 308 dialysis facilities in seven DOPPS countries: France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States (1996-2001). Almost half of patients (49%) experienced poor SQ. Patients with poor SQ were more likely to take

medication (antihistamines, antidepressants, anti-inflammatories, narcotics, gastrointestinal drugs, asthma drugs, or hypnotics).[3]

The risk of mortality was 16% higher for HD patients with poor SQ.

Exercise at least once a week (compared with less than once a week) was associated with a lower likelihood of poor SQ.

While further research will help determine the complex nature of individual factors involving poor SQ, programs that encourage exercise, smoking cessation, and therapeutic measures (e.g., relieving pruritus and reducing bodily pain) may be explored to benefit HD patients suffering from poor SQ. Simple bedside screening in clinical evaluation of HD patients is a potential tool, and may be beneficial as the subject of future studies.

3. Pruritus

Pruritus affects many patients on HD. In the DOPPS, pruritus has been studied in relation to morbidity, mortality, QOL, and SQ.

Analyzed in the article were 18,801 HD patients (1996-2004). Analyses were adjusted for age, sex, black race, Kt/V, hemoglobin, serum albumin, serum calcium corrected by albumin, serum phosphorus, 13 comorbidities, depression, years on dialysis, country, and facilities.[4]

According to the DOPPS, the feeling of moderate to extreme pruritus was experienced by 42% of HD patients (2002-2003).

Pruritus was slightly less common in patients starting HD than in patients on dialysis for more than 3 months. Pruritus in end-stage renal disease (ESRD) may be the result of pre-existing conditions, even in individuals not on HD, indicating the need to understand the development of pruritus before ESRD. Patients with moderate to extreme pruritus were more likely to feel “drained”, have poor SQ, depression, and poor QOL. Pruritus in HD patients was associated with 17% higher mortality risk.

The association between pruritus and mortality can be attributed to poor SQ, along with other factors. Bad related pruritus results highlighted the need for better therapeutic agents to provide relief for 40%-50% of patients affected by pruritus.

4. Sexual Dysfunction

There is a high rate of sexual dysfunction (SD) in HD patients. In the general population, many medications may negatively affect individuals’ sexual function. The DOPPS attempts to establish the relationship between prescription drugs and SD in patients on dialysis.

There were 16,237 patients studied who were prescribed antihypertensives and antidepressants (7346 patients in DOPPS phase I and 8891 patients in DOPPS II).[5]

The study showed interesting results regarding drugs and SD. Antihypertensive and tricyclic antidepressants increased the chances of having an SD, which is consistent with the findings of the general population.

Not surprisingly, patients with a diagnosis of depression also had a risk of worsening SD, so the overall effect on sexual function may reflect improvements in clinical depression being offset by the difficulties caused by drugs.

Benzodiazepines were associated with a high incidence of SD in the study of HD patients.

For patients with SD related to antihypertensive treatment, a reduction in the dose of medication or a change to angiotensin-receptor blockers, angiotensin-converting enzyme inhibitors, or calcium channel blockers, may help alleviate the problem.

Knowledge of associations between SD and prescription drugs may offer opportunities for intervention.

5. Depression

Depressive symptoms and depression are the most common psychological problems in HD patients. The prevalence of depressive symptoms (as evaluated through a self-reported questionnaire) and depression (as diagnosed by a physician) were assessed across DOPPS countries. Associations with antidepressant treatment, mortality, hospitalization, and the withdrawal of dialysis were also evaluated.

A systematic evaluation of depression in patients undergoing HD would provide information on the sense of well-being of patients.

Data suggest that depression is underdiagnosed and undertreated among HD patients. The Center for Epidemiologic Studies (CES-D) can help identify HD patients at increased risk of death and hospitalization. Interventions should target these patients to improve survival and reduce hospitalizations.[6]

6. "Do Not Resuscitate" Orders

Global statistics on practice patterns related to a patient's "Do Not Resuscitate" (DNR) orders and withdrawal of dialysis had not been collected or analyzed evenly.

The DOPPS has analyzed DNR on 8615 adult HD patients randomly selected from 308 dialysis centers in France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States.[7]

The United States had the highest prevalence of DNR orders (7.5%) and rate of HD withdrawal (3.5 per 100 patient-years). HD patients living with a high disease burden are at increased risk of death compared with the general population.

Within the international nephrology community, there is not consensus on how DNR orders can be analyzed and processed. There are also no uniform practice patterns established for stopping dialysis in relation to DNR orders. Once a patient has decided to request a DNR order, this order may change depending on clinical context of the patient. For example, in the United States, while undergoing HD, even for those patients who have chosen the DNR, it is likely that DNR patterns and withdrawal of practice varies by doctor, dialysis facility, and geographic region.

The highest prevalence of DNR and rate of HD withdrawal in the United States are compatible with legal and cultural emphasis on patient autonomy. By showing the characteristics associated with

these findings, this study contributes to our understanding of why HD patients requested DNR or withdrawal from treatment.

7. Recovery Time

After an HD treatment, many patients describe feeling tired and in need of rest or sleep.

The study on recovery time was based on patients attending three-times weekly HD; 68% of patients reported needing more than 2 hours to recover from a dialysis session, and 27%, more than 6 hours.[8]

Recovery time was longer if patients were older, female, or had high BMI, diabetes, or a psychiatric disorder. Patients who had symptoms of kidney disease, such as itching, cramping, poor SQ, and depression were more likely to need a longer recovery time.

In addition, patients less able to withstand stress may experience symptoms for longer. The symptoms may be related to the cumulative effects of renal impairment or treatment of HD because the likelihood of a longer recovery time increased with duration of ESRD and dialysis.

Additional studies are needed to investigate whether recovery time can be modified by changes in the prescription of HD. Recovery may be faster after treatments in which liquid displacements are slower and have smaller volume-concentration.

Studying recovery time may help determine how to incorporate adequate recovery time into clinical practice and how to use it as a guide to develop better QOL for patients.

Interventions to reduce recovery time and possibly improve clinical outcomes, such as increasing sodium concentration of the dialysate, need to be tested in randomized trials.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

Each patient's personal resources (cognitive, emotional, psychological elements, and perceived QOL) affect the way they approach the disease.

Health workers' important contributions include determining contextual factors and external resources. Early intervention is needed to get the greatest degree of adaptation to the disease process and treatment and achieve the greatest degree of integration in a patient's health regimen and routine.

As published in numerous articles, the DOPPS has provided the international community with detailed analyses of HD treatment standards and outcomes for patients.

One of the main functions of nursing is to help individuals, sick or healthy, to perform activities they would perform if they had the strength, will, and knowledge – while recognizing patients are the real protagonists of their health.

Nursing should promote healthy lifestyles. Renal patients' care must be integral and should be directed to interventions derived from nursing diagnoses as collaborative problems. Nurses must enhance self-care, provide emotional support, and help educate patients and their families on how working together creates a strong environment for ongoing care.

The DOPPS results allow monitoring changes in policies and standards of treatment and their effects on clinical outcomes, such as mortality, hospitalization, QOL, and survival.

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Mineral Bone Disorders in Hemodialysis Patients

A Review of Findings from the DOPPS

By Marisa Pegoraro

INTRODUCTION

With the definition of Mineral Bone Disorders (MBD), the nephrology community indicates a certain type of mineral alteration which leads to degeneration of the bone physiology, and abnormal mineral calcification in soft tissues and vessels.

The MBD pathophysiology is quite complex and, due to the longer survival of ESRD patients on dialysis, the complex chain of metabolic events can now be studied. Proper drugs, diet instruction, and life style education are necessary, and now finally available, in order to improve clinical outcomes and quality of life for dialysis patients.

This article aims to highlight findings and queries that DOPPS data collection and analyses shed light on during its first 20 years of activity, to make nurses aware of MBD disorders, and to enhance the nursing role in MBD management on patients' education and drug adherence.

PUBLICATIONS REVIEW

Papers will be analyzed in publication order, which reflects the clinical research interest approach following the first findings, mainly mentioned in the first paper, to more recent trends and medication use.

THE FIRST PAPER

The first paper from DOPPS data analysis on MBD was published in 2005 by Young et al.[1]using data collected in the first phase of DOPPS (1996-2000), from seven countries (US, Europe, and Japan) representing a total sample of 17,236. From this large sample, as per DOPPS protocol, in each unit a prevalent cross section sample of patients were randomly selected. A total of 8,621 patients were studied with lab tests, drug treatments, and cardiovascular conditions, which were collected every 4 months. The paper studied all different components involved in the "puzzle" that is MBD management: phosphorus and calcium levels, calcium and phosphorus product, parathyroid hormone, vitamin D therapies, phosphorous binding therapies, and dialysate calcium concentrations. This article represents a cornerstone of DOPPS data and is the basis of future article considerations.

Phosphorus (P): End-stage renal disease (ESRD) induces hyperphosphoremia which in turn stimulates a rise in higher parathyroid hormone. The article reports that only the 41% of patients had a P range within the guidelines (GL) of 3.5-5.5 mg/dl. All-cause and cardiovascular mortality were significantly associated with serum P concentration in a bimodal correlation either with P lower than 3.5 (10% of

patients) or P above 6.5 (29% of patients). Parathiroidectomy (PTX) was associated with higher P concentrations.

Calcium (Ca): ESRD induces hypocalcemia. According to GL, Ca should have a target range of 8.5 to 9.5 mg/dL. 9.3% of patients had lower concentrations and 50% had higher concentrations compared to GL recommendations. Serum Ca concentrations below 7.8 mg/dL were nevertheless associated with lower mortality risk.

Calcium &and Phoshorus Product (Ca x P): This mathematic product of lab test data is used by clinicians for dosing drugs and Ca dialysate concentrate prescription. The recommended GL upper limit of Ca x P is 55 $mg^2/dL^{2.}$. All-cause and cardiovascular mortality had a strong association with Ca x P > 65 mg^2/dL^2.

Parathyroid Hormone (PTH): . Optimal PTH in HD patients ranges at the start of the study was from 150 to 300 pg/mL. In DOPPS analyses, 51% of patients had a PTH below 150, correlated with low albumin, low Hb, higher Ca dialysiate concentration, females, older patients, and being treated in Japan; 27% had PTH above 300 pg/mL, correlated with male sex, black race, vitamin D therapy, and longer duration of ESRD. Higher PTH exposure was associated with increased risk of parathiroidectomy (PTX).

Vitamin D therapy (Vit D): Vit D is given to correct Ca levels in order to limit PTH rise and in consideration of P level. There are oral and IV drug formulations. A great variety of uses of Vit D IV was observed among HD unit clinical practice (ranging from 0% to 100% of patients treated) with larger IV use in US and lower use in Japan. Vit D was given to 46% of patients with low PTH and to 65% of patients with high PTH. This gap remained even after considering less stringent PTH target values. No statistical correlation was found between Vit D therapy and mortality.

Phosphorus binder therapy (P bind): Pbind is used to decrease serum P levels by inhibiting the internal absorption. They need to be taken during meals. A large variety of drugs has become available in the last 10 years. At the time of the study, 53% of patients were on Ca Carb., 26% on Ca Acet., 1% on Ca Citrate, 6% on Aluminum salts, and 1.5% in magnesium salts. Sevelamer was available only for 1% of patients and Lantanium Carb, was not available at all. The 77% of treated patients had low P. Among patients with higher P, the 85% were under some binder treatmeant. Similar percentages of patients were overusing and underusing when less stringent serum P concentrations (<3 and >6 mg/mL) were applied.

Dialysate calcium concentration (DsCa): Ca balance after HD treatment rises in direct proportion to DsCa concentration. At the time, K/DOQI GL recommended 2.5 mEq/L, while EBPGL did not set any specific value. Lower DsCa was used in Europe and Japan. In the US, DsCa ≤ 2.5 mEq/L was used in the 36% of patients with low serum Ca (<8.4 mg/dL), and in the 53% of patients with higher serum Ca (>9.5 mg/dL). All-cause mortality risk (but not strictly cardiovascular) was associated with higher DsCa use, even after adjustment for Ca and P serum concentrations.

Conclusions and Consideration for Clinical Practice

The first DOPPS findings supported other local or national data, and confirmed that MBD was not strictly related to bone conditions but had direct influence on the cardiovascular status and life expectancy of patients. Altered levels of Ca, P, and Ca x P induced a process of vascular calcification

(called “mineralization”) that suggested a contribution to occlusive vascular disease, including coronary, peripheral, and cerebral circulation. It showed evidence concerning the relationship between patients’ survival and mineral metabolism indicators and clinical practice options.

Applying statistical analysis and albumin correlation, the study supported the connection between mineral markers and patient nutritional status, enhancing the need for a more comprehensive and holistic evaluation of single patient lab tests.

The study also demonstrated that better knowledge about areas of clinical management improvements (i.e., dialysate concentration), better patient outcomes criteria (i.e., sex and race, age and ESRD duration), health economy issues (i.e., under/over drug prescription), and areas for further pharmaceutical research (i.e., P binders) was needed.

Allowing benchmarking among existing GL, the study also suggested revision and dissemination of more harmonized clinical practice guidelines.

THE SECOND PAPER

Published in 2006 by M Jadoul et al.[2], the second paper describes the prevalence of hip and other bone fractures among hemodialysis patients. The authors hypothesized a possible association between hyperparathyroidism and various medications, known to cause falls in the non-uremic elderly, as independent risk factors for bone fracture in HD patients. Data were collected in the second phase of DOPPS (2002-2004) from 320 dialysis units, in 12 different countries from a total sample of 12,782 patients.

Among a prevalent cross-section of HD patients, 2.6% had a previous hip fracture, with differences among countries that ranged from 3.9% in France, 2.7% in US, and 1.4% in Germany.

The incidence of new fractures among dialysis patients was 8.9 per 1000 patient/years (pts/y) and 25.6 per 1000 pts/y for any new fractures. Being female, older age, a prior kidney transplant, longer time on dialysis, and low albumin were predictors of new fractures. After controlling for an array of demographic, lab factors, and comorbidities, Spain and Sweden had significantly lower odds ratios for fractures than the US; none of the EU countries exhibited a higher incidence than the US.

Other variables were associated with higher incidence of hip fractures: living in a nursing home, needing assistance to walk, being diabetic, and being white (vs. black). No correlation was found with congestive heart failure and lung disease.

Very low (< 150 pg/mL) or very high PTH (>900 pg/mL) was associated with elevated risk of any fracture, suggesting that PTH may be an independent risk factor for fractures. A post-hoc analysis demonstrated a benefit in the use of Cinacalced vs. no drug.

Several medications were associated with elevated risk for new fractures: narcotic and pain medication, benzodiazepines, adrenal corticosteroids, and a combination of narcotic medications.

CONCLUSIONS AND CONSIDERATION FOR CLINICAL PRACTICE

The authors' hypothesis had been confirmed: HD patients are much more frail and likely to have hip and other bone fractures (up to two-fold more), compared to the general population at any age range.

For the aged population, previous fracture, PTH alteration, low BMI, needing aid to walk, and living in a nursing home are factors requiring more attention and coordinated nursing care. In younger patients, high PTH alteration plays an increased risk for fractures, thus requiring better adherence to medication while stressing the need for maintaining good physical condition. The use of Cinacalcet shows a positive influence on decreasing fracture risk. Its use needs to be clearly understood by the patient in order for them to be as compliant as possible**.**

Similarly, the use of antidepressants, painkillers, and corticosteroids could increase the risk for fractures, suggesting the need to consider potential benefits and risks when prescribing them.

THE THIRD PAPER

In 2008, Tentori et al. published an article[3] in order to clearly identify calcium, phosphorus, and PTH categories associated with the lowest mortality risk and possibly inform development of new GL. Data were collected throughout the first three phases of the DOPPS from 1996 up to 2007; 25,588 patients were included, for longer than 180 days, from 925 dialysis units in 12 different countries.

The number of patients with the lowest mortality risk for P and Ca categories increased internationally over time.

In both categories, Ca and Ca_{alb} levels greater than 10.0 and greater than 9.5 were associated with greater all-cause and cardiovascular mortality risk in both baseline and time-dependent models. Ca and Ca_{alb} of 7.5 mg/dL or less were associated with increased mortality risk, but only in the presence of albumin higher than 3.8 g/dL. ***The lower mortality risk was defined as 8.6-10.0 and 7.6-9.5 mg/dl for Ca and Ca_{alb}, respectively.***

Phosphorus levels of 2.0 mg/dL or less were associated with all-cause mortality risk in both baseline and time-dependent models. Very high P levels > 6.5 were associated with all-cause mortality. Cardiovascular mortality was higher even at lower P levels of 5.1 -6.0 mg/dL. That's why the **lower mortality risk category was set at 3.6-5.0 mg/dL.**

Mortality risk showed an increase only for PTH levels greater than 600 ng/dl (pg/dL), which is 2 to 4 times greater than the maximum recommended level. However, considering the great amplitude in PTH distribution and variety of assay used for PTH, these data suggested an unpaired ability to detect mortality categories. The connection with Ca x P product was evaluated, in order to include the magnitude of effect on mortality in patients with high level of both. ***PTH values higher than 300 ng/dL were associated with greater mortality risk in the presence of a Ca x P values greater than $55mg^2/dL^2$.***

CONCLUSIONS AND CONSIDERATION FOR CLINICAL PRACTICE

Lower mortality risk categories were identified and PTH values need to be considered along with Ca and P values. After this paper was published, several GL were modified, giving clinicians clearer therapeutic suggestions. Patients' drug adherence should be monitored and supported through education and shared lab test results in order to empower via knowledge.

THE FOURTH PAPER

The fourth paper, also written by Tentori et al.[4] , explored the survival advantage for patients using Vitamin D. The question arose from a great difference in Vitamin D prescription between the US and the other DOPPS countries. Data were analyzed from a sample of 38,066 patients, from 12 countries, between 1996 and 2007 (DOPPS I, II, III). Mortality risk was assessed using different statistical methods: standard baseline, time varying Cox regression models, and marginal structural models adjusted for demographics, detailed comorbidities, and the facility percentage of patients treated with Vitamin D; they also considered patient case mix to predict patient mortality. Vitamin D prescription varied widely among countries, ranging from 33% in France to 66% in the US, remaining almost stable throughout the duration of the observation period. Only in the US was there an increase of 8% recorded during DOPPS ll. The oral route was the most used in all European countries, while 62% of US patients were on the IV route (calcitriol 66.8%, paracalcitol 25.6%, and2.4 % in doxercalciferol).

The study did not find an association between Vitamin D therapy and survival, either in the patient-level or facility-level models. In addition, no survival advantages were in different Vitamin D analogs.

The patients prescribed Vitamin D had longer survival but were also younger and had case mix and lab characteristics that are generally associated with greater longevity (like higher Hb and albumin levels) than patients not prescribed Vitamin D. Survival benefit virtually disappeared in baseline models and it attenuated in time varying models. No difference in mortality was found when considering the route of administration between oral and IV prescription, thus rejecting a possible bias for noncompliance.

CONCLUSIONS AND CONSIDERATION FOR CLINICAL PRACTICE

Vitamin D should be guided by each patient's specific conditions. The results indicate an ethical need for clinical trials to clarify Vitamin D impact on mortality. From a nursing point of view, patient nutritional status supervision and education support seem to still be the most important aspects.

THE FIFTH PAPER

In 2014, Tentori et al.[5], following Jadoul's previous findings, analyzed DOPPS data in consideration of death and hospitalization following bone fractures in an in-hospital cohort of 34,579 patients among the HD patient population from DOPPS phases II, III, and IV. Fracture rates and death across all countries where higher (3-fold more) in HD population compared to the general population.

Three percent of this cohort (1,122) experienced a fracture (491 hips and 643 other), were older, female (and white in North America), had longer time on dialysis, lower BMI, and had higher PTH and KT/V compared with those with different data for the same mentioned values who did not Fracture rates did not vary over time, but a substantial difference in the fracture incidence existed among countries ranging from 12 per 1000 pts/y in Spain to 45 per 1000 pts/y in Belgium. Medium hospitalization length ranged from 7 days in the US up to 37 days in Japan (where rehabilitation takes place immediately, during hospitalization).

Patients who had experienced a fracture had a mortality rate exceeding 500 per 1000 pts/y; this rose to 1500 per 1000 pts/y, if subsequent hospitalizations were considered. Even though females had higher fracture rates, men had slightly higher mortality rates in the follow-up period. Higher

mortality rates were recorded in all countries in the first year of follow-up, declining with time. Major causes of death were cardiovascular events and infections, and other minor conditions correlated to bleeding, prolonged immobilization, and malnutrition which may precipitate pre-existing conditions.

CONCLUSIONS AND CONSIDERATION FOR CLINICAL PRACTICE

Bone fractures represent high health and economic burdens for HD patients. All possible action focused on preventing them should be identified and implemented, particularly for the frailest subgroup of patients. Physical therapy, avoidance of hypotensive episodes, and careful prescriptions of psychoactive medications and Vitamin D supplementation (resulting in the normalization of serum 25-hydroxy Vitamin D level), may reduce the risk of falls. Nutritional intervention aimed at maintaining or improving healthy body weight may contribute to decreasing the risk of bone fractures, as well.

THE SIXTH PAPER

The 2015 Tentori et al.[6] article analyzed recent changes in therapeutic approaches related to secondary hyperparathyroidism, taking into consideration all DOPPS data, for a total of 18 years of observation. The latest published GL suggested higher PTH levels than the previous standard. This was correlated with a medium increase of PTH values in all DOPPS countries (excepted in Japan which kept a very strict PTH range and did not show any increase with time). Use of IV Vitamin D and cinacalcet also increase in co-existence with higher PTH. Various statistical methodologies were used to identify realistic trends and predictors, taking into consideration all MBD markers and interactions: the DOPPS confirmed previous outcomes and found further evidence for an increased mortality risk for PTH exceeding >300 pg/mL.

At 3 - 6 and 12 months of observation, PTH represented the main predictor for all-cause and cardiovascular mortality and all-cause and cardiovascular hospitalization. In patients treated for secondary hyperparathyroidism (SHPT), the medium increase of PTH was seen from DOPPS I to V, ranging from 150 to 300 with similar variation from Eu, A/NZ, and US data. Patients with PTH from 300 - 450 ng/mL had a hazard ratio (HR) increase by 9%, while in those having PTH higher than 600 ng/mL, the HR increased up to 23% (corresponding to 11% of study sample). Also in non-SHPT treated patients, the HR rose up to 25% for PTH lower than 50 ng/mL. HR reached 15% for patients with PTH higher than 600 ng/mL (corresponding to 7% of study sample). PTH increased both for patients with higher or lower serum calcium and phosphorus, in all categories of age and time of dialysis, suggesting that patient characteristics (age, vascular access, longer duration of ESRD) may have contributed. However, these outcomes do not include Japan, where a very strict GL had been kept with a slight decrease in PTH levels occurred over time. Although there was an increase in PTH, rates of parathyroidectomy decreased over time, apparently consistent with the increased use of Vitamin D and Cinalcalcet. The study revealed also that among SPTH treated patients, 43% had a PTH <150 ng/mL and 41% had PTH <50ng/mL, suggesting areas of medication overuse and great possibility for clinical improvements. However, it seems that changes in therapeutic approach were not the only contributor: clinicians may have grown to accept higher PTH targets, allowing the lack of strong evidence to advocate for tighter control. DOPPS data fully endorse the notion that SHPT treatment should consider the most related serum markers (calcium and phosphorus), and possibly also fibroblast growth factor 23, because they show a robust association of high PTH and adverse outcomes in combination with mean PTH levels rising internationally.

Conclusions and Consideration for Clinical Practice

PTH is an important marker of bone and mineral metabolism and should be kept in the correct range value. The availability of new therapies should be considered as tools to control mineral metabolism, but they need wise and personalized management. Clinician attitude plays an important role for making patients and healthcare personnel aware of PTH changes over time. From a specific nursing point of view, often in clinical practice nephrologists need support to define adequate lab test routine practice and their evaluation related to single patient history and attitude.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

DOPPS data support correlation between mineral metabolism disorders with morbidity and mortality among dialysis patients. MBD management is complex, with several different varieties of serum tests as markers of management. Recent new drugs should help to contrast and control adverse outcomes, but: 1) for some new drugs (see cinacalcet, IV vitamin D) their net benefits are not fully supported by evidence; 2) clinicians' attitude and knowledge play a pivotal role concerning the starting treatment time and current treatment management; 3) it seems the knowledge has been acquired, but clinical practice has not yet been implemented and harmonized; and 4) patient education regarding treatment adherence and compliance, supported by knowledge and empowerment, are areas needing major improvements.

As it occurred 20 years ago for anemia management, it may be time to involve nurses to support nephrologists in their clinical practice, and monitor patients' understanding and compliance on MBD therapies, in a more structured and organized way. The cost of some new drugs, the cost of morbidities treatment (see all heath disease treatments), and the complexity of involved variables should justify such a possible choice.

Nursing activities are patient centered; therefore, greater involvement in therapy management should not just complement some doctor's activities. Seen in the context of care continuity and shared management, where the patient is known, a care-plan drawn, and the patient is empowered, step by step, to understand and participate to the complexity of MBD clinical management, nurses' involvement in therapy management should be considered an opportunity for clinical improvement.

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Vascular Access
A Review of Findings from the DOPPS

by Yolande Pirard

INTRODUCTION

Vascular access is the Achilles heel and the lifeline of patients receiving hemodialysis (HD). Vascular Access (VA) practice patterns are highly variable across the world. Thus, the Dialysis Outcomes and Practice Patterns Study (DOPPS), since 1996, has analyzed and transformed the data of this important topic into knowledge for care providers in the renal field. This helped to improve care and outcomes of dialysis patients. The large size of the DOPPS coupled with its study design provides a powerful approach for investigating HD practices that yield the best outcomes.

Arteriovenous fistulae (AVF), the first choice access type, are associated with a lower number of procedures, longer overall survival, lower risk of thrombosis and infection, fewer hospitalizations, and reduced overall health care expenditure. Arteriovenous grafts (AVG) are easier to cannulate, have shorter maturation time and may be appropriate if vascular anatomy does not allow an AVF construction. However, grafts have an increased risk of thrombosis, infection, and need for interventional procedures compared to AVFs. Catheters are necessary if after multiple access failures suitable blood vessels are no longer available for a fistula or a graft, and are also necessary when an AVF or a graft is not ready for use, and starting HD therapy is urgent. However, Combe et al. showed that tunneled and untunneled catheters have five to eight times higher rates of infection than fistulae.[1] This article reviews several DOPPS papers devoted to VA, helping us to understand more about VA practices, a key topic for nurses.

VASCULAR ACCESS USE IN EUROPE AND THE UNITED STATES

In an article by Pisoni et al.,[2] the DOPPS analyzed factors associated with AVF, AVG, and catheters use for incident and prevalent patients in the United States and Europe (EUR). Data for 6400 HD patients were analyzed from 1996 to 2000 (US) and from 1998 to 2000 (five European countries, France, Spain, Italy, United Kingdom, and Germany, DOPPS 1). In EUR, 80% of all VA were AVF whereas in the US, 58% were AVG. Results demonstrated a high level of AVF use in EUR both for patients with low or high comorbidity. AVF use was lower in the United States especially in patients who were younger, non-diabetic status, and without peripheral vascular disease. The creation of permanent VA was generally (65% to 89%) performed by a vascular surgeon in four EUR countries, but in Italy, 80% were placed by a nephrologist.

There was a large difference between VA use in the United States and EUR in incident patients: 66% of incident patients had an AVF in EUR compared with only 15% in the United States, whereas AVG use was about 2% in EUR and 24% in the United States. Sixty percent of new patients in the United States started with a catheter compared with 31% in EUR. This large difference was associated with pre-ESRD care and the unit preference for type of vascular access. In EUR, the practice of establishing a permanent functional access for the first HD treatment was more successful than in the United States where 46% of patients did not have a permanent VA versus 25% in EUR. It is important to observe that both in the United States and EUR, 55% of these patients without permanent VA had seen a nephrologist >30 days before starting dialysis.

Survival of AVF was better compared with AVG in patients starting HD with a permanent access. It is important to observe that both AVF and AVG survival was better if used for first HD treatment compared with AVF or AVG used after starting HD with a catheter. This is in line with reports[3] recommending avoiding catheter placement in the subclavian vein to minimize central vein stenosis and other complications that may complicate future placement of VA.

HEMODIALYSIS VASCULAR ACCESS PREFERENCES AND OUTCOMES

Young et al.[4] analyzed association between preference at the unit level, AVG and AVF use, based on a US sample of 133 units from 1996 to 1999.

Facility preference influenced the type of access created. Patients in units where medical directors (typically nephrologists) and nurse managers (or head nurse) expressed a preference for AVG were more than twice as likely to have an AVG than an AVF; these findings were clinically significant. Regarding new patients starting HD in their unit, the majority of respondents expressed a preference for AVF (59% to 79%), a sizable minority preferred AVG (21% to 40%).

This study and others also strongly suggested that on average, the practice of placing an AVF was associated with longest access survival but some reasons may exist to prefer an AVG: ease and speed of creation, ease of needling, high blood flow, avoidance of prolonged use of catheter, and usefulness in case of poor vascular anatomy. Still there is agreement that an AVG was inferior to AVF due to higher rates of infection and failure.

The optimal VA type also depends on local conditions such as training and skill of staff (surgeons, nursing). It is notable that grafts were more frequently placed even though a majority of dialysis providers expressed preference for fistulae. The relatively low prevalence of fistulae has been also attributed to unfavorable patient characteristics.

CONVERSION OF VASCULAR ACCESS AMONG US INCIDENT HD PATIENTS: DESCRIPTION AND ASSOCIATION WITH MORTALITY

The DOPPS study by Bradbury et al.[5] was the first to observe the patterns of VA type conversions among 4532 incident US patients and their association with mortality (data from DOPPS-1996 to 2004). Sixty-nine percent had a catheter, 17% an AVG, and 13.1% an AVF. Mean age was 62 years and 48.4 % had diabetes as cause of ESRD.

VA conversions are common in incident patients. Among patients who started hemodialysis therapy with an AVF or AVG, 22% experienced a conversion to a catheter due to failure of the original access. The median time of conversion was 62 days and 84 days, respectively. Conversion to a catheter was associated with an adjusted mortality HR of 1.81.

Among patients who started hemodialysis with a catheter, 59% converted to an AVF or AVG (for 57%) with a median time of 92 and 66 days respectively. The conversion to a permanent access was associated with an adjusted mortality HR of 0.69. Thus, there was a 31% lower risk of death in patients converting to permanent VA versus those who did not.

The unit practices also influenced the preference and type of conversions. It's important to note that 62% patients who initiated HD using a catheter never converted to a permanent VA during the first year.

In recent years in the United States, efforts have been implemented to reduce the use of catheters; thus prevalent patients dialyzing with a catheter were only 27% compared with 70% of incident patients starting HD with a catheter. However, despite decreasing mortality rates in prevalent HD patients, the mortality and infection rates in incident patients has not decreased. Early nephrologist referral for placement of a permanent access will help to decrease the mortality risk. Factors such as decisions about maturity of permanent access, time to cannulation, and expertise of individuals performing the cannulation might influence conversion decisions.

TIMING OF FIRST CANNULATION AND VA FAILURE IN HD

Saran et al.[6] used DOPPS data to examine the impact of two facility-level practices: time to first cannulation and blood flow rate as potential predictors of access outcomes. Data were analysed between 1996 and 2001 among 309 HD units in the United States, Japan, and Europe, covering 2730 grafts and 2154 fistulae. Based on responses of nurse managers, fistulae were commonly first cannulated when the nephrologist or the dialysis nurse clinically determined if veins are well developed and palpable to allow for cannulation.

Early first cannulation time (less than one month after creation) was not associated with an increased risk of primary fistulae failure. However, cannulation within 2 weeks would not be advisable (study of Rayner).[7] First cannulation between 2 and 4 weeks could be attempted if clinically indicated and deemed feasible based on clinical assessment without necessarily increasing the risk of fistula failure. The presence of access monitoring protocols as a facility-level practice pattern was not associated with significant changes in the results of primary patency of AVF in a subanalysis. These findings are important as they indicated the potential to reduce time with catheter or eliminate catheter use.

The current study noticed that significant differences in blood flow rate existed across countries. The facility median blood flow rate in Japan was 196.5ml/min, 300ml/min in Europe, and 412 ml/min in the United States. There was no statistical significant difference in relative risk of AVF or AVG failure between blood flow rate categories.

These findings suggest that the reduced time required for VA maturation has the potential to decrease reliance on catheters, while not compromising long-term access survival. It is notable that typical time to first cannulation for fistulae was considerably shorter in Europe than in the United States despite the European facility practice of placing fistulae at a higher rate in patients with diabetes, peripheral vascular and coronary artery disease. Lower blood flow rates can be used for AVF with excellent results as indicated in EUR where AVF are typically used at blood flow rates of approximately 300 ml/min. Future studies will help to analyze staff experiences, surgical commitment, and cannulation techniques.

FACILITY HD VASCULAR ACCESS AND MORTALITY

Pisoni et al.[8] studied the relationship of VA use with mortality and hospitalization risks as a practice-based analysis at the HD unit. The data collection included 28,196 HD patients from more than 300 units participating in the DOPPS in 12 countries from 1996 to 2004.

The use of graft and catheter was greater in United States than in Japan and many European countries with an increased mortality risk (30% to 40%), attributable to differences in VA practice. Considerable variations in vascular access were observed across Europe, for example AVF use was considerably lower in Belgium (52%) and Sweden (55%). Japanese HD units had very high AVF use (91%) and low catheter use (1% to 2%). Results were based on data collected largely before the start in 2003 of “Fistula First Initiative” in the United States.

Hence, an increase of 45% in AVF use was seen in the United States in 2006 compared with 24% in 1996 to 2000. However, catheter use increased from 17% to 27% from 1997 to 2002/2003 and subsequently remained at this higher level. It is important that units not only achieve a high level of AVF use but also have low catheter use. The relatively large increase in catheter use could lead to a net increase in mortality and hospitalization rates even if AVF use increases.

Greater use of catheter as a dialysis unit practice was associated with 20% greater mortality risk (for every 20% increase in patients with a catheter), and greater use of AVG was associated with 9% greater mortality risk (for 20% increase in patients with AVG) after adjustment.

The study assessed if units with greater catheter and graft use had also on average older patients and greater morbidity. Only three comorbidities (diabetes, lung disease, and cardiovascular disease), were significantly related to greater levels of case-mix adjusted unit catheter use.

The results also strongly suggested that the relationship between catheter and graft use with mortality and hospitalization was due to unit use rather than patient-level VA use. The hospitalization risks for any infection or VA-related infections were substantially greater with higher catheter or graft use than was all cause hospitalization; 18.6% of all hospitalization-related infections were attributed to VA infections. Catheter use was strongly related to sepsis in many other studies.

Higher doses of erythropoiesis stimulating agent (ESA) are also used for patients with a catheter versus permanent VA, suggesting that clinical or subclinical infection and chronic inflammation contribute to higher ESA requirements.

VASCULAR ACCESS: USE AND OUTCOMES

This summary about VA by R.L. Pisoni[9] is interesting and still relevant even though published in 2002. We learned the following from facilities successful in placing AVF at a high rate in a broad range of patients: a strong commitment to AVF as the permanent access as first choice for nearly all patients which is facilitated by a multidisciplinary team well trained in placement; referral; needling and maintenance of AVF; and applying highly skilled surgical technique with variations in procedure to successfully accommodate differences in patient vasculature and comorbidity.

At least four months of pre-ESRD care is generally required for new patients in order to have a well matured AVF for HD therapy. This is to accommodate the wide variation in the time necessary for access maturation depending upon the nature of a patient's vasculature, and the considerable imprecision associated with predicting the onset of HD. The surgical success rate impacts the probability of new ESRD patients starting HD with a functioning AVF.

Countries with a low median time for first needling of AVF did not demonstrate worse adjusted AVF survival rates than countries with long median needling times and this gives many patients the opportunity to start dialysis with a functioning AVF rather than with a catheter. This is also advantageous to dialysis units as it may not be necessary to refer patients earlier for AVF creation.

For a large group of patients who started HD with a catheter but did not have a permanent access created, more than half (55%) had seen a nephrologist for >1 month prior to starting HD. The high use of catheters among incident patients can have detrimental consequences for future permanent access survival. Recent studies indicate that prior catheter use is associated with a 1.4- to 2.1-fold higher risk of failure for subsequently used grafts or AVF, and that the side and location of the temporary access relative to the permanent access are important factors associated with survival of subsequently used permanent VA.

Catheters often are viewed as a temporary access for HD patients until an AVF or graft is ready for use. However, recent results from the DOPPS suggest that in some facilities, central vein catheters are routinely used for dialysis in a large proportion of patients. Part of this high prevalence of catheter use within these units is due to the extended use of

tunneled central vein catheters. Adjusted rates for VA infection in the DOPPS have been found to be 7-fold higher for catheters compared with AVF or grafts.

RECENT OUTCOMES FROM THE DOPPS

Recent DOPPS results[10] have shown a large improvement in the use of AVF in the United States from 1997 to 2013 with an increase from 24% to 68%, and a decrease in catheter use from 27% to 15% since the introduction of the prospective payment system in 2011. Across 20 DOPPS countries in 2013, for all accesses, AVF use ranged from 49% (Canada) to 92% (Russia) and catheter use from 1% (Japan) to 45% (Canada).

However, AVF use for incident patients in the United States remains low (28%), with catheter use at 67%. Recent results in DOPPS countries have shown catheter use between 11% in Japan and 81% in the Gulf Cooperation Council (GCC) countries, and AVF use ranging from 19% in the GCC to 84% in Japan.

Among patients having seen a nephrologist ≥4 months prior to ESRD only 55% had a permanent access in the United States compared with other DOPPS countries ranging from 28% in GCC to 81% in the United Kingdom. Reforms affecting pre dialysis care may be necessary to incentivize improvements in AVF rates at therapy initiation in countries with high use of catheters.

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

It is understandable that barriers in VA creation exist such as emergency situations, patient fear, preference or refusal, non-availability of a skilled surgeon, and patient vasculature differences. In several nephrology units, patient care pathways exist to follow and guide new patients to arrive well prepared for the onset of renal therapy. Multidisciplinary visits are planned during the pre-ESRD period with some financial advantages.

In order to empower patients to choose the renal replacement therapy (RRT) that is the best fit for him/her, timely pre-dialysis information is important to explain the different possibilities in treatment. If HD technique is chosen, nurses should explain VA and the importance of having a first choice VA.

Optimal timing for VA creation is difficult to determine due to the unknown or variation in disease progression. The planning of permanent access should occur early in Stage 4 CKD (GFR<30ml/min/1,73m$^{2)}$ to allow for VA creation and maturation. In order to have more patients starting HD with a permanent access, it is important to organize early referral for placing VA, minimize delays in AVF placements during pre-ESRD period, and perform pre-operative vascular mapping.

For every type of VA, the survival depends on local conditions, i.e. experienced nurses and skill level of staff. The nursing role is crucial in VA management, for example: timing of

cannulation, optimal cannulation techniques, access flow measurements, infection prevention, VA clinical assessment to identify changes in blood flow, arterial or venous pressure, stenosis identification, dry weight changes, and hypotension avoidance. Patient education is also important. Nurses have to explain how VA surveillance and care must be done by the patient.

As patients on home dialysis increase, quality of VA and their care is crucial. A good functioning fistula with well developed veins allows easier self-needling. The increase in the number of elderly patients with additional cardiovascular comorbidities and diabetes makes the creation and maintenance of functioning VA more difficult, and the high use of central venous catheters used for these patients is associated with an additional risk, specifically, infection and lower survival. Therefore, care should limit the utilization of catheters to clinically undisputable indications.

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Patients Undergoing Maintenance Hemodialysis and Quality of Life
A Review of Findings from the DOPPS

By Jeanette Wallin and Zehra Aydin

INTRODUCTION

Patients undergoing maintenance hemodialysis suffer not only from kidney disease; they also have comorbidities that require significant care. Increased focus on patient-centered care in recent years and health-related quality of life (HRQoL) have become increasingly important as an outcome measure in the evaluation of dialysis treatments. It has been suggested that for patients receiving renal replacement therapy (RRT), quality of life measures can be used to predict future morbidity and mortality[1].

HEALTH AND QUALITY OF LIFE

Health and quality of life are broad concepts and reflect different aspects of well-being. Quality of life is a broader concept than merely health. HRQoL refers mainly to function and well-being in disease and treatment[2]. The World Health Organization's (WHO) definition of health states that, "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[3]. Measuring HRQoL is a great addition to medical treatment. Especially important to note is that outcomes of health related quality of life measurement can be in groups of incurable chronic diseases.

DOPPS AND THE KIDNEY DISEASE QUALITY OF LIFE SHORT FORM (KDQOL-SF)

The Dialysis Outcomes and Practice Patterns Study (DOPPS) is an international prospective cohort study of a random sample of patients on hemodialysis. The goal of the DOPPS is to identify clinical practices that will allow hemodialysis patients to not only live longer, but also improve the quality of their lives. The DOPPS has been one of the first sources to report an international description of HRQoL and the prevalence of depression in hemodialysis patients across countries and clear evidence of the impact of psychosocial factors on morbidity and mortality[4].

Patients participating in the DOPPS are asked to complete a self-administered survey on an annual basis. The patient questionnaire, KDQoL-SF, is used to determine the score of the physical component summary (PCS), mental component summary (MCS), and kidney disease component summary (KDCS). KDQoL-SF is a self-reported instrument that measures patients' physical, psychological, and social well-being. The KDQoL-SF measures different aspects of HRQOL, including

items that capture social support and psychological factors. The KDQoL-SF was developed to be used by patients on dialysis[5] and it has been translated to several different languages [6].

FACTORS AFFECTING QUALITY OF LIFE

DOPPS analyses have assessed comorbidities, socioeconomic indicators, and potentially modifiable factors associated with HRQoL. Patients with more comorbid conditions, psychiatric disease, or hypoalbuminemia and those who were unemployed, with lower educational level, or lower income had lower HRQoL summary scores [4].

MORTALITY AND HOSPITALIZATION

Recent studies have suggested that poor HRQoL was strongly related to increased risk of mortality in patients on dialysis. DOPPS data were analyzed to assess associations between HRQoL and the risk of death and hospitalization. 17,236 patients from seven countries answered questionnaires (KDQOL-SF). The association between different components of HRQoL and clinical outcomes was assessed among participants in DOPPS[1,7]. Lower HRQoL summary scores were associated with significantly higher risk of hospitalization and mortality ($p < 0.001$)[4]. HRQoL was related to hospitalization and mortality. Both mortality and hospitalization increased significantly when quality of life was reduced from the highest to the lowest score for physical health (PCS), mental health (MCS), and kidney disease (KDCS). HRQoL was still significantly related to mortality and hospitalization when adjusted for several risk factors of death and hospitalization. The association between HRQoL and death was stronger than the association between HRQoL and hospitalization. This study also found that HRQoL was a better indicator to identify mortality and hospitalization than serum album [1,7].

DEPRESSION

Depression is a key HRQoL indicator and has been reported to be the most frequent psychological problem among hemodialysis patients[4]. Several studies identified that depression decreases adherence to treatment and has been associated with poorer HRQoL scores.

Lopez et al.[8] studied depression among hemodialysis patients in the context of the DOPPS, investigating whether the risks of death and hospitalization may be predicted from the presence of depression. The main analyses were restricted to 5256 patients who had a medical questionnaire (completed by the nurse coordinator in the unit) and who had responded to a patient questionnaire filled out by the patient. As part of the KDQOL-SF, and were asked to respond to the following two questions: (1) “have you felt so down in the dumps that nothing could cheer you up?” and (2) “have you felt downhearted and blue?” A response of “a good bit, “most,” or “all” of the time was classified as depressed. In the analysis, physician-diagnosed depression was reported in the medical records of 17.7% of patients; depression as measured by the “so down in the dumps” question was observed in 19.5% of patients. For the “downhearted and blue” question, a total of 21.5% of patients were classified as depressed. Depression was independently associated with higher risks of mortality and hospitalization. These results are consistent with those from other studies which have shown that depressed people are at increased risk for several diseases and related outcomes[8]. The two simple question assessment of depression can help to identify patients on hemodialysis at higher risk of death and hospitalization and are stronger predictors than a doctor's diagnosis of depression.

RECOVERY TIME AFTER HEMODIALYSIS SESSION

Rayner et al.[9] found that patients reporting a recovery time greater than 12 hours had a higher risk for hospitalization and higher mortality compared with patients reporting a recovery time between two to six hours. 6,040 patients in the DOPPS answered the question "How long does it take you to recover from a dialysis session?" categorized as: fewer than 2, 2-6, 7-12, or longer than 12 hours. Thirty-two percent reported recovery time less than 2 hours; 41%, 2-6 hours; 17%, 7-12 hours; and 10%, longer than 12 hours. Older age, diabetes, psychiatric disorders, greater intradialytic weight loss, and longer dialysis session length were associated with longer recovery time. Patients reporting a recovery time greater than 12 hours had a higher risk for hospitalization and higher mortality compared with patients reporting a recovery time between 2 to 6 hours. The conclusion of the study was that the question "How long does it take you to recover from a dialysis session?" is a simple question but says a lot about the patient's quality of life. This question could be a help to identify patients with lower quality of life.

The clinical problem of long recovery time it is very common. One possibility to help with this is changing hemodialysis schedules to respond to long recovery times, i.e., to possibly reduce to twice weekly treatment in patients nearing the end of life or to consider peritoneal dialysis (PD) or assisted PD[10].

SOCIAL SUPPORT

The DOPPS has investigated the influence of social support and other psychosocial factors on mortality, adherence to medical care recommendations, and physical quality of life among patients on hemodialysis. Data on 32,332 hemodialysis patients enrolled in 12 countries between 1996-2008 were analyzed. Untas[11] found that patients who reported that their health interfered with social activities had higher mortality; they were isolated, felt like a burden, and were dissatisfied with family support. There was a higher risk of non-adherence with medical care when the patient had lower levels of social support and other psychosocial factors. Higher social support and other psychosocial factors are associated with better physical quality of life. The conclusion for this study was that a greater focus on increased social support might improve quality of life for patients on hemodialysis. A focus on increasing social support may increase patients' adherence to treatments and ultimately might also contribute to reducing rates of death and hospitalization[11].

HOW DATA FROM THE DOPPS CAN INFORM PRACTICE: INFORMATION FOR NURSING COLLEAGUES

The complex situation patients on hemodialysis live with makes nursing extremely important. Hemodialysis patients experience significantly poorer quality of life than the general population and this restricts their ability to participate in normal daily activities. Understanding the perceived HRQoL of dialysis patients could facilitate health care planning in renal service. Psychosocial nursing interventions (assessment, encouragement, and support) would be better to begin at diagnosis and should be adapted to the progress of the disease and focus on the physical, psychological, and social functioning of people in order to facilitate the adaptation of patients to the changes of the disease. The role of nurses in providing patients with the best optimal dialysis involves minimizing technical errors, adhering to strict infection control practices, working closely with the multidisciplinary team, and maintaining current professional knowledge.

It is essential that nurses identify areas of patient treatment regimens which may be adversely affecting the patient's HRQoL and develop strategies to reduce them. Depression, more frequent hospitalizations, longer recovery time, and how social support are examples from DOPPS that can affect the patients' quality of life. Maximizing patient function and well-being should be a priority in nursing care alongside actions that reduce morbidity and mortality. Psychosocial aspects of a patient's HRQoL have been shown to be equally important as physical aspects and nurses can assist in improvements in this area [12].

While this is not new information, renal nurses armed with this ever-increasing evidence can focus on the quality of life of these patients and explore new ways to identify individual's specific problems and initiate corrective action. The use of quality of life indicators or tools will assist in this process[13].

Assessment with self-reported quality of life instruments is a good compliment to medical assessments and can be used in nursing and also for the dialog between the nurse and the patient. That means that the patient's experience is used as part of nursing care, which will get patients involved in their own care. When using HRQoL instruments, the nurse can, in a structural way, detect when the patient's quality of life is changed and identify when nursing modification is required. Quality of life is also one predictor to consider when discussing the need for palliative care. HRQoL assessment is a benefit for nursing, quality reports, and for research. The DOPPS research compares quality of life data between countries. This makes it possible for nurses to see patients' quality of life in other countries and if there any changes that can be taken in nursing quality development.

Lopes et al.[8] mentioned that even a single assessment of depression by simple questions can help identify hemodialysis patients at higher risk of death and hospitalization. These questions, particularly the "so down in the dumps" question, can be used in clinical practice to identify hemodialysis patients with depressive symptoms so that they can receive more detailed evaluation and special psychosocial or medical attention to reduce the risks of hospitalization and death[8].

Nurses are an important educational resource for patients concerning coping strategies and available support groups. Patients' expectations of their illness, treatment, and subsequent health status affect how they perceive their HRQoL; therefore, education is vital as it can provide patients with the opportunity to develop realistic expectations. Nurses play a central role in the multidisciplinary team and can link the patient with other members of the team who can provide the patient with services that may improve their HRQoL[12].

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