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Introduction

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At its annual meeting in 1995, the Canadian Society of Nephrology recognized the need for Canadian clinical practice guidelines for the treatment of patients with chronic renal failure and established a committee to identify areas for guideline development. The objectives were to establish national guidelines based on evidence and supplemented by expert clinical opinion, and improve the quality of health care for patients with chronic renal failure.

The guidelines are intended to be flexible, rather than prescriptive. They represent the best available knowledge and are to guide and inform practice. The guidelines will be important not only for nephrologists, but also for primary care physicians, patients, and families.

Care for patients with chronic renal failure consumes considerable human and financial resources. At times, there may be conflict between perceptions of the needs of these patients and the needs of society in general. These guidelines recognize that the physician's primary responsibility is to his or her patient.

Materials and Methods

The Canadian Society of Nephrology Committee for Clinical Practice Guidelines used teleconferencing to discuss and establish priorities. The areas selected for the first set of guidelines were vascular access for hemodialysis patients, treatment of anemia for patients with chronic renal failure, adequacy of peritoneal dialysis, and adequacy of hemodialysis. These areas, which are the same ones chosen by the National Kidney Foundation Dialysis Outcome Quality Initiative (NKF-DOQI) (1) in the United States, were selected for the following reasons:

- Vascular access represents the majority of hospitalizations for patients treated with hemodialysis.
- Anemia can be successfully treated with erythropoietin, but there is considerable controversy regarding target hemoglobin values, mode of administration, and iron therapy.
- Inadequate dialysis continues to be a major problem for patients treated with both peritoneal dialysis and hemodialysis and contributes significantly to morbidity and mortality.

In addition, these guidelines cover a fifth area not directly addressed by NKF-DOQI: the management of patients with chronic renal failure before dialysis, particularly with respect to timing of initiation of dialysis.

Work groups were formed to develop the guidelines for each area. Although nephrologists will be the most frequent physician users of these guidelines, patients will be most affected by their use. The guidelines will also have an impact on the practice of other care providers involved on renal care teams. To represent the different interests involved, each of the guideline work groups was composed of nephrologists, a patient representative (appointed by the Kidney Foundation of Canada), and at least one representative from another health profession (*e.g.*, nurse, dietitian, pharmacist, interventional radiologist).

Levels of Evidence for Rating Studies of Treatment, Prevention and Quality Assurance

I. A randomized, controlled trial (RCT) that demonstrates a statistically significant difference in at least one important outcome (*e.g.*, survival or major illness)

or

if the difference is not statistically significant, an RCT of adequate sample size to exclude a 25% difference in relative risk with 80% power, given the observed results.

II. An RCT that does not meet the level I criteria.

III. A nonrandomized trial with contemporaneous controls selected by some systematic method (*i.e.*, not selected by perceived suitability for one of the treatment options for individual patients)

or

Subgroup analysis of a randomized trial.

IV. A before-after study of case series (of at least 10 patients) with historical controls or controls drawn from other studies.

V. Case series (at least 10 patients) without controls.

VI. Case report (fewer than 10 patients).

Review of the Literature

The NKF-DOQI had completed an extensive content and methodologic review of the relevant literature and shared these data with the Canadian Society of Nephrology Clinical Practice Guidelines group while the DOQI recommendations were still in draft form. These were published in 1997 (1). We reviewed all relevant publications, in the major English language nephrology journals, subsequent to submission of the DOQI document. This was supplemented by review of abstracts from the 1997 and 1998 meetings of the Canadian Society of Nephrology and the American Society of Nephrology. The evidence was classified according to the methodologic strength using the system suggested by Carruthers and colleagues (2).

The nephrologists who participated in this process included

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both university-based and community nephrologists. All areas of the country were represented. The work groups met in June 1997 and developed the first draft of the guidelines, which were reviewed and modified by the chairs of the working groups in August 1997. The document was formally reviewed by six nephrologists and was available for comment by any member of the Canadian Society of Nephrology. A second draft was completed in April 1998 and was distributed to all members of the Canadian Society of Nephrology for further review. It was also sent to the Canadian Council of Nephrology Social Workers, Canadian Association of Nephrology Dietitians, and the Canadian Society of Nephrology Nurses and Technicians. The guidelines were then presented at an interactive workshop at the September 1998 meeting of the Canadian Society of Nephrology. Based on the reviews, feedback from other health care provider organizations, and the workshop discussions, the guidelines were revised.

Implementation and Evaluation

These recommendations are guidelines, not standards. Implementation is voluntary and requires an understanding of the evidence and opinions on which the recommendations are based. Evaluation of the effectiveness of the clinical practice guidelines will be both process- and outcome-orientated. These activities will be performed through the Canadian Organ Replacement Registry.

Sponsorship

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Chapter 1: Clinical Practice Guidelines for Initiation of Dialysis

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Guideline 1.1: Referral for Management of Renal Failure

1.1.1. Measure or calculate creatinine clearance for all patients with a serum creatinine >200 μmol/L (opinion).

1.1.2. Measure creatinine clearance by a 24-h urine collection with a concurrent serum creatinine or calculate it using the Cockcroft-Gault formula (evidence: level I).

1.1.3. Refer patients with a creatinine clearance <30 ml/min to a nephrologist for opinion regarding management of renal failure (opinion).

The symptoms of renal failure appear late and cannot be used for the early diagnosis of renal failure. Use of serum creatinine as the only indicator of renal failure will fail to diagnose an abnormally low creatinine clearance in 35% of those 40 to 49 yr old, and this increases to 92% of those >70 yr old (1). These data are derived from a comparison of serum creatinine to calculated creatinine clearances, uncorrected for body surface area, in a cross-sectional study of 2712 patients in British Columbia, Canada. A serum creatinine of 200 μmol/L in a 60-yr-old man weighing 70 kg corresponds to a creatinine clearance of 34 ml/min. The same serum creatinine value in those older than 60 yr, in females, and in those weighing less than 70 kg would represent a lower creatinine clearance.

Creatinine clearance is traditionally calculated from creatinine excretion in a 24-h urine collection and a concurrent serum creatinine. This is subject to collection error and is considered a burden by many patients. The Cockcroft-Gault formula permits calculation of steady-state creatinine clearance, uncorrected for body surface area, from serum creatinine, age, weight, and gender (2). This formula was derived from a cross-sectional study design and is the most common formula used to calculate creatinine clearance without urine collection. More recently, a formula has been developed to calculate GFR without urine collection (3). This formula has been derived from the Modification of Diet in Renal Disease (MDRD) study and appears to be more precise and accurate than the Cockcroft-Gault formula. However, it cannot be calculated at the bedside without a programmed calculator and is currently not expressed in SI units. Although the Cockcroft-Gault formula tends to overestimate GFR and is less precise than the MDRD formula, the ease of calculation and extensive experience with this formula are the reasons for selecting it for the initial assessment of creatinine clearance.

$$C_{Cr}(\text{ml/s}) = \frac{(140 - \text{age})(\text{wt in kg})}{(\text{Serum creatinine; } \mu\text{mol/L})\ (50)} \text{ in males}$$

$$C_{Cr}(\text{ml/s}) = \frac{(140 - \text{age})(\text{wt in kg})}{(\text{Serum creatinine; } \mu\text{mol/L})\ (50)} \times 0.85 \text{ in females}$$

Referral to a nephrologist is associated with better clinical outcomes than with non-nephrologist care (4). With early referral, patients should be managed using strategies to slow the rate of progression of renal disease and to deal with the complications of uremia, including treatment of anemia, cardiovascular disease, bone disease, and nutrition. Decisions regarding choice of modality require patient and family education. Early referral provides sufficient time to prepare patients for the selected modality and to permit timely initiation of either dialysis or renal transplantation.

Guideline 1.2: Managing Patients with a Creatinine Clearance <0.5 ml/s or <30 ml/min

1.2.1. Each center should establish a multidisciplinary clinic for the management of renal failure (evidence: level IV).

1.2.2. Measure renal function at least every 3 mo (opinion).

1.2.3. Measure renal function using a valid estimate of GFR corrected to a body surface area of 1.73 m^2. The recommended method is the mean of urea and creatinine clearances (evidence: level I).

1.2.4. Evaluate nutritional status every 3 mo using either protein equivalent of nitrogen appearance (PNA) or the subjective global assessment (SGA) of nutritional status. (opinion).

1.2.5. The frequency of clinical evaluation should be based on the clinical judgment of the responsible nephrologist (opinion).

Although nephrologists can provide excellent clinical care, most patients have complex problems that are often better managed by a multidisciplinary team. This team should include a nurse, renal dietitian, pharmacist, and a social worker. Psychology, psychiatry, physiotherapy, and occupational therapy, if available, would add other important professional skills to

the team. Different models can be used. One model, described by Levin *et al.* (5), demonstrated better patient outcomes at the initiation of dialysis in a cohort of renal failure patients followed in a renal failure clinic compared to those followed in nephrologist offices. The only exclusions were those known to the nephrologist for less than 4 mo.

The recommendation that referral occur at a creatinine clearance of 0.5 ml/s or 30 ml/min will allow more time to treat complications of uremia and to prepare for end-stage renal disease (ESRD) treatment, either by dialysis or transplantation. In a Canadian prospective cohort study of 288 patients with initial C_{Cr} of 25 to 75 ml/min, 23% had stable renal function over a 12-mo follow-up (6). The mean rate of loss of residual renal function, expressed as C_{Cr} uncorrected for body surface area, among the remaining patients was 0.1 ml/s or 6.4 ml/min per yr. This is comparable to the data reported in the United States by Hakim and Lazarus in 1989. They found a mean decline of 0.08 ml/s or 4.8 ml/min per yr (7).

The recommendation that renal function be measured at least every 3 mo is based on the mean rate of decline of 0.8 to 1.0 ml/s or 5 to 6 ml/min C_{Cr} per year. This interval will detect those with a more rapid rate of decline and permit interventions to slow this process or, alternatively, speed preparation for dialysis.

Residual renal function should be monitored with a valid estimate of GFR. The serum creatinine value could be used for calculation of the C_{Cr} from the Cockcroft-Gault formula, but the precision and accuracy are diminished at lower levels of GFR. Calculation of C_{Cr} from 24-h urine collections and concurrent serum creatinine measurement systematically overestimates GFR due to tubular secretion of creatinine. Use of cimetidine to suppress creatinine secretion increases accuracy and precision but is difficult to use in clinical practice. Iohexol and radioisotopic methods are accurate but expensive and are also difficult to use in usual clinical practice. Van Olden and colleagues have shown strong agreement between inulin clearance and the mean of urea and creatinine clearance at low levels of GFR (8), and this is the recommended method for estimation of residual renal function.

Traditionally, estimates of GFR and creatinine clearance are corrected for body surface area. However, there is concern that this normalization may underestimate the severity of renal failure in smaller, older, and malnourished patients. Alternative approaches include correcting ideal body surface area or using uncorrected values. In the absence of data to support these alternatives, the guidelines will use the conventional correction to 1.73 m^2 body surface area.

Malnutrition at the initiation of dialysis is associated with worse patient survival (9). Nutritional status should be monitored regularly both to guide nutritional interventions among patients with chronic renal failure and to assist in deciding the optimum time to initiate dialysis. PNA, assuming neither anabolism nor catabolism, is an estimate of protein intake. There are several formulas available for this calculation. The one recommended is that described by Maroni *et al.* (10). A clinical assessment of nutritional status that has been validated in ESRD is the SGA (11). Although it has not been formally validated in chronic renal failure for patients not on dialysis, it is a simple and reproducible bedside estimate of nutritional status. Additional estimates of nutritional status are caloric intake as determined by a registered dietitian, anthropometric measurements, and serial serum chemistry values (*e.g.*, serum albumin, serum bicarbonate). These would enrich the evaluation of nutritional status.

Guideline 1.3: Initiation of Dialysis

1.3.1. When the GFR is less than 120 L/wk per 1.73 m^2 (0.2 ml/s or 12 ml/min), look for symptoms or signs of uremia or evidence of malnutrition. If there is evidence of uremia or if the PNA is $<$0.8 g/kg per d or if there is clinical malnutrition (SGA), recommend dialysis. The GFR value of 120 L/wk corresponds to a C_{Cr} of approximately 0.3 ml/s or 18 ml/min and a weekly Kt/V of 2.0 (evidence: level IV).

1.3.2. If there is no evidence of uremia or malnutrition, increase the frequency of observation to monthly and recommend dialysis when indicated (uremia or malnutrition) (opinion).

1.3.3. When the GFR is less than 60 L/wk per 1.73 m^2 (0.1 ml/s or 6 ml/min), recommend initiation of dialysis (opinion).

Several studies have reported worse outcomes for patients with less residual renal function at initiation of dialysis (12–14). These outcomes have included rehabilitation (12), hospitalization (12,14), and patient survival (12–14). These observational studies are subject to biases (patient selection, referral time, starting time) that may confound the conclusions. The patient selection bias refers to the possibility that more compliant and/or healthier patients would agree to earlier initiation. Patients who initiate dialysis late may have been referred late and would not have had appropriate preparation for dialysis. Those referred late may also include a greater proportion with hypertension and noncompliance (15). In a study from Italy (12), the results are confounded by the starting time bias.

A lower GFR at initiation of dialysis is associated with worse nutritional status at that time. The latter is associated with worse patient survival with an effect lasting for at least 2 yr (16). Both in the usual clinical setting (17) and, to a lesser extent, in clinical trials with excellent dietary intervention (18), progressive loss of renal function is associated with a decline in nutritional status.

The traditional approach of restricting protein to delay initiation of dialysis has been challenged by these data. In highly controlled research settings (18) or in clinical settings with a major interest in nutrition (19), protein restriction may be safe and associated with excellent clinical outcomes. These data are not generalizable to usual clinical practice with late referral and decreased access to dietary counseling (20).

The objective of these guidelines is to identify a level of residual renal function at which the patient should be closely examined for signs and symptoms of uremia or malnutrition related to chronic renal failure. For patients treated with continuous peritoneal dialysis, a weekly Kt/V $>$2.0 has been recommended as representing adequate dialysis (21). Use of weekly Kt/V as the estimate of residual renal function is an unfamiliar concept for nephrologists. These guidelines recom-

mend GFR, estimated from the average of urea and creatinine clearance, as the preferred method of following changes in residual renal function. The relationship between Kt/V and GFR is different for patients with chronic renal failure predialysis than for patients treated with continuous ambulatory peritoneal dialysis (CAPD) (22). For a predialysis patient, the relationship has been described by Mehrotra *et al.* (22).

$$GFR\ (L/wk\ per\ 1.73\ m^2) = (54.6 \times weekly\ Kt/V_{urea}) + 17.48$$

For a weekly Kt/V of 2.0, the corresponding GFR is 126 L/wk per 1.73 m^2. Although the relationship between GFR and C_{Cr} is variable, the renal creatinine clearance would be approximately 180 L/wk per 1.73 m^2.

Initiation of dialysis should be recommended if there are clinical signs and symptoms of uremia or if there is any clinical evidence of malnutrition based on the SGA or if the PNA is $<$0.8 g/kg per d. If there are no uremic symptoms or evidence of malnutrition, the patient should be followed monthly.

Recent data from the MDRD study (23) and from the Health Care Financing Administration in the United States document initiation of dialysis at a higher mean GFR than has been reported historically. Patients in the MDRD study initiated dialysis at a mean GFR (mean of urea and creatinine clearances) of 0.14 ml/s or 8.4 ml/min (24)), and the Health Care Financing Administration data report a mean GFR of 0.12 ml/s or 7.1 ml/min. The median was 0.11 ml/s or 6.6 with 25th and 75th percentiles at 0.09 ml/s or 5.1 ml/min and 0.14 ml/s or 8.5 ml/min, respectively.

There are no data to suggest a level of GFR at which dialysis should be recommended regardless of symptoms, but as residual renal function decreases, clinical follow-up should increase in frequency.

The recommendation that dialysis be initiated at a GFR of 60 L/1.73 m^2 is based on opinion rather than evidence. With a mean rate of loss of 4.8 to 6.4 ml/min C_{Cr} per year, unacceptably low levels of residual renal function will be reached within 6 mo.

These recommendations do not address the issue of whether dialysis should be initiated fully or in an incremental manner with changes based on progressive loss of residual renal function. All decisions regarding the timing of initiating dialysis should be based on discussion of the biochemical and nutritional data with the patient and family, and should take into account the social impact of these decisions.

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Chapter 2: Clinical Practice Guidelines for the Management of Anemia Coexistent with Chronic Renal Failure

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Anemia in patients with chronic renal failure may be caused by a number of various and often inter-related factors. In diagnosing and managing the causes of anemia, it is particularly important to focus on the individual patient and his/her comorbidities and general well-being, rather than on specific laboratory values. References to specific doses and laboratory values are intended as guidelines only and should be superseded by the clinician's assessment and management of the individual patient.

Guideline 2.1: Target Population

2.1.1. These guidelines are intended to assist in the management of renal anemias (opinion). Renal anemias may occur in patients:

- with chronic renal failure before renal replacement therapies are required,
- receiving hemodialysis,
- receiving peritoneal dialysis, or
- with renal allografts, including perioperative situations and when the graft is functioning suboptimally.

These guidelines are intended for use in adult patients.

2.1.2. The costs associated with the optimal management of renal anemias may be significant. Patients should not incur financial hardship to receive this management (opinion).

Guideline 2.2: Evaluation of Anemia

2.2.1. Evaluate patients with chronic renal failure for anemia when (opinion):

- the hemoglobin is lower or has dropped faster than expected for the clinical situation or
- the hemoglobin is <110 g/L.

2.2.2. The minimal initial evaluation of anemia consists of (opinion):

- a clinical history including diet, weight loss, and medication use,
- a complete blood count (including red cell indices),
- reticulocyte count, and
- iron indices including transferrin saturation (serum iron ×100/total iron binding capacity) and ferritin.

2.2.3. The patient's clinical history may prompt further investigation of vitamin B12 status, red cell folate status, iron status, or thyroid function. The complete blood count provides significant information about bone marrow function. A mean corpuscular volume (MCV) that is low or falling within the normal range may indicate iron deficiency. If macrocytosis is present, vitamin B12 or folate deficiency may be present (red cell folate parameters) (opinion).

Discussion

Anemia, related to inadequate erythropoietin production, is an expected outcome of many of the conditions that cause chronic renal failure. However, all patients with anemia should have the likely cause(s) understood. Clinicians should initiate a search for the cause(s) of anemia when the severity of the anemia is out of keeping with the clinical course or when the patient's hemoglobin drops below the target of erythropoietin therapy in that individual.

Since there is no difference in hemoglobin between adult men and postmenopausal adult women (1), the threshold for evaluation should be the same for both men and women with chronic renal failure. This threshold is equal to the lower limit of the target hemoglobin, and happens to be 2 SD below the normal population mean.

Iron deficiency is common among patients with chronic renal failure and may be difficult to identify. No readily re-

peatable investigations that provide adequate sensitivity and specificity are currently available, although iron deficiency is strongly suggested by a transferrin saturation of <20% (80% sensitivity) or a serum ferritin of <100 g/L (75% specificity) (evidence: level IV). As an acute phase reactant, the serum ferritin value may be artificially increased by several different pathologic processes (2).

Guideline 2.3: Evaluation of Iron Status

2.3.1. Assess iron status by monitoring the MCV, transferrin saturation, and serum ferritin over time (3) (evidence: level IV).

2.3.2. In patients with transferrin saturation <20% and/or ferritin <100 g/L, consider providing iron supplementation (evidence: level IV). Because iron stores are used to make red blood cells, these iron indices will drop. In patients in whom hematopoiesis is expected to result in an increase in hemoglobin and these iron indices are borderline, iron deficiency will develop and may be prevented with the coadministration of iron supplementation (evidence: level III). Some patients may respond to higher levels of these iron indices with higher hemoglobin values (evidence: level IV).

2.3.3. In the initial evaluation for a suspected or diagnosed iron deficiency, include three stool collections for occult blood. If the test is positive, consider a formal gastrointestinal workup. If the test is negative, review the patient's diet and medication (opinion).

Discussion

Despite their imperfect sensitivity and specificity, MCV, transferrin saturation, and ferritin are used to follow iron status trends over time or to support clinical suspicion. Given the high prevalence of iron deficiency in patients with ESRD, there must be a high index of suspicion and a low threshold for iron therapy in this population. However, other causes for iron deficiency should also be considered. The evaluation of iron status should include a careful clinical evaluation with investigations when indicated.

Guideline 2.4: Treating Iron Deficiency

2.4.1. Administration of supplemental iron is an essential component of the treatment of patients who are either (evidence: level III):

- suspected of having iron deficiency as a contributing factor to their anemia or
- expected to develop iron deficiency as a result of ongoing erythropoiesis (see guideline: 2.2.2.).

2.4.2. Starting with a low dose of oral iron supplementation, gradually increase the dose over a few weeks until as high a dose as can be tolerated by the individual is achieved (opinion).

2.4.3. If there is not enough time for an adequate trial or if an adequate trial fails because of poor tolerance or inadequate response, consider intravenous iron replacement (opinion).

2.4.4. Follow iron status every month during therapy designed to increase the hemoglobin level, and at least every 3 mo in stable patients. Laboratory assays for transferrin saturation and serum ferritin may be inaccurate if the patients have received intravenous iron therapy within the previous 2 wk (evidence: level IV).

Discussion

Oral iron is poorly absorbed in patients with renal failure, even when they are iron-deficient (4) (evidence: level IV). The patient's ability to absorb iron is further reduced by:

- concomitant therapy with phosphate binders, cholestyramine, antacids, H2 blockers, and proton pump inhibitors and
- reduced compliance prompted either by side effects or by poor understanding of the details of iron therapy (5) (evidence: level VI).

Although the ideal time of day for a patient to take iron and the concomitant medications is not clear, there is support for patients to take iron on an empty stomach, if tolerated. The presence of gastrointestinal intolerance has been overcome by discontinuing oral iron temporarily followed by an escalating dose trial over 1 or 2 wk. If gastrointestinal intolerance reoccurs, administration with a small quantity of food may provide some absorption of iron despite its binding to the food or the associated phosphate binder.

The ideal oral iron salt has not been established (Table 1). The absorption of enteric-coated preparations is variable and unpredictable (6,7) (evidence: level V). The bioavailability of iron polysaccharide preparations is not detectable using transferrin saturation measurements within hours of ingestion, as is standard with the other iron salts. Serum transferrin saturation varies diurnally, and is sensitive to recently ingested (hours) oral iron (evidence: level V).

Discontinue oral iron therapy when patients are intolerant or when oral iron therapy fails. However, continue oral iron therapy when it is partially effective over the long term as it may reduce the patient's overall requirement for intravenous iron replacement (opinion).

Clinicians can provide intravenous iron replacement after a one-time test dose of 25 mg, in single doses varying from 25 mg to more than 1000 mg, depending on individual patient requirements. For convenience, hemodialysis patients frequently receive regular low doses of 100 mg infusions, whereas predialysis patients, peritoneal dialysis patients, or patients receiving dialysis in the absence of medical backup may find it more convenient to receive larger infusions at less frequent time intervals (8,9). Despite the apparent cost of intravenous iron, its superior bioavailability compared with oral preparations makes it the preparation of choice in treating iron deficiency in many patients. The cost of intravenous iron is low compared with the cost of the erythropoietin required to correct the anemia caused by iron deficiency (10) (evidence, level IV).

Iron utilization may be impaired by high-dose vitamin E therapy, aluminum intoxication, and concomitant therapy with desferoxamine. Additional studies are required to identify the most appropriate iron salt, the most appropriate ingestion environment, the most appropriate intravenous iron preparation,

Table 1. Comparison of iron content and cost of various iron preparations[a]

Iron Preparation	Unit Dose (mg)	Elemental Iron Content (mg)	Average Cost[b] of 100 mg of Elemental Iron
Ferrous gluconate	300	34	$0.05
Ferrous sulfate	325	65	$0.03
Ferrous sulfate liquid (5 ml)	625	210	$0.81
Ferrous fumarate	200	66	$0.06
Ferrous fumarate	300	99	$0.32
Ferrous fumarate liquid (5 ml)	300	99	$0.22
Iron polysaccharide	150	150	$0.06
Ferrous succinate	100	35	$0.75
Iron dextran (iv) (2 ml) (MW 96,000 or MW 267,000)	100	100	$20.00[c]
Ferric gluconate (iv)	100	100	NA[c,d]
Ferric hydroxysaccharate (iv)	100	100	$42.00[c,d]
Blood (1 unit iv)		250	$210.00[e]

[a] iv, intravenously; MW, molecular weight; NA, not available in Canada outside research protocols.
[b] Cost approximates average retail cost to the Canadian consumer, February 1999. Dispensing fee is not included.
[c] The bioavailability of intravenous iron (near 100%) is 5 to 20 times greater than that of oral iron supplements.
[d] Not yet approved by the Health Protection Branch of the Department of Health and Welfare for use in Canada.
[e] Estimate.

and the most appropriate dose, frequency, and mechanism of infusion.

Guideline 2.5: Assessing for Erythropoietin Therapy

2.5.1. Erythropoietin is not the routine treatment for all renal anemias. It should only be considered if the other major potential causes of the anemia have been eliminated. When assessing a patient for erythropoietin therapy, focus on the patient and his or her comorbidities and general well-being, rather than on specific laboratory values or on whether the patient is receiving dialysis. Consider erythropoietin therapy in the absence of nutritional deficiencies (Fe, B12, folate, protein) when the cause of the anemia is most likely to be erythropoietin deficiency and when the patient would either (opinion):

- be exposed to increased risk either with a lower hemoglobin or by alternate treatments (transfusion) or
- derive significant benefit from a higher hemoglobin. This threshold hemoglobin will vary among patients, based on their comorbidities. In general, the threshold will be slightly below the patient's target hemoglobin while receiving erythropoietin therapy, usually near 100 g/L.

2.5.2. Initiation of erythropoietin therapy will be required in many patients before the initiation of dialysis, both in the predialysis population and in patients with a failing renal transplant (evidence: level IV).

2.5.3. The target hemoglobin during erythropoietin therapy is 110 to 120 g/L for both adult males and adult females (opinion).

Discussion

The optimal physiologic hemoglobin in the ESRD population has not been established. However, in patients with a hemoglobin <100 g/L, there is clear evidence of deterioration in left ventricular hypertrophy, cerebral function, and quality of life (11,12) (evidence: level IV).

Patients whose hemoglobin is increased to >100 g/L receive documented reduction in left ventricular mass toward normal. Significant increases in physical function of 2.0 points (SF-36) are achieved with each increase of 10 g/L in hemoglobin to 140 g/L (13) (evidence: level III). Patients with myocardial ischemia related to atherosclerosis or peripheral vascular ischemia related to diabetic (or other) vascular disease may benefit from a higher hemoglobin. However, using erythropoietin and intravenous iron to achieve a hemoglobin of 130 to 150 may be associated with increased mortality in patients with clinically evident congestive heart failure or ischemic heart disease (13) (evidence: level II). Therefore, patients' hemoglobin should usually not plateau below 100 g/L or above 130 g/L. Accounting for fluctuations in the hemoglobin resulting from both laboratory and physiologic factors, if 115 g/L is used as a target hemoglobin, 96% of patients will have their hemoglobin maintained between 110 and 120 g/L.

Guideline 2.6: Administering Erythropoietin

2.6.1. Erythropoietin is available in prefilled unit dose syringes and in multidose vials. The choice of preparation should be individualized for the patient's needs (opinion).

2.6.2. Administer erythropoietin subcutaneously. Rarely, there are patients in whom intravenous therapy may be preferable (opinion).

2.6.3. The commonly used starting dose is 100 to 200 U/kg per wk, divided into two to three doses each week, and rounded to the closest unit-dose available. Maintenance doses and dosing frequency may require adjustments, according to the patient's response.

2.6.4. Patients should administer their own erythropoietin

whenever possible. To minimize wastage and maximize compliance, ensure that patients who are self-administering have access to appropriate instruction on how to store and administer the drug, and take other follow-up measures.

2.6.5. When prefilled unit doses of erythropoietin are not available:

- use insulin (not tuberculin) syringes to minimize the wastage in the dead space,
- for comfort, use the smallest possible gauge needle for injection,
- use preparations containing phosphate buffer or benzyl alcohol because these are associated with less local stinging, and
- to reduce discomfort, minimize the volume of injection that can still be accurately measured.

2.6.6. When administering subcutaneous erythropoietin, rotate injection sites between upper arm, upper leg, and abdominal wall.

2.6.7. Intraperitoneal administration of erythropoietin is rarely, if ever, indicated for adults. Intraperitoneal dose requirements significantly exceed those needed with intravenous or subcutaneous administration, and may be most effective when administered into a dry peritoneum (14) (evidence: level VI).

Discussion

With erythropoietin therapy, the optimal rate of rise in hemoglobin is such that the patient should reach target hemoglobin within 2 to 4 mo of treatment. At this rate, the optimal initial erythropoietin dose will equal the maintenance erythropoietin dose.

Self-administration of erythropoietin allows patients to vary the speed of delivery of the injection, thus controling some of the discomfort that may accompany subcutaneous injections. Self-care allows patients to be more independent of the health care team and to control part of their medical care. This provides a sense of empowerment and is associated with better adjustment to ESRD.

Guideline 2.7: Monitoring Erythropoietin Therapy

2.7.1. Monitor hemoglobin every 1 to 2 wk during initiation of erythropoietin therapy or after a major change in dose (if an unexpected rapid response occurs). Once the patient has achieved a stable hemoglobin, monitor hemoglobin every 4 to 12 wk or when clinically indicated (opinion).

2.7.2. During initiation of erythropoietin therapy, the optimal rate of rise of hemoglobin is that which will achieve the target hemoglobin within 2 to 4 mo. If this rate of rise is inadequate (<5 g/L in a month), then increase the erythropoietin dose by 25 to 50%. If the rate of rise of hemoglobin is excessive (>10 g/L in 2 wk), reduce the erythropoietin dose by 25% (opinion).

2.7.3. Erythropoietin therapy should not be interrupted perioperatively or during a brief intercurrent illness, and may well be beneficial. Erythropoietin therapy may be indicated in the perioperative transplant period (15) and should be considered on an individual basis (opinion).

2.7.4. When an inadequate response to erythropoietin is documented in the iron-replete patient, consider other causes for anemia, including occult infections, inflammatory disorders (including the failing transplant), chronic blood loss or hemolysis, hyperparathyroidism, aluminum bone disease, bone marrow malignancies, insufficient dialysis, and malnutrition (including folate or vitamin B12 deficiencies).

Discussion

Although weekly hemoglobin monitoring during induction is prudent and evidence-based, the risk of monitoring only every 2 wk is minimal compared with the cost savings, particularly when using lower doses. When the patient's hemoglobin and the erythropoietin doses are stable, regular monitoring with routine blood work is likely sufficient (opinion).

Carefully consider any decision to hold the erythropoietin dose for a period of time. The impact of holding the erythropoietin dose is most evident approximately 2 mo after this change, so holding may cause a "roller coaster effect (opinion).

When a patient is less responsive to erythropoietin than expected, particularly when the patient did not initially have any erythropoietin resistance, consider other acquired causes of anemia, in particular iron deficiency (opinion).

Guideline 2.8: Adverse Effects of Therapies in the Treatment of Anemia

2.8.1. Adverse effects related to erythropoietin therapy include hypertension and access thrombosis. There is no increased risk of seizures or hyperkalemia (16–20) (evidence: level III).

2.8.2. Oral iron therapy is frequently associated with gastrointestinal side effects that may be correlated with the total dose ingested, or with the amount of iron absorbed (opinion).

2.8.3. Intravenous iron supplementation may be associated with short-term side effects to free iron, or to the carbohydrate moiety to which the iron is bound. The severity of these reactions may be related to the form, dose, or rate of iron supplement administered, and may be more prevalent in patients with active rheumatoid arthritis or systemic lupus erythematosus. The total dose of administered iron may not be available for erythropoiesis for many weeks. Long-term risks are also related to the form of iron administered and other factors that are not well understood (13,21) (evidence: level VI).

Guideline 2.9: Supplemental Therapies in the Treatment of Anemia

2.9.1. There is insufficient evidence, without controlled trials, to support the use of carnitine to maximize erythropoietin effectiveness. Although androgens have been used in the past, the risk and side effects in both females and males makes them generally unacceptable as a treatment for anemia (22,23) (opinion).

2.9.2. Consider red cell transfusions as therapy in ESRD patients (regardless of whether the patient is receiving erythropoietin) who have the same indications as the general population (24,25) (opinion).

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Chapter 3: Clinical Practice Guidelines for Vascular Access

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Guideline 3.1: Planning for Vascular Access

3.1.1. Each center should have in place a dedicated team for vascular access, including a nephrologist, an access surgeon, an interventional radiologist, and a dialysis nurse (opinion).

3.1.2. Preserve arm veins suitable for placement of vascular access, regardless of arm dominance. Instruct hospital staff and patients with developing ESRD (*i.e.*, serum creatinine >300 μmol/L) to protect the arms from venipuncture and intravenous catheters (opinion).

3.1.3. Avoid using subclavian vein catheterization for temporary access in all patients with chronic renal failure due to the risk of central venous stenosis (1–3) (evidence: level III).

3.1.4. To determine the type of access most suitable for an ESRD patient, the clinician should take the patient's history and perform a physical examination of the patient's venous, arterial, and cardiopulmonary systems. When indicated, the clinician should also order a diagnostic evaluation (4,5) (opinion).

3.1.5. For patients requiring chronic hemodialysis, the preferred type of access is native arteriovenous (AV) fistula. The preferred sites for placing the AV fistula are (in order of preference) (6–16) (evidence: level II):

- the wrist (radial-cephalic) and
- an elbow (brachio-cephalic).

If it is not possible to establish either of these types of fistula, access may be established using:

- an AV graft of synthetic material (*e.g.*, polytetrafluoroethylene [PTFE]) or
- a transposed brachial-basilic vein fistula.

In patients who are at high risk for limb ischemia with AV vascular access and who are unsuitable for peritoneal dialysis, use cuffed central venous catheters for AV access (17–20) (opinion).

Discussion

AV access-related complications result in considerable morbidity (1). With a dedicated access team, a center can develop and maintain skills that will lead to better patient care. Arm veins, particularly the cephalic veins of the nondominant arm, should not be used for venipuncture or intravenous catheters. In patients with chronic renal failure, the dorsum of the hand should be used for intravenous line. When venipuncture of the arm veins is necessary, sites should be rotated.

Patients should wear a Medic Alert bracelet to inform hospital staff to avoid intravenous cannulation of essential veins. The preferred type of access is a native AV fistula, followed by grafts and then the use of central venous catheters (6–20).

The clinician must assess the patient carefully to determine the most appropriate type of access for that person (21). If, before establishing vascular access, clinicians identify or anticipate problems with the patient's vascular anatomy and/or the potential for limb ischemia, they can decide between the merits of central venous catheters and an alternative therapy, such as peritoneal dialysis. A recent multicenter study shows the relative risk of bacteremia to be 7.6 (95% confidence interval, 3.7 to 15.6) with central venous catheters compared with AV fistulae (22). Data from the Canadian Organ Replacement Registry show equivalent patient survival on hemodialysis and peritoneal dialysis (23). This information should be taken into consideration before making a decision to use central venous catheters for long-term hemodialysis as opposed to peritoneal dialysis, when both are technically feasible.

Venography is indicated in patients with the following (5) (evidence: level III):

- edema in the extremity in which an access site is planned,
- collateral vein development in any planned access site,
- differential extremity size, if that extremity is contemplated as an access site,
- current or previous subclavian catheter placement of any type in venous drainage of planned access,
- current or previous transvenous pacemaker in venous drainage of planned access,
- previous arm, neck, or chest trauma or surgery in venous drainage of planned access, or
- multiple previous accesses in an extremity planned as an access site.

Additional or alternate imaging techniques are indicated when previous multiple vascular accesses have been placed or

when residual renal function makes contrast studies undesirable. Appropriate diagnostic techniques may include:

- venography using CO_2 or Doppler ultrasound or
- venous mapping using Doppler ultrasound.

To improve the quality and consistency of vascular access, future research should include:

- a multicenter trial to determine which methodologies (*e.g.*, clinical assessment *versus* venous mapping) should be used to evaluate patients before access creation and
- an evaluation of the incidence of hand ischemia with primary AV fistula compared to AV grafts, with a view toward identifying a test that would predict when this will occur.

Guideline 3.2: Access Timing, Placement, and Maturation

Timing

3.2.1. Establish AV fistulae when the patient has a creatinine clearance of 15 to 20 ml per min or serum creatinine of 300 to 500 μmol/L, depending on the size and weight of the patient (opinion).

3.2.2. Place dialysis PTFE AV grafts at least 3 to 6 wk before an anticipated need for hemodialysis (opinion).

3.2.3. Cuffed and noncuffed hemodialysis catheters can be inserted immediately before their use, since they do not require maturation time (opinion).

Placement

3.2.4. The preferred site for tunneled cuffed venous catheters is the right internal jugular vein. Adjust the catheter tip to the level of caval atrial junction or beyond. Subclavian access should be used only when jugular options are not available (evidence: level III).

3.2.5. Do not place subclavian hemodialysis catheters on the same side as a maturing AV access (evidence: level II).

Maturation

3.2.6. Do not use an AV fistula sooner than 1 mo and preferably 3 to 4 mo after construction (evidence: level IV).

3.2.7. Do not use PTFE grafts routinely until 14 d after placement (opinion).

3.2.8. Use a venogram or other noncontrast study to evaluate central veins in patients with swelling that does not respond to arm elevation or that persists more than 2 wk after dialysis AV access placement (evidence: level III).

Discussion

Access Timing and Placement. It is difficult to predict exactly when patients will need to begin dialysis, but creatinine clearance and serum creatinine levels, adjusted for the patient's size and weight, can help considerably in planning for the timing of AV fistula placement (the preferred type of access for hemodialysis).

It is important to create an AV fistula at least 3 to 4 mo before its anticipated use. Grafts can be used in patients who are not candidates for a primary AV fistula. The preferred sites and types of graft are (in order of preference) (16):

- a forearm curved looped brachial cephalic graft and
- an upper arm straight graft.

The least preferred sites and type of grafts are forearm straight radial cephalic and looped thigh grafts. However, the location for the graft placement is determined by each patient's unique anatomical restrictions, the surgeon's skill, and the anticipated duration of dialysis (opinion).

According to the available evidence, PTFE tubes are preferred over other synthetic materials (evidence: level III). There is no evidence available yet on the efficacy of newer synthetic materials. When using these materials, follow manufacturers' recommendations. There is no convincing evidence to support a tapered tube over a uniform tube, externally supported over unsupported grafts, thick- *versus* thin-walled configurations, or elastic *versus* nonelastic material (21) (evidence: level III).

Cuffed tunneled central venous catheters can be a valuable alternative to grafts, although there are concerns about infection, thrombosis, and dialysis adequacy. Catheter position should be confirmed using radiography, and the catheter tip should be readjusted as necessary to ensure proper position. The use of real-time ultrasound-guided insertion may be an advantage in reducing insertion-related complications, particularly in patients who have had previous catheter insertions.

For patients with chronic renal failure who need acute hemodialysis vascular access, use a noncuffed or a cuffed percutaneously inserted catheter. These catheters are suitable for immediate use and should not be inserted before needed (24). Femoral catheters should be at least 19 cm long to minimize recirculation. Noncuffed femoral catheters should be sutured in place and can be left in as long as there are no complications.

Nonfunctional noncuffed catheters can be exchanged over a guidewire as long as the exit site and tunnel are not infected (for guidelines on infection, see 3.5.10. to 3.5.14.).

Maturation. AV fistulae need time to mature (at least 1 mo and preferably 3 to 4 mo) before cannulation (evidence: level IV). AV fistula maturation also depends on artery and vein size. The following procedures may enhance maturation of AV fistulae:

- Fistula hand-arm exercise (*e.g.*, squeezing a rubber ball with or without a lightly applied tourniquet) will increase blood flow and speed maturation of a new native AV fistula.
- Selective obliteration of major venous side branches will speed maturation of a slowly maturing AV fistula.
- When a new native AV fistula is infiltrated (*i.e.*, presence of hematoma with associated induration and edema), it should be rested until swelling is resolved.

A new PTFE dialysis AV graft should not be cannulated until swelling has gone down enough to allow palpation of the course of the graft—ideally 3 to 6 wk after placement. No attempt should be made to cannulate the graft for at least 14 d after placement.

Guideline 3.3: Monitoring and Maintenance

3.3.1. Establish a quality assurance program to monitor vascular access (evidence: level III).

3.3.2. Monitor AV fistulae bimonthly for hemodynamically significant stenoses, using an on-line total access flow measurement. Investigate an access flow less than 500 ml/min or a drop in access flow >20% of baseline for possible reversible lesions (25) (opinion).

3.3.3. When on-line blood flow measurements are not available, monitor AV fistulae using regular recirculation studies (evidence: level II). Measure recirculation using a non-urea-based dilutional method or by using the two-needle urea-based method (26–28). Do not use the three-needle peripheral vein method of measuring recirculation (29,30) (evidence: level II). When recirculation exceeds 15% (on two separate measurements) using the recommended two-needle urea-based or is greater than 5% on non-urea-based methods (25) on two separate measurements, investigate the cause. Confirm that the needles are placed correctly before conducting additional studies.

3.3.4. Monitor grafts monthly for hemodynamically significant stenoses, using an on-line total access blood flow measurement (31–42) (evidence: level III) and static or dynamic venous pressure measurements (43,44) (evidence: level II). Investigate an access flow <650 ml/min or a drop in flow >20% of baseline for potentially reversible stenosis (opinion).

3.3.5. Investigate any finding of access dysfunction or elevated levels of access recirculation using angiography (43) (evidence: level II).

3.3.6. Until investigations are complete, adjust the dialysis prescription to ensure that the patient is receiving adequate dialysis during this period of access dysfunction (opinion).

Discussion

Monitoring AV fistulae and grafts for hemodynamically significant stenosis, combined with corrective treatment, improves patency and decreases the incidence of thrombosis (43). The quality assurance program should collect and maintain data on each patient from the monitoring tests, clinical assessment, and dialysis adequacy measurements, and make this information available to all staff. The data should also be tabulated and tracked within each dialysis center.

Although recirculation studies have been shown to be useful for detecting AV fistulae stenosis, the recirculation only occurs when the total access flow is lower than the blood flow in the dialysate circuit. Therefore, the preferred method for monitoring AV fistulae is direct on-line flow measures. When clinicians do not have access to on-line flow measures, they can monitor vascular access using regular recirculation studies (31–44).

When using on-line flow measures, clinicians should be aware that AV fistulae are capable of sustaining a lower blood flow than an AV graft without clotting, so a flow measurement <650 ml/min in an AV fistulae is less likely to indicate a reversible stenosis or subsequent clotting. However, relative changes in flow measurement are still a cause for concern. In AV fistulae, clinicians should investigate an access flow <500 ml/min and any drop in blood access flow >20% from baseline (25,41) (opinion).

When using access recirculation measures, clinicians should be aware that any access recirculation is abnormal and should be investigated. Non-urea-based methods of measuring access recirculation have been shown to be more accurate and, if appropriate equipment is available, easy to perform.

Recirculation >5% using non-urea-based methods and recirculation >15% (15% cutoff for urea-based measurement is due to imprecision in measurements and cardiopulmonary recirculation) measured using urea-based method is significant and should lead to angiography, which will determine whether stenotic lesions are impairing access blood flow (25,26). The methods for monitoring AV grafts are, in order of preference:

- intra-access flow—monitoring for changes in flow (31–42) (evidence: level II),
- static venous pressures (43,44) (evidence: level II), and
- dynamic venous pressures (evidence: level II).

Blood access flows through AV grafts can be measured by indicator dilution or conductivity tracer techniques, using the Krivitski reversed line technique. Low blood access flows (<650 ml/min) have been found to be predictive of:

- significant graft stenosis (by angiography) and
- subsequent access failure by clotting.

In addition, any drop in flow >20% from baseline observed from serial access flow monitoring is a strong predictor of access dysfunction. Therefore, any access flow measurement <650 ml/min or any drop in flow >20% from baseline, confirmed by retesting, should be investigated (opinion).

When using pressure measurements to monitor access, clinicians should be aware that static pressure measurements are more accurate. Methods to measure dynamic and static pressure are listed below.

Other studies or information that can be useful in detecting AV graft stenosis include:

- measurement of access recirculation using urea concentrations (evidence: level II),
- measurement of recirculation using dilution techniques (non-urea-based),
- unexplained decreases in the measured amount of hemodialysis delivered (urea reduction ratio, Kt/V),
- physical findings of persistent swelling of the arm with the graft, prolonged bleeding after needle withdrawal, or altered characteristics of pulse or thrill in a graft,
- elevated negative arterial prepump pressures that prevent increasing to acceptable blood flow, and
- venography/Doppler ultrasound.

Any finding of access dysfunction, whether based on the presence of access recirculation, low or deteriorating access blood flow rates, positive pressure tests, or any other test should be investigated using angiography, to determine the appropriate intervention (*e.g.*, angioplasty, surgery).

In the process of investigating the dysfunction and taking corrective measures, it is vital that the clinician take interim measures to protect the patient. When the dialysis circuit blood flow exceeds the access flow, access recirculation will occur, which leads to inadequate dialysis. To optimize dialysis treatment, the dialyzer blood flow should be reduced to a level at or just below the patient's measured access blood flow rate. The clinician should make the appropriate corrections by time and dialyzer surface area to ensure that patient receives the desired and prescribed Kt/V (urea).

To improve the clinicians' ability to monitor and intervene successfully, future research should include a randomized prospective trial on intervention, based on access flow measurements in both AV fistulae and PTFE grafts.

Dynamic Venous Dialysis Pressure Monitoring Protocol

- Establish a baseline initiating measurements when the access is first used.
- Measure venous dialysis pressure from the hemodialysis machine at Qb 200 ml/min during the first 2 to 5 min of hemodialysis at every hemodialysis session.
- Use 15-gauge needles (or establish own protocol for different needle size).
- Assure that the venous needle is in the lumen of the vessel and not partially occluded by the vessel wall.
- Pressure must exceed the threshold three times in succession to be significant.
- Assess at same level relative to hemodialysis machine for all measurements.

Interpretation

The clinician must obtain three measurements in succession above the threshold to eliminate the effect of variation caused by needle placement. Hemodialysis machines measure pressure with different monitors and tubing types and lengths. These variables, as well as needle size, influence venous dialysis pressure. The most important variable affecting the dynamic pressure at a blood flow of 200 ml/min is the needle gauge. It is essential to set thresholds for action based on machine manufacturer, tubing type, and needle gauge.

The proposed method for static venous pressure measurement:

1. Turn the blood pump off.
2. Clamp tubing between the dialyzer and the venous drip chamber.
3. Make static measurement (P) from venous transducer exactly 30 s after stopping blood flow.
4. Determine in centimeters the height difference between the arm of the chair and blood in the venous drip chamber (H).
5. Calculate estimated intra-access pressure (eIAP).

$$\text{eIAP} = \text{P} + (0.35 \times H + 3.4)$$

6. Measure mean arterial pressure (MAP).
7. Calculate eIAP/MAP.
8. Absolute eIAP/MAP > 0.5 or a progressive rise on repeated measurements indicates a stenosis/thrombosis beyond the venous needle site in AV grafts.

Guideline 3.4: Preventing Infections

3.4.1. Include instruction on infection control measures for all hemodialysis access sites in staff and patient education (opinion).

3.4.2. Use a clean technique for needle cannulation for all cannulation procedures (see below).

3.4.3. Ensure that only trained dialysis staff change hemodialysis catheter dressings and manipulate catheters that access the patient's bloodstream (evidence: level III).

3.4.4. Examine the catheter exit site at each hemodialysis treatment for signs of infection. Change catheter exit site dressings at each hemodialysis treatment. Use dry gauze dressings and povidone iodine or mupirocin ointment at the catheter exit site whenever possible (22,46) (evidence: level II).

3.4.5. Minimize contamination when manipulating a catheter and accessing the patient's bloodstream (opinion).

Discussion

Proper infection control procedures can significantly reduce the risk of infection. Catheter care and accessing the patient's circulation should be sterile procedures. During catheter connect and disconnect procedures, nurses and patients should wear a surgical mask or face shield. Nurses should also wear gloves during all connect and disconnect procedures, although the evidence for sterile as opposed to nonsterile gloves is inconclusive.

A randomized control trial of dry gauze dressing with povidone iodine ointment at the catheter exit site, along with sterile dressing technique, resulted in a significant reduction in staphaureus exit site infections, bacteremia, and catheter tip colonization. The beneficial effect was most evident in staphaureus carriers. Similar results have recently been reported using mupirocin ointment (46,47).

Routine monitoring for staph nasal carrier status and its management remains controversial. Although some studies have shown reduction in staphaureus bacteremia in hemodialysis patients with nasal mupirocin ointment, development of antimicrobial resistance remains an important concern. Moreover, a recent multicenter study did not show nasal staph carriage as an independent risk factor for bacteremia. More research is needed on the impact of mucipuricin ointment in reducing staphaureus nasal carriage and its influence on catheter exit site infection/blood infection in hemodialysis patients (47).

It has become common practice for clinicians to prescribe prophylactic antibiotics for dialysis patients who are undergoing dental procedures. There is little evidence to support this use of antibiotics, but they may offer more benefit to patients with grafts than those with AV fistulae or catheters (opinion).

Cannulation Technique

1. Locate and palpate the needle cannulation sites before skin preparation.

2. Wash access site using an antibacterial soap or scrub (*e.g.*, 2% chlorhexidine) and water.
3. Cleanse the skin by applying 70% alcohol and/or 10% povidone iodine using a circular rubbing motion.

Notes:

- Alcohol has a short bacteriostatic action time and should be applied in a rubbing motion for 1 min immediately before needle cannulation.
- Povidone iodine needs to be applied for 2 to 3 min for its full bacteriostatic action to take effect and must be allowed to dry before needle cannulation.
- Clean gloves should be worn by the dialysis staff for cannulation. Gloves should be changed if contaminated at any time during the cannulation procedure.
- New, clean gloves should be worn by the dialysis staff for each patient.

Guideline 3.5: Managing Complications

3.5.1. Monitor all patients, particularly those in high-risk groups, for the development of limb ischemia following AV access construction (opinion).

3.5.2. In the case of primary AV fistulae, intervene when any of the following occur (48,49):

- inadequate flow (evidence: level III),
- hemodynamically significant venous stenosis (evidence: level III), or
- aneurysm formation if the skin overlying the fistula is compromised, there is a risk of fistula rupture, or available puncture sites are limited (opinion).

3.5.3. With grafts, intervene when any of the following occur:

- inadequate flow,
- hemodynamically significant stenosis (50–52) (see Guideline 3.3) (evidence: level II), or
- graft degeneration and pseudoaneurysm formation (opinion).

3.5.4. Surgically revise grafts when:

- there is severe degenerative changes of the graft or overlying skin (opinion),
- skin above the graft is compromised (opinion),
- there is a risk of graft rupture due to poor eschar formation or evidence of spontaneous bleeding (opinion), or
- limited puncture sites are available due to the presence of a large (or multiple) pseudoaneurysm(s) (opinion).

Stenosis

3.5.5. Treat stenosis that occurs in a dialysis AV graft or primary AV fistula (venous outflow or arterial inflow) if the stenosis is >50% of the lumen diameter and is associated with hemodynamic change (48–54) (see Guideline 3.3) (evidence: level II).

3.5.6. Use angioplasty to treat stenosis. If percutaneous angioplasty is not possible, use surgical revision (48–54) (evidence: level III).

Discussion

Angioplasty is the preferred treatment for both fistulae and graft stenosis (48–54). In native vessel AV fistulae, the most common site of stenosis/thrombosis is near AV anastomosis, distal to the insertion of arterial needle (48,49). Stenosis, as well as the clinical parameters used to detect it, should return to within acceptable limits after the intervention.

Centers should monitor stenosis treatment outcomes on the basis of patency. Reasonable patency goals (for the center as a whole) for angioplasty and surgical revision in the absence of thrombosis are:

- angioplasty - 50% unassisted patency[a] at 6 mo; no more than 30% residual stenosis postprocedure and resolution of physical indicator(s) of stenosis.
- surgical revision - 50% unassisted patency at 1 yr.

If angioplasty is required more than 2 times within 3 mo and the patient is a good surgical candidate, the patient should be referred for surgical revision if available. Stents are useful in selected instances (*e.g.*, limited residual access sites, surgically inaccessible lesions, contraindication to surgery) when angioplasty fails.

Thrombosis

3.5.7. Correct thrombosis of an AV graft with pharmacomechanical or mechanical thrombolysis or surgical thrombectomy.

Discussion

The choice of technique to correct thrombosis should be based on the center's expertise. However, the following standards are essential (48–52):

- Treatment should be performed as rapidly (within 24 h) as possible after detection of thrombosis to minimize the need for temporary access.
- Access should be evaluated by fistulogram for residual stenosis postprocedure.
- Residual stenosis should be corrected by angioplasty or surgical correction. Note that outflow venous stenosis are present in >85% of instances of thrombosis. The need for percutaneous transluminal angioplasty or surgical revision is expected in most instances (evidence: level III).
- The treatment should be performed as an outpatient procedure under local anesthesia. Access revision may require up to a 24-h observation to evaluate swelling and steal.

Monitoring tests used to screen for venous obstruction should return to normal after the intervention. Centers should monitor outcome results on the basis of patency. Minimum

[a] Unassisted patency is defined as patency until either a thrombosis or access failure or an intervention to prevent thrombosis is performed.

reasonable goals (for the center as a whole) for percutaneous thrombolysis and surgical revision thrombectomy should be:

- Percutaneous thrombolysis with angioplasty: 40% unassisted patency and functionality at 3 mo.
- Surgical thrombectomy and revision: 50% unassisted patency and functionality at 6 mo and 40% unassisted patency and functionality at 1 yr.
- Immediate patency (patency to next hemodialysis session): 85% for both techniques.

Prophylaxis of access thrombosis is not well studied. There is some question whether the widespread use of acetyl salicylic acid may be counterproductive. A randomized, controlled multicenter trial (*i.e.*, placebo *versus* dypridamole *versus* low dose coumadin *versus* other agents) would help determine the most effective way to prevent AV graft/catheter thrombosis, a common problem in dialysis patients.

Central Vein Stenosis

3.5.8. Treat central vein stenosis with percutaneous transluminal angioplasty (evidence: level III). Place a stent only after failed angioplasty (55,56).

Discussion

Central vein stenosis can result in significant arm swelling when an AV access is created on the ipsilateral side. When a patient has central vein stenosis and significant arm swelling, percutaneous angioplasty should be performed. Angioplasty can be repeated in case of recurrence. A stent should be placed after more than one recurrence or a failed angioplasty.

Dysfunctional Permanent Catheter

3.5.9. Treat a dysfunctional permanent catheter in the hemodialysis unit using the protocol for systemic urokinase[b] administration. Perform any further treatment based on the radiographic findings. If adequate flow is not achieved, repeat systemic urokinase. Patients who require more than one systemic urokinase should be considered for anticoagulation with warfarin, if there is no contraindication.

Discussion

Catheter dysfunction is defined as failure to attain and maintain an extracorporeal blood flow sufficient to perform hemodialysis without significantly lengthening the hemodialysis treatment.

The most common cause for this dysfunction is the development of a fibrin sheath around the catheter, which is often caused by thrombosis around the catheter. According to a recent study, systemic administration of 250,000 U of urokinase was effective in achieving adequate blood flow in more than 80% of cases. A second administration was often effective if the first dose failed to achieve adequate flow (57) (evidence: level III).

[b] Urokinase was temporarily withdrawn from the market due to concerns regarding the manufacturing process. There are insufficient data to make recommendations on other thrombolytic agents (except for streptokinase) for this purpose.

In patients with contraindications to systemic administration of urokinase, other procedures for dealing with catheter dysfunction include:

- fibrin sheath stripping using a snare if a fibrin sheath is present (58), and
- exchanging the thrombosed catheter over a guidewire if a fibrin sheath is present or if the catheter is malpositioned or of inadequate length.

Protocol for Urokinase Administration

1. Attempt to aspirate the occluded catheter lumen to remove heparin.
2. Slowly inject urokinase (1 ml or volume sufficient to fill lumen) with Tuberculin or other small syringe into the occluded catheter lumen (urokinase 5000 U/ml).
3. If needed, fill remainder of the catheter lumen with saline in the same manner (*e.g.*, for a 1.3-ml catheter lumen use 1 ml of urokinase and 0.3 ml of saline).
4. Add 0.3 ml of saline every 10 min $\times$ 2 to move active urokinase to distal catheter.
5. Aspirate catheter.
6. Repeat procedure if necessary.

Protocol for Administering Systemic Urokinase for Dysfunctional Hemodialysis Catheters

Systemic urokinase is used when intraluminal urokinase has been ineffective. All patients must be monitored by a registered nurse. Systemic urokinase must be administered by a physician. A full resuscitation cart must be immediately available.

1. Contraindications

- evidence of active bleeding,
- recent significant injury, fall, or surgery,
- arterial puncture within the last 24 h, and
- risk of intracranial bleeding.

2. Premedication

- Chlorpheniramine 10 mg intravenously and/or hydrocortisone 100 mg intravenously.
- Acetaminophen 650 mg orally given 30 min before urokinase.

3. Administration of Urokinase

- Five milliliters of sterile water or normal saline is added to 250,000 U vial of urokinase and dissolved by rolling, not shaking.
- The reconstituted urokinase is added to 100 ml of normal saline bag.
- The reconstituted urokinase is infused through the venous port over 3 h. This can best be done with patients on hemodialysis. The blood flow is gradually increased as venous and arterial pressure allow.

4. Monitoring

- Vital signs, including heart rate, BP, respiratory rate, and temperature, are monitored every 15 min for 1 h and then every hour for 3 h.

- Special attention should be paid to signs of bleeding, fever, chills, nausea, vomiting, and level of consciousness. In the event of an allergic reaction or anaphylaxis, epinephrine, solucortef, and benadryl must be available immediately.
- Note that heparin is not used in the dialysis run after systemic urokinase is given.

Infection

3.5.10. Treat local infection of a dialysis AV graft with appropriate antibiotics based on culture results and/or by incision/resection of the infected portion of the graft (59) (evidence: level III).

3.5.11. Treat extensive infection of a dialysis AV graft with parenteral antibiotics and total resection of the graft (59).

3.5.12. Initial antibiotic treatment should cover both Gram-positive and Gram-negative organisms.

3.5.13. Treat infections of primary AV fistulae, which are rare, as subacute bacterial endocarditis with 6 wk of antibiotic therapy. Fistula take-down is required in cases of septic emboli (opinion).

3.5.14. In patients with cuffed or noncuffed central venous catheters and suspected bacteremias, start treatment with cefazolin 1 to 2 g depending on patient weight, and gentamycin 1.5 mg/kg postdialysis after blood cultures are drawn. In patients with known cephalosporin allergy, use vancomycin 15 mg/kg instead of cefazolin. Once blood culture results are available, the catheter should be changed over a wire and antibiotic treatment continued for 2 to 4 wk as clinically indicated (60,61).

3.5.15. Treat catheter exit site infections—characterized by redness, crusting, and exudate at the exit site in the absence of systemic symptoms and negative blood cultures—as follows:

- Give oral antibiotics based on culture and sensitivity, ensure proper local exit site care, and do not remove the catheter (evidence: level IV).
- If there is tunnel drainage, treat with parenteral antibiotics (anti-*Staphylococcal*, anti-*Streptococcal* therapy pending culture report) in addition to following appropriate local measures. Definitive therapy should be based on culture results. Do not remove the catheter unless the infection fails to respond to therapy. If the infection fails to respond to therapy, remove the catheter and replace it using a different tunnel and exit site.

Discussion

Use of central venous catheters is associated with a significantly higher risk of bacteremia compared with AV fistulae. With AV grafts, the infection risk is moderate. It may be possible to eradicate a local graft infection with a combination of incision and local resection of the infected portion of the graft and systemic antibiotics. However, extensive infection of a graft requires total resection of the graft along with parenteral antibiotics (59). Tunneled cuffed catheter infection is a serious problem. Appropriate treatment depends on the nature of the infection (60,61).

Catheter-related bacteremia should be treated by initiating parenteral treatment with an antibiotic(s) appropriate for the organism(s) suspected, usually *Staphylococcus* and *Streptococcus*. Definitive therapy should be based on the organism(s) isolated. The catheter should be removed in all instances if the patient is clinically unstable or if the patient remains symptomatic for more than 36 h (60,61).

Preliminary reports suggest that after obtaining a bactericidal level of the antibiotic in the blood, stable asymptomatic patients without exit site or catheter tunnel tract involvement should be treated by changing the catheter over a guidewire plus a minimum of 3 wk of systemic antibiotic therapy (60,61).

Blood cultures should be repeated periodically during and immediately after this treatment to monitor its effectiveness. In patients with difficult access, clinicians can attempt antibiotic treatment without changing the catheter. However, the success of such catheter salvage is low (60,61).

A new permanent access should not be placed until blood cultures, performed after cessation of antibiotic treatment, have been negative for at least 48 h.

Guideline 3.6: Quality of Care Standards

3.6.1. Construct primary AV fistulae in all suitable new patients who elect to receive hemodialysis as their initial form of renal replacement therapy (6) (evidence: level III).

3.6.2. Reevaluate patients for possible construction of a primary AV fistula after failure of every dialysis AV access (6).

Discussion

Ultimately, more than 60% of prevalent patients should have a native AV fistula (6). Each center should establish a database to track the types of accesses created and the complication rates. Centers should work to achieve the following target rates:

- The rate of graft thrombosis should not exceed 0.5 thrombotic episodes per patient year at risk (51,62).
- After adjusting for initial failures (*e.g.*, failures within the first 2 mo of fistula use), the rate of thrombosis of native AV fistulae should be less than 0.25 episodes per patient year at risk. Dialysis centers should examine their thrombosis rates and the underlying causes as part of an ongoing Quality Assurance/Continuous Quality Improvement program.
- The rate of infection should not exceed 0.01 episodes per patient year at risk for primary AV fistula and 0.1 episodes per patient year at risk for AV grafts (22).
- For tunneled cuffed catheters, the recommended target rate of systemic infection is 0.5 per patient year at risk (22).
- The primary access failure rates of dialysis AV grafts in the following locations and configurations should not be more than 15% in forearm straight grafts, 10% in forearm loop grafts, and 5% in upper arm grafts.
- The cumulative patency rate[c] of all dialysis AV grafts should be at least 70% at 1 yr, 60% at 2 yr, and 50% at 3 yr.

[c] The cumulative patency rate of dialysis AV grafts refers to the number of grafts that remain patent (regardless of the number of primary interventions and/or thrombectomies) during the given time period.

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Chapter 4: Clinical Practice Guidelines for the Delivery of Hemodialysis

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Note to clinicians: The dosages of hemodialysis delivered (regardless of measurement technique) listed in these guidelines should be viewed as minimum targets, rather than optimal goals. Clinicians should also note that dialysis dose delivered and its measurement are only one component in providing high quality care to the renal patient. In making treatment decisions, the clinician must also consider other laboratory measurements and findings, as well quality of life measures (opinion).

Guideline 4.1: Dosage of Hemodialysis Delivered

4.1.1. For adults, the minimum acceptable target for the dose of hemodialysis delivered is a Kt/V of 1.2 or percent reduction of urea (PRU) of 65% 3 times per week (1–9) (evidence: level III).

4.1.2. There is no equivalent pediatric data.

4.1.3. The hemodialysis center must have a review system in place to recognize and respond quickly to any fall in the delivered dose of hemodialysis (opinion).

Discussion

This delivered dose of dialysis is a minimum acceptable target. Any dose below Kt/V of 1.2 or PRU of 65% 3 times per week will lead to an increase in mortality (evidence: level III). Information from slow nocturnal hemodialysis suggests that there are benefits, at least for some patients, from delivering substantially more hemodialysis, and there is no evidence to suggest that there is no benefit from delivering more dialysis (opinion).

In addition to considering the dose of hemodialysis, the clinician must consider many other measures and indicators in assessing a patient's health and prescribing treatment, including, for example: hemoglobin, nutritional status, acid base status, and hyperparathyroidism (opinion).

Units that reprocess dialyzers must be sensitive to the fact that dialyzer performance may deteriorate with reprocessing. They should ensure that the dose of dialysis delivered is monitored more closely when dialyzers are reused a number of times.

Hemodialysis centers should have a review system in place that recognizes changes in the delivered dose of hemodialysis, identifies the basis or cause (particularly for a drop in dose), and corrects it (see Guideline 4.8 for algorithm) (opinion).

Guideline 4.2: Measuring Delivered Dose

4.2.1. All patients (including those on home hemodialysis) should have the delivered dose of hemodialysis measured at regular intervals (2,7–13) (evidence: level V).

4.2.2. The dose of hemodialysis should be measured using a technique that can be performed accurately and consistently by available personnel. Use the same technique for all patients (opinion).

4.2.3. Three acceptable dose measurement techniques are:

- formal single pool urea kinetics (14),
- percent reduction of urea or urea reduction ratio (15,16), and
- Kt/V natural logarithm formula (17) (opinion).

Discussion

Even when the dialysis prescription is followed rigorously, certain events (*e.g.*, access recirculation) may prevent that dose of dialysis from being delivered. To ensure that patients are receiving the prescribed dose, the clinician must regularly monitor and measure the dose delivered. The measurement schedule will vary depending on the clinical setting, but delivered dose should be measured at least every 6 to 8 wk (opinion).

Of the three techniques, single pool urea kinetics predicts the dose delivered most accurately. However, the treatment priorities are to ensure that:

- patients receive at least a minimum dose of therapy, and

- the measurement technique used is easy to perform consistently, which will make it easier to compare doses from treatment to treatment.

Given these priorities, all three modes of measurement are considered acceptable. Although PRU does not take into account urea removal by ultrafiltration, measurements using this technique will underestimate (rather than overestimate) the dialysis dose and therefore are not considered a problem.

In the initial development and use of the PRU, it was customary for clinicians to convert the PRU to Kt/V using various imprecise mathematical manipulations. Now that there are data indicating that PRU correlates directly with mortality, there is no reason to introduce any errors through mathematical manipulation. The clinician can assess the dose of dialysis directly using the PRU, being aware of its limitations (opinion).

Clinicians should recognize that staff and patients may conduct themselves differently on the day when the dose of therapy is being measured. Therefore, clinicians are encouraged to use some additional techniques, which may be less precise but permit the measurement of the dose of hemodialysis delivered on a daily basis (*e.g.*, volume of blood processed, average pump speed, and duration of treatment), and to correlate them with the more formal dosage measurement (opinion).

Because the goal of measurement of the dose of hemodialysis delivered is to ensure that patients receive at least a given minimum dose of therapy and not to calculate precisely the dose received, the clinician can ignore the contribution of residual renal function (opinion).

Calculations for Dialysis Dose Delivered

Percent Reduction of Urea (PRU)

$$\frac{\text{Pre[Urea]} - \text{Post[Urea]} \times 100}{\text{Pre[Urea]}}$$

Urea Reduction Ratio (URR)

$$100 \times (1 - \text{Post[Urea]}/\text{Pre[Urea]})$$

PRU and URR are identical.

Natural Logarithm Formula

$$\text{Kt/V} = -Ln(R - 0.008 \times t) + (4 - 3.5R) \times UF/W$$

where Ln is the natural logarithm, R is postdialysis blood urea nitrogen divided by predialysis blood urea nitrogen, t is session length (hours), UF is ultrafiltration volume (liters), and W is postdialysis weight (kg).

Guideline 4.3: Drawing Samples

4.3.1. Predialysis and postdialysis samples must be drawn at the same dialysis session (opinion).

4.3.2. Draw predialysis blood from the arterial needle before administering any saline or heparin (opinion).

4.3.3. When central lines are used and if heparin and/or saline is used, withdraw at least 10 cc of blood before drawing the blood sample. The blood withdrawn may then be returned to the patient (opinion).

4.3.4. The postdialysis [urea] blood sample must not be diluted by either recirculation or saline (18).

4.3.5. For formal urea kinetic modeling, the sample must be drawn before any rebound; therefore, the slow flow/stop pump technique must be used (19) (see method below).

4.3.6. For other techniques (PRU and log prediction of Kt/V), the blood sample may be taken postdialysis, when the possibility of access and cardiopulmonary recirculation is eliminated. To eliminate the possibility of cardiopulmonary recirculation, draw the sample at least 2 to 3 min postdialysis (20–22) (evidence: level III). To facilitate longitudinal comparisons, the sampling technique for the unit should be clearly stated, documented, and consistent from treatment to treatment and between patients. Depending on the preferences of the unit, different measurements of the delivered dose of hemodialysis may be used under different circumstances (*e.g.*, in the course of studies), and thus different protocols for the postdialysis sample may be used at different times. The specific protocol should be documented in each circumstance (opinion).

Discussion

Because the goal is to ensure at least a minimum standard, a postdialysis sample is preferable and easier to obtain than a stop flow sample. Although the postdialysis sample may be more variable (due to rebound) (23), it will not be influenced by any factors that would suggest that more dialysis has been delivered than was actually received by the patient (opinion).

Each unit should document its sampling technique to facilitate national comparisons (opinion).

The precision of urea determination by the laboratory is sufficient (SD of [urea] of 15 mM is 0.5 mM), so it is not critical that all samples be processed in the same batch (opinion).

Recommended Method For Blood Sampling: Using the Slow/Flow Stop Pump Sampling Technique[d]

1. When hemodialysis is complete, turn off the dialysate flow and decrease the ultrafiltration rate (UFR) to 50 ml/h, to the lowest transmembrane pressure (TMP)/UFR setting, or off. If the dialysis machine does not allow for turning off the dialysate flow, or if doing so violates unit policy, decrease the dialysate flow to its minimum setting.

   Purpose: Stops the hemodialysis treatment without stop-

[d] For accurate single pool urea kinetic modeling, this technique must be used. However, given that ensuring the delivery of a minimally acceptable dose of dialysis is more important than an accurate measure of the dose delivered, it is quite acceptable for those units not doing formal single pool urea kinetics to draw the less complex sample, at least 2 to 3 min postdialysis. This sample can be drawn after retransfusion when the risk of access recirculation is totally eliminated. The longer the interval between terminating dialysis and blood sampling, the less influence "urea rebound" (23) (up to 30 min postdialysis) will have on the PRU, but the more inaccurate the single pool urea kinetics calculation. It is important for each unit to adhere to its procedure and to document when the postdialysis sample is drawn.

ping the blood flow completely; thus, the risk of clotting the extracorporeal circuit is low.

2. Decrease the blood flow to 50 to 100 ml/min for 15 s. To prevent pump shutoff as the blood flow rate is reduced, it may be necessary to adjust the venous pressure limits downward.

   Purpose: Fills the arterial needle tubing and the arterial blood line with nonrecirculated blood (in case there is any access recirculation) by clearing the dead space in the arterial needle tubing and the arterial blood line.

   At this point, proceed with either the slow flow or stop pump technique:

Slow Flow Sampling Technique

3. With the blood pump still running at 50 to 100 ml/min, draw the blood sample for the postdialysis urea from the arterial sampling port closest to the patient.

   Purpose: Drawing blood from the arterial sampling port ensures that the postdialysis urea measurement is performed on undialyzed blood.
4. Stop the blood pump and complete the patient disconnection procedure as per dialysis unit protocol.

Stop Pump Sampling Technique

5. After flushing the dead space in the arterial needle tubing of any access-recirculated blood by decreasing the pump speed for 15 s, immediately stop the blood pump.
6. Clamp the arterial and venous blood lines. Clamp the arterial needle tubing.
7. Blood for postdialysis urea measurement may be sampled by needle aspiration from the arterial sampling port closest to the patient by releasing arterial needle clamp. Alternatively, blood may be obtained from the arterial needle tubing after disconnecting it from the arterial blood line and attaching a Vacutainer or syringe without a needle.
8. Blood is returned to the patient, and the patient disconnection procedure proceeds as per unit protocol.

Guideline 4.4: Dialyzer Reprocessing

4.4.1. Dialyzer reprocessing must be done in accordance with the guidelines of the Association for the Advancement of Medical Instrumentation (AAMI) and with recommended practices for hemodialyzer reprocessing (opinion).

4.4.2. All units reprocessing dialyzers must be familiar with the AAMI guidelines (opinion).

4.4.3. Reprocessed dialyzers with a total cell volume (TCV) less than 80% of the batch mean value should not be reused (24,25) (evidence: level IV).

Discussion

The subcommittee accepts the AAMI standard of using the batch mean TCV for comparison with individual dialyzers rather than establishing the TCV for each dialyzer before use. Although this recommended approach will allow the extra use of the "very good" dialyzer, it will limit the reuse of those dialyzers at the lower end of TCV, which the subcommittee considered more important (opinion).

Guideline 4.5: Managing Inadequate Values for the Delivered Dose of Hemodialysis

4.5.1. Institute the following algorithm when a patient fails to receive the minimum target dose of dialysis or when there is a significant drop in the dose of dialysis being delivered (details below):

1. Check procedural issues,
2. Check for recirculation, and
3. Ensure no machine malfunction (opinion).

4.5.2. If no obvious cause is identified, either increase dialyzer surface area or dialysis time (evidence: level V).

Discussion

When the patient fails to receive the minimum target dose of dialysis or when there is a significant drop in the dose of dialysis being delivered:

Check Procedural Issues

1. Was the dialysis prescription followed? Check blood flow rate, duration of treatment, dialysate flow, specific dialyzer, and volume of blood processed.
2. Was the anticoagulation adequate? Routine rating system of degree of dialyzer clotting is useful. If it seems appropriate, check a parameter of anticoagulation (activated clotting time).
3. Was the dialyzer TCV adequate? (for reprocessed dialyzer)
4. Were there changes in machine recorded parameters?

- arterial and venous pressures
- TMP

5. Was blood sampling appropriate? Review pre- and post-values.

Check for Recirculation

1. Compress the access between the arterial and venous needles, observing arterial and venous pressures (opinion). Significant recirculation may be revealed by compressing the access between the two needles. The cause may be:

- **Anastomotic stenosis**: arterial pressure (prepump) becomes more negative.
- **Venous outflow stenosis**: venous pressure (postpump) becomes more positive.

Recirculation due to turbulence within the access may be present, and no change in arterial or venous pressure will occur during compression. Therefore, this maneuver should not replace the measurement of recirculation. If recirculation is present and compression does not reveal the basis, turbulence within the access is the most likely cause, and can be reduced by placing a tourniquet between the needles during dialysis (opinion).

2. Review needle placement and access configuration. Using loop grafts, ensure accurate knowledge of direction of flow. With needles inserted, compressing the graft between the needles results in pulsation only in the arterial needle.

3. Measure recirculation. If its presence is suspected, pursue suspected cause (anastomotic stenosis or venous stenosis).
4. Check the ports of the central lines.

Personnel often reverse the ports of central lines to improve flow. This process improves flow but, due to the anatomy of the lines, it can increase recirculation. If the ports are reversed frequently in a given patient, the dose of dialysis will be significantly compromised (evidence: level IV).

Ensure No Machine Malfunction

Check blood pump speed calibration (check other patients). If other patients dialyzed on the same machine have also had a reduction in their dialysis dose delivered, then a machine malfunction is the likely cause (opinion).

No Obvious Cause Identified

When clinicians can find no obvious mechanical or procedural cause for the drop in dialysis delivered, then measure the equilibration of urea across the dialyzer (with pre- and post-dialyzer samples at the beginning and end of dialysis). This will identify deposits on the membrane that may reduce the dialytic function of the dialyzer (opinion).

If there is no obvious cause for the reduced dialysis dose identified, the clinician can either increase the dialyzer surface area or the dialysis time (evidence: level V). Very muscular patients will require more clearance than obese patients of the same weight, due to their larger volume of distribution of urea (opinion).

Guideline 4.6: Optimizing Patient Compliance

4.6.1. Patient compliance is critical to the long-term success of therapy. The patient is an important member of the care team. To optimize patient compliance with therapy, identify why the patient is "noncompliant" and work with the patient and other caregivers to address those issues (opinion).

Discussion

All members of the team should be committed to the entire well-being of their patients and foster an environment that encourages appropriate care. This involves including the patient's primary care physician and appropriate specialists (*e.g.*, gynecologists, endocrinologists) in the patient's care (opinion).

Noncompliance may be the result of a number of factors (*e.g.*, socioeconomic, educational, emotional) that are beyond the patient's attitude or control. The clinician should be aware of these factors, which may require specific professional attention.

The clinician should help patients become educated about renal failure and ensure there is a teaching plan in place that ensures ongoing patient follow-up on issues such as access care, medications, and dietary interventions. Patients should also be educated about other important health issues, including hormone replacement therapy, the hazards of smoking, osteoporosis, and prostate cancer. The clinician should encourage patients to have continuing contact with their primary care physicians, who are best able to provide this education (opinion).

Guideline 4.7: Limiting Intradialytic Symptoms

4.7.1. Patient compliance will be enhanced by limiting intradialytic symptoms (opinion).

4.7.2. To limit adverse intradialytic symptoms, use the following strategies (opinion).

Ultrafiltration

1. Review appropriateness of current dry weight.

- Which is the patient's best day postdialysis (during long interval)?
- Patients whose dry weight is too low will feel progressively better with each successive day postdialysis.

2. Educate patient in role of weight gain in determining symptoms.
3. Extend dialysis time when volume of ultrafiltration exceeds predetermined symptomatic rate.
4. If available, monitor changes in blood volume in symptomatic patients during dialysis and change prescription accordingly.

- Mirror UF to dialysate [Na] if appropriate.
- Consider tensors to facilitate fluid removal.

Dialysate

1. Use hypertonic dialysate tailored to the individual patient.
2. Use bicarbonate dialysate.
3. Decrease dialysate temperature to minimize hypotension.

Patient

1. Optimize hematocrit in patients with heart disease.
2. Encourage the symptomatic patient to limit interdialytic weight gain.
3. Ask patient to limit eating before or during dialysis.
4. Review medications.
5. Consider diuretics when appropriate.

Discussion

The major reason dialysis is terminated early for some patients is intradialytic symptoms, such as cramps and low BP. In addition, protracted low BP may exaggerate rebound. Without compromising delivered dose, clinicians can take steps to modify the hemodialysis prescription to minimize these intradialytic symptoms. The potential role of pharmacologic agents remains to be established (26).

Guideline 4.8: Quality of Care

4.8.1. A single person or a multiprofessional team should be responsible for the quality of the medical care and have the authority to establish universal standards of care for the unit (opinion).

4.8.2. Multiprofessional management of the patient with ESRD should be a high priority (opinion).

Discussion

To ensure the quality of medical care for all patients, all those involved in providing care must be accountable. In a multiprofessional setting, the combination of a number of different professionals with different priorities, dealing with complex situations, may lead to variations in standards of practice and care. To ensure that the guidelines are applied uniformly to all patients in the unit, the individual or management team accountable for the quality of medical care must be clearly identified (opinion).

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Chapter 5: Guidelines for Adequacy and Nutrition in Peritoneal Dialysis

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This chapter focuses on the issues of adequacy and nutrition in peritoneal dialysis (PD), which reflects the mandate of the working group. It does not address many other issues in the management of PD patients, such as infection, access problems, bone disease, anemia, mechanical and metabolic complications, or cardiovascular disease (the largest single killer of most of our patients).

The working group emphasizes that adequacy and nutrition issues should not be viewed in isolation from the other medical and social problems that patients on PD may develop. In clinical practice, there is always the risk that defining absolute clearance and nutritional targets will lead to medicine by numbers, rather than a more integrated approach. To avoid this, the working group recognizes that all measured values must ultimately be interpreted in the clinical context of the individual patient. A clinical decision to switch dialytic modality must take into account more than adequacy and nutrition. There is no substitute for speaking with and examining our patients.

Most of the working group's guidelines and recommendations have not been validated by high-level clincal evidence. However, they represent the consensus opinion of a group of interested and experienced caregivers. Members of the working group hope they will stimulate thought and help improve clinical practice and outcomes for our patients.

Guideline 5.1: Target Clearances in Peritoneal Dialysis

5.1.1. For CAPD and automated PD (APD), the minimum weekly Kt/V clearance target would be 2.0/wk and the minimum weekly corrected creatinine clearance target would be 60 L/wk in high and high-average peritoneal transporters, and 50 L/wk in low and low-average peritoneal transporters (opinion).

5.1.2. Clearance values less than a Kt/V of 1.7/wk and a corrected creatinine clearance of 50 L/wk would be considered unacceptable, except in rare circumstances (opinion).

5.1.3. Apply all clearance targets in the context of the patient's personal and clinical circumstances (opinion).

Discussion

The high mortality in dialysis patients generally is a cause for concern. Evidence from hemodialysis indicates that increases in dialytic dose are associated with improved outcomes, including survival. Many patients on PD have clinically been underdialyzed. Evidence from the literature indicates an association between high clearances and better outcomes in patients on PD, although the relative contributions of peritoneal clearance and residual renal clearance have not yet been clarified (1,2) (evidence: level I).

Definitive clearance targets for PD have not been identified, and more research is required in this area. Nevertheless, the proposed minimum clearance targets for PD patients would be a Kt/V of 2.0/wk and, in the case of high and high-average transporters, a creatinine clearance of 60 L/wk, corrected for 1.73 m^2 body surface area (1,2). A lower creatinine clearance target of 50 L/wk, corrected for 1.73 m^2 body surface area, for low and low-average transporters is being proposed for the following reason. Low and low-average transporters, even on standard CAPD prescriptions, have very good clinical outcomes with markedly better patient and technique survival rates than their high and high average peritoneal transport counterparts (3). However, once low and low-average transporters lose residual renal function, it is physically almost impossible for most of them to achieve a corrected creatinine clearance of 60 L/wk (4). Thus, setting such a target in these patients might lead to their inappropriate transfer to hemodialysis, when they are in fact a group of patients who are particularly likely to do well on PD. In high and high-average transporters, in contrast, a corrected creatinine clearance of 60 L/wk is achievable, even without residual renal function, and the relatively less successful outcomes described in these patients make it desirable to maximize clearances. This emphasizes the need not to look at clearances in isolation from other patient characteristics (opinion).

The above are recommended minimum clearance targets; optimal targets remain unclear and may be higher. Therefore:

- If patients substantially exceed these clearance targets on an easily tolerated regimen such as 2 L 4 times daily, it is not desirable to reduce the dialysis dose to the target levels.
- If a patient has achieved these targets but has clinical evidence of uremia or is becoming nutritionally more compromised, and if no other etiology for the poor nutritional status is identified, the dose of PD should be prospectively raised, regardless of the levels of clearance already achieved.
- It is acceptable if a patient can only achieve one of the two suggested targets despite maximization of the PD prescription, provided the patient is not manifesting significant uremic symptoms or declining nutritional status without other apparent cause. The most common example of this is where urea, but not creatinine, clearance targets can be achieved. This is seen most often in patients with little or no residual renal function, in low transporters, or in patients who are on APD. The opposite scenario, in which creatinine but not urea clearance targets are achieved, is sometimes seen in patients with substantial residual renal function and relatively large body size.
- If the patient can achieve neither clearance target despite maximization of the PD prescription, the clinician should consider giving the patient a trial of well-prescribed hemodialysis. However, if the patient is clinically well with no evidence of significant uremic symptoms or of declining nutritional status, and is not willing to switch modality, it may be appropriate to continue with PD.
- If the patient has a Kt/V of <1.7/wk and/or corrected creatinine clearance of <50 L/wk, the clinician should consider giving the patient a trial of well-prescribed hemodialysis. However, in some cases, a switch may not be feasible.

For the sake of simplicity and in the absence of strong evidence suggesting otherwise, the same targets and the same approach should be used for APD, although this modality is usually more intermittent than CAPD (opinion). Intermittent PD (IPD) two or three times weekly should not be used as a definitive therapy for ESRD, because clearance targets can rarely be achieved with this modality.

Guideline 5.2: Clearance Measurements in PD: Methodology, Frequency, and Pitfalls

5.2.1. Monitor Kt/V and creatinine clearance in PD patients using 24-h collections of dialysate and urine, within 6 to 8 wk of commencing PD and, ideally, every subsequent 6 mo (opinion).

5.2.2. If the patient's clinical status changes unexpectedly, or if the prescription is altered, take supplemental clearance measurements (opinion).

5.2.3. Be more aware of the possibility of noncompliance with exchanges in PD patients.

Methodology

Calculate Kt/V and creatinine clearance in CAPD patients by measuring:

- the urea and creatinine content of 24-h dialysate and urine collections, and
- the urea and creatinine level in a serum sample taken during the same 24 h, or 12 h before or after.

Correct dialysate creatinine values for any interference with the assay consequent to high dialysate glucose levels. For the purpose of calculating creatinine clearance, estimate the urinary component using the mean of the renal urea and creatinine clearances, because this is likely to be a better measure of true GFR (5) (evidence: level II). Estimate the *V* value, used to normalize Kt to Kt/V, using the Watson formula. Normalize creatinine clearance to 1.73 m^2 body surface area, using the DuBois formula (2). All of these calculations can be done simply, using commercially available computer software (see end of this section for formula details).

To avoid a situation in which malnourished patients with significant weight loss have misleadingly high clearance values after normalization, calculate *V* and body surface area based on a "desirable" rather than the patients actual body weight (6) (opinion). (see Guideline 5.6 for discussion on calculating "desirable" body weight).

Twenty-four-hour dialysate collections may not be practical in APD patients. An alternative approach is to have the patient or an assistant collect a sample of the 24-h dialysate effluent, provided the effluent has all been collected in a single container and fully mixed. Because the drain volume can be recorded from the cycler, appropriate calculations can be made (opinion).

Frequency

Take the initial clearance measurements within 6 to 8 wk of commencing PD and plan to repeat these every subsequent 6 mo. In the case of patients who are functionally anephric when they begin PD, and so at high risk of underdialysis, take the initial clearance measurement within 2 wk. In the cases of patients whose ability to achieve clearance targets depends on residual renal function, measure the urinary contribution to clearance every 3 mo. In the case of patients who are clinically very stable and who are achieving clearance targets by peritoneal clearance alone, it may be reasonable to reduce the frequency of clearance measurements to once every 12 mo (opinion).

In all patients, take additional measurements any time unexplained and possibly uremic symptoms or complications or unexpected alterations in serum biochemistry arise, or if the patient has a history of decreasing urine output or unexplained fluid overload. The clinician should also take additional measurements within 4 wk of any alteration in the PD prescription (opinion).

Repeat 24-h collections if very unexpected results occur (*e.g.*, a major change in urea or creatinine equilibration between blood and dialysate, a major increase or decrease in the residual renal component of clearance, an unusually high or

low drain volume). Such findings often indicate inaccurate collections, patient noncompliance on the day concerned, or laboratory errors and should not be an indication to alter prescriptions.

Clinic Visits

Patients should be seen in clinic and their status on PD evaluated at least every 2 to 3 mo, and more often if patients are not doing well (opinion). In occasional circumstances (*e.g.*, the patient has logistical problems traveling to the clinic) and when the patient is clinically well with stable blood work, longer intervals between clinic visits may be acceptable.

Blood Work

Take blood samples for measurement of urea, creatinine, and electrolyte levels at least every 2 to 3 mo, and more often if patients are not doing well. Consider increases in serum creatinine and blood urea levels as indications to review the clearances being achieved and consider decreases in urea and creatinine levels as an indication to review nutritional status (opinion).

Noncompliance

Interpret measurements of clearance in PD patients in light of the patient's clinical and nutritional status, giving attention to the possibility of patient noncompliance. However, it is important to note that even regularly noncompliant patients are likely to be compliant on the days of their 24-h collections. Monitor clues to noncompliance, which include:

- a rising serum creatinine, despite an apparently unchanging creatinine clearance;
- uremic symptoms or poor biochemistry results, despite adequate prescribed clearances;
- an increasing 24-h creatinine excretion in urine and dialysate, which might suggest the dialysing out on the day of the collection of creatinine that had accumulated on previous noncompliant days;
- failure to attend clinics, poor record-keeping, or unexplained inability to achieve target weight;
- large accumulations of unused dialysate noticed on home visits;
- insufficient ordering of dialysate supplies; and
- a prompt improvement in the patient's clinical condition and biochemistry after hospitalization.

Address the possibility of noncompliance, when suspected, with the patient in a sympathetic manner, focusing on education. To deal effectively with this problem, be aware also of other types of noncompliance in PD, such as:

- incomplete filling and excess flushing on CAPD and
- skipping or shortening of cycler sessions on APD.

(See Appendix 5A for a form for following clearance and nutritional indices in PD patients).

Computational Formulas for Peritoneal Dialysis Clearances

Kt/V_{urea}:

$$\text{Weekly Kt/V} = 7[D/P_{urea}\,(\text{mmol/L}) \times \text{Effluent volume (L)} + U/P_{urea}\,(\text{mmol/L}) \times \text{Urine volume (L)}]/\text{Total body water (L)}]$$

Weekly creatinine clearance:

$$C_{Cr} = 7[D/P_{creat}\,(\mu\text{mol/L}) \times \text{Effluent volume (L)} + \text{Urine volume (L)} \times [U/P_{urea} + U/P_{creat}\,(\text{mmol/L})/2] \times 1.73\ \text{BSA}$$

Watson formulas for total body water (V):

$$\text{Male: } V(\text{L}) = 2.447 + 0.3362 \times \text{Weight (kg)} + 0.1074 \times \text{Height (cm)} - 0.09516 \times \text{Age (yr)}$$

$$\text{Female: } V(\text{L}) = -2.097 + 0.2466 \times \text{Weight (kg)} + 0.1069 \times \text{Height (cm)}$$

DuBois formula for body surface area:

$$\text{BSA} = 0.007184 \times \text{Weight } 0.425\ (\text{kg}) \times \text{Height } 0.725\ (\text{cm})$$

Note: All formulas have been converted to SI units for convenient use in Canada.

Guideline 5.3: Peritoneal Transport and Volume Status

5.3.1. Perform a peritoneal equilibration test within 6 wk of initiating PD, and repeat it when/if unexplained changes in peritoneal ultrafiltration or equilibration occur (opinion).

5.3.2. Pay particular attention to hydration, serum albumin, and nutritional status in patients who are high transporters on peritoneal equilibration testing (opinion).

5.3.3. Emphasize clinical detection and treatment of volume overload and hypertension in all patients on PD (opinion).

Peritoneal Equilibration Test

Knowing a patient's peritoneal transport characteristics, as measured by the peritoneal equilibration test (PET), is essential to prescribe APD and very desirable to prescribe CAPD (4,7) (opinion). The PET should be carried out within the first 6 wk of initiating PD, but not within the first 2 wk, because values at this stage may not yet be stable (8) (evidence: level II). The PET does not have to be repeated routinely unless:

- the patient switches, more than 1 yr later, from CAPD to APD, or
- the clinician has reason to suspect a change in transport status (*e.g.*, a rise or fall in urea or creatinine equilibration in 24-h dialysate collections, a decrease in ultrafiltration).

The PET should be done with careful attention to methodology and not within 1 mo of an episode of peritonitis (7) (evidence: level II).

Recent observations suggest that high transport status on the PET is an adverse prognostic risk factor for patient survival in PD (3) (evidence: level I). This may relate to poor ultrafiltration and consequent fluid overload, to high peritoneal protein losses, or to other reasons that are still unclear. Clinicians should consider patients who are high transporters to be at particular risk and pay special attention to their volume status, serum albumin levels, and other nutritional indices. It may be useful to measure 24-h dialysate protein losses as an index of the severity of their problem. Patients who are high transporters and who are having fluid overload problems on CAPD should be considered for transfer to APD (opinion). If they continue to have severe hypoalbuminemia (serum albumin >30 g/L) or clinical fluid overload despite optimization of their PD prescription, the clinician should consider giving them a trial of well-prescribed hemodialysis (opinion).

Hydration Problems and Hypertension

Cardiovascular morbidity and mortality are high in all dialysis populations (9) (evidence: level I). Because there is some evidence that PD patients have a tendency for chronic fluid overload (10) (evidence: level VI), clinicians should pay particular attention to volume status in this population. Staff and patients should be continually educated about the importance of watching for symptoms and signs of fluid overload and reducing the target weight accordingly. Particular effort should be made to normalize BP by appropriate reduction of patients' target weights before antihypertensive medications are introduced or added. In the future, newer PD solutions with more effective osmotic agents may be of use in resolving chronic fluid overload. In the meantime, consider the following strategies (opinion):

- the use of loop diuretics in patients with persisting urine output,
- the addition of a fifth exchange via a night exchange device in patients who tend to resorb their nocturnal dwell,
- switching patients who do not ultrafitrate well on CAPD to APD,
- short day dwells on APD, and
- if volume status is not well controlled, switching patients to well-prescribed hemodialysis.

Because overhydration occurs most frequently in patients who are high transporters on PET (evidence: level II), clinicians should pay particular attention to overhydration and hypertension in these patients (11).

Guideline 5.4: Strategies to Increase Peritoneal Clearance

5.4.1. Encourage caregivers to familiarize themselves with simple strategies to increase the dialytic dose in PD and to apply these strategies with an awareness of the individual patient's clinical and personal circumstances (opinion).

5.4.2. Remeasure the patient's total clearances soon after each alteration in the dialysis prescription (opinion).

"Incremental" Versus "Maximal" Approach

In prescribing PD, a number of strategies may be used to achieve desirable targets, including:

- An "incremental" approach, which measures residual renal clearance and aims to provide enough dialysis to bring total clearances up to the target values. Implicit in this approach is the need to monitor closely the inevitable decline in renal clearance that occurs with time and to raise the peritoneal clearance to ensure that targets are maintained (12).
- A "maximal" approach, which attempts to provide from the beginning sufficient peritoneal clearance to achieve the targets, treating residual renal function as an additional bonus that will eventually and inevitably be lost (12).

The difference between the two approaches will become particularly stark with earlier initiation of dialysis. With the "incremental" approach, patients might receive only one or two exchanges daily, whereas with the "maximal" approach, they would have very high total clearances when dialysis was initiated.

There is no consensus on the best approach at this time. The advantage of the "incremental" approach is that the patient will need less dialysis in the first 1 to 2 yr on PD, which will mean savings in cost and time and, perhaps, a lower risk of dialysis-related complications such as hyperglycemia, obesity, hyperlipidemia, and even peritonitis, as well as less risk of "burnout." The advantage of the "maximal" approach is that it obviates the need to monitor declining residual renal function with the same rigorous attention and avoids the disruption of frequent switches in prescription, as well as the associated concern that patients will be unwilling to increase intraperitoneal dwell volumes above those that they had when they started PD. The "maximal" approach is also consistent with the view that suggested targets represent a minimum rather than an optimal amount of clearance. In practice, an "in-between" approach may be an acceptable compromise.

"Empiric" Versus "Modeled" Approach

A second issue in determining a PD regimen is whether to choose the initial prescription empirically or with computer-assisted kinetic modeling:

- With the "empiric" method, the clinician chooses a prescription taking into account the patient's size, residual renal function, and, if known, peritoneal transport status, but without the use of formal mathematical calculations. Treatment is commenced, clearances are subsequently measured, and the dialytic dose is adjusted accordingly until targets are achieved.
- With the "modeled" approach, the clinician uses computerized kinetic modeling, which takes into account body size, residual renal function, and peritoneal transport status, and selects prescriptions that are predicted to achieve the targets, with or without residual renal function (4,13,14).

The "modeled" approach has the advantage of being somewhat more scientific. However, computer programs are not always accurate in their prediction of clearances and, with both approaches, it is essential to measure and remeasure clearances until targets are achieved. Even with the modeled approach, initial prescription selection is empiric as the PET is not typically known until 4 to 6 wk after initiation.

When using the "empiric" approach, bear in the mind the following:

- When dealing with patients with minimal residual renal function (<2 ml/min creatinine clearance), or when following the "maximal" approach, patients with a body surface area >1.7 m^2 or a body weight >65 kg should be routinely prescribed 2.5-L rather than 2-L dwell volumes in both CAPD and APD. Those with body surface area >2 m^2 or body weight >80 kg might be prescribed 3-L dwell volumes on both CAPD and APD.
- Patients requiring five exchanges daily to achieve targets should ideally use a night exchange device to deliver the fifth exchange, because this maximizes "spacing" of exchanges, improving urea and creatinine equilibration. This may also improve compliance.
- Patients on APD should do one or more day dwells unless they are of very small body size, are high transporters, or have very substantial residual renal function.
- In patients on APD, increases in clearance are best achieved by increasing dwell volumes or cycler time, or by adding a second day dwell. Increasing the frequency of cycles above 5 to 7 per nightly cycling session leads to relatively little or even no increase in clearance and is not very cost-effective.

As a general principle, selecting a prescription should take into account not only the clearances that may be achieved, but also the patient's preferences and lifestyle. A prescription that is compatible with the patient's preferences is likely to reduce the risk of patient "burnout" and noncompliance.

Guideline 5.5: Nutritional Issues in Peritoneal Dialysis

5.5.1. Ensure that all PD patients are counseled by a registered dietitian at the initiation of PD and every 6 mo thereafter, with a view to achieving a normalized PNA (nPNA) of 1.2 g/kg per d and a total energy intake of 35 kcal/kg per d (opinion).

5.5.2. Monitor nutritional indices in PD patients, including the serum albumin and the nPNA, with a view to detecting those at high risk of adverse outcome (opinion).

5.5.3. Calculate the nPNA whenever clearance measurements are being made, using the Bergstrom formulas, and have patients with values <0.9 g/kg per d reassessed by a registered dietitian (opinion).

5.5.4. Investigate patients identified as malnourished for possible contributory causes, and implement a strategy to try to correct the malnutrition (opinion).

Discussion

With the strong correlations between nutritional or nutritional-related indices and patient outcomes on PD, clinicians should give more intensive attention to nutritional factors, both before and after initiation of PD (1,2,15). To identify patients at highest risk for adverse outcomes, clinicians should monitor serially the following nutritional or nutritional-related indices in PD patients.

Serum Albumin

Measure serum albumin (SA) at least every 2 to 3 mo in association with the regular blood work, and consider patients with falling values or values <30 g/L at high risk. However, clinicians should note that:

- SA levels are greatly affected by peritoneal transport, by comorbidity, by the presence of inflammation (which may be estimated by C-reactive protein levels), and by nutritional intake (15,16) (evidence: level I).
- Different laboratory methodologies give different results for SA, and, in each center, the approach may need to be modified accordingly.

In some patients who are high transporters by PET, low SA may be relatively refractory to intervention. Given that the prognosis for patients with low SA (<30 g/L) and high transport status is poor (3,15), clinicians should consider switching these patients from CAPD to APD or, if this is not feasible or effective, offering them a trial of well-prescribed hemodialysis (opinion).

Normalized Protein Equivalent of Nitrogen Appearance

Calculate nPNA in PD patients each time a clearance measurement is done. Although other formulas can be used, the Bergstrom formulas are the best-validated (17–19)) (evidence: level II) (see reference list and text below). Normalize the PNA to give nPNA using "desirable" rather than actual body weight (20) (opinion). To estimate "desirable" body weight, use one of the following two methods:

- The National Health and Nutritional Evaluation Study table, which requires an estimate of body frame and is based on the median weight of North Americans of the same age, gender, height, and frame size as the patient.
- A back calculation from the "V" value determined by the Watson formula, which multiplies this V by 1.72 to give a standardized weight.

The disadvantage of the back calculation from V is that, because the Watson V is calculated from the patient's body weight, height, gender, and age, the calculation is circular and, in a malnourished patient, may be misleading. Each PD patient should receive nutritional counseling from a registered dietitian at the time of initiating PD and every 6 mo thereafter, with a view to achieving an ideal nPNA of 1.2 g/kg per d. However, for many patients, this target may not be realistic, and a value of 0.8 to 0.9 g/kg per d or greater may be considered acceptable

if the patient is clinically stable and appears to be nutritionally relatively healthy (opinion). Values less than 0.8 g/kg per d, or falling values are considered cause for concern and intervention (opinion) (see end of this section for details of formulas).

Total Energy Intake

In the past, too little attention was paid to energy intake in dialysis patients and its impact on health outcomes. It is suggested that energy intake be assessed with the same frequency as nPNA (17) (opinion). Glucose absorption from dialysate may be measured (rather than estimated) when the 24-h collection is being done, by subtracting the quantity of glucose in the daily dialysate effluent from the total quantity of glucose instilled that day (estimated from the strengths and sizes of the bags used). Dietary energy intake is best estimated by an experienced dietitian. Target energy intake for patients on PD should be 35 kcal/kg per d (17) (opinion).

Subjective Global Assessment

This technique, which is a simple extension of history taking and physical examination, is a potent predictor of patient survival (1,21) (evidence: level I). These guidelines suggest that patients have a formal SGA every 6 mo. Based on the SGA, they can be placed in various nutritional categorizes (*i.e.*, normal nutrition, mild-to-moderate malnutrition, or severe malnutrition). The SGA may be done by a dietitian, nurse, or physician. To increase experience and maximize reproducibility, each center should have a limited number of people doing SGA. Low or falling SGA status would be considered a marker for high risk and require intervention (for a suggested form for carrying out an SGA on a PD patient, see Appendix 5B).

Lean Body Mass by Creatinine Excretion

Each patient's percentage lean body mass (or edema-free, fat-free body mass) may be monitored serially, calculated using the Keshaviah adaptation of the Forbes and Bruining formula, converted to SI units (22). Another option to consider is monitoring serially total creatinine excretion, which provides at least an approximate indicator of somatic protein mass. Creatinine excretion can be measured as part of the calculation of clearance, so these calculations can be done whenever creatinine clearance is measured. Falling values for creatinine excretion or for lean body mass, or a percentage lean body mass $<70\%$ in a male or $<60\%$ in a female, are considered markers of a patient at high risk. Although there is some controversy as to the accuracy of lean body mass estimations made using creatinine kinetics, these indices—regardless of what they measure—have been shown to be highly predictive of survival in PD patients (1) (evidence: level I).

Other simple nutritional indices that care teams may use include blood urea, serum creatinine, and serum potassium. Falling values merit investigation, explanation, and possible intervention (opinion).

It may not be feasible for all PD programs to measure all of these nutritional indices. However, to identify patients who are nutritionally compromised, each program should measure the SA, the nPNA, and other indices, as required (opinion) (see Appendix 5A for a form for following clearance and nutritional indices in PD patients).

Interventions

Using nutritional indicators, it is relatively easy to identify nutritionally compromised, high-risk patients. However, it is less easy to intervene to reverse these nutritional abnormalities. Most interventions are not well validated and are often unsuccessful. Nevertheless, given the poor prognosis associated with these abnormalities, clinicians should consider taking an aggressive diagnostic and therapeutic approach that uses multiple strategies (opinion), including:

- nutrition counseling;
- assessment of socioeconomic and possible cultural factors, when relevant;
- prospective increases in the dose of peritoneal dialysis;
- treatment of comorbidities, including, for example, depression, gastrointestinal disease, and drug side effects;
- oral nutritional supplements that provide protein and/or calories, as well as intraperitoneal amino acids;
- feeding tubes; and
- a trial of well-prescribed hemodialysis.

The treatment of malnutrition in dialysis patients should also be a focus for future research.

Hyperlipidemia

The dialysis population suffers from high rates of cardiovascular disease, and the PD population from high prevalence of hyperlipidemia (9). Given the recent evidence that treating even mild hyperlipidemia with lipid-lowering agents in the nondialysis population significantly improves cardiovascular outcome and survival, consideration should be given to measuring cholesterol, triglycerides, high-density lipoproteins (HDL) and low-density lipoproteins (LDL) every 6 to12 mo. Furthermore, it may be reasonable to treat those with elevated values using dietary counseling and lipid-lowering agents. However, there are no studies addressing the effectiveness of treating hyperlipidemia in PD patients, in terms of cardiovascular end points or patient survival, and these should be a priority for future research (opinion). Nevertheless, hypocholesterolemia, which may be a marker of malnutrition, is associated with adverse outcomes in dialysis patients (23) (evidence: level I).

Computational Formulas for Nutrition

1. PNA for peritoneal dialysis (Bergstrom formulas)

$$PNA = 13 + 0.204 \, UNA \, [mmol/d] \text{ plus dialysate protein losses } [g/d]$$

$$PNA = 19 + 0.213 \, UNA \, [mmol/d]$$

UNA mmol/d is urea nitrogen appearance in the total urea in daily dialysate + urine measured in mmol/d.

The above results are then corrected to normalized body weight.

2. Creatinine kinetics for lean body mass (Keshaviah formula)

$$\text{Cr production [mmol/d]} = \text{Cr excretion} + \text{Extrarenal Cr degradation}$$

$$\text{Cr excretion [mmol/d]} = (\text{Urine volume [L]} \times \text{Urine Cr concentration [mmol/L]} + (\text{Dialysate volume [L]} \times 0.001(\text{Dialysate Cr concentration } [\mu\text{mol/L}])$$

$$\text{Extrarenal Cr degradation [mmol/d]} = 0.00004 \times \text{Serum Cr } [\mu\text{mol/L}] \times \text{Body weight [kg]}$$

$$\text{Lean body mass [kg]} = (3.29 \times \text{Production}) + 7.38$$

Guideline 5.6: Monitoring Clinical Outcomes in a PD Program

5.6.1. Monitor patient and technique survival in all large PD programs (opinion).

5.6.2. Monitor the percentage of patients in all PD programs who fail to achieve clearance targets on their most recent evaluation (opinion).

5.6.3. Record the percentage of patients in all PD programs with inadequate nPNA values and severe hypoalbuminemia (opinion).

Discussion

To judge the quality of their practices compared to other programs and to assess how practices change with time and various interventions, all Canadian PD programs should collect data on patient outcomes.

Record patient survival and technique survival. Constructing these survival curves may require some statistical advice. In small programs (*i.e.*, fewer than 50 patients), survival rates may vary randomly and substantially from year to year and may best be measured over 2- or 3-yr periods.

The use of technique survival as an end point may also be problematic. When interpreting these data, clinicians and researchers should keep in mind that:

- Rates of technique survival may be misleadingly high in programs in which, because of the lack of hemodialysis spots, the threshold for switching a patient who is not doing well from PD to hemodialysis is very high.
- Rates of technique survival may be misleadingly low in programs in which patients can switch easily from PD to hemodialysis.

Each program should also follow clearance and nutritional indices. Although the mean values of Kt/V and creatinine clearance can be estimated, the results may be misleading, because a small number of patients with marked residual renal function can skew mean values upward. Moreover, it should be noted that a mean value equivalent to the recommended targets suggests that approximately half of the patients are receiving less than the target. A better approach is to record the percentage of patients who, at any given time, are reaching or exceeding the Kt/V and/or creatinine clearance targets. In a good program, this number should exceed 80 to 85%. To ensure that adequate prescription policies are being practiced, programs should review the proportion of patients exceeding targets every 3 to 6 mo.

Nutritional indices such as serum albumin and nPNA can be monitored in the same way. In the case of serum albumin, it may be useful to measure the percentage of patients with the most recent value >30 g/L and >35 g/L. However, due to peritoneal protein losses, it is inevitable in most PD programs that a large proportion of patients will have a serum albumin <35 g/L. In the case of nPNA, programs should monitor the percentage of patients with a value >0.8 and/or >0.9 g/kg per d.

Guideline 5.7: Quality of Care

5.7.1. A single person or a multiprofessional team should be responsible for the quality of the medical care and have the authority to establish universal standards for PD care (opinion).

Discussion

To ensure the quality of medical care for all patients, all those involved in providing care must be accountable. In a multiprofessional setting, the combination of a number of different professionals with different priorities and dealing with complex situations may lead to variations in standards of practice and care. To ensure that the guidelines are applied uniformly to all PD patients, the individual or management team accountable for the quality of medical care must be clearly identified and responsible for monitoring clinical outcomes.

Appendix 5A
PD Adequacy and Nutrition Monitoring Form

Patient's primary disease: ____________________________________

Initiation date of PD: ____________________________ PET Status *(date: ____________)*______________________

Dates					

Current Prescription					
Kt/V	Total				
	Kpr				
	Kr				
CrCl	Total				
	Kpr				
	Kr				
Weight	Kg				
	Volume				
Dialysate volume	Net				
	UF				
	Urea				
	Cr				
Urine	Volume				
Serum	Urea				
	Cr				
	Albumin				
Protein	nPNA				
	DPI				
	Dialysate				
Energy	DEI				
	PEI				
Cr Kinetics	CrEx				
	%LBM				
Changes/ Comments					

Appendix 5B

Description of Subjective Global Assessment Technique

Subjective global assessment (or SGA) was developed for use in assessing the nutrition of general surgery patients. Based on this technique, validity testing indicated that PD patients could be assessed by four items. The items used in the history section include weight loss, nutritional intake, and gastrointestinal symptoms. The physical examination section assesses loss of subcutaneous adipose tissue and muscle wasting at various sites. Each item is given a subjective weight: 6 to 7, or normal (well nourished); 3 to 5, or mild-to-moderate malnutrition; and 1 to 2, or severely malnourished.

History Section

Weight Loss. The patient's weight loss over the past 6 mo, as well as the past 2 wk, is evaluated. If actual weights are available, these weights would be preferable. Otherwise, historical data from the patient may be used. If over the past 6 mo, the weight loss has been: >10%, then the rating would be severe; 5 to 10%, then the rating would be mild-to-moderate; and <5%, then the rating would be normal. In addition, the patient's weight loss over the past 2 wk is rated as: stabilization being normal and increasing weight and ongoing weight loss being severe.

Food Intake. The interviewer will rate the patient's food intake with lower scores indicative of a decreasing intake over a longer time duration and greater changes in food type.

Gastrointestinal Symptoms. This section deals with gastrointestinal symptoms that have been persistent over the past 2 wk. The more severe the symptoms, the lower the rating.

Physical Examination

Loss of Subcutaneous Fat. Subcutaneous fat can be evaluated by examining three sites: fat pads under the eyes and the adipose tissue above the triceps and biceps. The fat pads should show a slight bulge in a well-nourished individual, but will be "hollow" in a malnourished patient. By pinching the adipose tissue over the tricep and bicep, the thickness of the skinfold should be used to rate the patient's nutritional status. The overall rating for loss of subcutaneous fat is scored on the basis of these three sites.

Muscle Loss. The following sites can be utilized for assessment of the patient's muscle mass: temporalis muscle, prominence of the clavicle, contour of the shoulders, visibility of the scapula and ribs, protrusion of the interosseous muscle between the thumb and forefinger and the amount of quadricep and calf muscle mass. The overall rating for muscle loss is based on the assessment of these sites.

Overall SGA Rating

The ratings from the history and physical examination sections are then aggregated into a global, or overall, score. The overall rating is not simply a numerical score. The strength of the SGA is the clinical judgment of the examiner. If the patient is deteriorating or improving, the examiner may apply different weights to each section to reflect these changes.

Subjective Global Assessment Rating Form

Patient Name: ______________________________ Date: ______________________

A. History	Rating Severe		Mild–Moderate			Normal	
1. Weight changes over past 6 months ______ <5% weight change (or gain) ______ 5 to 10% weight loss ______ >10% weight loss over past 2 weeks ______ increasing weight ______ stable weight ______ ongoing weight loss	1	2	3	4	5	6	7
2. Food intake overall: ______ usual intake ______ <usual and decreasing duration: ______ weeks type of change: ______ suboptimal solids ______ full liquid intake ______ hypocaloric fluids ______ unable to eat	1	2	3	4	5	6	7
3. GI symptoms ______ none ______ anorexia ______ nausea ______ vomiting ______ diarrhea duration: ______ weeks	1	2	3	4	5	6	7

B. Physical examination							
1. Loss of subcutaneous fat	1	2	3	4	5	6	7
2. Muscle wasting	1	2	3	4	5	6	7

C. Overall SGA classification	Final Rating
1. Normal or well nourished Rating of 6 to 7 in most categories or significant and sustained improvement	
2. Mild to moderately malnourished 3 to 5 rating is indicated in most categories	
3. Severely malnourished 1 to 2 ratings in most categories	

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