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Select Ion and Preparation of Patients for Dialysis

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1. Introduction

The prevalence of chronic kidney disease (CKD) is increasing [1]. This rise is probably attributable to the progressively aging population and to the increased prevalence of comorbid conditions namely obesity, diabetes, and hypertension. According to the data from the National Health and Nutrition Examination Surveys, the prevalence of CKD in participants 70 years old and older is 46.8% compared to 6.7% in those between 40–59 years of age [1]. Many patients with CKD are unlikely to exhibit sufficient progressive decline in renal function to require renal replacement therapy (RRT), in fact according to the findings present in literature only a small percentage of CKD patients ultimately require RRT [2-5]. In part, this low rate is explained by the increased risk of death from cardiovascular causes before progression to end-stage renal disease (ESRD) can occur [6]. In part, it is secondary to the earlier referral than in the past to nephrologists with improvement of nondialytic maximum conservative management (MCM) focused on quality of life and patient comfort (i.e. maximizing renoprotective therapies, additional dietary interventions) [7,8]. In 2008, more than 110,000 Americans were started on maintenance RRT, a life-saving therapy for patients with ESRD [6]. Ideally, when patients begin RRT they should meet the following conditions: firstly, they should not require hospitalization for the management of untreated acute or chronic complications of uraemia; secondly, they should have a thorough understanding of the different treatment options; and thirdly, they should have a functioning, permanent access for the RRT of their choice [9].

Unfortunately still a sizable proportion of patients in the USA are not adequately prepared for starting RRT. In 2008, 44% of patients received no predialysis nephrology care and only 25% had received ongoing care by a nephrologist for more than 12 months prior to initiating dialysis [6]. Despite the critical importance of lifestyle management fewer than 10% of pa-

tients receive dietary counselling prior to starting RRT [6]. Furthermore, many patients newly diagnosed with ESRD are not offered alternatives to RRT (such as home dialysis or preemptive transplantation), even in the absence of medical contraindications [10,11]. More than 80% of patients in the USA initiate RRT with a central venous catheter (CVC), a type of access associated with significantly higher rates of infectious complications and of long-term non-infectious complications compared with a permanent vascular access [6, 12-14]. Inadequate preparation for RRT in the USA can only partially be accounted for delayed referral to nephrologists; as a considerable number of patients who have received more than 1 year of specialist care prior to initiating RRT are also inadequately prepared for this treatment [6]. In 2006, the annualized mortality in the first 3 months of starting RRT for patients in the USA was approximately 45%, which was in part due to inadequate preparation and education [15]. The available data on RRT preparation practices outside the USA are limited but seem highlight the same challenge, the need of a better selection and preparation to RRT [16]. Analyses from the Dialysis Outcomes and Practice Patterns Study (DOPPS) and findings from studies conducted in the 1980s and 1990s indicate a high rate of delayed referrals to a nephrologist in Europe, and contemporary data from Canada also demonstrate a high incidence of suboptimal RRT initiation [1,16-19].

Although dialysis prolongs the lives of many individuals with ESRD, the burden of RRT might not justify the potential benefits of treatment in certain patients, such as the elderly [20]. However, as illustrated by the North Thames Dialysis Study and by one Canadian study, judgment on the appropriateness for RRT should not depend solely upon chronological age but should instead be based on a composite assessment of the health and functional status of the individual [21,22]. Results from other studies suggest that there are subgroups of patients who have a low likelihood of benefiting from RRT [23-25]. For example, initiating RRT does not reverse the progressive decline in functional status; instead this decline seemingly accelerates after RRT initiation [23]. For selected individuals with advanced CKD, nondialytic MCM might, therefore, be superior to initiating RRT [24] this suggestion highlights the importance of considering the appropriateness of RRT for individuals with CKD early in the disease course. Assessment of disease management requires shared decision-making between patients, their family members, and the treating physicians [25]. Most of the data on the principles of management and outcomes of patients with advanced CKD who elect to have MCM are derived from the United Kingdom [24,26,27]. In most of the published studies to date, the life expectancy of patients with advanced CKD who choose MCM is shorter than that of patients with matching characteristics who choose RRT; the median life expectancy of patients with ESRD who forgo RRT has been reported to range from 14 months to 23 months [24,26,27]. However, the primary goal of care in patients who opt for MCM should be focused on symptom management to enhance quality of life and ensure patient comfort [9].

2. How is the choice made between hemodialysis and peritoneal dialysis?

Global comparisons show interesting differences between countries in the proportion of patients with ESRD treated by peritoneal dialysis and hemodialysis. The wide discrepancy between countries such as UK [45% of patients treated by peritoneal dialysis), and its

neighbour France, where only 10% are so treated, indicates strong non-medical influences on the choice of dialysis modality [28].

Economic reasons: the reimbursement to the physicians and the dialysis facilities for the cost of providing treatment varies widely around the world. There are also large differences between the levels of payment for hemodialysis and peritoneal dialysis in many countries. For example in French the facility is not reimbursed for peritoneal dialysis and the physicians receive no fee. Conversely in countries such as Hong Kong, where dialysis is only available in the private sector, more patients are treated by peritoneal dialysis than by hemodialysis, as the former is less expensive. If the physician has a financial interest in the hemodialysis facility, this may directly influence the decision on which modality of treatment to recommend.

Physician preference: there is a strong preference for hemodialysis among some influential nephrologists on both sides of the Atlantic. This is supported by data from USRDS [29]. In a large US-based survey reported in 1997, only 25% of patients remembered having peritoneal dialysis discussed with them. In contrast 68% of patients on peritoneal dialysis had had discussions on hemodialysis. Interestingly, a much greater proportion of patients on hemodialysis felt that the choice had been made by the medical team rather than by either themselves or by joint decision [29].

Geography and sociocultural influences: home dialysis, peritoneal dialysis or hemodialysis, is a much more attractive proposition if the alternative is a long journey to the dialysis facility. For example in New Zealand, in 1990 only 58% of dialysis patients lived in cities with dialysis facilities. As a result, 50% of patients received peritoneal dialysis and 32% home dialysis. In countries, such as Japan, most patients prefer to receive their medical care in a hospital setting [27]. They feel that is not appropriate for treatment to be done in the home and are often reluctant to take responsibility for delivering their own care, as a result only 6% of Japanese dialysis patients are on continuous ambulatory peritoneal dialysis.

3. Medical indications for peritoneal dialysis and hemodialysis

The majority of patients with ESRD are suitable for treatment with either peritoneal dialysis or hemodialysis. There are no completely reliable data comparing mortality or morbidity for these treatments and it is difficult to envisage an ethically acceptable trial where patients are allocated randomly to different dialysis modalities [30,31].

3.1. Contraindications to dialysis modalities

3.1.1. Peritoneal dialysis

There are few situations where there is a consensus that peritoneal dialysis is contraindicated. The consensus panel of the NKKF-DOQI has agreed the following relative contraindications to peritoneal dialysis [32]:

- Fresh intra-abdominal foreign body (e.g. aortic graft, ventriculo-peritoneal shunt): patients with prosthetic aortic grafts have been successfully treated with peritoneal dialysis. Hemodialysis is usually used initially for up to 16 weeks to allow the graft to be covered with epithelium and so avoid the risk of graft infection via peritoneal dialysate. However this risk must be balanced against that of bacterial seeding from the patient's hemodialysis access.
- Body size limitations and intolerance of intra-abdominal fluid volume: body size can be a problem at both ends of spectrum. The effect of increased intra-abdominal pressure can be particularly marked in patients with chronic respiratory disease, with low back pain and with large polycystic kidneys. In general, it is hard to predict a patient's tolerance of intra-abdominal fluid and so these limitations usually appear after a patient has started peritoneal dialysis.
- Bowel disease and other sources of infection: the presence of ischemic bowel disease, inflammatory bowel disease or diverticulitis is likely to increase the incidence of peritonitis due to organisms passing through the bowel wall into the peritoneum. Abdominal wall infection may lead to peritonitis via the exit site and catheter tunnel.
- Severe malnutrition or morbid obesity: patients should ideally commence peritoneal dialysis in an adequate nutritional state. Severe malnutrition may lead to poor wound healing and to leakage from the catheter tunnel. In addition peritoneal protein losses during dialysis may exacerbate hypoalbuminemia. At the other end of the spectrum it may prove difficult to satisfactorily place a catheter through the abdominal wall in patients with morbid obesity. Thereafter absorption of glucose from the dialysate may contribute to further weight gain.

3.1.2. Hemodialysis

Contraindications to hemodialysis are few. Access to the circulation can usually be obtained even in patients with extensive vascular disease or previous surgery. An aversion to needle puncture of the arteriovenous (A-V) fistula is common in the early stages but can usually be overcome by careful use of local anaesthetic and nursing encouragement. Some patients with severe cardiac disease may not tolerate the shifts in volume and electrolytes that occur during hemodialysis treatment. However, there are no objective measurements that will reliably identify such patients. Severe coagulopathy may make management of anticoagulation for the extracorporeal circuit difficult.

4. Vascular access for hemodialysis: Surgical considerations

The maintenance of adequate, durable vascular access for hemodialysis is essential for the wellbeing of the patient with ESRD. The provision of hemodialysis requires repetitive vascular access that can achieve a blood flow in excess of 350 mL/min. If vascular access cannot be achieved for even short period of time the patient will die from uraemia. Hemodialysis is

employed in chronic maintenance hemodialysis, acute renal failure and elimination of poisons from the body. For the provision of chronic maintenance hemodialysis the requirements for vascular access are very different from those for acute hemodialysis.

5. Vascular access for acute hemodialysis

5.1. Dual-lumen cuffed catheters

The vascular access requirements for acute hemodialysis are best served by the use of dual lumen, non-cuffed, temporary catheters. These catheters are made of a variety of materials including polyurethane or polytetrafluoroethylene. These materials have the useful property that at room temperature they are rigid, which facilitates their insertion, but when in place, they achieve body temperature and become much more flexible. Dialysis catheters are most commonly placed in the femoral, subclavian or jugular vein. Each of these sites has advantages and disadvantages depending on specific clinical circumstances. The femoral vein is in most patients the easiest site to insert a catheter and is associated with the lowest risk of life threatening complications. The major disadvantages of using the femoral vein are that the patient must remain recumbent while the catheter is in place and the high rate of infection if the catheter is left in place for more than 72 hours. It is preferable to use femoral catheters of 24 cm length as the recirculation in these catheters has been shown to be considerably lower than in the shorter 15 cm catheters. For patients who require longer periods of renal replacement (>72 hours and <3 weeks), a dialysis catheter placed in the jugular vein is preferable. The acute complications associated with both jugular and subclavian line insertion are similar. However subclavian line insertions are associated with the longer-term complication of subclavian vein stenosis, thus compromising the use of ipsilateral limb for long term vascular access. Catheters placed under aseptic conditions in either the jugular or subclavian vein may be left in place for up to 3 weeks. Complications associated with subclavian or jugular catheters include pneumothorax and arterial or great vein puncture with associated mediastinal, pleural or pericardial haemorrhage. The risk of great vein perforation is probably greatest in patients who have previously had multiple line insertions and have developed subclavian vein stenosis. Patients with a previously documented subclavian vein stenosis should never have a temporary catheter inserted on that side. It is imperative that a chest X ray is taken prior to the initiation of hemodialysis after either jugular or subclavian lines are inserted. This is to exclude the development of either a pneumothorax or hemothorax and to confirm that the catheter is in a position compatible with the desired vessel. If there is any doubt that the tip of the catheter is within a great vein, a small amount of contrast should be injected into the catheter under fluoroscopic control.

Although a far inferior choice for vascular access than a primary artero-venous (A-V) fistula or polytetrafluoroethylene (PTFE) graft, dual-lumen cuffed catheters have assumed an important role in the provision of vascular access for ESRD patients. Whenever possible some form of vascular access other than a cuffed catheter should be sought for a patient who has a

prognosis of more than 6 months. In our opinion the cuffed catheter is best used as a bridge between failed access and the establishment of permanent access.

6. Permanent vascular access

There is no doubt that a pre-emptively placed forearm primary A-V fistula is the most effective form of long-term vascular access for the uremic patient. It is important for physicians caring for patients with renal insufficiency to begin making plans for the provision of renal replacement therapy at an early stage and this usually begins when creatinine clearance is < 25 mL/min or serum creatinine > 4 mg/dL. Pre-emptive planning for the provision of vascular access is certainly cost-effective; it avoids emergency placement of femoral or subclavian catheters and also reduces hospital admissions for infection and temporary access failure.

7. Types of permanent vascular access

7.1. Primary fistula

In 1962 Cimino and Brescia described the technique of anastomosing the radial artery to the adjacent veins [33]. This technique allowed repeated puncturing of veins for dialysis access. The most frequent problem associated with A-V fistula is a failure to mature, as manifested by early thrombosis or inadequate blood flow rates. For patients in whom it is not possible to create a primary radio cephalic A-V fistula, an upper arm brachiocephalic fistula is a second best alternative and preferable to the use of a polytetrafluoroethylene (PTFE) graft. An upper arm brachiocephalic fistula takes few weeks to mature. Up to 80% of primary A-V fistulae will be functioning 3 years after creation.

7.2. PTFE grafts

PTFE was introduced in 1976 as a material for vascular bypass grafts. Since that time this material has become the mainstay for vascular access in dialysis when autologous A-V fistula is either technically impossible or has failed to mature. Using PTFE as a conduit, a fistula is created between an upper limb artery and vein.

More than 80% of the vascular procedures performed in the US [34]. Recent studies have demonstrated that the use of PTFE grafts is actually increasing rather than decreasing. These discrepancies between the US and other parts of the world have been attributed to the increased age of the dialysis population in the US and the increased proportion of ESRD patients with diabetes and with poor quality vessels that provide inadequate vascular access, as well as to the surgical practices that have evolved. More than 40% of patients who present ESRD in the US have not had vascular access created prior to the initiation of hemodialysis. Studies looking at the survival of PTFE grafts have noted cumulative patency rates for PTFE grafts of between 63-90% at 1 year and 50-77% at 2 years; fewer than 50% survive beyond

the third year. Newly inserted PTFE grafts should not be needed for at least 14 days because adhesions of the subcutaneous tunnel and graft has not yet occurred; potential bleeding into the graft tunnel and hematoma thereof may ruin the access site.

Prior to the creation of a new vascular access route, it is important to evaluate the patient for possible central vein stenosis. Clinical clues that should raise suspicion include oedema in the extremities, collateral vein development, differential size of the extremities, and current or previous placement of a cardiac pacemaker. If any of these findings are present the patient should undergo venography or duplex ultrasound. If venous stenosis is identified, it is preferable to plan access for the contralateral side if possible, although we have had occasional success in performing angioplasty on proximal veins and then proceeding with A-V fistula or PTFE graft insertion.

8. The importance of preparation for dialysis

Every patient would make an informed choice between peritoneal and hemodialysis after a period of counselling and preparation, unfortunately RRT is frequently started in less than ideal circumstances. Reports from both Europe and US clearly document the excess of morbidity and mortality associated with patients presenting late in ESRD and requiring RRT as an emergency procedure [14,15]. In fact patients starting RRT as an emergency usually receive hemodialysis and require a temporary CVC. Compared with non-emergency patients, their length of hospital stay is significantly greater and during this time there is a higher incidence of major complications and death. Data from USRD report [1997] showed that 25% of hemodialysis and 16% of peritoneal dialysis patients stated that a nephrologist first saw them less than one month before starting RRT; many of these patients would not have sought any medical attention prior to their presentation but it is clearly important that GPs promptly refer these patients for a specialist opinion.

Predialysis care by the nephrologist is focused on preventing or treating complications of CKD, preserving residual renal function, ensuring that the patient has sufficient understanding of his condition to choose between different RRT, and then arranging for appropriate access to be created in time before dialysis is required. In addition to the nephrologist giving advice, further benefits may be gained if patients are offered a multidisciplinary educational program.

Although few clinical trials have been conducted, there is enough evidence of clear benefits of CKD education [35-41]. Early patient education is highly effective when focused on health promotion, shared decision-making and discussion of treatment options [36]. In one randomized, controlled trial on patient education, a one-on-one educational session followed by phone calls every 3 weeks significantly extended the time to requiring dialysis [38]. *Post hoc* analyses from this clinical trial, as well as findings from other observational studies, demonstrate a variety of additional benefits from patient education, including the following: reduced patient anxiety; reduced number of hospitalizations; reduced numbers of emergency room and physician visits; increased likelihood that the patient will remain em-

ployed in work and be more adherent to therapy; and reduced mortality [37,39,40]. Furthermore, results from several studies have demonstrated a substantially reduced need for CVCs following patient education [40,41]. Consequently, it is important to maximize these benefits by engaging patients in CKD education prior to planning dialysis access placement. Patient education involves messengers, messages, receivers and a process. Before patient education can begin, the physician must initiate the discussion of what is often called breaking the bad news [42,43]. Patients do not want insensitive truth telling but prefer for the truth to be told with support to assist them in decision-making [44]. It is estimated that it takes an average of five encounters before individuals actually understand the message; therefore, patient education on CKD should be iterative [45]. The initial message should be delivered in a private room that is free of interruptions, and preferably when the patient has a supportive friend or relative with them [45]. Components of successful CKD education programs have also included individualized and ongoing education throughout the course of the disease, tours of dialysis facilities, meeting patients who are undergoing treatment with different dialysis modalities, use of videos and written materials, and behaviour changing protocols with small group problem-solving activities [37,46,47]. These and other strategies can be incorporated into any CKD education program. The educator needs to possess skills in patient communication and to understand the nature of the patient's barriers to receiving the information.

Presenting treatment options to the patient is a major undertaking for the educator, and offering decision support is an important goal of successful CKD education. There is a large variability in the uptake of home dialysis options (peritoneal dialysis or hemodialysis) between centres, regions, and different countries [6]. Data from the USA indicate that the low uptake of peritoneal dialysis in the country does not reflect patient choice but is instead more often a reflection of the choice not being offered to patients by healthcare providers [10,11]. Results from recent studies indicate that the 5-year and 10-year survival rates of patients treated with in centre hemodialysis are equivalent to survival rates with peritoneal dialysis [48]. Accordingly, for the vast majority of patients with CKD, decisions about dialysis modality should be based on what fits best with their lifestyle a decision that patients and their families must make for themselves [49]. Widespread, comprehensive CKD education will also empower patients to assume responsibility for their dialysis care, thereby increasing the uptake of home dialysis options. Expansion of home dialysis therapy is likely to be safe as the equivalency of outcomes of home peritoneal dialysis with in centre hemodialysis are maintained even when much larger proportions of patients are treated with the former therapy [48]. This therapy is also potentially more cost-effective given the lower societal costs for providing peritoneal dialysis, compared with in centre hemodialysis, in many countries[50].

The discussion about treatment options should begin with open questions and can be followed by introducing the two choices available to patients, dialysis or MCM. If the patient's preference is for dialysis, the choice of home dialysis versus in centre dialysis should be discussed next. Notably, fear and/or lack of knowledge of home dialysis has been shown to dissuade many patients from selecting this option [51]. One of the goals of patient education

should be to offer patient support and help overcome such fear. Regular contact between the educator and the patient over the weeks to months after starting education is important in the process of decision-making. However, it should be noted that the patient's choice of dialysis modality is simply the treatment with which they begin RRT, as many patients will actually transition between different therapies (for example, changing dialysis modalities, or from dialysis to transplantation and possibly back to dialysis again).

9. When RRT should be started?

In the 1990s, expert groups recommended that initiation of dialysis be considered when renal function declines to a predetermined level (mean of urea and creatinine clearance of ≤ 10.5 ml/min/1.73 m²) [52]. Over the past years, however, the mean estimated Glomerular Filtration Rate (eGFR) of patients starting dialysis in the USA has progressively increased [6,53]. Notwithstanding this change over time, there is no relationship between the duration of pre-dialysis nephrology care and eGFR at the time of starting dialysis [54]. Furthermore, patients who start dialysis with a high eGFR are as likely as patients with a lower eGFR to use CVCs as the first dialysis access [54]. These observations suggest that nephrologists might be recommending patients for dialysis for the same general reasons, irrespective of eGFR. For example, individuals with low levels of serum creatinine (and a high eGFR) might need to start dialysis if they are likely to have poor tolerance for the consequences of renal function decline. Findings from several observational studies demonstrate that patients who start dialysis with a high eGFR are substantially more likely to have characteristics associated with an increased mortality (such as older age, male sex, white ethnicity, diabetes mellitus and other cardiovascular comorbidities). Concerns about the rising trend of starting RRT in patients with a high eGFR have been raised, particularly since many studies now show a direct association between a high eGFR at the time of RRT initiation and subsequent risk of death [54-64]. This risk persists even after statistical adjustment for potential confounders and also when analyses are restricted to the healthiest subgroup; however, there is always the issue of residual confounding in observational studies [57,58]. Furthermore, with decreasing renal function, muscle mass becomes a more important determinant of serum creatinine level than is eGFR [65]. It follows then that the association between high eGFR and an increased risk of death might, in part, be a reflection of the effect of cachexia (muscle loss causing lower levels of serum creatinine at any given level of eGFR) on mortality [56]. Given the limitations of observational studies, it is fortuitous that the importance of renal function at RRT initiation has been tested in a randomized controlled clinical trial. In the IDEAL study, there was no difference in terms of survival between patients randomly assigned to begin dialysis early (at a creatinine clearance of 10–14 ml/min) or late (at a creatinine clearance of 5–7 ml/min) [66]. It is important to note that three-quarters of patients randomly assigned to starting dialysis late actually needed to begin treatment earlier, primarily owing to the development of uremic symptoms [66]. These data suggest that initiation of dialysis simply when renal function approaches a predetermined threshold, as measured by eGFR, is not appropriate. Indeed, it seems that dialysis can be safely delayed in otherwise

asymptomatic individuals with advanced CKD. This is particularly important in patients in whom a permanent dialysis access is not ready for use, and deferring dialysis might mitigate the need for CVCs. However, findings from the IDEAL study also indicate that it might not be universally possible to defer initiation of dialysis until patients reach an eGFR < 7 ml/min/1.73 m² as many patients with advanced CKD can develop uremic symptoms at high levels of renal function [66]. In addition to the indications for emergent dialysis (hyperkalaemia, volume overload, pericarditis and encephalopathy), dialysis therapy has been shown to be effective in ameliorating uremic anorexia and is associated with improvement in measures of protein energy wasting [67]. Hence, it is important to observe patients with advanced CKD for the early development of symptoms and/or uremic complications and begin dialysis at an appropriate time such that it precludes the development of complications that might require hospitalization or emergency intervention.

10. Conclusions

It is extremely important to ensure that the resources dedicated to ESRD treatment are used to best effect. If the greatest benefit is to be gained from RRT, the importance of selection and preparation of patients reaching ESRD must be recognised and addressed. Educating these individuals about CKD might, nevertheless, facilitate their participation in selection of RRT modality and might also result in an earlier transition to a permanent RRT. Several studies show that those measures lead to a reduction of the proportion of patients who start RRT as an emergency procedure (higher incidence of major complications and death) [14,15] and to an increasing number of patients that actively participate in developing their care plan and who start dialysis with a permanent access [68,69].

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