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CKJ REVIEW

An update on absolute and relative indications for dialysis treatment modalities

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ABSTRACT

Background. Choosing a dialysis modality is an important decision for people to make as their kidney failure progresses. In doing so, their options should be informed by any absolute or relative indications that may favour one modality over another.

Methods. In creating this update, we reviewed literature using a framework that considered first, high-level outcomes (survival and modality transition) from large registry data and cohort studies when considering optimal patient pathways; second, factors at a dialysis provider level that might affect relative indications; and third, specific patient-level factors. Both main types of dialysis modality, peritoneal (PD) and haemodialysis (HD), and their subtypes were considered.

Results. For most people starting dialysis, survival is independent of modality, including those with diabetes. Better survival is seen in those with less comorbidity starting with PD or home HD, reflecting continued improvements over recent decades that have been greater than improvements seen for centre HD. There are provider-level differences in the perceived relative indications for home dialysis that appear to reflect variability in experience, prejudice, enthusiasm, and support for patients and carers. Absolute contraindications are uncommon and, in most cases, where modality prejudice exists, e.g. obesity, Adult Polycystic Kidney Disease, and social factors, this is not supported by reported outcomes.

Conclusion. Absolute contraindications to a particular dialysis modality are rare. Relative indications for or against particular modalities should be considered but are rarely more important than patient preferences.

Keywords: automated peritoneal dialysis, diabetes, heart failure, home dialysis, obesity

INTRODUCTION

The choice of dialysis modality is inevitably one that involves compromises. Few people want to start dialysis and their personal preferences and what is considered feasible or the 'best' option by their clinicians may not align. Early findings from the Inter-CEPt study [1], which is examining the large variation in home dialysis use in the UK [2], point to dialysis modality choice being an act of faith for many, largely dependent on the trust placed by them in the clinical team. The success of a dialysis modality for any given individual is not simply a function of 'medical' suitability, but crucially dependent on the continued support and the effectiveness of the dialysis provider. For most people, both the main dialysis modalities, haemodialysis (HD) and peritoneal dialysis (PD) are feasible and a long life lived on kidney replacement therapy may well be best achieved by integrating more than one modality over time, typically in combination with transplantation [3, 4]. This update will look at the range of modality choices available and their relative and

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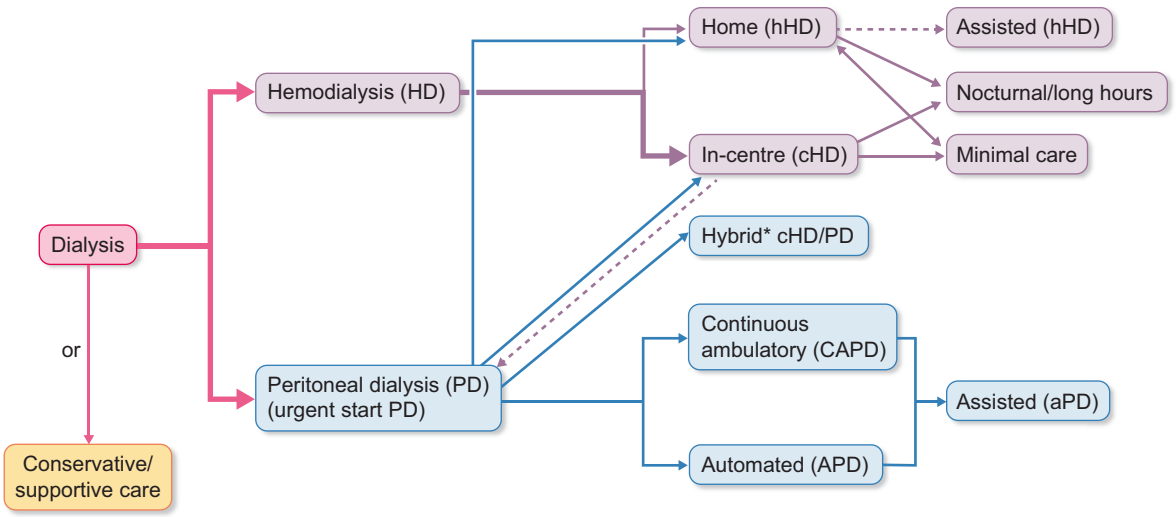

Figure 1: Hierarchy of dialysis modalities (reading from left to right) and their abbreviations. Arrows indicate potential patient pathways. For example, PD is more likely to lead to a transfer to HD compared than the other way around, but data supports the possibility of successful transfer from PD to hHD. *Hybrid cHD/PD is almost entirely confined to Japan where transplantation is relatively infrequent. See text for more detailed discussion of the different submodalities and potential pathways.

absolute indications, in the context of optimal patient pathways, provider-level limitations, and patient-level factors. Of course, when considering choice of dialysis modality, it is important to consider whether non-dialysis options (supportive care) might be more appropriate [5], but in this review we will focus on the pros and cons of different dialysis modalities.

Dialysis modalities and treatment pathways

In 2018 KDIGO held a controversies conference on dialysis initiation and modality choice, access, and prescription [6]. It noted that there is considerable global variation in the availability and practice of different dialysis modalities. Although there has been a proliferation in how the main dialysis modalities, HD and PD can be delivered, expressed hierarchically in Fig. 1, this has not translated into their availability for all people with kidney failure. Nevertheless, it would be important to consider how these different modalities and submodalities affect clinical outcomes and to consider whether this constitutes a contraindication, relative or absolute for some patient groups.

Several studies published over many years have compared the outcomes of HD with PD, based entirely on observational registry data, given that trials have not proved able to randomize sufficient people to obtain generalizable findings. For the last 10 years or so, these data have shown that for all people new to dialysis, 5-year survival is equivalent on these modalities [7–11]. Many have shown an early survival benefit for younger, less comorbid individuals starting on PD, and this had been attributed to several things including case-mix (for example, transplant eligibility), 'as is' bias, i.e. selection bias that favours patients with certain characteristics (e.g. in the case of PD this might reflect its preferential use by people with greater autonomy), avoiding the risk of unplanned start in HD with a line rather than a fistula [12] and better preservation of residual kidney function [13]. Given that no observational data can fully account for these biases, it cannot be certain which of these factors dominates, but what is clear is that the relative improvement in survival observed over the last 20 years for both of the main modalities has been about double that for PD when compared to HD, and the early survival advantage has extended for longer periods of time as documented by the European Renal Registry (ERA-EDTA RR [14]), Australia/New Zealand database (ANZDATA [15]), and the US renal data system (US-RDS [16]). This relative benefit does not appear to be due to a powerful patient selection effect as the doubling in PD rates since the start of the altered care bundle in the USA in 2008 has been associated with a sustained improvement in PD outcomes [17]. This would suggest that, all being equal with respect to patient preference, PD is relatively indicated in younger, fitter patients, for example as a bridge to transplantation, whereas for a less than optimally planned start with a dialysis line, HD is relatively contraindicated. This has led some centres to routinely default to starting dialysis urgently with a PD catheter, avoiding HD line dependency with good results reported in single centre experience, systematic reviews, and one recent trial [18–21].

The only subgroup of patients in these comparative registry analyses that has raised concern is those with diabetes. Some have suggested that older, diabetic women, once they have been on PD for a few years, have worse survival [22, 23]. However, more recent analyses have not confirmed this (ERA-EDTA RR, ANZDATA) [14,15] and the ERR indicates that it is younger diabetic women who appear to be at greater risk than men, a finding that is common to both modalities [24]. Thus, there does not appear to be a contraindication to either modality according to diabetes status or gender.

Another important subgroup to consider is those returning to dialysis after transplantation. In the past, concerns have been raised that these individuals are less suitable for PD due to an infection risk and more rapid loss of residual kidney function [25–27]. This concern is not borne out by the ANZDATA analysis, which shows that survival and transfer to HD risk is not different to new starters on PD [28]. It is common practice to continue low dose immunosuppression in the context of continued graft function in this situation, but this approach has not been tested in a randomized trial.

By contrast, the risk of needing to transfer to HD from PD, previously referred to as technique failure, is not symmetrical, being more frequent than modality transfer in the opposite

direction. Transfer to HD is important because it is associated with an early risk of mortality, observed in all the large national and international registries (ERA-EDTA RR, CORR, ANZDATA, and US-RDS [29]), although this risk has been falling steadily for the last 20 years. Transfer from PD to HD because of infection, the most common reason, or due to social factors was associated with least good survival following modality switch in the ANZDATA [30]. The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) has confirmed that peritonitis remains by far the most common reason for transfer to HD, responsible for just under one half of transitions [31, 32]. However, this is not the most important determinant of the large national differences in time spent on PD therapy, which are largely governed by the chances of receiving a kidney transplant [33]. It is not possible to predict with certainty who will have a high peritonitis risk before their starting PD and in fact this is as much a function of centre performance in peritonitis prevention, as will be discussed in the next section. Patients returning to PD after a brief period on HD due to infection requiring catheter removal do not experience an increased risk of peritonitis going forward [34]. Fear of getting peritonitis is often given as a reason for not selecting PD, by both clinicians and patients, but perceived peritonitis risk should not be a contraindication to PD as a rule and should be balanced with the risks associated with HD access-related infection. HD is associated with five times the risk of hospital acquired bacteraemia [35], especially when using a central line compared to fistula [36] and the potential for associated endocarditis.

Looking further down the hierarchy of dialysis modality choices (Fig. 1), studies reporting the outcomes for home HD (hHD) have consistently reported the best survival rates [37, 38]. However, this is likely to represent the high selection pressures at the patient-level given the relatively low absolute numbers and proportions of patients opting for this modality, although the survival benefit remains after adjusting for common comorbidities. Home HD is especially attractive in individuals who wish to continue their treatment at home but are no longer able to do PD and are, for whatever reason, challenging to transplant. ANZDATA has tracked patients transitioning from PD to hHD and shown that their survival advantage is not lost by integrating these two therapies, giving support to this strategy, although again it is clear that these individuals were highly selected from a much larger pool transitioning to centre HD (cHD) [4]. Most of the published data on hHD reflects similar dialysis regimes to cHD, but undoubtedly some of these individuals do longer hours (e.g. overnight, nocturnal) or extra sessions. Relatively small randomized controlled trials undertaken by the frequent HD network have not shown survival benefits for starting hHD with nocturnal frequent dialysis, an intervention that was associated with more rapid loss in residual kidney function [39]. It could therefore be argued that this approach is relatively contraindicated in people with well-preserved residual kidney function, who may in fact benefit from an incremental start to dialysis [40]. There is a growing appetite for incremental dialysis, which does not appear to be harmful but remains quite controversial [41], (both HD and PD) and as yet there is insufficient data to recommend this strategy, which by definition would be indicated in those with significant residual kidney function [42, 43].

In terms of submodalities of PD, the choice between continuous ambulatory PD (CAPD) and automated PD (APD) has shown a general trend towards using the latter when it is available (PDOPPS data submitted for publication). There is no clear evidence of a survival or transfer to HD advantage for either of these modalities, supporting the view that the main indication for choosing these treatments should be patient preference (PDOPPS, ANZDATA) [15, 44]. Some countries, for example Finland and China have found superior survival in APD [45, 46], but it is likely that this reflects patient selection factors. Both can be used to support assisted PD (aPD), aCAPD being initially well developed in France [47, 48], with aAPD available in several countries including the UK [49] and Canada [50], but very variably used in the rest of Europe [51]. As would be expected for this dialysis population, mortality rates are relatively high, but not worse than cHD, whereas transfer to HD is relatively less frequent, explained largely by the competing risk of death [52]. aPD has been shown to be similar to cHD in terms of most patient reported outcomes for the elderly frail, with the exception of treatment satisfaction which does appear to be greater for aPD [53].

The use of hybrid dialysis—i.e. both PD and cHD in combination—is a practice almost exclusive to Japan. Indications vary, but the primary reasoning for this approach relate to concerns of obtaining sufficient ultrafiltration and solute clearance once residual kidney function has gone, in the context of a country that has experienced relatively high levels of encapsulating peritoneal sclerosis [54] and a low transplantation rate resulting in long periods of time on treatment [33]. Generally, outcomes are good but rates vary considerably by unit [55]. Evaluation of outcomes on hybrid dialysis is currently the subject of analysis by the PDOPPS.

In summarizing the big picture (see Fig. 2), whether looking at all-comers or important subgroups such as diabetics and the frail elderly, there is nothing to suggest an absolute contraindication for the use of either the main modalities or their subcategories. There is a relative indication to favour PD in less comorbid individuals, especially when residual kidney function is still present either as a bridge to transplantation or as a strategy to avoid HD using a central line, but these benefits should be part of shared decision making and are not such that they should override patient preferences.

Are dialysis providers an issue?

Not all dialysis providers offer all modalities and even when they do, they are variably successful in making these available. Whereas at first sight this would not seem to be an issue of whether a specific modality is indicated or not, in practice it is a major determinant of who gets which treatment modality. The reasons for this are multiple and include financial constraints and how health services are organized, but there are particular issues at the dialysis facility level that affect whether a modality is perceived as contraindicated or more strongly indicated.

This especially applies to the use of home dialysis therapies, the subject of a recent KDIGO controversies conference, which highlighted several dialysis provider factors that translate into perceptions of patient suitability [56]. First, it is clear that unit size and experience are important factors [57, 58], and these are especially challenges for facilities early in their process of setting up these services. It could be argued that until the facility has gained experience in provision of home dialysis, including aPD, that it would be wise to start with relatively low risk patients, which would inevitably lead to some restrictions in offering (a)PD or hHD to people in whom in other more experienced centres these treatments would not be contraindicated. This may especially apply to patients with a perceived high infection risk even though this cannot be predicted. In fact, data from ANZDATA and PDOPPS show that dialysis facility factors are more important than patients level factors when it comes to PD peritonitis prevention and treatment [32, 59].

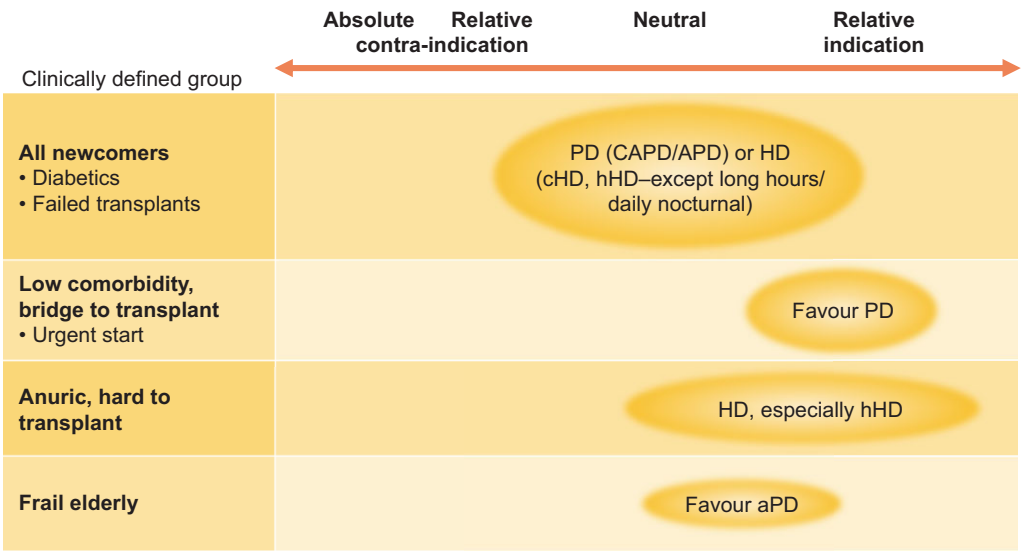

Figure 2: The horizontal double pointed arrow represents the spectrum of modality indications from absolute contraindication (to the left) to relative indication (to the right), according to large patient groupings as clinically defined on the left side of the figure. In no case is there a clear or absolute indication or contraindication, and in most cases the choice of modality on medical grounds is neutral, indicating that the choice of modality should focus on patient preferences.

Second, it seems that when it comes to 'relative' contraindications to PD that clinicians interpret these very differently. In the PDOPPS study, directors of PD services were far more likely to see a patient as being suitable for PD than directors of HD services across a wide range of patient characteristics, including having diabetes, age over 75, previous laparoscopic cholecystectomy, planned kidney transplant within 6 months, presence of a functioning fistula, wheelchair dependency, living alone, BMI >30 kg/m^2, and having polycystic kidney disease (APKD) [60]. The same study also found similar, albeit less dramatic differences when looking at clinician perceptions of known barriers to home therapies, such as financial burden to patients, their perceived capability of doing the therapy, lack of social support, and perceived quality of care. In other words, clinicians have strong prejudices that influence their interpretation of the relative contraindications to dialysis modalities. This is reflected in the large variation in the uptake of home therapies in the UK [2], where the healthcare system does not remunerate clinicians differently by modality, but it appears that clinician enthusiasm for home dialysis is a major determinant of the likelihood of an individual getting a home-based modality [61]. These inequalities of access are magnified in people from ethnic minorities and lower socio-economic groups [2, 62]. Undoubtedly enthusiasm for home therapies will lead to making available the extra support that is frequently required to enable patients with more complex needs to do home treatment [51, 63].

Specific patient groups

There are very few absolute contraindications for the two main dialysis modalities. In both cases the ability to obtain peritoneal or vascular access is essential. In the case of PD, a functioning peritoneal membrane is absolutely necessary, and a history of major abdominal surgery associated with extensive peritoneal membrane adhesions would be the main cause of losing this. Even then, it is reasonable to attempt laparoscopic PD catheter insertion as it is often impossible to predict whether a membrane will function adequately regardless of adhesions. PD is not advised in the context of an enteric fistula or stoma but can be done with a ureteric conduit (provided a PD catheter can be placed) and with a gastric feeding tube, provided the latter has a fully healed track. Gastric tube feeding is regularly undertaken in children on PD. For HD the ability to sustain sufficient blood pressure during a dialysis session so that the treatment can actually be delivered is essential. All these circumstances are relatively uncommon. However, as we have seen, there are certain patient groups that raise particular concern and lead to varying interpretations of what are seen as relative contraindications and these will be discussed separately next, and are summarized in Fig. 3. The issue of diabetes, the frail elderly, and specific patient pathways have already been discussed.

Obesity

Perceptions that obesity should be considered as a relative contraindication to PD seem to stem from the assumption that the use of glucose containing dialysate will make this worse, reducing survival and access to transplantation. In reality, there is no strong evidence for this and in fact data indicates that fat weight gain is greater in HD [64]. Comparison of body composition between HD and PD patients matched for age, comorbidity and gender show no difference in fat mass, and relatively better-preserved lean tissue in PD, which may be in part better preserved because of calories derived from dialysate [65, 66]. It is also the case that increased BMI does not appear to translate into a survival disadvantage in either dialysis modality, indeed may be protective in HD patients [67, 68]. Daily dialysate glucose exposure does have a detectable association with increased blood glucose levels, but the effect is small and not associated with clinical outcomes [69]. A much greater concern for survival in dialysis patients is low BMI [70, 71] and glucose derived calories from dialysate may be of value [72]. Increased BMI has been associated with a modest increased risk of transfer to haemodialysis and risk of exit site infection [73], although this was not observed in the PDOPPS [74]. This risk is not more than the modest

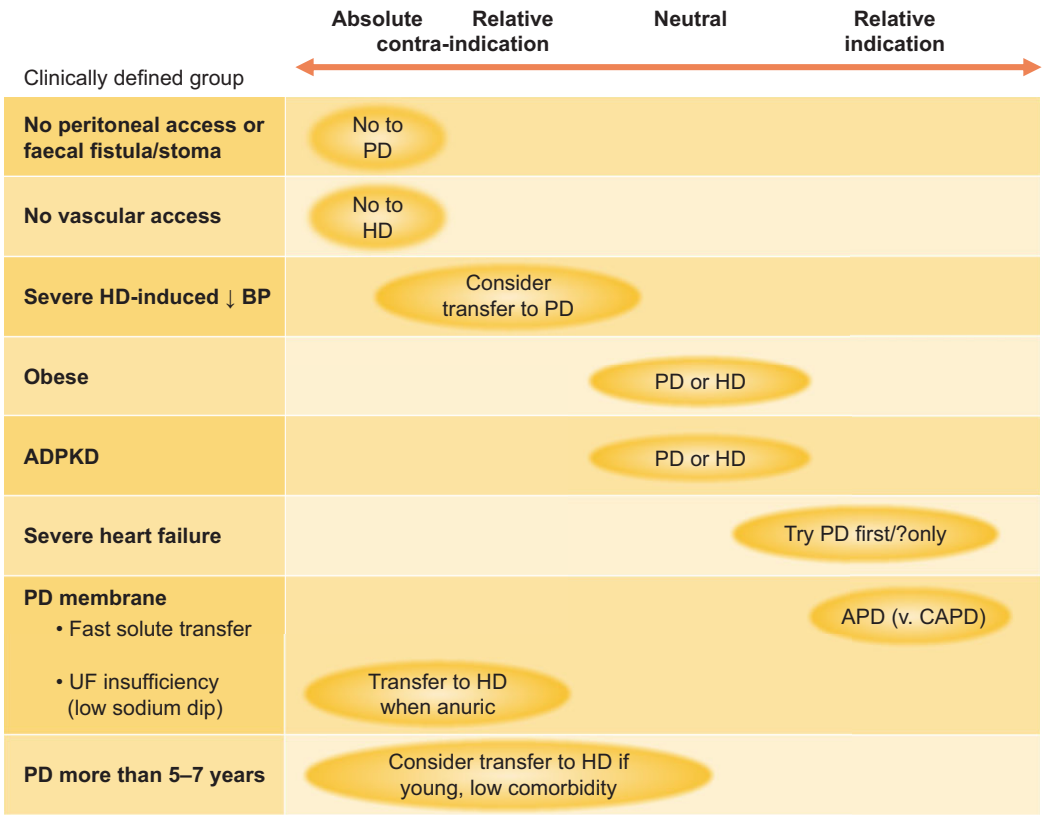

Figure 3: As in Fig. 2, the double ended arrow represents the spectrum of modality indications, but this time according to specific patient-level groups in which there is either a clear contraindication or where specific concerns have been raised. For example, lack of dialysis access is an absolute contraindication.

increase in risk of modality transfer in men compared to women. Severe obesity (BMI > 40) is a challenge to PD access and requires the insertion of pre-sternal catheters by surgeons with expertise in this method [75].

Low albumin and malnutrition

Blood albumin levels are lower in PD patients compared to HD, which can lead to reservations in recommending PD in people with low levels or malnutrition pre-dialysis. The reason for low albumin levels in dialysis patients is the negative effect of systemic inflammation on albumin synthesis (which is otherwise increased in non-inflamed PD patients, compensating for increased peritoneal protein losses), and additionally in PD, intra-peritoneal inflammation that increases the peritoneal surface area and leakiness to protein, exacerbating the peritoneal losses [76]. However, it is only poorly correlated with malnutrition once inflammation, the main determinant of muscle wasting and frailty in dialysis patients, is taken into account. A low albumin is associated with an increased risk of death in both HD and PD, but the relative adjusted risk is a little higher for HD, especially at lower albumin levels [77]. A low albumin and inflammation are associated with an increased risk of tissue oedema in both HD and PD patients, but not of intravascular volume expansion in PD [78, 79]. In the rare cases where a low albumin in PD is clinically problematic, switching to conventional HD will increase the albumin levels on average [80]. It is not known whether this applies to HD using 'leakier' membranes for haemodiafiltration.

Adult polycystic kidney disease (ADPKD)

Due to the perception that the presence of large polycystic kidneys might prevent PD from working, or be too uncomfortable, this is sometimes considered as a contraindication. ADPKD is associated with an increased risk of leaks and hernias, but there is no evidence of a survival disadvantage. Data from the ERA-EDTA shows that outcomes for APKD have improved for both PD and HD since the 1990s, with no difference by modality [81]. Some studies have indicated a survival advantage for PD and none a disadvantage [82].

Heart failure

Severe heart failure associated with frequent hospital admission for fluid overload, frequently associated with hypotension is sometimes considered as an indication for dialytic therapy. There is observational data, including systematic reviews showing that PD can be used in this setting with reasonable outcomes given the overall poor prognosis of these patients [83, 84]. The main advantage appears to be a reduction in hospital admissions. Randomized controlled trials have proved very difficult to conduct [85]. If it is considered clinically appropriate, a trial of therapy with PD is indicated as a first option.

Reduced peritoneal membrane efficiency and time on therapy

Successful PD is dependent on a peritoneal membrane that can deliver adequate ultrafiltration, especially as residual kidney function declines. This has consistently been demonstrated to be more important than peritoneal solute clearance [86]. For

how to assess membrane function and optimize therapy, the reader should refer to the recent ISPD guidelines [87]. Briefly, the nomenclature has been revised, changing from ultrafiltration (UF) failure as defined by a single UF capacity cut-off, to *UF insufficiency*, recognizing that this is a continuum of membrane function. If due to rapid small solute transfer rate, then shortening exchanges using APD as the modality of choice makes logical sense, and this is supported by observational studies [88, 89]. If due to low UF capacity of the membrane and a reduced 1-hour sodium dip then high concentration glucose solutions will be needed and transfer to HD might be appropriate, especially if this is an acquired problem [54]. There is also the concern of developing encapsulating peritoneal sclerosis, for which time on therapy is the strongest risk factor, although acquired membrane injury remains a concern. Competing risk analysis indicates that this risk is very low in older, more comorbid individuals and all incident patients, but in the young, especially when transplantation is going to be difficult time on therapy should be carefully discussed [90]. The International Society of Peritoneal Dialysis position statement suggests that clinicians should adopt a shared decision-making approach when discussing this risk with patients, taking into account quality of life, effectiveness of PD, likelihood of transplantation, relative contraindications to HD, and patient preferences [54].

Children

Choice of dialysis modality is mentioned here for completeness, but given the relative rarity of irreversible kidney failure, the high use of transplantation and the complexity from early childhood to adolescence the reader is referred to the literature for more detail. PD is strongly indicated in infants (aged under 2 or < 8–10 kg) due to the technical challenges of HD (e.g. obtaining vascular access), but HD can be done if the expertise is available [91]. Overall survival and morbidity rates by modality for children and adolescents are independent of modality and the relative indications are largely determined by social factors and developmental requirements.

In conclusion, the choice of treatment modality should be less affected by absolute or relative medical indications than is perhaps perceived by many clinicians. This should be factored in to shared care decision making that in most cases should focus on the individuals' lived life on dialysis and how this is accommodated by an appropriate and well supported modality choice.

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