# Is Kt/V useful in elderly dialysis patients? Pro- and Con- arguments

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# **Abstract**

Current guidelines for dialysis specify a minimum Kt/V. For HD patients, minimum treatment time and frequency is also specified. The guidelines allow for modification to take account of renal function. The guidelines are not specifically aimed at the elderly and may not be appropriate all patients in this group.

Increasing age is accompanied by physiological and pathological changes with may modify the patient’s response to uraemia and dialysis. Frailty and multi-morbidity is likely but to a variable extent. Elderly patients could be more susceptible to the effects of uraemia and require a higher dose of dialysis. Conversely, the generation rate of uraemic toxins is lower in elderly patients, potentially reducing the need for dialysis. In the elderly, quality of life may be more adversely affected by multi-morbidity than uraemic symptoms so dose of dialysis may be less relevant. Higher doses of dialysis may be more difficult to achieve in the elderly and may be less well tolerated.

We conclude that the prescription of dialysis in the elderly should be individualized, taking multiple factors into account. An individualized Kt/V may be useful in controlling dialysis dose and detecting problems in the delivery. However, achievement of a specified Kt/V may not result in any benefit to an elderly patient and could be counter-productive.

# Introduction

Kt/V, is the urea clearance, expressed as a fraction of the body water volume. In haemodialysis, it is a measure of the dose of a single dialysis session[[[1]](#endnote-1)]. In PD it includes the effect of renal function and is a measure of clearance over a defined period, normally a week. Kt/V is one of the principal quality indicators for dialysis. Current guidelines for dialysis all recommend ensuring that Kt/V exceeds a specified minimum level. The guidelines do not explicitly consider the age or frailty of the dialysis patient in setting the minimum Kt/V [[[2]](#endnote-2)][[[3]](#endnote-3)][[[4]](#endnote-4)][[[5]](#endnote-5)].

For practical purposes, in Europe, a person may be considered elderly at age of 65 years. This originates from “Gesetz betreffend der Invaliditäts-und Altersversversicherung”, a law enacted in 1883 by Otto von Bismarck, regulating financial support in case of incapacity and in old age, defined as beginning at age 65. Since then, in many developed countries, the age of retirement has been defined more flexibly, taking biological functional capacity into account. In other parts of the world, particularly in underdeveloped and developing countries, the age of 60 is considered the limit between adulthood and old age. The WHO defines elderly as age 60 or over, which would include the majority of all dialysis patients. Current guidelines for treatment of the elderly disagree in the definition of ‘elderly’ or lack definition entirely [[[6]](#endnote-6)]. Dialysis patients are usually considered as elderly when they are over 75 years old [[[7]](#endnote-7)][[[8]](#endnote-8)]. For the purpose of searching and analysing the literature, we used age 65 or over as the definition of elderly. This value was selected after much discussion as higher age cut-off would exclude much of the literature and include a greater proportion of atypical ‘super-survivors’ with low multi-morbidity.

Frailty in dialysis patients has been defined as a combination of exhaustion, weakness, low physical activity and weight loss [[[9]](#endnote-9)]. Frailty has multiple causes in addition to advancing age.

A joint initiative of the European Renal Association-European Dialysis Transplant Association (ERA-EDTA) and the European Union of Geriatric Medicine Societies (EUGMS) prioritized the development of guidance on interdisciplinary referral of older patients with chronic kidney disease stage 3b-5 and listed “the usefulness of Kt/V” in this special population as a topic of interest[[[10]](#endnote-10)].

Effect of increasing dialysis dose

Variations in dialysis dose are likely to be accompanied by advantages and disadvantages (table 1) and the optimal dose of dialysis will take account of both. It is conceivable that the priorities for the elderly patient will differ from those of younger patients and the optimal dose will also differ.

Haemodialysis

The current European guidelines recommend a minimum of three dialysis sessions per week totalling at least 12 hours, with a Kt/V of at least 1.2 each session. This can be reduced if there is significant renal function. The recommendation was based on the findings of a re-analysis of the National Co-operative dialysis study (NCDS) published in 1982[[[11]](#endnote-11)]. Numerous observational studies have shown an association between Kt/V and outcome.

Peritoneal dialysis

Current guidelines recommend that the total of dialysis and renal Kt/V should be at least 1.7 per week. This was informed by Adequacy of PD in Mexico (ADEMEX) study[[[12]](#endnote-12)], one of the very few RCTs designed to investigate the effect of different Kt/Vs (it showed no benefit in increasing Kt/V above 1.7/week). Numerous observational studies suggested worse outcome associated with lower dose.

## How age and frailty may influence dialysis dose.

Increasing age is accompanied by physiological and pathological changes which could influence the generation of uraemic toxins and the ease at which they may be removed by dialysis (Table 2). These changes may influence the relationship between Kt/V and outcome and, therefore, the optimal dose of dialysis.

Metabolic rate and energy expenditure falls as a function of age in healthy individuals [[[13]](#endnote-13),[[14]](#endnote-14)]. On average, a person age 80 years will have a reduction in energy expenditure 20% lower compared to a 40 year old. In theory, the rate of generation of uraemic toxins will be reduced by a similar amount. Dialysis patients aged 65 or over have approximately 25% lower salt and protein intake compared to younger patients[[[15]](#endnote-15)]. Therefore, compared to younger patients, the elderly would tend to have lower serum concentrations of these toxins if clearance remains the same. In these circumstances dialysis dose could be reduced in elderly patients without allowing toxin levels to rise above those considered acceptable in younger patents.

Elderly dialysis patients tend to have lower interdialytic fluid weight gain [[[16]](#endnote-16)] and better compliance with sodium restrictions [[[17]](#endnote-17)]. This will tend to reduce the requirement for ultrafiltration allowing either a slower ultrafiltration rate at the same dialysis time or a shorter dialysis with the same ultrafiltration rate, compared to a younger patient.

Muscle contains relatively more water, especially intracellular water, compared to other tissues. The reduction in muscle mass, which accompanies increasing age[[[18]](#endnote-18)], results in relatively lower total body water volume[[[19]](#endnote-19)]. In general, the proportion of body water which is intracellular is lower in the elderly, compared to younger patients. Elderly persons with immobility have been shown to have increased total body water, compared to the mobile elderly[[[20]](#endnote-20)]. This is likely to be due to water retention. Body water volume, as V, has a major influence on Kt/V, regardless of the concentrations of uraemic toxins. When Kt/V is calculated using online clearance, a V calculated using anthropometric data is often used. This is likely to be highly inaccurate in the elderly. V calculated using bioimpedance may provide a better estimate [[[21]](#endnote-21)]. During intermittent dialysis, a rapid fall in solute concentrations in plasma causes a disequilibrium or difference in osmotic pressure between body compartments, which could cause symptoms. The magnitude of this disequilibrium will depend on initial solute concentration and the K/V ratio.

Elderly patients are more likely to have multi-morbidity, including heart failure, arterial disease and autonomic dysfunction. These conditions reduce the patients’ tolerance to HD ultrafiltration and increases the risk of hypotension during HD. Hypotension usually causes symptoms and may result in early termination of dialysis. Repeated episodes may result in damage to heart and brain[[[22]](#endnote-22)].

Older age is a risk factor for receiving a lower dialysis dose[[[23]](#endnote-23)]. This may be because age-associated cardio-vascular disease predisposes the patient to intra-dialytic hypotension, resulting in shortened or interrupted dialysis. Similarly, cardio-vascular disease may contribute to poor vascular access, resulting in inadequate extracorporeal blood flow or interrupted dialysis figure 1.

The multi-morbidity, likely in elderly dialysis patients, could render the patient more susceptible or sensitive to the effects of uraemia. On the other hand, survival and quality of life could be overwhelmingly limited by the multi-morbidity so that uraemia and dialysis dose could be irrelevant.

The frailty of advanced age may be associated with cognitive dysfunction, immobility, motor dysfunction and incontinence. These will cause logistical and practical problems in providing an adequate dialysis. The ability of the patient to become involved in their care will be reduced. The patient could be distressed by dialysis, especially when dialysis sessions are longer, more frequent or hospital-based.

## Palliative dialysis

Conservative management of end-stage renal failure, without dialysis is increasingly accepted as an appropriate option for selected elderly patients, especially those with severe multi-morbidity and frailty. It makes sense for the options for such patients to include an intermediate “palliative dialysis” aimed at controlling uraemic symptoms but not necessarily avoiding long-term complications[[[24]](#endnote-24)]. Such a “palliative dialysis” would be designed to have lower treatment burden than standard dialysis and may include twice weekly or shorter sessions with lower Kt/V. All available means for controlling symptoms and maximizing physical and cognitive function would be considered to augment the effect of dialysis. These might include non-dialysis treatments such as drugs, dietary restriction, maximising residual renal function, physical and psychological therapy in combination with dialysis. The risk that palliative options might be used as a means of ageist rationing of dialysis may be reduced by a rigorous patient-centred approach[[[25]](#endnote-25)].

## Twice weekly dialysis

In observational studies, patients dialyzing twice weekly have better preservation of renal function[[[26]](#endnote-26)] and improved survival [[[27]](#endnote-27)] compared to those dialyzing with conventional thrice weekly dialysis regimes. These associations are likely to be due to patient selection, patents with more renal function are more likely to be selected for and to remain on twice-weekly dialysis. Elderly patients may have lower rates of generation of uraemic toxins, and lower fluid weight gains so may be better able to tolerate twice weekly HD. An RCT is needed to compare outcome of twice weekly compared to thrice weekly dialysis in selected patients.

## Incremental dialysis

Renal function is known to contribute significantly to clearance during the first few years of dialysis[[[28]](#endnote-28)]. Residual renal function is known to have even greater effect on outcome than dialysis dose for both haemodialysis[[[29]](#endnote-29)] and peritoneal dialysis[[[30]](#endnote-30)]. The effect of renal function on fluid balance, reducing the need for ultrafiltration may be particularly important.

With incremental dialysis, residual renal function is taken into account in the prescription. Patients with significant renal function are prescribed a shorter, less frequent and/or less intense dialysis. The dialysis dose may be increased later to compensate for declining renal function. The combined effect of the renal function plus the reduced dose dialysis should be equivalent to or exceed what constitutes a full-dose of dialysis in an anuric patient.

Renal function has different effects on patients compared to dialysis, so it is not sufficient to simply add a function of dialysis dose (e.g. Kt/V) to a measure of renal function. Compared to standard full-dose dialysis, patients treated by incremental dialysis require more careful monitoring of fluid status, nutrition and the levels of key uraemic toxins to ensure that they are getting sufficient dialysis as renal function falls[[[31]](#endnote-31)].

Multiple observational studies have confirmed that patients with significant renal function has improved survival, compared to anuric patients[[[32]](#endnote-32)], even if dialysis dose is reduced as part of an incremental dialysis program[[[33]](#endnote-33)].

A recent large observational study found that there was no difference in survival between patients treated by incremental vs standard haemodialysis. However, when in patients with urine volume less than 600ml/day or renal urea clearance less than 3ml/min/1.73m2, incremental dialysis was associated with significantly reduced survival[[[34]](#endnote-34)].

Incremental dialysis has a lower burden of treatment. There appears to be no adverse clinical effects, during the first few years of dialysis[46] and when there is significant renal function. The advantages of incremental dialysis might be particularly important for elderly patients with short life expectancy, where transplantation is not an option [[[35]](#endnote-35)]. Incremental dialysis is typically employed in PD. There is increasing interest in incremental haemodialysis, particularly as a way to allow once- or twice-weekly dialysis. An RCT is required to compare safety and efficacy of incremental dialysis, compared to standard full-dose HD in incident dialysis patients.

### Intensive dialysis

It has been hypothesized that Intensive dialysis would result in better clearance of uraemic toxins and that this would result in reduced symptoms and improved survival. Observational studies have found associations between longer, more frequent or more intensive dialysis and improved outcome, particularly for home treatments[[[36]](#endnote-36)]. If dialysis time is also increased, fluid balance is easier to achieve, with lower ultrafiltration rates.

The HEMO study did not show improved survival in patients randomized to receive an increased dose of dialysis. Pruritus was reduced in the high-dose group but there were no other significant benefits. In the FHN trials, patients randomized to frequent nocturnal dialysis had reduced survival compared to standard home dialysis. Frequent short dialysis was associated increased survival but more numerous infections and access interventions.

A recent pro- con debate on dialysis regimens in the elderly found concluded that, while there was no strong evidence to support intensive dialysis in general, a limited trial of intensive dialysis may be justified in more problematic patients[[[37]](#endnote-37)].

# Kt/V is useful in the elderly: The pro argument

Malnutrition is prevalent in elderly dialysis patients[18] and has been associated with an increased risk of death[[[38]](#endnote-38)][[[39]](#endnote-39)]. Anorexia is a known symptom of uraemia and is likely to contribute to malnutrition. It has been hypothesized that low Kt/V could be a risk factor for malnutrition in dialysis patients[[[40]](#endnote-40)][[[41]](#endnote-41)]. While there are likely to be multiple other potential causes of malnutrition in elderly dialysis patients[[[42]](#endnote-42)][[[43]](#endnote-43)][[[44]](#endnote-44)], low Kt/V is an easily identifiable and potentially modifiable risk factor[[[45]](#endnote-45)].

Multiple observational studies have shown that low Kt/V is associated with mortality[[[46]](#endnote-46)][[[47]](#endnote-47)] especially in anuric patients[33]. This has been shown in a dialysis population with a relatively high percentage of elderly patients[[[48]](#endnote-48)]. Low Kt/V is considered as a modifiable risk factor for mortality in dialysis patients[[[49]](#endnote-49)]. There is no evidence that elderly patients are any less susceptible to any adverse effects of low Kt/V.

The Haemodialysis (HEMO) and ADEMEX RCTs have shown no benefit of increasing Kt/V above standard dose. This does not mean that reducing Kt/V below standard dose is safe or that Kt/V is not a valuable quality measure to detect inadequate dialysis. There is no RCT evidence that reducing Kt/V in anuric patients is safe.

One of the aims of medical treatment in the elderly is to improve quality of life. In a pre-specified secondary analysis of the HEMO study, a significantly slower decline in physical health, as expressed by the physical component summary, and a slower worsening in bodily pain were observed in patients assigned to an eKt/V of 1.45 compared to a lower dialysis dose (1.05)[[[50]](#endnote-50)]. While the mean age of patients in the HEMO study was 57.6 years, the study included a significant number of patients aged 65 years or older. Other studies have shown that older people who are adequately dialyzed (Kt/V > 1.2) have a relatively good health-related quality of life (HRQOL), similar to that of the general population of the same age and gender[[[51]](#endnote-51)], and experience a similar decline in HRQOL compared to younger patients undergoing hemodialysis[[[52]](#endnote-52)].

Kt/V can be calculated for both renal function and dialysis and combined in a single measure. An incremental dialysis, minimizing the negative impact on the patient by minimizing treatment time and/or frequency yet maintaining overall adequacy, guided by measurements of renal and dialysis Kt/V, has been shown to have superior outcome[34]. Incremental dialysis, with its reduced dose, might potentially increase the risk of developing uraemic symptoms and fluid overload, especially when residual renal function fails completely[[[53]](#endnote-53)]. As a consequence, additional evidence is required to inform daily clinical practice. If it is implemented, incremental dialysis would require careful control and monitoring, including serial measurements of renal function and clearance by Kt/V.

One of the aims of medical treatment in the elderly is to reduce symptoms. Unfortunately, many of the potentially reversible symptoms of uremia are difficult to distinguish from the unavoidable effects of ageing and age-associated multi-morbidity. Pruritus is one of the few symptoms which is relatively specific for uraemia. Higher Kt/V has been associated with reduced pruritus in the majority[[[54]](#endnote-54)][[[55]](#endnote-55)][[[56]](#endnote-56)] but not all[[[57]](#endnote-57)] of the observational studies where this was reported. This association was shown in DOPPS 1[[[58]](#endnote-58)] but failed to reach significance in DOPPS II.

While urea is not particularly toxic, it has several characteristics which make it suitable as a tracer to quantify dialysis. These include free movement across the erythrocyte and tissue cell membranes[[[59]](#endnote-59)], stability in blood samples, relative lack of non-renal, non-dialysis clearance and low cost of measurement. Since Kt/V is calculated from the ratios of urea concentrations in pre-, post-HD blood, urine or dialysis fluid samples, calibration errors affecting all samples equally will not result in an error in Kt/V. The urea-based Kt/V is the best studied marker of dialysis adequacy. The use of Kt/V is supported by a well-known and studied urea kinetic model (UKM). UKM can be applied to all types of dialysis. Computer applications to run UKM are widely available and run on most computing devices. UKM can be used to calculate protein nitrogen appearance a marker of dietary protein catabolism. UKM can predict Kt/V for any dialysis prescription, so can be used to ensure adequate dialysis and detect unaccounted inefficiency in the dialysis process. Modern dialysis machines can now measure Kt/V continuously and inexpensively without blood samples using online measurements of conductivity or ultraviolet absorbance. There is much more published evidence linking Kt/V to outcome than for any other marker of dialysis adequacy.

While other measures of dialysis adequacy, using arguably more realistic uraemic toxins, have been proposed[[[60]](#endnote-60)][[[61]](#endnote-61)][[[62]](#endnote-62)], none are as well-validated as Kt/V. Many of these alternative methods increase complexity and cost.

# Kt/V is not useful in the Elderly: The con argument:

The use of the urea-based Kt/V has been questioned recently [[[63]](#endnote-63)]. The handling of urea by dialysis and the kidneys is not typical of uraemic toxins. Compared to other toxins, urea diffuses more rapidly, is reabsorbed in the renal tubules and, due to specific channels, transfers much more readily across cell membranes. Therefore, urea is more easily cleared by dialysis and less easily cleared by the kidneys, compared to other toxins. Protein-bound toxins, are hardy cleared by dialysis at all. Non-dialysis clearance and generation rates are highly variable between patients and have relatively greater influence on the levels of uraemic toxins than dialysis clearance. Kt/V does not predict levels of uraemic toxins in dialysis patients[[[64]](#endnote-64)][[[65]](#endnote-65)].

The hypothesis that increasing Kt/V improves nutrition has not been supported by evidence. Nutritional markers were not different between standard and high dose groups in both ADEMEX and HEMO studies[[[66]](#endnote-66)]. In the NECOSAD study, longitudinal observation of serum albumin showed a significant decrease in haemodialysis patients with the highest Kt/V, compared to lower Kt/V [[[67]](#endnote-67)].

The calculation of the renal component of Kt/V makes assumptions on the renal handling of urea and creatinine, which are known to change with advancing age[[[68]](#endnote-68)]. Therefore Kt/V is likely to be inaccurate in older patients.

Kt/V has been validated only in younger patients. The only RCT in HD which has shown a significant effect of Kt/V on outcome excluded elderly patients[11]. The changes in physiology which occurs with age are likely to influence the relationship between Kt/V and outcome. Few studies have specifically assessed the utility of Kt/V in elderly patients. Kt/V may have little or no relevance in the elderly and, in any case, we do not know how to interpret Kt/V in the elderly.

Much of the rationale for using Kt/V, rather than symptoms and clinical signs, is to prevent uraemic complications occurring in future. This may require increases in dialysis dose even while the patient is asymptomatic. This strategy may have no benefit for the elderly patient with limited life expectancy.

Clearance by haemodialysis may be limited by cardiovascular disease and access problems in elderly patients. Attempts to achieve a specified Kt/V may involve additional access interventions, more frequent or longer dialysis[[[69]](#endnote-69)]. These will be disadvantageous to the patient and may impair quality of life. The disadvantages of attempting to achieve a pre-defined Kt/V are likely to outweigh the benefits.

In the elderly, quality of life will be dominated by the “geriatric giants”: immobility, cognitive impairment, abnormalities of gait and incontinence. These are unlikely to be affected by Kt/V.

Measuring dose of dialysis or prescribing dialysis using Kt/V in elderly dialysis patients may be misleading and a distraction from assessments which are more likely to be meaningful for the patient. Good geriatric care is aimed at slowing the deterioration in physical and cognitive function and in maintaining the patients’ quality of life and independence for as long as possible. Any negative effects of treatment on these aims should be taken into account.

## Alternative metrics or biomarkers for the elderly dialysis patient

#### Geriatric assessment

Ideally, the patient should have a full geriatric assessment before starting dialysis[[[70]](#endnote-70)]. The assessments would include objective tests of mobility and cognitive function as well as subjective assessment of quality of life, symptoms and burden of treatment. The assessments should be repeated periodically and the impact of any treatment estimated.

#### Dialysis time

In haemodialysis, total diffusive time or dialysis time (td) is the duration of treatment during which clearance is applied. Modern dialysis machines automatically display elapsed td. Some of the harmful effects of HD are due to haemoconcentration and falls in blood volume associated with high ultrafiltation rates[[[71]](#endnote-71)]. Shorter dialysis time will require higher ultrafiltation rates. The clearance of uraemic toxin molecules, which are larger than urea, will be influenced less by blood and dialysis fluid flows, compared to urea clearance. So the cleared volume for uraemic toxins will be lower during a shorter dialysis, compared to a longer dialysis, even if Kt/V is the same. Some of the negative impact of dialysis is proportional to dialysis time. These include cost, inconvenience to patient and time away from home. Patients are more likely to prefer shorter and less frequent dialysis[[[72]](#endnote-72)].

There is at least as much evidence for a negative association between primary outcomes (e.g. mortality, hospitalization, symptoms) and td as there is for Kt/V[[[73]](#endnote-73)]. As with Kt/V, the evidence from RCTs that varying td can influence outcome is mixed or lacking. There is no direct evidence to support a requirement for any specific dialysis time. An RCT comparing the effects of varying td, without varying Kt/V is required to prove an independent causative relationship between primary outcomes and td.

#### Fluid status

There is more evidence for an association between fluid status and outcome than there is for Kt/V. The significantly improved survival associated with longer dialysis has been hypothesized to be due to better control of fluid overload[[[74]](#endnote-74)]. Fluid overload may result in symptoms and reduced cardiac function, reducing quality of life and physical function and is more likely in elderly dialysis patients[[[75]](#endnote-75)]. Pulmonary oedema may occur in the absence of fluid overload when there is impaired left ventricular function. Dehydration may be associated with loss of renal function and hypotension, which may be symptomatic and is a potential cause of falls, a major cause of loss of independence in the elderly. For these reasons, a comprehensive adequacy assessment would include an assessment of fluid and cardiac status. This may be particularly important in incremental dialysis, when fluid homeostasis is more critically dependent on residual renal function. Various objective measure of fluid status are available. Bioimpedance spectroscopy can quantify any over- or under- hydration. Lung ultrasound can detect and quantify sub-clinical pulmonary oedema[[[76]](#endnote-76)].

#### Ultrafiltration rate

In haemodialysis, ultrafiltration rates greater than 13ml/kg/hr are associated with reduced survival[[[77]](#endnote-77)]. For this reason, it has been suggested that ultrafiltration should be limited to below this rate. Other studies have not confirmed this association. It has been pointed out that limiting ultrafiltration rates to a specified limit could result in fluid overload unless dialysis time is increased or fluid accumulation between dialysis sessions is reduced.

#### Concentrations of key toxins

Uraemic toxicity is generally considered to be dependent on the concentrations of uraemic toxins, which depend on generation rate as well as clearance. Generation rates are more likely to be a function of body surface area than volume. It is already becoming apparent that optimal Kt/V levels might be different for females and smaller patients[[[78]](#endnote-78)], due to their differing relationship between surface area and V. This may be particularly true in the elderly, in whom V is hard to predict. Therefore, it has been suggested that surface area, not V should be used to normalize clearance in dialysis[[[79]](#endnote-79)].

Since the generation rates may differ in elderly patients compared to younger patients, it may be more valid to quantify dialysis adequacy from the serum levels of key uraemic toxins or surrogates, rather than Kt/V. Candidate toxins might include beta-2-microglobulin, phosphate, hydrogen ion, p-cresol sulphate, etc [[[80]](#endnote-80)]. An individualized treatment might target specific toxins which were present in particularly high concentration or were causing symptoms. The reduction of a specific toxin may be achieved by non-dialysis means[[[81]](#endnote-81)]. A high level of serum phosphate, for example might be better controlled by binders and diet, rather than increasing dialysis dose. Further research is needed to link patterns of uraemic toxin levels to specific symptoms.

#### Self-reported outcomes

The SONG-HD initiative has identified outcomes which are important to dialysis patients, their carers and nephrologists[[[82]](#endnote-82)]. These include multiple self-reported outcomes. Fatigue is the first of these to be prioritized. The aim is to develop a core outcome measure (i.e. short survey) for fatigue that is validated and feasible for use in all clinical trials involving patients on haemodialysis.

# Conclusions

According to both the pro- and the con-arguments (table 3), providing dialysis with a fixed minimum Kt/V as specified in the guidelines is probably not appropriate for many elderly patients. Clinical guidelines are not intended to be applied rigorously in every patient. The individual needs of the patient should always take precedence.

Elderly and frail patients, in particular, require more individualization, appropriate to their clinical condition, stage of life and priorities from their own perspective. Clinical decisions would be made jointly with the informed patient or their appointed attorney.

According to the pro argument, measuring Kt/V has little or no cost, especially when automatically calculated by the dialysis machine. While the elderly patient may not be dialysed to a standard, pre-defined Kt/V level, it may be helpful to use an individualized Kt/V. While the elderly patient would certainly benefit from a full geriatric assessment as described in the con arguments, knowledge of the Kt/V could assist in achieving an individualised ideal dose for that patient and in helping to troubleshoot problems with dialysis delivery.

Incremental and palliative dialysis are options which may be of particular interest to the elderly or frail CKD patient and might deliver a relatively low Kt/V. In these patients, a trial of reduced dose dialysis may be justified. Possible ways to reduce dose are listed in table 4.

There is clearly a need for studies designed to determine the factors which would influence optimal dialysis dose in elderly patients. More sophisticated measures of adequacy than Kt/V are required.

# Conflicts of interest

The authors have declared no conflicts of interests regarding the subject of this paper.

**Legends to Tables and Figures**

**Table 1**

Positive and negative effects of increasing dialysis dose

**Table 2**

Physiological differences between older and younger patients and their potential consequences

**Table 3**

Summary of the pro- and con-arguments regarding utility of Kt/V in elderly dialysis patients.

**Table 4**

Potential modification of standard haemodialysis prescription in elderly patients

**Figure 1**

Cycle of inadequate dialysis caused by and contributing to uraemia.

|  |  |  |
| --- | --- | --- |
|  | Positive | Negative |
| Physiological effects | * Reduced level of uremic toxins * Reduced fluid overload (with more frequent haemodialysis) * Reduced ultrafiltration rate (for nocturnal dialysis) | * Increased exposure to bio-incompatible material. * Increased solute disequilibrium (for more intensive haemodialysis). * Loss of residual renal function (for nocturnal dialysis). |
| Potential, outcome, not proven | * Improved survival * Reduced symptoms due to reduced uraemia. * Improved nutrition | * Increased symptoms due to inflammation. * Increased symptoms due to disequilibrium (more intensive dialysis) |
| Outcome supported by evidence | * Improved volume management (frequent short dialysis)[[[83]](#endnote-83)] * Increased overall survival (frequent short dialysis)[[[84]](#endnote-84)] | * Increased frequency of surgical/access interventions (frequent haemodialysis)[[[85]](#endnote-85)]. * Increased infections (frequent haemodialysis)[[[86]](#endnote-86)] * Increased time having treatment * Reduced survival (frequent nocturnal dialysis)[[[87]](#endnote-87)] |

**Table 1:** Positive and negative effects of increasing dialysis dose

|  |  |  |
| --- | --- | --- |
| **Quantifiable physiological differences between elderly and younger patients** | | |
| Differences | Approximate relative difference (%) | Consequences |
| Reduced metabolic rate[15] | -20 | Lower levels of uraemic toxins, potentially less need for clearance. |
| Reduced dietary intake[[[88]](#endnote-88)] | -20 |
| Reduced inter-dialytic weight gain[16] | -20 | Reduced need for ultrafiltration.  Potential for relatively shorter dialysis and/or lower ultrafiltration rate. |
| **Other differences in physiology between elderly and younger patients** . | | |
| Differences | | Consequences |
| Reduced cardiac function | | More frequent symptomatic hypotension during dialysis. More likely to terminate dialysis early. |
| More likely to have vascular disease | | Harder to establish fistula. More likely to experience vascular steal. More frequent hypotension during dialysis. |
| Reduced mobility | | Logistical difficulties in providing dialysis. |
| Reduced cognitive function | | Harder to self-care. More likely to require hospital treatment. Likely to find dialysis distressing. |
| More likely to have incontinence | | Difficulties in providing longer dialysis. |
| Increased number of chronic medical conditions. | | Survival and quality of life limited by multi-morbidity. |

**Table 2:** Physiological differences between older and younger patients and their potential consequences

|  |  |
| --- | --- |
| Pro | Con |
| Kt/V is the only validated and generally accepted measure of dialysis adequacy. | Kt/V is a poor reflection of the uraemic state. |
| There is no evidence that target Kt/V should be different in elderly compared to younger patients. | There are physiological changes associated with aging which are likely to influence dialysis requirement. None of the studies on Kt/V and outcome have taken account of such issues. |
| Elderly patients are more susceptible to malnutrition. Malnutrition is associated with and probably caused by inadequate dialysis. The nutritional consequences of inadequate dialysis may be more important in elderly patients. UKM provides nPCR, an objective measure of nutrition, as well as Kt/V. | None of the RCTs testing increasing Kt/V demonstrated any effect on nutrition.  Elderly patients are susceptible to malnutrition even if they have normal renal function. Dialysis adequacy may have no significant additional impact on nutrition in the elderly. Subjective global assessment can be used to assess nutrition, independent of UKM. |
| The clinical effects of uraemia are hard to distinguish from the normal ageing process. An objective measure of dialysis adequacy, such as Kt/V is required. | Quality of life in the elderly is more likely to be influenced by age and multi-morbidity than by dialysis dose. |
| Elderly dialysis patients are particularly prone to inadequate dialysis. Objective monitoring of Kt/V is required to detect and manage this inadequacy. | Adequate dialysis is harder to achieve in the elderly and may have less influence on outcome. Monitoring Kt/V may be a distraction from more important clinical findings. |
| Dialysis dose may be deliberately reduced in elderly patients to take account of their changing priorities. Kt/V needs to be measured to ensure that the dose remains adequate to avoid overt uraemic symptoms. | Subjective assessment of the patient’s function, quality of life and the impact of dialysis may be more appropriate than any surrogate biomarker. |

**Table 3:** Summary of the pro- and con-arguments regarding utility of Kt/V in elderly dialysis patients.

**Table 4:** Potential modification of standard haemodialysis prescription in elderly patients

|  |  |  |
| --- | --- | --- |
| Measure | Standard | Possible modification for elderly patient |
| Kt/V | 1.2 /session (3x/week HD)  1.7/week (PD) | Reduce or ignore, especially if there is significant renal function. |
| Maximum ultrafiltration rate | 13ml/Kg/Hour(HD) | Same |
| Minimum dialysis time | 12hrs/week (HD) | 9hrs or lower if ultrafiltration rate acceptable. |
| Minimum dialysis frequency | 3x/week (HD) | 2x/week if ultrafiltration rate acceptable |

**Figure 1:** Cycle of inadequate dialysis caused by and contributing to uraemia.

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