

## What Does an Adequate Dialysis Dose in The Elderly Mean? Usefulness of Kt/V, Functional Status and Incremental Dialysis in Elderly Patients

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### Abstract

What is currently considered an adequate hemodialysis dose for young patients has been determined by Gotch equation which is mainly based on urea generation rate, volume of urea distribution, total body water, and water compartmental distribution. However, all these parameters are usually modified by ageing and senescence (pathologic ageing). Because of that in the present article, it is hypothesized that hemodialysis prescription in elderly patients, particularly in those affected by geriatric syndromes, should require not only an individualized Kt/V value, where incremental dialysis could be the way to achieve it, but also the periodic evaluation of the functional status (frailty assessment) which could be even a better marker than Kt/V for adjusting dialysis dose in this group.

### Keywords

Kt/V; Dialysis; Elderly

### Introduction

In order to assess the Kt/V utility in elderly dialysis patients, it should take into account the procedure usually used to prescribe and monitor the hemodialysis dose in young patients but paying attention particularly to those aspects which can lead to inexact prescriptions in aged patients. Firstly, which of the parameters usually take into account for calculating the dialysis dose differs between young (18-64 years old), elderly (65-79 years old), and very ( $\geq 80$  years old) patients? Secondly, which dialytic parameters are usually changed if elderly patients suffer from the geriatric syndromes (dementia, falls, immobility, incontinence)? These conditions are also known as "geriatric giants" since they have high prevalence and significant health impact in the elderly [1]. Thirdly, does the current dialytic prescription usually take into account the structural and physiological changes that ageing induces to those organs involved in homeostasis, such as the heart, lungs and liver? Fourthly, is there a specific dialysis dose for old and very old patients?

Finally, have all these questions a precise answer? Clearly, they have not. The most common method worldwide currently used for calculating the hemodialysis dose is the formal variable-volume single-pool urea kinetic model of Gotch (standard Kt/V), although this method has been questioned [2,3]. In this sense, what is currently considered an adequate hemodialysis dose for young patients has been determined by Gotch equation which is mainly based on: urea generation rate, volume of urea distribution, Total Body Water (TBW), water compartmental distribution [4-6]. However, all these parameters suffer changes induced by normal ageing, and pathologic ageing (senescence) too [7-9]:

- **Urea generation rate:** It depends on protein diet and basal metabolism, both usually reduced in old individuals, and particularly in malnourished elderly and in the oldest old.
- **TBW:** It is progressively reduced along ageing, changing from around 65% in young people to around 50% in male, and 40% in female elderly people. Thus, old people have 10-20% lower TBW content compared to young people. Conversely, TBW is relative high (60%) in elderly patients suffering from immobility syndrome.
- **Volume of urea distribution:** It is related to TBW, so it is reduced in the elderly.
- **Water compartmental distribution:** It has been reported that the lower TBW content in the elderly is mainly based on the reduction in the intracellular water content. However, in untreated intellectual impairment syndrome an alteration in intracellular, extracellular and TBW has been documented. Deterioration of verbal learning has been associated with an increase in TBW, while the decline in verbal ability has been

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associated with a shift of water from the extracellular to the intercellular compartment. Based on the above analyzed ageing related changes, it could reasonably question why there is currently no different dialysis dose for dialyzing young and old patients? It seems that stable elderly patients could be treated using at least a 10% lower dialysis dose (for instance  $eKt/V$  of 1.1), while water balance requires more precise care in those elderly suffering from geriatric syndromes.

Additionally, there are other important variables which should also be taken into account, such as Body Surface Area (BSA), and Residual Diuresis (RD). Characteristically, ageing induces a progressive BSA reduction, as well as body composition modification, such as less TBW and Lean Body Mass (LBM). Thus, BSA and LBM estimation should be interpreted cautiously in old people since they have a greater proportion of fat in their body weight compared to young people [11,12]. Moreover, BSA and LBM are particularly reduced in very old individuals, sarcopenic, and frail elderly patients [13,14]. In regards with RD, it is known that its preservation is crucial even in dialysis patients since it is significantly associated to longer survival. This phenomenon has been attributed not only to a better handling of water balance but also to a better uremic toxins excretion by tubular secretion [15]. In these sense, creatinine and urea renal handling, for calculating the residual renal function, differs between young and elderly people, since urine excretion of urea and creatinine in elderly people is higher and lower respectively, compared to young people [7,16,17].

Because of the criticisms to  $Kt/V$ , alternative methods for scaling dialysis such as body weight, BSA, resting energy expenditure, high metabolic rate organ mass, liver size and bioelectrical resistance have been proposed [11-20]. Regarding the alternative methods proposed, extensive validation of them is lacking and/or their validity has not been proved in large studies yet, and they are based on indirect measurements of the amount of urea removed from patients during their dialysis sessions [20]. We have been looking for any evidence in the literature which could answer at least one of the previously exposed questions regarding which is the appropriate dialysis dose in elderly patients, and we have found that there was no study which had specifically determined which were the optimum and the minimum dialysis dose in old people, and which were these doses in elderly dialysis patients who suffer from any of the geriatric syndromes. In Europe, it is consider a standard dialysis dose an  $eKt/V$  of 1.2 three times per week [21]. The European Renal Best Practice Group (EBPG) has determined, based on the available evidence, that a hemodialysis dose of an  $eKt/V < 1$  three times per week is associated to bad prognosis. Consequently, the EBPG recommends a hemodialysis dose of an  $eKt/V \geq 1.2$  (standard  $Kt/V \geq 1.4$ ) per session in a thrice-weekly program [21,22]. However, the HEMO study failed to document any beneficial outcome between an  $eKt/V$  of 1.05 and 1.45. Moreover, this study suggests that to achieve adequate targets is more important than the target level itself [20]. Another clinical problem which requires to be solved is the difficulty usual found in achieving the prescribed hemodialysis dose in elderly patients, due to many variables such as suboptimal vascular access, low  $Q_b$ , and short dialysis sessions usually motivated by episodes of hypotension, arrhythmias, cramps, or vomiting [23,24]. Because of the above exposed facts, it seem reasonable to admit that an  $eKt/V$  of 1.2 as the only reference value, is not the best way to dose dialysis and to control its quality in the elderly with CKD undergoing renal replacement therapy.

Due to the lack of information on this topic we have started two research lines in order to learn more about it.

On one hand, Doctors Deira and Suarez are performing a prospective multi-center study to evaluate the possible advantages and disadvantages of individualized dialysis dose in elderly patients, using the concept of incremental hemodialysis. They have followed incident elderly patients who started hemodialysis at the Nephrology Division of San Pedro de Alcántara and Virgen del Puerto Hospital. In this study, serum urea, creatinine, and electrolytes have been

assessed twice a month, while urine volume and renal urea clearance (KRU) have been assessed monthly. Since 2012, Deira et al. have prescribed a progressive regimen of once-weekly hemodialysis to 40 incident end-stage chronic kidney disease patients (14 male) with  $KRU > 4$  ml/min/1.73 m<sup>2</sup>. Twenty of these patients were older than 75 (mean age: 81 year, range: 75-81). Hemodialysis dose was increased in those patients who required an ultrafiltration rate  $> 13$  ml/kg/hour for achieving volume control, or whose KRU had fallen below  $< 4$  ml/minute/1.73m<sup>2</sup> [25]. In this study,  $Kt/V$  value has also been measured and dialysis dose increase has been achieved by increasing the frequency of dialysis sessions. However, no comparison with conservative treatment has concomitantly been performed. In a preliminary analysis, they have documented that this dialytic procedure allow very elderly patients to avoid serum electrolytes alterations, abrupt overhydration, as well as to maintain good functional status and wellbeing (personal communication).

On the other hand, Musso CG et al. [13] (Frailty in Dialysis Study Group) have recently started a prospective multi-center study in order to evaluate which is the impact of different dialysis doses on functional status in the elderly, as well as to explore if the functional evaluation could be useful for guiding dialysis dose prescription in this population. For instance, evaluating if any increase performed in  $Kt/V$  value could induce some functional improvement in elderly dialysis patients. This study is based on two geriatric principles:

1. Since the goal of any treatment in geriatrics is to maintain the patient in the best functional status (physical, psychological, and social); consequently any dialytic treatment given to elderly patients should evaluate periodically its effect on patient's functional status [13].
2. Since the precise interrelationship between the systems in the organism (complexity) is an essential condition for making the organism capable of keeping homeostasis, and ageing is characterized by a progressive loss of complexity, then this loss of complexity makes old individuals frail. Additionally, current epidemiology has documented that detrimental social-behavioral factors such as isolation, influence overall mortality, particularly in the elderly. The idea is that global functional-social variables could be better prognosis markers than the organ specific variables in frail population. Thus, it has been proposed that these variables should be considered at time of prescribing drugs or medical procedures in the elderly, and they should also be considered for following patient's response to prescribed organ replacement therapies in the aged group [14].

## Conclusion

In the present article, it is hypothesized that hemodialysis prescription in elderly patients, particularly in those affected by geriatric syndromes, should require not only an individualized  $Kt/V$  value, where incremental dialysis could be the way to achieve it, but also the periodic evaluation of the functional status (frailty assessment) which could be even a better marker than  $Kt/V$  for adjusting dialysis dose in this group. From this new perspective not only the variables considered by the Gotch's  $Kt/V$  equation, such as urea generation rate, volume of urea distribution, total body water, and water compartmental distribution, would be necessary to adjust the dialysis dose in the elderly, but also the evaluation of their frailty markers, such as gait speed, hand-grip, and daily life activities geriatric tests.

Prospective studies are currently performed in order to evaluate the validity of this proposal.

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