

Complying with ethical principles in elderly and frail patients with advanced chronic kidney disease

Cumprir com os princípios éticos em doentes idosos e frágeis com doença renal crónica avançada

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Keywords

Ethical principles; Palliative care; Conservative renal care

Abstract

Introduction: In 2016, in Europe (EU), 27.3 million people were aged > 80 (the so-called “elderly people”), and this value will likely increase up to 7 million more in ten years time. Portugal follows that world trend and has presently the fifth highest proportion of elderly people in the EU. According to the data records from the Portuguese Society of Nephrology, the cohort of

dialysis patients aged > 80 years appears in the tables as an individualized group with a significant and increasing prevalence since 2015. Overtreatment of elderly patients ESRD has gained attention in professional journals and the lay media fueled by disturbing outcome data. Therefore, it is imperative to review the application of dialysis treatment. Patients should be informed about the options of treatment, including the more conservative, non-dialytic ones and the implications of the different options for their lives.

Aims: To analyze ethically the problems faced in renal replacement therapy resulting from the aging of the population in Portugal.

Materials and methods: A critical review and analysis was conducted to discuss the dilemmas and challenges to deal with the above critical situation, namely the approach dialysis versus conservative treatments.

Results: The basis for all processes involved are, namely: (i) the ethics’ principles that are the key support to guide the care providers through the treatment options; (ii) the estimation of prognosis and shared decision-making and (iii) the palliative care, which is an area where the awareness of clinicians needs to be urgently improved.

Conclusions: It is crucial the presentation to the patients of the several options of treatment aiming to achieve a better balance between risks and benefits and the best possible response to the goals and expectations of the patients.

Palavras-chave

Princípios éticos; cuidados paliativos; tratamento renal conservador.

Resumo

Introdução: Na Europa (EU), em 2016, 27,3 milhões de pessoas apresentavam mais de 80 anos de idade (os denominados pessoas muito idosas), número com tendência para aumentar em sete milhões no espaço de 10 anos. Portugal acompanha esta tendência e é, atualmente, o 5.º país da EU com a maior proporção de pessoas idosas. De acordo com dados da Sociedade

Portuguesa de Nefrologia, a proporção de doentes em diálise nestas faixas etárias tem aumentado significativamente desde 2015.

O sobretratamento dos idosos com Insuficiência renal crónica em estágio terminal tem ganho atenção nas publicações científicas médicas, tendo em conta os resultados obtidos. Deste modo, é imperativo rever a introdução/continuação dos tratamentos de diálise nesta população. Os doentes devem ser informados acerca das diferentes opções terapêuticas, nelas incluindo cada vez mais as mais conservativas, não dialíticas, assim como as implicações que cada opção terá na sua vida.

Objetivos: Analisar eticamente os problemas do processo de tomada de decisão perante a terapêutica de substituição renal na população idosa em Portugal.

Materiais e métodos: Realizar uma revisão e análise crítica para discutir os dilemas éticos no processo de decisão destas situações, nomeadamente a opção entre diálise e tratamento conservador.

Resultados: As bases de todos os processos envolvidos são, nomeadamente: (i) os princípios éticos, que constituem um suporte fundamental para guiar os profissionais de saúde através das várias opções de tratamento; (ii) a estimativa de prognóstico e a formulação de uma decisão partilhada e (iii) os cuidados paliativos, área em que a consciencialização dos profissionais de saúde precisa urgentemente de ser melhorada.

Conclusões: É crucial a apresentação aos doentes das várias opções de tratamento, por forma a conseguir um bom equilíbrio entre riscos e benefícios e dar a melhor resposta possível aos objetivos e expectativas dos mesmos.

I don't know what awaits us but I know what worries me: is that medicine, excited by science, seduced by technology and stunned by bureaucracy, erases her human face and ignores the unique individuality of each person who suffers, because although more and more ways to treat are invented, it has not yet been discovered how to relieve suffering without empathy or compassion.

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Introduction

The world's population is aging rapidly.¹ In 2016, in Europe (EU), 27.3 million people were aged > 80 (the so-called "elderly people"), and this value will likely increase up to 7 million more in ten years time. Portugal follows that world trend and has presently the fifth highest proportion of elderly people in the EU.²

Following the above scenario, diseases such as diabetes mellitus and systemic arterial hypertension became more prevalent, and the risk of patients developing chronic kidney disease increased, leading to the rising prevalence of old and frail patients on dialysis.

In Portugal, when dialysis units were first established in the seventies, dialysis was restricted to younger and fitter patients. That situation changed dramatically over the years, and all the indicators such as number, age, and comorbidity of the patients rose significantly. According to the data records from the Portuguese Society of Nephrology, the cohort of dialysis patients aged > 80 years appears in the tables as an individualized group with a significant and increasing prevalence since 2015.

In 2018, among the 12227 patients on hemodialysis (HD) in Portugal, more than 2700 (22%) are in the age group > 80 years. That group accounted for 578 new HD starts in 2018 (almost 25% of the new starts).³

Following the international tendency, in Portugal, there is a continuous and significant increase in the number of patients with end-stage renal disease (ESRD), who besides that, have multiple severe conditions and display high mortality and morbidity rates. The leading causes of this situation are related to cardiovascular diseases, infections, dialysis vascular access problems, as well as prolonged and

frequent hospitalizations.^{4,5} Presently HD is offered as the primary life-prolonging therapy overcoming the conservative treatments for ESRD.^{6,7}

The accumulated experience indicates that the benefits of dialysis are modest in specific populations.⁸⁻¹⁰ Overtreatment of elderly patients ESRD has gained attention in professional journals^{11,12} and the lay media¹³ fueled by disturbing outcome data.¹⁴⁻¹⁶ Therefore, it is imperative to review the application of dialysis treatment. Patients should be informed about the options of treatment, including the more conservative, non-dialytic ones and the implications of the different options for their lives.

The challenge for the healthcare providers and in particular for nephrologists is to balance the benefits and adverse effects of dialysis, bearing in mind the cardinal ethical questions (respect for autonomy, beneficence, nonmaleficence, and justice). One key aspect for care providers is to be able to help patients to make decisions about the options presented by the clinicians according to their goals and expectations in life.

First steps are being taken in Portugal; for example, public hospitals offer now outpatient consultation for conservative renal treatment. Also, there are increasing efforts from the nephrologist community in acquiring skills in communication with patients and palliative care, and the trend is to increase the number of palliative care unities significantly both in hospitals (public and private) and for outpatients.

Materials and methods

In this paper, we address the challenges to deal with renal treatment in line with ethical questions and consider ways in which care providers can approach the issue of dialysis versus conservative treatments in the elderly and frail patients.

Prospective controlled studies demonstrate that for a patient aged >75 years with comorbidities (especially ischemic heart disease), dialysis seems not to offer a survival advantage over conservative management (CM). Also, with the initiation of dialysis, the quality of life deteriorates and does not recover. While the CM patients maintain a stable quality of life until typically one or two months before their demise.^{9,17,18} Moreover, some patients do not tolerate in-center hemodialysis well and have a suboptimal quality of life, or even suffer harm from the treatment.¹⁹ Qualitative studies have uncovered a significant symptom and treatment burden associated with HD.²⁰⁻²² One example is

functional status and independence that is a most important issue for elderly patients^{16,24,25} and is rapidly lost after HD is initiated.

First-year mortality for incident dialysis patients, by age group, is 26.7% for patients aged 70-79 years, 34.6% for 80-84 years, and 40.4% for > 85 years. As many as 35% of the elderly patients discontinue dialysis.²⁶ Compared with non-dialytic conservative management, elderly patients who undergo dialysis can expect to spend more of their remaining life years in dialysis units or hospitals and are 2 to 3 times more likely to die in the hospital.²⁷

Taking into account the above reasons it is important not to rush to initiating dialysis. Several recent studies have highlighted the lack of benefit and potential harm from earlier initiation of dialysis, and this also pertains to the elderly patient²⁸⁻³⁰. Frailty increases the risk of early start of dialysis^{31,32}. Canadian guidelines nowadays recommend intention-to-defer dialysis.²⁹ This is especially important for the oldest patients because one-third of octogenarians with advanced CKD do not progress to ESRD and require only observation and conservative management.³² This is in line with increasing evidence obtained during the past decade, which suggests that the overall benefit of dialysis is modest for specific populations, in particular frail, elderly patients with multimorbidity.

Ethical principles should be considered in all health care decisions. They aim at respecting autonomy, beneficence, nonmaleficence, and justice.³³ Ethical decisions should be based on the understanding by the patients of the goals of treatment, risks, and benefits and considering their values and preferences.³⁴

Decision making in dialysis often involves ethical dilemmas such as an example: is dialysis the most appropriate treatment for the individual patient? When the decisions are difficult, ethics provides a structure, a guide of thinking that gives moral comfort and support for the care providers finding the right things to do.

In many countries, respect for the patient's autonomy is the most important of the four ethical principles. Autonomy is particularly relevant when different principles are in conflict and the balance between beneficence and nonmaleficence is complex and delicate.^{35,36} Respect for patient autonomy means offering the patient the possibility to hold his views and to make choices among the options presented by the clinicians. Ideally, the discussions with patients should begin well before the need

for dialysis is urgent, so that patients have time to think carefully about their goals for care, values, and preferences.

According to Kaldjian *et al.*, six goals should be explored with patients facing CKD. They are: (i) Be cured; (ii) Live longer; (iii) Improve or maintain function/quality of life/ independence; (iv) Be comfortable; (v) Achieve life goals; (vi) Provide support for family/caregiver to allow them to articulate the treatments that will help them to accomplish their goals.³⁷

The information about the kidney disease prognosis and the renal replacement options must be forwarded to the patients in due time and in such a clear way that they can understand the options and the likely implications of their choices. There are several factors that can decrease the quality of the patients' decision and its implementation, namely (i) poor or not well-explained information about the treatment options; (ii) timing and expected benefits of dialysis; (iii) insufficient time for decision making; (iv) limited or no existing resources; (v) influence of colleagues and family and (vi) reluctance to deviate from the status quo.³⁸

Indeed, most patients (dialysis-dependent or not) are willing to engage in end-of-life discussions and desire some form of advance directive. These documents (written or oral) are conceived and legitimated as enactments of the principle of "patient autonomy". They emphasize individuals being in control of their own life, even in cases of future severely incapacitating illnesses or loss of mental faculties, which preclude their capacity to make choices. They may also work as an "icebreaker", allowing it easier for healthcare professionals and relatives to communicate about the patient's preferences and interests. It is not by chance that a randomized controlled study concluded that advance care planning, including the formulation of an advance directive "improves end of life care and patient as well as family satisfaction reducing stress, anxiety, and depression in the loved ones".³⁹

According to surveys and interviews of patients undergoing hemodialysis, it seems that most patients feel that the information given to them on their ESRD and hemodialysis or other viable choices is not enough.⁴⁰⁻⁴²

One crucial aspect of being considered is the capacity of the patients to make an informed decision about dialysis starting or continuation. Indeed, increasing evidence indicates that a significant proportion of patients in the pre-dialysis

setting and currently on dialysis may lack that capacity.⁴³

In line with the ethical principle of beneficence, all clinicians (including nephrologists), have the moral obligation to act for the benefit of the patient. This includes carefully balancing treatment's benefits and burdens (such as dialysis), and to communicate their recommendations to the patient and his family. However, the wishes of the patient and family, although should be considered, should not, taken alone, be determinative of the final decision.

Also, according to the principle of nonmaleficence, health providers should not recommend potentially harmful treatments with few chances of benefit. Therefore, it must be born in mind that HD may do more harm than good for some of the frail elderly patients. The experience in nursing homes and community-dwelling elders, suggests that the onset of HD may bring rapid functional decline.^{24,25} Many older HD patients regret having started HD.^{41,44} The symptom burden in the elderly HD patient is heavy and approximates to that of cancer.¹⁴ In these cases, palliative care can significantly alleviate the situation (even in patients who withdraw from HD), but it is unfortunately underutilized.

Similarly, elderly patients with dementia have particularly poor survival on HD. Disruption in their routine such as caused by HD treatment, can trigger fear and agitation leading to rapid functional decline.⁴⁵

The ethical principle of justice implies the just and equitable distribution of health resources such as dialysis and the set of resources required when conservative management is adopted. Regarding conservative management, a study focused on the experiences of patients opting not to have dialysis or withdrawing from dialysis, showed that one problem felt by the patients was the sense of abandonment due to little follow-up care after their decision.⁴⁶ This raises the importance of an ethical approach to these patients, which should include palliative support and awareness and education of nephrologists in this dimension of care.

To summarize, health providers and in particular nephrologists must face significant challenges to guide the elderly and frail renal patients with multimorbidity through the treatment options that best fit their medical condition supported by the four ethical principles and taking into account the goals and expectations of the patients and their families.

Resulting considerations

Our review analysis points out to several resulting considerations, as follows. Providing ethical multicare solutions for elderly and frail renal patients with multimorbidity put significant challenges on the care providers. These challenges became more acute along the years, mainly due to population aging. This situation creates a huge impact on the health care system in view of: (i) the limited health resources; (ii) the low effectiveness in the elderly group of population of more intrusive treatments such as dialysis and (iv) the little practice of conservative treatments leading to insufficient development of palliative care, which requires specific knowledge and supportive structures.

Limitations and recommendations

The first step to improve the situation is to develop methodologies to select the more suitable and ethical option for the patient, preferably via a process of shared decision-making (SDM). This is the recommended model for dialysis decision-making because it heads the need for ethical considerations, to entirely inform patients about the risks and benefits of dialysis, as well as the need to guarantee that patients' values and preferences play a leading role.⁴⁷

SDM guideline established limits in the SDM process. These limits were set to protect the rights of patients and the professional integrity of health professionals. In the ethical structure of SDM, the patient has the right to deny dialysis even if the nephrologist disagrees with the patient's decision. Likewise, the nephrologist has the right to decline to offer dialysis when the foreseen benefits do not justify the risks. Acknowledging that there are situations in which patients and nephrologists might disagree about the decisions to start, continue, or withdraw dialysis. The guidelines of SDM stipulates recommendations of how to resolve such challenges by comprising the use of time-limited trials and ethics counseling.

Shared Decision aids to improve patients' knowledge of their options, give them realistic expectations of benefits and harms and helps to make choices concordant with the patient's values and goals of care. Several studies show that patients undergoing dialysis are eager to have more information.^{48,49} Discussing options with patients is crucial, but it is critically important to avoid

presenting treatment options as “Do hemodialysis or do ‘nothing’ or even worse as “Do hemodialysis or die.” The full spectrum of treatment options should be on the table when discussing options with patients. For seriously ill patients, clinicians must be prepared to face patients’ decisions that may be modulated by interferences from family members, which can be biased by an unrealistic optimism motivated by the nonacceptance of losing their loved ones.

Presently, many nephrologists and nephrology fellows feel poorly prepared to address those challenging discussions.^{50,51}

Specific clinical training, especially in communication with the patient, is urgently needed. Among the goals is, for example, to develop alternatives to present ambiguous medical terms to ensure that the patient understands as clear as possible the treatment options and the associated risks and benefits. Providers should also be prepared to address patient misunderstanding and to cope with their emotional responses.

Communication can be further complicated or jeopardized by the low health literacy of the patient. This may even impede the patient’s capability to understand medical concepts. Therefore, clinicians should develop skills (especially for older patients) to explain to the patient his prognosis and treatment options in more straightforward terms and make sure by cross-questioning that the patient got the most essential part of the message.

Concerning palliative care services, there is an increasing awareness of nephrologists and health systems of the importance of being able to provide end-of-life care to these patients.⁵² Nephrologists should get familiarized with palliative services and consider palliative care as part of their professional responsibilities.

The term *palliative dialysis* starts to be used to indicate a form of patient-centered dialysis that is focused on the patient’s quality of life.

Dialysis promotes an extension of life but requires an increased burden of four hours of tri-weekly hemodialysis treatments, which may result in an unacceptable decrease in the quality of life of old and sick people.²³ However, dialysis can be adapted to the patient’s needs and wishes and need not be “a prison”.

However, there is still no agreement on the definition and establishment of “incremental” dialysis as a regular procedure. Some changes are being considered, for example, U.S. experts suggest an

approach based on twice-weekly dialysis, and in Italy, where it is often part of an integrated approach which includes nutritional management, dialysis start involves typically one session per week, while continuing the diet prescribed in the pre-dialysis phase (usually with a moderate protein restriction, at 0.6–0.8 g/Kg/day).⁵³⁻⁵⁷

Conclusions

Although dialysis is, without any doubt, a valuable and life-extending treatment which has enabled thousands of old patients with ESRD to live longer with improved quality of life, current evidence does not support the moral and technological imperative to dialyze all elderly patients with ESRD- irrespective of their comorbidity and functional status.

Therefore, treatment options that best suit the patient’s goals should be presented by the care providers. Shared decision-making should be implemented as it fulfills the ethical principles of autonomy, beneficence, and non-maleficence, which are a vital support to guide the options of treatment. Unlike standardized medicine aiming to achieve the best medical solution, in an ethical discussion, there is no medical best solution. Instead, the goal is to reach a personalized choice adapted to the individual’s context.

Indeed, there is room and an urgent need for “personalized medicine” in renal replacement therapy such as it happens already in chemotherapy, where protocols are increasingly being adapted to the patients.

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References

1. Colby SL, Ortman JM. Projections of the size and composition of the U.S. population: 2014 to 2060 (current population reports). Washington: U.S. Department of Commerce, U.S. Census Bureau; March 2015 [cited 2017 Aug 14]. Available from: <https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf>.
2. <https://ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20200402-1>
3. Portuguese Registry of Dialysis and Transplantation, 2018.

4. Thompson S, James M, Wiebe N, et al. Cause of Death in Patients with Reduced Kidney Function. *J Am Soc Nephrol*. 2015;26(10):2504–2511. DOI: 10.1681/ASN.2014070714.
5. Jager KJ, Lindholm B, Goldsmith D, et al. Cardiovascular and non-cardiovascular mortality in dialysis patients: where is the link? *Kidney Int Suppl*. 2011;1(1):21–23. DOI: 10.1038/kisup.2011.7
6. Nissenson AR. Improving outcomes for ESRD patients: shifting the quality paradigm. *Clin J Am Soc Nephrol*. 2014;9(2):430–434. DOI: 10.2215/CJN.05980613.
7. Anand S, Kurella Tamura M, Chertow GM. The elderly patients on hemodialysis. *Minerva Urol Nefrol*. 2010;62(1):87–101.
8. Kurella M, Covinsky KE, Collins AJ, Chertow GM. Octogenarians and nonagenarians starting dialysis in the United States. *Ann Intern Med*. 2007;146:177–83. DOI: 10.7326/0003-4819-146-3-200702060-00006
9. Murtagh FE, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE: Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. *Nephrol Dial Transplant*. 2007; 22: 1955– 1962. DOI: 10.1093/ndt/gfm153
10. Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K: Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. *Clin J Am Soc Nephrol*. 2012; 7: 2002–2009. DOI: 10.2215/CJN.01130112
11. Rosansky SJ. The sad truth about the early initiation of dialysis in elderly patients. *JAMA*. 2012;307:1919–20. DOI: 10.2215/CJN.03330414
12. Thorsteinsdottir B, Swetz KM, Albright RC. The Ethics of Chronic Dialysis for the Older Patient: Time to Reevaluate the Norms. *Clin J Am Soc Nephrol*. 2015;10(11):2094–2099. DOI: 10.2215/CJN.09761014
13. Span P. Dialysis Is a Way of Life for Many Older Patients. Maybe It Shouldn't Be. *The New York Times* 2019 Feb 15: Sect. Health. Available from: <https://www.nytimes.com/2019/02/15/health/dialysis-kidney-disease.html>.
14. Murtagh FEM, Addington-Hall J, Higginson IJ. The Prevalence of Symptoms in End-Stage Renal Disease: A Systematic Review. *Adv Chronic Kidney Dis*. 2007;14:82–99. DOI: 10.1053/j.ackd.2006.10.001
15. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med*. 2009;361:1539–47. DOI: 10.1056/NEJMoa090465.
16. Jassal SV, Chiu E, Hladunewich M. Loss of independence in patients starting dialysis at 80 years of age or older. *N Engl J Med*. 2009;361:1612–3. DOI: 10.1056/NEJMc0905289
17. O'Connor NR, Kumar P: Conservative management of end-stage renal disease without dialysis: a systematic review. *J Palliat Med*. 2012; 15: 228–235. DOI: 10.1089/jpm.2011.0207
18. Schell JO, Da Silva-Gane M, Germain MJ: Recent insights into life expectancy with and without dialysis. *Curr Opin Nephrol Hypertens*. 2013; 22: 185–192. DOI: 10.1097/MNH.0b013e32835ddb69
19. Jassal SV, Watson D. Dialysis in Late Life: Benefit or Burden. *Clinical Journal of the American Society of Nephrology*. 2009;4(12): 2008-2012. DOI: 10.2215/CJN.04610709
20. Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. *Nephrol Dial Transplant*. 2011;26:1608–14. DOI: 10.1093/ndt/gfq630
21. Gorodetskaya I, Zenios S, McCulloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Int*. 2005;68:2801–8. DOI:10.1111/j.1523-1755.2005.00752.x
22. Yong DS, Kwok AO, Wong DM, Suen MH, Chen WT, Tse DM. Symptom burden and quality of life in end-stage renal disease: a study of 179 patients on dialysis and palliative care. *Palliat Med*. 2009;23:111–9. DOI: 10.1177/0269216308101099
23. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional Status of Elderly Adults before and after Initiation of Dialysis. *New Engl J Med*. 2009;361(16): 1539-1547. DOI: 10.1056/NEJMoa0904655
24. Berger JR, Hedayati SS. Renal replacement therapy in the elderly population. *Clin J Am Soc Nephrol*. 2012;7(6): 1039–1046. DOI: 10.2215/CJN.10411011.
25. US Renal Data System: USRDS Annual Data Reports. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010.
26. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? *Clin J Am Soc Nephrol*. 2009;4(10):1611–1619. DOI: 10.2215/CJN.00510109
27. Liberek T, Warzocha A, Galgowska J, Taszner K, Clark WF, Rutkowski B. When to initiate dialysis—is early start always better? *Nephrol Dial Transplant*. 2011; 26(7):2087–91. DOI: 10.1093/ndt/gfr181
28. Leurs P, Machowska A, Lindholm B. Timing of dialysis initiation: when to start? Which treatment? *J Ren Nutr*. 2015;25(2):238–41. DOI: 10.1053/j.jrn.2014.10.015
29. Nesrallah GE, Mustafa RA, Clark WF, Bass A, Barnieh L, Hemmelgarn BR, et al. Canadian Society of Nephrology. Canadian Society of Nephrology 2014 clinical practice guidelines for timing the initiation of chronic dialysis. *CMAJ*. 2014;186(2):112–7. DOI: 10.1503/cmaj.130363
30. Johansen KL, Delgado C, Bao Y, Kurella Tamura M. Frailty and dialysis initiation [published correction appears in *Semin Dial*. 2015 Jul–Aug;28(4):455]. *Semin Dial*. 2013;26(6):690–696. DOI: 10.1111/sdi.12126
31. Nixon AC, Bampouras TM, Pendleton N, Woywodt A, Mitra S, Dhaygude A. Frailty and chronic kidney disease: current evidence and continuing uncertainties. *Clin Kidney J*. 2018;11(2):236–245. DOI: 10.1093/ckj/sfx134
32. El-Ghoul B, Elie C, Sqalli T, Jungers P, Daudon M, Grünfeld JP, et al. Nonprogressive kidney dysfunction and outcomes in older adults with chronic kidney disease. *J Am Geriatr Soc* 2009; 57: 2217–2223. DOI: 10.1111/j.1532-5415.2009.02561.x
33. Berglund C. *Ethics for Healthcare*. Oxford: Oxford University Press; 1998.
34. Moss AH, Holley JL, Davison SN, Dart RA, Germain MJ, Cohen L, et al. Core Curriculum in Nephrology: Palliative Care. *Am Kidney Dis*;2004;43:172-185. DOI:10.1053/j.ajkd.2003.10.011
35. Not just autonomy—the principles of American biomedical ethics. *J Med Ethics*. 1995;21(6):332–8. DOI: 10.1136/jme.21.6.332
36. Gillon R. Ethics needs principles—four can encompass the rest—and respect for autonomy should be “first among equals”. *J Med Ethics*. 2003;29(5):307–12. DOI: 10.1136/jme.29.5.307
37. Kaldjian LC, Curtis AE, Shinkunas LA, Cannon KT: Goals of care toward the end of life: a structured literature review. *Am J Hosp Palliat Care*, 2008; 25: 501–511. DOI: 10.1177/1049909108328256
38. Morton RL, Tong A, Howard K, Snelling P, Webster AC. The views of patients and carers in treatment decision making for chronic kidney disease: a systematic review and thematic synthesis of qualitative studies. *BMJ* 2010; 340: c112. DOI: 10.1136/bmj.c112
39. Detering KM, Hancock AD, Reade MC, Silvester W. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. *BMJ*. 2010;340:c1345. DOI: 10.1136/bmj.c1345
40. Davison SN: End-of-life care preferences and needs: Perceptions of patients with chronic kidney disease. *Clin J Am Soc Nephrol* 5: 195–204. DOI: 10.2215/CJN.05960809
41. Song MK, Lin FC, Gilet CA, Arnold RM, Bridgman JC, Ward SE: Patient perspectives on informed decision-making surrounding dialysis initiation. *Nephrol Dial Transplant*. 2013; 28: 2815–2823. DOI: 10.1093/ndt/gft238
42. Kurella Tamura M, Periyakoil VS. The patient perspective and physician's role in making decisions on instituting dialysis. *Nephrol Dial Transplant*. 2013; 28: 2663–2666. DOI:10.1093/ndt/gft379
43. Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, et al. Cognitive impairment in hemodialysis patients is common. *Neurology*. 2006; 67:216–23. DOI: 10.1212/01.wnl.0000225182.15532.40
44. Stringer S, Baharani J. Why did I start dialysis? A qualitative study on views and expectations from an elderly cohort of patients with end-stage renal

- failure starting hemodialysis in the United Kingdom. *Int Urol Nephrol.* 2012;44:295–300. DOI: 10.1007/s11255-011-0045-4
45. McAdams-DeMarco MA, Daubresse M, Bae S, Gross AL, Carlson MC, Segev DL. Dementia, Alzheimer's Disease, and Mortality after Hemodialysis Initiation. *Clin J Am Soc Nephrol.* 2018 Set; 13 (9) 1339-1347. DOI:10.2215/CJN.10150917
 46. Ashby M, op't Hoog C, Kellehear A, Kerr PG, Brooks D, Nicholls K, et al. Renal dialysis abatement: lessons from a social study. *Palliat Med.* 2005; 19:389–96. DOI:10.1191/0269216305pm1043oa
 47. United States. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. Making Health Care Decisions. U S Code Annot U S. 1982; Title 42 Sect. 300v as added 1978. P. 30-44.
 48. Long BD, Shuman AG. Could good care mean withholding information from patients? *AMA J Ethics.* 2016;18(1):6–11. DOI: 10.1001/journalofethics.2016.18.1.ecas1-1601
 49. Berger JT. Redefining the domains of decision making by physician and patient. *Int J Clin Pract.* 2011;65(8):828–30.
 50. Methven S, Caskey F. Putting the patient first: should we nudge them or shove them? *Nephrol Dial Transplant.* 2014;29(5):941–3. DOI: 10.1093/ndt/gft504
 51. Grubbs V, Moss AH, Cohen LM, Fischer MJ, Germain MJ, Jassal SV, et al. Dialysis Advisory Group of the American Society of Nephrology. A Palliative Approach to Dialysis Care: A Patient-Centered Transition to the End of Life. *Clinical Journal of the American Society of Nephrology,* 9(12):2203-2209. DOI: 10.2215/CJN.00650114.
 52. Rope RW, Pivert KA, Parker MG, Sozio SM, Merrell SB. Education in Nephrology Fellowship: A Survey-Based Needs Assessment. *J Am Soc Nephrol.* 2017;28(7):1983–1990. DOI: 10.1681/ASN.2016101061
 53. Park JI, Park JT, Kim YL, Kang SW, Yang CW, Kim NH, et al, on behalf of the CRC for ESRD investigators. Comparison of outcomes between the incremental and thrice-weekly initiation of hemodialysis: a propensity-matched study of a prospective cohort in Korea. *Nephrol Dial Transplant.* 2017;32(2):355–63. DOI: 10.1093/ndt/gfw332
 54. Obi Y, Chou J, Kalantar-Zadeh K. Introduction to the critical balance-residual kidney function and incremental transition to dialysis. *Semin Dial.* 2017; May;30(3):232-234. DOI: 10.1111/sdi.12600
 55. Morfin JA, Fluck RJ, Weinhandl ED, Kansal S, McCullough PA, Komenda P. Intensive Hemodialysis and treatment complications and tolerability. *Am J Kidney Dis.* 2016;68(5S1):S 43–50. DOI: 10.1053/j.ajkd.2016.05.021
 56. Bossola M, Vulpio C, Tazza L. Fatigue in chronic dialysis patients. *Semin Dial.* 2011;24(5):550–5. DOI: 10.1111/j.1525-139X.2011.00956.x
 57. Bellizzi V, Cupisti A, Locatelli F, Bolasco P, Brunori G, Cancarini G, et al; "Conservative Treatment of CKD" study group of the Italian Society of Nephrology. Low-protein diets for chronic kidney disease patients: the Italian experience. *BMC Nephrol.* 2016;17(1):77. DOI: 10.1186/s12882-016-0280-0