

Withholding and Withdrawing Dialysis in the Intensive Care Unit: Benefits Derived from Consulting the Renal Physicians Association/American Society of Nephrology Clinical Practice Guideline, Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

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Despite advances in the technology of dialysis, mortality in patients who develop acute renal failure remains high. Scoring systems have been developed to improve the ability to define prognosis in seriously ill patients with acute renal failure but predicting outcomes for individual patients is uncertain. Decisions to withhold or withdraw dialysis in seriously ill patients are difficult for patients, families, and health care providers. The clinical practice guideline, *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis*, provides evidence-based recommendations to aid nephrologists in discussions and the process of medical decision-making about starting and stopping dialysis. Estimating prognosis and addressing the issues of advance directives and patient and family preferences through the process of shared decision-making can clarify appropriate strategies for clinical management and interventions. Time-limited trials of dialysis may be an invaluable tool in this process. Increasing nephrologists' awareness of the guideline may facilitate decision-making around the issues of withholding and withdrawing dialysis in part by clarifying patients and situations in which it may be appropriate to withhold or withdraw dialysis.

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Withdrawing and withholding dialysis has received increasing attention since the seminal article by Neu and Kjellstrand in 1986 in which withdrawal from chronic hemodialysis accounted for 22% of all patient deaths (1). According to the U.S. Renal Data System, approximately one in five patients on chronic hemodialysis withdraw from therapy before death (2). A growing number of studies over the past 2 decades have now addressed withdrawal and withholding of dialysis in ESRD patients; however, far fewer have focused on withholding and withdrawing dialysis in acute renal failure (ARF). Decision-making about withholding or withdrawal of renal replacement therapy (RRT) in a critically ill patient with ARF may be more complicated than in an ESRD patient, in large part because of the potential for recovery of renal function. For example, poor candidates for chronic dialysis may be considered more favorably for temporary dialysis. Furthermore, acute illness, however severe, may be perceived

by patients and health care decision-makers alike as reversible and in isolation from significant chronic illness (3). Finally, and perhaps most importantly, critically ill patients are frequently unable to make medical decisions. Few critically ill patients have advance directives and even if they do, the directive does not appear to aid in the decision-making process for their surrogates (4).

In February, 2000, the Renal Physicians Association (RPA) and the American Society of Nephrology (ASN) published the clinical practice guideline *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* (5). The guideline is evidence-based and contains nine specific recommendations addressing shared decision-making, informed consent or refusal, estimating prognosis, conflict resolution, advance directives, withholding or withdrawing dialysis, special patient groups, time-limited trials of dialysis, and palliative care. The recommendations pertain to patients with ARF as well as those with ESRD. The available literature is graded using standard levels of evidence (levels A through C) to support the rationale for each recommendation (5).

Although only 21% of US nephrologists are aware of the guideline, 84% of those who are aware of the guideline use it in clinical decision-making (6). Thus, the guideline can be an

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invaluable source for information and guidance when making decisions to withhold or withdraw dialysis. In this manuscript, we review the primary issues affecting decisions to withhold or withdraw dialysis in ARF, focusing specifically on patients in the intensive care unit. Specifically, these issues are (a) the prognosis of ARF, (b) feasibility and initiation of dialysis in ARF, (c) preferences/shared decision-making/advance directives for withholding and withdrawal of dialysis in ARF, (d) the cost of dialysis for critically ill patients, and (e) legal aspects of dialysis for critically ill patients.

The Expected Outcome/Prognosis for Patients with ARF

In-hospital mortality rates of ARF in intensive care unit (ICU) patients remain high, from 28 to 90% in studies of heterogeneous populations (7). One of the largest prospective studies to examine survival in seriously ill patients, the SUPPORT trial (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment), included 490 patients who developed ARF and initiated dialysis during the study period (8). Sixty-nine percent of these patients had acute respiratory failure or multiorgan system failure with sepsis as the qualifying diagnoses for trial enrollment. In the SUPPORT trial, as in other studies, variables most often associated with high mortality included multiorgan failure, mechanical ventilation, liver failure, and malignancy (9). Median survival from dialysis initiation was 32 d and only 27% of patients were alive 6 mo later (9).

Multiple scoring systems have been offered to predict survival in patients with ARF or acute kidney injury (AKI) (10–13). Recently, the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) investigators examined 29,269 critically ill patients in 23 countries and found 1738 developed ARF during their ICU stay; 1260 patients underwent RRT (14). Overall in-hospital mortality was 60%. Independent risk factors for hospital mortality included use of vasopressors, mechanical ventilation, septic shock, cardiogenic shock, and hepatorenal syndrome (14). It should be noted that although mortality from ARF remains high, recent large epidemiologic studies indicate that it may have declined over the past 2 decades (15), even for individuals that required dialysis (16).

In an effort to improve the approach to ARF in the ICU, the RIFLE criteria were developed (17). The acronym is defined as Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage renal failure and provides definitions and classification for ARF as well as establishing criteria for evaluating management and outcomes (17). Preliminary application of the RIFLE criteria appear promising (18), but prognostic models to predict mortality in ICU patients have only an 80 to 85% discriminating ability to identify specific patients with a poor prognosis (19,20). Despite their less than 100% predictive value for individual patients, estimates of prognosis remain useful for patients, families, and health care providers in the process of shared decision-making (5,18–20).

In addition to estimating survival, the issue of recovery of kidney function after ARF needs to be considered to make informed decisions throughout the clinical course of ARF. Post-

survival quality of life of both the patient and his or her family may be markedly affected by whether or not chronic dialysis is required. Depending on the setting and the cause of ARF, recovery of kidney function generally occurs in 70 to 90% of survivors (14,18,19,21,22). However, only a few studies have examined long-term outcomes and quality of life of survivors (9,23–26). In the SUPPORT trial, 62% of survivors rated their quality of life as good or better; functional outcome was acceptable although patients with ARF had a median of one dependency in activities of daily living (9). Several recent studies examining quality of life in ARF survivors report diminished quality of life and physical functioning, but preserved satisfaction with life (25–27).

The Feasibility of Dialysis

Feasibility of dialysis is listed as one of the pertinent questions to be considered within the analytic framework of evidence for decision-making about dialysis in ARF (5). Although there are clinical circumstances in which conditions may adversely influence the ability to perform or deliver dialysis (e.g. hypotension, bleeding diathesis, unstable angina), the availability of continuous RRT has largely made dialytic treatment possible for most patients. Rarely, therefore, is the feasibility of dialysis an isolated impediment. More commonly, the feasibility of dialysis is intimately linked with issues involving prognosis and the ethical principles of beneficence and maleficence.

Decision-Making for the Initiation of Dialysis in Critically Ill Patients

Although technically feasible in most patients, dialysis may not benefit all patients with ARF. The ethical issues surrounding withholding and withdrawing dialysis in ARF are similar to those in chronic kidney disease. The ethical principles of autonomy and beneficence play key roles; the patient (or proxy) must consent, and benefit must outweigh the risks. Available clinical and ethical evidence supports withholding dialysis in ARF in several situations, as described in Recommendation 6 of the RPA/ASN guidelines and detailed in Table 1.

Furthermore, as noted in the RPA/ASN guideline, prognosis is an important factor to consider when making decisions to initiate dialysis because this addresses the principle of beneficence. Recommendation 7 of the RPA/ASN guidelines states it is “reasonable to consider” withholding or withdrawing dialysis in patients who have a terminal illness from a nonrenal cause or whose medical condition precludes the technical process of dialysis (5). Terminal illness was defined as a life expectancy of 6 mo or less from nonrenal disease(s) in patients not deemed to be candidates for solid organ transplantation (5). This recommendation provides a clinical practice guideline for withholding dialysis from patients with cirrhosis who are not candidates for liver transplantation, patients with widespread malignancy unresponsive to treatment, and those with severe congestive heart failure or end-stage pulmonary disease (5). The ethical principles of beneficence and nonmaleficence support this recommendation because in certain situations dialysis does not offer a reasonable expectation of benefit (28).

Despite the presence of the guideline, dialysis may be offered

Table 1. Appropriate situations for withholding or withdrawing dialysis

- A fully informed patient with decision-making capacity who refuses dialysis or asks that dialysis be discontinued.
- A patient who does not currently possess decision-making capacity but previously indicated refusal of dialysis in an oral or written advance directive.
- A patient who does not currently possess decision-making capacity and whose properly appointed legal agent refuses dialysis or asks that dialysis be discontinued.
- A patient who has irreversible, profound neurological impairment such that he or she lacks signs of thought, sensation, purposeful behavior, and awareness of self and environment.

Adapted from *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* (5).

or continued in certain patients if providers remain sensitive and cognizant of individual patient and family goals and circumstances. A time-limited trial of dialysis (5,29) may be a good option in patients with ARF when prognosis is not clear or wishes for aggressive care are unknown (5,29). Time-limited trials of dialysis are initiated with the understanding that dialysis will be withdrawn in a given period of time if clinical improvement does not occur. Goals of treatment, clinical outcomes to be assessed, and the duration of the dialysis trial should be clear to all parties (patient, family, consulting, and primary health care providers) and re-assessed as needed. During time-limited trials, medical decision-making is an ongoing process and allows for changes in the patient's clinical status and re-assessment of prognosis but within defined endpoints.

Preferences/Shared Decision-Making/ Advance Directives about Withholding Dialysis

Preferences of the Patient or Proxy

As noted in Recommendation 6 of the guideline, a competent patient's advance directive or the instruction of an appropriate surrogate or health care proxy to withhold dialysis should be respected. Advance directives are recommended to facilitate decision-making as well as to strengthen interfamily relationships, prepare for death, and allow patients and families control over medical decision-making (30–32). The presumption of informed consent under the ethical principle of patient autonomy is inherent in the process of advance care directives and planning. Advance care planning generally occurs within the patient-family relationship rather than in the patient-physician sphere. But, patients and families overwhelmingly expect health care providers to raise the subject of advance care planning and discuss the utility of medical interventions (30–32).

Unfortunately, advance care directives are often not completed, and even when available, they do not appear to function as intended. One study of 872 patients in a cancer center ICU

found that the presence of an advance directive did not affect decisions to initiate life-supporting interventions (33). However, the presence of an advance directive may have helped to promote earlier decisions about duration of therapy and resuscitation status (33). Although advance directives can facilitate the process of medical decision-making, their existence does not ensure the patient's wishes will be honored (32,34).

Programs that put advance directives in the form of medical orders show promise in ensuring patient wishes are properly heeded in the areas of resuscitation and end-of-life care (35). Physician Orders for Life-Sustaining Treatment (POLST) is a special medical order form completed by the physician and patient to establish end-of-life orders (www.polst.org). POLST has been used primarily for patients with chronic illness and in nursing home facilities in Oregon and the state of Washington. West Virginia and New York have similar programs under slightly different names, and several more states are developing similar programs. The orders generally address cardiopulmonary resuscitation, hydration, and feeding (36). Hopefully, other interventions such as dialysis would be included by the physician, particularly if ARF could be predicted, such as in patients with pre-existing chronic kidney disease.

Preferences of the Health Care Team

Clinician discomfort with interventions perceived to be too intensive is common, more likely for older, severely ill medical patients and for those with ARF (37). Clinician discomfort is also variable across ICU centers and more common among nurses (37). Discomfort among providers occurred most often during the first week of a patient's ICU stay and was most commonly reported by the bedside nurse (41.7%, $n = 551$), followed by attending physicians (34.7%, $n = 459$), and residents (23.6%, $n = 312$) in one study evaluating 657 mechanically ventilated ICU patients in 13 medical-surgical ICUs in four countries (37). Discomfort with the care plan was significantly more common when the plan was perceived to be too intense rather than not intense enough (1241/1322, 93.9% versus 81/1294, 6.1%, $P < 0.001$) (37). The sources of provider discomfort with the intense plans of support included perceptions that the patient and family were overestimating the chance for survival (51.7%), overestimating the patient's future quality of life (45.8%), that life support was inappropriately prolonging the dying process (35.6%), and there was inappropriate use of resources (30.3%) (37). Decision-making in ARF in these mechanically ventilated patients was strongly associated with clinician discomfort, both in plans to provide dialysis (odds ratio of 2.5) and to withhold dialysis (odds ratio of 2.0). However, nearly 40% of the patients in this study survived to hospital discharge, showing that factors other than physicians' discomfort determine decisions to withdraw life support and that end-of-life decisions should not be made hastily by a single physician (37). Conflict among physicians, between physicians and nurses (38), and among physicians and families is common in such situations.

Offering or continuing dialysis may in the some circumstances violate the principle of professional integrity if the treatment is considered medically inappropriate (28,39). Physi-

cians should not recommend treatments they think are medically inappropriate because of patient or family insistence. However, physicians may feel compelled to treat ARF with dialysis by default because it is a feasible therapy that shows objective signs of short-term effectiveness (e.g. normalization of electrolytes, lowering of BUN). When dialysis is presented in this way to family members or loved ones, it may be difficult for them to withhold an “effective” treatment because of feelings of guilt.

A better approach may be to describe dialysis as something that is generally withheld in the patient’s circumstances rather than something that simply can be done to maintain biologic function. Recently, Volandes and Abbo have argued for “flipping the default” option for cardiopulmonary resuscitation (CPR) in patients with advanced dementia (40). They argue that patients with end stage dementia should not be given CPR by default, but only upon specific request. Their statements are based on data that show the majority of individuals/health care decision makers do not want CPR if they have advanced dementia. Additional study of patient preferences regarding acute dialysis treatments would help guide physicians to “set the default” for dialysis or no dialysis.

Ethically, decisions to withhold medical therapies are analogous to decisions to withdraw therapies (41,42). However, discussions about such decisions may be different and documenting decisions to stop dialysis is more common than documenting decisions to withhold dialysis (43). Additional study of withholding and withdrawing dialysis in the setting of ARF would be helpful to isolate aspects of patient/family and provider discussions that lead to decisions and comfort or discomfort with those decisions.

Considering the Cost of Dialyzing Acutely Ill Patients

On the basis of the ethical principle of justice, the equitable distribution of resources is an important aspect of health care provision, particularly when the care provided is expensive and limited to a few beneficiaries. Therefore, in considering withholding or withdrawing dialysis treatment for the critically ill, a concrete assessment of cost and benefit is reasonable. Quality of life-years saved is a frequently used metric for assessing the cost-effectiveness of a treatment. In considering the cost-effectiveness of dialysis for ARF, the largest trial examining this issue was the SUPPORT trial (9). Four-hundred ninety of the patients enrolled in this trial developed ARF and were started on dialysis. Cost-effectiveness analysis of only direct medical costs found the estimated cost per quality-adjusted life-year was \$128,200 for patients started on dialysis (9). For the 103 patients in the worst prognostic category, the estimated cost per quality-adjusted life-year was \$274,100 and for the 94 patients in the best prognostic category, the cost per quality-adjusted life-year was \$61,900 (9). The commonly cited threshold for cost-effective care is \$50,000 per quality-adjusted life-year, thereby making dialysis a cost-ineffective treatment for seriously ill patients (9).

Additional studies on cost effectiveness of treatment of ARF are available but not as extensive as the SUPPORT trial. Gopal

et al. reported on the outcomes of 85 survivors of multi-organ failure including ARF that required continuous RRT (23). Given an approximate survival rate of 20% in their cohort, the cost of each year of survival was \$44,000 US dollars. This is substantially less than the SUPPORT trial results, although this was a group with poor prognosis on the basis of the inclusion criteria of multisystem organ failure. However, a formal cost analysis was not performed as part of the study (non-ICU hospital care was not included) nor was quality-adjusted life-years calculated. Korkeila and colleagues performed a more detailed examination of 62 patients with ARF requiring renal replacement therapy (24). The hospital mortality in their group was 45%, which rose to 55% at 6 mo and 65% at 5 yr. The cost per 6-mo survivor was just over 80,000 US dollars, an estimate closer to the results of the SUPPORT trial.

Legal Aspects of Withholding or Withdrawing Dialysis

Patients have the right to refuse life-saving health care, including hydration and artificial nutrition. US case law history, particularly the Quinlan case [In Re Quinlan, 355 A.2d. (New Jersey, 1976)], and the Supreme Court decision in 1990 for the Cruzan case [Cruzan *versus* Director, MO Department of Health, 497 US 261, 110 Sct 2841 (1990)], strongly reinforces an individualistic, autonomous perspective to withholding and withdrawing medical care. The Patient Self Determination Act of 1990 (included in the Congressional Omnibus Reconciliation Act of 1990, Public Law 101 to 508) protects by federal statute the rights of patients to consent to or to refuse any medical treatment, including stopping dialysis. Although it is clear that patients have the right to refuse life-saving treatment, whether they may demand interventions that are deemed medically futile by the caregiver remains contested. The question of initiating or continuing care when patients or their decision-makers and the caring physicians do not agree on the benefits of therapy is a major ethical and potentially legal issue. As medical interventions such as dialysis have become more effective at prolonging life, the issue of determining the potential futility of such interventions has become increasingly important. However, universal agreement on a measure or definition of futility has not been reached and the issue is likely to remain unresolved (44–47).

Withholding and withdrawing dialysis should occur only with consent of the patient or designated health care decision-makers. Physicians may cite medical futility but should avoid acting unilaterally, without patient knowledge, or over patient’s or surrogate decision-maker’s objections, to withhold or withdraw a treatment. Physicians retain the right to withhold and withdraw treatment that they believe is medically inappropriate, but should inform the patient about the treatment option within the context of benefit or lack of benefit and the physician’s judgment of futility if appropriate. This approach is critical, because it allows the patient an opportunity to obtain a second opinion (48). Although court decisions have consistently sided with patients and surrogates in cases of futility, they have been reluctant to punish physicians who refuse to provide medically inappropriate treatment if the physicians

follow the accepted standard of care. The usual determinants of malpractice pertain to such patients; therefore, the physician should meet the requirements of standard medical care for the particular clinical condition (48).

Interprofessional team consensus is needed in situations perceived to be medically futile. It is imperative that nephrologists participate in discussions with family and that they document the discussions in the medical record to support informed decision-making. If a nephrologist disagrees with the critical care team about the suitability of a patient for dialysis, then a discussion among all providers is needed. An Ethics Committee Consultation may be helpful in cases in which providers disagree about appropriate interventions, or when providers and patients disagree. A time-limited trial of dialysis can be invaluable in such situations, and negotiations almost always resolve disagreements in care.

Discontinuation of Life Support Therapy

Once a decision is made to change healthcare goals to a less aggressive course, discontinuation of life support may occur in a stepwise manner. Dialysis discontinuation is probably one of the first things to occur whereas discontinuation of artificial feeding and hydration and mechanical ventilation are likely to be the last interventions withdrawn (49). A palliative care consultation should be considered to aid in pain and symptom management, hospice referral, and support of family adjustment to end-of-life care. Part of palliative care for ARF may include ultrafiltration to treat dyspnea. Families should be prepared for the possibility that patients may recover from ARF as well. Transfer to a general medical or surgical floor should occur only if adequate nursing care is available.

Time to death after discontinuation of dialysis has been fairly well established to be a median of 9.6 d for patients with ESRD on chronic dialysis therapy (50). ARF patients in the SUPPORT trial who withdrew from dialysis ($n = 96$) all died in the hospital or within 3 d of hospital discharge. All but 2 patients in whom dialysis was withheld ($n = 92$) died in the hospital or within 6 d of discharge; one of these patients survived 25 d and the other 77 d postdischarge (43). The time frame may be much shorter in critically ill patients due to comorbidities and the fact that other life sustaining therapies may be reduced or discontinued. Most patients die within several hours of withholding life-sustaining treatment and may require continued ICU monitoring for palliative care (51). Remarkably, some patients (up to 10%) may continue to live for 1 or more days after ventilator discontinuation.

Summary

Mortality remains high for seriously ill patients who develop ARF, and dialysis in this population is generally not cost effective. Little is known about the long-term outcome and quality of life of survivors of ARF in ICUs but most patients appear to recover kidney function and enjoy acceptable quality of life. Scoring systems to estimate prognosis in such patients are not perfect but often provide information useful in medical decision-making. The RPA/ASN guideline, *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* pro-

vides general recommendations to follow when withholding and withdrawing dialysis is considered. Time-limited trials of dialysis with predetermined measures of improvement, reasonable goals and duration of the trial, and ongoing assessment and communication of clinical status with patients, families, and care providers may enhance decision-making, reduce discomfort among providers and families, and lead to fewer cases of extended intensive care for seriously ill patients with poor prognoses. Greater awareness and dissemination of the RPA/ASN guidelines may facilitate decision-making and care of seriously ill patients who develop ARF.

Disclosures

None.

References

1. Neu S, Kjellstrand CM: Stopping long-term dialysis. An empirical study of withdrawal of life-supporting treatment. *N Engl J Med* 314: 14–20, 1986
2. US Renal Data System: *US Renal Data System Annual Data Report 2007*, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2007
3. Teno JM, Stevens M, Spornak S, Lynn J: Role of written advance directives in decision making: Insights from qualitative and quantitative data. *J Gen Intern Med* 13: 439–446, 1998
4. Teno J, Lynn J, Wenger N, Phillips RS, Murphy DP, Connors AF Jr., Desbiens N, Fulkerson W, Bellamy P, Knaus WA: Advance directives for seriously ill hospitalized patients: Effectiveness with the patient self-determination act and the SUPPORT intervention. SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment *J Am Geriatr Soc* 45: 500–507, 1997
5. *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* Renal Physicians Association and American Society of Nephrology, Washington, DC, 2000
6. Davison SN, Jhangri GS, Holley JL, Moss AH: Nephrologists reported preparedness for end-of-life decision-making. *Clin J Am Soc Nephrol* 2: 1256–1262, 2007
7. Metnitz PG, Krenn CG, Steltzer H, Lang T, Ploder J, Lenz K, Le Gall JR, Druml W: Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. *Crit Care Med* 30: 2051–2058, 2002
8. The SUPPORT Principal Investigators: A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). *JAMA* 274: 1591–1598, 1995
9. Hamel MB, Phillips RS, Davis RB, Desbiens N, Connors AF Jr, Teno JM, Wenger N, Lynn J, Wu AW, Fulkerson W, Tsevat J: Outcomes and cost-effectiveness of initiating dialysis and continuing aggressive care in seriously ill hospitalized adults. SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Ann Intern Med* 127: 195–202, 1997
10. Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHE II: A severity of disease classification system. *Crit Care Med* 13: 818–829, 1985

11. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology score (SAPS II) based on a European/North American multicenter study. *JAMA* 270: 2957-2963, 1993
12. Liano F, Pascual J: Outcomes in acute renal failure. *Semin Nephrol* 18: 541-550, 1998
13. Paganini EP, Halstenberg WK, Goormastic M: Risk modeling in acute renal failure requiring dialysis: The introduction of a new model. *Clin Nephrol* 46: 206-211, 1996
14. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C: Acute renal failure in critically ill patients: A multinational, multicenter study. *JAMA* 294: 813-818, 2005
15. Xue JL, Daniels F, Star RA, Kimmel PL, Eggers PW, Molitoris BA, Himmelfarb J, Collins AJ: Incidence and mortality of acute renal failure in Medicare beneficiaries, 1992 to 2001. *J Am Soc Nephrol* 17: 1135-1142, 2006
16. Waikar SS, Curhan GC, Wald R, McCarthy EP, Chertow GM: Declining mortality in patients with acute renal failure, 1988 to 2002. *J Am Soc Nephrol* 17: 1143-1150, 2006
17. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P: Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 8: R204-R212, 2004
18. Abosaif NY, Tolba YA, Heap M, Russell J, El Nahas AM: The outcome of acute renal failure in the intensive care unit according to RIFLE: Model application, sensitivity, and predictability. *Am J Kidney Dis* 46: 1038-1048, 2005
19. Chertow GM, Christiansen CL, Cleary PD, Munro C, Lazarus JM: Prognostic stratification in critically ill patients with acute renal failure requiring dialysis. *Arch Intern Med* 155: 1505-1511, 1995
20. Douma CE, Redekop WK, van der Meulen JH, van Olden RW, Haecck J, Struijk DG, Krediet RT: Predicting mortality in intensive care patients with acute renal failure treated with dialysis. *J Am Soc Nephrol* 8: 111-117, 1997
21. Himmelfarb J, Tolkoff RN, Chandran P, Parker RA, Wingard RL, Hakim R: A multicenter comparison of dialysis membranes in the treatment of acute renal failure requiring dialysis. *J Am Soc Nephrol* 9: 257-266, 1998
22. McCarthy JT: Prognosis of patients with acute renal failure in the intensive-care unit: A tale of two eras. *Mayo Clin Proc* 71: 117-126, 1996
23. Gopal I, Bhonagiri S, Ronco C, Bellomo R: Out of hospital outcome and quality of life in survivors of combined acute multiple organ and renal failure treated with continuous venovenous hemofiltration/hemodiafiltration. *Intensive Care Med* 23: 766-772, 1997
24. Korkeila M, Ruokonen E, Takala J: Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. *Intensive Care Med* 26: 1824-1831, 2000
25. Maynard SE, Whittle J, Chelluri L, Arnold R: Quality of life and dialysis decisions in critically ill patients with acute renal failure. *Intensive Care Med* 29: 1589-1593, 2003
26. Noble JS, Simpson K, Allison ME: Long-term quality of life and hospital mortality in patients treated with intermittent or continuous hemodialysis for acute renal and respiratory failure. *Ren Fail* 28: 323-330, 2006
27. Ahlstrom A, Tallgren M, Peltonen S, Rasanen P, Pettila V: Survival and quality of life of patients requiring acute renal replacement therapy. *Intensive Care Med* 31: 1222-1228, 2005
28. Keating RF, Moss AH, Sorkin MI, Paris JJ: Stopping dialysis of an incompetent patient over the family's objection: Is it ever ethical and legal? *J Am Soc Nephrol* 4: 1879-1883, 1994
29. MacKay K, Moss AH: To dialyze or not to dialyze: An ethical and evidence-based approach to the patient with acute renal failure in the intensive care unit. *Adv Ren Replace Ther* 4: 288-296, 1997
30. Davison SN: Facilitating advance care planning for patients with end-stage renal disease: The patient perspective. *Clin J Am Soc Nephrol* 1: 1023-1028, 2006
31. Ikonomidis S, Singer PA: Autonomy, liberalism and advance care planning. *J Med Ethics* 25: 522-527, 1999
32. Lynn J, Goldstein NE: Advance care planning for fatal chronic illness: Avoiding commonplace errors and unwarranted suffering. *Ann Intern Med* 138: 812-818, 2003
33. Kish WS, Martin CG, Shaw AD, Price KJ: Influence of an advance directive on the initiation of life support technology in critically ill cancer patients. *Crit Care Med* 29: 2294-2298, 2001
34. Somogyi-Zalud E, Zhong Z, Hamel MB, Lynn J: The use of life-sustaining treatments in hospitalized persons aged 80 and older. *J Am Geriatr Soc* 50: 930-934, 2002
35. Hickman SE, Hammes BJ, Moss AH, Tolle SW: Hope for the future: Achieving the original intent of advance directives. *Hastings Cent Rep*: S26-S30, 2005
36. Hickman SE, Tolle SW, Brummel-Smith K, Carley MM: Use of the Physician Orders for Life-Sustaining Treatment program in Oregon nursing facilities: Beyond resuscitation status. *J Am Geriatr Soc* 52: 1424-1429, 2004
37. Griffith L, Cook D, Hanna S, Rucker G, Sjokvist P, Dodek P, Marshall J, Levy M, Varon J, Finfer S, Jaeschke R, Buckingham L, Guyatt G: Clinician discomfort with life support plans for mechanically ventilated patients. *Intensive Care Med* 30: 1783-1790, 2004
38. Breen CM, Abernethy AP, Abbott KH, Tulskey JA: Conflict associated with decisions to limit life-sustaining treatment in intensive care units. *J Gen Intern Med* 16: 283-289, 2001
39. Paris JJ, Schreiber MD, Statter M, Arensman R, Siegler M: Beyond autonomy: Physicians' refusal to use life-prolonging extracorporeal membrane oxygenation. *N Engl J Med* 329: 354-357, 1993
40. Volandes AE, Abbo ED: Flipping the default: A novel approach to cardiopulmonary resuscitation in end-stage dementia. *J Clin Ethics* 18: 122-139, 2007
41. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research: *Deciding to Forego Life-Supporting Treatment*. US Government Printing Office, Washington DC, 1983.
42. Brody H: Withdrawing versus withholding therapy: Still a pernicious distinction. *J Am Geriatr Soc* 43: 716-717, 1995
43. Wenger NS, Lynn J, Oye RK, Liu H, Teno JM, Phillips RS, Desbiens NA, Sehgal A, Kussin P, Taub H, Harrell F, Knaus W: Withholding versus withdrawing life-sustaining

- treatment: Patient factors and documentation associated with dialysis decisions. *J Am Geriatr Soc* 48: S75-S83, 2000
44. Helft PR, Siegler M, Lantos J: The rise and fall of the futility movement. *N Engl J Med* 343: 293-296, 2000
 45. Schneiderman LJ, Jecker NS, Jonsen AR: Medical futility: Its meaning and ethical implications. *Ann Intern Med* 112: 949-954, 1990
 46. Truog RD, Brett AS, Frader J: The problem with futility. *N Engl J Med* 326: 1560-1564, 1992
 47. Cranford RE: Medical futility: Transforming a clinical concept into legal and social policies. *J Am Geriatr Soc* 42: 894-898, 1994
 48. Cantor NL: Twenty-five years after Quinlan: A review of the jurisprudence of death and dying. *J Law Med Ethics* 29: 182-196, 2001
 49. Faber-Langendoen K, Lanken PN: Dying patients in the intensive care unit: Forgoing treatment, maintaining care. *Ann Intern Med* 133: 886-893, 2000
 50. Cohen LM, McCue JD, Germain M, Kjellstrand CM: Dialysis discontinuation. A 'good' death? *Arch Intern Med* 155: 42-47, 1995
 51. Hall RI, Rocker GM: End-of-life care in the ICU: Treatments provided when life support was or was not withdrawn. *Chest* 118: 1424-1430, 2000