

To Dialyze or Not: The Patient with Metastatic Cancer and AKI in the Intensive Care Unit

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Summary

AKI severe enough to necessitate renal replacement therapy occurs in approximately 5% of patients admitted to the intensive care unit (ICU) and is associated with in-hospital mortality in excess of 50%. Complicating factors, such as cancer, can increase in-hospital mortality to 85%. Intensivists often expect that consulted nephrologists will provide dialysis when asked to do so, without considering whether it is likely to benefit the patient and therefore is medically and ethically appropriate. In this Attending Rounds, on the basis of the evidence and recommendations in *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis*, a clinical practice guideline, a case of anuric AKI in the ICU is presented and analyzed. Woven into the discussion are insights from the clinical and ethics literature on this topic, along with the experience of the author. This Attending Rounds presents an approach to deciding when it is not appropriate to dialyze patients with AKI in the ICU.

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Case (Presented by Sarina Ahuja, MD, Nephrology Fellow)

A 58-year-old woman with morbid obesity (body mass index > 90 kg/m²) was admitted to the hospital with back pain and was incidentally found to have iron deficiency anemia due to postmenopausal bleeding. She had normal baseline kidney function with a serum creatinine level of 0.4 mg/dl (laboratory reference range, 0.49–1.10 mg/dl) and an estimated GFR > 60 ml/min per 1.73 m². Her urinalysis was normal with the exception of 30 mg of protein per deciliter on dipstick testing, which was not further quantified. During evaluation of her anemia and endometrial bleeding, imaging studies revealed multiple mediastinal masses and large lymph nodes. A lymph node biopsy revealed metastatic squamous cell cancer of unknown primary. Her course was further complicated by multiple drug-resistant infections, septic shock, respiratory failure necessitating mechanical ventilation and tracheostomy, and anuric AKI. At least in part because of the patient's multiple medical problems, she was somnolent and unable to interact with her family or hospital staff most of the time. She lacked decision-making capacity, and her husband was appointed her healthcare surrogate. The husband and wife had never discussed her wishes for goals of treatment should she become incapacitated.

Four weeks into her hospitalization, the nephrology service was consulted for evaluation and management of AKI, which was thought to be due to acute tubular necrosis from septic shock. The patient was poorly responsive and could not respond to questions or commands. After 7 days of anuria, her blood urea nitrogen peaked at 86 mg/dl and her serum creatinine peaked at 3.6 mg/dl. The patient was on high ventilator settings (fraction of inspired oxygen, 50%; positive end-expiratory pressure, 10 cm H₂O; and

pressure control, 22 cm H₂O). She was unable to be weaned from mechanical ventilation, with PCO₂ levels of approximately 70 mmHg. She was 30 L positive for the admission and had anasarca. Potential indications for dialysis included uremia and fluid overload with compromised oxygenation.

The oncology service had evaluated the patient on two separate occasions and deemed her an unsuitable candidate for chemotherapy. Given her poor prognosis and her terminal metastatic malignancy, the consulting renal service did not consider her an appropriate candidate for dialysis. On several occasions the nephrologist and the intensivist had frank discussions with the husband about his wife's poor prognosis and the tremendous suffering that his wife was undergoing. Her husband was unprepared to have his wife die; he demanded a second opinion and a transfer to another hospital where she could undergo dialysis.

The nephrologist was troubled by the husband's outburst at the refusal to provide dialysis for his wife and was reassured by his nephrology colleagues and the medical literature that refusal to dialyze this patient was appropriate. No nephrologist at the present hospital or at another hospital would accept her in transfer. An ethics consult was obtained, and the consultants agreed with the nephrologist that the patient should not be treated with dialysis. She remained at the initial hospital, and her renal failure was managed conservatively. Over time, her urine output increased to 500 ml/d, and her serum creatinine level decreased to 2.9 mg/dl. After months of hospitalization, the husband wanted to take his wife home and declined transfer of the patient to a long-term acute care hospital or other facility where she could be maintained on mechanical ventilation. He had come to accept that his wife was going to die and wanted her to die at home. He agreed

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to her being discharged home on a ventilator with hospice services. She died shortly thereafter.

Introduction

The RIFLE classification system defines AKI according to severity: risk, injury, failure, loss, and ESRD (1). AKI occurs in as many as 36%–67% of intensive care unit (ICU) patients (2) and is frequently caused by acute tubular necrosis from septic shock, as occurred in our patient. Approximately 5% of ICU patients with AKI develop the failure stage of RIFLE and require renal replacement therapy (3). For patients with AKI requiring dialysis, observational studies have indicated that the hospital mortality rate for AKI in the ICU is in excess of 50% (1–5). Multiple independent risk factors for in-hospital death have been identified, including use of vasopressors, mechanical ventilation, septic shock, presence of pre-existing end-stage chronic illness, and multiple organ system failure (1,3). Our patient had all of these risk factors, including end-stage chronic illness, ventilator-dependent hypercarbic respiratory failure, and untreatable metastatic cancer.

Patients with cancer admitted to the ICU who have AKI that necessitates dialysis have a particularly high mortality. The in-hospital mortality rate was 86% in one study (6) and the 60-day survival rate in another was only 14% (7). In the latter study, the adjusted odds ratio for 60-day mortality in patients with cancer and AKI was 14.3 compared with cancer patients who did not have AKI (7). Morbid obesity has also been associated with a two-fold increase in hospital mortality in one study (8), although another study did not confirm this finding (9).

Our patient had an overall very poor prognosis with three significant comorbid illnesses (morbid obesity, hypercarbic respiratory failure, and metastatic cancer) and AKI associated with multiple independent risk factors for hospital mortality. Quite appropriately, the nephrologist asked the ethical question, “Should I dialyze this patient?” This article will address this question using the seven-step process for ethical decision-making presented in the nephrology clinical practice guideline, *Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis* (10). The process is presented in Table 1.

Table 1. The seven-step process of ethical decision-making in patient care

<p>Step 1. What are the ethical questions? Step 2. What are the clinically relevant facts? Step 3. What are the values at stake for all relevant parties? Step 4. List options. What could you do? Step 5. What should you do? Choose the best option from the ethical point of view. Step 6. Justify your choice. Give reasons to support your choice. Refer back to the values and explain why some values are more important in this case than the others. Step 7. How could this ethical issue have been prevented? Would any policies/guidelines/practices be useful in changing any problems with the system?</p>

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Step 1: What Are the Ethical Questions?

This case poses multiple ethical questions: (1) Is the nephrologist ethically obligated to dialyze the patient? (2) How should the nephrologist respond to the husband’s demand for dialysis? and (3) What is a fair way to resolve the conflict between the husband and the nephrologist? Fortunately, the intensivist consulting the nephrologist did not believe that dialysis would improve the patient’s chances for survival to discharge and did not object when the nephrologist declined to dialyze the patient. In many cases, however, intensivists consult nephrologists with the expectation that if the intensivist wants the patient dialyzed, the nephrologist will do it without question. Nephrology fellows from many different academic programs report to me the same experience. They feel as if they are “dialysis technicians” and that they are being consulted to “do dialysis,” and not for their independent expertise with regard to whether dialysis is likely to benefit the patient. This issue will be addressed further in step 3.

Step 2: What Are the Clinically Relevant Facts?

A first relevant fact to address is the patient’s kidney function. The two most commonly used formulas for estimation of GFR, the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) formula, have not been validated in patients with morbid obesity, advanced malignancy, or severe multiorgan failure and critical illness; thus, they are probably inaccurate in these settings (11). The patient’s initial serum creatinine level was lower than the normal range, and even when she was in anuric kidney failure for 1 week her serum creatinine level did not rise above 3.6 mg/dl. Nonetheless, she met the failure criteria for RIFLE with a three-fold increase in her serum creatinine level and anuria lasting for more than 12 hours (1).

A second fact to address is the relationship of the patient’s morbid obesity to her respiratory failure. Patients with morbid obesity have reduced lung volumes with hypoventilation at the lung bases causing arterial hypoxemia. They also have been found to have increased work of breathing resulting from increased airway resistance, abnormal chest elasticity, and inefficiency of the respiratory muscles. Not surprisingly, pneumonia, hypoxia, hypercarbic respiratory failure necessitating mechanical ventilation, increased length of stay in the ICU and the hospital, and longer period of weaning from mechanical ventilation have all been identified as respiratory complications of morbid obesity (8,9). Despite several months of attempts, our patient was unable to be weaned from mechanical ventilation during her extended hospital stay.

A third fact to consider is the patient’s overall prognosis. This patient had a terminal illness from a nonrenal cause, metastatic cancer, as well as end-stage lung disease. Critical care physicians do not have clinical practice guidelines that address which patients are appropriate candidates for long-term mechanical ventilation. If patients (or their legal decision-makers) do not consent to removal from mechanical ventilation (recognizing that this usually results in the patient’s death), discharge to a facility that can provide long-term mechanical ventilation is often arranged.

In these circumstances, recommendation 6 in the *Shared Decision-Making* clinical practice guideline states that the

nephrologist is ethically justified in not offering dialysis. It reads, “Consider forgoing dialysis for AKI, CKD, or ESRD patients who have a very poor prognosis or for whom dialysis cannot be provided safely.” It further notes that patients included in the category covered by the recommendation include “those who have a terminal illness from non-renal causes” (10).

Needless to say, the husband was not pleased with the nephrologist’s decision not to offer dialysis and requested transfer to another hospital where his wife could receive dialysis. The subsequent events will be described in step 4.

Step 3: What Are the Values at Stake for All Relevant Parties?

This case involves several competing values. The husband valued prolongation of his wife’s life. Well into her hospital course, he remained emotionally unprepared for her death. For this reason he requested that everything possible be done, including cardiopulmonary resuscitation, use of vasopressors, and dialysis. He did not trust the doctors. Only late in the hospital course did he understand that his wife was going to die and that long-term life prolongation was not possible.

A standard approach to “doing medical ethics” that preserves the value of integrity of physicians is the one presented in the ethics textbook, *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*, seventh edition (12). The authors refer to their approach as the “Four-Topic Method” (see Table 2) and state that the first factor to be examined in an ethical analysis is whether the treatment is medically indicated. By this, they mean “the expected medical benefits of the treatment outweigh the burdens.” Professional integrity requires nephrologists to refrain from offering dialysis if the burdens of dialysis substantially outweigh the benefits. In this case, the patient’s posthospital survival was extremely unlikely, and the nephrologist saw dialysis as an intervention that would increase the patient’s suffering and possibly prolong the patient’s dying without restoring her to a reasonable quality of life. The nephrologist did not believe that dialysis would be in the patient’s best interest and therefore did not offer it.

A value that has crept into medical care in the United States in the past 50 years is the “technological imperative.” In short, as applied to dialysis, the technological imperative states, “If we can dialyze the patient, we must dialyze the patient.” Victor Fuchs, the health economist who coined the term, stated that healthcare driven by this approach is not effective, efficient, or equitable (13). In short, this value increases cost without necessarily improving quality of care. Observers of the application of the technological imperative to implantable cardioverter-defibrillators, another life-sustaining technology like dialysis, note that in the United States two cultural moves—from new technique to standard technique and then from standard technique to ethical necessity—are evident in the growing trend to use aggressive interventions such as dialysis and implanted cardioverter-defibrillators for older or sicker patients. The irony is that such interventions prolong debilitation, suffering, and the dying process, something that patients report they want to avoid (14). Hence, in this case the nephrologist did not want to violate his professional and moral standards,

Table 2. Deciding what to offer: the four topics to be considered in ethical analysis

Medical indications Patient preferences Quality of life Contextual features
Data obtained from reference 12.

yield to the technological imperative, and dialyze the patient just because “it could be done.”

The nephrologist’s position is supported by the *Shared Decision-Making* guideline. Shared decision-making recognizes the importance of both patient preferences and medical indications. In shared decision-making, the health care provider is the expert in diagnosis, prognosis, and treatment alternatives, and the patient is the expert in his or her own history, values, preferences, and goals. The two work together to reach decisions that are individualized to the patient’s particular circumstances and preferences. The guideline, however, recognizes limits to the shared decision-making process that protect the rights of patients and the professional integrity of health care professionals. The patient has the right to decline dialysis even if the renal care team disagrees with the patient’s decision and wants the patient to undergo dialysis. Similarly, the renal care team has the right to refuse to offer dialysis when the possibility of prolonging the patient’s life is not justified by the significant suffering that such life prolongation is likely to entail. The nephrologist concluded the latter.

Some have also recognized that physicians are not ethically or legally obligated to provide medically ineffective treatment. In the Maryland Code, “medically ineffective” treatment means that to a reasonable degree of medical certainty, a medical procedure will not prevent or reduce the deterioration of the health of an individual or prevent the impending death of an individual (15). For this patient, with terminal cancer and ventilator-dependent respiratory failure, dialysis would have been ineffective in preventing her deterioration and her death. Because of her altered mental status before the onset of uremia, it also would not have afforded her even a few days more of survival with meaningful interaction with her family.

Step 4: List Options. What Could You Do?

In this case, the nephrologist has the following options:

- He could dialyze the patient as requested by the husband.
- He could unilaterally refuse to dialyze the patient without seeking further consultation.
- He could request an ethics consultation.
- He could seek to transfer the patient’s care to another nephrologist or institution.

For situations like this one in which there is conflict between the husband and the nephrologist, recommendation 8 in the dialysis *Shared Decision-Making* clinical practice guideline states, “Establish a systematic process for conflict

resolution if there is disagreement about what decision should be made with regard to dialysis." This process is displayed in Figure 1. The nephrologist followed the recommendation and first obtained an ethics consultation. The ethics consultants agreed with the decision of the nephrologist and spent some time talking to the husband about his and his wife's values and what would be most important to him at this time in her illness. The husband indicated that he still wanted to fight for his wife's life; when presented with the possible option of transfer of his wife's care to another hospital when no other nephrologist at the present hospital was willing to dialyze the patient, he accepted it. This course of action is also recommended in the guideline when it suggests attempting transfer of care to another institution if a plan of care cannot be agreed upon with the patient or legal agent after ethics consultation and an attempt to transfer care within the institution. No other hospital was willing to accept the patient in transfer and do as the husband requested. The ethics committee followed up with the husband and raised the possibility of discharge home with hospice, with the understanding that his wife was dying. Transfer home would allow the husband to accomplish his goal of his wife dying at home.

Step 5: What Should You Do? Choose the Best Option from the Ethical Point of View

With an understanding that he had no other option for getting his wife home, the husband accepted the recommendation of discharge of his wife to her home on a ventilator with hospice care. Because the husband was initially so emotionally unprepared for his wife's death, he had been in denial with regard to her actual overall condition for most of her hospitalization. The refusals by the oncologist and the nephrologist at the present hospital and the physicians at other hospitals to agree to the husband's requests finally brought him to the point at which he understood that his wife was dying and that his desire for long-term life prolongation for her was not achievable. The ICU social worker found a hospice willing to accept the patient on mechanical ventilation in the home.

Step 6: Justify Your Choice. Refer Back to the Values and Give Reasons Why Some Values Are More Important in This Case Than Others

The husband wanted the patient to return home. The hospice discharge option allowed the care team to honor the husband's value of wanting his wife to die at home. All other options for her longer-term survival, such as discharge to a long-term acute care hospital, had been explored and were not acceptable to the husband. The husband grieved his inability to prolong his wife's life, which had been his main value during the long hospitalization. He did establish a supportive relationship with one of the hospice nurses, and the hospice instituted bereavement counseling immediately after the patient's death.

Step 7: How Could This Ethical Issue Have Been Prevented? Would Any Policies/Guidelines/Practices Be Useful in Changing Any Problems with the System?

The *Shared Decision-Making* clinical practice guideline was used at multiple points in this case to guide decisions and

address conflict. Following it prevented the patient from suffering from dialysis treatments that would not have prolonged her survival. The nephrology team reported gratitude for having the guideline as a resource to guide them through this difficult decision making process.

Questions

Dr. Perry Wilson (Senior Research Nephrology Fellow): You allude multiple times to the "suffering" inflicted by dialytic therapies. Often, in the ICU, patients are sedated or otherwise unresponsive and it is unclear whether they are suffering at all. It is doubtful that the dialytic process is painful (though catheter insertion may be). What are the ethical considerations when a patient is unconscious? Are all ICU patients "suffering"?

Dr. Moss: Suffering is an experience involving factors that are distressful to a patient and that undermine patient quality of life. ICU patients who lack decision-making capacity may suffer and indicate it by their behaviors of restlessness, agitation, groaning, grimacing, pushing away or striking doctors and nurses, and clenching their fists. In our case the patient demonstrated many of these behaviors and pulled out her nasogastric tube and peripherally inserted central catheter line multiple times. Because of her behavior she was intermittently placed in restraints, which increased her suffering and necessitated sedation with fentanyl and midazolam drips to calm her. When these drips were stopped for a "drug holiday," these behaviors returned. From an ethical perspective, professionalism requires physicians to be compassionate and to attempt to relieve suffering and refrain from inflicting it on their patients.

Dr. Jeffrey S. Berns: We often talk about time-limited trials of dialysis to resolve conflicts with other physicians or patient families. Do you find this to be a useful approach that helps others come to terms with the nephrologists' recommendation to not initiate dialysis, or does this just delay the need to make a definitive decision?

Dr. Moss: Time-limited trials can be very useful in circumstances when the benefit of dialysis is uncertain for a particular patient and the patient (or appropriate legal agent for a patient who lacks decision-making capacity) is requesting it. For such a patient who improves with dialysis, the benefit is proved, and dialysis is continued. For a patient who does not improve with dialysis or who cannot tolerate it, then dialysis can be stopped with the increased knowledge that it did not help. For families who are very insistent that dialysis be performed when the nephrologist is hesitant to employ it because the likely burdens outweigh the benefits, a time-limited trial with the goals agreed upon in advance can provide families with a better understanding of the burdens of dialysis. Often this additional information is helpful in reaching a decision with the family to stop dialysis after a time-limited trial has failed to achieve the agreed upon goals.

Dr. Barry Fuchs (Medical ICU Medical Director): Critical care physicians often make judgments about patient prognosis to help decide the most appropriate treatments to offer and to help families make informed decisions. However, prognostication about survival from critical illness is not a science and failure to offer a life-sustaining intervention could result in premature death. Given the

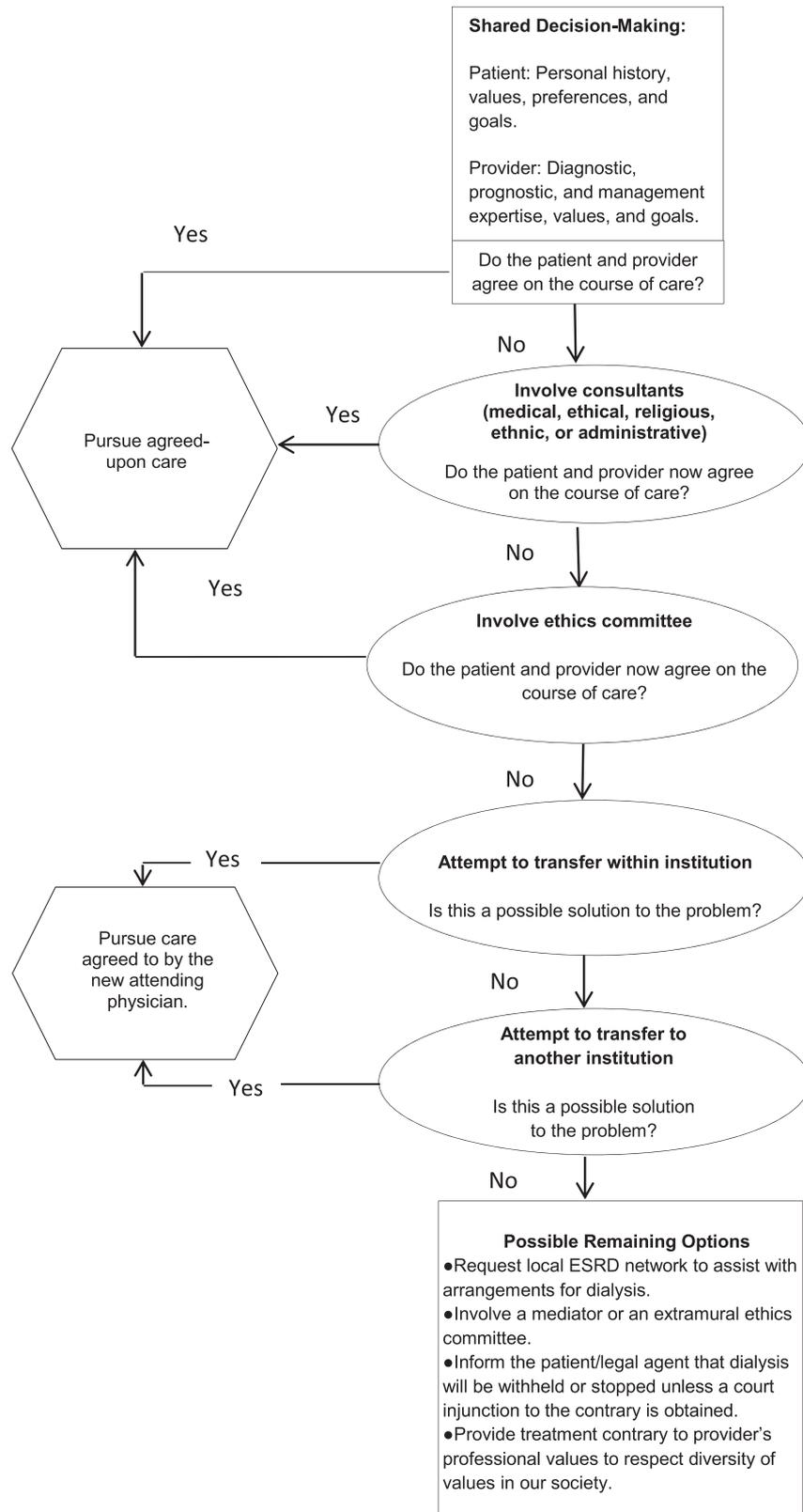


Figure 1. | Systematic approach to resolving conflict between patient and kidney care team. Reprinted from reference 10, with permission.

gravity of the decision to withhold or discontinue dialysis in an individual patient, what recommendations would you give to colleagues about how they should approach decisions about patient prognosis before deciding about whether to offer dialysis?

Dr. Moss: The process of shared decision-making is recommended for making these decisions. In shared decision-making, the patient (or family) is the expert in the patient's history, values, and goals and the nephrologist is the expert in diagnosis, prognosis, and treatment options. In the process, it is important for nephrologists to be clear about the patient's prognosis in light of the patient's (or family's) goals for treatment. Prognosis is based on the number and severity of comorbid conditions, functional status, and nutritional status. Her poor prognosis was clear before the patient developed AKI. The husband's goal was for his wife to return home without the need for mechanical ventilation. This goal was not achievable and dialysis would not have helped achieve it, but potentially dialysis could have prolonged her suffering. The decision not to offer dialysis was justified in this case by the Hippocratic maxim, "Be of benefit and do no harm" and the recommendations in the dialysis *Shared Decision-Making* clinical practice guideline.

Disclosures

None.

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