human.” Hence, a capacity to generate an appropriate stromal population from human pluripotent stem cells or the elucidation of the signaling pathways required for the appropriate response in human ureteric epithelium is clearly required. Reinvestigating what we know already around ureter patterning in mouse will likely once again provide solutions, although profiling of the human fetal kidney stroma will also provide important information. In the meantime, if proven to work for human stem cell–derived ureteric epithelial cultures, the classic anatomic coculture approach adopted in Sallam et al.8 may become a standard functional assay of ureteric competence with which to assess the growing number of protocols for differentiation to this epithelial end point.

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Do-Not-Resuscitate Orders among Patients with ESKD Admitted to the Intensive Care Unit: A Bird’s Eye View

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The goal of advance care planning (ACP) is to help elucidate, clarify, and communicate patients’ values, goals, and care preferences.1 Engaging patients and their families in an iterative and ongoing process of ACP can help to ensure that they receive care that is congruent with their core values in situations where they may be unable to speak or advocate for themselves.1–3 During ACP, patients’ preferences related to cardiopulmonary resuscitation and other treatments along with their preferred surrogate decision maker(s) are typically documented in their medical record (e.g., advance directive, do-not-resuscitate [DNR] order, Provider Orders for Life Sustaining Treatment, and Medical Orders for Life Sustaining Treatment). To uphold personhood throughout the course of illness and across the continuum of care, ACP should ideally

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be integrated with patients’ other care processes; informed by their evolving experience of illness, prognostic awareness, and understanding of treatment options; and grounded in their cultural and social identities. Having an opportunity to engage in ACP is especially important for patients with ESKD as many have limited life expectancy and will face complex medical decisions during the course of illness. Also, a disproportionate number of patients with ESKD are Black, a population with relatively low rates of advance directive completion.

In this issue of JASN, Danziger et al. describe their work to characterize documentation of DNR orders among patients with different underlying health conditions on the basis of national data from the Intensive Care Unit Research Institute Database. Using this novel data source, the authors were able to compare the prevalence of DNR orders among patients with ESKD admitted to an intensive care unit (ICU) over a 1-year period with that among patients with other serious illnesses (i.e., stroke, cancer, heart failure, dementia, chronic obstructive pulmonary disease, and cirrhosis).

The adjusted odds of dying in the hospital was 47% higher for patients with ESKD compared with the reference group of patients without any of the aforementioned health conditions. However, unlike patients with other serious illnesses, those with ESKD were no more likely than the reference group to have a DNR order in place at the time of ICU admission. Although the interaction term for race did not reach statistical significance, the apparent disconnect between practice and prognosis seemed to be most pronounced among Black patients with ESKD who were no more likely to have a DNR order than Black cohort members without underlying health conditions, despite having a 62% higher adjusted odds of dying in the hospital. Overall, 12% of patients with ESKD changed their code status to DNR while in the ICU, compared with 8% of those without ESKD. In adjusted analysis, patients with ESKD were 43% more likely to transition to DNR status during an ICU stay than those without ESKD, usually within the first few days after admission.

These findings add granularity to earlier work documenting relatively low rates of completion of advance directives, intensive patterns of end-of-life care, unfavorable family ratings of quality of end-of-life care, and racial-ethnic disparities in both ACP and intensity of end-of-life care among patients with ESKD. Because intensive life-prolonging interventions represent the default option in many health systems, failure to engage in ACP can expose patients to care that is incongruent with their values and goals. This is an especially prominent concern for the substantial number of patients with ESKD who say they would want to prioritize comfort and relief of suffering over life prolongation if they were seriously ill or dying. Observational studies in patients with ESKD suggest that timely engagement in ACP is associated with less intensive patterns of end-of-life care. Although there have been very few interventional studies of ACP in patients with ESKD, limited trial data suggest that engagement in ACP can also help the surrogate decision makers of patients with ESKD to prepare for their role and reduce their levels of anxiety, depression, and distress after the patient’s death.

The study by Danziger et al. is important because most patients with ESKD spend at least some time in an ICU and episodes of critical illness are relatively common among members of this population. This is especially true as patients approach the end of life. Among fee-for-service Medicare beneficiaries with ESKD, >60% were admitted to the ICU at least once during the last 90 days of life. The ICU is thus an important part of the health care landscape for patients with ESKD, and ICU teams probably play a significant role in shaping the care that many of these patients receive at the end of life.

The authors’ findings raise important questions that could motivate more detailed work to characterize the care of critically ill patients with ESKD and identify opportunities to optimize their experiences and those of their family members. For example, why, despite comparatively high in-hospital mortality rates, were patients with ESKD less likely than those without underlying health conditions (and those with other serious illnesses) to have a DNR order in place at the time of ICU admission? Additionally, why did there seem to be an especially large disconnect between mortality rates and the prevalence of DNR orders among Black versus White patients with ESKD? Although not a primary focus of the paper, one also wonders why patients with ESKD were more likely than other groups to transition to DNR status while in the ICU. More broadly, because documentation of treatment preferences is only as meaningful as the conversations on which it is based, these findings beg the question of whether the presence or absence of a DNR order at the time of ICU admission was an accurate reflection of the values and goals of individual patients. Perhaps most importantly, one wonders whether the care that patients received while in the ICU honored what mattered most to them and to what extent this was supported by the presence or absence of a DNR order.

The bird’s eye view of resuscitation status for patients with ESKD admitted to the ICU afforded by the study by Danziger et al. broadens our understanding of care practices for seriously ill patients with ESKD. A more detailed characterization of the arc of care planning, clinical decision making, and experience of illness for members of this population could provide a deeper understanding of these findings, offer insight into the role of ICU teams in shaping end-of-life care for members of this population, and identify opportunities to optimize care and uphold personhood when patients with ESKD become critically ill.

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See related article, “Use of Do-Not-Resuscitate Orders for Critically Ill Patients with ESKD,” on pages 2393–2399.

Two Tales of Single-Cell RNA Sequencing: Gene Expression and Alternative Splicing in Mouse Kidney Development

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Mammalian nephrogenesis is a process of cell fate acquisition and segregation driven by the reciprocal interactions between the ureteric bud (UB) and adjacent metanephric mesenchyme (MM).1 In response to signals released from MM, the UB branches extensively, forming the collecting duct system. In turn, the tip of the UB induces the MM to self-organize into the Six2-expressing cap mesenchyme, which represents a pool of nephron progenitor cells. These Six2-expressing cells subsequently undergo a mesenchymal-to-epithelial transition, forming the nephron epithelium. As nephrogenesis proceeds, the distal ends of nephrons interconnect with the collecting duct system, giving rise to a network of continuous renal epithelial tubules. At the same time, vascular and other nonepithelial cells develop in parallel with epithelial cells, generating a highly organized and heterogeneous kidney tissue.

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