Kidney transplant failure is an important cause of dialysis initiation in the United States. In 2011, this group represented 4.7% of patients new to dialysis, a 30% increase in the number of patients initiating dialysis after transplant failure since 2000 (1). Improvements in short-term kidney allograft survival have surpassed improvements in long-term graft survival (2). Therefore, the transplant failure dialysis population will continue to increase because of a relatively fixed duration of graft survival, an increasing number of kidney transplants performed, improving patient survival after kidney transplantation, and more limited opportunities for repeat versus initial kidney transplantation (1).

Quantifying the morbidity and mortality of patients with transplant failure needs to be interpreted in the context of the control group against which the mortality risk is being compared. Relative to patients with ongoing kidney allograft function, patients returning to dialysis after transplant failure face an increased risk of death and reduced quality of life (3). The risk is highest in the early period after dialysis initiation, and is particularly driven by higher susceptibility to infection-related morbidity (3,4).

Conclusions comparing the mortality risk of patients with transplant failure relative to transplant-naïve incident dialysis patients are less clear. Inherent differences between the two groups in terms of the duration of uremia cannot be fully accounted for. Reports from the dialysis registry data in Canada comparing the mortality risk between all transplant-naïve patients versus all patients with transplant failure demonstrated similar survival (5). A more recent analysis from the French Renal Epidemiology and Information Network, utilizing a robust case-control design and accounting for extensive comorbidity and biochemical adjustments between transplant-naïve patients and patients with transplant failure, similarly demonstrated equivalent survival between the two groups (6). By contrast, two analyses, one using data from the Scientific Registry of Transplant Recipients (SRTR) among a United States population and the second from the Dialysis Outcomes and Practice Patterns Study (DOPPS), yielded different results (7,8). Both the SRTR and DOPPS studies restricted comparisons to transplant-naïve dialysis patients who, similar to patients with transplant failure, were potentially transplant eligible by virtue of being placed on a transplant waiting list. In these studies, the transplant failure groups had a higher mortality risk compared with the transplant-naïve, wait-listed patients.

Opportunities to improve the outcomes of patients returning to dialysis after transplant failure have largely focused on the role of transplant-related factors. The observation that these patients suffer from disproportionately high rates of sepsis and infection-related mortality has led to the hypothesis that a history of prolonged and ongoing exposure to chronic immunosuppression may be mediating these risks (4,8,9). Moreover, the transplanted kidney itself may be an ongoing source of systemic inflammation and hypoalbuminemia even in the absence of overt clinical evidence of rejection (10). Taken together, the role of transplant-specific modifiable practices after graft loss, including the method and rapidity of immunosuppression tapering and/or the indications for and timing of transplant nephrectomy in improving outcomes after transplant failure, remain unclear (11–14).

The provision of appropriate multidisciplinary CKD care may be equally important in improving outcomes for patients with transplant failure. This approach would include management of the complications of progressive transplant CKD, education regarding ESRD treatment options, and timely referral for both appropriate dialysis access creation and initiation of RRT.

In this issue of CJASN, Chan et al. use US Renal Data System (USRDS) data to examine the distribution of vascular access type at dialysis initiation comparing a cohort of 16,728 patients who initiated dialysis after transplant failure versus 509,643 transplant-naïve incident dialysis patients (15). The authors found that 34.6% of patients with transplant failure initiated hemodialysis with a surgical access (arteriovenous fistula [AVF] or arteriovenous graft [AVG]) compared with 19.2% of patients in the transplant-naïve groups, whereas the remainder of patients in both groups started dialysis with a central venous catheter (CVC). With regard to an AVF or AVG that was placed before dialysis but was not used at the time of hemodialysis initiation, 51.4% of the patients with transplant failure initiated hemodialysis with a CVC without a concomitant AVF or AVG in place compared with 62.1% of the transplant-naïve patients. These findings are quite concerning considering that patients with transplant failure receiving hemodialysis are at greater risk for infection and that high rates of CVC use may be part of this causal pathway (4).
Is the high rate of CVC use at dialysis initiation and low rate of pre-emptive AVF/AVG placement a proxy for the absence of appropriate CKD care among patients with transplant failure? Existing clinical practice guidelines strongly recommend pre-emptive placement of surgical vascular access, and the morbidity and mortality of CVC use among maintenance hemodialysis patients is ingrained into kidney care practitioners (16). Moreover, other studies found that patients with transplant failure are less likely to meet other dialysis clinical practice targets (serum phosphorus, BP, hemoglobin) compared with transplant-naïve patients (8,17,18). Although the rates of surgical vascular access use at hemodialysis initiation were indeed higher among patients with transplant failure (34.6% versus 19.2%), rates of pre-emptive AVF/AVG placement among patients with transplant failure who started hemodialysis with a CVC were slightly lower (21% of CVCs) compared with transplant-naïve patients (23% of CVCs), suggesting that a larger proportion of patients with transplant failure may not have had any predialysis access planning (15).

Should the bar be set higher for our expectations for surgical access placement and use among patients initiating hemodialysis after transplant failure? Unlike a significant proportion of transplant-naïve hemodialysis patients, patients with transplant failure should be well known to the transplant nephrology care team. Moreover, as a group, these patients have fewer comorbidities than their transplant-naïve counterparts, factors that Chan et al. and others have found to be more predictive of AVF/AVG use at hemodialysis initiation (15,19).

Surprisingly, Chan et al. reported that >31% of patients with transplant failure were classified as having either no nephrology referral or a referral of ≤1 year before dialysis initiation. Despite being known to transplant nephrologists, this figure may relate to perceptions that American patients with transplant failure are referred late for predialysis care rather than the actual receipt of any form of nephrology care per se. This perception may be driven by the fragmentation of care between the transplant and dialysis centers where elements of care in late-stage CKD may overemphasize efforts to salvage renal allograft function while placing an underemphasis on predialysis planning. Unlike the United States, the similar survival observed between patients with transplant failure and transplant-naïve patients in France may reflect differences in the delivery of care received (6). Indeed, French patients with transplant failure have greater planned elective dialysis starts than transplant-naïve patients, a finding that may relate to a more optimal continuum of care whereby the provision of transplant, general CKD, and dialysis care occur within the same nephrology units (6).

Are there patient-related factors among patients with transplant failure that may affect the lower rates of AVF/AVG placement and use at dialysis initiation? Although estimating equations to predict dialysis risk are well established among the general CKD population, the risk in the late stages of transplant CKD is less clear (20). Conceivably, transplant patients may face a more unpredictable trajectory of kidney function decline, with a higher proportion of patients with unanticipated and rapid loss of kidney allograft function. Contrary to other populations, among patients with transplant failure, Chan et al. found younger age to be more predictive of CVC use and older age to be more predictive of AVF/AVG placement (19). This finding may relate to issues surrounding immunosuppression nonadherence, which is demonstrated to be more common among younger transplant recipients and may lead to abrupt allograft loss and unplanned dialysis initiation (21). Moreover, Chan et al. did not examine the role of pretransplant factors. It is plausible that with an extended duration of uremia and with an extended pretransplant hemodialysis period for many patients with transplant failure, exhaustion of vascular access sites may have occurred before transplantation. This may be further compounded by the effects of uremia and immunosuppression in promoting poor blood vessel caliber and impairing suitability for successful post-transplant vascular access placement. In addition, a significant proportion of patients with transplant failure must face the reality of a return to dialysis after previously experiencing the negative effect dialysis has had on their quality of life, well-being, and vocational abilities. It may be even more difficult for this young group of patients to face this reality for the second time and accept the need for dialysis planning.

Are we scapegoating kidney transplant care teams for their failure in facilitating pre-emptive and successful surgical hemodialysis vascular access creation in patients with transplant failure? Arguably, a more valid “apples to apples” comparison than that provided by Chan et al. would be to examine the rates of surgical vascular access placement and use comparing patients with transplant failure against transplant-naïve patients who have experienced an extended duration (>12 months) of predialysis nephrology care. Using the most recent data from the USRDS annual report reveals that among these patients, only 36.6% of incident transplant-naïve hemodialysis patients initiated dialysis with a permanent surgical vascular access (AVF/AVG) in 2011, a figure that disappointingly has changed very little in the last 5 years (1). This figure is strikingly comparable to the incident AVF/AVG use rate of 34.6% reported by Chan et al. among transplant failure incident hemodialysis patients. With unacceptably high reported primary AVF failure rates among American centers ranging between 29% and 64% (22–25), it is clear that the high rates of CVC use and low rates of successful surgical vascular access among patients with transplant failure may just scratch the surface of a more pervasive problem across the entire CKD population. The findings by Chan et al. only stand as further proof to the nephrology community as a whole of our overall hemodialysis vascular access failings.

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References


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