Comparing kidney transplant outcomes; caveats and lessons

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Keywords: graft survival; international comparison; kidney transplant

The number of people with end-stage renal disease (ESRD) is growing not only in the USA but worldwide secondary to the global epidemic of diabetes and other causes of kidney disease. Dialysis costs are expensive and access to this care is difficult in developing countries. The majority of patients starting dialysis in low-income countries die and or stop treatment within the first 3 months secondary to financial restraints [1]. Kidney transplantation is the treatment of choice for patients with ESRD and improves long-term survival compared with dialysis [2]. As first shown by Wolfe et al. [2], kidney transplantation increases life expectancy as well as quality of life. Later studies have shown that this increase in survival is tied in with the quality of the organ and renal function obtained [3, 4]. However, mortality after transplantation has great variability and is influenced by many known factors (i.e. diabetes), but also unknown factors that contribute to the low R² of most models and thus provides an incomplete understanding of the reasons behind this variability.

Undoubtedly, an important component of long-term survival is adequate care delivery to kidney transplant recipients. It is likely that better and more frequent specialist care would potentially preserve renal function and also help mitigate mortality from hypertension, diabetes and atherosclerotic disease. In addition, earlier infection and malignancy detection could decrease mortality from these very common causes of death in this population. It is possible that the long-term outcomes of kidney transplant in the USA are hampered by financial barriers leading to
non-adherence and lack of access to specialists in the field of transplant. In the USA, Medicare beneficiaries lose their coverage for their immunosuppressive drugs 3 years after transplant and care providers receive low reimbursements for these patients. These factors undoubtedly contribute far greater than in other countries that have nationalized healthcare or provide medication coverage for all constituents including Spain [5].

Ojo et al. evaluated the rates of graft failure and death among USA and Spanish kidney transplant recipients. The authors showed a significant difference among the 10-year graft and patient survival, which was significantly better in the Spanish population. The USA had a greater fraction of transplants going to recipients 70 years of age or older compared with Spain. The two countries had similar rates of glomerular disease and polycystic kidney disease as the primary cause of ESRD. The differences, including recipient age at transplant and a higher number of patients with diabetes as a cause of ESRD, could be strong predictors of patient and allograft survival. Diabetes and hypertension are associated with multiple comorbidities including cardiovascular disease which is the leading cause of death for renal transplant patients. However, it is important to note that the US registry data are limited and do not account for data on blood pressure, hemoglobin A1C, cholesterol and other factors that could contribute to death with a functioning graft. Kidney transplant recipients from Spain receive their care from the same medical team from the onset of ESRD through the post-transplant period which could contribute to long-term patient and allograft survival. In Spain, patients have access to medications including immunosuppression paid by a publicly funded National Health Service regardless of their ability to pay [6]. This is an important difference between the two countries that cannot be understated.

Other studies have compared clinical outcomes in the USA with Canada, Australia-New Zealand and the UK. A significant portion of recipients received transplants for diabetes compared with the other countries and US recipients had lower graft and patient survival rates [7, 8]. These studies compare USA with other countries with a national type of healthcare and the data are limited to what is entered into the SRTR database.

There are also differences documented among centers themselves. The center effect in renal transplantation has been defined as the variation in the center-specific renal allograft outcomes beyond that which can be explained by random variation and adjustments for factors known to impact on these outcomes (piece taken from article) [9, 10]. There have been a number of studies supporting the importance of center effect as a prognostic factor for kidney transplantation in the USA and UK [11–13]. The variability in 1-year graft survival among US transplant centers, unexplained by adjustments for case-mix, has been shown to range from 30 to 40% [14, 15]. This effect has persisted despite the many advances in transplantation and improvements in patient outcomes [16]. The center effect has also been documented in Canada which included 20 centers in data analysis and found that larger centers, defined >200 transplants a year, showed superior graft and patient outcomes [17].

The specialty of kidney transplantation has made huge strides over the last 20 years, evolving from an experimental procedure to now being standard of care for treatment of ESRD. Surgical techniques and pharmaceutical gains have helped to improve outcomes; however, most of the improvements are driven primarily in first-year survival, whereas long-term graft attrition remains largely unchanged. It is difficult to measure long-term survival because of documentation and the fact that in the past long-term graft survival was far too short to allow for competing risks associated with mortality. While long-term renal allograft survival in the USA has improved slightly, renal graft half-life for deceased donor transplant was 6.6 years in 1989, increased to 8 years in 1995, then after the year 2000 further increased to 8.8 years by 2005. This change is still insufficient to allow one to totally divorce death with a functioning graft from death-censored graft loss (as many patients who lose their graft sooner are not sampled) [18]. However, in this elegant analysis, death-censored graft survival was not different. This would indicate that the difference in mortality is unlikely to be related to differences in renal function and makes it more difficult to make the case that it is due to greater adherence to immunosuppressive medication. As the multivariate models were corrected for known comorbidities and available recipient and donor risk factors, one cannot ascribe the increased risk of mortality in the USA as opposed to Spain to any of these factors. This then begs the question alluded to in the introduction. What accounts for the variability in mortality between two countries or even two centers?

It is easy to ascribe the differences between Spain and the USA to the differences in healthcare delivery and it is likely this may play a part. The fact is the data at hand do not offer us easy answers. Given the variables available, the risk of death is lower in Spain than the USA, but the data does not give us the reasons. The points made in the discussion of this important paper are well taken and likely explain much of the variability (i.e. healthcare delivery differences). We must also offer a note of caution in inferring too much into the data. The fact is we simply do not know the reasons of why one individual thrives and one does not. This paper is a wonderful start to explore this issue and adds invaluable knowledge that hopefully will allow us to improve our understanding of the variability in mortality and ultimately allow us to take better care of these very special and complicated patients. However, the study by Ojo et al. also highlights that mortality in renal transplant recipients can be influenced by factors not easily captured on databases and challenges us to consider variables in national registries that are currently unavailable.

Conflict of interest statement. None declared.


References

To improve clinical outcomes of patients with chronic kidney disease (CKD), there has been increasing research on the impact of individual psychological processes and social environment factors (known as psychosocial factors) on the CKD population [1–3]. Psychosocial factors are shown to significantly contribute to the overall health outcomes, for example, by alleviating patients’ perception of their disease burden, enhancing their rehabilitation [1, 4, 5], as well as helping to explain the proportion of variance in their quality of life (QoL) and level of depression [2, 3].

The Poppe et al. study [6], published in the current issue of Nephrology Dialysis Transplantation, contributes to this growing body of research by demonstrating the effects of psychosocial factors on the health outcomes of patients with CKD. Their study focuses on the role of acceptance in patients’ health-related QoL (HRQoL) and the effect of neuroticism on acceptance. With cross-sectional data from 99 patients with CKD and on mixed treatment modalities (including pre-dialysis, dialysis and transplant) as well as the use of path analysis, Poppe et al. [6] examined the direct and mediating effects of acceptance and the direct