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INVITED COMMENTARY

Early death after kidney transplantation - can the risk be reduced?

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Farrugia and colleagues present their analysis on the incidence and risk factors for mortality within the first year after renal transplantation in England between 2001 and 2012 in this issue of the journal [1]. The authors made use of two national databases, the Hospital Episode Statistics and the National Mortality Statistics, which were linked for this analysis. Of the 19 103 renal transplantations performed in that period in England, 566 or 3% have died within the first years after transplantation. The main causes of death were infections followed by cardiovascular events and malignancies. Of subjects with a pretransplant history of myocardial infarction, 39% of death could be attributed to cardiovascular death. Accordingly, in patients with a malignancy before transplantation, cancer was the attributable cause of mortality in 62% of cases. Entries in the database listed kidney failure in 22% of deceased persons as contributing event. The investigators furthermore identified deceased donor transplantation, recipient age, a history of selected medical comorbidities as well as the socioeconomic factor as risk factors for death within the first post-transplant years. Based on these findings, the authors concluded that although the risk of death within the first years after renal transplantation is low, specific groups of patients exhibit a dramatically higher mortality rate.

This paper is of great interest to the transplant community, as it is among the few recent that thoroughly analyzed the incidence and cause of death in the early post-transplant period and showed that selected groups are at clearly elevated risk. These findings have the potential to start a discussion in the transplant community, whether the diagnostic check-up and follow-up of wait-listed candidates as well as recommendations in guidelines for a deceased donor transplant are adequate/up to date. In fact, the EDTAs EBPG updated their recommendations very recently [2]. In this guideline paper, the ERBP group together with experts in this field forms the EDTA-DESCARTES working group highlighted the importance of thorough pretransplant cancer as well as cardiovascular screening. The authors suggested that cancer screening should be carried out according to the recommendations that apply to the general population. It remains, however, not entirely clear how patients with a past diagnosis of a malignancy should be handled. The EBPG refer in the situation of a malignancy history to the published risk estimate of very early recurrence and mortality to the guidelines in oncology and thus somehow neglecting the additional risk, specifically of virally induced malignancies, after transplantation. Furthermore, the discussion of each individual case with an

oncologist is recommended, and a potential delay of active listing should be considered depending on cancer type, grading and staging patient age and the degree of comorbidities. The remaining uncertainty in this area can be appreciated by the labeling of 'ungraded statement' in almost all domains of this carefully written guideline paper.

As almost all patients with a long history of CKD and renal replacement therapy of ESRD suffer from cardiovascular disease, invasive evaluation of the cardiovascular status may be recommended, although the type and pathophysiology of atherosclerosis do not mirror the processes in the general population. Thus, although diagnostic coronary angiography has not even been shown to reduce events and death in the general population, it is now performed in most of the center as part of the wait-listing workup especially in patients above 50 years and with a long-standing disease history.

The data presented by Farrugia *et al.* support these thorough evaluation recommendations, given the fact that the death due to cancer and cardiovascular causes within the first year in the population with such pre-existing conditions should be minimized. The high rate of very early cardiovascular and cancer mortality indirectly suggests that either the wait listing was inappropriate or the interval of the sequentially workup of listed patients with foregoing events was too long. It may be speculated that the dramatically reduced risk of mortality in the first year after live donor kidney transplant recipients supports this hypothesis. Although it is certainly correct that renal transplantation reduces the risk of cardiovascular death in the long term when compared with dialysis, patients have an elevated risk very early on. Well-accepted perioperative risk factors for cardiovascular events include modifiers such as surgery, hospitalization, infection, higher medical immunosuppression and comedication as well as immobility and comorbidity. As also shown in the recent analysis by Farrugia, pre-existing diabetes contributes in 25% of cases to early cardiovascular mortality.

The analysis exhibits all limitation of an observational retrospective study. Specifically, the propensity for listing specific patients with ESRD and underlying disease for transplantation could not be elucidated. Accordingly, the procedure or pretransplant workup of candidates as well as the regular update of wait-listed patients were not available. However, all intrinsic limitations were adequately discussed, and the recommended guidelines for observational studies such as the STROBE statement have been provided.

In summary, the analysis by Farrugia and colleagues very nicely showed that there are nonmodifiable and potentially modifiable risk factors that are responsible for the early death after renal transplantation. As in all observational studies, patient age and socioeconomically deprived living areas as proxy of low socioeconomic status are strong predictors of mortality. Among the potentially modifiable factors, the underlying comorbidities, cardiovascular disease and malignancies specifically exhibit a dramatically increased risk of early events. These findings suggest that these patients should receive a carefully workup at shorter intervals while wait-listed for a deceased donor graft.

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