

INVITED COMMENTARY

Good, not great

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Rejection, infection and malignancy continue to dominate the long-term clinical courses after solid organ transplantation. Overall, little progress has been made with the reduction of omission of maintenance immunosuppression. This continues to haunt the field and significantly impacts patient survival, graft survival and quality of life. Particularly for non-live saving transplantations, such as transplantations of the hand or the face, a critical assessment and reflection on the actual implications of immunosuppression is necessary.

The study presented by Anne Conrad *et al.* [1], adds an important clinical assessment of the real-world experience to the existing understanding of infections in VCA. The authors add a matched comparison with patients receiving a kidney transplant in order to benchmark the findings with another transplant population. The results of the study reveal a high infection rate in the early phase after upper extremity allotransplantation (UEA), whereas the long-term risk for infections seems to level out with kidney transplant recipients. These findings are not surprising and possibly relate to two factors specific for VCA in comparison with KTx: (i) The external position and the cumulative surgical trauma during the transplant of a VCA enhances the risk for

wound and tissue infections. This is underlined by the predominance of mucocutaneous infections and the (not reported) skin associated microbes causing the infections. (ii) The relative high number of rejections during the early phase after VCA triggers the use of pulsed steroid and antibody treatment together with a less well-understood application of steroid and tacrolimus ointments. The balance between rejection and immune responsiveness can be considered to shift forth and back, giving room for infections and, for example, virus replication. The authors do not refer to the difference between the two groups with respect to the treatment for rejection. It is likely, that VCA recipients received an overall more profound immunosuppression during the course.

On the contrary, VCA recipients can be considered to be in an overall better health state than the comparator. In that sense, the matching as attempted faces a significant limitation and adds a negative bias to the kidney group since it levels out the factor of the pre-existing kidney disease. Another limiting factor is the data source and the differences between the two registries utilized in the trial. Data self-reporting is not mandatory in the IRHCTT and the completeness of the data

depending on the good intentions of the centers providing the data. While this is equivalent to the situation in a large number of registries, the willingness to share and openly discuss complications in VCA only gradually matured to the level of full transparency. The limitation is within the nature of such an assessment, but requires consideration in the reading of the article.

A further limitation is the duration of the follow-up. While the dynamics of the prevalence of infections indicates a lesser relevance of infections late after UEA, the long-term immunological risk and development of DSAs may eventually result in a more intense immunosuppression and hence bare the risk of late infections, particularly in cases of partial or complete graft loss [2].

The article does reiterate a critical issue. Hand and face transplantations remain high-risk procedures for non-life saving indications. It is all the more important to carefully reflect and balance the risks and benefits in the decision making. Considering the high prevalence of immunologic complications, the increasing evidence for development of donor specific antibodies, the deterioration of function over time in some cases, the loss of grafts and the mortality, the decision to offer hand and face transplantation needs to be seen with caution. The initial experience with hand and face transplantation was almost overwhelmingly positive. Not surprisingly, more complicated courses after VCA occurred and illustrated, that transplantation of vascularized tissue would be no less complicated than transplantation of solid organs.

This study illustrates, that the long-term risk for infections is not higher than that in kidney transplantation. The observation, that infectious complications are equivalent with kidney transplant recipients does underline, that no chronic site infection hamper the

long-term fate of the graft and the patient. While this is helpful, the long-term complications both in kidney as well as hand/face transplantation are more defined by the risks for graft loss and the oncological risks.

In the context of the assessment of outcomes in VCA, the clear-cut definition of endpoints remains an important and unsolved issue. The authors display the rate of graft losses, but a clear-cut definition of graft loss in UEA remains to be established. The loss of function is generally not considered an indicator for graft loss, yet the deterioration of function in hand transplantation must be considered as an endpoint. In kidney transplantation, graft loss is defined by return to dialysis and in congruity to this comparison, the lower level of function that constitutes a function as insufficient to adequately serve the patient requires a definition in UEA.

All in all, the authors provide a valuable contribution to the understanding of the infectiological risks following UEA. They point out, that the picture may be different for other types of VCA. The relative low rate of late infections is reassuring, but the immunological risks, the risks for graft loss and the risks for malignancy remain to be assessed in the long-term follow-ups. The IRHCTT is a valuable asset for the field and should be maintained with great care. It remains the sole registry in the field and multicenter assessments of results largely depend on the registry – at least as a basis for data collection. VCA has matured from its early days of experimental procedures with a huge number of unknowns to a field with a greater understanding of the benefits and the risks. A careful appreciation of the current knowledge and potential risks in the long run remain the basis for decision making in an overall still fragile environment and context of this novel procedure.

REFERENCES

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