

Trends and determinants for graft survival among kidney transplanted patients in Sweden

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i lokal Arvid Carlsson, Medicinaregatan 3, Göteborg, torsdagen den 29 februari 2024, klockan 13.00

av

Salmir Nasić

Fakultetsopponent:

Docent Therese Andersson

Medicinsk epidemiologi och biostatistik, Karolinska institutet, Stockholms Universitet

Avhandlingen baseras på följande delarbeten:

- I. Nasic S, Peters B, Stegmayr B, Kenne Sarenmalm E, Afghahi H, Eriksson M. **Sex-specific time trends of long-term graft survival after kidney transplantation – a registry-based study.** *Ren Fail* 2023; 45(2):2270078.
- II. Nasic S, Mölne J, Stegmayr B, Peters B. **Histological diagnosis from kidney transplant biopsy can contribute to prediction of graft survival.** *Nephrology (Carlton)* 2022;27(6):528-536.
- III. Mölne J, Nasic S, Bröcker V, Stegmayr B, Felldin M, Peters B. **Glomerular macrophage index (GMI) in kidney transplant biopsies is associated with graft outcome.** *Clin Transplant* 2022;36(12):e14816.
- IV. Nasic S, Mölne J, Eriksson M, Stegmayr B, Afghahi H, Peters B. **Changes in numbers of glomerular macrophages between two consecutive biopsies and the association to renal transplant graft survival.** *Submitted.*

Trends and determinants for graft survival among kidney transplanted patients in Sweden

Salmir Nasić

Avd. för molekylär och klinisk medicin, Institutionen för Medicin, Sahlgrenska akademien, Göteborgs Universitet, Sverige.

Abstract

According to literature, even after a successful kidney transplantation approximately 50% of the patients risk losing the transplant within ≈ 15 years. A return to dialysis or a new transplantation is then necessary. Therefore, it is important to identify determinants for graft survival.

This thesis is based on data from two large registries. The linking of the registries and the analyses carried out on the extensive amount of data required an accurate and careful statistical approach.

The overall aim of the thesis was to evaluate and investigate association between recipient characteristics, clinical and histological variables related to graft survival (GS) in a population of kidney transplanted patients. Association between the variables and GS as outcome was analyzed by various survival models.

In study I focus was on GS after kidney transplantations based on the quality register TIGER containing data from kidney patients transplanted in the transplantation center in Gothenburg. The study showed that graft survival in general has improved over time but in the last study period 2006-2017 women had shorter graft survival compared to men.

In study II-IV focus was on different aspects of kidney transplant biopsy findings and associations to GS based on data from both a regional kidney biopsy registry and the TIGER-registry.

The association between biopsy-proven diagnoses and GS was investigated showing that some diagnostic groups were associated with a higher risk of graft loss. Compared to normal biopsy findings, shorter GS was mainly found in transplants with glomerular diseases, rejections, acute tubular injuries, borderline changes and chronic changes.

Another biopsy-based variable is glomerular macrophage index (GMI) - a biomarker for inflammatory processes in the transplant. The increased levels of GMI were found to be strongly associated with worsened graft survival.

Also, the change in GMI between two consecutive biopsies and the magnitude of the change was associated to graft survival. High levels of GMI and categories where GMI increased were associated to higher risk for graft loss compared to groups with low or decreasing GMI-level.

The thesis showed that results from transplant biopsies need further attention from clinicians in regard to the overall histological results in relation to time of biopsy and presence of high GMI-levels at the first but also at the follow up biopsies. GMI can be useful even in case of insufficient other histological findings. Female kidney transplant patients need additional surveillance. Future studies regarding these risk variables will help to reveal how to improve therapy and prolong graft survival.

Keywords: kidney transplantations, graft survival, kidney transplant biopsy

ISBN 978-91-8069-605-0 (PRINT)

ISBN 978-91-8069-606-7 (PDF)

<http://hdl.handle.net/2077/79339>