

Surveilling hearts

A New Biomarker for the Non-Invasive Diagnosis of Rejection after Heart Transplantation

Akademisk avhandling som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, fredagen den 13:e december, klockan 9:00

av

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Avhandlingen baseras på följande delarbeten

- I. Böhmer J, Wasslavik C, Andersson D, Stahlberg A, Jonsson M, Wahlander H, Karason K, Sunnegardh J, Nilsson S, Asp J, Dellgren G, Ricksten A
Absolute Quantification of Donor-Derived Cell-Free DNA in Pediatric and Adult Patients After Heart Transplantation: A Prospective Study
Transplant International, 2023; 36, 11260
- II. Böhmer J, Wahlander H, Karason K, Sunnegard J, Wasslavik C, Jonsson M, Asp J, Ricksten A, Dellgren G. **Clinical Examples of the Additive Value of Absolute Quantification of Cell-Free DNA after Heart Transplantation**
Clinical Transplantation. 2024 Oct;38(10):e15477
- III. Böhmer J, Wahlander H, Tran Lundmark K, Odermarsky M, Sjöborg Alpman M, Asp J, Nilsson S, Karason K, Sunnegardh J, Ricksten A, Dellgren G
PCR-based Absolute Quantification of Donor-Derived Cell-Free DNA after Heart Transplantation: A Population-based Study on 94 Consecutive Cases
Under revision

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



Surveilling hearts - A New Biomarker for the Non-Invasive Diagnosis of Rejection after Heart Transplantation

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Abstract

Introduction: Heart transplantation (HTx) is the ultimate treatment for advanced heart failure. Survival after HTx is hampered by rejection. Endomyocardial biopsies (EMB) are the cornerstone of surveillance after HTx to diagnose rejection. Donor-derived cell-free DNA (dd-cfDNA) in the blood stream has been proposed as an alternative marker of rejection.

Methods: We aimed to establish a method to quantify levels of dd-cfDNA after HTx. For this purpose, we used retrospective analysis of stored samples and prospectively collected samples from HTx patients in study I. In study II, we wanted to depict relevant clinical scenarios such as infection and rejection and their influence on levels of dd-cfDNA. Prospectively investigated HTx patients were in study III enrolled in two arms: a national study for pediatric patients, and a regional study for adult patients. We obtained blood samples for the analysis of dd-cfDNA in parallel to EMB during the first year after HTx.

Results: In study I, we successfully implemented droplet digital PCR (ddPCR) after targeted preamplification to determine levels of dd-cfDNA and presented normal values of dd-cfDNA in the first 52 HTx patients. We then characterized the trajectories of dd-cfDNA levels in HTx patients suffering from different infections and rejection types in study II. Investigating the final cohort of 94 patients, we found significantly elevated dd-cfDNA levels in patients suffering from rejection as diagnosed by EMB in study III.

Conclusion: ddPCR is a feasible method to measure dd-cfDNA levels after HTx and can be used to successfully rule out rejection in stable patients.

Keywords: donor-derived cell-free DNA, droplet digital PCR