

PHD THESIS SUMMARY

Prognostic factors and prediction of complications after heart transplant

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Introduction: Heart transplant, after more than 50 years since first human-to-human procedure, remains the gold-standard treatment for patients with end-stage heart failure who remain symptomatic despite optimal medical therapy. The transition from an experimental surgery to a lifesaving procedure has increased the number of patients waiting for heart transplant. Preoperative inflammatory status, as an independent predictive factor for the postoperative outcome, is one of the most intensely studied fields of research in modern medicine, backed by a large number of research in this regard. The improvement of current therapeutic algorithms is only possible by studying new fields and factors and their predictive value in the context of a complex surgical procedure, such as cardiac transplantation.

General objectives: The aim of the studies was to identify prognostic factors which can anticipate the apparition of posttransplant complications.

General methodology: The general methodology of our studies consisted in a retrospective analyses of heart transplant patient's data between May 2014 and January 2021, from Emergency Institute for Cardiovascular Diseases and Transplantation Târgu Mureş, Romania. A total number of 38 patients met the inclusion criterias of the studies.

Study 1: In the first study, the associations between the chronic medical treatment before the cardiac transplant with the apparition of postoperative complications in the first two months. Secondly, we determined the cut-off of preoperative C reactive protein (CRP), total cholesterol (TC), respectively, the low-density lipoprotein cholesterol (LDL-c) levels, investigating the relationship between these markers and two-month complications after heart transplant, and analysing the correlations between these markers and the statin treatment.

Study 1 conclusions: In summary, chronic preoperative administration of statins represent a protective factor against the development of two-month postoperative complications of any cause in heart transplant recipients, simultaneously presenting an elevated risk for early-postoperative acute kidney injury (AKI). From the statin group, atorvastatin therapy had a higher risk of newly diagnosed postoperative type 2 diabetes mellitus (T2DM). Furthermore, higher body mass index (BMI) presented a higher additional risk of T2DM. Second, we determined that CRP, TC, and LDL-c above the cut-off levels might be poor prognostic factors in the first two months after heart

transplantation. Atorvastatin administration was associated with lower CRP values, underscoring the anti-inflammatory role of lipid-lowering therapy.

Study 2: The second study's aim was to identify pro-inflammatory markers from the complete blood counts determined before heart transplantation. Neutrophil to monocyte ratio (NMR) and monocyte to white blood cells ratio (MWR), with the same cut-off values previously studied, were analysed in the anticipation of postoperative complications. Moreover, we investigated the associations between these markers and the risk of acute graft rejection in the first two years after cardiac transplant.

Study 2 conclusions: Using previously studied cut-off values, we noticed that preoperative $NMR > 8.9$ was associated with the apparition of newly diagnosed paroxysmal atrial fibrillation (AFib). At the same time, $MWR > 0.09$ was a protective factor against this supraventricular arrhythmia. Elevated MWR was a risk factor of postoperative complications of any cause in the first two months after heart transplantation. The patients with $NMR \leq 6.63$ had 2.88 higher risk of acute graft rejection in the first two years after the transplant, compared with those below this cut-off value.

Study 3: In the third study we investigated the markers based on the albumin concentrantions, such as platelet to albumin ratio (PAR) and monocyte to albumin ratio (MAR) before heart transplantation. The associations between this markers and post-transplant complications were determined in the first two months. The statistical analysis was made using the same cut-off values previously studied, as well as the optimal values.

Study 3 conclusions: By using previously studied cut-off values, we observed that preoperative $MAR > 0.14$ represented a risk factor for the development of postoperative infections. The optimal cut-off values determined by Receiver Operating Characteristics (ROC) curve and Youden's index, we showed that $PAR > 38.84$ was an independent risk factor for the occurence of postoperative infections and complications regardless of cause.

General conclusions: Chronic statin treatment before heart transplantation together with multiple preoperative pro-inflammatory markers might provide additional information in the anticipation of early postoperative complications. Further prospective studies with larger patient cohorts are needed in order to evaluate the involvement of these markers in postoperative complications after a heart transplant and subsequently make drastic conclusions.