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Cellular immunodeficiency in patients with Failing-Fontan

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Introduction:
3-15% of all Fontan-patients develop a failing of their Fontan circulation with manifestation of a protein-loosing enteropathy (PLE). Clinically a PLE includes hypoalbuminemia, hypogammaglobulinemia and dysregulation of the salt water homeostasis. According to low IgG levels, an altered risk of bacterial infections is expected but can not be observed. Instead they show an increased risk or vulnerability of acute and chronic viral and fungal infections.

Methods:
Venous blood was obtained from Failing-Fontan (n=10) and Non-Failing patients (n=15) and a control group of patients with biventricular heart (after thymectomy during cardiac surgery) (n=20) at different time points. The control group minimized the predescribed effect of temporary T-cell depletion after thymectomy. Absolute and relative count of T-cells (CD3+, CD4+, CD8+), natural killer cells (CD16, CD56+, CD3-) and B-cells (CD19+) were determined using flow cytometry. Duodenal and colorectal biopsies of Failing-Fontan patients with PLE (n=2) who received a coloscopy and gastroscopy were analysed by immunohistochemistry to differentiate between B- and T-cell infiltration.□□Results:
Patients with Failing-Fontan had significant ($p<0.01$) lower absolute and relative T-cell subsets of CD3+, CD4+ and CD8+ cells than Non-Failing patients and the control group. Absolute count of CD45 lymphocytes was significantly ($p<0.01$) reduced in Failing-patients. Relative count of natural killer cells was significantly ($p<0.05$) higher in Failing-patients. Failing patients showed a significant ($p<0.05$) higher B-cell count.
The immunohistochemistry analysis of the duodenal and colorectal biopsies showed an increased CD3+ T-cell infiltration in the descending colon and duodenum.
□Conclusions: □For the first time we describe a cellular immunodeficiency in patients with Failing-Fontan with an extensive T-cell depletion. This can explain the clinical vulnerability against recurrent viral and fungal infections. Based on our results frequent substitution of immunoglobulins does not seem reasonable since the B-cell lineage is increased and frequent bacterial infections are not present in these patients. Long term effects on immunomodulation due to chronic immunoglobulin substitution can not be estimated. The alteration of T-cells in the descending colon and duodenum might represent a migration of T-cells from peripheral blood into the gastrointestinal wall. Underlying pathophysiological mechanisms of T-cell depletion in Failing patients need to be further analyzed.