MP3-11

Gut inflammation in Fontan patients is associated with increased enteric protein-loss, augmented systemic inflammation and alterations in vitamin D homeostasis.

ten Dam K. (1,2), Germund I. (3), Haustein M. (3), Khalil M. (4), Koopman L.P. (1,2), Apitz C. (5), Duijnhouwer A.L. (6), Tjwa E.T.T.L. (7), Huntgeburth M. (8), Brockmeier K. (3), Helbing W.A. (1,2), Hannes T. (3), Herberg U. (8), Sreeram N. (3), Tanke R.B. (1,2), Kerst G. (10), Udink ten Cate F.E.A. (1,2) [for the Fontan Care Network].
Amalia Children's Hospital, Radboud University Medical Center, Nijmegen, the Netherlands (1); Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, the Netherlands (2); Heart Center Cologne, University Hospital Cologne, Cologne, Germany (3); Pediatric Heart Center, Justus-Liebig University, Giessen, Germany (4); University Children's Hospital Ulm, Ulm, Germany (5); Department of Cardiology, Radboud University Medical Center, Nijmegen, Netherlands (6); Department of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, the Netherlands (7); Clinic III for Internal Medicine, Department of Cardiology, Heart Center, University Hospital Cologne, Cologne, Germany (8); University of Bonn, Bonn, Germany (9); University Hospital RWTH Aachen, Aachen, Germany (10)

Objectives: Gut inflammation (GI) has been observed in Fontan patients with protein-losing enteropathy (PLE). The clinical relevance of this finding is unknown. The aim of the present study was to identify factors associated with IF in a Fontan cohort.

Methods: A retrospective chart review was performed of Fontan patients who had been screened for both enteric protein-loss and presence of GI, by measuring fecal alpha-1 antitrypsin (A1AT) and fecal calprotectin (FC) levels, respectively. Associations between laboratory parameters (serum albumin level, markers of systemic inflammation, vitamin D metabolism) and clinical characteristics were explored. Patients without ≥ moderate ventricular dysfunction, ≥ moderate valvular regurgitation, cyanosis, or PLE, and classified as NYHA class I were defined as good Fontan. Patients not fulfilling these criteria were classified as failing Fontan.

Results: From 2011 to 2018, 41 Fontan patients (31.7% female, age 9.3 ± 3.6; PLE: n = 18, 43.9%) were screened. Increased FC levels (> 50 ug/g) were found in 16 patients (39%, PLE n = 10). A strong correlation between FC and A1AT levels was found (r 0.689, p <0.0001). This association was independent of having a good Fontan circulation, presence of GI or PLE (all $p < 0.05$). GI was found in 6 Fontan patients without PLE (14.6%). Interestingly, significant enteric protein-loss developed in 4 of these patients (median A1AT 683 ug/g, normal 100 – 500 ug/g) within 11 - 26 months. Furthermore, PLE patients with active GI had lower albumin levels, lower lymphocyte count, higher NLR and A1AT than PLE patients with normal FC concentrations (all $p < 0.05$). Furthermore, strong correlations were found between FC, measures of systemic inflammation, serum albumin levels, and markers of vitamin D metabolism in PLE patients, patients with GI, and failing Fontan patients (all $p < 0.05$), but not in good Fontan patients (all $p > 0.1$).

Conclusions: GI seems an emerging mechanism of disease in Fontan, and is strongly associated with severity of enteric-protein loss, augmented systemic inflammation, and altered vitamin D metabolism. Future studies are needed to determine whether alterations in intestinal function are responsible for these findings.