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

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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.