Towards a proposal for a universal diagnostic definition of protein-losing enteropathy in Fontan patients


Department of Pediatric Cardiology, Heart Center Cologne, University Hospital of Cologne, Cologne, Germany (1); Pediatric Heart Center, Justus-Liebig University, Giessen, Germany (2); Department of Cardiology, Heart Center Cologne, University Hospital of Cologne, Cologne, Germany (3)

Objectives: The definition of protein-losing enteropathy (PLE) in Fontan patients is variable and lacks standardization. A universal definition of PLE would significantly contribute to better comparison of treatment options and outcome, thus supporting essential clinical research in this critical area. The present study sought 1) to determine whether a clear definition of PLE in Fontan patients is routinely used, and (2) to identify useful diagnostic building blocks for composing a uniform PLE definition.

Methods: A systematic search of Medline (PubMed) was performed. Two reviewers independently screened titles and abstracts, and then evaluated full-text versions of all articles deemed potentially relevant. Clinical studies, written in English and comprising 4 or more Fontan with PLE were eligible for inclusion. PLE definitions were quantitatively analyzed using the so-called ‘building block approach’, in which definitions were fractionated into constituent pieces of diagnostic information.

Results: We identified 363 papers. In the final analysis, data from 55 published articles were extracted. A definition of PLE was used in only 24/55 (43.6%) of the studies. PLE definitions were very heterogeneous. We identified 6 different diagnostic building blocks: (1) hypoalbuminemia (n = 22 studies, 91.7%), (2) hypoproteinemia (n = 9, 37.5%), (3) clinical presentation (n = 17, 70.8%), (4) documentation of enteric protein-loss (n = 14, 58.3%), (5) exclusion of other causes of hypoproteinemia (n = 15, 62.5%), and (6) hypoimmunoglobulinemia (n = 1, 4.2%). Most studies used 3 diagnostic building blocks (range 1 – 5) to compose a PLE definition (n = 13/24, 54.2%). Cut-off values for laboratory parameters (serum albumin, protein, or fecal alpha-1-antitrypsin) were frequently incorporated in the PLE definition (n = 15, 62.5%).

Conclusions. Our study emphasizes the need for a uniform and consequent use of a PLE definition in clinical studies concerning Fontan patients. Establishment of a universal diagnostic PLE definition is urgently needed, and the proposed building blocks may help constitute such a clinically useful definition.