Chylothorax and pleural effusion in contemporary extracardiac fenestrated fontan completion

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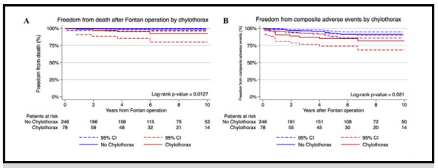
ABSTRACT

Background: We hypothesized that chylothorax could be a sign of intolerance to the Fontan physiology, and thus patients who develop chylothorax or pleural effusion have worse medium-term to long-term survival.

Methods: A total of 324 patients who underwent the Fontan operation between 2000 and 2013 were included. Chylothorax was defined as ≥5 mL/kg/day of chylomicron-positive chest drainage fluid no earlier than postoperative day 5 or drainage with >80% lymphocytes. Outcomes were compared between the chylothorax and non-chylothorax groups by the Kaplan–Meier method and log-rank test. Independent predictors of chylothorax and number of days of any chest drainage were analyzed with multivariable logistic regression and multivariable generalized negative binomial regression for count data, respectively.

Results: Chylothorax occurred in 78 patients (24%). Compared with the non-chylothorax group, the chylothorax group had a longer duration of chest tube requirement (median, 18 days vs 9 days; $P < .000$) and a longer length of hospital stay (median, 19 days vs 10 days; $P < .000$). Eight patients (10.3%) required thoracic duct ligation. The chylothorax group had lower freedom from death ($P = .013$) and from composite adverse events ($P = .021$). No predictor was found for chylothorax. Pulmonary atresia ($P = .031$) and pre-Fontan pulmonary artery pressure ($P = .01$) were predictive of prolonged pleural effusion (>14 days).

Conclusions: Occurrence of chylothorax following the Fontan operation can be a marker of poorer medium-term clinical outcomes. It is difficult to predict occurrence of chylothorax owing to its multifactorial nature and involvement of lymphatic compensatory capacity that is unmasked only after the Fontan operation. (J Thorac Cardiovasc Surg 2017;■:1-9)



Kaplan–Meier curve showing lower freedom from composite adverse events in the chylothorax group.

Central Message

Chylothorax after the Fontan operation is a marker of intolerance to the Fontan circulation that is associated with poorer medium-term clinical outcomes.

Perspective

The occurrence of chylothorax following the Fontan operation can be a marker of poorer medium-term clinical outcomes. Patients with chylothorax are at increased risk of late death, protein-losing enteropathy, and plastic bronchitis. The occurrence of chylothorax is difficult to predict owing to its multifactorial nature and the involvement of lymphatic compensatory capacity that is unmasked only after the Fontan operation.

CONG

With incremental refinements of patient selection, surgical techniques, and perioperative management, the contemporary form of the Fontan operation for patients with a functional single-ventricle physiology is associated with excellent early survival.[1,2] Nonetheless, redirection of the inferior vena cava to the pulmonary circulation in the context of the lack of a subpulmonary ventricle inevitably exposes the systemic venous and lymphatic system to substantially higher pressure, which is associated with the majority of the acute and late postoperative complications following Fontan completion.

Chylothorax and prolonged pleural effusion are common and important complications after Fontan completion.[3,4] One of the proposed mechanisms of pleural effusion and

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Abbreviations and Acronyms
AV = atrioventricular
IQR = interquartile range
MCT = medium-chain triglycerides
PA = pulmonary artery
PLE = protein-losing enteropathy
TPN = total parenteral nutrition

chylothorax in the Fontan physiology is the increase in hydrostatic capillary pressure, resulting in excessive filtration in the interstitial space and overwhelming drainage into the lymphatic system.[5] A large multicenter study showed that chylothorax is associated with longer hospital stay, higher in-hospital mortality, and higher cost in children who underwent various types of congenital heart surgeries.[6] In that study, the Fontan operation had the highest incidence of associated chylothorax, but a detailed subanalysis of the patients who underwent the Fontan operation was not performed.[6]

The primary aim of the present study was to identify predictors for chylothorax and prolonged pleural effusion in the contemporary Fontan cohort. We hypothesized that chylothorax may be a sign of intolerance to the Fontan physiology, and thus patients who develop chylothorax or pleural effusion have worse medium-term to long-term survival.

METHODS

This retrospective study included all patients who underwent the Fontan operation between 2000 and 2013 at The Hospital for Sick Children, Toronto. The hospital's Research Ethics Board approved the study and waived the need for patient consent. Patient demographic and preoperative characteristics are summarized in Tables 1 and 2.

Criteria and Patient Selection

Pre-Fontan cardiac catheterization is performed between 2 and 3 years of age to determine candidacy for Fontan completion. Standard criteria, including mean pulmonary artery (PA) pressure of ≤15 mm Hg, end-diastolic pressure of the systemic ventricle of ≤10 mm Hg, and the absence of important anatomic lesions, are used. Arteriopulmonary collaterals of significance are coil embolized at the pre-Fontan catheterization. Important anatomic lesions, such as atrioventricular (AV) valve regurgitation, aortic arch obstruction, or pulmonary vein stenosis, are typically addressed in an interim procedure, not as a concomitant procedure at the time of Fontan operation. Patients with elevated PA pressure and/or pulmonary vascular resistance are treated with a pulmonary vasodilator, typically sildenafil, and are reassessed with repeated cardiac catheterization after 3 to 6 months of treatment.

Surgical Procedures

The surgical technique has been described in detail elsewhere.[7] In brief, an extracardiac Fontan operation using a polytetrafluoroethylene tube graft (typically 22 or 20 mm) has been our standard approach throughout the study period. A 4-mm fenestration was routinely created unless technically difficult. A lateral tunnel Fontan was performed only when standard extracardiac Fontan operation was not feasible, typically in patients with isomerism hearts with unusual systemic and pulmonary venous arrangements. Procedures were done under normothermic or mild hypothermic cardiopulmonary bypass. Cardioplegic arrest was used only if concomitant intracardiac procedure was required. Modified ultrafiltration was routinely performed. Starting in the late 2000s, all patients were subjected to extubation in the operating room.

Chylothorax: Definition and Treatment

Our institutional diagnostic and treatment protocol has been outlined previously.[8] In brief, pleural fluid in patients with persistent chest tube drainage ≥5 mL/kg/day beyond postoperative day 5 is routinely tested for chylomicrons, lymphocyte fraction, and triglycerides. The presence of chylomicrons or a lymphocyte fraction ≥80% is defined as chylothorax. The medical treatment for confirmed chylothorax consists of 4 phases: phase 1, introduction of the medium-chain triglyceride (MCT) formula; phase 2, total parenteral nutrition (TPN) and nothing by mouth; phase 3, prednisone administration (1 mg/kg/day); phase 4, octreotide (0.5-4 mg/kg/hour intravenous continuous infusion). The duration of each phase is 5 to 7 days. Patients also undergo a vascular ultrasound to rule out occlusive thrombosis of the upper venous systems. The chylothorax is considered resolved and the chest tubes are removed once drainage is ≤2 mL/kg/day for each individual drain, with the minimal fat diet continued for an additional 6 weeks after drain removal. If a patient does not respond to the first cycle of the treatment regimen, cardiac catheterization is performed to measure Fontan pressure, to rule out any anatomic issue, and to coil embolize any arteriopulmonary collaterals that potentially increases Fontan pressure. Thoracic duct ligation is considered when 2 cycles of medical treatment fail, and no anatomic lesions are detected on cardiac catheterization.

In this study, prolonged pleural effusion was defined as the need for a chest tube due to drainage of >4 mL/kg/day/tube for >14 days. Prolonged but nonchylous pleural effusion was treated with diuretics and fluid restriction, not with the chylothorax treatment regimen.

Data Collection and Outcome Assessment

All patients' clinical charts, echocardiography and cardiac catheterization reports, and operation records were reviewed. The Nakata index was calculated as the summation of the right and left PA cross-sectional areas indexed to the patient's body surface area.[9] Qualitative assessments of ventricular function and degree of AV valve regurgitation were performed as described previously.[10] Ventricular function was graded as normal, mildly reduced, moderately reduced, or severely reduced. The degree of AV valve regurgitation was graded as none/trivial, mild, moderate, or severe. Composite adverse events included death from any cause, transplantation, requirement for Fontan takedown, and development of protein-losing enteropathy (PLE) or plastic bronchitis.

Statistical Analysis

Continuous variables are summarized as median with interquartile range (IQR), and differences between groups were assessed with the Wilcoxon rank-sum test. Categorical and ordinal variables are presented as frequency and percentage, and differences were assessed with the χ^2 or Fisher exact test according to group size. A P value < .05 was considered significant. Independent predictors of chylothorax and the total number of days of any chest drainage were analyzed with multivariable logistic regression and multivariable generalized negative binomial regression for count data, respectively. The time-related freedom from death was assessed nonparametrically using the Kaplan–Meier method in patients otherwise censored at last known date to be alive or at the date of heart transplantation or Fontan takedown. Analyses were also conducted adjusted for age, body weight, and cardiopulmonary bypass time. All analyses were performed with R statistical packages (R Institute for