Effect of Gastrointestinal Malformations on the Outcomes of Patients With Congenital Heart Disease

Carlos M. Mery, MD, MPH, Luis E. De León, MD, J. Rubén Rodriguez, MD, R. Michael Nieto, MD, Wei Zhang, PhD, Iki Adachi, MD, Jeffrey S. Heinle, MD, Lauren C. Kane, MD, E. Dean McKenzie, MD, and Charles D. Fraser, Jr, MD

Divisions of Congenital Heart Surgery and Pediatric General Surgery, Texas Children's Hospital, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston; and Outcomes and Impact Service, Texas Children's Hospital, Houston, Texas

Background. **The goal of this study was to assess the effect of associated gastrointestinal malformations (GI) on the outcomes of patients undergoing congenital heart operations.**

Methods. **Neonates and infants with thoracic (esophageal atresia, tracheoesophageal fistula) and abdominal (duodenal stenosis/atresia, imperforate anus, Hirschsprung disease) GI malformations undergoing congenital heart operations between 1995 and 2015 were included. Two control groups were created, one for each group. Patients were matched by diagnosis, procedure, history of prematurity, presence of genetic syndrome, and a propensity score including weight and year of operation.**

Results. **The cohort included 383 patients: 52 (14%) with thoracic GI malformations and 98 (25%) thoracic GI controls, 80 (21%) with abdominal GI malformations and 153 (40%) abdominal GI controls. Median follow-up was 6 years (range, 16 days to 20 years). Patients with thoracic GI malformations had longer length of stay ($p < 0.001$), longer intubation times ($p = 0.002$), and higher perioperative death ($p = 0.015$) than controls. There was a tendency for worse overall survival than controls, mainly explained by the higher risk of early death ($p = 0.06$). No difference was found in outcomes between patients with abdominal GI malformations and controls.**

Conclusions. **Patients with thoracic GI malformations have worse perioperative outcomes than controls, but their long-term survival does not seem to be significantly different. Abdominal GI malformations do not have a significant effect on outcomes. The presence of GI malformations should likely not preclude patients from undergoing congenital heart operations, but careful family counseling is necessary, especially for thoracic GI malformations.**

(Ann Thorac Surg 2017;■:■–■)

The association of congenital heart defects (CHDs) and congenital gastrointestinal (GI) malformations is well known [1–3]. CHDs affect approximately 0.5% to 1% of the general population, and the incidence of GI malformations has been reported to be between 1.3 and 1.8 per 1,000 live births [4]. Previous reports have identified a higher incidence of congenital GI malformations in patients with CHDs, with numbers reported between 8% and 15% [5–9]. GI malformations in the setting of CHD may occur as an isolated defect or in the setting of chromosomal abnormalities, in which case the incidence is even higher [10, 11].

It is widely believed that the presence of congenital GI malformations significantly worsens the perioperative course and increases the risk of morbidity and mortality of patients undergoing congenital heart surgery (CHS) [11–13]. Furthermore, this risk has sometimes been considered prohibitive in terms of undergoing further operations for CHDs in some patients [12–14].

Previous studies of extracardiac malformations have focused on the prevalence of GI malformations in patients with congenital heart disease [5, 8, 15]; however, the effect of congenital GI malformations on the short- and long-term outcomes of patients undergoing CHS have not been well defined. The goal of this study was to assess the effect of associated congenital GI malformations on the outcomes of patients undergoing operations for CHDs.

Patients and Methods

The study cohort included all neonates and infants with congenital GI malformations (esophageal atresia [EA], tracheoesophageal fistula [TEF], duodenal stenosis or atresia, imperforate anus [IA] and Hirschsprung disease) who underwent operations for CHD at Texas Children's Hospital between July 1995 and December 2015. The

Accepted for publication April 17, 2017.

Presented at the Fifty-third Annual Meeting of The Society of Thoracic Surgeons, Houston, TX, Jan 21–25, 2017.

Address correspondence to Dr Mery, Congenital Heart Surgery, Texas Children's Hospital, 6621 Fannin St, Houston, TX 77030; email: cmmery@texaschildrens.org.

Published by Elsevier Inc.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2017.04.042

study excluded patients who had a diagnosis of congenital diaphragmatic hernia in association with any of the GI malformations and those who underwent prior cardiac surgical intervention at another institution. Because malrotation is a condition that includes a wide spectrum of disorders of intestinal fixation (rather than an actual malformation of the GI tract) with different degrees of severity, most of which are repaired in the elective setting in the absence of obstructive symptoms, patients with this condition were not included in the study. This study was approved by the Baylor College of Medicine Institutional Review Board, and informed consent was waived.

Patients were classified by the anatomic location of their GI malformations into two groups: thoracic GI malformations (EA or TEF, or both) or abdominal GI malformations (duodenal stenosis or atresia, IA, or Hirschsprung disease). Patients who had both thoracic and abdominal GI malformations were classified according to the most severe condition, usually the thoracic GI malformation; for example, a patient who had TEF and IA would be included in the thoracic GI malformation group.

Patients who met all inclusion criteria were then matched to patients with CHD who underwent CHS but without congenital GI malformations in a variable ratio, either 1:2 or 1:1, according to the available number of patients. Patients were exactly matched by cardiac diagnosis, primary procedure, history of prematurity (<37 weeks' gestation), and the presence of a genetic syndrome or chromosomal abnormality. A propensity score including weight and year of operation was calculated for further matching. Nearest-neighbor matching without replacement was applied to propensity scores and restricted on exact matching for diagnosis, procedure, prematurity, and syndrome. Weights were used to account for the variable matching [16] and were used at the time of statistical analysis. Two control groups were created from this matched set of patients, one for the thoracic GI malformations group and one for the abdominal GI malformations group.

Medical records, operative reports, procedure, discharge, and clinic notes were retrospectively reviewed to obtain data on demographics, presence of comorbidities, fundamental diagnoses, and number of cardiothoracic and abdominal procedures. Follow-up was obtained by a combination of patient records and structured telephone interviews with patients and referring cardiologists or primary care physicians.

Statistical Analysis

Data are described as percentages and medians with ranges, as appropriate. Comparisons of categoric variables between patients with congenital GI malformations and controls were performed using the χ^2 or Fisher exact test, as appropriate. Continuous variables were analyzed using the Wilcoxon rank test. Time-to-event variables were analyzed using the Kaplan-Meier method and log-rank tests. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc, Cary, NC). A p value of less than 0.05 was considered statistically significant.

Results

The cohort included 383 patients: 52 (14%) had thoracic GI malformations, and 80 (21%) had abdominal GI malformations. Included were 98 patients (25%) as thoracic GI controls and 153 (40%) patients as abdominal GI controls. Median follow-up of the cohort was 6 years (range, 16 day to 20 years). Follow-up exceeding 6 months was complete for 95.4% of the patients. A genetic syndrome or chromosomal abnormality was present in 29 patients (56%) with thoracic GI malformations and in 59 (74%) with abdominal GI malformations. The demographics and clinical characteristics of the cohort by groups can be found in Table 1, and the complete distribution of CHD diagnoses by groups can be found in Table 2.

Thoracic GI Malformations

Of the 52 patients with thoracic GI malformations, 6 (12%) had isolated EA, 29 (56%) had isolated TEF, and 5 (10%) had EA with TEF. Also included in this group were 12 who had both thoracic and abdominal GI malformations: 7 (13%) had both TEF and IA, 3 (6%) had EA with TEF and IA, 1 (2%) had EA and duodenal atresia, and 1 (2%) had EA with TEF and duodenal atresia. In 42 patients (81%) with thoracic GI malformations, the surgical intervention for the GI malformation was performed before the cardiac repair, and in 37 patients (71%), the GI and cardiac malformations were both addressed during the same hospitalization (Table 3).

Compared with controls, patients with CHD and thoracic GI malformations had longer intensive care unit ($p = 0.002$) and hospital lengths of stay ($p < 0.001$) and required longer mechanical ventilation days ($p < 0.001$; Table 4).

Operative mortality was higher in patients with thoracic GI malformations (13%) than in controls (3%; $p = 0.03$; Table 4). Overall actuarial survival at 5 years was 76% for patients with thoracic GI malformations and 88% for controls (Fig 1A). There was a tendency for worse overall survival than controls, mainly explained by the higher risk of early death; however, this did not reach statistical significance ($p = 0.06$).

Conditional long-term survival after hospital discharge was similar between both groups, with an actuarial conditional survival at 5 years of 86% for those with thoracic GI malformations and 88% for their controls ($p = 0.59$; Fig 1B).

Four of the 12 patients (33%) with both thoracic and abdominal GI malformations died perioperatively: 2 patients with TEF and IA at 98 and 47 days postoperatively; 1 patient with TEF, EA, and IA at 35 days postoperatively; and 1 patient with TEF, EA, and duodenal atresia at 9 days after the operation.

Abdominal GI Malformations

Of the 80 patients with abdominal GI malformations, 34 (43%) had IA, 29 (36%) had duodenal atresia, 4 (5%) had duodenal stenosis, 1 (1%) had both duodenal atresia and IA, and 12 (15%) had Hirschsprung disease. Surgical