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ORIGINAL ARTICLE

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Outcomes in patients with cor triatriatum sinister

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ABSTRACT

Objective: To describe outcomes in patients with cor triatriatum sinister (CTS).

Design: Retrospective review of patients with CTS followed at Mayo Clinic Rochester from 1990 to 2016. Clinical notes, operative reports, and baseline imaging studies were reviewed including echocardiogram, magnetic resonance imaging, computed tomography, and cardiac catheterization.

Results: Fifty-seven patients (median age 34 years; men 32 (56%)) were enrolled. Definitive or suspected CTS diagnosis was made by transthoracic echocardiogram in 41 (72%) patients, and additional multimodality imaging was required in 39 (68%) patients. Of these 57 patients, initial diagnosis was made in adulthood in 35 (61%) patients, and 33 of 57 (58%) patients had additional congenital heart disease (CHD) diagnosis. A total of 27 (47%) patients required surgical resection of CTS membrane during median follow-up of 76 months, and these patients were younger at the time of CTS diagnosis (26 vs 41, $P = 0.01$) and more likely to have associated CHD (55% vs 45%, $P = 0.02$). There was one perioperative mortality and no late mortality. There was no recurrence of CTS membrane obstruction in the patients that underwent surgery. Similarly there was no significant increase in CTS membrane gradient in the patients that were managed conservatively.

Conclusions: The natural history of CTS is stability without progressive left atrial obstruction, especially in patients with isolated CTS and in those with initial CTS diagnosis made in adulthood. In patients requiring surgical membrane resection due to flow obstruction, surgery is safe and effective with very low risk of recurrence.

KEYWORDS
cor triatriatum, echocardiography, left atrial obstruction, surgical resection

1 | INTRODUCTION

Cor triatriatum, first described by Church in 1868, is a rare congenital heart defect involving abnormal division of the atrial chambers by an accessory membrane.[1] This membrane can result in varying amounts of flow obstruction within the chamber depending on the number and size of membrane fenestrations present. Cor triatriatum can occur in the right atrium (cor triatriatum dexter) or in the left atrium (cor triatriatum sinister, CTS).[1]

CTS is a rare congenital anomaly that is estimated to be present in 0.4% of patients with congenital heart disease.[2,3] It can occur in isolation but often is associated with other congenital heart disease, most commonly atrial septal defect and anomalous pulmonary venous connection.[4] Many early case series describe the presentation to be similar to mitral stenosis, with symptoms of dyspnea, signs of heart failure, and imaging consistent with pulmonary edema.[2] The extent and orientation of the left atrial membrane can be quite variable, and pathologic study demonstrates that while described as a "membrane," the tissue in fact contains cardiac muscle covered by fibrous endocardium.[5] The embryologic basis for CTS remains uncertain, and has been theorized to result from abnormal incorporation of the pulmonary veins into the left atrium, or alternately overgrowth of the septum primum.[4]

Abbreviations: CTS, Cor triatriatum sinister.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

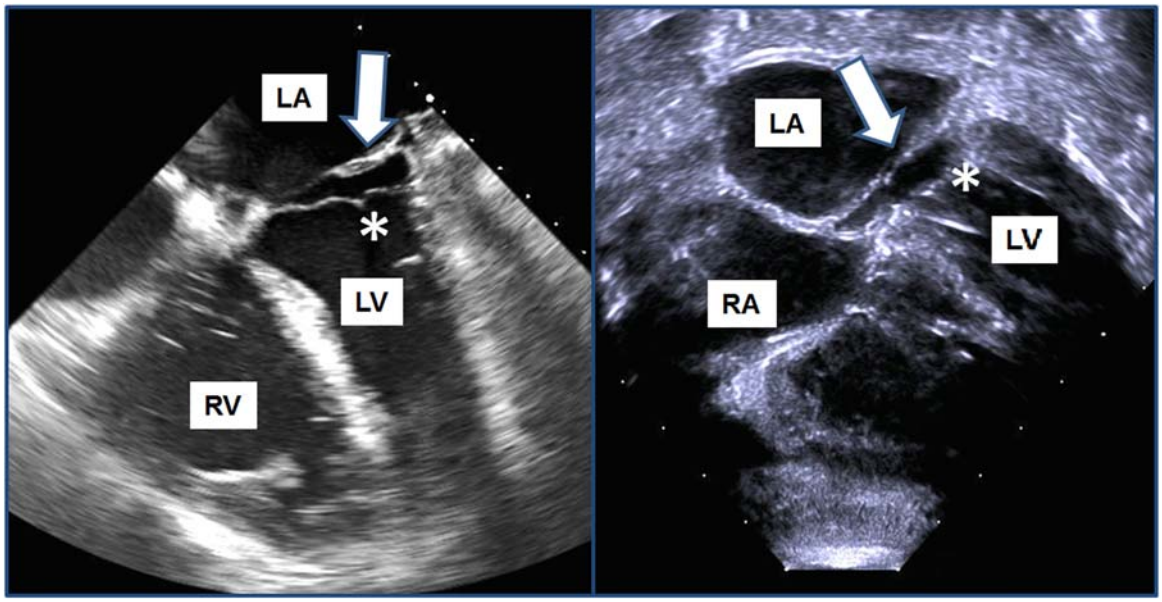

FIGURE 1 Echocardiographic images of cor triatriatum sinister (CTS). Left: Transesophageal echocardiogram (mid-esophageal level) showing CTS membrane (white arrow) in the left atrium above the mitral valve (asterisk). Right: Transthoracic echocardiogram (subcostal window) showing CTS membrane (white arrow) in the left atrium above the mitral valve (asterisk). Abbreviations: LA, left atrium, RA: right atrium, lV, left ventricle, rV, right ventricle

When describing the atrial anatomy in CTS, the chamber receiving pulmonary venous drainage is referred to as the "proximal" chamber, while the chamber containing the left atrial appendage and connecting to the atrioventricular valve is called the "distal" chamber. Multiple classification schemes have been developed to describe the anomaly.[5–7] Frequently cited is the Lam system, which classifies CTS based on the location of pulmonary venous drainage (to the proximal chamber, the coronary sinus, or elsewhere) and presence or absence of an atrial septal defect.[7] Representative images of CTS by echocardiography are depicted in Figure 1. While the condition was initially documented primarily in children, recent series have reported late presentations in adults, likely owing to variable atrial obstruction and increasing availability of high quality multimodality imaging.[8] There are limited data about the natural history of CTS because of the rarity of this diagnosis. The purpose of this study is to describe patient outcomes, specifically of progressive left atrial obstruction and need for surgical intervention, based on a series of patients with CTS diagnosis seen at a referral center.

2 | METHODS

2.1 | Patient selection and data collection

This is a retrospective review of all patients with CTS diagnosis seen at Mayo Clinic Rochester from January 1, 1990 through December 31, 2016. The Mayo Clinic Institutional Review Board approved this study and waived informed consent. Medical records were reviewed in detail including clinical notes, electrocardiograms, echocardiograms, magnetic resonance imaging, computed tomography, cardiac catheterization and surgical notes. Demographic, clinical, and hemodynamic data at the time of initial diagnosis (baseline data) were collected and analyzed. Clinical, surgical, and hemodynamic data during follow-up were also collected and analyzed.

2.2 | Statistical analysis

Analyses were performed with JMP software (version 10.0; SAS Institute Inc, Cary, North Carolina). Categorical variables were reported as percentages, and continuous variables were reported as mean ± standard deviation or median (interquartile range, IQR) for skewed data. Categorical variables were compared using the chi-square test or Fisher's exact test, and continuous variables were compared with a 2-sided, unpaired *t* test, paired *t* test, or Wilcoxon rank-sum test, as appropriate. For all statistical analyses, a *P* value less than 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Baseline characteristics

There were 57 patients with a diagnosis of CTS seen at Mayo Clinic from January 1, 1990 to December 31, 2016. The mean age at the time of initial diagnosis was 34 ± 28 years (median age 34 years, IQR 17–49 years), and 32 (56%) were men. A definitive or suspected CTS diagnosis was made with transthoracic echocardiography in 41 (72%) patients, and additional imaging and hemodynamic evaluation were obtained in 39 (68%) patients. These additional imaging and hemodynamic evaluations were transesophageal echocardiogram, N = 22; cardiac magnetic resonance imaging, N = 4; cardiac catheterization, N = 3; and cardiac computed tomography, N = 2. Atrial fibrillation and flutter were common in the population, present in 16 (28%) patients. Median age at CTS diagnosis in patients with atrial fibrillation or flutter was 58

(IQR: 44–71) years, while median age at CTS diagnosis in patients without atrial arrhythmia was 26 (IQR: 0–55) years, $P < 0.001$. Of the patients with atrial fibrillation or flutter, one patient had an obstructive CTS membrane (mean gradient 5 mm Hg), and 6 patients had other structural heart lesions. Among the 57 patients with CTS diagnosis, 33 (58%) had additional congenital heart disease diagnosis, the most common being patent foramen ovale/atrial septal defect in 25 (44%) followed by mitral stenosis in 4 (7%), and partial anomalous pulmonary venous connection in 4 (7%), Table 1. Of the patients identified with atrial-level communication, only 7 had nonrestrictive shunts resulting in right-sided chamber enlargement. The remainder (n = 18) had a hemodynamically insignificant patent foramen ovale without right ventricular enlargement. Anatomy of CTS was described based on the LAM classification,[7] and the most common CTS subtype was LAM class A in 38 (67%) patients, Table 2.

3.2 | Surgical intervention

Over a median follow-up of 76 (IQR: 51–93) months, 27 (47%) patients underwent surgical resection of CTS membrane and the median age at the time of surgery was 26 (IQR: 17–35) years. Table 3 shows a comparison of the baseline clinical and echocardiographic data between the patients that had surgical intervention and those that were managed conservatively. The patients that had surgical intervention were younger at the time of CTS diagnosis, 26 (IQR: 17–35) vs 41 (32–49) years, $P = 0.01$; and were more likely to have associated congenital heart disease, 18 (55%) vs 15 (45%), $P = 0.02$. Initial diagnosis of CTS was made in adulthood in 35 patients, and 13 (37%) of those patients required surgery. Lam A1 classification, with atrial shunt in the proximal chamber, was present in 5 patients, one of whom had delayed presentation with CTS diagnosis at age 73. The remaining 4 patients were young children or had other associated congenital heart disease.

Among the 27 patients that had surgical intervention, the primary indication for surgery was an obstructive CTS membrane in 10 (37%) patients, while the remaining patients had additional indications for surgery. Of the 10 patients with obstructive membranes, 9 presented with symptoms which prompted their evaluation and diagnosis. These symptoms were failure to thrive or respiratory distress in 4 infants and young children, and exertional fatigue, dyspnea, and hemoptysis in 5 older children and adults. The diagnosis of obstructive CTS membrane was made incidentally in a 10 year old boy who underwent imaging evaluation for pericarditis. Among patients with obstructive CTS

TABLE 1 Baseline Characteristics (N = 57)

Age at diagnosis, years	34 ± 28
Male	32 (56%)
Associated lesions	33 (58%)
PFO/ASD	25 (44%)
Ventricular septal defect	3 (5%)
Mitral valve stenosis	4 (7%)
Anomalous pulmonary vein	4 (7%)
Bicuspid aortic valve	3 (5%)
Pulmonary stenosis	2 (4%)
Patent ductus arteriosus	2 (4%)
Comorbidities	
Atrial fibrillation/flutter*	16 (28%)
Hypertension	16 (28%)
Hyperlipidemia	11 (19%)
Smoking	11 (19%)
Obstructive sleep apnea	5 (9%)
Coronary artery disease	4 (7%)
Diabetes mellitus	3 (5%)
NYHA class III-IV	3 (5%)

Abbreviations: PFO/ASD, patent foramen ovale/atrial septal defect; NYHA, new York Heart Association, atrial fibrillation/flutter*, all atrial arrhythmia diagnoses including postoperative arrhythmia.

TABLE 2 LAM classification

LAM	Description	N (%)
A	Proximal chamber receives all the pulmonary veins; No ASD	38 (67%)
A1	ASD between right atrium and proximal chamber.	5 (9%)
A2	ASD between right atrium and distal chamber.	2 (4%)
B	Pulmonary veins drain into the coronary sinus	0
C	No connection between pulmonary veins and the proximal chamber	1 (2%)

Abbreviations: ASD, atrial septal defect. Classification could not be determined in 11 patients.

TABLE 3 Comparison of clinical and imaging data

	Surgery (N = 27)	No surgery (N = 30)	*P*
Age at diagnosis, years	26(IQR: 17–35)	41(IQR: 32–49)	0.01
Male	12 (44%)	20 (67%)	0.26
Isolated CTS	9 (38%)	15 (63%)	0.02
Associated CHD	18 (55%)	15 (45%)	0.01
Hypertension	5 (19%)	11 (36%)	0.08
Hyperlipidemia	3 (11%)	8 (27%)	0.18
Coronary artery disease	1 (4%)	3 (10%)	0.31
NYHA class III-IV	2 (7%)	1 (3%)	0.29
Creatinine clearance <60 ml/min	2 (7%)	2 (7%)	0.34
Echocardiography			
CTS mean gradient, mm Hg	3.4 ± 0.6	1.2 ± 0.7	0.07
Tricuspid regurgitation velocity, m/s	3.1 ± 0.8	2.8 ± 0.4	0.09
≥ Moderate RV dysfunction	2 (7%)	1 (3%)	0.66
Left ventricular ejection fraction, %	60 ± 6	62 ± 4	0.29

Abbreviations: RV, right ventricular; IQR, interquartile range; CTS, cor triatriatum sinister; CHD, congenital heart disease; NYHA, New York Heart Association.

membrane, the average membrane gradient at the time of surgery was 8 mm Hg. For the patients with additional indications for surgery, the concomitant surgical procedures performed at the time of CTS membrane resection were ASD closure (n = 6), mitral valve repair or replacement (n = 5), atrial septectomy and ligation of pulmonary artery (n = 3), partial anomalous pulmonary venous return repair (n = 2), aortic valve replacement (n = 1), Fontan operation (n = 1), patent ductus arteriosus ligation (n = 1), ventricular septal defect closure (n = 1), pulmonary valve replacement (n = 1), and coronary artery bypass grafting (n = 1). Note that some patients had multiple surgical indications and procedures. The patients with obstructive CTS membrane were younger at the time of surgery compared to those with additional surgical indications 13 (IQR: 6–17) vs 31 (IQR: 23 −38) years, $P = 0.03$.

There was 1 (4%) early postoperative death. This occurred in a 2-month-old male with obstructive CTS, mean gradient of 10 mmHg, pulmonary hypertension with suprasystemic pulmonary pressures, and evidence of moderate right ventricular dysfunction at the time of surgery. This patient underwent membrane resection, closure of patent foramen ovale, and ligation of patent ductus arteriosus. The postoperative course was complicated by hemodynamic instability requiring mechanical circulatory support and subsequent death due to multi-organ failure on postoperative day 8. There were no late deaths.

3.3 | Imaging follow-up

Postoperative imaging was available in 24 of the 27 patients, and the median duration of follow-up from the time of surgery was 65 (IQR: 34–89) months. There was no significant increase in CTS membrane gradient from the time of hospital dismissal after surgery compared to the last imaging follow-up, 1 mm Hg vs 1 mm Hg, $P = 0.89$. Among the 30 patients that were managed conservatively, 13 of them (43%) had available follow-up imaging, and the median duration of follow-up was 47 (IQR: 32–61) months. There was no significant increase in CTS membrane gradient from the time of diagnosis to the time of last follow-up, 1.2 mm Hg vs 0.5 mm Hg, $P = 0.18$.

4 | DISCUSSION

The current study describes the outcomes in patients with a diagnosis of CTS based on a cohort of patients followed at a single tertiary center. Some of the surgical patients in the current study have been previously reported.[9] The key findings in this study are: (1) the diagnosis of CTS may require multimodality imaging; (2) majority of the patients seen at our center were managed conservatively without surgical intervention; (3) obstruction severity related to CTS membrane is not progressive.

Although the diagnosis of CTS was made or suspected based on TTE in 41 patients (72%) in the current study, 68% of the cohort required an alternate imaging modality to confirm diagnosis and assess for associated congenital heart lesions. Several studies have reported increased diagnostic yield when multimodality imaging is used for the diagnosis of CTS.[10–13] Sakamoto and colleagues described two cases of CTS in adults where the use of cardiac MRI provided additional anatomic information that was not evident on TTE, specifically regarding the location of atrial communication and anatomy of the pulmonary veins.[13] In a different study, the utilization of agitated contrast echocardiography provided additional information regarding membrane fenestration that was not apparent on TTE alone.[11]

Of the 57 patients in the study, only 47% underwent surgical intervention during the study period. The majority of these patients (58%) had associated congenital heart lesions that could have influenced the decision for and timing of surgery. Among the 30 patients that were managed conservatively, serial echocardiograms did not show any significant temporal increase in the severity of obstruction during follow-up. Another important observation from this study was the low likelihood of surgical intervention in patients with isolated CTS and those with initial CTS diagnosis made in adulthood. Of the 24 patients with isolated CTS, and 35 patients with CTS diagnosis made in adulthood, only 38% and 37%, respectively, underwent surgery. This finding has clinical implications for patient counseling and frequency of echocardiographic monitoring.

It seems logical that a patient with an obstructive CTS membrane and an atrial-level shunt in the “proximal” chamber might have delayed presentation, as the atrial shunt could provide decompression of the pulmonary venous chamber and thereby mitigate symptoms. Due to small sample size, this question was difficult to answer in the current study. Observationally, however, only 1 of the 5 patients with Lam A1 anatomy was an adult with a delayed presentation, suggesting that this anatomy did not mask symptoms in the majority of patients. Atrial fibrillation and flutter were common in the population, and those patients with atrial arrhythmias were older at the time of CTS diagnosis. Notably, however, only one patient with atrial arrhythmia had an obstructive CTS membrane, and only six had other associated structural heart disease. Thus, the majority of cases of atrial fibrillation and flutter in this series are likely related to acquired, age-related heart disease.

Although it is difficult to make recommendations based on a retrospective case series, our data suggest that patients with an isolated CTS diagnosis, or an initial CTS diagnosis in adulthood, may not require close monitoring in the absence of significant obstruction. Additionally, surgical resection of CTS membrane was safe and effective in relieving obstruction without recurrent obstruction during follow-up. Similar to our findings, prior studies have reported low risk of residual or recurrent obstruction after resection of CTS membrane, a finding that has clinical implications for postsurgical recommendations.[14–16]

4.1 | Limitations

This is a single center retrospective study and as a result it is subject to the inherent bias associated with this type of study design. Patients were seen at a tertiary medical center, introducing referral bias. The majority of the patients that underwent surgical resection of CTS membrane also had other structural lesions that were addressed at the time of surgery. This makes it difficult to accurately determine the primary indication for surgery in such cases. Although we propose that isolated CTS with mild obstruction and initial diagnosis of CTS in adulthood

were associated with low risk of surgical intervention, we did not control for confounding factors or perform any rigorous statistical analysis because of small size.

5 | CONCLUSIONS

The natural history of CTS is stability without progressive left atrial obstruction, especially in patients with isolated CTS and in those with initial CTS diagnosis made in adulthood. In patients requiring surgical membrane resection due to flow obstruction, surgery is safe and effective with very low risk of recurrence.

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTIONS

Concept/design, Alexander Egbe; Data collection, Margaret Fuchs; Data analysis, Alexander Egbe; Drafting article, Margaret Fuchs; Critical revision of article, Alexander Egbe, Sameh Said, Heidi Connolly.

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