Congenital Heart Disease

Tech Science Press

DOI: 10.32604/CHD.2021.014276

ARTICLE

Surgical Correction of Coronary Artery Ectasia Combining Congenital Coronary Artery Fistula

Yulin Wang[1,#], Ye Yang[1,#], Limin Xia[1,3], Wenjun Ding[1], Qiang Ji[1,*] and Chunsheng Wang[2,*]

[1]Department of Cardiovascular Surgery of Zhongshan Hospital Fudan University, Shanghai, China

[2]Shanghai Municipal Institute for Cardiovascular Diseases, Shanghai, China

[3]Department of Cardiovascular Surgery of Xiamen Branch of Zhongshan Hospital Fudan University, Xiamen, China

[*]Corresponding Authors: Qiang Ji. Email: ji.qiang@zs-hospital.sh.cn. ChunSheng Wang. Email: zscardiacs2016@163.com.

[#]Yulin Wang and Ye Yang: Contributed equally as the co-first author

Received: 15 September 2020 Accepted: 12 October 2020

ABSTRACT

Background: Coronary artery ectasia (CAE) complicated with concomitant congenital coronary artery fistula (CCAF) is rare. This study characterizes the clinical characteristics of CAE combining CCAF, and reports a single-institution experience with surgical correction of CAE combining CCAF. **Methods:** A total of 24 symptomatic patients (8 males, median 52.5 years old) who underwent surgical correction of CAE combining CCAF in this center were reviewed. Based on the size of ectatic segment, the CAE were classified as a giant CAE (>20 mm, n = 14) and a non-giant CAE (≤20 mm, n = 10). Individualized surgical approaches were chosen. The patients were followed up for a median of 3.8 years. **Results:** The overwhelming majority of CAEs were solitary, and only 4.2% of CAEs were associated with multiple lesions. CAEs were predominantly located in the right coronary artery with predilection to women more than to men (2:1). 95.8% of patients with the CCAF had single fistula defect. The right atrium was the most frequent drainage site (33.3%) followed by the left ventricle (25.0%). Surgical mortality was 4.2%. All 22 follow-up patients survived with recovery from symptoms and New York Heart Association (NYHA) functional class I-II. In 10 patients with non-giant CAEs undergoing closure of fistula alone, favorable in-hospital outcomes were recorded, but residual fistula (one patient) and acute inferior wall myocardial infarction related to intracoronary thrombosis (one patient) were observed at follow-up. In 11 patients with giant CAEs undergoing aneurysm resection plus distal bypass grafting at the time of closure of fistula, favorable in-hospital outcomes and encouraging midterm results were recorded. Additionally, in 3 patients with giant CAEs undergoing closure of fistula plus aneurysmal plication, adverse events occurred, including surgical death related to rupture of the ectatic segment (one patient), perioperative myocardial infarction caused by acute thromboembolism (one patient), nonfatal inferior wall myocardial infarction related to intracoronary thrombosis (one patient) at follow-up.Conclusion: Individualized surgical approaches based on the size and the location of ectatic coronary artery as well as fistula should be offered to symptomatic patients with CAE combining CCAF.

KEYWORDS

Coronary artery ectasia; congenital coronary artery fistula; surgical approach; giant coronary artery ectasia

1 Introduction

Abnormal dilation of coronary arteries was first described by Bougon in 1812 [1]. It is accepted that there are two different phenotypes of coronary aneurysmal dilation: Coronary artery ectasia (CAE) and coronary artery aneurysm. CAE is defined as a diffuse (exceeding more than a third of the coronary artery length) dilation of coronary segments of at least 1.5 times the adjacent normal segment or the patient's largest coronary artery, whereas the term aneurysm is used to define similar, but more focal lesion [2–6]. Abnormal dilation of coronary arteries can be found in up to 5% of patients undergoing coronary angiography [7,8], while CAE is rare [7]. The epidemiologic data of CAE varies, which may be related to different causative factors. Atherosclerosis is reported to be the most frequent cause of CAE followed by Kawasaki disease, with congenital coronary artery fistula (CCAF) being rare [9]. CAE has been reported to be associated with an unfavorable prognosis irrespective of the presence of atherosclerotic coronary artery disease or concomitant congenital disorder [2–5].

For symptomatic patients with CAE complicated with CCAF who are not suitable or unsuccessful for percutaneous coronary intervention, surgical correction is generally accepted as the preferred treatment [9–12]. Besides closure of fistula, reported surgical approaches of CAE complicated with CCAF include aneurysm plication or resection, saphenous vein patch repair of the aneurysm, marsupialization with interposition graft, and distal bypass grafting [6,12–26]. Unfortunately, quite a few studies take both CAE and coronary artery aneurysm as one unit, rather than separately. In addition, the majority of previous studies are single case studies with focusing on perioperative results [17–26]. In patients with CAE complicated with CCAF, the appropriate surgical approaches, precise success rates, and the mid- and long-term results following surgery remain to be further discussed.

This single-center study reviews 24 documented symptomatic patients who underwent surgical correction of CAE combining CCAF, characterizes the clinical characteristics of CAE combining CCAF, and evaluates in-hospital outcomes and follow-up results, to provide a reference for surgical correction of CAE combining CCAF.

2 Material and Methods

2.1 Study Protocol

This study protocol was approved by the ethics committee of *Zhongshan Hospital Fudan University* and was consistent with the *Declaration of Helsinki*. All included patients signed an informed consent approved by the ethics committee.

From January 2009 to December 2018, symptomatic patients who underwent surgical correction of CAE combining CCAF in this center were identified. Baseline characteristics, surgical data, and perioperative outcomes were obtained from our institutional database and were analyzed. Patients were regularly followed up at 3- and 6-month following surgery and in 12-month intervals thereafter. Follow-up data were obtained through clinic visits, WeChat, or telephone interviews with patients or their families. All patients received clinical evaluation and noninvasive coronary computed tomography (CT) angiographic examination (iCT 64, Philips Healthcare, Amsterdam, Netherlands) at follow-up. Data collection was performed retrospectively by trained staff (two people). The trained staff, however, were not informed of the purpose of this study.

Perioperative outcomes were surgical mortality and major postoperative morbidity. Surgical mortality included both death events within the first 30 post-operative days and any death event that occurred during the hospital stay. Major postoperative morbidity included new-onset myocardial infarction, re-thoracotomy, prolonged mechanical ventilation (>48 hours), renal replacement therapy, stroke, and wound infection. Follow-up results included all-cause death, cardiac death, nonfatal myocardial infarction, New York Heart Association (NYHA) functional class, and residual fistula, intracoronary

thrombosis, and bypass graft failure determined with coronary CT angiography. In the analysis of NYHA functional status and angiographic results, the most current follow-up information was used.

2.2 Surgical Procedure and Postoperative Medication

According to the maximum diameter of the ectatic segment, the CAE was classified into a giant CAE (>20 mm) and a non-giant CAE (20 mm or less) [6]. In patients with a non-giant CAE, closure of fistula alone was conducted in this center. The surgical approaches for a giant CAE were chosen according to the size of CAEs and coronary ramification, but the decision was ultimately left to the discretion of the operating surgeon. Besides closure of fistula, other surgical options for a giant CAE were aneurysm plication, or aneurysm resection or ligation with concomitant bypass grafting of the affected coronary arteries.

All patients received full median sternotomy under general anesthesia with single-lumen endotracheal intubation. Cardiopulmonary bypass was instituted by the ascending aortic and right atrium/bicaval cannulation with aortic cross-clamping and cold blood cardioplegic arrest. The ectatic segment was entered through a longitudinal incision, and thrombotic material was removed. Coronary ostia were identified. The fistula defect was closed via direct suture with a 5-0 polypropylene suture and a continuous suturing technique or using an autologous pericardium patch and a running suture of 5-0 polypropylene. Aneurysm plication, including longitudinal arteriotomy of the ectatic segment followed by reconstruction using direct suture of trimmed aneurysmal wall tissue with several running sutures of 5-0 polypropylene, was carried out to form a new coronary artery close to normal size. The surgical practice of aneurysm resection or ligation with concomitant bypass grafting of the affected coronary arteries was to open the ectatic segment, suture its afferent and efferent vessels, and finish with bypass grafting of the affected coronary arteries by using *in situ* left internal thoracic artery or saphenous vein. Bypass grafting of affected coronary arteries included distal bypass grafting and bypass grafting of other coronary larger ramification. Weaning from cardiopulmonary bypass was regular with no evidence of myocardial ischemia.

Postoperative antiplatelet and anticoagulation therapies were as follows. First, subcutaneous injection of 2500 IU low-molecular-weight heparin once every 12 hours was initiated within 4 hours of surgery and continued until oral anticoagulant therapy was administrated. Second, aspirin (100 mg/d), clopidogrel (75 mg/d), and warfarin (titrated to a target international normalized ratio of 2.0–2.5) were administered for patients undergoing aneurysm plication, or aneurysm resection with concomitant bypass grafting at the time of closure of fistula after the initiation of oral intake; and aspirin (100 mg/d) and clopidogrel (75 mg/d) were administered for patients undergoing closure of fistula alone. Finally, warfarin and clopidogrel were discontinued 6 months and one year following surgery, respectively; however, aspirin was continued indefinitely.

2.3 Statistical Analysis

Categorical variables were expressed as frequency distributions and single percentages and were compared between groups using Fisher's exact test. Continuous variables were expressed as the median with an inter-quartile range (IQR) and were compared between groups with the Wilcoxon rank sum test. Statistical analysis was performed with SPSS statistical package version 22.0 (SPSS Inc., Chicago, IL, USA).

3 Results

3.1 Study Population

A total of 29 symptomatic patients with coronary aneurysmal dilation, including 24 patients with CAE and 5 patients with coronary artery aneurysm, underwent surgery in this center between January 2009 and December 2017. The CCAF was identified in all the 24 patients with the CAE. No patients were identified as Kawasaki disease or had a history of Kawasaki disease. The 24 symptomatic patients with CAE combining CCAF were eligible to this study and their information was analyzed.

There were more female (66.7%) than male patients (33.3%) with a median age of 52.5 (IQR, 44.5–58.5) years. All patients manifested with drug refractory symptoms including progressive dyspnea and/or chest pain, with NYHA class III or IV in 75.0% of the population. Six (25.0%) patients were diagnosed during invasive coronary angiography following symptoms of chest pain, and the remaining 18 (75.0%) patients complained of progressive dyspnea, leading to non-invasive computed tomography scan and finally invasive coronary angiography. Four (16.7%) patients received unsuccessful percutaneous coronary intervention prior to surgery. Two patients underwent unsuccessful percutaneous closure of fistula with coil embolization. In other 2 patients, the guide wire failed to reach the distal end of the fistula due to the tortuosity of the coronary artery. Seven patients suffered from concomitant other cardiac lesions. The baseline characteristics are shown in Tab. 1.

Table 1: Baseline characteristics

Variable	Value
Number of patients	24
Age (years), median (IQR)	52.5 (44.5–58.5)
Gender (females/Males)	16/8
Obesity (body mass index >30 kg/m^2)	2 (8.3%)
Recent smoking	3 (12.5%)
Concomitant diseases	
Diabetes mellitus	3 (12.5%)
Hypertension	5 (20.8%)
Dyslipidemia	1 (4.2%)
Chronic obstructive pulmonary disease	1 (4.2%)
Marfan's syndrome	1 (4.2%)
Concomitant other cardiac lesions	n = 7 (29.2%)
Severe mitral regurgitation	1
Severe aortic insufficiency	2
Infective mitral regurgitation and aortic insufficiency	1
Severe mitral regurgitation and tricuspid regurgitation	1
Atrial septal defect	1
Aortic aneurysm (Marfan's syndrome)	1
Preoperative cardiac status	
Recent myocardial infarction	2 (8.3%)
Atrial fibrillation	3 (12.5%)
Failure of PCI	4 (16.7%)
NYHA functional class	
II	1 (4.2%)
III	17 (70.8%)
IV	6 (25.0%)
LVEF (%), median (IQR)	61.0 (58.5–69.0)
LVEDD (mm), median (IQR)	56.5 (45.8–63.8)

IQR, inter-quartile range; PCI, percutaneous coronary intervention; NYHA, New York Heart Association (classification); LVEF, left ventricular ejection fraction; LVEDD, left ventricular endo-diastolic diameter.

3.2 Description of CAE and CCAF

The description of CAE combining CCAF is listed in Tab. 2. The maximum diameter of the ectatic coronary arteries ranged from 15.0 mm to 73.0 mm (median 25.0 mm). Ten patients were identified as having the non-giant CAE, and their median diameter of the CAE was 18.0 mm (ranging from 15.0 mm to 20.0 mm). And the remaining 14 patients suffered from the giant CAE, and their median diameter of the CAE was 38.5 mm (ranging from 23.0 mm to 73.0 mm). Based on the number of involvements of coronary arteries, Markis's CAE classification type III was observed in 23 patients (95.8%) and type I in 1 patient (4.2%). The right coronary artery was the most affected artery (66.7%) followed by the left anterior descending artery (20.8%). In addition, multiple fistula defects were observed in 4.2% and single fistula defect in 95.8% of patients. The right atrium was the most frequent drainage site (33.3%) followed by the left ventricle (25.0%), with the right ventricle being the least frequent drainage site (4.2%). (Fig. 1) showed radiological findings of 4 patients with CAE secondary to CCAF.

Table 2: Description of CAE combining CCAF

Variable	Value
Number of patients	24
Maximum diameter of CAE (mm), median (IQR)	25.0 (18.8–41.0)
Classification based on the size of CAE	
Non-giant CAE (20 mm or less)	10
Size of CAE (mm), median (IQR)	18.0 (17.3–19.0)
Giant CAE (more than 20 mm)	14
Size of CAE (mm), median (IQR)	38.5 (32.0–49.8)
Markis's classification of CAE	
Type III	23 (95.8%)
Type I	1 (4.2%)
Location of CAE	
Right coronary artery	16 (66.7%)
Left anterior descending artery	5 (20.8%)
Left circumflex artery	2 (8.3%)
Right coronary artery + left anterior descending artery	1 (4.2%)
Defect of CCAF	
Single fistula defect	23 (95.8%)
Multiple fistula defects	1 (4.2%)
Drainage site of CCAF	
Right atrium	8 (33.3%)
Left ventricle	6 (25.0%)
Coronary sinus	5 (20.8%)
Pulmonary artery	3 (12.5%)
Right ventricle	1 (4.2%)
Right atrium + pulmonary artery	1 (4.2%)

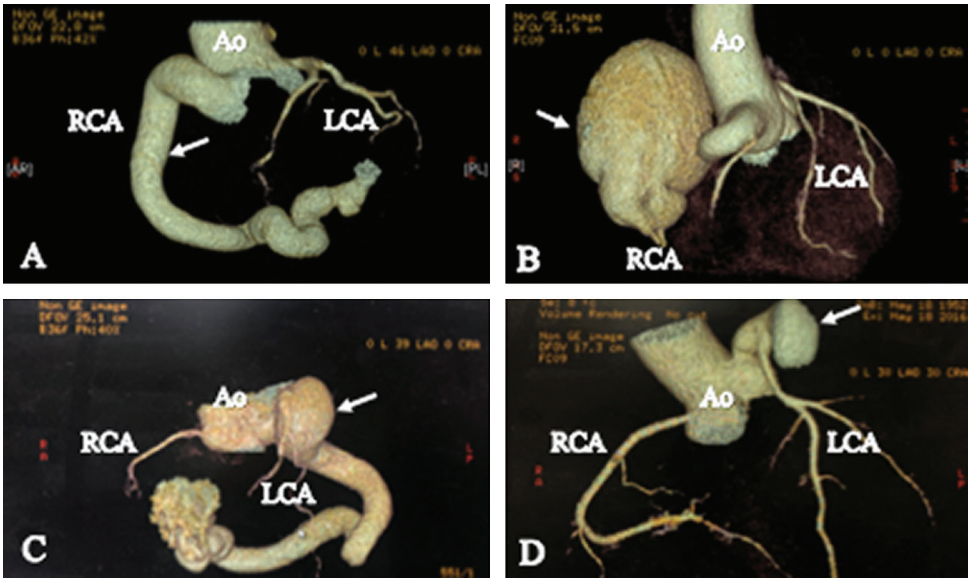

Figure 1: Radiological findings of CAE secondary to CCAF. (A, the right coronary artery ectasia (at the arrowhead, the maximum diameter of 16.0 mm) with fistula to the left ventricle; B, the right coronary artery ectasia with a giant coronary artery aneurysm (at the arrowhead, the maximum diameter of 60.0 mm), with fistula to the coronary sinu; C, coronary artery ectasia located in the left main and the left anterior descending artery (at the arrowhead), with fistula to the right ventricle; D, coronary artery ectasia located in the left main and the left circumflex coronary artery (at the arrowhead), with fistula to the pulmonary artery. AO, aorta; RCA, right coronary artery; LCA, left coronary artey; CAE, coronary artery ectasia; CCAF, congenital coronary artery fistula)

3.3 Surgical Data

Ten patients with non-giant CAEs underwent closure of fistula alone, with a median aortic cross-clamping time of 45.0 (IQR, 25.0–50.0) min. Among the 10 patients, 4 patients received failure of percutaneous coronary intervention, 3 other patients had concomitant additional cardiac lesions, and the remaining 3 were not suitable for percutaneous coronary intervention due to coronary sinus being the drainage site.

Among 14 patients with giant CAEs, 11 patients with the size of the CAE ranging from 32.0 mm to 73.0 mm underwent aneurysm resection and bypass grafting of the affected coronary arteries (saphenous vein grafting to the posterior descending artery in 10 patients and the left internal mammary artery grafting to the left anterior descending artery in one patient) at the time of closure of fistula. Histopathology of the excised aneurysm showed widespread myxoid degeneration and lymphocytic aggregations in the medial layer, without extensive calcification of the arterial wall or plaque formation (Fig. 2). Note that one patient who suffered from the right coronary ectasia with fistula to the left ventricle and aneurysmal dilatation of aortic sinus as well as ascending aorta related to Mafan's syndrome underwent closure of fistula and aneurysm resection, followed by Yacoub's procedure, and finish with bypass surgery with saphenous vein grafting from aorta to the posterior descending artery. And the remaining 3 patients with the size of the CAE of 23 mm, 24 mm, and 26 mm, respectively, underwent closure of fistula plus aneurysmal plication. Surgical data of this series are summarized in Tab. 3.

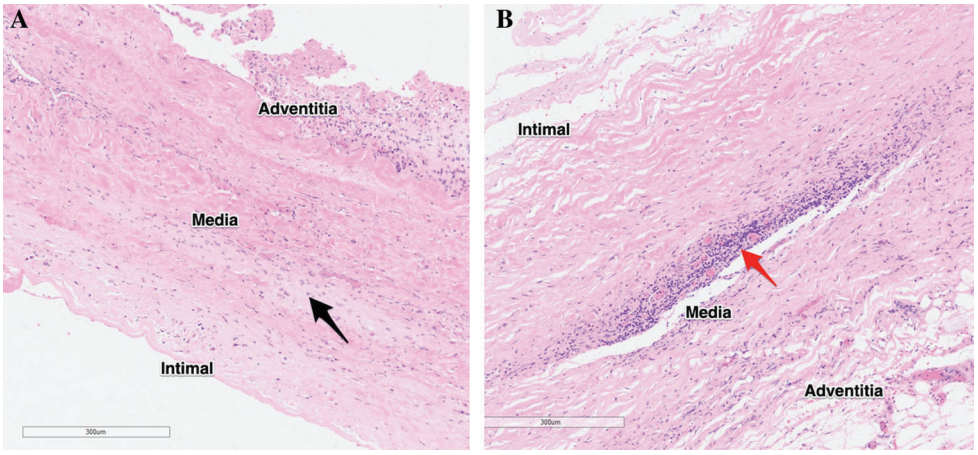

Figure 2: Histological analysis of the resected aneurysmal wall (Hematoxylin and Eosin staining. Original magnifications, ×100. A, Myxoid degeneration of the medial layer was observed. B, Lymphatic cells had accumulated in the medial layer)

Table 3: Surgical data

Variables	Total (n = 24)	Non-giant CAE (n = 10)	Giant CAE (n = 14)
CPB (min), median (IQR)	67.0 (46.0–80.0)	39.5 (34.3–49.0)	76.0 (70.0–81.0) #
ACC (min), median (IQR)	45.0 (25.0–50.0)	22.5 (19.5–25.8)	49.0 (48.0–52.0) #
Procedures for CAE			
Closure of fistula alone	10	10	0
Plus aneurysm resection + bypass grafting	11	0	11
Plus aneurysmal plication	3	0	3
Procedures for other cardiac lesions	7	3	4
Mitral repair	1	0	1
Aortic valve replacement	2	1	1
Mitral repair and aortic valve replacement	1	0	1
Mitral repair and tricuspid valvuloplasty	1	1	0
Atrial septal defect repair	1	1	0
Yacoub's procedure	1	0	1

#, $p<0.05$ for dada of the giant CAE group versus data of the non-giant CAE group.
CPB, cardiopulmonary bypass; ACC, aortic cross-clamping.

3.4 In-Hospital Outcomes

In 10 patients with non-giant CAEs undergoing closure of fistula alone, no surgical mortality or major postoperative morbidity was observed. The median maximum value of cardiac troponin T following surgery was 0.16 (IQR, 0.11–0.23) ng/ml. All the 10 patients recovered smoothly with the median intensive care unit time of 1 day and the median postoperative hospital length of 5 days.

In 11 patients with giant CAEs undergoing aneurysm resection and bypass grafting of the affected coronary arteries at the time of closure of fistula, no surgical mortality or major postoperative morbidity

was recorded. The median maximum value of cardiac troponin T following surgery was 0.29 (IQR, 0.25–0.36) ng/ml. All the 11 patients recovered smoothly with the median intensive care unit time of 2 days and the median postoperative hospital length of 6 days.

In addition, in 3 patients with giant CAEs undergoing closure of fistula plus aneurysmal plication, 2 patients received re-thoracotomy following surgery and before discharge. The one with the size of the CAE of 24 mm developed acute inferior myocardial infarction on the third day postoperatively which may be related to acute embolism of ectatic right coronary artery and received emergency operation; and the other with the size of the CAE of 26 mm developed rupture of the ectatic right coronary artery on the second day postoperatively and underwent emergency operation. The latter received the second emergency operation due to pericardial tamponade on the sixth day postoperatively, and finally died of low cardiac output on the seventh day postoperatively. The median maximum value of cardiac troponin T following surgery was 3.15 (IQR, 1.67–5.20) ng/ml.

In-hospital outcomes of this series are listed in (Tab. 4). No renal replacement therapy, stroke, or wound infection was recorded.

Table 4: Clinical outcomes

Variables	Total (n = 24)	Non-giant CAE (n = 10)	Giant CAE (n = 14)	
			S1 (n = 11)	S2 (n = 3)
In-hospital				
Surgical death	1 (4.2%)	0	0	1
New-onset MI	1 (4.2%)	0	0	1
Re-thoracotomy				
Rupture of the ectatic segment	1 (4.2%)	0	0	1
Acute thromboembolism	1 (4.2%)	0	0	1
Prolonged ventilation	1 (4.2%)	0	0	1
Blood transfusion	6 (25.0%)	0	4	2
#Troponin T (ng/ml), median (IQR)	0.25 (0.18–0.32)	0.16 (0.11–0.23)	0.29 (0.25–0.36)	3.15 (1.67–5.20)
ICU stay (d), median (IQR)	2.0 (1.0–3.0)	1.0 (1.0–1.0)	2.0 (2.0–3.0)	3.0 (2.0–7.0)
PLOS (d), median (IQR)	6.0 (5.0–7.0)	5.0 (5.0–6.0)	6.0 (5.0–7.0)	6.0 (6.0–7.0)
Follow-up				
Number of patients	22	9	11	2
Follow-up time (y), median (IQR)	3.8 (1.6–5.9)	4.3 (1.9–5.4)	3.5 (1.8–7.8)	3.3 (3.1–3.4)
Survival	22 (100%)	9	11	2
NYHA class				
I	10 (45.5%)	5	5	0
II	12 (54.5%)	4	6	2
Nonfatal MI	2 (8.3%)	1	0	1
Residual fistula	1 (4.2%)	1	0	0

S1, patients with giant CAEs undergoing aneurysm resection plus bypass grafting at the time of closure of fistula; S2, patients with giant CAEs undergoing aneurysmal plication at the time of closure of fistula.

#Troponin T, the maximum value of cardiac Troponin T postoperatively (the upper limit of normal in this center is 0.03 ng/ml).

MI, myocardial infarction; ICU, intensive care unit; PLOS, postoperative length of stay.

3.5 Follow-Up Results

A total of 22 patients (including 9 patients with non-giant CAEs and 13 patients with giant CAEs) received a follow-up visit with a median duration of 3.8 (IQR, 1.6–5.9) years. All patients survived with significant improvement of quality of life with recovery from symptoms and NYHA functional class I–II.

Among 9 patients with non-giant CAEs, 2 patients developed adverse events. The one was found to have a residual fistula (the size of 1.0 mm) with drainage into the left ventricle 12 months following surgery. The patient was asymptomatic with no obvious enlargement of the CAE, and dynamic evaluation was continued. The other patient developed nonfatal inferior posterior wall myocardial infarction 15 months following surgery, which may be associated with intracoronary thrombosis. The patient preferred medical treatment instead of invasive intervention and discharged two weeks later. The patient was categorized as NYHA functional class II, and dynamic evaluation was continued with a future perspective of reintervention.

Among 11 patients with giant CAEs undergoing aneurysm resection and bypass grafting of the affected coronary arteries at the time of closure of fistula, encouraging results were recorded at follow-up, including no adverse cardiac events or adverse angiographic results.

In addition, in 2 patients with giant CAEs undergoing closure of fistula plus aneurysmal plication, one patient with the size of the CAE of 23 mm developed nonfatal inferior wall myocardial infarction 13 months following surgery, which may be associated with intracoronary thrombosis. The patient underwent emergency percutaneous coronary intervention and survived.

4 Discussion

This study summarized the clinical characteristics of a series of Chinese patients with CAE complicated with CCAF. Also, this study suggested that aneurysm resection combined with bypass grafting of the affected coronary arteries at the time of closure of fistula may be an appropriate surgical approach for the giant CAE combining CCAF, and closure of fistula alone may be a surgical option for the non-giant CAE complicated with CCAF. To the best of our knowledge, this is the largest experience of adult patients undergoing surgical correction of CAE combining CCAF published to date.

The overwhelming majority of CAEs in this series were solitary, and only 4.2% of CAEs were associated with multiple lesions. This was in line with previous reports [24–26]. Devabhaktuni et al. [9] reported that the majority of CAEs were located in the proximal and middle segments of the right coronary artery with male to female ratio of 3:1. Recently, Luo et al. [2] investigated a series of 51 CAE patients and reported that the right coronary artery was the most involved coronary artery. CAEs in this series were predominantly located in the right coronary artery with predilection to women more than to men (2:1). These results were in line with previous studies [2,9] about the location of the CAE but were different from gender ratio. The epidemiologic data of CAE varied, which may be related to different causative factors. Devabhaktuni et al. [9] reviewed previous literatures until 2015, and found that atherosclerosis was the most frequent cause of CAE followed by Kawasaki disease, with CCAF being even rare. In this series including 24 Chinese patients with the CAE, all patients suffered from CCAF. Histological analysis of the resected aneurysmal wall showed myxoid degeneration and lymphocytic aggregations in the medial layer, without histological evidence of severe atherosclerotic changes, such as extensive calcification of the arterial wall and plaque formation, suggesting that coronary artery ectasia in

this series may be not closely related to atherosclerosis. No patient in this series was diagnosed as having atherosclerosis, Kawasaki disease, or had a history of Kawasaki disease. This result was different from the evidence from the majority of previous studies [6,9]. The reason for this difference may be related to ethnic differences.

The ideal surgical approach for the CAE combining CCAF has not been established [6,16,23]. This study divided 24 patients with CAE combining CCAF into two groups based on the size of the ectatic coronary artery [6], and evaluated their in-hospital and midterm results following different surgical approaches. First, 10 patients with non-giant CAEs (the size of the CAE of 15–20 mm) underwent closure of fistula alone. Although adverse events including nonfatal myocardial infarction (one case) and residual fistula (one case) were recorded, favorable in-hospital outcomes and no midterm death with recovery from symptoms and NYHA functional class I-II suggested that closure of fistula alone may be a surgical option for the non-giant CAE combining CCAF. Second, 11 patients with giant CAEs (the size of the CAE of more than 30 mm) underwent aneurysm resection and bypass grafting of the affected coronary arteries at the time of closure of fistula, and received favorable in-hospital outcomes and encouraging mid-term results, suggesting that aneurysm resection and bypass grafting of the affected coronary arteries at the time of closure of fistula may be an appropriate surgical option for the giant CAE combining CCAF. And finally, 3 patients with giant CAEs (the size of the CAE of 23 mm, 24 mm, and 26 mm, respectively) underwent plus aneurysmal plication, and developed more adverse events, including surgical death related to rupture of the ectatic segment, perioperative myocardial infarction caused by acute thromboembolism, and nonfatal inferior wall myocardial infarction related to intracoronary thrombosis at follow-up. Results from this study did not support closure of fistula plus aneurysmal plication as a surgical option for the giant CAE combining CCAF. Therefore, results from this study indicated that individualized surgical approaches based on the size and the location of ectatic coronary artery as well as fistula should be offered to patients with CAE combining CCAF.

There was a concern about increased risks of intracoronary thrombosis following surgery. In this series, all patients received strict antiplatelet and anticoagulation therapies. Perioperative acute inferior myocardial infarction secondary to acute embolism of the ectatic segment was observed in only one patient, and redo for bleeding was not recorded, suggesting that strict antiplatelet and anticoagulation therapies may be contribute to the low incidence of perioperative myocardial infarction, and the risk of bleeding may be overstated. Additionally, 2 patients developed nonfatal myocardial infarction related to intracoronary thrombosis after discontinuation of warfarin and clopidogrel, suggesting that longer strict antiplatelet therapies needed further research.

This study had some potential limitations. First, this was a single-center, observational study with a limited sample size, which may have influenced the generalizability of the results. A final determination would require multicenter, prospective, randomized studies involving a larger sample size. However, to our knowledge, this was the largest experience of adult patients undergoing surgical correction of CAE combining CCAF published to date. Second, due to a limited sample size, this study did not compare results of different surgical approaches. Finally, this study summarized the clinical characteristics of the CAE and evaluated in-hospital and midterm results following surgery, but did not explore the underlying mechanisms.

5 Conclusion

This study suggests that aneurysm resection and bypass grafting of the affected coronary arteries at the time of closure of fistula may be an appropriate surgical option for the giant CAE combining CCAF, and closure of fistula alone may be a surgical option for the non-giant CAE combining CCAF. Therefore, individualized surgical approaches based on the size and the location of ectatic coronary artery as well as

fistula should be offered to symptomatic patients with CAE combining CCAF. Our data contribute to accumulating evidence of individualized surgical approaches for CAE combining CCAF.

Acknowledgement: There are no acknowledgements.

Availability of Data and Materials: The datasets used in the current study are available from the corresponding author or the first author on reasonable request.

Authors' Contributions: (I) Conception and design: C. Wang and Q. Ji; (II) Administrative support: C. Wang; (III) Provision of study materials or patients: Y. Wang, Y. Yang, L. Xia, W. Ding; (IV) Collection and assembly of data: Y. Wang, Y. Yang, L. Xia, W. Ding; (V) Data analysis and interpretation: Q. Ji, Y. Wang, Y. Yang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Competing Interests: The authors declare that they have no competing interests.

Consent for Publication: All authors have read and approved the content and agree to submit it for consideration for publication in your journal.

Ethics Approval and Consent to Participate: Prior consent from all patients and approval from the ethics committee of Zhongshan Hospital Fudan University were obtained.

Funding Statement: This study was supported by a grant from National Natural Science Foundation of China (No. 81100140).

Conflicts of Interest: The authors declare that they have no conflicts of interest or report regarding the present study.

References

1. Jarcho, S. (1969). Bougon on coronary aneurysm. *1812 American Journal of Cardiology, 24(4),* 551–553. DOI 10.1016/0002-9149(69)90500-1.
2. Luo, Y., Tang, J., Liu, X., Qiu, J., Ye, Z. et al. (2017). Coronary artery aneurysm differs from coronary artery ectasia, angiographic characteristics and cardiovascular risk factor analysis in patients referred for coronary angiography. *Angiology, 68(9),* 823–830. DOI 10.1177/0003319716665690.
3. Boles, U., Zhao, Y., David, S., Eriksson, P., Henein, M. Y. (2012). Pure coronary ectasia differs from atherosclerosis, morphological and risk factors analysis. *International Journal of Cardiology, 155(2),* 321–323. DOI 10.1016/j.ijcard.2011.12.010.
4. Boles, U., Wiklund, U., David, S., Ahmed, K., Henein, M. Y. (2019). Coronary artery ectasia carries worse prognosis, a long-term follow-up study. *Polish Archives of Internal Medicine, 129(11),* 833–835.
5. Warisawa, T., Naganuma, T., Tomizawa, N., Fujino, Y., Ishiguro, H. et al. (2016). High prevalence of coronary artery events and non-coronary events in patients with coronary artery aneurysm in the observational group. *International Journal of Cardiology, Heart & Vasculature, 10,* 29–31.
6. Kawsara, A., Núñez Gil, I. J., Alqahtani, F., Moreland, J., Rihal, C. S. et al. (2018). Management of coronary artery aneurysms. *Cardiovascular Interventions, 11(13),* 1211–1223. DOI 10.1016/j.jcin.2018.02.041.
7. Doi, T., Kataoka, Y., Noguchi, T., Shibata, T., Nakashima, T. et al. (2017). Coronary artery ectasia predicts future cardiac events in patients with acute myocardial infarction. *Arteriosclerosis, Thrombosis, and Vascular Biology, 37 (12),* 2350–2355. DOI 10.1161/ATVBAHA.117.309683.
8. Swaye, P. S., Fisher, L. D., Litwin, P., Vignola, P. A., Judkins, M. P. et al. (1983). Aneurysmal coronary artery disease. *Circulation, 67(1),* 134–138. DOI 10.1161/01.CIR.67.1.134.
9. Devabhaktuni, S., Mercedes, A., Diep, J., Ahsan, C. (2016). Coronary artery ectasia—A review of current literature. *Current Cardiology Reviews, 12(4),* 318–323. DOI 10.2174/1573403X12666160504100159.

10. Badmanaban, B., Mallon, P., Campbell, N., Sarsam, M. A. I. (2004). Repair of left coronary artery aneurysm, recurrent ascending aortic aneurysm, and mitral valve prolapse 19 years after Bentall's procedure in a patient with Marfan syndrome. *Journal of Cardiac Surgery, 19(1),* 59–61. DOI 10.1111/j.0886-0440.2004.02052.x.
11. Kochar, A., Kiefer, T. (2017). Coronary artery anomalies, when you need to worry. *Current Cardiology Reports, 19 (5),* 154. DOI 10.1007/s11886-017-0854-x.
12. Pham, V., Hemptinne, Q., Grinda, J. M., Duboc, D., Varenne, O. et al. (2020). Giant coronary aneurysms, from diagnosis to treatment, a literature review. *Archives of Cardiovascular Diseases, 113(1),* 59–69. DOI 10.1016/j.acvd.2019.10.008.
13. Crawley, P. D., Mahlow, W. J., Huntsinger, D. R., Afiniwala, S., Wortham, D. C. (2014). Giant coronary artery aneurysms, review and update. *Texas Heart Institute Journal, 41(6),* 603–608. DOI 10.14503/THIJ-13-3896.
14. Singh, S. K., Goyal, T., Sethi, R., Chandra, S., Devenraj, V. et al. (2013). Surgical treatment for coronary artery aneurysm, a single-centre experience. *Interactive Cardiovascular and Thoracic Surgery, 17(4),* 632–636. DOI 10.1093/icvts/ivt282.
15. Izumi, K., Hisata, Y., Hazam, S. (2009). Surgical repair for a coronary-pulmonary artery fistula with a saccular aneurysm of the coronary artery. *Annals of Thoracic and Cardiovascular Surgery, 15(3),* 194–197.
16. Beckmann, E., Rustum, S., Marquardt, S., Merz, C., Shrestha, M. et al. (2017). Surgical treatment of coronary artery aneurysms. *Journal of Cardiac Surgery, 32(11),* 674–679. DOI 10.1111/jocs.13227.
17. Hillebrand, J., Rukosujew, A., Martens, S., Boese, D. (2016). Redo operation of recurrent giant coronary artery aneurysm, optimizing surgical strategy. *The Thoracic and Cardiovascular Surgeon Reports, 5(1),* 57–59. DOI 10.1055/s-0036-1586232.
18. Dolapoglu, A., Ott, D. A. (2016). Giant right coronary artery aneurysm. *Texas Heart Institute Journal, 43(4),* 360–362. DOI 10.14503/THIJ-15-5450.
19. Narren, A., Reddy, P., Notarstefano, C., Kudavali, M. (2017). Giant coronary artery aneurysm in a middle-aged woman. *Annals of Thoracic Surgery, 103(4),* e313–e315. DOI 10.1016/j.athoracsur.2016.09.018.
20. Komoda, S., Komoda, T., Ivanitskaia-Kuehn, E., Dreysse, S., Pasic, M. et al. (2010). Giant aneurysm of the right coronary artery and fistula to the coronary sinus. *General Thoracic and Cardiovascular Surgery, 58(2),* 78–81. DOI 10.1007/s11748-009-0453-x.
21. Voth, V., Usta, E., Schneider, W., Ziemer, G. (2011). Multiple giant coronary aneurysms-exclusion by vein graft interposition. *Thoracic and Cardiovascular Surgery, 59(7),* 439–441. DOI 10.1055/s-0030-1270898.
22. Khan, H. R., Shajar, M., Naik, S. (2016). Giant right coronary artery aneurysm. *Journal of Cardiac Surgery, 31(8),* 527–528. DOI 10.1111/jocs.12779.
23. Uchida, T., Hamesaki, A., Sadahiro, M. (2017). A modified surgical approach for giant left coronary arterial aneurysm. *Journal of Cardiac Surgery* , *32(8),* 489–491. DOI 10.1111/jocs.13177.
24. Yoneyama, F., Sakamoto, H., Tokunaga, C., Enomoto, Y., Hiramatsu, Y. (2017). Complex coronary artery aneurysm. *Journal of Cardiac Surgery, 32(1),* 26–27. DOI 10.1111/jocs.12868.
25. Li, D., Wu, Q., Sun, L., Song, Y., Wang, W. et al. (2005). Surgical treatment of giant coronary artery aneurysm. *Journal of Thoracic and Cardiovascular Surgery, 130(3),* 817–821. DOI 10.1016/j.jtcvs.2005.04.004.
26. Keyser, A., Hilker, M. K., Husser, O., Diez, C., Schmid, C. (2012). Giant coronary aneurysms exceeding 5 cm in size. *Interactive Cardiovascular of Thoracic Surgery, 15(1),* 33–36. DOI 10.1093/icvts/ivs111.