# Unilateral and Multilateral Congenital Coronary-Pulmonary Fistulas in Adults: Clinical Presentation, Diagnostic Modalities, and Management With a Brief Review of the Literature

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ABSTRACT

*Background:* Congenital coronary-pulmonary fistulas (CPFs) are commonly unilateral, but bilateral and multilateral fistulas may occur. In multilateral CPFs, the value of a multidetector computed tomography (MDCT) imaging technique as an adjuvant to coronary angiography (CAG) is eminent. The purpose of this study was to describe the clinical presentation, diagnostic modalities, and management of coincidentally detected congenital CPFs.

*Hypothesis:* Unilateral and multilateral coronary-pulmonary fistulas are increasingly detected due to the wide speard application of multidetector computed tomography which might be a supplementary or replacing to conventional coronary angiography.

*Methods:* We evaluated 14 adult patients with congenital coronary artery fistulas (CAFs) who were identified from several Dutch cardiology departments.

*Results:* Fourteen adult patients (5 female and 9 male), with a mean age of 57.5 years (range, 24–80 years) had the following abnormal findings: audible systolic cardiac murmur (n = 4), chronic atrial fibrillation (n = 2), nonsustained ventricular tachycardia (n = 1), and cardiomegaly on chest x-ray (n = 2). Echocardiography revealed normal findings with trivial valvular abnormalities (n = 9), depressed left ventricle systolic function (n = 3), and severe mitral regurgitation and atrial dilatation (n = 2). The findings in the rest of the patients were unremarkable. CAG and MDCT were used as a diagnostic imaging techniques either alone (CAG, n = 6; MDCT, n = 1) or in combination (n = 7). Single modality and multimodality diagnostic methods revealed 22 fistulas including CPFs (n = 15), coronary cameral fistulas terminating into the right (n = 2) and the left atrium (n = 1), and systemic-pulmonary fistulas (n = 4). Of all of the fistulas, 10 were unilateral, 6 were bilateral, and 6 was hexalateral. $^{13}$N-ammonia positron emission tomography-computed tomography was performed in 3 patients revealing decreased myocardial perfusion reserve.

*Conclusions:* CAG remains the gold standard for detection of CPFs. An adjuvant technique using MDCT provides full anatomical details of the fistulas.

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## Introduction

Congenital coronary-pulmonary fistulas (CPFs) were first described postmortem in an adult male by Krause in 1865.[1] CPFs may rarely be acquired subsequent to iatrogenic


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nonsurgical intervention[2,3] and surgical procedures,[4] or due to accidental thoracic traumas.[5,6] Congenital unilateral or multilateral CPFs are increasingly recognized during routine coronary angiography (CAG) or multidetector computed tomography (MDCT) for analysis of chest pain, but remain uncommon anomalies, characterized by a communication between 1 or more coronary arteries and the pulmonary artery. The majority of CPFs are single (unilateral) communications,[7] but bilateral (dual) fistulas[8,9] and multilateral, triple,[10] and quadruple[11] fistulas have previously been described. Congenital fistulas in adult population are usually detected with noninvasive[12,13] and invasive[14] diagnostic imaging modalities. Functional assessment of CPFs may be achieved by myocardial perfusion imaging (MPI), cardiac magnetic resonance imaging, positron emission tomography-computed tomography (PET-CT), right heart catheterization, oximetric series, and recently by fractional flow reserve (FFR) of the nutrient artery.[15] A case series of 14 Dutch patients who underwent diagnostic catheter CAG (n = 13) and MDCT (n = 8) with coincidentally found unilateral and multilateral congenital CPFs is presented herein, and the literature is briefly reviewed.

## Methods

Between 2010 through 2013, 14 subjects were identified and evaluated from different Dutch cardiology departments. From the databases of 6 cardiac catheterization suites, adult patients with congenital fistulas were collected (Gerle Ziekenhuis, Apeldoorn-Zutphen; Scheper Hospital, Emmen, Medisch Spectrum Twente, Enschede; Ziekenhuis Groep Twente, Almelo-Hengelo; Universitair Medisch Centrum St. Radboud, Nijmegen; Orbis Medisch Centrum; and Hospital Sittard-Geleen). The indications for CAG, and the demographic and clinical presentation of the patients were retrieved from the patient's files. Baseline clinical features, angiographic analysis, and coronary artery fistula (CAF) characteristics (origin, pathway, and outflow) were collected. All patients, except 1 diagnosed by MDCT, underwent selective CAG for symptoms suspected of myocardial ischemia. CAG (n = 13) was performed using a femoral (n = 11) and radial (n = 2) approach. Coronary arteries were visualized in the standard planes.

Fistula characteristics (singularity and multiplicity) were determined according to their mode of origin, pathway, and termination Table 1.

The years of data collection were: 2010 (n = 4), 2011 (n = 4), 2012 (n = 4), and 2013 (n = 2). The individual hospital's participation was as follows: (Gerle Ziekenhuis, Apeldoorn-Zutphen (n = 3); Scheper Hospital, Emmen (n = 1), Medisch Spectrum Twente, Enschede (n = 2); Ziekenhuis Groep Twente, Almelo-Hengelo (n = 6); Universitair Medisch Centrum St. Radboud, Nijmegen (n = 1); Orbis Medisch Centrum and Hospital Sittard-Geleen) (n = 1).

In all patients, physical examination, electrocardiography (ECG), and transthoracic echocardiography were routinely performed. When needed for further clarification of the clinical presentation and fistula characteristics, tailored diagnostic methods were undertaken in the individual patient at the clinician's discretion (CAG, n = 13; MDCT, n = 8; MPI, n = 7; PET-CT, n = 3; ambulatory ECG monitoring, n = 1).

MDCT was performed in 8 patients, with the following techniques: 128-slice Somatom Definition AS+ (Siemens Medical Solutions, Erlangen, Germany) and 320-row detector Aquilion-One (Toshiba Medical Systems Europe, Zoetermeer, the Netherlands) with retrospective ECG-gating following intravenous administration of 70 to 90 mL of iodinated contrast medium (400 mg/mL) at a rate of 6 mL/s. A 0.6-mm collimation, with a helical pitch of 0.22, rotation time of 0.3 seconds, tube voltage of 100 to 120 kV (weight-dependent), and tube current 150 to 170 mAs was used. Scanning was performed in the craniocaudal direction at a regular heart rate of <63 bpm. Source images were reconstructed in both systolic and diastolic phases at a 0.75-mm slice thickness with an overlap interval of 0.4 mm. Ultimately, 3-dimensional series were obtained.

## Definitions

Definitions are adopted from earlier publications.[16–18] CAFs are defined as an abnormal direct communication between 1 or more coronary arteries with a cardiac or thoracic structure bypassing the capillary network. Coronary cameral fistulas (CCFs) are fistulas that communicate with 1 or more cardiac chamber (right atrium [RA], left atrium [LA], right ventricle [RV], left ventricle [LV]). This includes solitary CCFs characterized by small or large vessels fistulating into a cardiac chamber and coronary artery-ventricular multiple microfistulas (MMFs) terminating with plural small vessels mainly into the lumen of the LV > RV. Coronary-vascular fistulas (CVFs) are fistulas that terminate into a thoracic vascular structure (pulmonary artery [PA], coronary sinus [CS], caval veins, pulmonary vein [PV], bronchial and mediastinal vessels). Coronary-pulmonary fistulas (CPFs) are characterized by a communication between 1 or more coronary arteries and the pulmonary artery. Coronary artery disease (CAD) is defined as a luminal narrowing of ≥75%. Unilateral fistula is a fistula originating (with single or multiple fistulous vessels) from 1 major epicardial coronary artery or its main branches, with 1 or more termination sites. Bilateral fistulas originate (with single or multiple fistulous vessels) from 2 major epicardial coronary arteries or their main branches with 1 or more termination sites. Multilateral fistulas originate (with single or multiple fistulous vessels) from all 3 major epicardial coronary arteries or their main branches and/or extracardiac vessels with 1 or more termination sites.

## Results

Fourteen patients who underwent diagnostic catheter CAG (n = 13) and MDCT (n = 1) were found to have congenital CPFs. There were 5 female and 9 male subjects, with a mean age of 57.5 years (range, 24–80 years).

## Clinical Characteristics

The demographic and clinical presentations are summarized in Table 2. The patients' main clinical presentations were asymptomatic (n = 3), chest pain (n = 3), dyspnea on exertion (n = 3), palpitation (n = 2), angina pectoris (n = 3), and 1 sustained acute inferior myocardial infarction (MI).

On auscultation of the heart, continuous murmur was heard in 1, and systolic cardiac murmur of variable grade


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Table 1. Angiographic and MDCT Fistula Characteristics of 14 Adult Patients

| Case | Fistula Course | Origin | Pathway | Termination | MDCT | Management |
|---|---|---|---|---|---|---|
| 1 | LAD-PA | Single | Multiple/tortuous | Single | Hexalateral | CMM |
| 2 | Cx-PA | Multiple | Multiple/tortuous | Single | Unilateral | PTE |
| 3 | LAD-PA | Multiple | Multiple/tortuous | Single | NA | PTE |
| 4 | RCA-RA (ectasia) | Single | Single/tortuous | Single | Unilateral | SL + MVpl |
| 5 | LAD-PA | No CAG | MDCT | | Unilateral | WW |
| 6 | RCA-PA | Multiple | Multiple/tortuous | Single | Bilateral | CMM |
| | LAD-PA | Multiple | Multiple/tortuous | Multiple | | |
| 7 | RCA-PA | Single | Multiple/tortuous | Single | NA | SL + MVpl, failed PTE |
| | LAD-PA (aneurysm) | Multiple | Multiple | Single | | |
| 8 | LAD-PA | Single | Multiple/tortuous | Single | NA | CMM + PCI, RCA |
| 9 | LAD-PA | Multiple | Multiple/tortuous | Single | Unilateral | SL + CABG |
| 10 | LAD-PA | Single | Single/tortuous | Single | Unilateral | PCI, LAD |
| 11 | LAD-PA | Multiple | Multiple/tortuous | Multiple | Bilateral | WW |
| | RCA-PA | Single | Single/tortuous | Single | | |
| 12 | LAD-PA | Single | Single/tortuous | Single | NA | CMM |
| 13 | LAD-PA | Single | Single/tortuous | Single | NA | PTE + PCI, LAD, and RCA |
| 14 | RCA-RA (ectasia) | Single | Single/tortuous | Single | NA | CMM |

Abbreviations: CABG, coronary artery bypass grafting; CAG, coronary angiography; CMM, conservative medical management; Cx, circumflex coronary artery; MDCT, multidetector computed tomography; LAD, left anterior descending coronary artery; MVpl, mitral valve plasty; NA, not applicable; PA, pulmonary artery; PCI, percutaneous coronary intervention; PTE, percutaneous therapeutic embolization; RA, right atrium; RCA, right coronary artery; SL, surgical ligation; WW, watchful waiting.

was audible in 4 patients. Two patients had chronic and 1 had paroxysmal atrial fibrillation (patients 4, 6, and 9). One female patient had frequent ventricular premature beats and nonsustained ventricular tachycardia (NSVT). The ECG depicted repolarization disturbances in 4 patients, incomplete right bundle branch block in 4 patients, complete left bundle branch block in 1 patient, signs of an old MI in 1 patient, and was otherwise normal in 6 of the patients. Chest x-ray revealed cardiomegaly in 2 patients.

Transthoracic echocardiography revealed normal findings with trivial valvular abnormalities in 9 patients, depressed LV systolic function in 3 patients (mild in 2 and severe in 1), and severe mitral regurgitation, left atrial dilatation, and biatrial dilatation in 2 patients who also had chronic atrial fibrillation (patients 4 and 6).

Exercise tolerance testing was performed in 8 subjects. It was normal in 7 patients and abnormal in 1 patient.

## Ambulatory ECG Monitoring

In 1 patient (patient 12), ambulatory ECG monitoring revealed NSVT.

## CAG

CAG findings and fistula characteristics (origin, pathway, and outflow) are presented in Table 2 (Figures 1–4). A total of 18 fistulas originated from the left anterior descending coronary artery (LAD) in 10 patients, from the right coronary artery (RCA) in 6 patients, left main coronary artery (LM) in 1 patient, and circumflex coronary artery (Cx) in 1 patient. The termination sites were into the PA in 15 patients, into the LA in 1 patient, and into the RA in 2 patients. Aneurysmal formation was found in 1 patient (patient 7), and significant dilatation and ectasia of the RCA was found in 2 patients (patients 4 and 14). Five had CAD, and of those, 3 had 1-vessel disease, and 2 had 2-vessel disease. Medical treatment was initiated in 1 patient. Percutaneous coronary intervention (PCI) was performed in 3 patients and coronary artery bypass grafting (CABG) in 1 patient. CAG and/or MDCT were used as a diagnostic imaging technique either alone (CAG, n = 6; MDCT, n = 1) or in combination (n = 7). Combined diagnostic modalities (CAG and MDCT) revealed that 10 of the 14 study patients had a single fistula, and 4 had multiple fistulas. One patient with a single CPF was initially detected by MDCT.

## MDCT

MDCT was performed in 8 patients. The total number of fistulas reached 22, including 10 unilateral, 6 bilateral, and 6 hexalateral (this was detected on CAG as a bilateral fistula). MDCT confirmed the findings of conventional CAG and added 4 more fistulas originating directly from the


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Table 2. Demographic Features, Clinical Presentations, Diagnostic Modalities and Management

| Case/Gender/ Age, y | Clinical Presentation | Fistula | Date of Detection | Associated Disorders | Transthoracic Echocardiography | Diagnostic Modalities | Management |
|---|---|---|---|---|---|---|---|
| 1/ F/48 | Angina pectoris | Hexalateral, LM LAD→PA, 4x aorta→PA | November 9, 2010 | None | Normal | CAG, MDCT, PET-CT, MPI | CMM (BB) |
| 2/M/61 | Routine check up, asymptomatic | Cx→LA | March 12, 2010 | COPD | Normal | CAG, MDCT, MPI | PTE-coils, residual fistula |
| 3/M/33 | ACP | LAD→PA | January 10, 2011 | None | Normal | CAG, MPI | PTE-coils |
| 4/M/56 | Dyspnea, AF | RCA→CS/RA | April 7, 2010 | COPD | Mildly depressed LV kinetics, MR, LA dilatation | CAG, MDCT | MVpl, SL, exclusion LAA |
| 5/M/24 | Asymptomatic, CM | LAD-PA | May 10, 2011 | None | Normal | MDCT | WW policy |
| 6/M/77 | Dyspnea, AF | RCA-PA, LAD-PA | August 24, 2011 | COPD, permanent AF | Mildly depressed LV kinetics, RA and LA dilatation | CAG, MDCT, PET-CT | CMM (CCB, VKA, ACE) |
| 7/F/44 | Palpitation, light headedness | RCA-PA, LAD-PA | May 12, 2012 | Melanoma, ventricular arrhythmias | MVp MR | CAG | MVpl, right minithoracotomy, SL RCA-PA, PTE: failure, LAD-PA |
| 8/M/77 | Angina pectoris | LAD-PA | May 31, 2012 | CAD (1 VD), asthma, ulcerative colitis, Gilbert syndrome | Normal | CAG, MPI | PCI-RCA, CMM (BB, aspirin, statin, MCR, prednisolon) |
| 9/M/66 | DOE chest pain, PAF | LAD-PA | November 11, 2011 | CAD (2 VD), AVNRT/stroke | Normal | CAG, MDCT, MPI | CABG, SL, removal of LAA |
| 10/F/61 | Chest pain | LAD-PA | October 9, 2012 | CAD (1 VD) | Normal | CAG, MDCT, PET-CT, MPI | PCI-LAD (aspirin, BB, statin, clopidogrel) |
| 11/M/65 | Asymptomatic | LAD-PA, RCA-PA | June 20, 2012 | CAD (1 VD), COPD | Normal | CAG, MDCT, MPI | WW policy |
| 12/F/80 | Palpitation NSVT | LAD-PA | February 28, 2013 | RR | Normal | CAG, Holter | CMM (aspirin, BB, ACE, CCB, statin, ezetrol) |
| 13/M/65 | Angina pectoris | LAD-PA | October 6, 2010 | CAD (2 VD), old IMI, OSAS | Severely depressed LV kinetics | CAG | PTE coils PCI- RCA PCI -LAD |
| 14/F/48 | Acute IMI | RCA-RA | February 7, 2013 | Breast carcinoma | Normal | CAG | CMM (VKA, BB, clopidogrel, tamoxifen) |

Abbreviations: ACE, angiotensin-converting enzyme; ACP, atypical chest pain; AF, atrial fibrillation; AVNRT, atrioventricular reentry tachycardia; BB, β-blocker; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CAG, coronary angiography; CCB, calcium channel blockers; CM, continuous murmur; CMM, conservative medical management; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; Cx, circumflex coronary artery; DOE, dyspnea on exertion; F, female; IMI, inferior myocardial infarction; LA, left atrium; LAA, left atrial appendage; LAD, left anterior descending coronary artery; LM, left main; LV, left ventricle; M, male; MCR, monocedocard retard; MDCT, multidetector computed tomography; MPI, myocardial perfusion imaging; MR, mitral valve regurgitation; MVp, mitral valve prolapse; MVpl, mitral valve plasty; NSVT, nonsustained ventricular tachycardia; OSAS, obstructive sleep apnea syndrome; PA, pulmonary artery; PAF, paroxysmal AF; PCI, percutaneous coronary intervention; PET-CT, positron emission tomography-computed tomography; PTE, percutaneous therapeutic embolization; RA, right atrium; RCA, right coronary artery; RR, hypertension; SL, surgical ligation; VD, vessel disease; VKA, vitamin K antagonist; WW, watchful waiting.

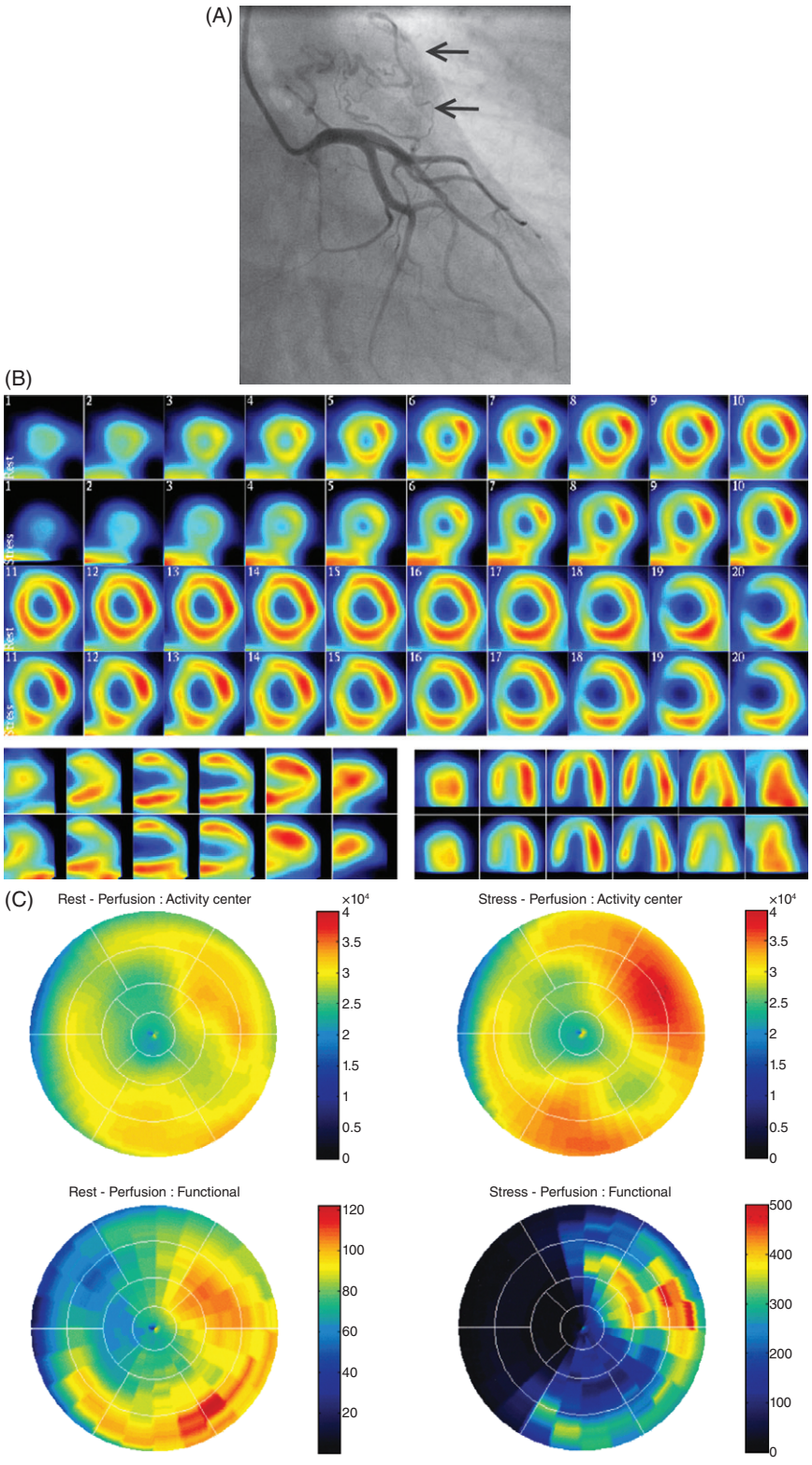


Figure 1. Patient 1: (A) Coronary angiographic frame of the left coronary artery demonstrating fistulous vessels from the LAD and LM to the PT (arrows). (B, C) Myocardial perfusion imaging and positron emission tomography-computed tomography scanning demonstrating reversible myocardial ischemic changes in several segments. (D, E) Schematic representation of multidetector computed tomography of the heart showing a hexalateral coronary artery fistula. Arabic numerals indicate anomalous vessels arising from the ascending aorta (1, 4), posterior aspect of the transverse portion of the aortic arch (5, 6), LM (2), and LAD (3). These vessels bifurcated and anastomosed, and finally terminated into the PT (asterisk). Abbreviations: AO, aorta; GCV, great cardiac vein; LAD, left anterior descending artery; LB, lateral branch; LCx, left circumflex artery; LMCA, left main coronary artery; MA, median artery; PT, pulmonary trunk; RA, right atrium; RCA, right coronary artery; RM, right marginal branch; SVC, superior vena cava.


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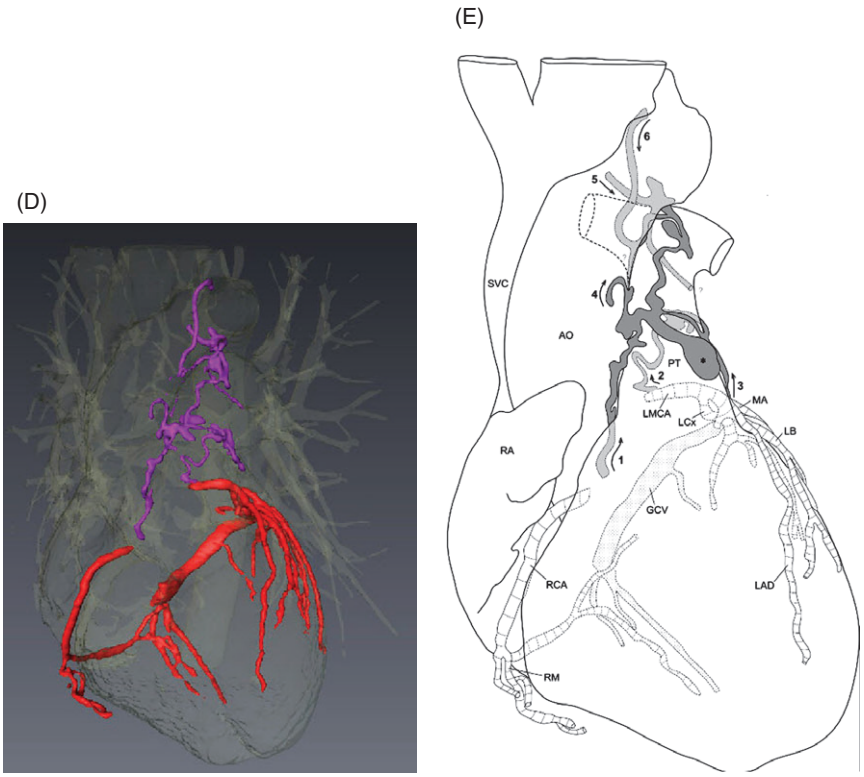


Figure 1. Continued

ascending thoracic aorta (n = 2) and aortic arch (n = 2). One hexalateral fistula (patient 1, Figure 1D,E) and bilateral fistulas were detected in 3 patients (patients 6, 7 and 11).

## Radionuclide Studies

***MPI:*** Exercise/rest MPI using technetium-99m-sestamibi was performed in 7 patients. Six patients were positive for myocardial ischemic changes.

***PET-CT:*** PET scanning demonstrated reversible ischemic changes (patient 1) during adenosine in the following areas: basal antero- and inferoseptal, mid antero- and inferoseptal, and distal septal segments. The global perfusion reserve (adenosine stress/rest ratio) was 1.79 (territories: LAD 1.11, RCA 1.40, and Cx 3.04). Blood flow through the Cx artery was 3-fold higher than the LAD artery. PET perfusion reserve was insufficient in the LAD region. PET-CT showed more ischemic changes than myocardial perfusion imaging (Figure 1B,C) and it revealed in patient 6 a global stress/rest ratio of 1.50 and an overall decreased perfusion reserve.

## Management

The applied treatment modalities were watchful waiting policy (2 patients), conservative medical management (CMM) (5 patients), percutaneous therapeutic embolization (PTE) (4 patients), and surgical ligation (SL) (3 patients). Residual fistula remained in an asymptomatic patient after PTE (patient 2, Figure 2B). SL was performed in 3 patients, accompanied by mitral valve plasty in 3 patients and in combination with CABG in 1 of the patients. CMM included β-blockers (6 patients), calcium channel blocker (2 patients), angiotensin-converting enzyme inhibitor (3 patients), statins (4 patients), aspirin (ASA) (4 patients), clopidogrel (3 patients), and oral vitamin K antagonists (4 patients).

## Discussion

Coronary-pulmonary fistulas are generally congenital in origin,[13] but acquired fistulas subsequent to penetrating[5] or nonpenetrating[6] chest traumas have been reported. Furthermore, although rare, they may be acquired late secondary to iatrogenic nonsurgical interventions such as PCI[2] and following endomyocardial biopsy[3] or after CABG.[4] Among our present case series, CPFs were found in 11 and solitary CCFs in 3 of the subjects, with the vast majority as unilateral (10/14, 71%) and multilateral (4/14, 29%) fistulas.

## Incidence

The incidence of CAFs encountering small and large fistulas accounts for 0.18%.[19] The true incidence of CAFs will vary among ethnic groups and geographic areas depending upon whether the reported series is based upon clinical, angiographic, echocardiographic studies, or autopsy series. The incidence in the echocardiographic series was 0.06 to 0.2%,[20,21] in the necropsy series 14%,[22] and in the angiographic series was 0.1% to 0.67%.[16,23–27]

As the true incidence is not known and prospective registration is lacking, we are planning to launch an international prospective registry to include patients with congenital or acquired CAFs in children and adults, aiming to establish a solid base for firm guidelines regarding current diagnostic capabilities, management, and treatment modalities.


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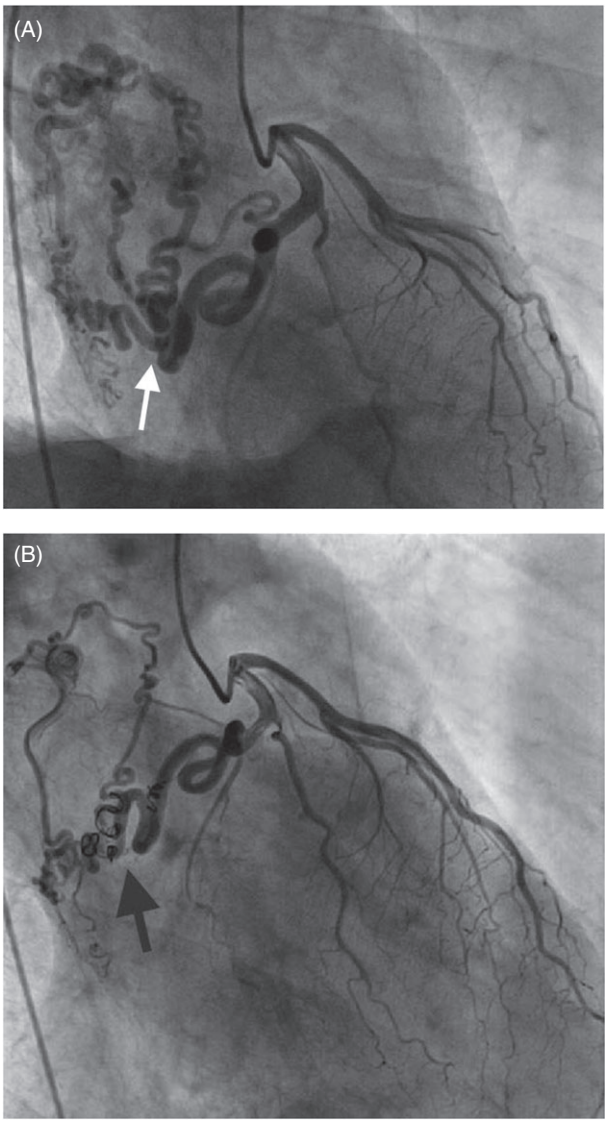


Figure 2. Patient 2: (A) Coronary angiographic frame of the left coronary artery showing the fistula from the circumflex coronary artery (Cx) ending in the left atrium (LA). The Cx turned into complete dilated fistulous channel (white arrow) turnicating the LA. (B) Residual fistula after coiling (black arrow) on repeat coronary angiography 7 months later.

## Etiology

The overwhelming majority of CPFs are congenital[13] in origin, as was the case in our current series, but acquired fistulas subsequent to penetrating[5,28] or nonpenetrating[6] chest traumas have been reported. Furthermore, acquired CPFs have been reported as a late complication after stenting of the left main trunk with a paclitaxel-eluting stent[2] and secondary to CABG occurring between the left internal mammary artery graft and the PA, which give rise to the recurrence of angina and occurrence of a novel cardiac murmur.[4,29] Recently, optical coherence tomography revealed the cause of an acquired fistula as a spontaneous rupture of a subadventitial hematoma of the RCA communicating with the lumen of the right cardiac chambers.[30]

## Embryology

Due to the reported high multiplicity rate of CPFs,[31,32] it may be postulated that CPFs are considered to have a different embryological background basis than other types of coronary fistulas. It has been noted that bilateral fistulas frequently[33] terminate into the PA (56%), compared to unilateral fistulas, which drain into the PA (17%)[31]; this might strengthen the theory that they are remnants of Vieussens' vascular circle. The circle of Vieussens is a ring between the pulmonary conal branch of the RCA and a branch of the LAD that supplies infundibular muscular tissue. Few hypotheses have been launched. In the mid 1950s, Hackensellner postulated an "involution-persistence theory," hypothesizing that there are 6 sprouts or anlages in the truncus arteriosus, of which 2 in the aortic sinuses persist in developing the coronary buds, whereas the other 4 disappear. According to this theory, the normally involuted sprouts or anlages from the pulmonary sinus may persist and communicate with the aortic sinus, resulting in unilateral or multilateral CPFs.[34] In the 1970s, it was postulated that CPFs were associated with the presence of an accessory coronary artery from the pulmonary artery.[35] In contrast, other coronary fistulas may embryologically occur due to persistence of intertrabecular spaces and fetal sinusoids, which normally obliterate to form the adult coronary capillary network.[36,37] In the current case series, approximately one-third of the patients had multilateral fistulas terminating into the PA.

## Classification

According to Angelini, CAFs are classified as anomalies of termination.[16] Congenital CAFs may be classified into 2 main categories: CVFs and CCFs, which are subdivided into solitary CCFs and coronary-ventricular MMFs.[17,18] CPFs are classified as CVFs among the variety of the CVFs that terminate into a thoracic vascular structure (eg, PA, CS, caval veins, PV, and bronchial and mediastinal vessels), in contrast with the CCFs, which communicate with 1 or more cardiac chambers (eg, RA, LA, RV, LV).[36,38]

## Diagnostic Modalities (Anatomical and Functional)

Generally, fistulas are readily detected by several noninvasive and invasive diagnostic imaging methods. Multimodality diagnostic approach is usually applied.[39] MDCT is a noninvasive imaging technique that has been successfully utilized for visualization of unilateral and multilateral fistulas[40,41] and for the diagnosis of coronary artery anomalies.[42] MDCT has been useful not only in detection but also in follow-up after surgical treatment of CPFs.[43] MDCT is considered the diagnostic procedure of choice in patients with coronary artery anomalies in whom conventional CAG may result in misinterpretation or the course and termination site of the unilateral or multilateral fistulas cannot be indentified.[44] MDCT demonstrates a complex coronary-pulmonary artery fistula via an aneurysmal Vieussens' arterial ring.[45] MDCT is the imaging method of choice for the delineation of multilateral fistulas. Multilateral fistulas were confirmed by MDCT in 3 patients of our case series, and 4 more fistulas were added arising from the thoracic aorta that were invisible on the CAG.


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***FFR:*** Although a continuous steal phenomenon in fistulas has been debated,[46] FFR is a promising diagnostic technique that has recently been reported to successfully depict the coronary steal phenomenon. In CVFs, (eg, CPFs) even in the presence of normal pulmonary artery pressure and small magnitude left-to-right shunt, MI can still develop without stenotic CAD.[15] Accurate functional assessment of CPFs using FFR measurement under maximal hyperemia of the distal segment of the nutrient coronary artery during temporary balloon occlusion of the fistulous vessel demonstrated the steal phenomenon. FFR increased from 0.78 to 0.95[15] when subsequently treated with PTE. On the other hand, Hollenbeck and Salloum reported a case of anterior wall ischemia, proven by MPI to be caused by a moderate LAD stenosis, and bilateral CPFs where FFR improvement occurred following stenting of the LAD lesion alone.[47] On the contrary, in CCFs (solitary CCFs or coronary artery-ventricular MMFs), FFR revealed normal hemodynamic parameters ruling out ischemia or a steal phenomenon.[48]

***Steal Phenomenon:*** Small as they are, CPFs can steal saturated blood away from the myocardium causing hypoperfusion and reduction of blood flow distally in the nutrient coronary artery. As was the case in 1 of our patients, it has been rarely reported that CPFs cause an ipsilateral MI in the absence of obstructive CAD due to the coronary steal phenomenon[15] or association with thrombotic CAD.[49]

***Singularity and Multiplicity:*** Postmortum reports of dual,[49,50] triple,[10] and quadruple,[11,51] CPFs have been published. The MDCT angiogram of 1 of our current patients (patient 1) demonstrated hexalateral fistulas (2 CPFs and 4 systemic-pulmonary) (Figure 1A,D,E). To the best of our knowledge, this female patient is the first ever antemortem reported with hexalateral fistulas having 6 donor vessels from the left coronary artery (2), ascending thoracic aorta (2), and aortic arch (2), all terminating into the PA. Postmortem, Takechi et al reported in a cadaveric heart of a 83-old Japanese male, who died of ascending colon cancer, pentalateral (4 CPFs and 1 systemic-pulmonary) fistulas.[52]

***Associated Anomalies:*** CPFs may be associated with systemic-pulmonary fistulas,[53] as was the case in the first patient of our case series. Fistulas, which are an anomaly of termination, may coexist with a coronary artery anomaly of distribution originating from the opposite sinus of Valsalva.[54] None of our patients had an anomaly of distribution. Infective endocarditis with vegetation of both mitral valve leaflets associated with CCF (RCA-LV) has recently been described.[55] CCFs are prone to the development of infective endocarditis,[56] contrasting with CVFs, which are more susceptible to the occurrence of ipsilateral MI.[15]

## Management

During the past decades, endovascular PTE techniques including coils and covered stent placement were introduced as alternatives to surgical ligation.[57] According to the recent American Heart Association/American College of Cardiology guidelines, a class I recommendation was indicated for transcatheter occlusion of symptomatic fistulas, whereas a class IIa recommendation was assigned

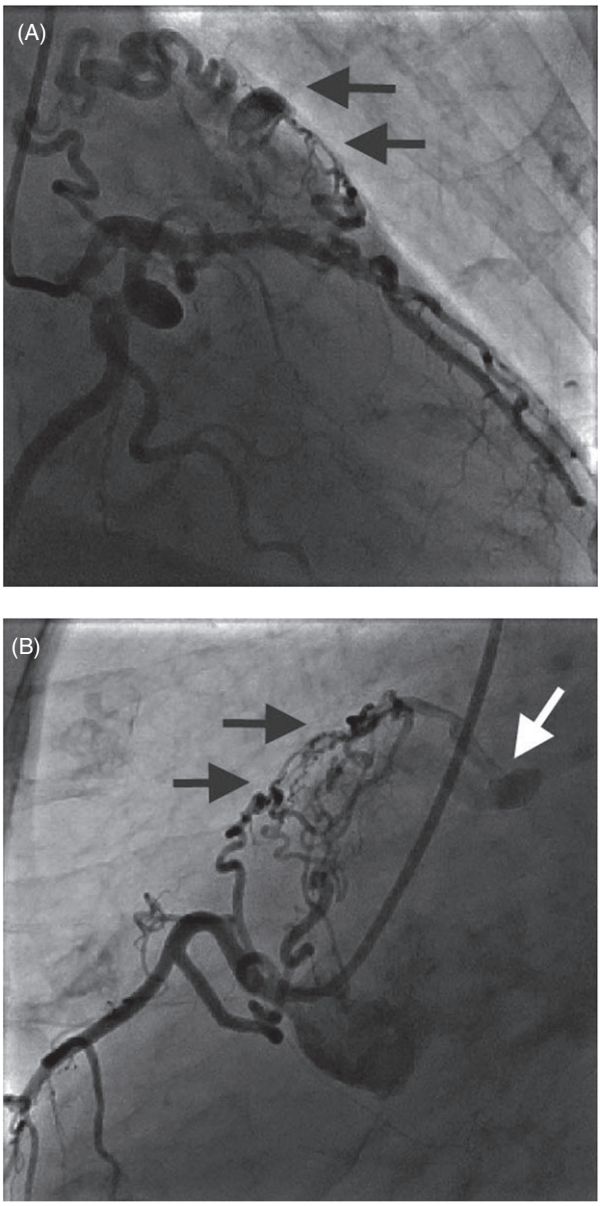


Figure 3. Patient 6: Coronary angiographic frame of the left (A) and right (B) coronary arteries in bilateral fistulas forming a crown-like figure (black arrows). The left anterior descending coronary artery-pulmonary artery fistula shows multiple origin, pathway, and outflow. The right coronary artery-pulmonary artery fistula has a single termination (white arrow).

for the transcatheter occlusion of moderate or large fistulas without clinical manifestations.[58] A review of the international literature in 2006 revealed that PTE was performed in only 5% of the patients,[59] but the rate had greatly increased to 22% by 2011.[38] Nowadays, PTE is the commonly used method and has been shown to be a safe and effective technique for the management of fistulas.[57] Furthermore, the presence of multiple origins (bilateral or multilateral fistulas)[9,60] or concomitant congenital or acquired cardiac disorders[14] requiring surgical correction advocate surgical intervention. In our series, 3 patients underwent surgical ligation of the


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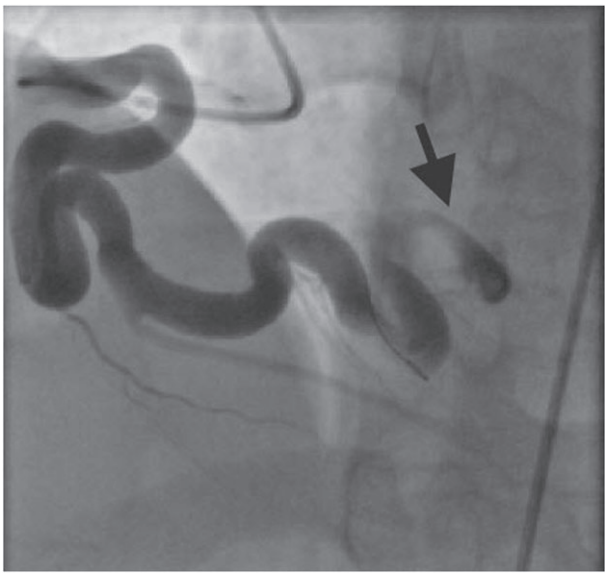

Figure 4. Patient 14: Coronary angiographic frame of the right coronary artery (RCA) demonstrating a severely dilated and tortuous RCA with slow flow and hypoperfusion of the distal segments (arrow). The fistula has a single origin, pathway, and outflow.

fistulous vessel performed in combination with CABG in 1 patient and combined with mitral valve repair in 2 of the patients. Generally, patients with multilateral fistulas are not suitable for PTE.

Percutaneous transfemoral[61] and transradial[62] approaches for embolization of a fistula have been reported. In our patients, PTE via the transfemoral approach was performed in 4 patients; in 1 of those, failure of PTE occurred due to fistulous vessel tortuosity and lack of guiding catheter support.

## Future Development and Use of Radiofrequency Energy

Recent developments have demonstrated that radiofrequency (RF) ablation may be applied for the ablation of CPFs. In animal experimental studies, it has been shown that percutaneous transluminal RF ablation closure of coronary arteries can be achieved in dogs. The application of RF energy was transcoronary, resulting in complete closure of the target vessels.[63] The first application of RF catheter ablation in humans was performed by Dietze et al in 2013.[64] They reported the successful RF ablation of a CPF via a transpulmonary approach after the failure of percutaneous closure with a duct occluder.[64] Furthermore, video-guided thoracoscopic clipping of a CPF case has been reported.[65]

## Conclusion

The clinical presentation of CPFs is highly variable. Morphologically, CPFs may be manifested as a unilateral or multilateral connections between the coronary artery, ascending aorta, descending aorta, and aortic arch with the pulmonary artery. CAG remains the gold standard imaging modality for detecting CPFs, especially when the morphological anatomy of the fistula is suitable for PTE. For functional assessment and further anatomical delineation, PET-CT and MDCT are of great diagnostic value, respectively. Multilateral CPF patients may be treated with conservative medical management, especially when they are not suitable for PTE or surgical intervention.


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