

Invasive Physiologic Study Across Various Spectrum of Coronary Artery Fistulas with Concomitant Coronary Artery Stenosis

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Abstract

Background: Most CAFs are asymptomatic but it might have serious hemodynamic consequences causing signs and symptoms of myocardial ischemia and heart failure prompting intervention, be it percutaneous or surgical, to manage the hemodynamic burden.

Case Illustration and Discussion: We presented 5 patients with CAFs undergoing FFR/iFR in our institution. Of all patients, only one showed significant iFR suggesting significant hemodynamic burden, probably due to a stealing phenomenon. Number of fistulas varied from 1 – 3 with most fistula arose from left anterior descending and terminated in pulmonary artery. Only one patient underwent RHC showing relatively normal flow ratio supported by normal iFR reading across different coronary artery segments. One patient presented with patent stents in LAD and OM2 despite existing subtotal occlusion in proximal PDA, the other one presented with insignificant stenosis in RCA, and the other two presented with no concomitant stenosis. We underwent no further intervention for 4 patients with normal FFR/iFR reading but we underwent stent implantation for one patient with significant FFR/iFR reading.

Conclusion: Whenever possible, further diagnostic work up should always be performed as an objective parameter of CAFs' hemodynamic burden. FFR/iFR might be considered as one of many modalities to do so.

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Keywords: *coronary artery fistula; coronary artery stenosis; free fractional reserve (FFR); instantaneous wave free ratio (iFR).*

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Introduction

Coronary artery fistulas (CAFs) are abnormal communications between coronary arteries and venous system where these abnormal conduits result in capillaries bypass within the myocardium. It represents around 0.002% of the population and it was first introduced by Krause in 1865. Most CAFs are asymptomatic but it might have serious hemodynamic consequences causing signs and symptoms of myocardial ischemia and heart failure prompting intervention, be it percutaneous or surgical, to manage the hemodynamic burden.^{1,2}

Currently, there's no widely accepted guidelines or consensus to manage patients with CAFs. The decision to undergo intervention is usually based on the presence of symptoms, size and also the anatomic features of the fistula. Here, we present the potential role of fractional flow reserve (FFR)/instantaneous-wave free ratio (iFR) that can be used to assess the physiological effect of CAFs as it is often incidentally diagnosed from invasive coronary angiography procedure hoping this modality might help in guiding management of CAFs.^{3,4}

Case Illustration

We presented 5 patients with CAFs undergoing FFR/iFR in our institution. Of all patients, only one showed significant iFR suggesting significant hemodynamic burden, probably due to stealing phenomenon. Number of fistulas varied from 1 – 3 with most fistula arose from left anterior descending and terminated in pulmonary artery. Only one patient underwent RHC showing relatively normal flow ratio supported by normal iFR reading across different coronary artery segments. One patient presented with patent stents in LAD and OM2 despite existing subtotal occlusion in proximal PDA, the other one presented with insignificant stenosis in RCA, and the other two presented with no concomitant stenosis. We underwent no further intervention for 4 patients with normal FFR/iFR reading but we underwent stent implantation for one patient with significant FFR/iFR reading. Details of each patients' case can be seen in Table 1.

Discussion

As previously stated, CAFs are rare coronary artery anomaly representing around 0.002% of population even though its incidence might increase up to 0.13 – 0.18% from invasive coronary angiography. There hasn't been any established guidelines or consensus regarding management of CAFs. Therefore, the decision to undergo intervention is usually based on the presence of symptoms, size and also the anatomic features of the fistula. Al-Hijji, et al stated CAFs can be classified as small, medium or large according to its size. CAFs are categorized small, medium, or large if the size is < 1, 1 – 2 and > 2 times the size of the largest coronary artery diameter that doesn't feed the CAFs, respectively. Most small CAFs will close spontaneously but medium and large CAFs may require intervention if it is accompanied by evidence of ischemia in the feeder artery territory, arrhythmia due to CAFs, endarteritis, vessel rupture, cardiac chamber enlargement, and ventricular dysfunction. Intervention can also be considered if there's high pulmonary-to-systemic flow ($Q_p:Q_s > 1,5:1$) and aneurysmal degeneration.⁶ Furthermore, Yun, et al also mentioned some other indications to undergo intervention by dividing the type of intervention as showed in Table 2.⁷

Signs and symptoms in patient with fistula might appear due to stealing phenomenon of CAFs where blood tends to flow from its origin in certain coronary artery segments to fistula that usually has lower resistance. The resistance of fistula is determined by the size, tortuosity and length of the fistula. The lower the resistance of the termination area, the more likely blood will be drawn away from normal coronary circulation followed by signs and symptoms of myocardial ischemia, myocardial infarction, congestive heart failure or even sudden death.⁸

The use of FFR/iFR to decide the need to undergo intervention in patients with CAFs hasn't been done in a well-designed study but its use has been reported in several case reports. Petit, et al underwent FFR in fistula originating from LAD to MPA (with no concomitant coronary artery stenosis) with baseline FFR reading of 0.88. Intravenous adenosine infusion was given 140 mcg/kg/min subsequently then pressure gradient decreased to 0.84 so it was decided no intervention was needed. Upon follow up, the patient hadn't had any or

Table 1. Characteristics of fistula from each case.

Characteristics	Patient A	Patient B	Patient C	Patient C	Patient D
Number of fistulas	One	Three	Two	One	One
Origin	Left anterior descending	Left anterior descending Left circumflex Right coronary artery	Left main Left anterior descending	Left anterior descending	Left main
Termination area	Left atrium	Pulmonary artery	Pulmonary artery	Pulmonary artery	Pulmonary artery
Qp:Qs	No available data	No available data	0.9	No available data	No available data
PVR/SVR	No available data	No available data	0.095	No available data	No available data
PARi	No available data	No available data	0.916	No available data	No available data
Concomitant stenosis	Absent	20-30% in proximal RCA	Absent	RCA: moderate stenosis in mid, subtotal stenosis in proximal PDA Prior history of DES implantation in LAD in 2014 and OM2 in 2015 (both stents are currently patent) Prior history of LAD-PA fistula coiling (2014)	LAD: 40 – 50% stenosis in proximal, 70% stenosis in mid LCx: 50 – 60% stenosis in proximal RCA: 90% stenosis in mid
iFR reading	iFR LAD: 0.97	iFR LAD: 0.95 iFR LCx: 1.0 iFR RCA: 1.07	iFR LAD: 0.96 iFR LCx: 1.0 iFR RCA: 1.0	Proximal LAD: 0.99 (located between LAD-PA coil and LAD stent) Distal LAD: 0.88	iFR LAD: 0.81 iFR LCx: 1.0
Intervention	Optimal medical therapy	Optimal medical therapy	Optimal medical therapy	Optimal medical therapy	DES implantation in mid RCA and mid LAD
Long-term outcome	No upcoming episodes of chest pain	No upcoming episodes of chest pain	No upcoming episodes of chest pain	No upcoming episodes of chest pain	No upcoming episodes of chest pain

been hospitalized due to episodes of chest pain.¹¹ This case is similar to our first and third patients suggesting the potential role of FFR/iFR to guide decision-making in patients with CAFs with no concomitant stenosis.

FFR/iFR can also be used in management of fistulas with concomitant stenosis as reported by Yew, et al. He reported an incidental finding of CAFs from LCx and LM that drained to PA with concomitant moderate

Table 2. Indications for surgical ligation and percutaneous transcatheter closure.

Surgical Ligation
Large symptomatic fistula with high fistula blood flow
Multiple communications and drainage sites
Tortuous and aneurysmal fistulous arteries
Need for simultaneous distal bypass
Large vascular branches that can be accidentally embolized
Percutaneous transcatheter closure
Proximal fistula origin
Single drain site
Non-tortuous vessel with distal portion of fistula accessible with the closure device
Extra-anatomic termination of fistula away from normal coronary arteries
Older patients with high risk of perioperative complications
Absence of concomitant cardiac disorders

stenosis (50-60%) in mid LAD. The FFR value of LAD prior and after intracoronary 200 mcg glyceryl trinitrate (GTN) and 300 mcg of adenosine was 0.96 and 0.91, respectively. Meanwhile, the FFR value of LCx after intracoronary administration of adenosine was 0.98. Despite the presence of moderate stenosis, no further intervention was undertaken.⁹ This case is similar to our second patient who presented with CAFs and insignificant stenosis of 20 – 30% where we also found insignificant iFR reading so we decided no further intervention was needed.

Another case of using FFR/iFR to guide decision-making for patients with CAFs and concomitant moderate stenosis was reported by Hollenbeck, et al. He reported a case of 65-year-old male with CAFs originating from proximal LAD and conus branch of RCA accompanied by moderate stenosis of mid LAD. He previously underwent SPECT procedure showing anterior wall ischemia that matched LAD region. FFR was evaluated in mid LAD showing significant FFR reading of 0.79 so a 3.0 x 23 mm drug-eluting stent (DES) and a 4.0 x 8 mm DES were implanted in mid and proximal LAD, respectively. FFR was evaluated afterwards showing FFR reading of 0.87 suggesting relief of ischemia.¹⁰ Our last patient presented with typical chest pain where we decided to undergo invasive coronary angiography examination showing moderate stenosis of 50 – 60% in proximal LAD and proximal LCx, 70% of stenosis in proximal LAD and 90% of stenosis in mid RCA. We underwent iFR in mid LAD

and LCx where we found significant reading of 0.81 in mid LAD. His case was brought to surgical conference deciding to undergo stent implantation in LAD and RCA. A 3.0 x 28 mm DES and a 3.0 x 33 mm DES were implanted successfully in mid RCA and mid LAD, respectively. Unfortunately, we didn't evaluate iFR afterwards as previously done by Hollenbeck, et al but we underwent regular follow up and found out he is currently able to engage in daily activities with no significant complaint of chest pain.

An intriguing issue in patient with CAFs and concomitant stenosis is to decide which one to intervene prior to another and whether it's possible to intervene both at the same time. The presence of CAFs with concomitant significant stenosis remains dilemmatic considering that both coronary artery stenosis and CAFs may cause ischemia with similar signs and symptoms. Previous reports haven't elaborated much regarding this but Hollenbeck, et al proposed one should first consider whether the CAFs is amenable to transcatheter occlusion. If it is amenable to transcatheter occlusion, CAFs embolization can be considered as the first approach. Yet, if the patient is a suitable candidate for revascularization, Hollenbeck, et al suggested PCI first as a reasonable approach to alleviate symptoms.¹⁰ In contrast with Hollenbeck, et al, Yew, et al suggested to undergo PCI first regardless the presence of CAFs and if FFR/iFR reading is still significant, one could consider embolizing the CAFs.⁹

FFR/iFR has also been used to guide decision-making in acute infarction as previously reported by Frampton, et al. She reported a case of 73-year-old man with ST-elevation with myocardial infarction (STEMI) with coexisting CAFs. From invasive angiography examination, a 95% stenosis in distal LAD with TIMI-2 flow, a dominant RCA with 90% distal stenosis and a prominent CAFs between LAD and right PA. Considering the emergent situation of STEMI, patient's age and his frailty, a minimally invasive strategy was chosen and the patient proceeded percutaneous coronary intervention (PCI) of LAD and RCA. A 2.25 x 16 mm drug-eluting stent (DES) was implanted to LAD and a 4.0 x 20 mm DES was implanted to distal RCA with TIMI 2 flow. Hemodynamic assessment of the LAD was performed afterward showing iFR of 0.88 and potential coronary steal physiology. This was confirmed by RHC showing Qp:Qs of 1.5 and significant step up at the level

of right PA. Further intervention was deferred and it was planned to optimize medical therapies. Two months after his index procedure, the patient complained of persistent angina despite maximally tolerated medical therapy. Therefore, embolization of the aneurysm sac and the feeding arteries were pursued. Angiographic evaluation after embolization of the fistula showed TIMI 3 flow and no residual communication between LAD and right PA. This was confirmed by iFR and RHC showing normal iFR and Qp:Qs reading of 0.98 and 0.99, respectively. The patient was discharged home afterward on dual antiplatelet therapy and returned for regular outpatient visit with complete resolution of angina.⁶

The rationale of utilizing FFR/iFR to decide the need to undergo intervention is the antegrade flow to both distal vessel and fistula. As more blood flows to the fistula, probably due to its lower resistance, less blood flows to distal vessels resulting in lower reading of iFR and vice versa. In addition, as more proximal the origin of the fistula, the more myocardium is at risk for ischemia. In contrast, if only insignificant amount of blood flows to the fistula, blood flowing to distal vessels will still be adequate to provide perfusion to distal myocardium that consequently result in higher reading of iFR.

The use of FFR/iFR isn't only useful to guide decision-making in CAFs with no existing coronary stenosis, it is also useful in CAFs with concomitant stenosis, be it insignificant or not. Despite the promising features and favorable outcome of patients whose treatments were guided using this modality, further well-designed studies are still needed to confirm the role of FFR/iFR to intervene the presence of CAFs with or without coronary artery stenosis. In the meantime, when it's possible to undergo this procedure, one may consider the use FFR/iFR to pursue a stepwise strategy of intervening CAFs with or without coronary artery stenosis.

Conclusion

Due to limited literature covering the issue of CAFs and coronary artery stenosis, the decision which to intervene first between these two is currently still in the discretion of the attending physician. Whenever possible, further diagnostic work up should always be

performed as an objective parameter of hemodynamic burden. FFR/iFR might be considered as one of many modalities to do so. Yet, further well-designed studies are needed to confirm the role of FFR/iFR hoping this modality might someday help in guiding decision-making in patients with CAFs.

List of Abbreviations

CAFs	Coronary Artery Fistulas
FFR	Fractional Flow Reserve
iFR	Instantaneous-Wave Free Ratio
LAD	Left anterior Descending
PCI	Percutaneous Coronary Intervention
RCA	Right Coronary Artery

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