

STATE-OF-THE-ART REVIEW

Management of Coronary Artery Aneurysms



Akram Kawsara, MD,^a Iván J. Núñez Gil, MD,^b Fahad Alqahtani, MD,^a Jason Moreland, MD,^a Charanjit S. Rihal, MD,^c Mohamad Alkhouli, MD^{a,c}

ABSTRACT

Aneurysmal dilation of coronary arteries is observed in up to 5% of patients undergoing coronary angiography. Due to their poorly elucidated underlying mechanisms, their variable presentations, and the lack of largescale outcome data on their various treatment modalities, coronary artery aneurysms and coronary ectasia pose a challenge to the managing clinician. This paper aims to provide a succinct review of aneurysmal coronary disease, with a special emphasis on the challenges associated with its interventional treatment. (J Am Coll Cardiol Intv 2018;11:1211–23) © 2018 by the American College of Cardiology Foundation.

Aneurysmal dilation of coronary arteries is found in up to 5% of patients undergoing coronary angiography (1). The presence of coronary aneurysm or ectasia has been associated with poor long-term outcomes irrespective of the presence of concomitant atherosclerotic coronary artery disease (2–4). Clinical presentations range from incidental finding on cardiac imaging to acute coronary syndrome (5). Treatment options include medical management, surgical excision, coronary bypass grafting (CABG), and percutaneous coronary interventions (PCI). However, due to the lack of randomized trials or societal recommendations, the management of these patients poses a clinical dilemma to the clinician. The aim of this paper is to provide a concise overview of the pathophysiology, classification, clinical presentation, assessment, and management strategies of aneurysmal coronary disease.

DEFINITIONS AND CLASSIFICATIONS

Bougon first described abnormal dilation of coronary arteries in 1812 (6). In 1953, Trinidad et al. (7) published the 49th case of “aneurysm of the coronary artery” in the published reports. Since then,

many publications have brought forth a deeper understanding of this entity. Interestingly, until recently, 2 terms have been used interchangeably to indicate the presence of aneurysmal dilation of coronary vessels: coronary artery aneurysm (CAA) and coronary artery ectasia (CAE) (8). This has often led to incertitude, as these synonymously used terms actually refer to 2 different phenotypes. Therefore, arbitrary criteria have been suggested to differentiate between these 2. By these criteria, a focal dilation of coronary segments of at least 1.5 times the adjacent normal segment is described as CAA, whereas the term CAE is used to define similar, but more diffuse, lesions (9,10). CAAs are then divided to saccular aneurysms if the transverse diameter exceeds the longitudinal diameter, and to fusiform aneurysms in the opposite case. Subclassification of CAA and CAE based on morphological or intravascular imaging factors has also been suggested (Table 1, Figure 1) (11,12).

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

The reported incidence of coronary aneurysms ranges from 0.3% to 5%, with predilection to men more than

From the ^aDivision of Cardiology, Department of Medicine, West Virginia University, Morgantown, West Virginia; ^bCardiovascular Institute, Hospital Clínico Universitario San Carlos, Madrid, Spain; and the ^cDepartment of Cardiology, Mayo Clinic, Rochester, Minnesota. Dr. Moreland has been a new products consultant for and receives reimbursement for related travel expenses from ABIOMED. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received September 11, 2017; revised manuscript received January 7, 2018, accepted February 20, 2018.

ABBREVIATIONS AND ACRONYMS

CAA = coronary artery aneurysm

CABG = coronary artery bypass grafting

CAE = coronary artery ectasia

IVUS = intravascular ultrasound

MACE = major cardiovascular adverse event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

SVGA = saphenous vein graft aneurysm

to women, and to proximal than to distal segments of the coronary bed (13). This wide range is likely due to the various reporting methods, with higher incidences found in studies including both CAE and CAA together versus those reporting CAA alone (14-20). In contemporary studies, the incidence of true CAA is <1% (17-20). The right coronary artery is usually the most affected artery (40%) followed by the left anterior descending (32%), and the left main being the least affected artery (3.5%) (21). Interestingly, saccular aneurysms were found to be more common in the left anterior descending coronary artery than in other coronary arteries (22,23). Atherosclerotic and vasculitic CAAs

usually affect more than 1 artery, whereas congenital and iatrogenic CAAs are typically confined to a single vessel.

The pathogenesis of CAA is not well understood. However, there is compelling evidence of particular associations between certain risk factors and CAAs:

1. An individual genetic susceptibility to the formation of CAA, especially in patients with congenital CAA has been suggested (24).
2. The strong association between CAA and coronary artery disease implies a possible common underlying etiology (25,26).
3. There is a high prevalence of noncoronary aneurysmal disease in patients with CAA and vice versa, suggesting another mechanism distinct from atherosclerosis that causes generalized arterial dilation (27,28).
4. Certain vasculitic and connective tissue diseases have a proven interrelation with CAA (e.g., Kawasaki disease, Marfan, and so on) (29).
5. Local wall injury following intracoronary manipulation (angioplasty, stenting, brachytherapy, and so on) has been shown to provoke the formation of CAA. However, notable differences seem to exist between these interventions, with CAAs being more frequently reported following brachytherapy due to the late effect of adaptive remodeling, and drug-eluting stent implantation due to the impaired intimal healing effects of the antiproliferative agents (20,30-32). Notably, there have been fewer published reports of CAA formation following second- and third-generation stent implantation (33,34). Whether this represents a reporting bias versus a true improvement with newer stents remains unknown. There has been, nevertheless, a concerning number of reports of CAA following PCI with biodegradable stents (35-38).

6. Post-infectious CAAs have been reported and are believed to be the result of direct wall invasion or immune complex deposition (39).

A summary of the existing published reports on the possible risk factors of CAA is provided in Table 2.

An uncommon, but an important, subset of aneurysms to allude to is the category of aortocoronary saphenous vein graft aneurysms (SVGAs). These aneurysms have distinctive characteristics compared with native coronary aneurysms: 1) they often present very late following bypass grafting. In a systematic review of 168 cases, 68.5% presented >10 years after CABG; 2) they are significantly larger than CAAs; 3) they usually progress over time; and 4) not uncommonly, they present with mechanical complications (e.g., compression of adjacent cardiac or venous structures, or rupture) (40).

CLINICAL PRESENTATION AND ASSESSMENT

Most CAAs are clinically silent and are only detected incidentally during coronary angiography or computed tomography. However, clinical symptoms can develop due to one of the following reasons: 1) the presence of concomitant obstructive atherosclerotic disease can result in both effort angina or acute coronary syndrome; 2) local thrombosis in the lumen of large aneurysms may lead to distal embolization and myocardial infarction (MI) (41,42) (Figure 1); 3) massive enlargement of some CAAs and SVGAs can result in compression of adjacent structures (40,43); 4) aneurysm rupture, albeit rare, can cause acute cardiac tamponade (40,42); and 5) stress-induced myocardial ischemia due to microvascular dysfunction has been documented even in the absence of significant coronary stenosis (44).

Coronary angiography remains the most common used imaging modality to assess ectatic or aneurysmal coronary arteries. However, delayed antegrade contrast filling, segmental back flow, and contrast stasis in the dilated coronary segment often hamper optimal imaging during angiography (13). A forceful and prolonged injection may be necessary to avoid misinterpreting slow aneurysmal filling as in situ thrombosis, especially in giant aneurysms. In these cases, intravascular ultrasound (IVUS) can be extremely helpful; it provides better delineation of vessel wall structures and helps to distinguish between true aneurysm, pseudoaneurysm, and segments with aneurysmal appearance due to plaque rupture or adjacent stenosis. IVUS can also accurately size the CAA and/or any adjacent stenoses and allows proper stent sizing if PCI is planned. However,

caution should be exercised when IVUS assessment is performed post-stenting to avoid dislodgment of the stent. The use of optical coherence tomography in assessing CAA is limited by the small scan diameter of the infrared light (45). Coronary computed tomography is gaining popularity in the assessment of these patients, because it allows more accurate evaluation of the aneurysm size and degree of thrombus and calcification than invasive angiography (Figure 2) (46). Computed tomography is particularly helpful in patients with giant CAA and those with SVGA, because it avoids the pitfalls of luminal angiography and provides a precise assessment of mechanical complications of these aneurysms (40).

Coronary aneurysms, especially the giant ones, were thought to act hemodynamically in a manner similar to that of a stenosis due to the turbulence of flow and energy loss as blood passes through the aneurysm. However, this hypothesis was refuted in studies using coronary and functional flow reserve techniques (47,48). In these studies, CAAs without a concomitant stenosis corresponded with normal coronary and functional flow reserve values and preserved regional myocardial function during stress.

MANAGEMENT STRATEGIES

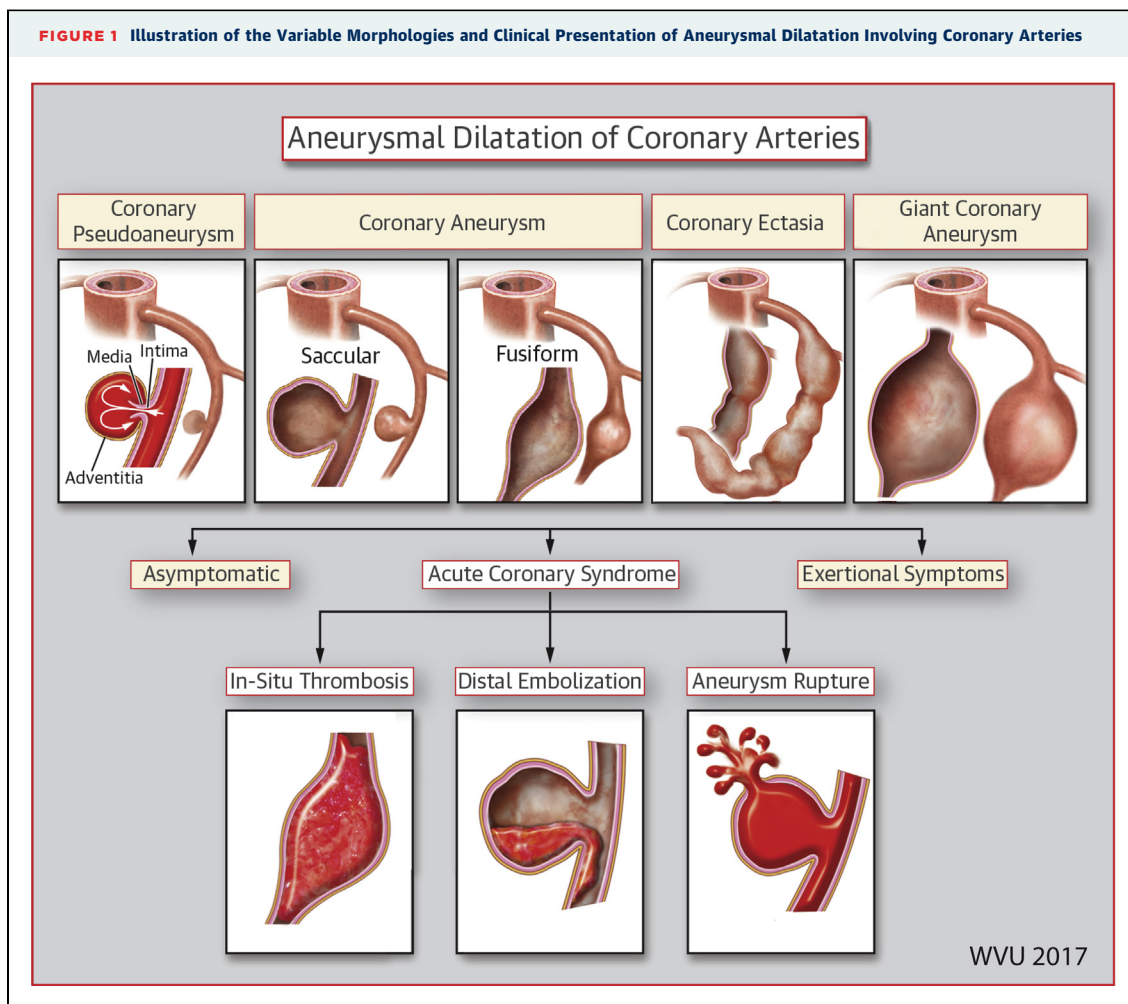
Management of patients with CAA presents significant challenges for several reasons: The natural history of coronary aneurysms is largely unknown. Hence, the optimal treatment of incidentally found CAA or coronary ectasia in the absence of a concomitant coronary stenosis or occlusion is uncertain. Also, for patients presenting with angina or acute MI of an aneurysmal culprit, in whom an intervention is warranted, both percutaneous and surgical revascularization are associated with technical challenges. Furthermore, in both symptomatic and asymptomatic CAA patients, we are faced with a substantial knowledge gap due to the lack of randomized trials or large-scale data. Most of the current recommendations are based on small case series, or anecdotal evidence. Acknowledging these limitations, treatment strategies should be individualized based on the location and morphology of the CAA, the patient's characteristics, and the clinical presentation.

MEDICAL MANAGEMENT. Atherosclerosis is implicated in the pathogenesis of a large proportion of CAA especially in older patients; therefore, the importance of aggressive risk factor modification in these patients cannot be overemphasized.

The role of dual antiplatelets or therapeutic anticoagulation in the management of patients with CAA

TABLE 1 Classifications of Aneurysmal Dilatation of Coronary Artery Disease	
Definition	Types and Classifications
Coronary artery aneurysm	
Focal dilation of at least 1.5 times the adjacent normal segment	Morphology: Saccular aneurysm: transverse > longitudinal diameter Fusiform aneurysm: transverse < longitudinal diameter Vessel wall structure by IVUS: True aneurysm: preserved vessel wall integrity with 3 layers (intima, media, and adventitia) Pseudoaneurysm: loss of vessel wall integrity and damage to the adventitia Complex plaque with aneurysmal appearance: stenoses with ruptured plaques or spontaneous or unhealed dissections Normal segment with aneurysmal appearance: normal segment adjacent to stenosis Diameter: Giant aneurysm: diameter >20 mm
Coronary artery ectasia	
Diffuse dilation of at least 1.5 times the adjacent normal segment	Type I: diffuse ectasia of 2 or 3 vessels Type II: diffuse disease in 1 vessel and localized disease in another vessel Type III: diffuse ectasia in 1 vessel Type IV: localized or segmental ectasia
IVUS = intravascular ultrasound.	

or CAE, especially those that are incidentally discovered, is an area of ongoing debate. Unfortunately, there is no high-quality evidence to support or contradict the use of an escalated antiplatelet or antithrombotic regimen in these patients. Previous retrospective studies have shown similar event rates in patients with and without CAE, suggesting that anticoagulation might not be necessary (15,49,50). However, other studies revealed contradictory results (2-4). Baman et al. (2) showed that the presence of CAA was associated with higher 5-year mortality in patients undergoing coronary angiography (all-comers) compared with those without CAA (adjusted hazard ratio: 1.56; 95% confidence interval: 1.01 to 2.41). In another study, patients who underwent coronary computed tomography for risk assessment before noncardiac surgery and were found to have incidental CAAs had a high rate of major cardiovascular adverse events (MACE) (54%) at 49-month follow-up (3). A recent study suggested a possible advantage of anticoagulation in patients with CAE and acute coronary syndrome (4). In this study, CAE was associated with 3.25-, 2.71-, and 4.92-fold greater likelihoods of MACE, cardiac death, and nonfatal myocardial infarction, respectively, at 49-month follow-up. Nonetheless, CAE patients who were treated with oral anticoagulation and achieved a

FIGURE 1 Illustration of the Variable Morphologies and Clinical Presentation of Aneurysmal Dilatation Involving Coronary Arteries

time-in-therapeutic range >60%, had 0% occurrence of MACE, compared with 33% in patients not on therapeutic anticoagulation ($p = 0.03$).

There is also limited evidence that anticoagulation may reduce thrombotic events in patients with Kawasaki disease. Therefore, the current guidelines recommend anticoagulation only in selected Kawasaki patients with large or rapidly expanding CAA (29).

Some authors suggest a potential role for angiotensin-converting enzyme in preventing or slowing the progression of CAA. However, this has not been proved in long-term studies (51). Of note, vasodilators such as nitrates have been shown to exacerbate myocardial ischemia in patients with an isolated large CAA or CAE, and therefore their avoidance is recommended (44). The use of intravenous immunoglobulin in patients with Kawasaki disease can result in higher rates of CAA regression and lower incidences of MACE (29,52).

It should be noted that all of the aforementioned studies have important limitations due to their retrospective nature, small sample size, and potential biases.

PERCUTANEOUS INTERVENTIONS. Outcome data on PCIs in patients with CAA or CAE are sparse (Table 3). However, important insights can be drawn from the existing limited published reports:

1. The majority of published studies assessed PCI outcomes in symptomatic patients presenting with acute MI (17-19,53,54). Outcomes of PCI in asymptomatic patients with CAA or CAE are limited to small case series (20,55).
2. PCI of an aneurysmal/ectatic culprit vessel in the setting of acute MI is associated with lower procedural success and a higher incidence of no-reflow and distal embolization (19,53,54).
3. Patients who survive STEMI after a PCI of an aneurysmal/ectatic vessel have higher mortality

TABLE 2 Common Underlying Pathologies in Patients With CAA

Etiology (Ref. #)	Pathogenic Mechanism	Examples
Genetic susceptibility (24)	Specific HLA class II genotypes, such as HLA-DR B1*13, DR16, DQ2, and DQ5, are more detectable in patients with CAA	Idiopathic CAA
Overexpression of certain enzymes (e.g., angiotensin-converting enzyme) (51)	Enhanced inflammatory response Induces proteolysis of extracellular matrix proteins	Atherosclerotic CAA
Autoimmune/inflammatory process (29)	Increased plasma level of intercellular adhesion molecule-1, vascular cell adhesion molecule-1, and E-selectin Imbalances in protein levels of matrix metalloproteinase and its tissue inhibitor	Systemic vasculitis (Kawasaki, Takayasu) Lupus Marfan syndrome
Dynamic wall stress changes (24)	Episodic hypertension and vasoconstriction ± endothelial damage	Cocaine use
Direct vessel wall injury (20,30–38)	Mechanical and shear wall stress Non-healing dissections, and so on	Iatrogenic CAA (post-balloon angioplasty, stenting, atherectomy) Post-stenotic CAA
Infectious (24,39)	Direct invasion of pathogens into the vessel wall Immune complex deposition	Bacterial, mycobacterial, fungal, syphilitic, Lyme, septic emboli, and mycotic aneurysm

CAA = coronary artery aneurysm; HLA = human leukocyte antigen.

and higher rates of definite stent thrombosis, target vessel revascularization, and MI during intermediate-term follow-up (17,18,20,53).

Therefore, the following discussion regarding the indications and techniques of PCI in these patients should be viewed as a general guide, in light of the limited available evidence:

In patients with acute coronary syndrome due to a CAA culprit, the emphasis is to restore flow. Due to the higher associated thrombus burden, PCI in ectatic

and aneurysmal arteries is frequently aided with thrombectomy (aspiration or mechanical), and glycoprotein IIb/IIIa inhibitors (Figure 3, Online Videos 1, 2, and 3). Despite these efforts, the occurrence of no-reflow or distal embolization is quite frequent (19,53,54). The decision to intervene on CAA in patients without acute coronary syndrome is rather complex, due to the lack of supportive data. Nevertheless, when an intervention is considered due to certain high-risk clinical or anatomic features, the treatment modality differs according to the shape and

FIGURE 2 Coronary Computed Tomography Assessment of Coronary Aneurysms



(A and B) Volume-rendered 3-dimensional and oblique sagittal imaging of a proximal left anterior descending coronary artery aneurysm (arrow), showing a large intramural thrombus (asterisk). (C) Volume-rendered 3-dimensional image of a proximal right coronary artery saccular aneurysm (arrow). Reprinted with permission from Diaz-Zamudio et al. (10).

TABLE 3 Summary of the Studies on Outcomes of PCIs in Patients With Aneurysmal Coronary Disease

First Author (Ref. #) Year	N	Diagnosis	Symptoms	Primary Outcomes	Results
Joo et al. (20) 2017	78	CAA	40% angina 60% ACS	MACE compared with 269 controls after PCI at 16.1 ± 14.6 months f/u	CAA group had higher MACE (26.9% vs. 2.2%; $p < 0.01$), driven by nonfatal MI and TVR
Bogana Shanmugam et al. (53) 2017	25	CAE	STEMI	In-hospital outcomes MACE compared with 80 controls after PCI at 36.6 ± 14.1 months f/u	CAA group had less angiographic success (24% vs. 77%; $p < 0.01$), and higher MACE at f/u (44.0% vs. 16.3%; $p = 0.01$), driven by nonfatal MI, TVR, and sudden death
Iannopollo et al. (18) 2017	32	CAA	STEMI	30-day and 1-yr MACE compared 2,280 controls after PCI	No difference in mortality, more ST in CAA group at 30 days (12.7% vs. 1.5%; $p < 0.01$) and 1 yr (15.5% vs. 2.2%; $p < 0.01$)
Szalat et al. (71) 2005	24	CAA	NR	Short-term MACE post-covered stents	At 4 months, 19 patients had f/u, of whom 4 had restenosis
Ipek et al. (19) 2016	99	CAA	STEMI	In-hospital and 1-yr MACE compared with 1,556 controls	Higher no-reflow rate in CAE patient, but no difference in in-hospital or 1-yr mortality, TVR, or ST
Campanile et al. (72) 2014	101	CAE	STEMI NSTEMI	In-hospital and 2-yr MACE	Procedural success 70.3%, MACE was 6.9%, 17.8%, and 38.5% at 30-day, 1-yr, and 2-yr f/u; 8.9% had ST
Yip et al. (54) 2002	24	CAA	STEMI	In-hospital outcomes, and survival at 19 ± 30 months f/u	No-flow 62%, cardiogenic shock 25%, in-hospital death 8.3%; survival at f/u was 90.9%
Briguori et al. (55) 2002	7	CAA	71% angina 29% none	In-hospital outcomes, and MACE at 35 ± 8 months f/u	Angiographic success 100% 1 (14%) MACE event (TVR)
Nunez-Gil et al. (17) 2017	256	CAA	82% NSTEMI 12% STEMI	MACE compared with 500 controls at 52 months median f/u	Higher odds of mortality (HR: 3.1; 95% CI: 1.8-5.6; $p < 0.01$) and MACE (HR: 2.3; 95% CI: 1.4-3.8; $p < 0.01$) with CAA

ACS = acute coronary syndrome(s); CAA = coronary artery aneurysm; CAE = coronary artery ectasia; CI = confidence interval; f/u = follow-up; HR = hazard ratio; MACE = major adverse cardiovascular event(s); MI = myocardial infarction; PCI = percutaneous coronary intervention; ST = stent thrombosis; STEMI = ST-segment elevation myocardial infarction; TVR = target vessel revascularization.

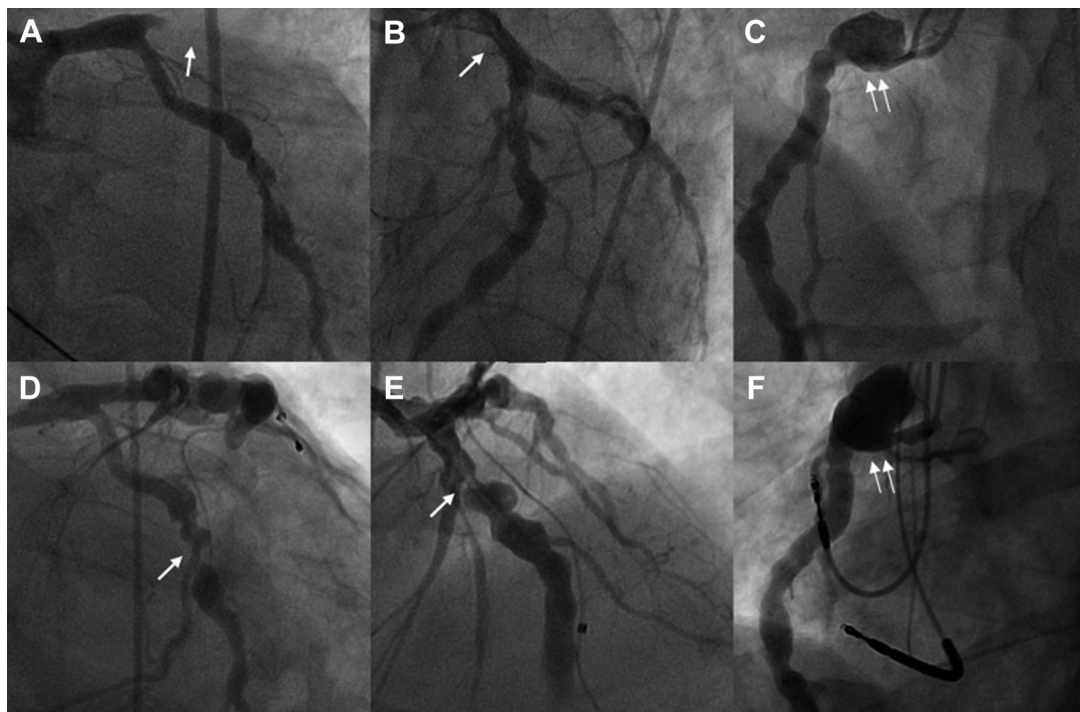
the extent of the aneurysm: 1) saccular aneurysms and small pseudoaneurysms not involving a major side branch can be treated with covered stent exclusion (**Figure 4**, **Online Videos 4** and **5**); 2) saccular or fusiform aneurysms that involve a major side branch can be treated with balloon or stent-assisted coil embolization, or with surgical exclusion (**Figure 5**, **Online Video 6**); 3) for CAA involving the left main coronary artery, multiple or giant (>20 mm, or >4× reference vessel diameter) CAAs, and for SVGAs, surgical resection is considered the first-line therapy; and 4) in patients with large or rapidly expanding SVGAs or in those causing symptomatic external compression, percutaneous closure with Amplatzer occluders or coil embolization with or without PCI of the native grafted vessel is a feasible alternative to surgery (40). A suggested algorithm for the treatment of CAA is outlined in **Figure 6**.

Percutaneous treatment of CAA brings, however, certain practical challenges:

1. Purpose-specific devices: There are no covered stents that are specifically designed for the treatment of CAAs. Nevertheless, several stent graft systems have been used off-label to exclude CAA.
2. Thrombus burden: In the setting of acute coronary syndrome, PCI of an aneurysmal culprit artery is associated with higher rates of adverse

For diameters between 2.75 and 5 mm, the GRAFTMASTER coronary stent graft (Abbott Vascular, Santa Clara, California) is most commonly used. The GRAFTMASTER stent is constructed using a sandwich technique, whereby an ultra-thin layer of expandable polytetrafluoroethylene is placed between 2 GRAFTMASTER stents, which are then pre-mounted on a balloon catheter delivery system. The new PK Papyrus covered stent (Biotronik, Berlin, Germany) achieves greater bending flexibility and a smaller crossing profile compared with the GRAFTMASTER stent, due to its advanced covered single stent design. However, it is currently not available for commercial use in the United States. If a larger diameter stent is needed (5 to 10 mm), the Atrium iCAST balloon expandable covered stent (MAQUET, Wayne, New Jersey), has been successfully used to treat CAA (56). A summary of covered stents suitable for the treatment of CAA is provided in **Table 4**.

FIGURE 3 Cine Angiography Illustrating Initial and Follow-Up Findings in a Patient With Diffuse Ectasia and a Fusiform Aneurysm Presented With Anterior Wall STEMI



(A) Initial angiogram showing a stumped ostial LAD (arrow). (B) Initial angiogram following proximal LAD stenting (arrow). (C) Initial angiogram showing proximal RCA fusiform aneurysm (double arrows). (D to F) Follow-up angiogram 4 years later showing patent proximal LAD stent but worsening mid-LAD and circumflex stenoses (arrow) and enlarging proximal RCA fusiform aneurysm (double arrows). See Online Videos 1, 2, and 3. LAD = left anterior descending coronary artery; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction.

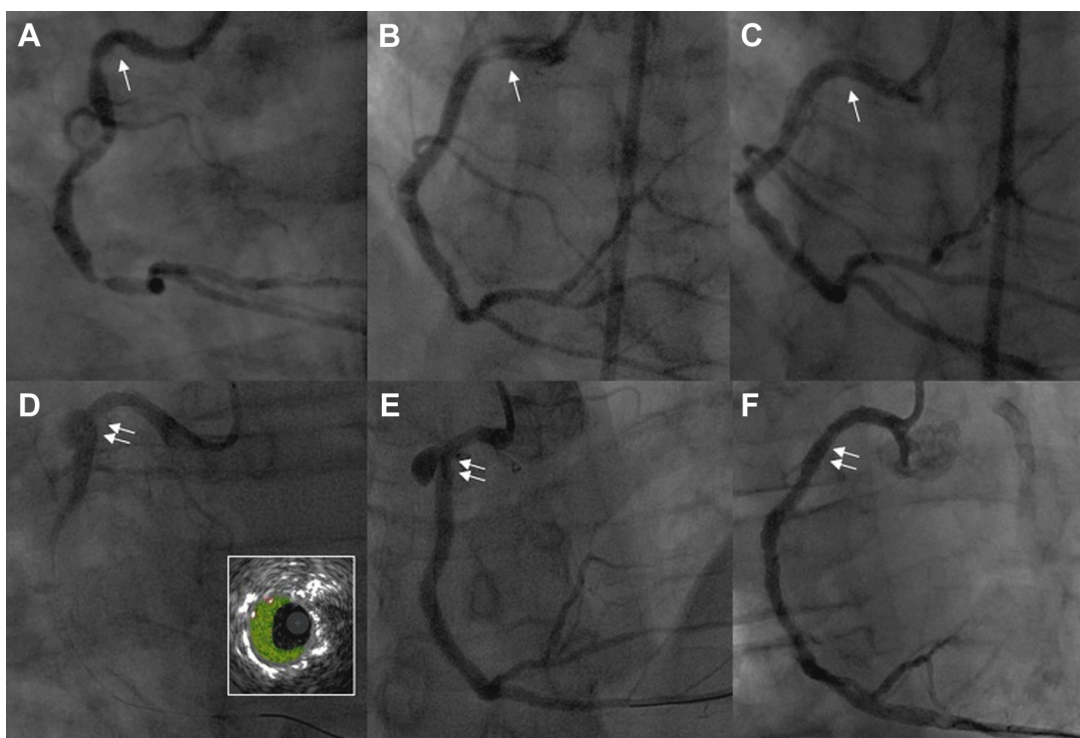
event and higher failure rates than non-aneurysmal culprit arteries, mainly due to the presence of a substantial thrombus burden (19,53,54). Although there is limited specific data on the use of rheolytic thrombectomy to treat aneurysmal or ectatic infarct related vessels, the AngioJet device (Boston Scientific, Marlborough, Massachusetts) demonstrated effectiveness in 2 randomized trials by decreasing embolization in patients who underwent PCI on venous grafts or native coronary vessel with massive thrombosis (57,58). A few case reports have also demonstrated its efficacy in patients with CAA (59,60).

3. Sizing and landing zone assessment: Proper sizing of the CAA is key to reducing the risk of stent thrombosis and stent migration (61). However, partially thrombosed CAA can result in underestimation of the true size of the aneurysm. Also, the full extension of the CAA is often difficult to delineate, rendering accurate assessment of the

stent's landing zone difficult. In long aneurysmal segments, several overlapping stents are often needed to cover the full length of the aneurysm (62,63).

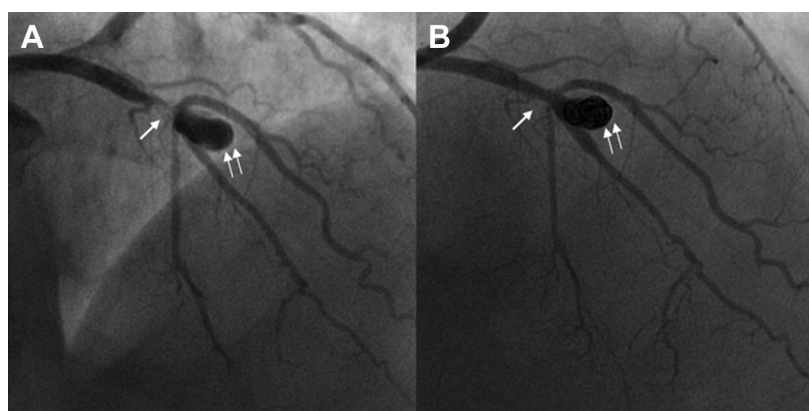
4. Challenges of covered stent delivery: covered stents are stiff and are delivered via large coronary guiding catheters or introducer sheaths, which increases the risk of procedural complications (stent migration, dissection, perforation, and so on), especially in tortuous vessels. They also limit access to side branches and may incompletely cover the aneurysm, leaving a persistent leak into the aneurysm sac. In such cases where covered stent placement is not possible due to severe tortuosity, calcification, or fear of side branch compromise, the stent-assisted coil embolization technique, a commonly used technique in the treatment of cerebral aneurysms, can be used. With this technique, a microcatheter is usually placed in the aneurysm before stenting. A regular

FIGURE 4 Cine Angiography Illustrating Initial and Follow-Up Findings in a Patient Without Baseline CAA Who Developed a Coronary Pseudoaneurysm Following PCI



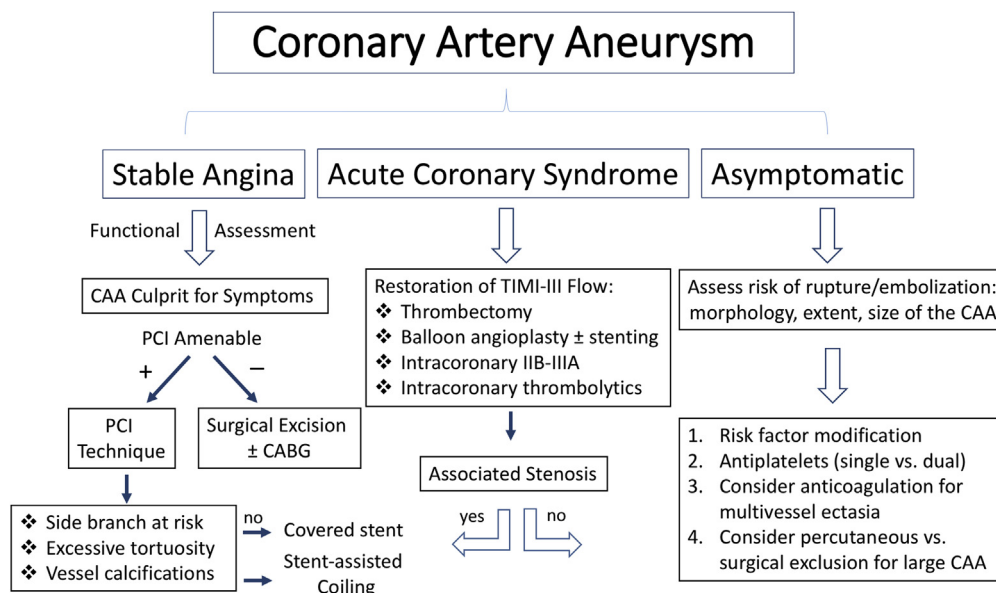
(A) Severe stenosis in the distal RCA. Note the deep-seated Amplatz guiding catheter in the proximal RCA (arrow). (B) Guide-induced proximal RCA dissection noted after stenting the distal RCA (arrow). (C) Successful treatment of the dissection with drug-eluting stents (arrow). (D) Angiogram 8 years later showing an occluded mid RCA (culprit for inferior wall STEMI) and a possible pseudoaneurysm of the proximal RCA (site of prior stenting) (double arrows correspond to IVUS image in the inset). (E) Successful treatment of the RCA STEMI with drug-eluting stents. (F) Successful exclusion of the coronary pseudoaneurysm with a GRAFTMASTER covered stent (double arrows). See Online Videos 4 and 5. CAA = coronary artery aneurysm; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention; other abbreviations as in Figure 3.

FIGURE 5 Cine Angiography Illustrating a Moderate Size Saccular Aneurysm in the Mid-LAD Treated With a Modified Stent-Assisted Coil Embolization



(A) Mid-LAD aneurysm at initial presentation; (B) mid-LAD aneurysm after coiling and drug-eluting stent placement. The single arrows shows the LAD stenosis before and after stenting. Double arrows show the coils. LAD = left anterior descending coronary artery.

FIGURE 6 A Suggested Algorithm for Management of Patients With CAA



See Online Video 6. CABG = coronary artery bypass grafting; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Figure 4.

coronary stent is then deployed in the aneurysmal segment at low pressure, and coils can then be passed through the microcatheter to wrap around the stent. Post-dilation of stent is then performed. Additional coils can be advanced via the stent struts if needed, but this can be difficult and is not usually necessary (53,64,65). Another modification of this technique is presented in Figure 7.

Experience with PCI of aneurysmal arteries in patients with Kawasaki disease is limited to small series in pediatric patients and young adults (29,66,67). These data do, however, highlight several intriguing findings: 1) the walls of a stenotic aneurysmal artery in Kawasaki patients may be lined with

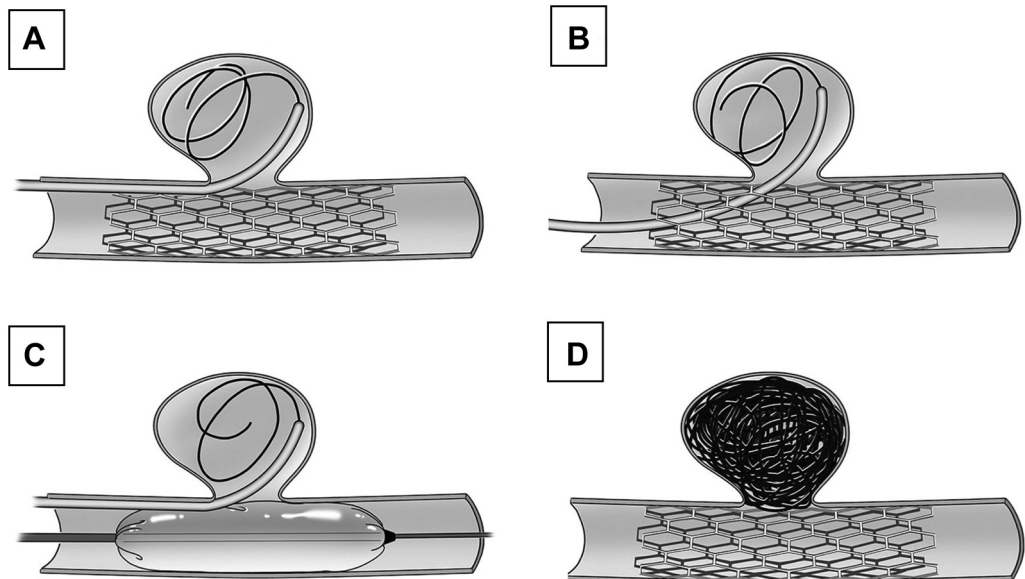
considerable thrombus, and therefore IVUS is often necessary to assess the true diameter of the vessel; 2) repeat intervention is common among Kawasaki patients following PCI; and 3) long-term outcomes might be superior with CABG as compared with PCI. Current American Heart Association guidelines recommend restricting PCI in Kawasaki patients to those with a single-vessel or focal multivessel disease (29).

SURGICAL INTERVENTIONS. The ideal surgical approach has not yet been formally studied. Operative therapy for CAA may include aneurysm ligation, resection, or marsupialization with interposition graft (68). The most common surgical practice is, however,

TABLE 4 Summary of Covered Stents Suitable for Treatment of CAAs

Stent System	Graftmaster	PK Papyrus	Direct-Stent	BeGraft	Aneugraft	Icast Atrium
Manufacturer	Abbott	Biotronik	InSite Tech	Bentley	ITGI Medical	Atrium Medical
Stent Design	Stainless steel, double layers	Cobalt chromium, single layer	Stainless steel, double layers	Cobalt chromium, single layer	Stainless steel, single layer	Stainless steel, double layers
Required Guiding Catheter	6–7 F	5–6 F	6–7 F	5 F	6 F	8–9 F
Diameter Range	2.8–4.8 mm	2.5–5.0 mm	2.25–6.0 mm	2.5–5.0 mm	2.5–4.0 mm	5–10 mm
Length Range	16–26 mm	15–26 mm	2.25–6.0 mm	2.5–5.0 mm	2.5–4.0 mm	16–59 mm
Availability in U.S.	Available	Not Available	Not Available	Not Available	Not Available	Available

CAA = coronary artery aneurysm.

FIGURE 7 Illustration of the Stent-Assisted Coiling Technique

(A) A microcatheter is advanced into the aneurysm, jailed by a noncovered stent, followed by coil delivery via the microcatheter. A final post-dilation of the stent is often performed. **(B)** Coils are delivered through the stent struts after initial stent deployment. **(C)** A microcatheter is advanced into the aneurysm, jailed by a coronary balloon, followed by coil delivery via the microcatheter. A noncovered stent deployment usually follows. **(D)** Final result of stent-assisted coil embolization. Reprinted with permission from Spiotta AM, Wheeler AM, Smithason S, Hui F, Moskowitz S. Comparison of techniques for stent assisted coil embolization of aneurysms. *J Neurointerv Surg* 2012;4:339-44.

to open the CAA, suture its afferent and efferent vessels, and finish with bypass grafting if necessary (69). The precise success rate of these techniques is not known due to the rarity of this surgery and the impact of reporting bias.

UNMET NEEDS AND FUTURE PERSPECTIVES

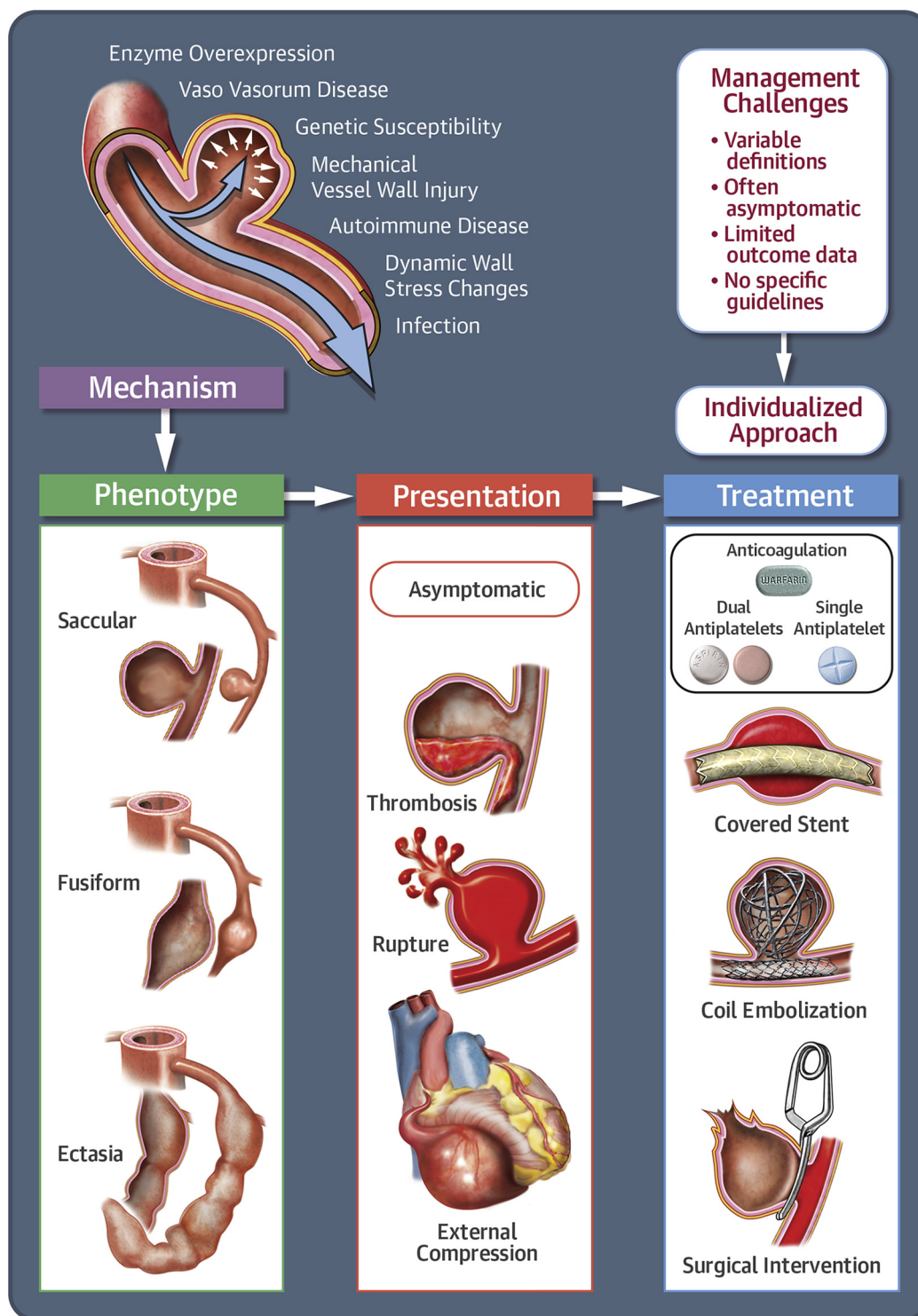
Controversies regarding the optimal approach to CAA and CAE persist, and there is an unmet need for additional investigations in this area (Central Illustration). Important questions to be addressed in future research in the field include the following. 1) What is the underlying etiology of CAA and CAE? Are these two completely separate entities, or different phenotypes of the same disease? 2) Do these abnormalities confer a higher risk of adverse events in asymptomatic patients? 3) Is there a role for long-term dual antiplatelets or anticoagulation in the primary or secondary prevention of thrombotic complications? 4) Do incidentally discovered CAAs have to be intervened upon? 5) What is the ideal interventional method to treat CAAs (bare-metal vs. drug-eluting stents, covered stent grafts, stent-assisted

coiling, surgical exclusion, and so on)? 6) If an intervention is undertaken, what is the optimal intra- and post-procedural medication regimen?

To resolve these questions, collaborative studies with clear definitions of the disease phenotypes and clinical endpoints are needed. For example, a prospective study collecting genomic and inflammatory markers in patients with CAA and/or CAE and 2 other control groups (one with normal coronary arteries, and another with atherosclerosis) may help in discerning the underlying pathophysiology of the disease. Intracoronary imaging with IVUS ± optical coherence tomography in a subset of patients can provide important insights into the mechanisms of vessel wall injury and the different phenotypic manifestation of the disease.

Another study focused on the outcomes of patients with CAA and/or CEA stratified by clinical presentations (asymptomatic, stable angina, acute MI) and management types (medical management with or without anticoagulation, PCI, surgery) will help in clarifying some of the outstanding management issues. In this regard, the CAAR (Coronary Artery Aneurysm Registry) is a promising example of a

CENTRAL ILLUSTRATION Coronary Artery Aneurysms



Kawsara, A. et al. J Am Coll Cardiol Interv. 2018;11(13):1211-23.

An illustration of the mechanisms, phenotypes, clinical presentations, and treatment modalities of coronary artery.

multicenter registry that aims to assess the short- and long-term outcomes of the various management strategies of CAA (70).

CONCLUSIONS

Aneurysmal dilation of coronary vessels is not uncommon, and its management is challenging.

Knowledge of the issues pertaining to the natural history, assessment, and interventional treatment of this entity is essential to achieve optimal results.

ADDRESS FOR CORRESPONDENCE: Dr. Mohamad Alkhouli, West Virginia University Heart & Vascular Institute, 1 Medical Drive, Morgantown, West Virginia 26505. E-mail: Mohamad.Alkhouli@wvumedicine.org.

REFERENCES

1. Swaye PS, Fisher LD, Litwin P, et al. Aneurysmal coronary artery disease. *Circulation* 1983;67:134–8.
2. Baman TS, Cole JH, Devireddy CM, Sperling LS. Risk factors and outcomes in patients with coronary artery aneurysms. *Am J Cardiol* 2004;93:1549–51.
3. Warisawa T, Naganuma T, Tomizawa N, et al. High prevalence of coronary artery events and non-coronary events in patients with coronary artery aneurysm in the observational group. *Int J Cardiol Heart Vasc* 2016;10:29–31.
4. Doi T, Kataoka Y, Noguchi T, et al. Coronary artery ectasia predicts future cardiac events in patients with acute myocardial infarction. *Arterioscler Thromb Vasc Biol* 2017;37:2350–5.
5. Cohen P, O'Gara PT. Coronary artery aneurysms: a review of the natural history, pathophysiology, and management. *Cardiol Rev* 2008;16:301–4.
6. Jarcho S. Bougon on coronary aneurysm (1812). *Am J Cardiol* 1969;24:551–3.
7. Trinidad S, Grayzel DM, Rapoport P. Aneurysm of the coronary artery. *Ann Intern Med* 1953;39:1117–24.
8. Packard M, Wechsler H. Aneurysms of coronary arteries. *Arch Intern Med* 1929;43:1.
9. Luo Y, Tang J, Liu X, et al. Coronary artery aneurysm differs from coronary artery ectasia: angiographic characteristics and cardiovascular risk factor analysis in patients referred for coronary angiography. *Angiology* 2017;68:823–30.
10. Diaz-Zamudio M, Bacilio-Perez U, Herrera-Zarza MC, et al. Coronary artery aneurysms and ectasia: role of coronary CT angiography. *RadioGraphics* 2009;29:1939–54.
11. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary arterial ectasia. *Am J Cardiol* 1976;37:217–22.
12. Maehara A, Mintz GS, Ahmed JM, et al. An intravascular ultrasound classification of angiographic coronary artery aneurysms. *Am J Cardiol* 2001;88:365–70.
13. Manginas A, Cokkinos DV. Coronary artery ectasias: imaging, functional assessment and clinical implications. *Eur Heart J* 2006;27:1026–31.
14. Robertson T, Fisher L. Prognostic significance of coronary artery aneurysm and ectasia in the Coronary Artery Surgery Study (CASS) registry. *Prog Clin Biol Res* 1987;250:325–39.
15. Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients. *Br Heart J* 1985;54:392–5.
16. Alfonso F, Perez-Vizcayno MJ, Ruiz M, et al. Coronary aneurysms after drug-eluting stent implantation: clinical, angiographic, and intravascular ultrasound findings. *J Am Coll Cardiol* 2009;53:2053–60.
17. Nunez-Gil IJ, Terol B, Feltes G, et al. Coronary aneurysms in the acute patient: incidence, characterization and long-term management results. *Cardiovasc Revasc Med* 2017 Dec 6 [E-pub ahead of print].
18. Iannopollo G, Ferlini M, Kozinski M, et al. Patient outcomes with STEMI caused by aneurysmal coronary artery disease and treated with primary PCI. *J Am Coll Cardiol* 2017;69:3006–7.
19. Ipek G, Gungor B, Karatas MB, et al. Risk factors and outcomes in patients with ectatic infarct-related artery who underwent primary percutaneous coronary intervention after ST elevated myocardial infarction. *Catheter Cardiovasc Interv* 2016;88:748–53.
20. Joo HJ, Woong Yu C, Choi R, et al. Clinical outcomes of patients with coronary artery aneurysm after the first generation drug-eluting stent implantation. *Catheter Cardiovasc Interv* 2017 Nov 22 [E-pub ahead of print].
21. Syed M, Lesch M. Coronary artery aneurysm: a review. *Prog Cardiovasc Dis* 1997;40:77–84.
22. Harikrishnan S, Sunder KR, Tharakan JM, et al. Saccular coronary aneurysms: angiographic and clinical profile and follow-up of 22 cases. *Indian Heart J* 2000;52:178–82.
23. Tunick PA, Slater J, Kronzon I, Glassman E. Discrete atherosclerotic coronary artery aneurysms: a study of 20 patients. *J Am Coll Cardiol* 1990;15:279–82.
24. Abou Sherif S, Ozden Tok O, Taskoylu O, Goktekin O, Kilic ID. Coronary artery aneurysms: a review of the epidemiology, pathophysiology, diagnosis, and treatment. *Front Cardiovasc Med* 2017;5:4:24.
25. Demopoulos VP, Olympios CD, Fakiolas CN, et al. The natural history of aneurysmal coronary artery disease. *Heart* 1997;78:136–41.
26. Ovali C, Morrad B. Associations between coronary artery disease, aneurysm and ectasia. *Kardiochir Torakochirurgia Pol* 2017;14:158–63.
27. Balderston JR, Giri J, Kolansky DM, Bavaria JE, Gertz ZM. Coronary artery aneurysms associated with ascending aortic aneurysms and abdominal aortic aneurysms: pathophysiologic implications. *Catheter Cardiovasc Interv* 2015;85:961–7.
28. Meindl C, Achatz B, Huber D, et al. Coronary artery ectasia are frequently observed in patients with bicuspid aortic valves with and without dilatation of the ascending aorta. *Circ Cardiovasc Interv* 2016;9:e004092.
29. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation* 2017;135:e927–99.
30. Bavry AA, Chiu JH, Jefferson BK, et al. Development of coronary aneurysm after drug-eluting stent implantation. *Ann Intern Med* 2007;146:230–2.
31. Aoki J, Kirtane A, Leon MB, Dangas G. Coronary artery aneurysms after drug-eluting stent implantation. *J Am Coll Cardiol Interv* 2008;1:14–21.
32. Condado JA, Waksman R, Gurdziel O, et al. Long-term angiographic and clinical outcome after percutaneous transluminal coronary angioplasty and intracoronary radiation therapy in humans. *Circulation* 1997;96:727–32.
33. Kim U, Seol SH, Kim DI, et al. Clinical outcomes and the risk factors of coronary artery aneurysms that developed after drug-eluting stent implantation. *Circ J* 2011;75:861–7.
34. Gadepalli R, Rayidi G, Pramod G, Srivastava SK, Venkata Balakrishna SN. A case of early development of giant coronary artery aneurysms after drug-eluting stents implantation: an unpredictable menace. *Interv Med Appl Sci* 2017;9:47–50.
35. Timmers L, Lim YC, Tan HC, Low AF. Coronary aneurysm without malapposition after bioresorbable vascular scaffold implantation. *Euro-Intervention* 2016;12:60.
36. La Manna A, Mangiameli A, Capodanno D, Longo G, Sgroi C, Tamburino C. Managing bioabsorbable vascular scaffold failure: combined scaffold restenosis and late-acquired coronary aneurysm treated with self-expandable stent. *Can J Cardiol* 2015;31:691.e1–3.
37. Varghese S, Lauer B, Ohlow MA. Coronary artery aneurysm after everolimus-eluting bioabsorbable vascular scaffold implantation. *J Am Coll Cardiol Interv* 2016;9:e23–5.
38. Lee WC, Chung WJ, Fang HY, Wu CJ. Coronary artery aneurysms formation within everolimus-eluting stents and bioresorbable vascular scaffolds. *Int J Cardiol* 2016;206:58–60.

39. Singh H, Singh C, Aggarwal N, Dugal JS, Kumar A, Luthra M. Mycotic aneurysm of left anterior descending artery after sirolimus-eluting stent implantation: a case report. *Catheter Cardiovasc Interv* 2005;65:282–5.
40. Ramirez FD, Hibbert B, Simard T, et al. Natural history and management of aortocoronary saphenous vein graft aneurysms: a systematic review of published cases. *Circulation* 2012;126:2248–56.
41. Rath S, Har-Zahav Y, Battler A, et al. Fate of nonobstructive aneurysmatic coronary artery disease: angiographic and clinical follow-up report. *Am Heart J* 1985;109:785–91.
42. Chrissoheris MP, Donohue TJ, Young RS, Ghantous A. Coronary artery aneurysms. *Cardiol Rev* 2008;16:116–23.
43. Ebina T, Ishikawa Y, Uchida K, et al. A case of giant coronary artery aneurysm and literature review. *J Cardiol* 2009;53:293–300.
44. Kruger D, Stierle U, Herrmann G, Simon R, Sheikhzadeh A. Exercise-induced myocardial ischemia in isolated coronary artery ectasias and aneurysms (“dilated coronopathy”). *J Am Coll Cardiol* 1999;34:1461–70.
45. Fathelbab H, Camacho Freire SJ, Leon Jimenez J, et al. Detection of spontaneous coronary artery spasm with optical coherence tomography in a patient with acute coronary syndrome. *Cardiovasc Revasc Med* 2017;18:7–9.
46. Murthy PA, Mohammed TL, Read K, Gilkeson RC, White CS. MDCT of coronary artery aneurysms. *AJR Am J Roentgenol* 2005;184 Suppl:S19–20.
47. Murakami T, Tanaka N. The physiological significance of coronary aneurysms in Kawasaki disease. *EuroIntervention* 2011;7:944–7.
48. Hamaoka K, Onouchi Z, Kamiya Y, Sakata K. Evaluation of coronary flow velocity dynamics and flow reserve in patients with Kawasaki disease by means of a Doppler guide wire. *J Am Coll Cardiol* 1998;31:833–40.
49. Boles U, Zhao Y, Rakhit R, et al. Patterns of coronary artery ectasia and short-term outcome in acute myocardial infarction. *Scand Cardiovasc J* 2014;48:161–6.
50. Zhang Y, Huang QJ, Li XL, et al. Prognostic value of coronary artery stenoses, Markis class, and ectasia ratio in patients with coronary artery ectasia. *Cardiology* 2015;131:251–9.
51. Gulec S, Aras O, Atmaca Y, et al. Deletion polymorphism of the angiotensin I converting enzyme gene is a potent risk factor for coronary artery ectasia. *Heart* 2003;89:213–4.
52. Friedman KG, Gauvreau K, Hamaoka-Okamoto A, et al. Coronary artery aneurysms in Kawasaki disease: risk factors for progressive disease and adverse cardiac events in the US population. *J Am Heart Assoc* 2016;5:e003289.
53. Bogana Shanmugam V, Psaltis PJ, Wong DTL, Meredith IT, Malaipaan Y, Ahmar W. Outcomes after primary percutaneous coronary intervention for ST-elevation myocardial infarction caused by ectatic infarct related arteries. *Heart Lung Circ* 2017;26:1059–68.
54. Yip HK, Chen MC, Wu CJ, et al. Clinical features and outcome of coronary artery aneurysm in patients with acute myocardial infarction undergoing a primary percutaneous coronary intervention. *Cardiology* 2002;98:132–40.
55. Briguori C, Sarais C, Sivieri G, Takagi T, Di Mario C, Colombo A. Polytetrafluoroethylene-covered stent and coronary artery aneurysms. *Catheter Cardiovasc Interv* 2002;55:326–30.
56. Kim TH, Marfatia R, Lee J, Azrin M. Giant coronary aneurysm management with Viabahn covered stent. *Cardiovasc Revasc Med* 2017;18 Suppl 1:56–9.
57. Kuntz RE, Baim DS, Cohen DJ, et al. A trial comparing rheolytic thrombectomy with intracoronary urokinase for coronary and vein graft thrombus (the Vein Graft AngioJet Study [VeGAS 2]). *Am J Cardiol* 2002;89:326–30.
58. Antoniucci D, Valenti R, Migliorini A, et al. Comparison of rheolytic thrombectomy before direct infarct artery stenting versus direct stenting alone in patients undergoing percutaneous coronary intervention for acute myocardial infarction. *Am J Cardiol* 2004;93:1033–5.
59. Giombolini C, Notaristefano S, Santucci S, Notaristefano F, Notaristefano A, Ambrosio G. AngioJet thrombectomy for the treatment of coronary artery aneurysm after failed thrombolysis in acute myocardial infarction. *Heart Int* 2006;2:94.
60. Lee MS, Nero T, Makkar RR, Wilentz JR. Treatment of coronary aneurysm in acute myocardial infarction with AngioJet thrombectomy and JoStent coronary stent graft. *J Invasive Cardiol* 2004;16:294–6.
61. Kaneko U, Kashima Y, Hashimoto M, Fujita T. Very late stent migration within a giant coronary aneurysm in a patient with Kawasaki disease: assessment with multidetector computed tomography. *J Am Coll Cardiol Interv* 2017;10:1799–800.
62. Cereda AF, Tiberti G, Pera IG, et al. A giant coronary artery aneurysm treated using multiple overlapping covered stents. *J Am Coll Cardiol Interv* 2017;10:e127–8.
63. Jurado-Roman A, Lozano-Ruiz-Poveda F, Lopez-Lliva MT, Sanchez-Perez I. Reconstruction of right coronary artery with 2 giant aneurysms in series using 3 overlapped covered stents. *J Am Coll Cardiol Interv* 2017;10:1060–2.
64. Win HK, Polsani V, Chang SM, Kleiman NS. Stent-assisted coil embolization of a large fusiform aneurysm of proximal anterior descending artery: novel treatment for coronary aneurysms. *Circ Cardiovasc Interv* 2012;5:e3–5.
65. Piao ZH, Jeong MH, Jeong HC, et al. Coronary artery fistula with giant aneurysm and coronary stenosis treated by transcatheter embolization and stent. *Korean Circ J* 2015;45:245–7.
66. Suda K, Iemura M, Nishiono H, et al. Long-term prognosis of patients with Kawasaki disease complicated by giant coronary aneurysms: a single-institution experience. *Circulation* 2011;123:1836–42.
67. Bang JS, Kim GB, Kwon BS, et al. Long-term prognosis for patients with Kawasaki disease complicated by large coronary aneurysm (diameter ≥ 6 mm). *Korean Circ J* 2017;47:516–22.
68. Singh SK, Goyal T, Sethi R, et al. Surgical treatment for coronary artery aneurysm: a single-centre experience. *Interact Cardiovasc Thorac Surg* 2013;17:632–6.
69. Izumi K, Hisata Y, Hazam S. Surgical repair for a coronary-pulmonary artery fistula with a saccular aneurysm of the coronary artery. *Ann Thorac Cardiovasc Surg* 2009;15:194–7.
70. Nunez-Gil IJ, Nombela-Franco L, Bagur R, et al. Rationale and design of a multicenter, international and collaborative Coronary Artery Aneurysm Registry (CAAR). *Clin Cardiol* 2017;40:580–5.
71. Szalat A, Durst R, Cohen A, Lotan C. Use of polytetrafluoroethylene-covered stent for treatment of coronary artery aneurysm. *Catheter Cardiovasc Interv* 2005;66:203–8.
72. Campanile A, Sozzi FB, Consonni D, et al. Primary PCI for the treatment of ectatic infarct-related coronary artery. *Minerva Cardioangiol* 2014;62:327–33.

KEY WORDS coils, coronary artery aneurysm, coronary ectasia, covered stent, surgical resection

APPENDIX For supplemental videos, please see the online version of this paper.