

Review Article

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Management of coronary artery perforation: A 2024 appraisal

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Abstract

Advances and innovations in technology have led to interventionists embarking on percutaneous coronary intervention in patients with increasingly complex anatomy, such as left main disease, heavily calcified, multivessel disease, and chronic total occlusion. Consequently, the interventionist encounters an infrequent, yet potentially serious complication of coronary artery perforation (CAP). While the incidence of CAP is low, it can lead to severe consequences, such as cardiac tamponade, myocardial infarction, or even death. This review aims to provide an in-depth exploration of coronary perforation encompassing its epidemiology, pathophysiology, clinical presentation, contemporary therapeutic options, and future directions.

Keywords: Percutaneous coronary intervention; Perforation; Covered stent.

Introduction

Interventional cardiology remains a vigorous discipline with continued rapid evolution since its beginnings in the late 1970s. With the improvement of technology and interventional tools, interventionists have started embarking on percutaneous coronary intervention (PCI) in patients with increasingly complex anatomy, such as left main disease, heavily calcified, multivessel disease, and chronic total occlusion (CTO). Consequently, the interventionist is confronted with coronary artery perforation (CAP) which is a rare, yet potentially dreadful complication of PCI leading to severe consequences, such as cardiac tamponade, myocardial infarction, or even death. This review summarizes the available information about CAP and details the contemporary therapeutic options.

Incidence and risk factors

The complexity of coronary anatomy determines the incidence of CAP. In the modern era of PCI, its incidence is 0.43% but rises to 2.9% in CTO interventions [1]. This is more common with long-standing CTOs, the absence of a visible stump, presence of bridging collaterals, that resist conventional guide wires leading to the use of more aggressive PCI techniques [2]. PCI, if performed through one of the collaterals increases the risk considerably. Once tamponade occurs, even if pericardiocentesis is performed, the in-hospital mortality increases to more than 5% in the vent of tamponade. There exist several patient and procedural risk factors for CAP. Older age, previous coronary artery bypass graft anatomy, and female gender constitute patient-related factors. CAP is frequent in

females due to anatomic tortuosity, smaller arteries, and hormonal estrogen levels influencing coagulation factors and inflammatory parameters [1].

Complex coronary lesions (American College of Cardiology/American Heart Association-defined type B2 and C), heavily calcified lesions, angulated tortuous lesions, CTOs, and narrow coronary arteries constitute procedural risk factors (Table 1). Furthermore, the use of hydrophilic guidewires, oversized balloons or stents, excessive post-dilatation, atheroablative devices, and lack of intravascular imaging, have been associated with coronary perforation (Table 1) [3-6].

Classification, Diagnosis, and Outcome

CAP is classified by location (large vessel, distal vessel, and collateral perforations) and by severity (Ellis's classification) [7-9]. Large-vessel perforations are normally caused by oversized balloons and stents, particularly when the balloon: artery ratio is > 1.2:1, and aggressive balloon inflations, especially in highly calcified lesions that are not pre-emptively remodeled by atheroablation before stenting. Distal perforations typically occur due to wire migration. Hydrophilic-coated, polymer jacketed, and stiff-tip guidewires have been pin-pointed as a common culprit of distal perforations. Epicardial vessel collateral perforation typically occurs during the retrograde technique for CTO PCI. It was reported that CAP occurred in 15% of total retrograde cases [10-12].

Ellis-graded perforations fall into types, ranging from small endovascular leaks into the adventitia (type I) to frank extravasation into the pericardial space (type III) [8]. In type IV perforations, anatomical cavities, such as the coronary sinus and the right ventricle, may be involved (Table 2). Muller et al. introduced type V perforation: distal perforation associated with the use of hydrophilic and/or stiff wires [13]. Type I perforations are less dangerous than type III perforations, which may lead to cardiac tamponade and hemodynamic collapse, myocardial infarction (MI), and death [14]. According to a recent investigation, "cloud-like" and "floating" patterns of perforations, in addition to proximal arterial perforation, are linked to poor clinical

Table 1: Factors related to coronary artery perforation.

Anatomical factors	Procedural factors
Heavy calcification	Hydrophilic-coated, polymer jacketed, and stiff-tip guidewires
Severe tortuosity	Oversized balloons (>1:2 vessel diameter) and stents
Smaller diameter coronary artery	High-pressure balloon inflation
Chronic total occlusion	Atherectomy devices
Mismatched proximal and distal segment	

Table 2: Classification of coronary perforation [8, 13].

Type	Morphology
I	Focal extraluminal crater without extravasation
II	Pericardial or myocardial blush without an exit hole larger than 1 mm
III	Frank streaming of contrast through an exit hole larger than 1 mm
IV	Contrast spilling directly into anatomic cavity chamber such as coronary sinus and the right ventricle
V	Distal perforation related to the use of hydrophilic and/or stiff wire

Table 3: Prevention of coronary perforation [18].

Device	Methods to prevent perforation
Angioplasty balloon	Low balloon: artery ratio, avoid high-pressure pre-dilatation
Stent	Avoid high-pressure initial inflation and oversizing in heavy calcification post-dilate the stent
Stiff and hydrophilic guidewire	Careful distal navigation to avoid side branches Maintain tip mobility to avoid subintimal space
Rotational atherectomy	Burr: artery ratio <0.8 Avoid angulated segments

outcomes for perforations that occur during CTO PCI [15]. Type III "cavity spilling" perforations, however, are associated with less catastrophic consequences [16].

CAP should be suspected if there is a sudden onset of acute and sharp chest pain and/or hemodynamic instability during balloon inflation or stent deployment. CAP can result in pericardial hemorrhage and cardiac tamponade, fistulae to the left ventricle or the right ventricle, or coronary arteriovenous fistulae [17]. Type 3 perforations are recognized by visualization of contrast extravasation warranting immediate treatment. However, perforations manifesting as tamponade are usually confirmed by echocardiography or occasionally by recognition of tamponade physiology in the laboratory. Fluoroscopy may reveal immobile heart borders. Although most CAPs are diagnosed by coronary angiography during PCI, distal vessel perforations may go undetected initially if they are subtle, especially if the shutters are used. So, it is critical to get longer image acquisition and planning to the distal vessels when there is a suspicion of CAP. There may be delayed manifestation of tamponade 8-14 hours later. Echocardiography should also be performed emergently and serially up to 48 hours afterward to assess for pericardial effusion and/or cardiac tamponade. In the case of CTO PCI, collateral flow can result in persistent leaking from a distal vessel perforation and should be carefully assessed via retrograde angiography.

Prevention

A guidewire's tip should be softly advanced without pushing against resistance to prevent perforation. It ought to be able to move freely. Once in the distal segment, the

interventionist must refrain from inserting the tip into small branches. The deflated balloon should be left in place after inflation, and the ECG should be monitored to see if it reverses to baseline. The patient should be asked if there is relief of chest pain after balloon deflation. With a small contrast injection, if there is good distal flow without obvious extravasation of blood, the balloon should be pulled back in the guide to be re-inflated should perforation occur [18].

Treatment

The treatment of CAP is dictated by the perforation type, site, vessel size, and mechanism of perforation. Regardless of location or size, initial treatment involves measures to stop extravasation and support the patient hemodynamically whenever warranted. Urgent bedside echocardiography should be performed to assess pericardial effusion and tamponade. Cardiothoracic surgeons should be notified immediately in case percutaneous measures are not successful and emergency cardiac surgery may be required.

Prolonged balloon inflation

Achieving immediate hemostasis with low-pressure (2-6 atm, maximum 8 atm) prolonged (up to 10 minutes) balloon inflation (balloon: artery ratio 1:1) proximal or at the site of the perforation is the first step to reduce extravasation of blood in the pericardium and to reduce the risk of cardiac tamponade. A second guidewire and

microcatheter can be advanced alongside the balloon to allow definitive treatment of the perforation (block and deliver technique). It is recommended that the patient's condition be stabilized with intravenous fluids, vasopressors, and mechanical circulatory support in the event of hemodynamic deterioration [19]. The maximum tolerated time a coronary can be occluded without causing significant myocardial damage is approximately 20 minutes; therefore, repeated 5- to 10-minute inflations can be done until the CAP is sealed. In case of failure of intermittent, complete occlusion to resolve the CAP, and partial occlusion to yield thrombolysis in myocardial infarction grade 2 flow can be held longer. If the inflation of the proximal balloon causes ischemia, a microcatheter alongside the balloon is positioned to inject fresh blood into the distal artery known as the microcatheter distal perfusion technique. With this method, the interventionist could prolong balloon inflation for 20 minutes, successfully achieving hemostasis [20]. The extravasation is often persistent despite prolonged balloon inflation in more extensive CAP (Ellis's grades II to III) needing alternative methods, such as subcutaneous fat embolization, or intracoronary injection of thrombin, occlusive coils, beads, or the implantation of covered stents (Figure 1, Table 4).

Pericardiocentesis

With Ellis type III CAP, as little as 100 mL of blood in the pericardial sac can lead to cardiac tamponade

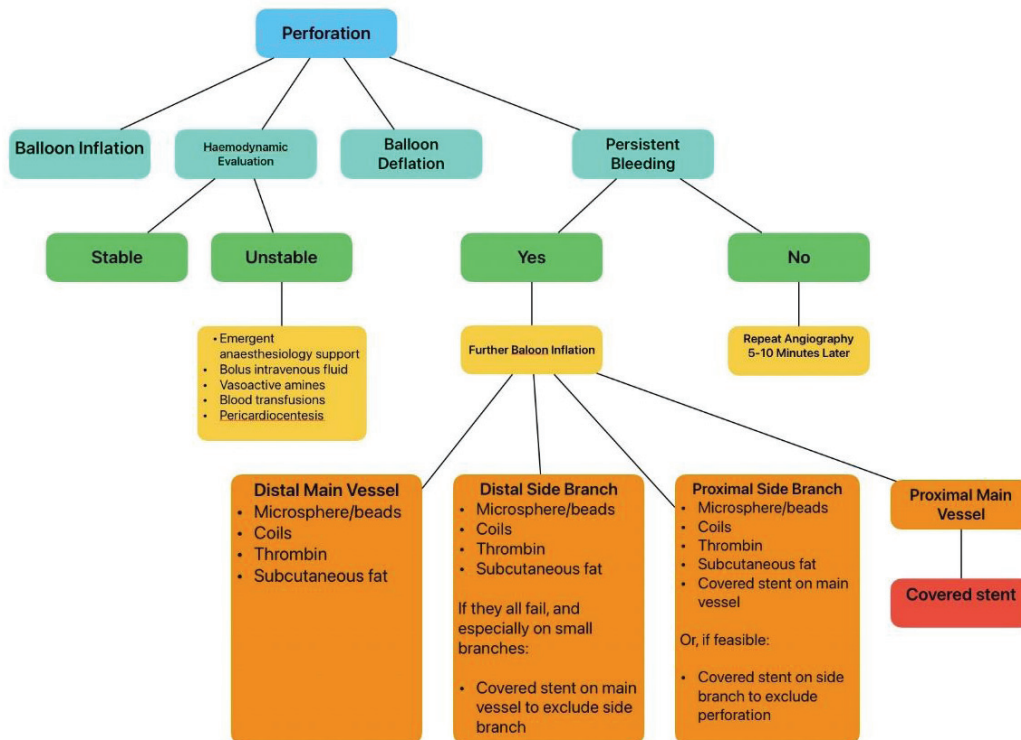


Figure 1: Approach to the management of coronary artery perforation.

Table 4: Techniques to manage coronary artery perforation.

Types of technique	Description	Indication	Merits	Demerits
Conservative	Watchful expectancy	Small, stable perforations; no active bleeding or hemodynamic instability	Noninvasive	Not suitable for all perforations; risk of perforation worsening
Covered stent	<ul style="list-style-type: none"> GraftMaster (PTFE covered) Papyrus (polyurethane covered) 	Proximal, larger perforations	Provides strong seal	Jailing side branches; inflexible and bulky, especially PTFE-covered stents
Autologous Fat/ Blood Clot	<ul style="list-style-type: none"> Fat globules or blood clots obtained from the patient Fat from the abdominal or femoral (next to the puncture point) site Can be dipped in contrast for a minute to render it radiopaque 	Distal coronary perforation	Widely available, biocompatibility, not expensive, any microcatheter can be used	Risk of thrombus embolization to other coronary arteries
Thrombin	Helps sealing by assisting in the formation of fibrin clots	Distal coronary perforation	Widely available, not expensive	Risk of thrombus embolization to other coronaries if
Coils	<ul style="list-style-type: none"> Detachable coils (predictable positioning). Pushable coils (unpredictable and irreversible delivery). The size of these coils should be larger than the size of the treated vessel. The choice of microcatheter is crucial. Progreat (Terumo), Transit (Cordis), and Renegade (Boston Scientific); can use only a 0.014 in. Finecross (Terumo) instead of a 0.018 in. microcatheter All neurovascular coils are compatible with 0.014 in. microcatheters. Commonly available coils: <ul style="list-style-type: none"> Interlock (Boston Scientific) Azur (Terumo) Micronester (Cook) Neurovascular coils (detachable): <ul style="list-style-type: none"> Axium (Medtronic) Smart coil (Penumbra) 	Distal coronary perforation	High visibility on fluoro, has controlled delivery; found to be very effective with distal perforations	Requires expertise in catheter-based techniques; pushable coils cannot be repositioned after deployment
Ringer balloon	Balloon with hollowed out center	Size of perforations not specified yet	Allows for longer inflation time (up to 1 hour)	Still undergoing investigational studies

if it accumulates rapidly. Urgent pericardiocentesis is warranted to rapidly decompress the cardiac compression from the pericardial effusion. Reinfusion of aspirated pericardial blood may decrease the need for blood transfusion. Reinfusion utilizes a closed circuit composed of a pigtail catheter in the pericardiac sac that is connected to central venous access. Once the cap is sealed, the pigtail catheter is left in place for at least 24 hours. It should be taken out if less than 50 mL of blood accumulates in less than 12 hours [21].

Dry tamponade (tamponade physiology without free fluid in the pericardium) is frequently caused by hematoma (whether myocardial or intramyocardial) that leads to compression and collapse of the cardiac structure. Typical pericardiocentesis is not useful because it is caused by a hematoma, or the pericardial fluid may be loculated and difficult to drain. Hemodynamic support with intravenous fluid resuscitation and vasopressors is of utmost importance while further steps, such as anticoagulation reversal or cardiac surgery, are considered.

Covered stent

Covered stents have revolutionized CAP therapy. The introduction of these devices has led to a substantial drop in cardiac tamponade, the requirement for emergency CABG [22], and death rates associated with coronary perforation [23]. Typically covered with polytetrafluoroethylene (PTFE), the main objective of a covered stent is to seal the perforation with a layer impermeable to blood. Deployment of a covered stent at the site of perforation can provide definitive treatment of large-vessel perforations, especially in vessels with a diameter > 2.5 mm (Figure 2). However, covered stents have some limitations. Covered stents should be avoided in vessels with sizable side branches as they carry the risk of side branch occlusion and periprocedural myocardial infarction. Also, thrombogenicity is of concern with covered stents, especially those covered with PTFE. The PTFE-covered stent is bulky, rigid, and challenging to deliver, necessitating techniques such as distal anchors and the use of guide extension catheters [24]. It frequently requires a dual guide technique to minimize bleeding into

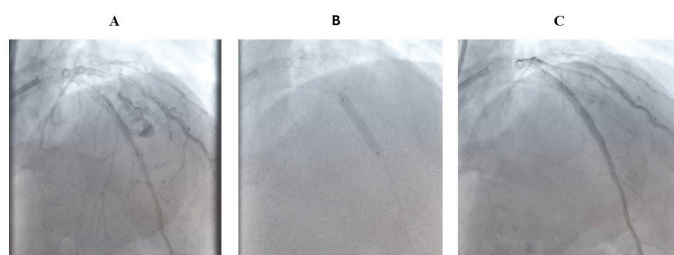


Figure 2: A. Coronary angiography depicting Grade III perforation in a native left anterior descending coronary artery (LAD) after the high-pressure post-dilatation of the stent. B. Sealing of the perforation by the covered stent. C. Final outcome.

the pericardium while preparing for covered stent delivery and deployment [25]. This technique involves contralateral access and the use of a separate guide catheter to deliver the stent. A second guidewire is advanced just proximal to the occluding balloon, which is then deflated and retracted, allowing passage of a new guidewire and covered stent for complete closure of the perforation [25]. These PTFE-covered stents have demonstrated a rather quite high risk of angiographic restenosis (32%) and stent thrombosis rate (5.7%) in various clinical settings [23]. Graft Master (Abbott Vascular, USA) is a PTFE-covered stent that is constructed using a sandwich technique in which a layer of PTFE is placed between two stainless steel stents. PK Papyrus (Biotronik, Berlin, Germany) is a newer-generation covered stent that is made of a single-layer electro-spun polyurethane-covered cobalt chromium stent thinner strut which allows exceptional flexibility and deliverability, even in challenging anatomy.

The Papyrus covered stent was associated with lower rates of target lesion revascularization compared to the Graft Master at 30-day follow-up and there were no significant differences in MACE or re-PCI between the Graft Master and Papyrus at 1-year follow-up in the CRACK-II Registry [26]. A makeshift covered stent can be created in the Cath lab by cutting both ends of a lightly inflated balloon to create a cylinder of balloon material. Then a stent is crimped over another remounted stent with the balloon cylinder in between [27].

Thrombin Injection

Thrombin is an enzyme that converts fibrinogen into fibrin in the final step of the clotting cascade which can be delivered through a microcatheter or over-the-wire balloon. Local and precise administration of thrombin can be used to seal distal CAP [28, 29].

Autologous Fat/Blood Clot Embolization

Autologous subcutaneous fat harvested from the local subcutaneous tissue, such as the patient's thigh near the arteriotomy site or autologous blood clots, can be utilized to seal distal CAP. A microcatheter or over-the-wire balloon

may be used to deliver fat globules and blood clots. The fat globules or blood clots can be dipped in contrast for a minute to render it radiopaque. Selective engagement of the microcatheter is critical to avoid fat or clot entry into major branches. Specific to the fat particles, the fat forms a physical barrier to seal the perforation, but also activates the coagulation pathway, thereby further sealing the coronary perforation. Accessibility, biocompatibility, low cost, and easy delivery through any coronary microcatheter are advantages of autologous fat or blood clot embolization [30-32].

Coils

Coils are permanent metallic (stainless steel or platinum) agents with a wiring framework made of synthetic wool or Dacron fibers and thrombogenic properties. Microcatheters are used to deliver coils, and the choice of coil size is important to ensure compatibility with the inner diameter of the delivery catheter to prevent the coil from being stuck and damaged. The currently available microcatheters have a wide range of internal diameters, with the smallest having an internal diameter of 0.015 inches at the tip. The narrowest internal diameter of the microcatheter determines the smallest diameter of guidewire, coils, or any other equipment that can be delivered through it. As a result, < 0.014 inch is the largest coil diameter that can be delivered through coronary microcatheters, such as the Axium coil (Medtronic) which has an outer diameter of 0.0108 to 0.0125 inch [33].

Coils can be categorized based on how they are delivered: pushable or detachable. When a detachable coil is attached to a wire that allows the coil to be delivered to the target area without being released. It can be retracted and repositioned if the position is not satisfactory. Once the desired position of the coil is achieved, the detachable coil can be released. As a result, the detachable coils may be positioned with greater accuracy and precision than pushable coils. There are two ways to deploy pushable coils. In the first technique, the coil is advanced and deployed past the catheter tip using a guidewire or designated pusher wire. In the second approach, the delivery catheter is forcefully flushed with saline using a Luer lock syringe, which also expels the coil from the catheter. Pushable coils, in contrast to detachable coils, are difficult to remove and reposition once they are deployed [34].

Most coils are classified as magnetic resonance imaging (MRI) conditional, which means that patients can get a safe scan if they are placed in MRI conditions. A static magnetic field can be used to scan most coils ranging from 1.5 to 3.0 Tesla, with the highest spatial field gradient of 5000 Gauss/cm. Additionally, there is a certain amount of MRI-related heating of the coils; however, this is very low, with a minimum of 0.6°C and a maximum of 3.1 °C at most. Coils

may result in a certain degree of artifact and compromise the image obtained. Image artifacts can extend between a diameter of 5.7–41.3 mm from the coil depending on individual products. It warrants optimization of MR imaging parameters to compensate for the presence of the coil may be necessary [34].

Balloon fragments

The distal end of a used balloon is snipped and loaded on the guidewire. The balloon fragment is then advanced with another balloon loaded on the wire, proximal to the balloon fragment. Once the fragment reached the distal portion of the vessel, the guidewire was withdrawn, leaving the balloon fragment in place and successfully sealing the CAP [35].

Ringer balloon

A new balloon for coronary perforation is the Ringer perfusion balloon catheter (Teleflex) which controls bleeding in the same way as a regular balloon catheter, but the balloon has a hollow center that is designed to allow blood flow through the vessel while simultaneously prohibiting blood from exiting the perforation site. This permits extended inflation up to one hour while the permanent treatment for CAP. Right now, it's in the investigative stage; the Ringer Perfusion Balloon Catheter Clinical Investigation is a prospective, multicenter, single-arm clinical investigation intended to evaluate the safety and efficacy of the Ringer perfusion balloon catheter [36].

Anticoagulation Reversal

It is recommended to reverse anticoagulation after removal of all intracoronary gears, including wire and balloons have been removed to avoid acute intracoronary thrombosis. Intravenous administration of protamine is needed to neutralize unfractionated heparin. The recommended dose is 1 mg protamine intravenously for every 100 units of heparin used to achieve an activated clotting time of < 150 seconds. The maximum amount of protamine that should be used is 50 mg. Infusion of fresh frozen plasma can be used to partially reverse anticoagulation due to bivalirudin. The relatively short life of bivalirudin is advantageous and may facilitate more rapid hemostasis after cessation of the infusion [4]. Platelet GP IIb/IIIa inhibitors should be discontinued once perforation occurs.

Conclusion

The incidence of CAP fortunately remains low, yet life-threatening complications of PCI may lead to high morbidity and mortality. It is critical to avoid oversized balloons or stents and high atmospheric inflations for larger vessels. Large vessel perforation is usually treated with a covered

stent if prolonged balloon tamponade fails. For distal vessels, changing to a non-hydrophilic wire after crossing the primary lesion and emphasizing the importance of holding onto the coronary guidewire during forceful injections to prevent distal movement of the guidewire tip can reduce the risk of perforation. Distal vessel perforation can also be treated with prolonged balloon inflation. In the event of failure of prolonged balloon inflation, various materials, such as coils, subcutaneous fat, thrombin, autologous blood clots, gelatin sponge, polyvinyl alcohol particles, and microspheres, can be used to cease active extravasation. Prompt recognition and timely interventions are vital to successful outcomes in CAP.

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