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In this chapter we perform a review of complications that may occur during CTO PCI. Over the past few years, tremendous improvement in PCI devices, as well as growth of new strategies has enabled us to treat with success even complex CTO. As CTO PCI is a complex procedure, it is associated with higher risk for complications as compared with PCI of non-CTO lesions [1]. Therefore it is critical to understand the potential complications with procedures, and steps that could be taken for mitigating risk. Patient-specific risk estimates can be calculated by using a dedicated scoring system, such as the PROGRESS-CTO complications score that uses 3 variables (age ≥ 65 years, lesion length > 23 mm, and application of retrograde approach) [2]. Ellis et al. [3] reported the following 2 independent correlates of complications: moderate to severe lesion calcium and low left ventricular ejection fraction.

10.1 The Frequency of Adverse Events with CTO PCI

Rates of inpatient mortality and MACE from a single-center series of 25 years of CTO PCI has, reassuringly, suggested success rates are increasing, while adverse events are declining over time [4]. A systematic review by Patel and colleagues of 65 studies with 18,061 patients and 18,941 target CTO vessels revealed low risk for death (0.2%), emergent coronary bypass graft (0.1%), stroke (0.01%), MI (2.5%), and contrast nephropathy (3.8%) [5]. Perforation was reported at 2.9% with cardiac tamponade in 0.3%. An analysis of 2596 target CTO lesions from Japanese

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Table 10.1 Frequency of complications on CTO PCI

Mortality	0.2%
Myocardial infarction	1.2%
Stroke	0.2%
Emergent coronary artery bypass graft surgery	0.0%
Coronary embolism	0.2%
Coronary perforation (tamponade)	0.4%
Vascular access complications	1.3%
Contrast induced nephropathy	1.7%
Radiation skin injury	0.2%

CTO-PCI Expert Registry revealed the complications consistent with above-mentioned study (Table 10.1) [6].

Regardless of the small numbers of serious complications, CTO operators should be aware of these events and should be able to treat them immediately if needed.

10.2 General CTO PCI Complications

10.2.1 Perforation

Coronary perforation is a well-known complication of CTO PCI. It is one of the most feared complications of CTO PCI which can lead to cardiac tamponade necessitating emergency pericardiocentesis and rarely, cardiac surgery to be controlled. It could be caused directly by the guidewire or by subsequent balloon advancement and dilatation. To avoid complications, balloon advancement or dilatation and microcatheter advancement should not be performed when the guidewire is not confirmed to be within the vessel. It is also important to size balloons appropriately using intravascular ultrasound (IVUS) and pay careful attention to tip hydrophilic or polymer-jacketed wire during attempts to delivery devices.

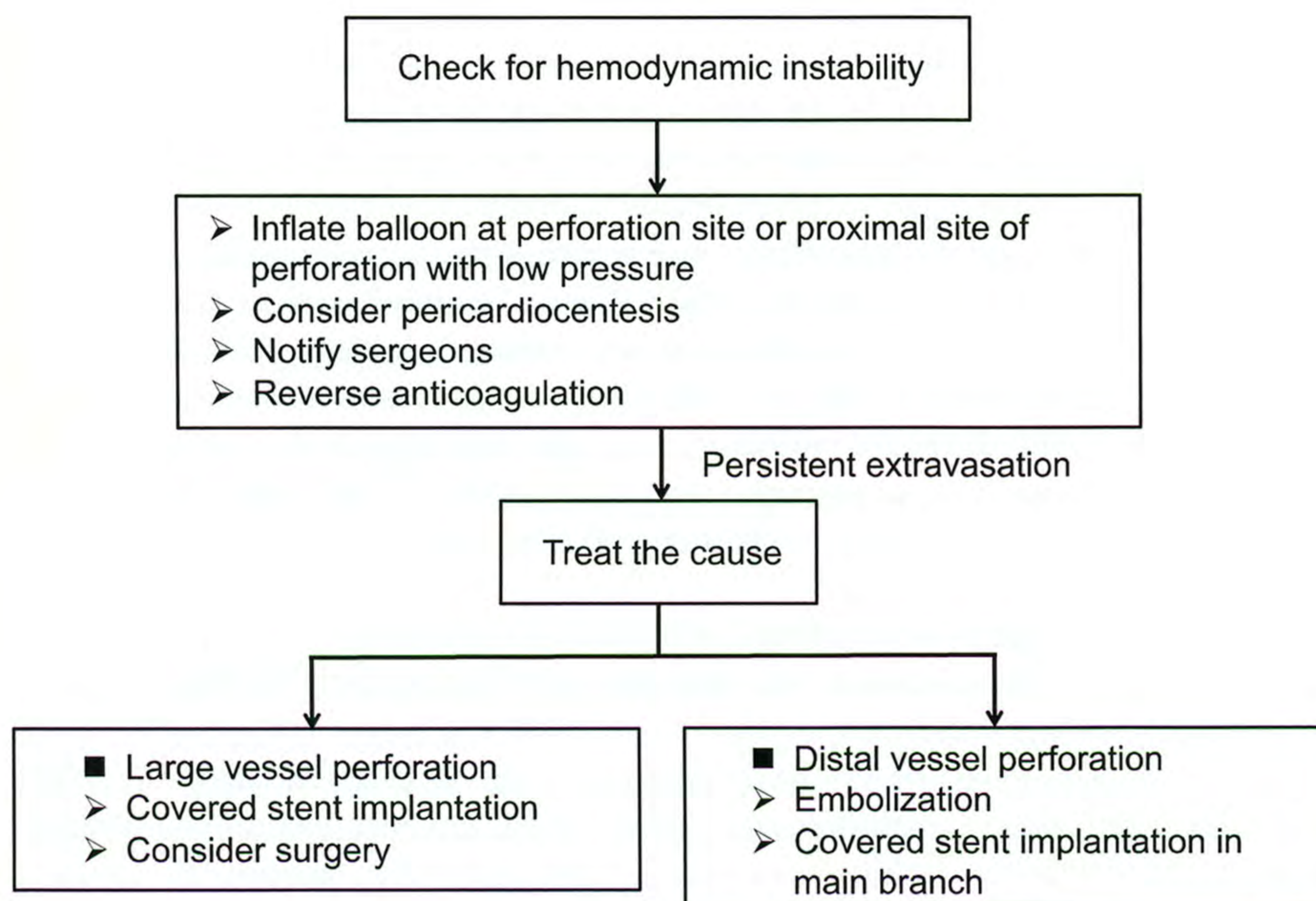
Coronary perforations are categorized according to location. There are three main perforation locations: large vessel perforation, distal artery perforation, and collateral vessel perforation, in either a septal or an epicardial collateral [7]. And the severity of coronary perforations has traditionally been classified according to the Ellis Criteria (Table 10.2) [8]. The general treatment of coronary perforations is shown in Fig. 10.1 [9] and the first step in any coronary perforation is inflation of a balloon to prevent additional bleeding into the pericardium. If there is a significant bleed while working with a 6Fr or 7Fr guide catheter, it is often useful to site a second guide catheter in the same vessel (a dual guide technique). However, a dual guide technique is not required if a 8Fr guide is used when covered stent delivery and continued balloon inflation can be managed via a single guide.

10.2.1.1 Coronary Perforation by Guidewire

Coronary perforation by a guidewire is the most frequent complication of CTO PCI. Guidewires for CTO have stronger penetrability than conventional guidewires; namely, some have a hard tip, some are tapered, and some are coated. Since the lesions are complex, the risk of perforation of the coronary arteries is high.

Table 10.2 Ellis criteria of coronary perforations

Perforation type	Description
Type I	Extraluminal crater without myocardial blush, extravasation or evidence of dissection
Type II	Myocardial or pericardial blush without extravasation
Type III	Extravasation through a ≥ 1 mm perforation
Type III: cavity spilling	Perforation and extravasation into an anatomic cavity chamber

**Fig. 10.1** Perforation management algorithm

Most of the time, operating a guidewire inside a CTO lesion is similar to relying on finger touch with only a vague image of the path of the coronary arteries. In perforations originating from inside a CTO lesion, blood is absent at the lesion and the plaque itself forms at the perforation site; as a result, blood rarely leaks from the blood vessel.

If coronary perforation occurs after the guidewire reaches the distal coronary arteries, it will be complicated by bleeding, which may be difficult to control. In situations in which a guidewire successfully passes through the lesion but the device has difficulty passing through it, moving the guidewire back and forth may cause coronary perforation during the procedure. In perforations occurring before the passage of the device through the CTO lesion, blood is supplied to the distal coronary arteries from the collateral circulation; therefore, perfusion pressure is low and only mild blood leakage results. However, even if the blood leak is mild, it may cause cardiac tamponade; thus, dilatation should be performed as quickly as possible at the CTO site, and proper hemostatic treatment is required as soon as possible.

Hemostatic interventions include pressure using a balloon, occlusion by a microcatheter, and embolization using thrombi, adipose tissue, or coil when appropriate, but coil embolization infallibly stops the bleeding.

A particularly serious issue is when the guidewire causes perforation of the distal coronary arteries before dilatation of the CTO lesion, making it impossible for the device to pass through the CTO lesion and causing hemodynamic failure due to cardiac tamponade. In such situations, hemostasis devices cannot be placed; therefore, hemodynamics must be maintained through vasopressor administration and pericardial drainage. In some cases, hemostasis through thoracotomy may also be needed. After hemodynamics are stabilized through procedures such as pericardial drainage, attempts can be made to pass the device through the CTO lesion while continuing observation, but if the effect of heparin is reversed, caution must be taken against thrombus formation.

Because perforation due to a guidewire is often asymptomatic in the period immediately following its occurrence; as a result, it may remain unnoticed during the procedure and left untreated once the patient is returned to their hospital bed. However, several hours later, the patient may suddenly develop a decrease in blood pressure, and perforation is only discovered after the patient develops cardiac tamponade. This is why the entire coronary artery that was subjected to revascularization must be subjected to angiography after the procedure. Confirming the absence of perforation due to the guidewire is of crucial importance.

10.2.1.2 Coronary Perforation by Balloon Dilatation

One way to help the guidewire pass through the CTO lesion is by introducing a microcatheter or intravascular ultrasonography (IVUS) into the CTO lesion before letting the guidewire pass through it. In such cases, the proximal site inside the CTO lesion is dilated using a small-diameter balloon; it has not been determined whether the tip of the guidewire is inside or outside the coronary artery. Although the balloon has a small diameter, a massive hemorrhage could occur if the balloon is inflated outside the coronary artery. As a countermeasure, one must stop the bleeding by re-inflating the balloon. Later, another guidewire is inserted inside the CTO lesion via another route or using the retrograde approach, the balloon is inflated, and hemostasis is achieved by compression of the plaque inside the CTO lesion at the site of the rupture; this makes hemostasis possible but requires tremendous skills and experience. First, efforts should be made to stop the bleeding and achieve hemodynamic stability. It is most important to carefully examine the benefits and risks associated with balloon inflation before passing the guidewire through the lesion.

10.2.2 Side Branch Occlusion

In most cases, CTO lesions start forming anteriorly and posteriorly to the site of the occlusion and ramify into the side branches. Most patients with CTO lesions also have cardiac dysfunction, and troubles commonly involve the side branches, leading to severe complications. If the side branches diverge from the proximal portion of

the occlusion, the guidewire must be inserted into side branches to prepare for unforeseen occlusions of the side branches and other troubles.

Further, the distal end of the occlusion in the CTO lesion often consists of bifurcation of the lateral branch. When the guidewire is pushed forward from inside the CTO lesion and penetrates the distal coronary arteries, effort should be made so that penetration occurs from the apex of the distal end of the occlusion. After the guidewire passes through the lesion, the CTO lesion is dilated using a small-diameter balloon; later, the remaining branches must be immediately secured using a double-lumen catheter. The situation that must be avoided the most is one in which the guidewire shortcuts the bifurcation and directly perforates either of the branches.

10.2.3 Coronary Dissection or Hematoma

Even if the guidewire successfully reaches the distal coronary arteries, dissection and hematoma formation can occur during the guidewire progression. This can go unnoticed, and angiography after balloon dilatation may reveal a dissection or hematoma that may have progressed to the distal. As a countermeasure, angiography should not be performed after balloon dilatation; instead, IVUS is first performed to confirm the presence of a dissection or hematoma, and later, indwelling stent placement should be performed under IVUS guidance.

10.3 Complications of the Retrograde Approach

The success rate of CTO PCI has improved due to the widespread use of the retrograde approach. In addition, suitable devices have been developed and its safety has improved; however, the retrograde approach has its own specific complications, most of which are likely to be fatal. This must be considered during the procedure.

10.3.1 Complications of Coronary Artery with CTO

10.3.1.1 Advance of Coronary Dissection or Hematoma

The reverse controlled anterograde and retrograde subintimal tracking (CART) method is currently the mainstream method in the retrograde approach. In this procedure, the condition is that the CTO lesion should be dilated before the guidewire reaches the distal coronary arteries. The space that was dilated by the antegrade balloon will expand as a dissection if it is inside the intima or as a hematoma if it is inside the subintima. If antegrade contrast injections are performed after antegrade balloon dilatation, it may cause the dissection and hematoma to extend more distally, giving rise to complications such as occlusion of the distal coronary arteries. This is why—in principle—antegrade contrast injections must not be performed under such circumstances. Even if antegrade contrast injections are not performed, the dissection and hematoma may still extend through antegrade coronary blood

flow, but there is no need to worry about such a risk as long as the antegrade balloon remains dilated during the procedure.

10.3.1.2 Proximal Coronary Injury by Retrograde Guidewire

The proximal end of the occlusion in a CTO lesion is often located at the bifurcation, and after a procedure consisting of making a retrograde guidewire pass directly inside a proximal coronary artery, IVUS must be performed for confirmation. In some cases, the retrograde guidewire may reach the proximal coronary artery by shortcutting the coronary bifurcation. If the operator fails to notice this and proceeds with the dilatation, the side branch on the proximal side could be obstructed; if this happens in patients with reduced cardiac function or large side branches, it may lead to lethal complications. If IVUS findings confirm shortcutting of the coronary bifurcation, switching to the reverse CART method inside the CTO lesion would be appropriate.

10.3.2 Collateral Channel Injury

When creating a system to perform the retrograde approach, one must first advance the guidewire and device to the distal coronary artery through the collateral channel. The pathways include the septal channel, epicardial channel, and bypass graft.

Damage to the collateral channel can be classified into two categories: damage due to the guidewire and damage due to the device. In terms of frequency, the more common types are guidewire-induced damage. Guidewire manipulation can obstruct the collateral channel, but in most cases, blood also flows in from other collateral channels; therefore, this issue is unlikely to cause any problems. Perforations due to the guidewire also often occur. When the damage involves the septal channel, the bleeding often penetrates the right and left ventricles as well as the coronary veins, rarely causing problems. However, guidewire-induced perforations in the epicardial channel can cause cardiac tamponade and hemodynamic collapse; therefore, the bleeding must be stopped through coil embolization or microcatheter occlusion. When bleeding occurs in the epicardial channel and the guidewire has already passed through the lesion, hemostasis should be achieved by pushing the microcatheter forward to block the blood flow, and the procedure has to be continued by using the retrograde approach. Finally, to confirm that the bleeding has stopped, angiography must be performed, while the retrograde guidewire is left in place; if the bleeding persists, bleeding from both the antegrade and retrograde directions must be stopped.

Damage to the collateral circulation due to passage of the device has become less common since devices have undergone improvements. The damage is often discovered after device removal; thus, when a retrograde device is removed, the guidewire must absolutely be left in place when angiography is performed, and the latter must be performed to confirm the presence or absence of bleeding or damage to the

collateral circulation. If the damage affects the septal channel, a hematoma forms inside the myocardial septum, causing ischemia or ventricular arrhythmia; therefore, a shunt with the cardiac ventricles should be formed using another guidewire, and the pressure inside the hematoma must be reduced. If the damage affects the epicardial channel, it may lead to cardiac tamponade; therefore, the bleeding must be stopped immediately using coil embolization from the anterograde and retrograde directions. To ensure that hemostatic treatment can be performed in emergency situations, the operator should ensure that the coil they are familiar with is always ready to be used during PCI.

10.3.3 Donor Artery Injury

A donor artery injury often induces extensive ischemia and hemodynamic collapse. This is due to the guiding catheter, which injures the proximal portion of the donor coronary artery. In the retrograde approach, stronger than usual forces are applied to the guidewire and the device; as a result, the guiding catheter can easily be drawn deep into the coronary artery. Under such circumstances, it is likely to injure the proximal portion of the donor coronary artery. If stenosis occurs at the proximal site of the donor coronary artery, the retrograde approach should be preceded by the deployment of stent to avoid complications. If externalization is successfully achieved, the procedure should be continued while the guiding catheters on both sides are completely removed from the coronary artery.

10.3.4 Ischemic Phenomenon of Donor Artery

If a moderate or severe stenosis occurs in the donor coronary artery, the stenosis must absolutely be treated before the retrograde approach is started. If device passage induces ischemia, chest pain and hemodynamic instability will occur. Even if the clinical course is uneventful immediately after the device passage, ischemia can sometimes be induced by the maneuvering of a retrograde device or the induction of vasodilation and vasospasm; therefore, procedures such as stent deployment should absolutely be performed before use of the retrograde approach.

Even if a collateral channel with abundant blood flow is used as a route for the retrograde approach, ischemia that may be induced by the procedure does not normally pose any problems in most cases. Even if the collateral channel is occluded by the retrograde device, blood flowing from other collateral channels will increase and chest pain as well as electrocardiographic changes will be mild. However, when a collateral channel with direct communication is used as a route for the retrograde approach, the ischemia that is induced by the occlusion of collateral channels will be strong; even if the hemodynamics are maintained, a strategic change may be imperative in some cases.

10.3.5 Embolization

Thrombus formation is among the complications that require the most caution with the retrograde approach. During the retrograde approach, the procedure is often continued for long hours without angiography or device replacement while a guiding catheter is left inserted in the coronary arteries on both sides; as a result, the blood inside the guiding catheter may stagnate and a thrombus may form. If the resulting thrombus flows into the donor coronary artery, it may cause hemodynamic collapse and could lead to lethal complications.

As a preventive measure, the activated clotting time (ACT) should be controlled and constantly maintained at 300 s or higher during the procedure. Because heparin has a short half-life, its effect is attenuated during the procedure; therefore, in our facility, the ACT is measured every 30–60 min, and additional heparin doses are administered when appropriate. Further, during a procedure using the retrograde approach, flash injections of heparin sodium are administered every 30 min through the retrograde guiding catheter.

10.4 Conclusions

Since CTO PCI is believed to carry a higher incidence of complications than conventional PCI, it must be performed with consideration of preventive measures and countermeasures against all possible complications. It is important to know that, as a pathological condition, CTO is stable to some extent; even if the first treatment is unsuccessful, it can be replaced with PCI or other treatment strategies at a later date. Thus, making the decision to terminate the procedure instead of pushing too far is also crucial in cases of complications.

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