How to Read and Find the Appropriate Collateral Channel for the Retrograde Approach

6

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6.1 Summary

Recent developments in the technical approach, both in strategy as well as available tools, have led to a greatly improved success rate for the recanalization of a chronic total coronary occlusion (CTO) which is now beyond 90% in experienced hands [1]. One of the major developments contributing to this success is the introduction and development of the retrograde approach accessing the distal vascular bed of an occluded vessel via collateral pathways [2]. The following chapter will focus on the anatomy and function of collaterals and their proper assessment by angiography, which are important criteria for the selection of the appropriate channel for a retrograde approach.

6.2 Anatomy of Collateral Connections

The fact that collaterals exist between occluded and open coronary segments was detected as early as 400 years ago. Ensuing was a century long debate among anatomists whether these collateral connections were pre-existent or developed anew in case of an occlusion. That debate was finally concluded by studies conducted by Baroldi and the Scot anatomist Fulton in the middle of the last century [3]. The in vivo study of the collateral anatomy then became possible with the introduction of coronary angiography. In 1974 Levin published an extensive analysis of the variation of collateral connections in the territories of occluded coronary arteries [4].

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His category of 22 individual pathways is still valid and a valuable source of information and can help to categorize possible interventional collaterals also for the retrograde approach [5].

Most importantly it needs to be realized that collateral pathways do coexist, and rarely do we find only one predominant connection. Even in that latter case, other pathways may be found by exploration with a wire as they may be dormant due to the fact that collateral supply will always pass via the ones with the lowest resistance [6]. For example, we may have a large collateral connection from the apical LAD to the RCA, but still we will find septal connections which are not active because of their higher resistance [7].

The predominant site of a CTO is the right coronary artery (RCA). Levin described ten predominant pathways, six of them originating from the left coronary artery (LCA) and four were ipsilateral pathways. The contralateral supply from the left anterior descending artery (LAD) can either run through the septum, which is the preferred interventional route, or via the apex, which is also often accessible for the retrograde approach. In addition, there may be connections via a LAD and acute marginal of the RCA connection which in practice often enters the occlusion close to the distal cap and therefore is not ideal for a retrograde access. The connections from the left circumflex artery (LCX) run through the atrioventricular groove and show varying degrees of tortuosity, making them viable retrograde options. More distal connections from the LCX run via epipericardial connections from an obtuse marginal (OM) to the distal posterolateral (PL) branch of the RCA. A rather rare connection is between the atrial branch and a proximal conus branch of the RCA. The ipsilateral connections are more difficult to utilize for a retrograde approach as they are of various tortuosity, but they may present an interventional option [8]. The Kugel's collateral connects a conus branch with the PL system, while there are connections from OMs to the distal RCA either directly to the distal bed or to another OM distal to the occlusion. Again, like in connections from the LAD to an OM, the collateralized OM often inserts close to the distal cap and therefore does not provide the angle towards the distal cap. In addition, we may find more exotic pathways running from a conus branch cranial around the heart to insert in to the distal PL system not observed in Levin's study.

In the recent application of Levin's approach to describing collateral pathways McEntegart et al. even described 20 collateral patterns in RCA CTOs, with the predominant supply via the septum in 72% of cases, the atrial connection in half of all cases followed by ipsilateral bridges, the apical LAD to RCA connection, LAD branches to OMs and the Kugel's collateral.

The second most frequent CTO is located in the left anterior descending artery (LAD). Levin observed seven major connections, four from the RCA, two ipsilateral as epicardial connections from a diagonal or obtuse marginal branch, and one ipsilateral between septal branches of the LAD proximal and distal to the occlusion. The RAO connections mirror the connections in case of a RCA CTO. The supply might run via the septum from the PDA, or from acute marginal branches from the RCA or via a proximal conus branch, and finally via the apex. In addition, in left dominant circulations there could a septal connection from the PDA originating from the LCX to the occluded LAD [4]. Interestingly, the frequency distribution observed by Levin with rare septal and more frequent epicardial connections does not reflect the daily practice, where the group of McEntegart described 13 distinct patterns [5]. They observed septal connections from the PDA to the LAD in half of all patients, then followed by the acute marginal to LAD and ipsilateral OM or diagonal to LAD pathways in about 20–25% each. Conus branch connections from the RCA were observed in 18%, septo-septal connections in 16%.

Whether these connections are accessible for an interventional approach again is determined by their tortuosity, distensibility, and the insertion point relative to the distal cap of the occlusive lesion.

The LCX is the least frequent CTO, and it is often the most difficult one to treat, which leads to the inclusion of the LCX as an adverse factor in the prediction of a successful recanalization by the PROGRESS score [9]. Levin observed five distinctly different pathways for a LCX CTO [4]. He found an ipsilateral connection via atrial branches as the most frequent, followed by ipsilateral OM connections or from the diagonal system. The RCA may supply the distal bed via atrial connections through the atrioventricular groove or distal OM branches. Also McEntegart et al. observed a less frequent number of coexisting collaterals for a LCX CTO [5]. The patterns are very much dependent whether the coronary circulation is left or right dominant. They categorized 12 different patterns of connections, the most frequent being diagonal to OM in about 30%, and connections from the RCA through the AV groove in 20–30% depending on the dominance, other connections are observed in the range of 10% or less.

For the sake of the interventional approach, the basic division is between septal, atrial, and epicardial connections (Table 6.1). The majority of connections for RCA and LAD CTOs are septal connections. These pathways run through the myocardium of the interventricular septum, but especially the basal connections of the first septal sometimes connect running across the right atrium and enter the distal RCA bed either separately through an intermediate branch at the crux cordis or into the proximal side branch of the PLA of the RCA. This is just one example that the rules about the anatomic course and distinctions between septal and epicardial pathways can vary individually. The general idea that septal pathways are less prone to severe complications when damaged during an interventional attempt to pass them as opposed to the more fragile epicardial connections should always be taken with caution, and the primary rule must be to avoid damaging collaterals.

It must be kept in mind that collaterals from septal origin may then pass towards the epicardium and vice versa. This is most evident in connections from the septal

Table 6.1 Collateral pathways and their interventional suitability

	Corkscrew-like morphology	Length of access route	Applicability	Distensibility
Epicardial	Various	Long	Moderate	Not dilatable
Atrial	Often	Medium	Moderate	Not dilatable
Septal	Slight	Short	High	Dilatable

branches of the LAD to the acute marginal branches of the RCA. Another example are branches which originate from the first septal and then turn towards the base of the heart and run across the right atrium before entering the RCA either very proximal in the PL branch or as a separate small intermediate branch. Damage to these connections will not be "protected" by the muscular septum but may create severe complications by intramural hematoma expansion and compression of cardiac cavities.

6.3 Angiographic Visualization and Assessment of Collateral Connections

The first and most important step when considering the retrograde approach is the angiographic visualization of the collateral pathways. For a perfect visualization it is important to avoid panning during filming, and to allow enough time for the contrast medium to reach the occluded segment. Contrast should be forcefully injected, and a large diameter catheter is helpful to reveal the smaller collaterals. The frame rate for the cineangiography should be increased (e.g., 15/s) to improve the detection of even tiny connections.

As the majority of CTOs are located in the right coronary artery (RCA), the main source of collateral supply runs through the septum, and these are the most frequently used interventional pathways. These septal channels can be best viewed in their entire course from a plain 30° right angle, with additional information on the entry into the channel provided from a cranial angulation, and the exit into the posterior descending artery (PDA) from a caudal angulation. Likewise, the connection from a RCA donor artery to an occluded left anterior descending artery (LAD) can be viewed. Other connections via the atrial grove between the left circumflex artery (LCX) and the RCA can be visualized both from the right and left anterior oblique projections at best with a caudal angulation. However, the takeoff of these channels may vary considerably and needs individually adjusted gantry angles.

Among the important features for the angiographic assessment of a possible suitable route for wire access to the distal occluded segment is the diameter of the collateral connection. This was initially graded in 3 categories of collateral connection size (CC) (CC0: no angiographic continuous connection; CC1: threadlike connection (<0.4 mm); CC2: side branch like connection (>0.4 mm)) [10]. There are also occasional large connections, especially via the apex of >1 mm diameter which could be labelled CC3 connections. Other important features to consider are the tortuosity of the connection and the angle of takeoff from the donor segment, as well as at the site of entry into the receiving segment. The length of the connection can be of relevance as the length of the interventional catheters is limited.

The tortuosity of a collateral can be of various relevance, as some bends will be straightened when a wire is advanced, some bends may be less distensible and then cause an increasing resistance to the advancement of the wire and microcatheter (Fig. 6.1). Therefore, the sheer fact of a tortuous connection alone should not determine the utility as an interventional pathway. Osamo Katoh in his first presentations on the retrograde transcollateral approach had used a ratio of amplitude and

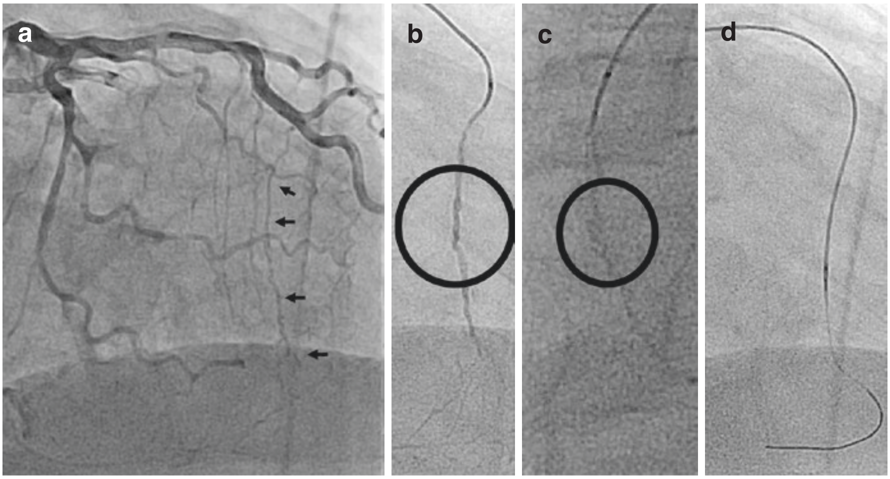

Fig. 6.1 (**a**) Several septal pathways are visible on this RAO 30° view. The one marked by arrows was selected for the interventional access. (**b**) However, the attempted wire passage with a Sion (ASAHI Intecc) stopped in the middle of the vessel. Selective injection did not reveal the cause on the RAO view (circle), but the LAO view (**c**) showed a severe tortuosity with a more than 180° reverse bend (circle). (**d**) Realizing this obstacle, the wire could be manipulated through this bend with a 90° tip angle

collateral diameter as a measure to determine the collateral suitability. A value of >2 would describe moderately tortuous connections, a value <2 would define severe tortuosity.

From their detailed analysis of collateral angiographies with a view to their interventional suitability McEntegart et al. suggested a collateral scoring system. This score is rather detailed and complex, and it has not yet been validated in a larger independent series. A much simpler score was suggested by Huang et al. limiting it to the collateral connection size and the tortuosity as the major determinants of success to pass the collateral by a wire [11]. The definition used by this group to define high tortuosity is the observation of high-frequency curves, that is, a curve of more than 180° when the vessel diameter is less than 3 times the size of the curve. If in epicardial connections two or more of these high-frequency curves are observed within a 2 mm distance this epicardial is considered tortuous. Regarding the septal connections, some of these bends will straighten themselves through the cardiac cycle. If more than one such bend stays unaffected by the cardiac cycle, it is considered as a tortuous septal.

The issue with validating these kinds of scores is the fact that passing collaterals with a wire requires above all a long experience and familiarity with these dedicated wires, which continue to receive further innovation and refinement. A difficult anatomy may pose an obstacle to less experienced operators, which can be overcome by others. Therefore, all scores can serve as a general guide especially for the novice, but they cannot replace the trial in case certain unfavourable collaterals may be the only option for a successful interventional treatment.

6.4 Time Variation of Angiographic Visualization of Collateral Connections

The assessment also has to take into account that several collateral pathways may coexist, and that their appearance may change depending on the haemodynamic status of the collateral donor artery (Fig. 6.2). Therefore, any previous angiograms should be carefully analysed. Disappearance of a collateral connection between two angiograms at different time points may not signify the actual closure of the collateral connection, but rather that it is functionally dormant. It is suggested by some operators to use a low-pressure balloon occlusion of one of the pathways to explore alternative routes, which are more likely accessible to a wire passage. A common practice is the selective injection into channels to identify by this direct contrast application possible distal run-off into the distal coronary bed of the occluded artery (Fig. 6.3).

Careful wire probing may still achieve wire passage even when connections are not clearly visible, especially in septal pathways. This is the basis of the so-called septal surfing approach to pass from the LAD towards the distal bed of an occluded RCA and vice versa [12].

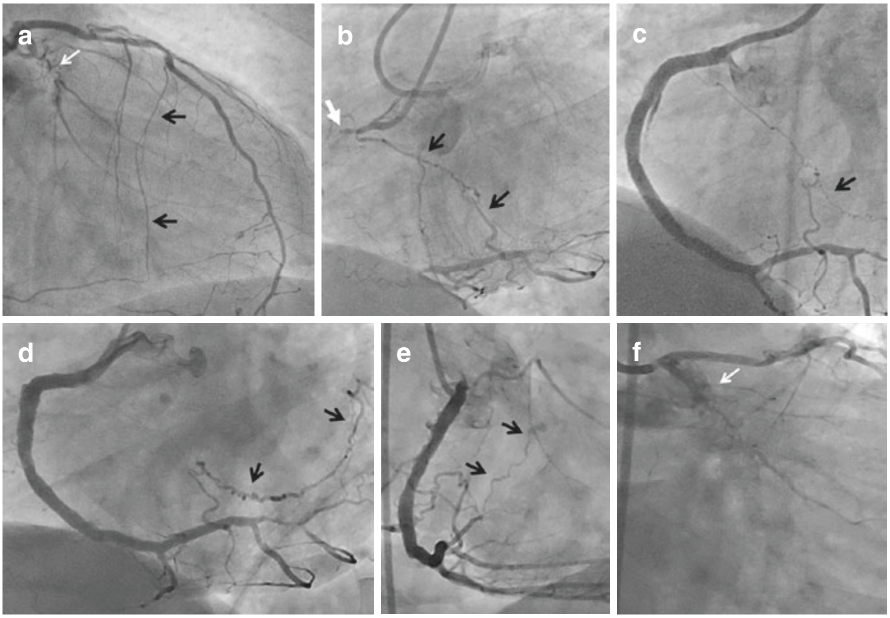

Fig. 6.2 (**a**) A patient with three-vessel disease and a circumflex occlusion (white arrow) with bridging collaterals. There are septal connections to the occluded right coronary artery (black arrows). (**b**) The occluded right coronary artery (white arrow) receives also ipsilateral collateral supply via a Kugel's artery (black arrows). (**c**) After staged recanalization of the right coronary artery a thin connection becomes already visible (arrow). (**d**, **e**) Four months later at the time of the planned circumflex recanalization, this connection is developed into the main supply for the distal left circumflex artery (arrows). (**f**) The bridging collaterals are no longer the major source of supply for the occluded circumflex (white arrow)

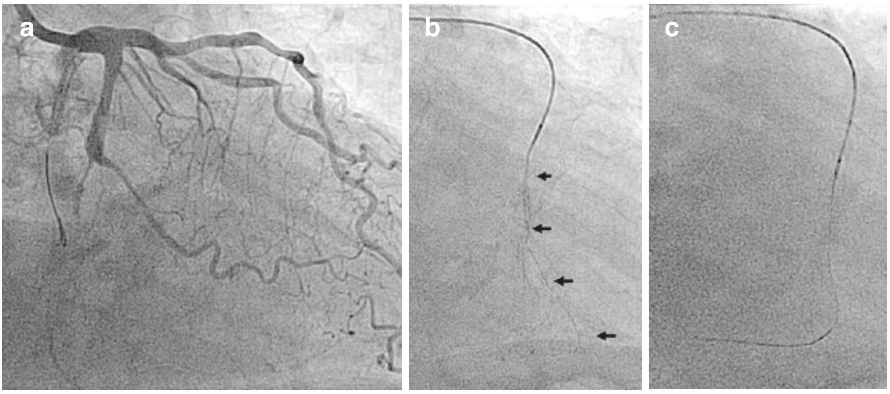

Fig. 6.3 (**a**) A left circumflex occlusion with ipsilateral filling of the distal PDA, but no clear collateral pathway. (**b**) Selective injection reveals a faint CC1 connections turning towards the PDA (arrows). (**c**) This could be passed by a Sion wire (ASAHI Intecc), but the distal turn of the wire looks like it took an invisible channel inward of the one visualized in (**b**)

6.5 Can We Augment Collateral Visualization?

Collateral filling by contrast medium is dependent on the pressure gradient across the collateral and its diameter. To improve the collateral visualization, we would ideally increase the collateral flow. In analogy to the epicardial coronary artery, however, collaterals do not typically have a smooth cell layer that would respond to vasodilators as nitroglycerin [13]. Collaterals do respond to shear stress as a principle of their recruitment from the initial arteriolar connection to a fully functional collateral, but this is not instantaneously affected [14]. Therefore nitrogylcerin will not enlarge the diameter of the collateral, but it may still improve their identification by increasing flow in the receiving vessel.

Furthermore, there is an obvious rule that there cannot be normal regional myocardial function without blood supply. Therefore, if a normally contracting area distal to a coronary occlusion must receive sufficient collateral supply to uphold the viability. If on a routine diagnostic angiogram, no such supply is observed there must be different sources present which were not yet detected. A typical case is a LAD occlusion supplied by a conus branch from the RCA that originates separate from the RCA ostium. These separate branches need to be searched for and sometimes provide even an interventional pathway.

6.6 The Functional Capacity of Collaterals

A detailed discussion of the collateral circulation relevant to coronary artery disease can be found in many reviews [13, 15, 16]. Collaterals develop through arteriogenesis, that is, through the recruitment of preformed and pre-existing inter-arterial connections mainly driven by shear forces along the pressure gradient that develops when the native vessel is occluded [14]. Some of these connections may be pre-existent to such an extent that they are immediately recruitable in case of a vessel occlusion, as shown during balloon occlusion in non-diseased coronary arteries [17]. The functional assessment of collaterals has revealed that in patients without well-developed pre-existing collateral connections, collaterals required between 2 and 12 weeks to fully develop their functional capacity [7].

The physiological assessment of collateral function is best done with combined pressure and flow velocity recordings with microsensors [7, 13]. This provides a complete picture of the haemodynamic of the collateralized territory distal to an obstruction [18, 19]. The assessment of a donor lesion by FFR may be influenced by the myocardial mass distal to the lesion including the collateralized territory. Therefore, physiologically driven revascularization in a donor segment needs to take into account that once the occluded myocardium is reperfused after recanalization, the FFR value may increase and the donor artery obstruction may no longer be below the cutoff value [20, 21].

Collateral function can develop to a similar functional level in patients postmyocardial infarction with large akinetic territories as in patients with normal preserved regional function. Therefore, the presence of viability is not a prerequisite for collateral development and the observation of excellent collaterals should not be the reason to perform the intervention, but rather the proof of viability [22]. On the other hand, the assessment of collateral function shows that the functional competence of collaterals in CTOs is limited even in patients with perfectly preserved left ventricular function distal to an occlusion. During a standard stress protocol with systemic infusion of adenosine the coronary flow velocity and pressure changes distal to an occlusion were well below cutoff values for assessing the functional reserve in non-occlusive coronary obstructions, that is, a flow velocity reserve above 2, and an *FFR* above 0.75. So even well-developed collaterals would not prevent ischaemia during exercise [23].

Collaterals will regress once the native artery that was supplied by the collaterals is revascularized. This process starts immediately after the re-established antegrade flow with immediate loss of collateral conductance, at least with CC1 collaterals, less so with CC2 collaterals. Acute reocclusion, for example, in the course of a late stent thrombosis can therefore lead to an acute coronary syndrome [24, 25], as the recruitment of collaterals is not instantaneous in most patients [26].

For the interventional approach it is important to realize that large epicardial collaterals have in general a lower resistance than septal connections, and thus will be a major source of collateral supply [7]. In case of damage to a collateral bed during an interventional approach that ultimately fails, the ensuing possible myocardial ischaemia will be greater if the major supply is interrupted. Therefore, if the operator has the choice of collateral pathways, he may select the one with the smaller diameter and prefer septal over epicardial pathways. At the same time, it is to be expected that the patient may experience chest pain during the retrograde procedure and this technique needs careful attention to the potential causes of this ischaemia. If no major obstruction is detected, the procedure may be continued despite the discomfort of the patient, and analgesia should be applied.

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