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Přehledový článek | Review

Percutaneous coronary interventions in bifurcation lesions: from theory to practical approach

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ABSTRACT

Coronary bifurcation lesions including unprotected distal left main stenosis remains challenging for percutaneous coronary interventions. This review will summarize the classification, histopathology and physiology of bifurcation lesions, as well as lessons learned from bench testing, different stenting strategies and two stent techniques including dedicated bifurcation devices. Due to the variety of anatomical configurations the Medina classification of bifurcation lesions is widely accepted. Lessons from histopathology reveal location of the atherosclerotic plaques most frequently in the lateral walls of both main vessel and side branches in the areas of low shear stress with turbulent flow. The diameter of the mother vessel is the sum of the daughter vessel diameters (distal main plus side) multiplied by 0.68 (Dm = 0.678*/D1 + D2/). *In vitro* bench testing of bifurcation stenting allows visualisation of stent deformations and lumen reductions after deployment of one or two stents. The role of final kissing inflation, proximal optimization technique, one or two stent strategy and different two-stent techniques are addressed (provisional T-stenting, TAP, crush, culotte, SKS, V-stenting). The role of imaging techniques is emphasized (IVUS, FFR and OCT) especially for the distal LMCA bifurcation lesions requiring the use of more advanced devices and specialized techniques as well as adjunctive pharmacologic agents.
Dedicated bifurcation devices and their potential indications are described. Practical tips and recommendations based on the European Bifurcation Club consensus are presented.

Klíčová slova:
Bifurkační léze
Bifurkační stent
Kmen levé koronární tepny
Lékové stenty
Perkutánní koronární intervence

SOUHRN

Bifurkační léze včetně nechráněné stenózy kmene levé věnčité tepny představují komplexní typy perkutánních koronárních intervencí. V přehledovém sdělení uvádíme jejich klasifikaci, histopatologické nálezy, fyziologii průtoku bifurkačních lézí a poznatky z testování na modelech bifurkací („bench testing“), které ovlivňují volbu typu a techniky stentingu včetně speciálních bifurkačních stentů. S ohledem na anatomickou variabilitu bifurkačních lézí byla v praxi přijata jejich klasifikace dle Mediny. Histopatologické studie prokázaly, že maximum aterosklerotických změn je na laterální stěně hlavní i boční větve, což odpovídá oblastem s nízkým střižným napětím a turbulentním průtokem. Průměr hlavní větve je dán matematickou formulí jako součet průměrů obou dceřiných větví násobeno koeficientem 0,68 (Dm = 0,678*/D1 + D2/). Virtuální testy na modelech bifurkací prokázaly různý stupeň deformace stentů v závislosti na počtu stentů (jeden versus dva stenty), použité technice implantace („T-stenting“, TAP, „crush“, „culotte“, „kissing“ stenty, „V-stenting“) a zdůrazňují úlohu konečné současné dilatace obou větví („kissing“ dilatace) či techniku proximální optimalizace. Zmiňujeme úlohu dalších pomocných metod (IVUS, FFR nebo OCT), zejména při intervencích na kmeni levé koronární tepny, které vyžadují využití speciálních technik stentingu, zobrazení i přídatné farmakoterapie.
Uvádíme přehled specifických typů bifurkačních stentů a v závěru pak řadu praktických rad, které byly formulovány v rámci setkání European Bifurcation Club.

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Introduction

Percutaneous coronary intervention (PCI) is widely accepted method of myocardial revascularization, life-saving in acute myocardial infarction with ST segment elevation (STEMI), superior to medical treatment in acute coronary syndromes (ACS) and concurrent to coronary artery bypass graft surgery (CABG) in many stable patients. With increasing complexity of coronary artery disease long-term results of PCI decline due to cummulative risk of restenosis, while CABG results are not affected by lesion complexity itself. Drug eluting stents led to dramatical decrease in restenosis within first year after the procedure, but some situations remain challenging for catheter treatment, namely bifurcation lesions, left main lesions and chronic total occlusions.

Definition of bifurcation

Anatomical definition: bifurcation lesion is a lesion occuring at, or adjacent to, a significant division of a major epicardial coronary artery. Simple description of bifurcation lesion is difficult due to the variety of anatomical configurations, sizes of the main vessel (MV) and side branch/es (SB), stenosis location and severity, presence of calcifications, angles between main branch and side branch/es. The main vessel is the largest and/or the longest vessel. Definition of significant side branch is related to the volume of vascularized myocardium or vessel diameter (in most cases 2.25 mm and bigger), while functional definition is related to the potential consequencies of SB occlusion in the global context of a particular patient (symptoms, viability, collaterals, left ventricular function…). The only classification which indicates the position of lesions and is easy to use in everyday life is the Medina classification [1]. It is comprised of three numbers and two commas. The first number represents the proximal main vessel segment, the middle number is the distal main vessel segment and the third number represents the SB. „1" accounts for the presence and „0" for the absence of > 50% stenosis. This classification was accepted by the general consensus from the second meeting of the European Bifurcation Club.

Pathology and physiology

Pathologic examination of coronary arteries and intravascular ultrasound studies reveals that location of the atherosclerotic plaques most frequently occurs in the lateral walls of both main vessel and side branches, while it is uncommon in the carina region [2].

Endothelial shear stress (ESS) is the tangential force exerted on the endothelial surface which results from the friction of the flowing blood. The pattern of fluid flow depends on the flow velocity and the presence of irregularities or obstructions. Flow is either laminar or turbulent. In a straight segment flow is laminar and undisturbed, and pulsatile ESS is varying between 15 and 70 dyne/cm^2 over the cardiac cycle. In irregular regions, like bifurcations, disturbed laminar flow (with areas of flow separation and recirculation) generate low and/or oscilatory ESS (< 10–12 dyne/cm^2). Low ESS typically occurs at the inner areas of curvatures and upstream of stenoses. Oscilatory ESS occurs primarily downstream of stenoses, at the lateral walls of bifurcations and in the vicinity of branch points. The wide angulation of the side branch take-off intensifies flow perturbations, increases the spatial ESS variations and low ESS in the lateral wall, thereby augmenting the atherogenesis. The ESS variations are augmented by pulsatile flow, which generates an oscilatory ESS and constitutes a proatherogenic factor. High heart rate prolongs the exposure of the coronary endothelium to the impaired systolic flow conditions of low and/or oscilatory ESS [3]. Regions exposed to the non-uniform and low shear stresses develop early atherosclerotic lesions (areas of minimum shear stress are mainly along the inner side of the curved coronary arteries) while areas exposed to uniform shear stresses (flow dividers) are usually, but not always, protected. Atherosclerotic plaque usually develops opposite the side branch and the same mechanism stimulates intimal hyperplasia and in-stent restenosis following stent implantation. Thus, high restenosis rates are expected with bare metal stents, which could be offset by drug eluting stent placement.

Although there is a correlation between the stenosis severity of the side branch (SB) and its physiological significance following stent implantation in the main vessel (MV), Koo has shown that about 70% of ostial SB lesions following MV stenting are not functionally significant. In this study [4], no lesion with < 75% SB stenosis by QCA had a fractional flow reserve (FFR) < 0.75. Wide variations in FFRs were shown even in SB lesions with > 75% stenosis by QCA suggesting that in some cases "significant" side branch lesions after main branch stenting should not be treated. On the opposite side, in this study, final kissing balloon inflation of functionally significant SB stenosis (FFR < 0.75), was associated with excellent clinical outcome. Therefore, FFR assessment of SB ostial lesions after MV stenting or the use of a better angiographic cut-off value may be advocated before stenting of the SB.

Fluid dynamics

In a conventional scheme of bifurcation the "main vessel" diameter is conserved before and after the origin of "side branch". The true representation of bifurcation is a mother vessel dividing into two daughter vessels. Strict relations are obtained between the flow rates and diameters of the three vessels. The diameter of the mother vessel is systematically greater than that of the larger daughter vessel. The sum of flow rates (Q) in two daughter vessels equals the flow rate in mother vessel (Qm = Qd1 + Qd2). Finet's adaptation [5] of Murray's law [6] calculates that the proximal mother (main) vessel is the sum of the daughter vessel diameters (distal main plus side) multiplied by 0.68 (Dm = 0.678*/D1 + D2/). This rule should be kept in mind: the proximal main vessels and distal main vessels are not of the same diameter (see the POT technique).

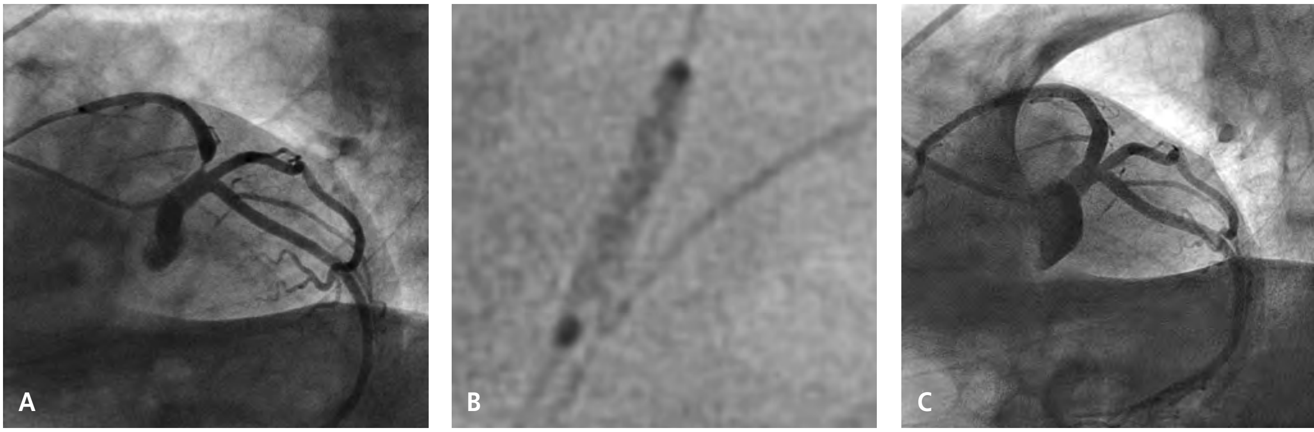


Fig. 1 – Single stent technique. Ostial LAD critical lesion, NSTEMI, Medina type 0,1,0 (A). Stent (DES 4.0/8 mm) positioned with an anchoring wire in the intermediate branch. The anchor wire is advanced through last proximal strut of the stent (after partial stent inflation and subsequent manual crimping – B). Final result after implantation (C).

Bench testing

In vitro bench testing of bifurcation stenting allows visualisation of stent deformations and lumen reductions after deployment of one or two stents into a silicone model tubes (anatomically correct phantoms). Virtual bench testing is a numerical technique using dedicated software to predict strut deformations occuring during bifurcation stenting in idealised or artificial models.

1. ***Stent design:*** one important factor is the size to which the stent cells can be expanded by balloon dilatation. Using stents with large cell sizes reduces the possibility of compromising SB lumen.
2. ***Single main vessel stenting:*** stenting over SB (without final kissing dilatation) leaves stent struts across side branch, which leads to disturbation of laminar flow, low ESS and recirculation, therefore increasing the risk of stent thrombosis and side branch stent restenosis. On the opposite, SB ostium dilatation produces MV stent distortion and malaposition opposite to SB [7] and must be corrected by final high pressure MV dilatation or final kissing inflation (FKI). For the stent cell design, optimal SB access is only when a cell is centrally placed with respect to the SB ostium. The amount of ostial SB scaffolding is affected by the site of guidewire recrossing and distal cell recrossing is recommended. Before recrossing, underdeployment of the proximal part of MV stent shoud be corrected by inflating short and bigger balloon just proximal to the carina with restoration of the original anatomical configurance (proximal optimization technique – POT).
3. ***T-stenting:*** the main problem of T-stenting is the precise placement of SB stent. A too distal deployment results in incomplete scaffolding, while too proximal leaves struts in the MV. Therefore the T-stenting with the small protrusion technique has been proposed (TAP-stenting). After MV stenting, the SB stent is positioned with a small protrusion to the MV with uninflated balloon within the MV before deploying the SB stent. After FKI a small neo-carina is present. This technique is usefull in bifurcations with wide angles (unless single stent strategy is not possible).
4. ***Crush stenting:*** complex stent deformations are induced by crush stenting. With the aim of providing complete ostium scaffolding gaps in strut scaffolding have been observed at the distal side of SB ostium after postdilatation. Despite optically good angiographical results, three layers of struts (and excessive drug release) in MV, difficulties in recrossing SB with excessive stent deformations are predictors of high stent thrombosis rate and restenosis [8].
5. ***Culotte stenting:*** this technique requires postdilatation through both the SB and MV stents to reduce the amount of "floating struts" with distal recrossing and FKI. Therefore stents with open cell design should be selected, this technique is usefull when dealing with large SB and sharp division angle [9].
6. ***V-stenting:*** this technique consists of simultaneous deployment of two stents from MV into two daughter vessels. These two stents form relatively long metallic "neo-carina" in the MV. A typical problem is uneven expansion in the MV segment, especially when using different stent sizes, and twisting of the stents. Although this technique is quick and easy, the substantial metallic carina predisposes to MV thrombosis.
7. ***Dedicated stent systems:*** *in vitro* testing may help to understand and improve the products in the early phase of their development.

IVUS, FFR and OCT in bifurcations

Coronary bifurcation lesion assessment with IVUS before intervention is valuable in angiographically intermediate lesions (to assess the severity of disease), left main (LMCA) lesions (characterising distal LMCA lesion signifi-

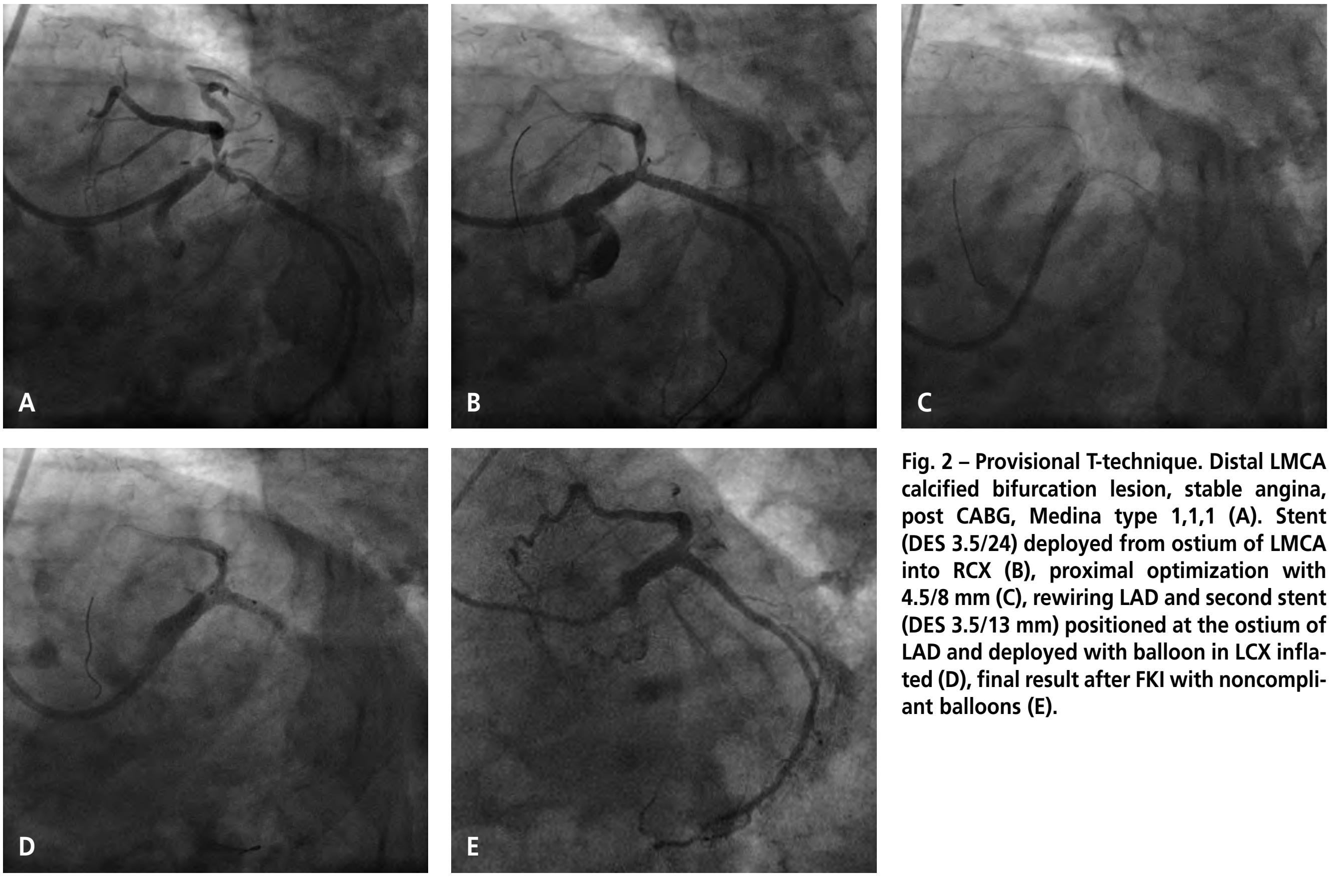


Fig. 2 – Provisional T-technique. Distal LMCA calcified bifurcation lesion, stable angina, post CABG, Medina type 1,1,1 (A). Stent (DES 3.5/24) deployed from ostium of LMCA into RCX (B), proximal optimization with 4.5/8 mm (C), rewiring LAD and second stent (DES 3.5/13 mm) positioned at the ostium of LAD and deployed with balloon in LCX inflated (D), final result after FKI with noncompliant balloons (E).

cance and morphology to ensure the lesion requires treatment) and ostial side branch lesions (to predict carina shift with increased risk of side branch occlusion). It has been demonstrated that IVUS determined minimal lumen diameter (MLD) and minimal lumen area (MLA) cut-off values of 2.8 mm and 5.9 mm^2, respectively, predict the physiological significance of a LMCA stenosis (well correlated with FFR cut-off point 0.75). IVUS guidance of PCI help to select the appropriate stent size and length, optimally expand the stent avoiding malposition and incomplete lesion coverage after stenting, especially in two stent techniques [10]. Stent underexpansion, incomplete coverage of the SB ostium, and stent deformations in the MV are predictors of restenosis and stent thrombosis. Routine use of IVUS in the unprotected LMCA interventions in the large MAIN-COMPARE multicentre registry showed a strong trend towards a lower mortality with IVUS guidance [11]. IVUS taught us about different stenting techniques and is used in a novel dedicated bifurcation stents (very low neointimal hyperplasia in the MV DES and dedicated Tryton SB stent as a result of optimal SB ostium scaffolding and radial diffusion of the antiproliferative drug).

Fractional flow reserve (FFR) represents the fraction of maximal myocardial flow that can be maintained in the presence of epicardial stenosis and is obtained by the ratio of distal coronary pressure and proximal coronary pressure. FFR can be used for the evaluation of the functional significance or the necessity of revascularization [12]. As the bifurcation lesion is basically the combination of three lesions, FFR overestimates the severity of SB lesion if there is a significant proximal stenosis. In contrast FFR underestimates the lesion severity when there is a significant distal lesion. It has been shown that geometric changes after MV stent implantation, carina shift and plaque shift are associated with SB jailing, but this is difficult to predict. Results from the Nordic Baltic Bifurcation III trial suggest that the angiographic evaluation overestimates the severity of jailed SB lesions and that functional status of jailed SB lesions after DES implantation does not change during follow-up [13]. Therefore only significant SB lesions (DS > 75% or FFR < 0.75) should be stented, this further emphasizes the role of simple stenting techniques. FFR for complex stenting strategies is not generally applicable for the complexity of procedure and difficulties of recrossing with FFR guidewire.

The optical coherence tomography (OCT) allows for assessment not just strut apposition (proximal MV, ostium of the SB, stent overlap), but also endothelisation at follow-up. It has been shown that paclitaxel eluting stents have the highest proportion of uncovered struts in the SB ostium, while sirolimus eluting stents in the main vessel opposite the ostium. This demonstrates some of the inadequacies of our existing stent technologies and the need of new bifurcation stenting technologies (dedicated DES). Routine clinical application of OCT is still limited [14].

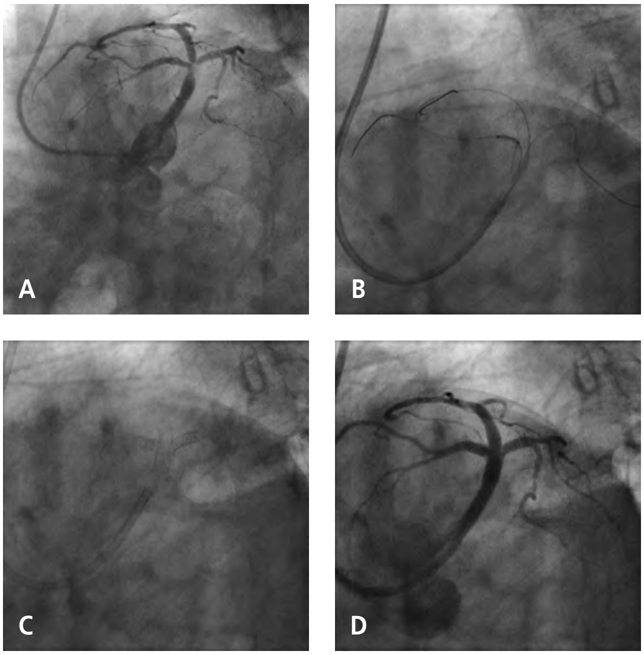


Fig. 3 – T and protrusion technique. Distal LMCA trifurcation, NSTEMI, Medina type 1,1,1,1, the biggest is intermediate branch (considered as MV – A). After stenting the intermediate branch (DES 3.5/20 mm across LAD and LCX), both SB rewired and sequentially stented (DES 2.5/8 mm in both branches) with a small protrusion into the main vessel (B). After double final kissing inflation small neo-carina is present (C, D).

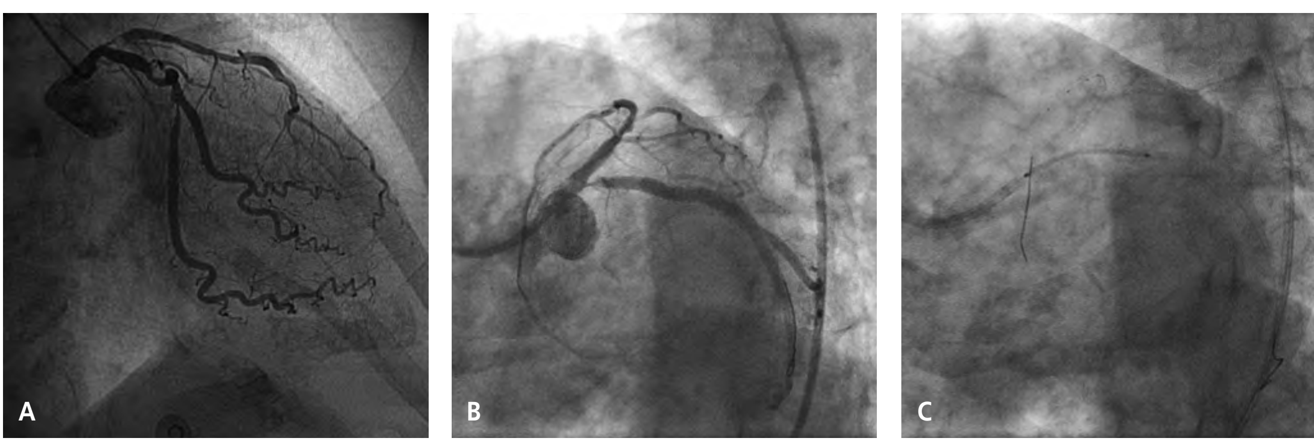
Techniques description

Stenting main vessel only

This is easy technique with single wire and MV stent across side branch, usefull in all 1,1,0, 0,1,0 or 1,0,0 lesions (Fig. 1A–1C). Stent size is respecting the distal MV diameter. To solve the problem of underdeployment of the proximal part of the MV stent inflation with a short and bigger balloon (0.5 mm bigger noncompliant balloon) just proximal to the carina is performed – so called proximal optimization technique (POT) to respect Murray's law (this also facilitates the insertion of the guidewire, balloon or stent into the SB). Final kissing is not mandatory, unless side branch is not large and significant – the role of FKI is to oppose struts over SB to vessel wall.

Final kissing inflation (FKI)

The final kissing inflation (FKI) is important to correct stent distortion and expansion, fully expanding the stent in the proximal MV where the diameter is much larger, providing better scaffolding of the SB ostium. The Nordic-Baltic Bifurcation study III looked at the role of FKI after MV stenting. The 6-month major adverse cardiac event rates were 2.1% and 2.5% (p = 1.00) in the FKI and no-FKI groups, respectively. At 8 months, the rate of binary (re)stenosis in the entire bifurcation lesion (MV and side branch) was 11.0% versus 17.3% (p = 0.11), in the MV was 3.1% versus 2.5% (p = 0.68), and in the side



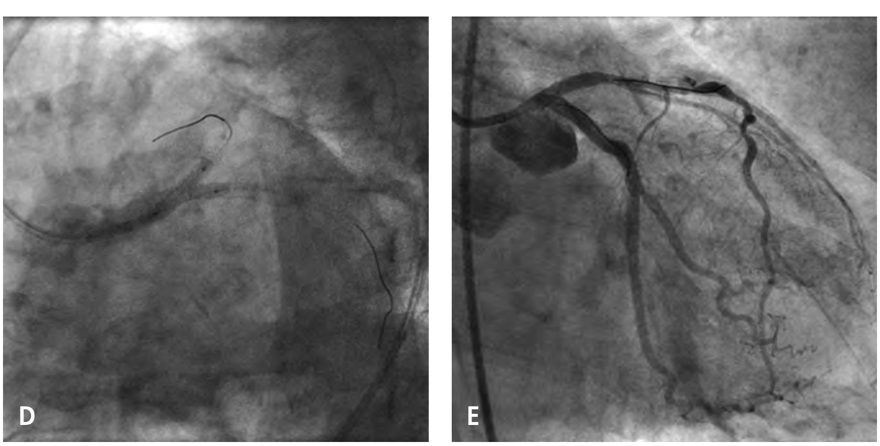


Fig. 4 – The culotte technique. Distal LMCA bifurcation lesion, Medina 1,1,1, diffuse mid LAD 70% stenosis, severe LCX/OM bifurcation lesion (Medina 1,1,0), diffusely diseased RCA, NSTEMI, SYNTAX Score 32, EuroScore 10.8% (A). After stenting LCx (DES 3.5/30 mm) with FKI, second stent (DES 3.5/24 mm) is positioned from ostium of LMCA into LAD and deployed (B). LCX is rewired and third stent (DES 4.3/24mm) is positioned from the ostium of LMCA into the LCx (C) and deployed. Final result after FKI with high pressure balloons (D, E).

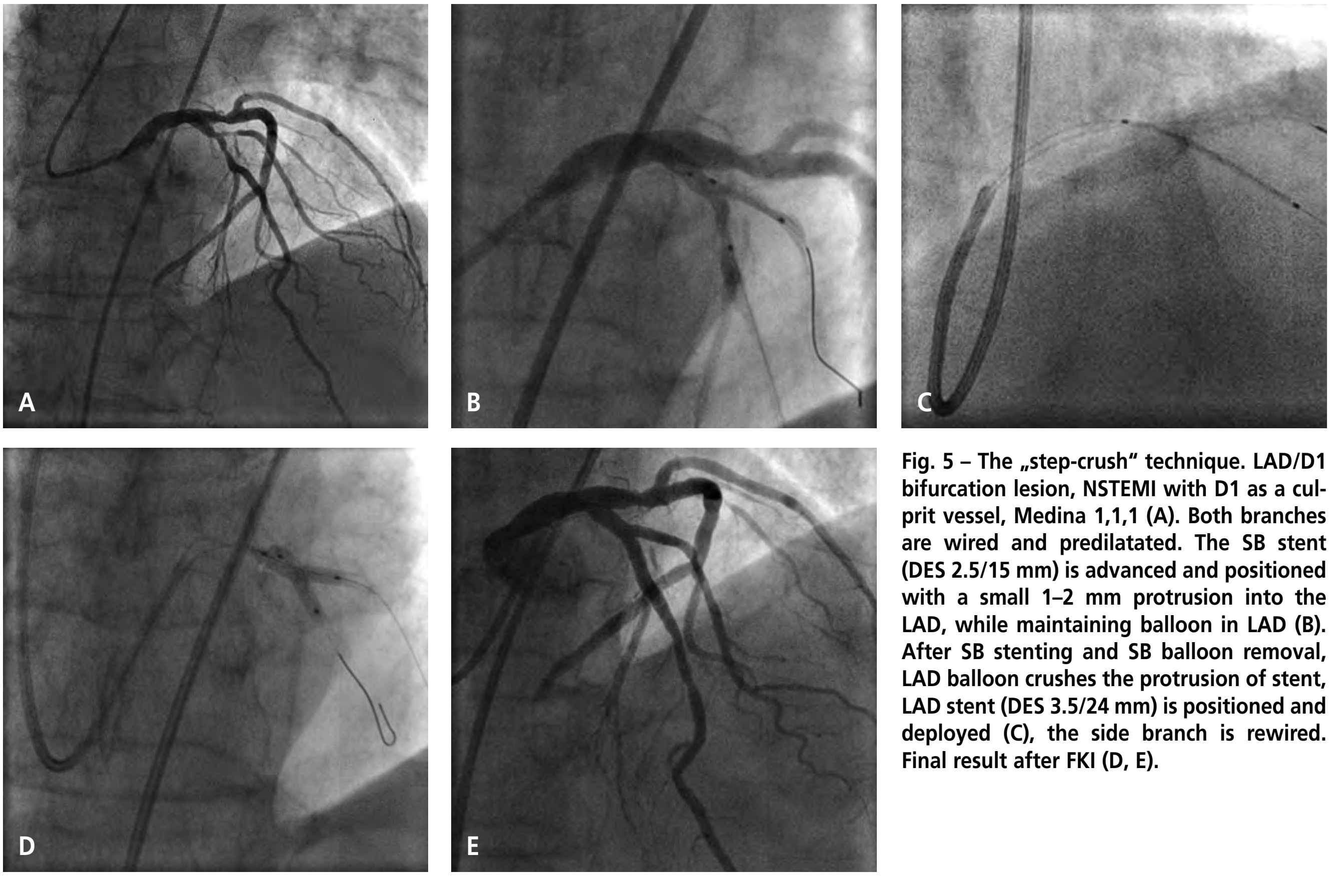


Fig. 5 – The „step-crush" technique. LAD/D1 bifurcation lesion, NSTEMI with D1 as a culprit vessel, Medina 1,1,1 (A). Both branches are wired and predilatated. The SB stent (DES 2.5/15 mm) is advanced and positioned with a small 1–2 mm protrusion into the LAD, while maintaining balloon in LAD (B). After SB stenting and SB balloon removal, LAD balloon crushes the protrusion of stent, LAD stent (DES 3.5/24 mm) is positioned and deployed (C), the side branch is rewired. Final result after FKI (D, E).

branch was 7.9% versus 15.4% (p = 0.039) in the FKI versus no-FKI groups, respectively. In patients with true bifurcation lesions, the side branch restenosis rate was 7.6% versus 20.0% (p = 0.024) in the FKBD and no-FKBD groups, respectively [15].

T-technique

This is the most frequently used technique with several modification from provisional stenting to stenting the SB and is most suited for bifurcations where the angle between the branches is close to 90°.

- Provisional T technique: place wire in the SB, second wire in the MV and stent the MV. If the SB result is unsatisfactory, use POT technique, rewire the SB through distal strut and after balloon dilatation implant second stent to the SB and perform FKI with high pressure noncompliant balloons (Fig. 2A–2E). Ideal technique to avoid the second stent, if the SB lesion is short (< 3 mm).
- Classical T-technique: position a stent at the ostium of the SB, avoid protrusion into the MV, deploy the stent and remove balloon. Advance and deploy the MV stent, re-wire the SB, remove jailed wire, perform SB dilatation and FKI.
- Modified T-technique: is a variation performed by simultaneously positioning stents in the SB and MV. The SB stent is deployed first, after balloon removal from the SB, the MV stent is deployed, followed by FKI. Ideal technique when the angle between the branches is close to 90°, larger guiding is required (7F). In lesions 0,0,1 useful technique, sometimes avoiding the MV stenting.

T and protrusion (TAP)

This is a modification of provisional T, compatible with 6 Fr guiding catheters. After the MV stenting the SB is wired (jailed wire removed), after balloon dilatation the SB stent is positioned with a small protrusion to the MV with uninflated balloon within the MV before deploying the SB stent. After FKI a small neo-carina is present (Fig. 3A–3D).

The culotte technique

It provides near perfect coverage of the carina and SB ostium with the best immediate angiographic results. Both branches are wired and pre-dilated. The first stent is deployed to the SB (most angulated branch), the MV is rewired ad dilated. The second one is deployed into the MV, the SB is rewired and FKI with noncompliant balloons at high pressure (> 16 atm) individually before last simultaneous inflation at 10 atm. Stenting the branch with the sharpest angle is recommended first, however in case of large dissection after predilatation there is a risk of closure of the secondly stented vessel and main vessel should be stented first (Fig. 4A–4E). The culotte technique is compatible with a 6 Fr guiding catheters.

The crush technique

It assures immediate patency of both branches – important when the SB is functionally relevant and difficult to wire. The classical crush technique has evolved and is performed with less SB stent protrusion into the MV – the *"mini-crush"*. Both branches are wired and fully dilated, the SB stent is positioned and the MV stent is advanced. The SB stent is pulled back to the MV about 1–2 mm (verified in 2 projections), deployed at least at 12 atm, balloon deflated and removed. Then the stent in the MV is deployed at high pressure. The SB stent is re-wired and two-step FKI performed – first step is dilatation of the stent towards the SB at 16 atm, then FKI with an inflation pressure 10–14 atm in both balloons. This technique can be used in almost all true bifurcation lesions but should be avoided in wide angle bifurcations. The main limitation is the need to re-cross multiple struts with wire and balloon to perform FKI. This technique, due to simultaneous advancement of two stents, requires 7 Fr guiding catheters. The *"step-crush"* is the modified balloon crush adapting this technique to a 6 Fr guiding catheters. This modification uses balloon instead of stent in the MV for crushing the protrusion of SB stent followed by positioning and deployment of the MV stent with FKI (Fig. 5A–5E). Another modification is the *double kissing crush* (DKI) as a modification of the step crush where kissing inflation is performed twice: firstly after the SB is crushed by the MV balloon and secondly the routine FKI at the end of procedure.

Simultaneous kissing stents (SKS) and V-technique

These techniques are performed by delivering and implanting two stents together. One stent is placed into the SB and the other into the MV. Both stents are pulled back to create a new carina (very short in V-technique and longer, double barrel in SKS technique), each stent is deployed individually at high pressure with medium pressure FKI. The V-stenting is relatively easy (usefull in emergencies) and ideal in Medina 0,1,1 lesions with large proximal MV free of disease (ostial LAD and LCX disease with short and large left main free of disease). The long-term risk of stent thrombosis is expected to be higher related to the unapposed and uncovered struts in the metallic neo-carina, in case of restenosis difficulties with re-crossing and frequent stent deformations requires converting to the crush technique.

One or two drug eluting stents

Drug eluting stents have been shown to minimize the angiographical and clinical restenosis by more than 80% and 50% respectively. With these stents several randomized studies in bifurcation lesions were published.

1. The NORDIC study used sirolimus eluting stents in a randomised comparison of main vessel stenting versus stenting of both MV and SB using several different techniques. Only 2.7% of patients randomized to MV stenting only received the second stent in the SB, MACE rate at 6 months was very low in both groups (2.9% vs 3.4% respectively). After 14 months the rates of MACE were 9.5% in the MV group and 8.2% in the MV + SB group (ns), no difference was found in stent thrombosis [16].
2. The BBC ONE study randomised patients with bifurcation lesions (82% true bifurcations 1,1,1–1,0,1 or 0,1,1) to a provisional T strategy versus complex culotte or crush 2 stents. The MACE rate was 8% for simple versus 15% for complex treatment, largely driven by a higher incidence of periprocedural myocardial infarction [17].
3. The CACTUS study compared crush stenting with provisional T strategy (FKI mandatory in both groups). The primary endpoint (6-month MACE) was not different (15% vs 16%) and there was no difference in the rate of restenosis [18].
4. The NORDIC stent technique study [19]: patients with a bifurcation lesions were randomized to crush and culotte stenting. At 6 months there were no significant differences in MACE rates between the groups; crush 4.3%, culotte 3.7% ($p = 0.87$). The rates of procedure-related increase in biomarkers of myocardial injury were 15.5% in crush versus 8.8% in culotte group ($p = 0.08$). Angiographically, in-stent restenosis was significantly reduced following culotte vs crush stenting (4.5% vs 10.5%, $p = 0.046$).

Metaanalysis of simple versus complex stenting strategy for DES treatment of coronary bifurcation lesions [20,21] revealed no significant differences with respect to the rates of cardiac death, target lesion revascularisation or definite stent thrombosis (ST). The restenosis risk of MV and SB did not differ between the simple strategy group and the complex strategy group. The risks of in-hospital or 30-day and follow-up myocardial infarction (MI) were markedly lower in patients treated with the simple strategy compared to the complex strategy. The simple strategy can be recommended as a preferred bifurcation stenting technique in the DES era and FKI is recommended to decrease side branch restenosis. Complex two-stent strategy is recommended if a SB stenosis exceeds 70% in diameter for more than 5 mm in length, supplying clinically significant territory of viable myocardium (> 2.5 mm in diameter). The ongoing BBC TWO and NORDIC IV are probably to be the last randomizing (non left main) bifurcations into one- versus two-stent strategy. Experienced operators use both of these techniques respecting more anatomy and physiology rather than selecting "simple" cases to avoid complex strategy. Dedicated bifurcation stents are expected to play a role, particularly for left main stem.

Left main coronary artery (LMCA)

Marked technical advances in PCI, stent technology, and availability of DES has led to re-evaluation of the role of PCI as a viable alternative treatment for unprotected LMCA disease. The choice of PCI or CABG depends on several clinical and anatomic features. PCI of unprotected LMCA disease has comparable safety and efficacy outcomes to CABG in following left main patient subsets: ostial and/or shaft left main disease, isolated left main disease, left main disease plus single vessel disease, distal bifurcation left main disease treatable by single stent (cross-over approach) and left main with low concomitant disease severity (SYNTAX Score < 23). However, true distal LMCA bifurcation lesions require unique and more integrated approach that combines more advanced devices with specialized techniques, adjunctive imaging support as well as adjunctive pharmacologic agents. Respecting the geometry and stent design, the T-stenting and culotte stenting IVUS assisted techniques are recommended on the basis of vessel size, bifurcation angulation and degree of obstruction of the SB. In a recent metaanalysis of four randomized trials at 12-month follow-up PCI, as compared to CABG, was associated with a significant risk reduction of stroke (0.12% vs 1.90%, $p = 0.004$), with an increased risk of repeat revascularization (11.03% vs 5.54%, $p < 0.001$) and similar risk of mortality and myocardial infarction [22–25]. Large randomized trial is ongoing (EXCEL) and dedicated LMCA bifurcation stents are currently being explored (Axxess stent, Tryton stent).

Dedicated bifurcation devices

Many devices are already under clinical investigation [26]. They may be devided into 4 groups: 1. devices treating the MV with some degree of SB scaffolding (XIENCE SBA, STENTYS, Petal, Twin-Rail, Nile), 2. side branch stents (Sideguard, Tryton), 3. proximal bifurcation stents (AXXESS), 4. bifurcated stents (Medtronic).

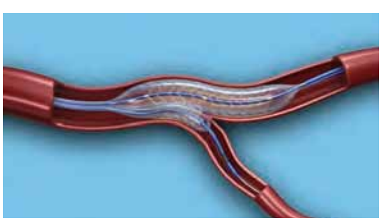


Fig. 6 – The XIENCE SBA Stent.

The XIENCE SBA (side branch access) is a modified Xience V-stent designed with an open portal for side branch access (Fig. 6). It is a double balloon, single shaft delivery system (similar to the FRONTIER stent). The stent is a cobalt-chromium DES (everolimus, permanent polymer) 18 mm in length and 2.5 and 3.0 mm in the MV diameter. After predilatation of the MV and the SB, the stent is delivered over a rapid exchange single extra support wire into the MV beyond the SB, then the joining mandrel is removed to separate the tip of the SB balloon, stent is pulled back and second wire (300 cm, OTW) is positioned into the SB (with careful rotation to prevent wire twisting). Then the device is advanced into the bifurcation, forward tension is held to maintain the position and stent is deployed by inflation through a single inflation lumen. Compatible with 6 Fr guiding catheters.

The STENTYS Self-Aposing Stent is a self-expandable nitinol closed cell design stent intended for side branch angulation between 30 and 70 degrees. The stent conforms to the shape of the artery and is available in three diameters (2.5–3.0 mm, 3.0–3.5 mm and 3.5–4.5 mm), two lengths (22 mm and 27 mm) and BMS or DES (paclitaxel 0.8 μg/mm^2) versions. At the carina, after disconnection, the stent expands to a maximum of 6.6 mm. The rapid-exchange delivery system allows the stent to be positioned and delivered in the MV by withdrawing a retractable sheath, disconnection at the SB is done by wire crossing at the carina level and balloon dilatation. If needed, any stent can be deployed into the SB (Fig. 7). In an APPOSITION II randomized trial the stent showed a 10-fold reduction in stent strut malposition compared to balloon expandable stents. Compatible with 6 Fr guiding catheters.

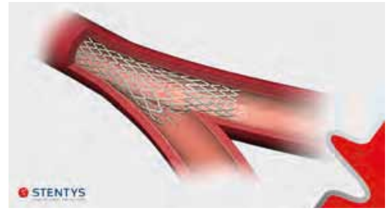


Fig. 7 – The STENTYS Self-Aposing Stent.

The Sideguard Stent is a bare 8 or 14 mm long self--expanding nitinol stent indicated for bifurcation angles from 45 to 135 degrees. It flares proximally at the ostium of the SB into a trumpet shape to achieve full ostial coverage (Fig. 8). After predilation of the SB the Sideguard Stent is advanced while three proximal and two distal radiopague markers aid positioning of the stent and allow angiographic visibility post implantation. Inflation of the balloon tears the protective sheath that enables self expansion of the Sideguard Stent. The delivery system and the guidewire are removed from the SB and main vessel is stented. Available in three sizes 2.5 mm, 2.75 mm, and 3.25 mm, compatible with 6 Fr guiding catheters.

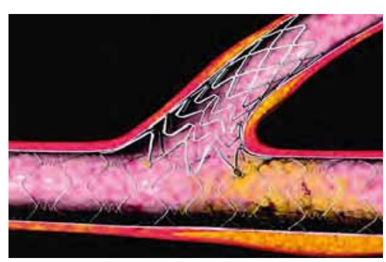


Fig. 8 – The Sideguard Stent.

The Tryton Stent is a balloon expandable cobalt chromium side branch stent with free distinct zones: a distal SB zone (slotted tube design), a central transition zone (three panels) and proximal MV zone (free undulating fronds that terminate proximally in two wedding bands). The stent is available in one length of 19 mm (the SB zone is 8 mm long) premounted on a stepped balloon with the SB diameters of 2.5 mm, 3.0 mm and the proximal diameter of 3.0 mm and 3.5 mm. After wiring of both the MV and SB and predilatation, the Tryton stent is advanced into the SB and positioned till two middle markers straddle the SB origin. After deployment the SB wire

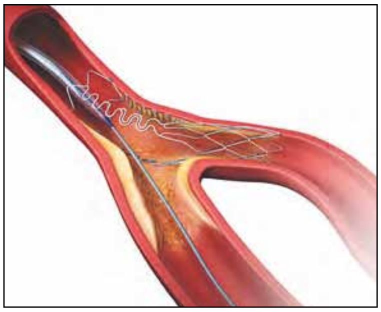


Fig. 9 – The Tryton Stent.

is retracted and repositioned through the fronds into distal MV, main vessel DES is advanced and deployed with recrossing the SB and FKI (Fig. 9). This stent can be used in a wide range of bifurcation angles, locations as well as for left main stenting (3.5–4.0 mm version). Compatible with 6 Fr guiding catheters.

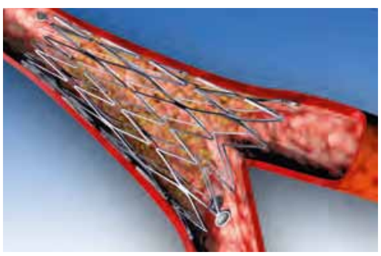


Fig. 10 – The AXXESS Stent.

The AXXESS Biolimus A9 Eluting Coronary Bifurcation Stent System is a self-expanding conically shaped laser--cut nitinol drug eluting stent with 150 μm strut thickness on a rapid exchange delivery system upon withdrawal of a cover sheath. Optimal deployment is guided by progressive flaring of three gold markers to effectively cover the proximal part of the MV and protrude over carina level (Fig. 10). The current version can accomodate vessels from 2.75 mm to 4.25 mm in two lengths (10 and 14 mm), special version is available for left main bifurcation lesions (up to 4.75 mm). Delivery is through a 7 Fr approach, after the proximal MV stenting one or two conventional DES is deployed into the distal MV and the SB respectively.

The Medtronic Bifurcation Stent System is a bare metal (cobalt based alloy) Y-shaped stent that consists of a 12-crown 7 mm proximal main vessel section, an

Fig. 11 – The Medtronic Bifurcation Stent System.

8-crown 4 mm side branch section and 8 mm distal main vessel section available in two versions, one with a proximal MV diameter of 3.8 mm, distal MV 3.0 mm and SB 2.5 mm, and the other with a proximal MV diameter of 4.3 mm, distal MV 3.5 mm and SB 2.5 mm. The stent is pre-mounted on a dual rapid exchange delivery system, uses two balloons (the SB balloon uses a stepped design to match the anatomy) compatible with 8 Fr guide catheters (Fig. 11). This device is intended for bifurcation angles less than 90 degrees. Like other self-alignment devices (Taxus Petal, Nile-PAX, Twin-Rail, Trireme, Side--Kick) guidewire twisting may limit proper stent positioning with the risk of miss alignment, especially when the vessel is calcified or tortuous, with a disappointing rate of device success.

Practical tips

When planning an interventional strategy for bifurcation lesion PCI several practical tips are recommended by the consensus from the 2nd and the 5th European Bifurcation Club meetings [27,28].

1. The proximal MV diameter is larger compared to distal MV diameter (by Murray's law), the primary stent should be sized according to the distal MV diameter and proximal MV segment should be postdilated with larger (or kissing) balloon inflations to optimize the proximal stent diameter (the POT technique).
2. Side branch diameter and area of muscle mass are responsible for functional significance of the SB.
3. Side branch lesion severity, length and the angle of bifurcation are responsible for selection between one or two stent strategy.
4. Jailed wire technique should be routinely used in functionally significant SB and in SB lesions whose access is particularly challenging.
5. The POT technique should be used prior to wire recrossing into a SB, efforts should be made to cross the main vessel stent distally, thereby ensuring stent coverage of the ostium of the SB (last strut technique).
6. The T-techniques remain the gold standard for most bifurcations with a single stent implantation.
7. FKI should be used when an angiographically significant (> 75%) SB lesion remains after main vessel stenting and is mandatory in all unprotected LMCA bifurcations.
8. Large side branches with ostial disease extending > 5 mm from the carina are likely to require a two/stent strategy. When two stents are required, the culotte technique offers advantages over crush stenting.
9. FKI is mandatory in any two/stent techniques with individual non-compliant high pressure ostial postinflations and final high pressure proximal MV stent inflation to correct possible MV stent distortion.
10. Dedicated bifurcation stent systems remain limited but are likely ultimately to prevail.

Conclusions

The strategy of provisional SB stenting is widely accepted in suitable bifurcation lesions and is accompanied by low rates of stent thrombosis. However it is not applicable to all lesions and clinical situations and 10% or more require two stents. To avoid excessive metal scaffolding, the classical crush technique should be avoided, replaced by culotte, T and protrusion or mini-crush techniques. Dedicated bifurcation devices must improve procedural outcome by simplifying the intervention and enhancing its safety to gain wider acceptance. Distal LMCA bifurcation lesions require unique approaches, more advanced devices and adjunctive imaging for optimal result. In the meantime maintenance of dual antiplatelet therapy without interruption with optimal duration at least 12 months is mandatory.

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