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Review

Coronary bifurcation lesions: Present status and future perspectives

Massoud A. Leesar [a,*], Abdul Hakeem [b], Kasra Azarnoush [c], Leif Thuesen [d]

[a] University of Alabama at Birmingham, United States
[b] University of Arkansas Health Sciences Center, United States
[c] Clermount-Ferrand University Hospital, France
[d] Aarhus University Hospital, Denmark

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ABSTRACT

Coronary bifurcation lesions (CBLs) are challenging and associated with a higher rate of adverse events than non-bifurcation lesions. In the era of drug-eluting stents, 2 primary interventional strategies for treating CBL include the complex strategy – the main vessel (MV) and side-branch (SB) stenting, and the simple strategy – MV stenting combined with provisional SB stenting. The meta-analysis of the simple vs. complex strategies demonstrated an increased incidence of myocardial infarction in the complex strategy. Likewise, the Tryton dedicated bifurcation stents, as compared with the simple strategy, increased the rate of myocardial infarction. In contrast, the Nordic–Baltic Bifurcation Study IV demonstrated that event rates were not significantly different comparing the simple vs. complex strategies in true bifurcation lesions involving a large SB. Fractional flow reserve (FFR) has emerged as a powerful catheter based tool for the functional assessment of a stenosis, but the role of FFR on the long-term outcomes of patients with CBL has not been studied. Given the recent evidence that Tryton stents (a dedicated bifurcation stent) increased event rates, and the lack of benefit from using 2-stent techniques (the Nordic Baltic Bifurcation Study IV) in true CBL, assessing the FFR of the SB seems now of outmost importance, but randomized data are lacking. An intravascular study showed that kissing balloon inflation (KBI) significantly reduced SB stenosis, restored stent lumen at the carina, and expanded stent in the proximal segment. However, a recent randomized study showed no significant benefit of routine KBI. This review highlights current concepts and future perspectives in patients with CBL.

1. Introduction

Coronary bifurcation lesions (CBLs) represent a technical challenge in percutaneous coronary intervention (PCI) [1–5]. Thus far, no uniform strategy has been established for the optimal management of CBL [6–11]. The treatment of CBL is associated with a relatively high rate of restenosis, myocardial infarction, and stent thrombosis [7,8]. Approximately 15% of all PCIs performed in the U.S. involve CBL. Furthermore, these lesions are referred for bypass surgery, particularly when they are located in the left main or left anterior descending coronary artery (LAD) [4,9]. In a large meta-analysis [10], CBLs were independent predictors of stent thrombosis, a complication that was associated with a 45% mortality rate. The STENT Study (Strategic Transcatheter Evaluation of New Therapies) [11] demonstrated that the 2-year major adverse cardiac event rate with drug eluting stents (DES) in CBL was significantly higher than in non-bifurcation lesions.

Approximately 1,313,000 PCIs were performed in the United States in 2006 [12] with an estimated cost of $22 billion. Given that the average 1-year cost of stenting per patient is approximately $16,813, the cost of PCI on bifurcation lesions is estimated to be $4.4 billion [13], but there is no established "optimal" treatment strategy, probably because, CBLs are characterized by both complexity and diversity and the lack of large randomized trials with long-term follow-up. Consequently, several techniques have been advocated by individual operators based on personal preference [1,2,4].

2. Randomized trials of coronary bifurcation lesions

The main vessel (MV) stenting may shift the carina to the side-branch (SB) and results in an apparently significant SB stenosis. Hence, kissing balloon inflation (KBI) or SB stenting is often undertaken to improve SB stenosis determined by angiography. In the era of DES, the two primary interventional strategies for managing CBL include the complex (2-stent) strategy – MV and SB stenting, and the simple (provisional) strategy – MV stenting combined with provisional SB stenting depending on the angiographic SB lesion severity after MV stenting.

A number of randomized trials compared the simple with complex strategies for the treatment of CBL (Table 1) [14–20]. Among these trials, there is a significant variability with respect to event rates. In the

* Corresponding author at: University of Alabama at Birmingham, 510 20th street South, FOT-920, Birmingham, AL 35294, United States.
E-mail address: mleesar@uab.edu (M.A. Leesar).

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Table 1
Summary of event rates comparing randomized bifurcation studies.

Trial	Complex MACE	Simple MACE	P	No of patients Complex/simple	Follow-up Months
CACTUS [14]	15.8%	15%	NS	173/177	6
Colombo et al. [15]	23%	22%	NS	63/22	6
Pan et al. [16]	8.5%	7%	NS	47/44	6
Ferenc et al. [17]	12.9%	11.9%	NS	101/101	6
NORDIC [18]	3.4%	2.9%	NS	207/206	6
NORDIC [19]	21.8%	15.8%	NS	202/202	60
BBC-ONE [20]	15.2%	8.0%	0.009	249/248	9

CACTUS (Coronary Bifurcation Application of the Crush Technique Using Sirolimus-Eluting Stents) trial [14], event rates were relatively high and similar following the complex vs. simple strategies. In the German BBK study by Ferenc et al. [17], event rates were intermediate and did not differ between the complex vs. simple strategies. In the Nordic trial (The Nordic bifurcation trial) [18], the rates of major adverse cardiac events (MACE), irrespective of the strategy employed, were low and similar in the two treatment groups. Likewise, the 5-year follow-up of the Nordic trial [19] demonstrated that the composite rate of MACE was not significantly different comparing the simple strategy vs. complex strategy. In contrast, in the BBC ONE (British Bifurcation Coronary Study: Old, New and Evolving Strategies) trial [20], event rates were lower in the simple strategy primarily due to the reduced rates of procedural related myocardial infarction.

The meta-analysis [6] of the above-mentioned randomized trials [14–19] demonstrated that the 2 CBL treatment strategies resulted in similar outcomes in terms of risk of cardiac death, target lesion revascularization (TLR), and stent thrombosis. However, the rate of periprocedural myocardial infarction was significantly higher in the complex vs. simple strategies based on the BBC-ONE study [20]. Likewise, Zimarino et al. [21] performed a meta-analysis of 12 major bifurcation studies with inclusion of 6961 patients and demonstrated that the complex strategy, compared with the simple strategy, was associated with an increased incidence of MI, likely driven by stent thrombosis.

A number of non-randomized series reported that dedicated bifurcation stents can be safely deployed in patients with CBL with good outcomes, but the randomized Tryton Bifurcation trial was presented at the TCT 2013 meeting and demonstrated that the Tryton stent (a dedicated bifurcation stent), compared with the simple strategy in 704 patients, did not meet the non-inferiority end-point and increased the rate of myocardial infarction. Along the same line, Dubois et al. [22] performed optical coherence tomography (OCT) 9 months after Tryton stenting in the bifurcation lesions and showed a high proportion of malapposed struts in the proximal MV and restenosis in the SB because the side-branch portion of the Tryton stent is a bare-metal stent. They concluded that such OCT results do not fulfill expectations of a dedicated bifurcation stent.

Taken together, the above randomized trials and the meta-analyses of bifurcation trials demonstrated that event rates were significantly higher in the complex compared with simple strategies. Even patients with true bifurcation lesions involving a large side-branch did not achieve a significant benefit comparing the complex vs. simple strategies. Likewise, Tryton dedicated bifurcation stent increased the complexity of procedure and the risk of myocardial infarction. Thus, the simple strategy with provisional side-branch stenting is now considered a preferred strategy. On the other hand, in the presence of a long lesion or dissection in the SB, a 2-stent strategy is needed to obtain optimal results.

3. The safety of jailing a guidewire in the SB

Protecting the SB with a guidewire to prevent the closure of the SB is very important because it has been shown that SB compromise is not inconsequential. The occlusion of a SB >1.0 mm has been associated with a 14% incidence of myocardial infarction [23,24], and the occlusion of a SB >2.0 mm during the simple strategy can be associated with a large periprocedural myocardial infarction [25]. The jailed SB wire would facilitate rewiring of the SB by widening the angle between the MV and SB [26] and prevent SB occlusion after MV stenting. Furthermore, Hahn et al. [27] reported that SB occlusion occurred in 187 of 2227 (8.4%) bifurcation lesions after MV stenting and that increased the rate of death, MI, or stent thrombosis. They also showed that jailed guidewire in the SB was associated with significant flow recovery in the SB and no incidence of wire trapping or fracture of the jailed guidewire was noted. Therefore, routine guidewire jailing in the SB with the use of simple strategy in patients with CBL is the key to keep the SB open and to prevent death or MI. Jailed polymer-coated guidewires can be pulled from underneath the stent easier than other wires. However, jailing of polymer-coated guidewires in the SB can lead to polymer shearing. We [28] compared the rate of polymer shearing in 2 commonly used polymer-coated guidewires (Whisper wire versus Terumo Runthrough wire) after jailing underneath the stent to protect the SB occlusion during MV stenting. We examined the distal 15 cm of the jailed guidewires with a scanning electron microscope and demonstrated no incidence of wire fracture by microscopic examination, however, the Whisper wire had higher area and length of polymer shearing as compared with the Runthrough wire [Fig. 1]. In this respect, the impact of polymer shearing on the periprocedural myocardial infarction will need to be investigated in randomized trials.

4. Management of side-branch stenosis after the main vessel stenting

There are no established guidelines for the treatment of SB stenosis after MV stenting and the visual assessment of SB stenosis is a challenge. The definition of a suboptimal SB results after MV stenting or KBI varies among randomized CBL trials [14–20]. Most studies used >50–60% residual stenosis of the SB as indication for SB stenting (Table 2). This definition had a major impact both on crossover rate from a one-to a- two-stent strategy ranging from 2.1% to 51.2%. In the Sirius Bifurcation study [15], a residual SB stenosis of >50% required SB stenting and resulted in a

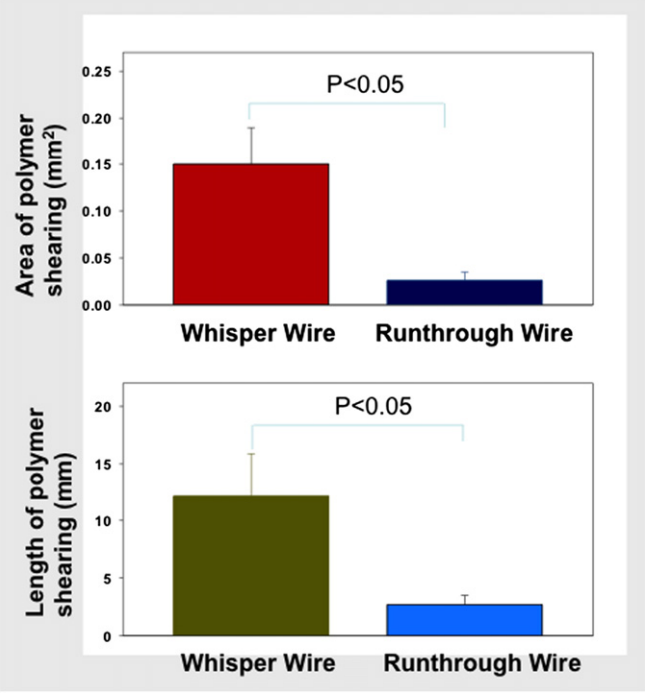

Fig. 1. Shows that the area and length of polymer shearing were significantly higher with Whisper wire than with Runthrough wire.