**VM VIA MEDICA**

EDITORIAL

# "The significant other": Evaluation of side branch ostial compromise in bifurcation stenting

Tinen L. Iles[1], Goran Stankovic[2], Jens Flensted Lassen[3]

[1]Visible Heart Laboratories, Department of Surgery, University of Minnesota, Minneapolis, MN, United States
[2]Department of Cardiology, Clinical Center of Serbia and Faculty of Medicine, University of Belgrade, Serbia
[3]Department of Cardiology B, Odense University Hospital and University of Southern Denmark, Odense, Denmark



## Article p. 507

*"Everything is nothing with a twist"*
Kurt Vonnegut

## Background

The overall numbers of percutaneous coronary interventions of bifurcation lesions continue to increase worldwide. Interventions however, remain challenging. Despite an increasing anatomical and physiological understanding of the dividing coronary tree and a fast-growing refinement of stenting techniques for bifurcation lesions, there remains a risk of side branch (SB) ostial compromise or in the worst-case scenario, SB closure during stent implantation [1]. Evaluating the risk of SB compromise or closure during bifurcation stenting is one of the major considerations when planning the procedure. Furthermore, deciding which coronary bifurcation lesions that require an elective two-stent procedure, because of the risk of SB closure, remains a fundamental controversy worldwide [2]. The European Bifurcation Club recommends a provisional stenting approach to most bifurcation lesions, the philosophy is to keep the procedure as simple as possible (but not simpler). It is recommended that the operator use two wires (with the SB wire, as protection for potential rescue procedures should the SB close). The procedure can then develop from one initial stent in the main branch (MB) across the SB. The stent is recommended to be implanted with respect to the distal diameter of the MB. According to the philosophy of provisional step-wise bifurcation stenting, the implantation of the initial stent is finalized by the proximal optimization technique to correct the proximal stent malapposition and to open stent struts towards the SB. Thereafter the SB is only treated (by balloon dilatation, kissing balloon dilatation or stenting) if needed [2, 3]. By using this approach, it is possible to reduce number of stents needed and layers of metal composites in the coronary vessels, minimizing long-term risks and optimizing angiographic outcomes and the procedure is also cost-effective [4].

---

Address for correspondence: Jens Flensted Lassen, MD, PhD, Department of Cardiology B, Odense University Hospital and University of Southern Denmark, Odense, Denmark, e-mail: Jens.Flensted.Lassen@rsyd.dk

Evaluation of whether or not to leave the SB without intervention when the SB ostium is impaired after MB stent implantation is a crucial step in the provisional approach. The angiographic evaluation (quantitative coronary assessment [QCA], eye balling) is difficult and can be misleading. Fractional flow reserve (FFR) evaluation carries a risk of compromising the SB by dissection during rewiring and FFR evaluations in bifurcations, which can be misleading because of signal crosstalk [4]. Accordingly, a deeper anatomical and physiological understanding of the stent — vessel wall interaction and its role in SB ostial compromise during stent implantation is needed.

## A novel mathematical approach to understanding SB compromise in bifurcation stenting

In this issue of 'Cardiology Journal', Vasilev et al. [5] present an excellent mathematical model and validation to understand the mechanism of SB compromise after MB stenting. The authors took an elegant approach to demonstrate that there is a severe overestimation of stenosis severity when the areas are estimated to be circular (mathematically) instead of an oval. This provides novel insight into the evaluation of SB compromise after stenting the MB across the SB. By bringing the clinical observations of the SB ostium from three-dimensional fluoroscopy reconstructions the authors quantitatively replicated the natural physiology and describe the flow reduction over the compromised SB ostium. These precise measurements described and calculated comparison highlights the multifactorial elements in SB compromise during stenting, and thereby increases the understanding of the final interaction between the stented segment and the paired anatomic and physiological system.

The model was accomplished through utilizing patient QCA analyses data from a clinical trial to test the hypothesis that accounting for the elliptical SB anatomy would elucidate the most accurate prediction of stenting strategy. FFR data was collected and mathematically determined the square area of the SB before and after stenting. Subsequently, three quantitative approaches were utilized to determine the most accurately representative approach in calculating the cross-sectional area.

The authors took significant quantitative considerations; it was accurately pointed out that previous works considered the primary equation to identify the ostial dimensions transcendental functions. However, the function described in these previous works do not satisfy the polynomial equation [6]. Uniquely, the authors have circumnavigated these pitfalls in detail, the basics of the assumptions were: 1) Circular SB ostium shape after main vessel (MV) stenting was in a standard estimate of SB ostial stenosis; 2) Elliptical ostium shape at SB assumed after MV stenting accounting for SB reference diameter, taking into account for long axis ellipse; 3) Elliptical ostium shape at SB assumed after MV stenting, calculated with minimal lumen diameter at SB ostium before stenting, considered for long axis ellipse calculation (Fig. 1) From this validation set, the authors concluded that the stenosis area was significantly larger when utilizing the circular formula when compared to the elliptical formula demonstrating a value of considering the mathematics in clinical decision-making (Fig. 1).

A consequence of solving for the elliptical area inadvertently sheds light on the quantitative effect of over dilation of the distal SB. Although the authors main focus was to better understand SB compromise and a true reflection of the ostial area, solving for this utilizing the clinical QCA data describes the close approximation from the Ramunjun formula. Thus, optimizing many of these parameters is highly important to transform the clinical observations into something that is possible to computationally simulate [7, 8].

## Translating the quantitative approach to SB ostial impairment into clinical practice

The cause of SB compromise during stenting of the MV has been attributed to as well, plaque shift from the MV into the SB as to carina shift due to pushing of the carina tip into the ostium of the SB during stent implantation. The coronary arteries divide in a fractal manner and the diameter of the branches correlate to the physical principle of minimal workload [9]. Because of these underlying biological principles, the coronary vessels taper (Fig. 1). This phenomenon is most prevalent after takeoff of a SB resulting in discrepancy in vessel diameter between the proximal vessel and the distal vessels in a bifurcation. If a tubular stent is implanted across the SB and implanted with respect to the proximal diameter of the MB it will be over-dilated in the distal MB, thereby increasing the risk of SB ostial compromise. The vessel will be overstretched in the area immediately below the takeoff of the SB, increasing the risk for an overstretched oval deformation and consequently
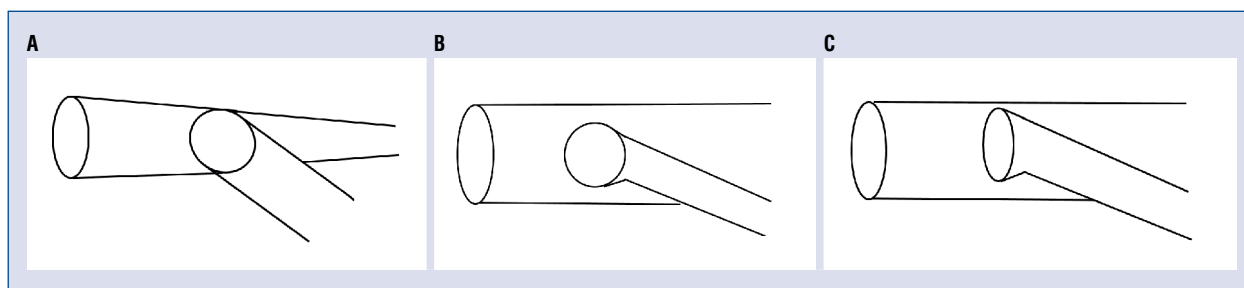
**Figure 1.** Quantification of ostial shift and effect on side branch (SB) shape by distal main branch (MB) over dilation. **A.** Tapered nature of MB. The formula Ac = $\pi$.ds$^2$/4 assumes the SB is circular and ds is the reference SB; **B.** Main branch after stenting with stent dilatation according to the proximal MB diameter. The SB diameter, ds, was taken as a reference in those calculations. The respective area stenosis (AS) was calculated as ASds = (1–Ae1/Asb) × 100, where ASds is ostial elliptic AS of the SB, Ae1 — SB calculated ostial area, Asb — reference SB vessel area (calculated based on vessel diameter 1 mm distal from the end of visually diseased end of plaque segment); **C.** Main branch after stenting with stent dilatation according to the proximal MB diameter, taking into account the overstretching of the distal part of the vessel, with oval transformation of the SB ostium. For the third calculation of SB ostial area after stenting, the same assumptions and formulas were used as in the second, but as a reference diameter instead of SB reference diameter the SB ostial minimal lumen diameter before stenting was used (i.e. this is the minimal lumen diameter before stenting, as measured from quantitative coronary assessment). The corresponding AS was labeled ASmld = (1–Ae2/Asb) × 100, where ASmld is ostial AS (in percentages), Ae2 — ostial SB area calculated according to the above assumptions, Asb — as above.

introducing the "nipping" appearance of the SB ostium, as seen on the angiograms (Fig. 1). It seems most likely that ostial compromise is due to mechanistic overstretching of the vessel by the stent implantation that will bring the circular ostium to an oval form. Plaque shift due to the reorganizations of the soft plaque by the pressure applied during stent implantation as well as the carina shift, partly due to overstretching and partly due to to pushing the carina toward the SB, which are likely to add to ostial compromise.

Vasilev et al. [5] shall be congratulated for bringing the SB ostial compromise attributed to distal vessel overstretching, during stent implantation into mathematical formulas. This achievement has clarified the mechanism behind the clinical optical coherence tomography observation of elliptical stretch and deformation of the SB ostium and increased understanding of SB ostial compromise. Furthermore, the formulas have founded the base for realistic calculations of cross-sectional area of the compromised SB ostium and thereby made it possible to evaluate the resulting FFR by simulation and explain the observed deviations from the actual measured FFR values calculated with the assumption of a circular SB ostium. In conclusion, mathematical modeling has increased the understanding of device and vessel wall interaction and made the simulation of the consequences of SB compromise possible.

## Future applications for mathematical modeling in bifurcation stenting

There are distinct advantages to leveraging mathematical models over computational fluid dynamics and other computational tools in certain aspects of clinical research. In this example, quantitative analysis was beneficial and acted as a powerful tool that both validates the peri-procedural work, provides evidence for our intuition and guides in clinical decision-making. In the future, this mathematical analysis may merge with fluid dynamics and other computational tools in order broaden the whole picture, merging multi-physics models, that couple contraction, electrophysiology and flow with a quantitative analysis within the procedure [7–9]. Therefore, mathematical modeling can be a cornerstone for translating biological observations into formulas that can be validated by simulation and broaden our view and understanding of device vessel wall interaction during stent implantation.

In an overall conclusion, numerical analysis, mathematical modeling and computational simulation has the potential to be the tool of choice in the evaluation of various technical issues and their relation to function and outcome in bifurcation stenting. The advancement of supercomputers can maximize the output and improve simulation by expansion. By including boundary conditions and

flow parameters that are more precise and based on mathematic modeling as part of the models, the possibility to test and simulate anatomy that is more realistic and physical conditions are widely open. By following this path, the future is open to integrate anatomy, physiology and device interactions in the simulations to finally mimic the laws of nature and improve stent implantation in coronary bifurcation lesions.

**Conflict of interest:** None declared

## References

1. Lassen JF, Burzotta F, Banning AP, et al. Percutaneous coronary intervention for the left main stem and other bifurcation lesions: 12th consensus document from the European Bifurcation Club. EuroIntervention. 2018; 13(13): 1540–1553, doi: 10.4244/EIJ-D-17-00622, indexed in Pubmed: 29061550.

2. Burzotta F, Lassen JF, Louvard Y, et al. European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. Catheter Cardiovasc Interv. 2020 [Epub ahead of print], doi: 10.1002/ccd.29071, indexed in Pubmed: 32579300.

3. Iles TL, Burzotta F, Lassen JF, et al. Stepwise visualisation of a provisional bifurcation stenting procedure - multimodal visualisation within a reanimated human heart utilising Visible Heart methodologies. EuroIntervention. 2020; 16(9): e734–e737, doi: 10.4244/EIJ-D-19-00606, indexed in Pubmed: 31951206.

4. Banning AP, Lassen JF, Burzotta F, et al. Percutaneous coronary intervention for obstructive bifurcation lesions: the 14th consensus document from the European Bifurcation Club. EuroIntervention. 2019; 15(1): 90–98, doi: 10.4244/EIJ-D-19-00144, indexed in Pubmed: 31105066.

5. Vassilev DI, Kassab GS, Collet C, et al. Elliptical stretch as a cause of side branch ostial compromise after main vessel stenting in coronary bifurcations: New insights from numerical analysis. Cardiol J. 2020; 27(5): 507–517, doi: 10.5603/CJ.a2018.0124, indexed in Pubmed: 30394509.

6. Vassilev D, Gil R. Clinical verification of a theory for predicting side branch stenosis after main vessel stenting in coronary bifurcation lesions. J Interv Cardiol. 2008; 21(6): 493–503, doi: 10.1111/j.1540-8183.2008.00400.x, indexed in Pubmed: 18973506.

7. Mortier P, De Beule M, Dubini G, et al. Coronary bifurcation stenting: insights from in vitro and virtual bench testing. EuroIntervention. 2010; 6 Suppl J: J53–J60, doi: 10.4244/EIJV6SUPJA9, indexed in Pubmed: 21930491.

8. Djukic T, Saveljic I, Pelosi G, et al. Numerical simulation of stent deployment within patient-specific artery and its validation against clinical data. Comput Methods Programs Biomed. 2019; 175: 121–127, doi: 10.1016/j.cmpb.2019.04.005, indexed in Pubmed: 31104701.

9. Murray CD. The physiological principle of minimum work applied to the angle of branching of arteries. J Gen Physiol. 1926; 9(6): 835–841, doi: 10.1085/jgp.9.6.835, indexed in Pubmed: 19872299.