Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Cardiovascular Intervention

Crush, Culotte, T and Protrusion: Which 2-Stent Technique for Treatment of True Bifurcation Lesions?

– Insights From In Vitro Experiments and Micro-Computed Tomography –

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Background: Percutaneous coronary intervention of complex true bifurcation lesions often fails to ensure continuous stent coverage and strut apposition in both the side branch and main vessel. Struts left unopposed floating in the lumen disturb blood flow and are increasingly recognized as increasing the risk of stent thrombosis.

Methods and Results: In this study, we compared the results of different bifurcation treatment strategies: Crush (n=5); Culotte (n=3); T-/T with Protrusion (TAP) (n=4) using drug-eluting stents deployed in-vitro in representative coronary bifurcation models. After final kissing balloon post-dilatation, the rate of malapposition within the bifurcation quantified from micro-computed tomography scanning was on average 41.5±8.2% with the Crush technique, reduced to respectively 31.4±5.2% with Culotte and 36.7±8.0% with T-/TAP approach. Overlaying layers of struts in the Crush and Culotte techniques lead to a significantly higher rate of strut malapposition in the proximal vessel than with the T-/TAP technique (Crush: 39.1±10.7%, Culotte: 26.1±7.7%, TAP: 4.2±7.2%, P<0.01). Maximal wall-malapposed strut distance was also found on average to be higher with the Crush (1.36±0.4 mm) and Culotte techniques (1.32±0.1 mm) than with T-/TAP (1.08±0.1 mm, P=0.04).

Conclusions: In this model, the Crush technique resulted in a higher risk of malapposition than either the Culotte or T-/TAP technique. (*Circ J* 2013; **77:** 73–80)

Key Words: Bifurcations; Malapposition; Percutaneous coronary intervention; Stents

Provisional T-stenting with stenting of the main vessel (MV) and optional side branch (SB) stenting in case of significant SB ostial occlusion is the strategy used nowadays by most interventionalists for treating bifurcation lesions. However, it remains open to discussion of the best technique to deliver a second stent in the SB during percutaneous coronary intervention (PCI) of complex true bifurcation lesions.

Crush or Culotte stenting theoretically provides full scaffolding of the SB ostium, but these approaches are associated with greater strut malapposition and higher rates of target lesion revascularization and myocardial infarction (MI) than provisional stenting. In this study, we used micro-computed tomography (CT) to compare in vitro 3 different well-described 2-stent bifurcation treatment strategies and to evaluate their different effects in terms of strut apposition.

Methods

Experimental Models

The 3 different 2-stent techniques (Crush, n=5; Culotte, n=3 and T-/T with Protrusion (TAP), n=4) were performed using commercially available drug-eluting stents (DES: n=24) deployed in representative coronary bifurcation models (Model 1: proximal MV=3.5 mm, distal MV=2.75 mm, SB=2.75 mm, MV/SB angle=45°; Model 2: proximal MV=3.0 mm, distal MV=2.5 mm, SB=2.25 mm, MV/SB angle=70°; the second model was used only once for each strategy to assess the effect of the SB angle on strut protrusion).

The stents used were the sirolimus-eluting stent (SES: n=2; Cypher, Cordis, Warren, NJ, USA), the paclitaxel-eluting stent (PES: n=10; Taxus, Boston Scientific, Natick, MA, USA), the everolimus-eluting Xience V (n=6; Abbott Vascular, Santa Clara, CA, USA) and the zotarolimus-eluting Endeavor stent

Received March 7, 2012; revised manuscript received July 19, 2012; accepted August 21, 2012; released online September 25, 2012 Time for primary review: 71 days

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ISSN-1346-9843 doi:10.1253/circj.CJ-12-0272

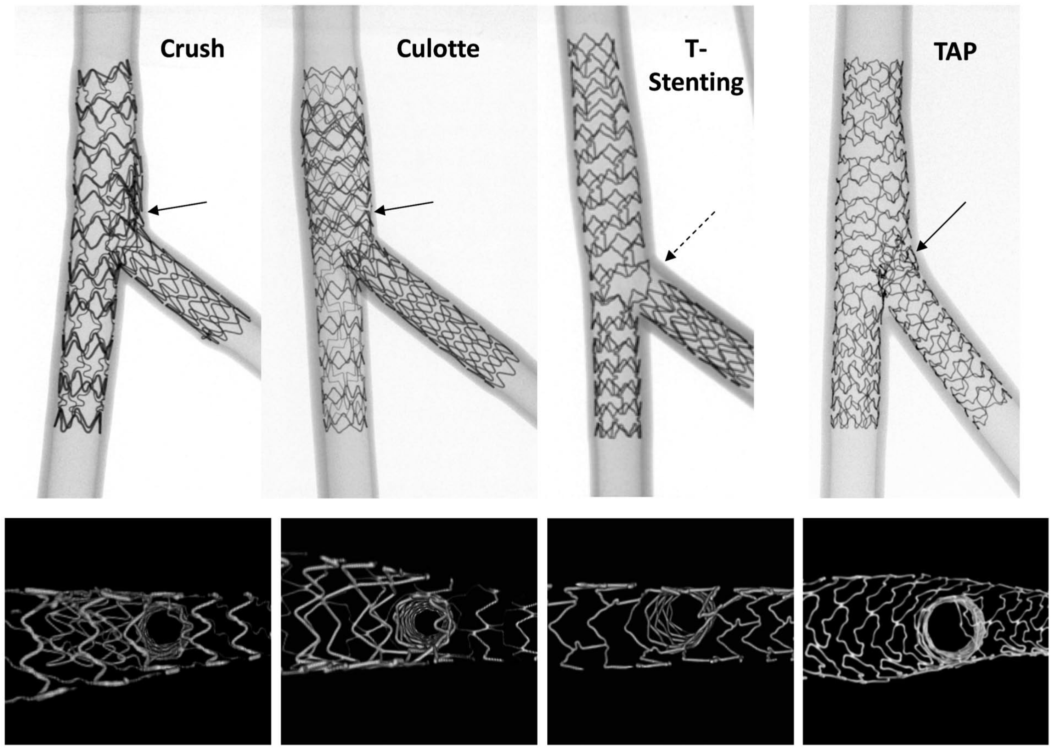

Figure 1. Planar projection and 3D view of the side branch (SB) ostium showing a comparison of 4 different bifurcation techniques: Crush, Culotte, T-stenting and T and Protrusion (TAP). Overlapping layers of struts proximal to the SB in the Crush and Culotte techniques (arrow) increase the metallic presence and the rate of malapposition proximal to the SB. T-stenting technique can leave a gap in stent scaffolding between the main vessel stent and the SB stent (dashed arrow), whereas TAP provides scaffolding of the ostium with minimal strut overlap and malapposition in the proximal vessel.

(n=6; Medtronic, Santa Rosa, CA, USA).

Kissing balloon (KB) post-dilatation using balloons sized according to the distal daughter vessel diameters was systematically performed. Cell recrossing of the wire was performed under visual control to try to get successful recrossing in the SB-ostium through the more distal struts to try to minimize strut unopposed near the carina.

2-Stent Techniques

Crush In the Crush technique, the stent is first positioned in the SB and then retracted to protrude into the MV (2–3 mm). The protruding portion of the SB stent is then crushed against the wall by dilatation with a balloon followed by deployment of the MV stent. The procedure is completed with the rewiring of the SB and FKI post-dilatation (Figure 1).

Culotte In the Culotte technique, the first stent is deployed in one of the SB, usually across the SB to the MV, with a protrusion similar to that with the Crush technique.[1,2] The MV then needs to be rewired through the strut of the first stent and after predilatation with a non-compliant balloon, a second stent is then implanted. The procedure is completed after rewiring of the SB by a final KB (Figures 1,2).

T- and TAP In the provisional T-stenting, a stent is implanted first in the MV followed by rewiring of the SB and KB to open the ostium; a second stent is then deployed in the SB and the procedure is then completed by a final KB.[1] T-stenting is the common approach for high angle (>70°) T-shaped bifurcations because it provides coverage of the SB with minimal protrusion into the MV.[1,2]

For angles <70°, the T-stenting technique is limited by the potential gap in scaffolding at the take-off of the SB (Figure 1). An adaptation of T-stenting that offers both good strut apposition and coverage of the ostium is the T with Protrusion (TAP). After stenting of the MV and a first KB to dilate the strut at the ostium and access the SB, the SB stent is advanced and left with minimal protrusion (<1–2 mm) into the MV in order to provide full continuity of stent scaffolding between the MV and SB stents[1,2] (Figures 1,2).

Quantification of Strut Apposition and 3D Reconstruction

The percentage of malapposed struts was quantified within the bifurcation as well as in the proximal reference and distal daughter vessels from micro-CT scanning (resolution up to 5 microns).

After post-processing, 3D reconstruction of the stent and reslicing, results were processed (ImageJ, rsbweb.nih.gov) to extract the rate of strut malapposition and the maximal strut-wall distance at different locations in the model (Figures 1,3,4)

Cut-open sections of the models were reconstructed, a providing longitudinal overview of the struts' apposition along the model for the different techniques. Ostial residual stenosis area was measured from the 3D reconstruction as previously described.[3]

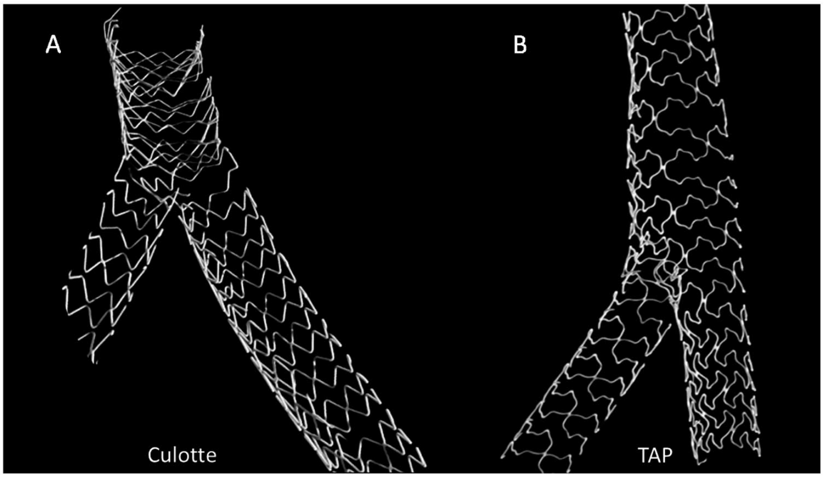

Figure 2. 3D micro-computed tomography reconstruction of (**A**) Culotte and (**B**) T-stenting with Protrusion (TAP). TAP can provide good scaffolding of the ostium with minimal strut overlap in the proximal vessel compared with the Culotte technique.

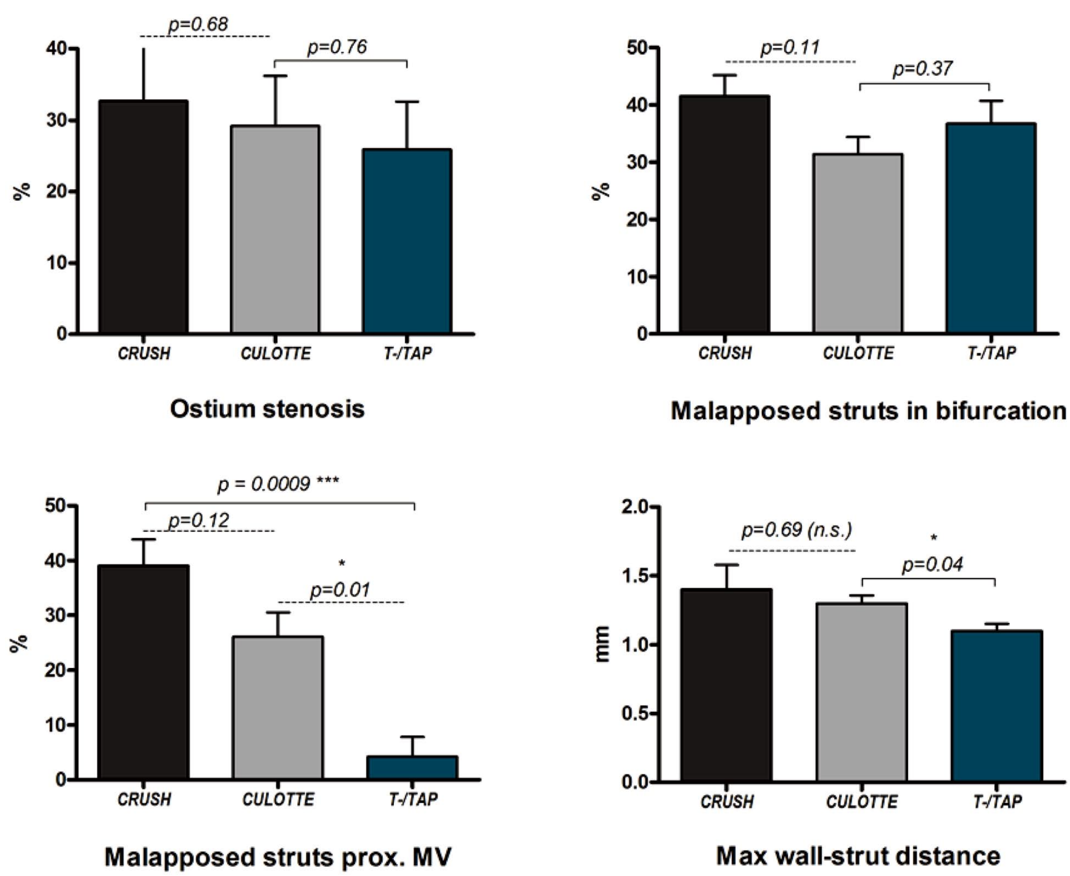

Figure 3. Rate of ostial stenosis and strut malapposition assessed by micro-computed tomography (CT) with different 2-stent techniques. 2-stent conventional stenting techniques using commercially available drug-eluting stents (Crush, n=5; Culotte, n=3 and T-/T-stenting with Protrusion (TAP), n=4) were compared. After kissing balloon post-dilatation using the same balloon sizes and inflation pressure, the percentage of malapposed struts was quantified from micro-CT scanning at different locations in the bifurcation. A trend was observed with Culotte and TAP techniques having lower rates of malapposition than the Crush technique. Note that measures are the results of in-vitro bench experimentations with optimal crossing and FKI post-dilatation. Results presented are representative of idealized deployment conditions and cannot predict the performance of each technique in patients with advanced diseases; therefore, data must be carefully interpreted.

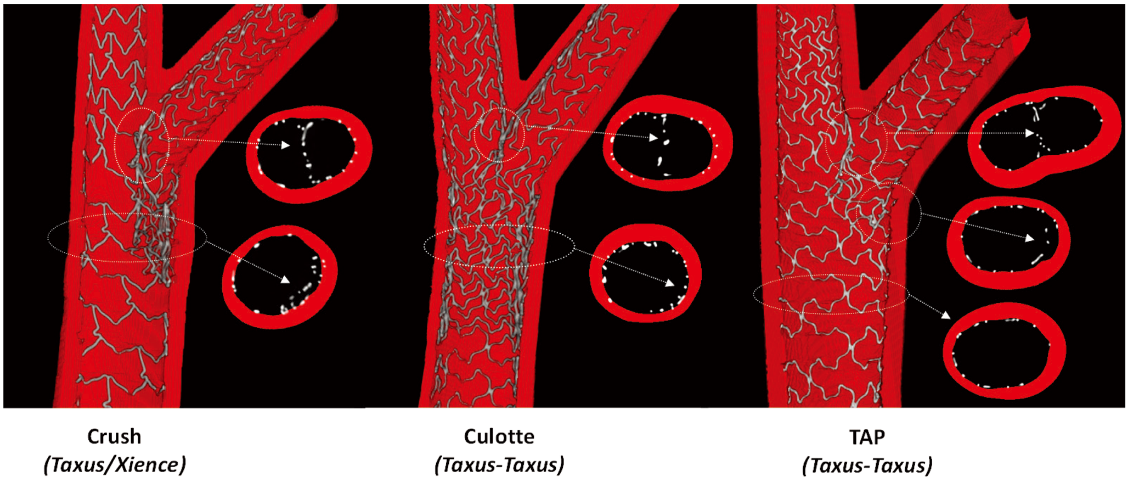

Figure 4. 3D reconstruction of representative cases of the Crush, Culotte and T-stenting with Protrusion techniques. Models were virtually cut open longitudinally. Multiple overlapping strut layers are clearly seen with the Crush and Culotte techniques, resulting in a large area of strut malapposition proximal to the side branch (circle).

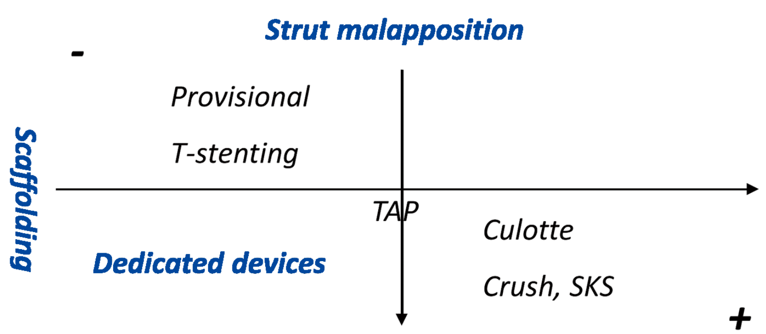

Figure 5. Trade-off between stent scaffolding and strut apposition depending on bifurcation treatment strategy. T-stenting and T-stenting with Protrusion techniques limit strut malapposition but can fail to ensure protection of the side branch ostium. More complex technique s,such as Culotte, Crush and Simultaneous Kissing-Stent (SKS), provide continuous scaffolding of the lesion in both branches, but the drawback of these techniques remains the large amount of metal that is generally left unapposed in the lumen.

Computational Flow Reconstruction

Flow patterns and shear rate were analyzed using computational fluid dynamics (CFD) to identify segments with higher risk of flow disturbance induced by unapposed struts.

Micro-CT scans from a representative case of the Crush technique after KB post-dilatation were imported to a commercial surface meshing software (Mimics, Materialise Inc, Leuven, Belgium) and CFD suite (CFX 12.1, ANSYS Inc, USA) for flow analysis. The inlet flow condition used was a flow waveform recorded in a human left anterior descending artery by ultrasound Doppler (Combowire, Volcano Corp, USA) and the flow split between the MB and SB was assumed to be 70% to the MB and 30% to SB.

Statistical Analysis

Results are expressed as mean±SD. Comparison between the different strategies was tested by analysis of variance. Paired t-tests were used to compare results between pairs of samples. Results were considered statistically significant for $P<0.05$.

Results

Strut Apposition

The rate of malapposition within the bifurcation was on average 41.5±8.2% with the Crush technique, reduced to 31.4±5.2% with Culotte and 36.7±8.0% with the T-/TAP approach. The percentage of residual stenosis at the SB ostium was on average similar for all 3 techniques (Crush: 32.7%, Culotte: 29.2%, T-/TAP: 25.9%).

The Crush technique not only produces an additional layer of strut near the carina, but the technique results in 3 layer of struts crushed against the vessel wall proximal to the SB, increasing as well the distance between the unapposed layer of struts and the wall (Figures 4–6).

The Culotte technique produces a layer of strut in front of the carina similar to the Crush technique. An extensive region of strut overlap can be created proximal to the bifurcation with large protrusion of both the SB and MV stents (Figure 4).

Overlapping layers of struts in the Crush and Culotte techniques leads to a significantly higher rate of strut malapposition in the proximal vessel than with the T-/TAP technique (Crush: 39.1±10.7%, Culotte: 26.1±7.7%, T-/TAP: 4.2±7.2%,

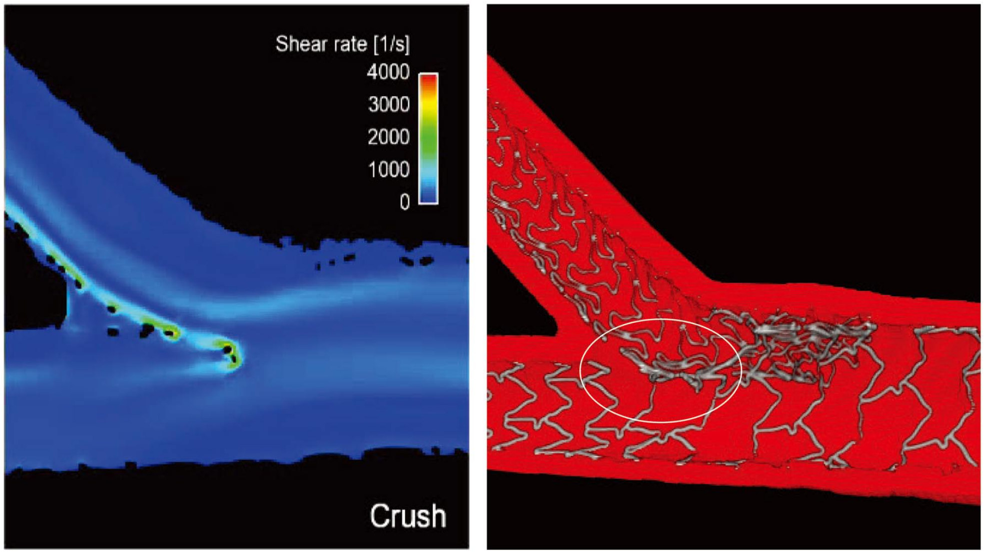

Figure 6. Unapposed struts create flow disturbances and may increase the risk of stent thrombosis. Computational flow dynamic reconstruction in the model bifurcation after the Crush technique with a Taxus liberte 2.75 in the side branch and a Xience 3.0 as the main vessel stent. Extensive layers of malapposed struts remain in the lumen despite kissing-balloon optimisation. Unapposed struts in the neocarina (circle) cause severe flow disturbances with high shear rate that may increase the risk of platelet adhesion and stent thrombosis.

P<0.01).

Maximal wall-malapposed strut distance was also found on average to be higher with the Crush (1.36±0.4 mm) and Culotte techniques (1.32±0.1 mm) than with T-/TAP (1.08±0.1 mm, P=0.04).

Lessons From Scanning Electron Microscopy (SEM)

SEM was performed using multiple DES deployed according to the Culotte technique. SEM analysis of polymer integrity revealed a high amount of polymer scratches in the areas of strut overlap in the MV (**Figure 7**). Strut overlap created a large area of polymer damage, including areas with delamination (peeling) of the coating of the stent. Multiple strut layers are likely to increase the frictional forces acting on the polymer coating, particularly during final KB post-dilatation of overlapping stents.

Lessons From CFD

Flow analysis detected extensive disturbance caused by unopposed struts left in the lumen after complex stenting. In the Crush technique, the 3 layers of stent struts left against the wall inevitably lead to a high rate of strut malapposition proximal to the SB ostium. Furthermore, high velocity components in the middle of the lumen can be observed hitting the layer of floating struts left in front of the carina (neocarina) (**Figures 5,6**).

The consequences of leaving an extensive amount of strut unapposed after bifurcation procedures are discussed next.

Discussion

Clinical Results of Complex and Simple Bifurcation Techniques

Randomized trials have demonstrated that for a lesion confined to the MV, stenting of both the MV and SB with 2 stents does not produce any clinical benefit compared with stenting the MV only.[4–6] In a recent meta-analysis of randomized trials including patients with coronary bifurcation lesions who were randomly selected to undergo PCI by either double or single stenting, Katritsis found an increased risk of MI with double stenting (risk ratio, 1.75, P=0.001), as well as an increase in the risk of stent thrombosis (risk ratio, 1.85, P=0.19).[7] In summary, a provisional T-stenting strategy with stenting of the MV and elective stenting of the SB appears to have equivalent efficacy with less risk of MI than a planned 2-stent strategy in most bifurcation lesions.[4–6,8–10]

Several recent reports have criticized the current dogma that provisional approach should be the default strategy in all bifurcation lesions and is better than an elective double stenting, even in more complex lesions.[11,12] Most report and trials comparing simple and complex strategies for bifurcation lesions have an inherent bias because they generally include a wide range of simple and complex lesions but patients with more severe disease involving the SB, usually ending by being treated with double stenting.[11,12] Little data are available on comparing elective double stenting with the provisional approach with 1 or 2 stents in the complex lesions subset. True bifurcations (Medina 1.1.1, 1.0.1, and 0.1.1) involving large-sized SB (>2.5 mm) with disease extending beyond the ostium (>5 mm from the ostium) are less likely to be treated optimally with a provisional technique and are still an area of uncertainty for interventionalists.[2,11,12]

Complex Techniques: Scaffolding vs. Apposition Dilemma

Whereas a simple provisional approach ensures good stent struts apposition and warrants preservation of MV patency, the technique often fails to protect the SB ostium, with the risk of a late focal renarrowing. Gaps in stent scaffolding and focal ostial restenosis remain a limitation of the T-stenting technique,

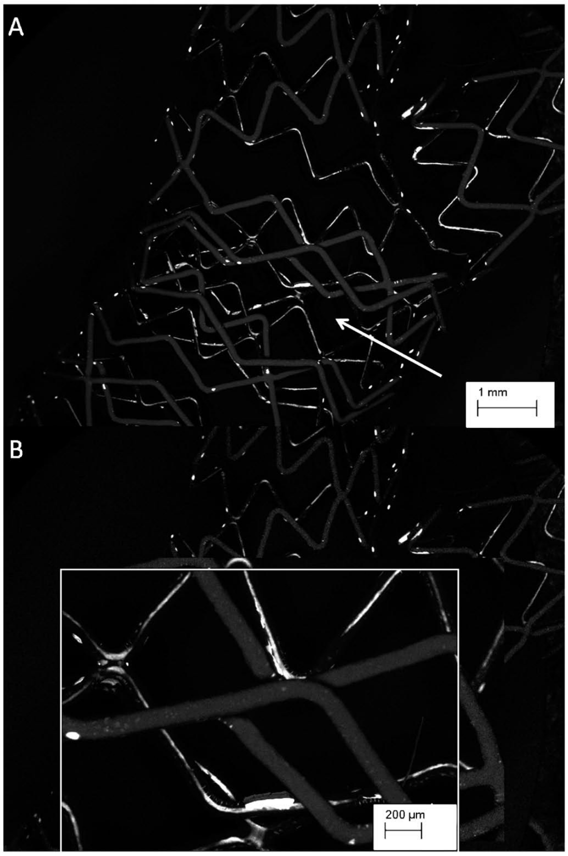

Figure 7. Scanning electron microscopy after the Culotte technique with deployment of 2 drug-eluting stents (Endeavor Resolute). Multiple strut layers in the area of stent overlap may increase the risk of damage to the polymer coating (arrow). Magnification: **A**=×35, **B**=×85. Pathological evidence[31,35] suggests a possible correlation between polymer damage and persistent inflammation with delayed coverage and high risk of stent thrombosis.

particularly for angles <50°.[2] Complex techniques such as the Crush and Culotte techniques have been designed to provide continuity in stent coverage between the SB and MV and to ensure protection of the SB.[3,13,14] These techniques are, however limited, by the significantly higher rate of struts left unapposed in the middle of the lumen, which usually translates into a high incidence of major adverse cardiac events (MACE).

This creates a dilemma for the interventionalist, as more complex techniques provide a better lesion scaffolding but at a cost in terms of strut apposition.

In the randomized Nordic stent technique study, the Crush and Culotte techniques were associated with similar MACE: 4.3% with Crush and 3.7% with Culotte at 6 months (P=0.87), but the in-stent restenosis rate after 8 months were 12.1% vs. 6.6% (P=0.10) in the MV, and 10.5% vs. 4.5% in the SB for the Crush and Culotte groups, respectively (P=0.046).[15]

Provisional T- and TAP

In a randomized study with sirolimus-eluting stents in 101 patients assigned either to provisional T-stenting or routine T-stenting, Ferenc reported binary restenosis rates in the main branch of 7.3% and 3.1% (P=0.32) respectively at 9 month follow-up with target vessel revascularization at 1 year of 10.9% after provisional and 8.9% after routine T-stenting. SB restenosis remained high in both groups, with 23.0±20.2% after provisional T-stenting and 27.7±24.8% (P=0.15) after routine T-stenting. They concluded that routine T-stenting is not significantly different in terms of angiographic outcome as compared with provisional SB stenting.[16]

PCI with 2 stents is nowadays performed mainly as a crossover from a provisional strategy in case of suboptimal results in a large-sized SB (ie, abrupt closure, flow-limiting dissection, >75% stenosis, TIMI flow <3); it is estimated that approximately 70% of true non-left main bifurcations are currently being tackled with a provisional T approach.[2,7]

For angles <70°, the T-stenting technique is limited by the potential gap in scaffolding at the SB ostium. A popular adaptation of the T-stenting that offers both good strut apposition and coverage of the ostium is the TAP method. The SB stent is advanced and left with minimal protrusion (1–2 mm) into the MB. The aim of the TAP technique is to provide full continuity of scaffolding between the MB and SB stents. Good clinical results have been observed with the TAP technique and long-term TLR rates as low as 6.8% have been reported.[17]

In our study, the T-/TAP approach led to significantly less malapposed struts than the more complex techniques. However, the main limitation of TAP compared with provisional T-stenting remains the risk of positioning the SB stent too low in the ostium, which can create a neocarina with many struts protruding extensively into the MV lumen (**Figure 4**).

Importance of Successful Recrossing and Post-Dilatation

With the Culotte and Crush techniques, there is a risk of compromising one of the branches in the case of failure to rewire or recross a balloon through the stent strut to complete the procedure and perform a mandatory final KB.

For example, in the CACTUS study, a final KB was performed in the majority of patients (91.1%), but the absence of a final KB was associated in both provisional and Crush stenting groups with a significantly higher rate of MI (29.0% vs. 7.5% with final KB, P<0.001), higher stent thrombosis (6.5% vs. 0.9 %, P=0.06) and a higher incidence of TLR (12.9% vs. 6.3%, P=0.25).[18]

Conversely, excellent results have been reported in true bifurcation lesions with the double-kissing post-dilatation crush (DK Crush) strategy,[19] where a first KB post-dilatation is performed after the implantation of the SB stent but before implantation of the second stent. Similar MACE rates and inferior TLR rates have been reported compared with controls treated with provisional stenting.[19] This underlines the importance of post-dilatation in complex strategies to achieve satisfactory clinical outcomes.

Risks Associated With Unapposed Struts

Delayed re-endothelialization with DES and malapposition are increasingly recognized as hallmarks risk for late stent thrombosis (LST).[20,21]

Absence of endothelial coverage has been frequently observed in pathological analysis and animal experiments with first-generation DES (SES, PES) compared with bare metal stents or second-generation DES.[20,22,23] Strut coverage with endothelium provides an antithrombotic barrier between the blood and the implanted stent, which seems critical for preventing LST.[24–26] A recent optical coherence tomography study in patients with LST confirmed the correlation between absence of coverage and a higher risk of LST.[21]

Unapposed struts have been associated in vivo with delayed coverage;[27] they have also been shown to create pro-thrombogenic flow disturbances with high shear.[28,29] High shear gradients and flow recirculation are a known risk factor for platelets activation[30,31] and large layers of unopposed struts, such as observed with complex techniques, may therefore increase the chance of stent thrombosis.[31]

Previous in vitro SEM analysis showed a high frequency of polymer cracks and damage with DES.[32,33] The consequences of leaving some damaged polymer coating in direct contact with the blood stream remains uncertain. Delamination of the polymer might be more frequent in the clinical setting when advancing the stent in the sheath and when attempting to cross difficult calcified lesions.[34] Pathological evidence suggest a possible correlation between polymer damage, delayed healing with persistent inflammation and the risk of stent thrombosis.[31,35] Such damage and delamination of polymer with DES[32,33] may alter re-endothelization and increase the risk of LST,[20,35] particularly in the bifurcation where coating damage can be largely found on unapposed struts,[36] also disturbing blood flow.[29,30]

Study Limitations

The number of experiments and statistical power were restricted by the limited availability of DES samples (n=24). Further experimental validation with larger sample sizes is required to confirm the present observations, and the results must be carefully interpreted because in-vitro experimentation is performed in an idealized model and under controlled deployment may not predict the in vivo results in the presence of advanced disease.

The present results suggest that the T-/TAP technique produces less malapposition than the more complex Crush and Culotte techniques. The position of the stents could be precisely controlled in our in vitro study, whereas cardiac and catheter motion in vivo might affect accurate stent positioning. Positioning of the SB stent too low in the ostium during the TAP technique can create a neocarina with a large amount of unapposed stent struts protruding into the MV lumen.

In all bifurcation techniques, including simple provisional stenting with only opening of the SB ostium, results are dependent on the location of the recrossing of the wire through the stent mesh. In our study, visual inspection of the location of the wire recrossing through the stent mid-distal cell was performed to ensure optimal balloon recrossing. If the balloon would not cross, a second wire was used to cross through a more favorable cell to prevent severe stent distortion. Such control is not possible in vivo techniques requiring several recrossings (Culotte) or wire recrossing though multiple layer of struts (Crush), which are therefore likely to lead to more risk of severe stent deformation or failure to recross the balloon.

Conclusions

The aim of this study was to evaluate which 2-stent technique (Crush, Culotte and T-/TAP) is better for the treatment of true bifurcation lesions, using an in vitro bench model and high resolution imaging to evaluate strut apposition.

In conclusion, we observed that final results in terms of strut apposition remained poor for all techniques, even after successful KB post-dilatation and despite visual inspection of wire recrossing.

More complex techniques, namely Crush and Culotte, led to a higher rate of strut malapposition than a T-/TAP approach. The more complex techniques may produce a higher risk of flow disturbance and polymer damage, which are both increasingly recognized as hallmarks for delayed healing and risk of LST.

Using an idealized in-vitro model, and despite following the recommendations for bifurcation treatment with a successful final KB, complete scaffolding of both branches and full apposition of the struts remained challenging. Further improvement of guidance and material are still required to reduce the rate of strut malapposition in the treatment of bifurcation lesions.

Disclosures

None of the authors has a conflict of interest to disclose.

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