Laboratory Research

Changes in coronary bifurcations after stent placement in the main vessel and balloon opening of stent cells: theory and practical verification on a bench-test model

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Objective To describe changes that occur in stent morphology and structure after its implantation in coronary bifurcation. Side branch (SB) compromise after stenting of main vessel in coronary bifurcation is a major intraprocedural problem and for the long term, as a place of restenosis. Methods We created an elastic wall model (parent vessel diameter 3.5mm, daughter branches 3.5mm and 2.75mm) with 30, 45 and 60 degree distal angulation between branches. After stent implantation, struts to the side branch were opened with 2.0mm and consequently 3.0mm diameter balloons. Subsequent balloon redilatations and kissing balloon inflations (KBI) were performed. All stages of the procedure were photographed with magnification up to 100 times. Results We found that the leading mechanism for side branch compromise was carina displacement, and discovered theoretical description for expected ostial stenosis severity. Based on our model we found that displacement of bifurcation flow divider cause SB stenosis with almost perfect coincidence with our theoretical predictions. Opening of stent cells through the proximal and distal stent struts always increased interstrut distance, but never achieved good apposition to the wall. Balloon diameter increase didn’t give proportional enlargement in stent cell diameters. KBI leads to some small better stent positioning, correcting main vessel strut dislodgment from wall, but never gave full strut-wall contact. Distance between struts and wall was minimal only when the stent cell perfectly faced ostium of SB. This was also our observation that the shape of ostium of SB became elliptically-bean shaped after stent implantation and generally kept that shape during consequent stages of experiment. Measured diameter and area stenosis were perfectly fitted and theoretically predicted from our concept. Conclusion We have described stent-wall deformations in stent-balloon technique for treatment of coronary bifurcation demonstrating carina displacement as possibly main mechanism of side branch compromise after main vessel stenting. We have shown that KBI could not give full strut-wall contact if there is no perfect facing of stent cell and SB ostium. (J Geriatr Cardiol 2008; 5(1):43-49)

Key Words coronary bifurcation; bench test; stent

Introduction

In the modern era, interventional cardiologists are faced more frequently with difficult procedures such as bifurcation lesion intervention, due to the complex anatomy of vessel branching points.¹ ² Side branch (SB) compromise after stenting of main vessel (MB) stenting is the big problem in short- and long-term prognosis. It creates a lot of controversies about a best treatment strategy. The reasons for SB compromise are still not clear, despite a widely accepted concept for so called “plaque shifting”, which was a conclusion by analogy from observations in non-branching vessels and from angiographic observations,¹ but never proved directly by intracoronary ultrasound (ICUS) examination. In general all research efforts were focused on achievement of optimal stent scaffolding of bifurcation points and of the proximal segments of both vessels. Attention was also paid to MB stent structural distortions after opening the cell leading to side branch (SB).⁵ ⁶ ⁷ Kissing balloons inflation (KBI) was proposed as a universal technique for restauration to optimally expanded BMS structure.⁸ ⁹ Recent randomized trials with drug eluting stents (DES) did not confirm the absolute necessity of KBI to achieve good long term results.¹⁰ ¹¹ However, little is known about the changes in vessel wall and in configuration of branching vessel region in real arteries. In the past, bench test models examining changes during stent implantation were executed on stiff models (Plexiglas plates, glass models), with geometry far from real anatomy.

The purpose of our study was to examine wall-stent interaction at the side branch ostium after stent implantation in the main vessel of coronary bifurcation and to test applicability of our theoretical predictions for measurement of side branch compromise.
Methods

We assume that every branching point in the circulation system could be represented as a connection between three tubes with different diameters. The connection region between daughter vessels is flow divider (FD), which faces the main blood stream of the parent vessel. When stent is placed from parent vessel (main vessel, MV) to main branch (MB), which is larger than daughter branches, a complex change in configuration of region occurs. As stent must scaffold all anatomical structures, its diameter is generally somewhere in-between diameters of MV and MB. After an ideal stent opening there is equalization of proximal and distal limbs of bifurcation, pushing the flow divider in direction of side branch ostium. As a result, stenosis at the ostium appears. The extent of this stenosis will depend on the extent of stent opening, or the extent of flow divider displacement.

Using this idealized model we can calculate (in two dimensional plane model) the extent of ostial diameter stenosis and subsequent area changes in the SB ostium. In our previous report we showed that with full stent expansion, the percentage DS at the ostium of the side branch is equal to cosine angle $\alpha$, which is the angle between the two axes of parent vessel before bifurcation and side branch. For a common case we have the $\%$DS = sin $(\alpha - \alpha')/\tan \alpha$, where $\alpha'$ is angle between parent vessel axis and actual position of lever arm (formed from SB wall facing main branch) after stent implantation. Theoretically predicted values using above mentioned angles and diameter of side branch were compared with those actually measured from experiments.

Bench – test model

Our test model was prepared from plastic tubes with wall thickness of 0.5 mm (equal to upper normal limit), glued at the site of bifurcation (Fig. 1). The tubes are very elastic and permit wall conformation to local pressure. The parent vessel internal diameter was 3.50 mm with branches of 2.75 mm and 3.50 mm, with several angulations between -30º, 45º and 60º (n=6). To obtain better visualization of changes in bifurcation we decided to implant stent to the slightly smaller branch.

We used for all tests the stent Chopin 2 (Balton, Warsaw, Poland), which is a platform for paclitaxel eluting stent Luc – Chopin. The stent has a four cells design with 160 μm strut thickness. For all experiments only 3.50 mm diameter and 18 mm length stent was used. With those sizes, stents have maximal cell opening diameter of 2.50 mm according to manufacturer specification. All stages in the experimental protocol were photographed (microscope Nikon, model NXZ 5239) using up to 100 times magnification of interior of a stent, from different angles for optimal visualization of changes in the walls and in the stent, when necessary with additional manual fixation. To obtain better visualization of changes around branching point, the distal part of side branch tube was cut on a different distance from ostium (in model 1 it was around 3.00 mm from ostium, in model 2 – on 5.00 mm distance).

Measurements from photographs were made with dedicated software Dicom Works version 1.3.5b, using fixed measure points for calibration. All measurements were performed at last 3 times and the results were averaged. Because of parallax, we used only photographs, which are in close proximity to orthogonal views of the plane of interest.

Experimental protocol

Experimental steps: (1) after wire placement at each branch for vessel stabilization, stent was implanted; (2) small balloon (2.0 mm or 2.25 mm diameters) was inflated through the stent cell facing side branch. In half of the models, the balloon was inflated in the proximal stent strut (close to the parent vessel) and in the other half in the distal strut (close to the main branch and flow divider); (3) the larger balloon, diameter 3.0 mm, was used for further dilatation of stent cell; (4) to correct changes during previous steps, balloon from stent was again inflated in main vessel. Fifth step - kissing balloon inflation with two balloons was made with 3.5 mm for stented vessel and 3.0 mm for side branch.

Inflations were performed with pressures up to 20 atmospheres for single balloon dilations and up to 14 atmospheres for KBI. At every step photographs were made from parent vessel, with main branch and side branch views, and additional views from lateral position.

The following parameters were measured and

Fig. 1. Different plastic models used for experiment. Numbers above represent distal branch angle.
was highly eccentric because of stent strut position (Fig. 2).

than that as we have shown. The 30° model placed for MLD formula with same %DS of 63%, %AS must be 86% higher close to the measured value. Using circular area calculation with angle $\alpha$ of 27º and $\alpha'$ = 8º, %DS = 63%, was very well close to the measured value. After dilatation through distal strut (for model 30º - 0.11 +/- 0.01mm, with 45º it was 0.19 +/- 0.01mm). The reason for that was that deformation resulted in stent deformation in diagonal direction of main vessel, because of no prolapse of struts in lumen of side branch. At the same time in improvement of side branch opening there is a decrease of MLD downstream from carina in main vessel. As minimal diameter was 3.25 +/- 0.02mm after stent implantation, it decreased to 3.11 +/- 0.04mm after small balloon inflation and further decreases to 3.01 +/- 0.02mm with larger balloon inflation.

There is no proportional increase in MLD and decrease of %DS with increasing balloon diameter in SB. After initial increase in MLD of 0.42mm with inflation of 2.00mm balloon, additional inflation of 3.00mm balloon up to 18 atmospheres was not followed with proportional increase in cell diameter. MLD further increased with 0.21 $\pm$ 0.01mm (12% from previous diameter of 1.81mm), which is much smaller than a 30% increase in balloon diameter.

After balloon dilatation of main vessel, flow divider returns almost to the initial position, giving MLD of 1.48 $\pm$ 0.02mm and %DS = 52 $\pm$ 2%, with pulling to the main vessel of lateral stent struts, and with maximal strut – lateral wall distance 0.28 $\pm$ 0.02mm (Fig. 3). Minimal diameter in

### Statistical analysis

All values are reported as mean $\pm$ SD; where it was necessary we used a sign-ranked test for detection of significant differences with level of significance $P<0.05$.

### Results

We present results on a step-by-step basis for 30 and 45 degree models. As there is some small, but in our point of view important differences in results from a 60 degree model, this is presented separately. Results from 30 degree and 45 degree models.

### Stent implantation.

After wire placement significant decrease in the distal bifurcation angle between branches at the level of flow divider occurs. It was in the range 8º-17º in different models. Stent implantation leads to several changes in the shape of bifurcation. There is displacement of carina in direction of side branch ostium, visualized in lateral views and from direct observation from lumen side of lateral vessel. Resulting diameter stenosis is as much larger as smaller in angulation between branches and especially as smaller in angle $\alpha$. Area occupied from carina is elliptical, as according to our prediction and markedly different from cylindrical shape configuration of distal side branch. There are two sections in side branch after stent implantation – proximal with elliptical shape and distal with regular cylindrical shape. The minimal lumen diameter region was in place where one of struts most prominently pushed carina. The result was that ostium of side branch tube took bean shape around the elliptically shaped displaced carina (Fig. 2 A-B).

We found that the general shape of ostial portion is elliptical with long diameter close to the diameter of proximal tube and short diameter close to original diameter of tube, before stent implantation with mean eccentricity ratio of 0.87. Because of difference in diameter of parent tube and main branch some underexpansion was observed distally from flow divider and overexpansion in proximal region.

Data for measured parameters at the ostial part of side branch are presented in Table 1. According to formula for MLD using cosine alpha predicted ostial diameter stenosis with angle $\alpha$ of 27º and $\alpha'$ = 8º, %DS = 63%, was very well close to the measured value. Using circular area calculation formula with same %DS of 63%, %AS must be 86% higher than that as we have shown. The 30º model place for MLD was highly eccentric because of stent strut position (Fig. 2 B). Distance between stent strut and wall of side branch varies between 0.66mm and 0.88mm.

### Opening of lateral stent strut with balloon

Because of relatively random, and according to cell placement positioning of stent in the main vessel we observed different patterns of strut distribution against opening of the lateral vessel. We tested stent and wall deformations with balloon inflations in distal strut and in proximal strut. Lumen of interstrut opening increased as a result of lateral displacement of struts and as a result small returning of carina to the lumen of main vessel. That leads to increase of MLD at ostium of SB (1.81 $\pm$ 0.07mm for 30 º models, 2.02 $\pm$ 0.21mm for 45 º models). With smaller balloons (2.00mm and 2.25mm diameter) there was no observable stent deformation in main vessel. With larger balloon (>2.25mm) marked stent apposition from wall of main vessel occurs (equal to 0.39mm in Fig. 2 D), which accounts for much better apposition between stent and lateral branch wall (MLD 2.02mm). We defined term extension distance as maximal distance which could be obtained after full dilatation of stent and strut to the side branch (double arrow on Fig. 2 C). In this example it is 4.95mm. At the ostium of side branch, stent cell has a larger diameter of 2.71mm after inflation of 3.00mm diameter balloon.

When dilatation through proximal strut was performed strut apposition to the wall of side branch vessel was better, now with displacement of struts to the carina region. With larger balloon again was observed small displacement from wall of main branch. This disposition was much smaller than observed from dilatation through distal strut (for model 30º - 0.11 +/- 0.01mm, with 45º it was 0.19 +/- 0.01mm). The reason for that was that deformation resulted in stent deformation in diagonal direction of main vessel, because of no prolapse of struts in lumen of side branch. At the same time in improvement of side branch opening there is a decrease of MLD downstream from carina in main vessel. As minimal diameter was 3.25 +/- 0.02mm after stent implantation, it decreased to 3.11 +/- 0.04mm after small balloon inflation and further decreases to 3.01 +/- 0.02mm with larger balloon inflation.

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main branch distally from carina increased to $3.32 \pm 0.02\text{mm}$.

Area of stent cell opening to the side branch was larger comparing with the initial one, mainly because of lateral strut displacement (Fig. 3 C), but maximal strut opening was smaller in comparison with the previous step ($2.62 \pm 0.04\text{mm}$ maximal interstrut distance). In the model of proximal strut opening there were almost no changes in strut position (strut – carina distance changes from $0.66 \pm 0.06\text{mm}$ after stent implantation to $0.48 \pm 0.02\text{mm}$ and $0.36 \pm 0.01\text{mm}$ after small, respectively large balloon inflations and to $0.38 \pm 0.02\text{mm}$ after redilatation of main vessel), again with returning of carina close to initial place and parameters of stenosis.

**Kissing balloon inflation**

Generally KBI corrects main vessel deformations, without visible disposition from vessel wall of struts. With distal strut dilatation it does not abolish distance between stent and lateral wall and does not ensure better stent scaffolding than after sequential balloon inflation in side and main branch. It does not correct displacement from wall observed after balloon inflation in previous steps. The limiting factor was extension distance compared with summed diameter of main and side branches at place of vessel divergence. Mean distance strut – wall was $0.23\text{mm}$.

In proximal strut dilatation KBI led to small additional decrease of strut – wall of flow divider distance (from $0.38 \pm 0.02\text{mm}$ to $0.30 \pm 0.01\text{mm}$). Kissing ballooning ensures better opening of stent cell (maximal diameter $2.76 \pm 0.02\text{mm}$, minimal $1.92 \pm 0.04\text{mm}$). Minimal diameter in main branch at the carina place decreases a little after KBI – from $3.34 \pm 0.02\text{mm}$ to $3.27 \pm 0.03\text{mm}$. Final MLD = $1.73 \pm 0.01\text{mm}$ and MLA = $4.75 \pm 0.19\text{mm}^2$ with %DS = $50 \pm \%$ and %AS = $52 \pm \%$, better than initial values. Mechanism of increase of SB ostial area is partial carina displacement to the main vessel and wider strut opening and proximal vessel over distention. Proximal vessel has an elliptical shape after KBI (maximal to minimal diameters $3.97\text{mm} \times 3.46\text{mm}$, ratio of eccentricity 0.87, Fig. 3 D). This is for the expense of $9.7\%$ diameter stenosis in main branch distally from carina.

**Model testing – results from 60 degree model**

General changes already described with 30 degree
and 45 degree models are valid also for this model. Predicted MLA and %DS (|Å|= 37º and |[^]= 17º) are 1.89mm and 46% and actually observed was 2.02 ±0.03mm and 40 ±1%. In those models however we can position stent cell exactly against side branch opening. That resulted in much smaller stent deformations during consecutive steps and smaller strut wall distances — maximal value of 0.11 ±0.01mm at the lateral wall and 0.21 ±0.02mm at flow divider mal (Fig. 4). Maximal cell opening was 3.23 ±0.02mm with mini 2.09 ±0.01mm. Compromise of main vessel diameter distal from carina was much smaller than in previous models (residual %DS 4.7%). In this model we observed the largest possible deviation from optimal stent equalization of side branch limbs. That emphasizes the role of vessel geometry on the results of stenting.

Summary from model experiments

On Fig. 5 we present changes during sequential phases of MLD, MLA, %DS and MLD in main branch downstream from flow divider. The graphic presents simultaneous changes in MLD - MLA and %DS – MLD distal branch well.

After initial increase in MLD and MLA associated with small balloon inflation, there is a small further increase in those parameters with larger balloon inflation. Main vessel redilatation almost returns parameters to the initial values and KBI again increases both of them, but without full correction to the maximal obtainable values. Decrease in %DS was accompanied with decrease in distal MLD in main branch, and simultaneous reverse change was detected with main vessel dilatation. This observation is associated with the changing position of carina.

Discussion

As far as we know this is the first report giving a full description in quantitative manner of side branch stenosis after stent placement in the main vessel. We concentrated our attention on the complex interaction between stent and vessel wall in a model close to a real anatomical situation, with elastic walls and thickness close to upper limit of normal in humans. All recent randomized studies clearly demonstrated superiority of one stent technique over two stent techniques. Moreover it became clear that clinical significance of stenosis at the ostium of side branch became important at levels much higher (more than 85% diameter stenosis than previously thought. We make a step forward and propose formulas for prediction of changes in side vessels.

Our results have shown that ostial side branch stenosis is a result to a great extent the displacement of flow divider of bifurcation to the direction of lateral vessel. This displacement depends on the so called from us angle á, which is the angle between axis of parent vessel and axis of side vessel. We assumed for our calculations that this angle is constant and doesn’t change during stent implantation. In an ideal situation the stent must be expanded fully, and equalization of limbs of branching points results. In reality and as we have shown in our bench test experiments, some stent underexpansion always occurs. In this regard we deem that only placement of a guidewire in the lateral vessel could ensure minimal, but enough for flow maintenance, displacement of carina despite small stent underexpansion at that site. This could explain a favorable effect of jailed wire technique.

The other important consequence from flow divider displacement is that it forms an elliptically shaped opening of side branch ostium. That results in much larger area at that point than expected if shape was circular. Finally that will result in stenosis overestimation if only diameter stenosis is used for estimate of ostial narrowing severity.

We strongly believe that the changes we described in our bench-test model occur in real arteries. Until now all studies on bench models were on rigid models and concentrated on stent deformations, without description of stent – wall interaction. We define two zones in side vessel – proximal elliptical, with lateral distention and invagination.
of walls of side vessel, and distal circular. Ostium of side branch takes a bean shaped configuration, far away from circular and keeps that form despite different types of intervention there. Place and extent of MLD depend strongly on strut positioning and angle \( \dot{a} \). It could be centrally or eccentrically positioned.

Balloon dilatation through the struts of stent leads to lateral displacement and opening of stent cell. However without regard to which strut is used (proximal or distal) there is always distance between strut and adjacent wall. We define a new parameter, namely extension distance, to describe capability of stent to accommodate the bifurcation region. This is maximal diameter at which stent could be stretched in radial direction with full expansion of one cell. In case of Chopin2 stent we used, it is 4.95mm for 3.5mm diameter stent. One important finding from our model is that there is small further increase in cell opening with using larger balloons. Because of angulated position of balloon during inflation, maximal diameter at the ostium is not equal to balloon diameter, but is much larger. Formula for calculation is \( D_{\text{max}} = D_{\text{act}} / \sin \dot{a} \), where \( D_{\text{max}} \) is maximal diameter and \( D_{\text{act}} \) is balloon diameter. For 2.00mm balloon \( D_{\text{max}} = 2 / (\sin 27^\circ) = 4.44\text{mm} \) distance, which is limited from stent material and cell geometry. We can state that opening of struts with a small balloon is quite enough to ensure good flow in branch vessel. Moreover, such a manipulation escapes deformation of stent in main vessel, and that is what theoretically decreases probability for in-stent restenosis.

It is our finding that kissing balloon inflation decreases, but does not eliminate strut-wall distance. When proximal strut is used resulting ostial diameter is generally larger. Only if stent cell is positioned exactly to the ostium of side vessel there are minimal gaps between stent and wall (Fig. 4). It is possible that with smaller side branches and larger extension distance there will be a better strut apposition. However, KBI ensures larger ostial area, by the mechanisms of strut displacement and proximal vessel overexpansion. What is important, KBI leads to small decrease in distal minimal lumen diameter of the main branch. The need for dedicated stent, which ensures centering of stent cell exactly against SB opening, is obvious.

We think that in face of our data it must be a strongly reconsidered necessity of KBI in every case of only main vessel stenting. Despite the fact that KBI gives larger final MLD in side branch it does not ensure strut – wall apposition and does not gives better results in main vessel. Our results are in accordance with one recent IVUS-controlled study using strategy of only main branch stenting with final KBI, which shows that despite KBI, the distal main branch lumen area is significantly smaller than proximal lumen area.\(^{13}\) We can speculate that only using a small balloon to open side stent cell with or without consequent KBI with same small balloon and nominal balloon in parent vessel is enough to achieve good result.

It is little known for the effect of stent implantation at that site in case of SB dissection in real arteries. On angiography because of overlapping of lateral portions of ellipse any underexpansion would be missed. If this stent is optimally expanded in side branch, flow divider will be displaced in main vessel direction and compromise there will be observed (see Fig. 5). One possible solution to this problem is proximal overdilatation of main branch stent with a very short balloon, which \textit{per se} will increase SB ostial diameter, without KBI. A clinical study for this method is under investigation from our group.

Comparing with previous studies our results are in some contradiction, especially with our observations for kissing balloon inflation. It is generally believed that KBI ensures best stent apposition and long term results. However our results put a point of caution in this concept. Actually best strut apposition to the vessel wall depends more on cell positioning against the side branch ostium than from KBI \textit{per se}. Our results give a good explanation of current results from randomized trials, which have shown no difference in long term results between single and double stent techniques and KBI and non-KBI groups.\(^{9, 10, 14, 15}\)

Limitations

Our study has several limitations. First, it is a bench-test study on a model, which only mimics real anatomy. It is possible that in arteries quantitative aspect of deformations is to some extent different. However all deformations follow quite well our theoretical predictions.

Secondly, the study was performed with the four cell designed, thick strut stent Chopin 2. The observed parameters during our study (as maximal cell opening distance) differed to some extent from parameters given from the manufacturer. As an open cell designed stent it could be considered a good option for bifurcation stenting. It is possible that with other stents, with different design and strut thickness some parameters to be different. In our view despite some differences between stents general tendencies will be the same as we show.

Third, it is important that this is a bench-test model without any plaque burden. In our viewpoint our study gives a basis for differentiating between changes occurring independently from atherosclerotic process. If we can predict with a mathematical armamentarium changes from stent placement we can subtract it from final changes where there is disease process.

Conclusions

We characterized bifurcation vessels, with respect of stenting, with simple geometric parameters; namely angle \( \dot{a} \), giving a basis for prediction of side branch compromise. Our bench tests on a model with elastic walls give direct evidence for flow divider displacement forming elliptical
shape of ostium of SB, and power of our theoretical concept and demonstrated big role of the flow divider position. We have given evidence that real area at the entrance of lateral vessel could not be estimated realistically from angiography. We have directly shown that kissing balloon inflation does not guarantee good stent apposition to the vessel walls.

References