QUANTITATIVE CORONARY ANGIOGRAPHY FOR IN-STENT RESTENOSIS

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Abstract: Quantitative coronary angiography is a technique directly based on contrast coronary angiography and is commonly used to assess early and late results after percutaneous coronary intervention. It is used to calculate several parameters useful in objective assessment of coronary lesions (continuous end points such as minimal luminal diameter at follow-up, percent diameter stenosis, late loss etc are used to test new stenting methods). Late loss is an angiographic surrogate for neointimal proliferation and has a great importance for drug eluting stent trials. Likewise late loss and percent diameter stenosis are used as surrogates of clinical effectiveness in trials. Of a great interests for researche is the study of coronary bifurcation and the development of three-dimensional techniques.

Keywords: restenosis, quantitative, angiography, late loss, stent

1. Introduction

Coronary angiography consists in visualization of coronary vessels and associated lesions by selective injection of contrast medium. The technique was introduced in the 1950’s by Sones. After more than 100 years since Claude Bernard (1844) made the first experimental catheterization on animal and Roentgen (1895) discovered X-rays, invasive coronary exploration plays a central role in coronary artery disease diagnostic and treatment. Coronary lesions can be evaluated qualitative and quantitative. Because visual interpretation is a subjective evaluation with a wide intraobserver and interobserver variability quantitative coronary angiography (QCA) can be considered the “golden standard” in coronary artery stenosis analysis, having the great advantage of being free from observer’s influences. QCA was introduced 30 years ago by Brown and colleagues. The first generation of QCA systems were based on 35-mm cinefilm analysis and over years multiple technique improvements were made for the next generation (improvements in the quality of the edge detection, solutions for the quantitative analysis of complex lesion morphology, specialized function etc). QCA utilizes most frequently, arterial contour detection and can be used in two ways: “on-line QCA” and “off-line QCA”. On-line QCA requires a situation in which QCA work station is directly connected to the image generating X-ray systems. On-line digital systems are used in clinically practice as a guide in coronary interventions, to decide on the type of intervention and to choose appropriate devices and their sizes. Off-line QCA based on data storage and transfer is uses for research purposes

2. QCA parameters and stent studies

QCA parameters are obtained analyzing all segments in at least two orthogonal projections. Selected images for analysis are identified using views where stenosis has the minimal foreshortening and the minimal overlap with other structures and display the stenosis in its “sharpest and tightest” view. With the contrast-filled catheter as the calibration source, QCA is performed using a validated automated edge detection algorithm.(figure 1)

For stent studies three main coronary segments are subject for quantitative angiography: in-stent, proximal edge and distal edge segment. The coronary segment of analysis is the part of the target vessel that is used for QCA analysis. The stented segment is the part of the coronary artery extending from the most proximal to the most distal stent marker. The edge segments positioned adjacent to the proximal and distal boundaries of the stented segment (up to 5 mm length from the boundaries). QCA uses specific software which allows obtaining parameters for objective quantification of coronary artery lesions. The main parameters obtained with QCA are:

- Minimal luminal diameter (MLD) - the smallest lumen diameter in the segment of interest (mm)
- Lesion length - the length of the stenotic segment calculated from the two points (proximal and distal) where the coronary margins changes direction and creates shoulders between the
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angiographically normal segments and the diseased segment (mm)

- **Diameter stenosis (DS)** - \((\text{RVD-MLD})/\text{RVD}\) (percentage %)
- **Reference vessel diameter (RVD)** - the average diameter of the coronary artery assumed without atherosclerotic disease (mm)
- **Late loss** - postprocedural MLD-MLD at follow-up (mm)
- **Acute gain** - postprocedural MLD-preprocedural MLD (mm)

**Fig. 1** QCA performing in patient with in-stent restenosis (MLD: 0.89 mm, RVD: 3.20 mm, %DS: 72%)

Binary restenosis (BR) is defined as DS >50% at follow-up coronary angiography in the treated coronary segment. QCA is used to evaluate short and long term results of interventional therapy and also to prove different stent types efficacy in clinical studies. Coronary stent leads to a higher residual lumen in comparison with balloon angioplasty, but is limited by restenosis occurrence. Several definitions have been used to describe angiographic restenosis. Widely accepted is the binary definition based on the percentage of DS (DS ≥ 50% at follow-up at the site of the treated coronary segment) as was shown in experimental physiology studies.

In-stent restenosis is observed in various patterns which largely have been described as diffuse or focal. (figure 2)

Frequently is used Mehran classification in four patterns (pattern I: focal and pattern II, III, IV: diffuse)

**Fig. 2** Patterns of in-stent restenosis: a) focal, b) diffuse

The loss of MLD at follow-up is defined as late loss. Because stents abolish elastic recoil and remodeling, late loss can be considered an angiographic surrogate for neointimal proliferation. Late loss calculation becomes more important in drug eluting stents (DES) studies where late loss can determine the effect on neointimal hyperplasia of agent under investigation.

Late loss is an objective parameter that can be related to stent’s type or design. Compared to bare metal stents (BMS), using DES has a favorable effect on late loss reduction as many clinical trials have been demonstrated.

The SIRIUS Angiographic Substudy compared the...
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efficacy of SES versus BMS using results of coronary angiography at 240 days follow-up at patients with high risk of restenosis. Using SES determined a 91% reduction of binary restenosis within the stent, a 75% reduction within the treated arterial segment, reduction in late lumen loss within the stent (0.17 mm) compared with BMS (~1 mm), this favorable effect being extended also to the edge segments. In the TAXUS IV trial angiographic measures at nine months showed a reduction in late loss within the stent at patients treated with PES (~0.39 mm) compared with BMS (~0.92 mm), a reduction of binary in-stent restenosis rate (5.5% vs 24.4%) and this benefit was also found in small coronary artery, long lesions or edge segments. Late loss and percent diameter stenosis are frequently used as surrogates of clinical effectiveness in trials. Pocock and colleagues, analyzing data from 11 randomized trials, showed that the risk of target lesion revascularization (TLR) in individual patients is strongly correlated to late loss and percent diameter stenosis. Several models have been described to analyze late loss in clinical trials. Mauri et al analyzing data from 22 published trials, have shown that there is a strong positive association and a monotonic relationship between late loss and risk of binary restenosis. A curvilinear relationship has been described between late loss and TLR by Ellis et al. Follow-up %DS is as efficient as late loss in predicting TLR. The risk of TLR is low when %DS < 50%, increase sharply when %DS>50-80% and reach a plateau when %DS>80%. QCA can be used in patients undergoing brachytherapy to analyze the local biologic effects of therapy and the „edge effect”. A great interest for interventional cardiology field is bifurcation treatment. Because applying standard QCA to coronary bifurcation is difficult, manufacturing companies developed a special software for the analysis of bifurcation. Techniques for reconstruction of the two-dimensional coronary angiogram in space have allowed the implementation of three-dimensional QCA and that seems to be a promising tool for the future.

QCA role in clinical practice is complementary to standard coronaryography and other imaging techniques (computed tomography, intravascular ultrasound etc). Several angiographic phenomena can bias QCA: thrombus, extensive calcium deposits, diffuse disease, and slow flow.

3. Conclusions

Developed in the last 30 years quantitative coronary angiography is a reliable technique with a proven efficacy in the management of patients undergoing percutaneous coronary intervention. Despite some limitations, angiographic parameters such as late loss, percent diameter stenosis etc. play an important role in stent studies.

Continuous improvements in software technology, bifurcation analysis, three-dimensional QCA represents a challenge for the next years.

4. References