Residual coronary dissections after drug-eluting stenting: the good, the bad, and the ugly

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This editorial refers to 'Incidence, predictors, and outcomes of coronary dissections left untreated after drug-eluting stent implantation' by G.G.L. Biondi-Zoccai et al., on page 540

The article of Biondi-Zoccai et al. provides a unique opportunity to review the management of coronary dissections induced during percutaneous coronary interventions. For more than 25 years, interventional cardiologists have been facing this challenging situation using different approaches. Initially, prolonged balloon inflation was the only available therapy. If unsuccessful, patients with acute or threatened vessel closure had only urgent coronary artery bypass surgery as a therapeutic alternative to prevent or limit myocardial damage. The introduction of coronary stents, with their inherent scaffolding properties, dramatically changed this scenario and allowed the dissection flap to be readily tackled. However, whether or not routine stenting is systematically required to seal even minor residual coronary dissections has been a matter of continuous debate for the last decade. Currently, the soliloquy 'To stent or not to stent: that is the question' is being revisited in the new era of drug-eluting stents. Only inquiring into the facts (the good, the bad, and the ugly) may guide us in solving this dilemma. However, what do we know about the pathophysiology, predisposing factors, prognostic implications, and management of residual coronary dissections?

The good

Coronary dissections represent the 'natural' response of the coronary wall to the mechanical injury of vessel stretching caused by high-pressure balloon inflation. In fact, the mechanism of lumen enlargement after angioplasty relies upon the occurrence of a 'controlled' coronary dissection. If this 'therapeutic' dissection is relatively confined, both in depth and in length, the lumen gain obtained guarantees a high coronary flow that largely offsets the associated drawbacks of high/low shear stress zones caused by winding dissection planes and the strong stimulus for thrombus formation generated as flowing blood interacts with subintimal vessel layers. Notably, several studies demonstrated that the presence of an angiographically detected residual dissection was associated with a lower risk of restenosis. This is in sharp contrast to our current overt insecurity when we need to proceed with balloon angioplasty alone, especially when final results are scrutinized with high-resolution digital angiography.

Residual dissections are also frequently noticed after coronary stenting, mainly in bailout situations. In some cases, particularly when the relatively rigid first-generation stents were used, this was the result of incomplete coverage of the dissected segment in the cases of severe tortuosity or long dissections in small/distal vessels. Several studies, however, consistently demonstrated a benign clinical and angiographic outcome in these patients and, interestingly enough, complete resolution of the dissection plane at late follow-up. At that time, conventional wisdom recommended a conservative management for unsealed dissections, providing they remained stable and were associated with normal coronary flow and only mild residual stenoses. Later on, detailed mechanistic studies using intravascular ultrasound after stenting uniformly confirmed a benign outcome in patients with residual dissections. Ultrasound-detected 'edge-tears' or 'dissection pockets' tend to be small (unnoticed by angiography) and disappear at late repeated imaging.

Finally, two previous studies failed to demonstrate a clinical benefit of additional stenting in patients with uncomplicated moderate residual coronary dissections. Therefore, the rationale supporting a conservative management in this setting stems from the evidence suggesting that most stable residual coronary dissections have an excellent prognosis and completely heal over a 6-month time frame.

The bad

Coronary dissections have consistently been found to be a predisposing factor for acute vessel closure after balloon angioplasty. In fact, the NHLBI classification was devised as
a tool to elucidate the risk of vessel closure after vessel dissection. Attempts to seal these dissections with prolonged low-pressure balloon inflation proved both risky and unreliable. Likewise, the time required to guarantee that a dissection had indeed stabilized (watchful waiting strategy) frequently 'disrupted' not only laboratory schedules, but also operator’s patience. The same is true for residual dissections after stenting where most studies identified this finding as a major predictor of stent thrombosis. Accordingly, the use of a 'conservative strategy' has been continuously challenged and blamed as nihilistic, especially with the advent of new generation stents—with superb trackability—able to guarantee pristine final angiographic results.

The ugly

Drug-eluting stents represent a breakthrough in interventional cardiology. However, the delayed endothelial healing process that characterizes these antiproliferative devices sets the basis for a higher thrombotic substrate requiring prolonged dual antiplatelet therapy (that is not compulsory after bare metal stenting). The dramatic consequences associated with stent thrombosis lead to an aggressive management of any factor—including residual dissections—that could increase this risk.

Once a drug-eluting stent has been implanted, the use of a similar stent to tackle a residual dissection would appear a reasonable choice. Nevertheless, although the influence of lesion length on restenosis has been dramatically blunted by these stents, longer stented segments still carry a higher risk not only of restenosis but also, more importantly, of stent thrombosis. Thus, there is a price to pay when multiple stenting is required to completely seal residual dissections. Moreover, why should we use a drug-eluting stent to treat a dissected vessel in the first place? Could this interfere or even prevent the normal healing process of the vessel wall? This is particularly relevant in the cases where the torn tissue originates from or extends into relatively healthy coronary segments. Prior reports demonstrating vessel remodelling, acquired incomplete apposition, hypersensitivity phenomena, and even aneurysm formation after drug-eluting stenting are not particularly reassuring in the setting of a dissected vessel. All these features may become a nidus for thrombus formation, which, in turn, may herald the dreadful complication of stent thrombosis.

The alternative of leaving alone stable residual dissections is also of concern. We should keep in mind that therapeutic strategies aimed to inhibit cellular proliferation can act as a double-edged sword, interfering with the normal healing process of the vessel wall. Studies have demonstrated that intracoronary brachytherapy affects vessel healing and may promote the persistence of residual dissections at late follow-up. Theoretically speaking, a similar phenomenon could occur after drug-eluting stenting. What should we do then? ‘To stent or not to stent’?

The facts

The interesting study of Biondi-Zoccai et al. analysed 4630 lesions treated with drug-eluting stents included in the RECIPE registry. Final residual dissections were identified by angiography in 77 (1.7%) of these lesions (71% type A–B and 80% normal flow). Dissections tended to arise from long and complex lesions and in the left anterior descending coronary artery. On multivariate analysis, coronary calcification and diffuse disease predicted the occurrence of final dissections. Residual dissections were associated with increased rates of in-hospital mortality and major adverse cardiac events at 1 month. In addition, the cumulative rate of stent thrombosis was also higher in these patients.

This work should not be considered as a ‘natural history’ study of residual dissections after drug-eluting stenting, as some initial dissections were eventually treated by the investigators. Therefore, only those residual dissections that could not be sealed and those that the operator decided to manage conservatively were adjudicated and analysed. External validation of the final models was not attempted, but a sound statistical analysis, including bootstrapping for internal validation and Hosmer–Lemeshow statistic to check fitting of logistic models, was reassuring. In addition, although a centralized core-lab was not used, the pre-specified analysis at each site of explicitly defined angiographic features and the large number of patients included support the robustness of the study findings. Finally, some tautological reasoning may always overshadow the link between procedural-related complications and subsequent adverse clinical outcomes. Despite these caveats, the current study provides compelling evidence, suggesting the adverse prognostic implications of residual dissections after drug-eluting stenting.

The restenosis rate in the study was relatively high and similar in patients with and without residual dissections. However, the lack of systematic angiographic follow-up precluded to gain further insights into the potential late implications of unsealed dissections. In this regard, the possibility that either local injury or residual dissections may predispose to ‘edge’ in-stent restenosis has been suggested. Lemos et al. recently demonstrated that residual dissections after drug-eluting stenting are frequently detected among patients who subsequently develop ‘edge’ in-stent restenosis. Likewise, in the Italian registry, a surprisingly high number of unhealed dissections (up to 37%) persisted at late angiography. Why should these residual dissections fail to heal? What will be their fate in the long run? The answers remain elusive, and these results should be considered just hypothesis generating, underscoring the need for further large-scale studies with systematic angiographic follow-up.

The need to treat complex or flow-limiting dissections appears to be undisputed. However, the key issue is whether all apparently benign and relatively small residual dissections also require an aggressive treatment. Although the data from this real world registry on the subset of non-flow-limiting type A–B dissections are unable to convincingly demonstrate their detrimental effect on clinical outcome, there was a strong trend in this regard, supporting the view that even these dissections confer an increased risk for complications. Surprisingly, residual dissections witnessed after a failed attempt to deploy an additional stent (38% of final dissections) were not associated with a poorer outcome than those that were intentionally left untreated. Whether a more comprehensive anatomical (intravascular ultrasound) or physiological (fractional flow reserve) evaluation of these apparently ‘benign’ dissections could be used to unravel their potential risk for
complications and to triage patients for further stenting remains as yet speculative.

The results obtained with drug-eluting stents are not evolutionary but revolutionary. However, the current study provides an interesting piece of new information, suggesting that residual dissections after drug-eluting stenting are indeed associated with adverse clinical and angiographic outcomes. More aggressive and prolonged antiplatelet regimens appear indicated in these patients. Although implantation of additional drug-eluting stents would appear not only justified but even the therapy of choice—as the Italian investigators dare to adventure—further studies are still warranted to confirm that this strategy translates into improved clinical outcomes. In the mean time, as in the Shakespeare's Hamlet soliloquy, the dilemma will stay with us and the decision-making process concerning the need for additional drug-eluting stenting in the vexing scenario of ‘benign’ residual dissections will be made on an individual basis, taking into account not only anatomical features but also economic considerations and operator’s criteria.

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References
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