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Spelling out risk reduction strategies for intracoronary stenting

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Introduction

Plain balloon coronary angioplasties often required prolonged inflations, coronary reperfusion, frequent angiographic controls, and repeat interventions because of imminent target vessel closure. In up to 10% of cases, emergency coronary bypass surgery was required. The introduction of intracoronary stents clearly simplified coronary interventions by markedly reducing post-dilatation mechanical complications[1,2], initially at the cost of risking specific stent-related complications, such as thrombotic vessel occlusions[3] and later increased rates of bleeding[4]. However, the efficacy of dual anti-platelet therapy in preventing thrombosis and reducing bleeding complications[5] and a convincingly low in-stent restenosis compared to post-angioplasty restenosis rates[6,7] have clearly established the central role of bare-metal stents (BMS) in PCI[8]. More recently, drug-eluting stents (DES) allowing better suppression of the biological restenosis processes even further increased the broad acceptance of intracoronary stenting[9]. Prompted by recent concerns regarding the long-term safety of DES[10], this article seeks to re-assess the current clinical practice of intracoronary stenting and to make explicit a number of strategies available for reducing intervention risk.

Stenting strategies

Indications for stenting in coronary interventions historically included two broad categories: rescue after failed balloon angioplasty and improvement of prognosis.

Based on intention-to-treat, six principle types of strategy of intracoronary stenting can be distinguished. We describe them in the order of increasing stenting probability:

- Originally, stents have been employed exclusively for rescue of failed angioplasties. Using this *"bail-out"* strategy, coronary stents are used exclusively in patients with acutely imminent or established vessel closure.
- In the *provisional stenting* strategy, the primary intention is to treat the lesion by plain balloon angioplasty and to resort to stenting only in case of unsatisfactory results as determined by angiography.
- In *conditional stenting*, the attitude is neutral: the lesion will be treated either by plain angioplasty or by stent angioplasty and the decision is based on angiography and a second modality such as IVUS or pressure-wire.
- In *primary stenting*, the intention is to treat the target lesion by stent angioplasty. However, balloon angioplasty is used first, providing important clues to the tracking ability of the proximal access pathway and the mechanical properties of the target lesion. If stent-like result has been achieved, e.g. defined as <20% diameter residual stenosis and absence of relevant dissection assessed by angiography, stenting may be omitted.
- In *unconditional stenting*, stenting is employed regardless of the result of the initial balloon angioplasty.
- In *direct stenting*, stent placement is the first and only intervention planned.

If multiple lesions are targeted, a different strategy can be employed for each. In current clinical practice, the majority of coronary interventions are performed using strategies with high a-priori probability of stenting – about 40% even with a direct stenting strategy[11]. Albeit there is no doubt that introduction of stents has markedly decreased the risks and increased the benefits of PCI[12]

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and expanded PCI indications[13] compared to stand-alone coronary angioplasty the increasingly indiscriminate use and growing reliance on stents has had at least two major problematic impacts on clinical practice. First, higher incidence of specific stent-related risks and complications potentially detracting from the overall benefits of stenting; second, neglect of careful consideration of different treatment options and strategic decision making. What are these stent-related risks?

Risk of stenting

Qualitatively, a risk is any undesirable event that may or may not occur. Quantitatively, risk is the extent of damage incurred by the event weighed by its probability – even if both damage and probability are known only very roughly. PCI, as any interventional treatment, attempts to take a course of action that minimises the overall risk and maximises the benefit for a given individual patient, relying on the power of judgement and technical skills of the interventionist[14]. To allow comparison of different PCI strategies comprehensive concept of latent and actional risk evaluation has been proposed[15]. Roughly speaking, latent risk arises from the patient's condition and can be reduced by intervention, while actional risk arises from the conduct of a given individual intervention and can be reduced by non-intervention. Thus, sensibly conducted PCI accepts modest actional risk in order to markedly reduce latent risk in a particular patient. The risks specific to stenting are those components of actional risk not present in plain balloon angioplasty. In clinical practice, coronary stents implanted in "bail-out" scenarios have clearly reduced the actional risk while immensely increasing the derived benefits in the majority of cases[16]. Outside of such cases, however, the actional risk specific to stenting must be considered in each individual patient not to actually exceed the actional risk of plain balloon angioplasty without added benefits[17]. Although statistical data on incidence of specific stent-related risks are rare in the literature[18] some of the risks and complications are well recognised including:

– Stent damage, malapposition, failed crossing, failed deployment, dislocation or loss[19-21].
– Stent- related edge dissections with increased latent iatrogenic risk (if left unattended) or the actional risk (if treated)[22-25].
– Stent- related thrombosis[26].
– Unplanned stenting and escalating stenting procedures[27-29].
– Stent related aneurysm, retrograde aortic dissection, inflammatory responses and allergy and other rare complications[30-33].

While each of these risks is relatively modest, together they are clearly large enough to warrant serious attempts at minimising them – something we feel is not done enough in current stenting practice. What can we do to reduce these risks?

Risk reduction by better case selection

To maximise the benefits of stenting pro and contra stenting factors must be always thoroughly considered. Decisions upon primary stenting strategies and unplanned stenting in evolving interventions must become a critical part of decision making in each individual patient. These factors can be divided into two basic categories, target site and patient related.

– *Pro-stenting target-site related factors:* plaque ruptures, mechanically unstable lesions, high recoil, high proximal target lesion in critical segments of critical target vessels, target lesion in the last remaining vessel, the most significant lesion in multi-vessel disease, severely compromised left ventricular function and type II diabetes, suboptimal result of plain angioplasty (>20% diameter residual stenosis).
– *Contra-stenting target site related factors:* "stent-like" results after plain angioplasty[17,18], particularly in target segments with low "Leaman score"[35], diffuse disease, multiple long target lesions, multi-vessel coronary artery disease with multiple focal and/or diffuse lesions, small vessels, poor outcome of previous stenting revascularisation attempts, target lesions in highly tortuous segments, "hostile" upstream vessel access.
– *Pro-stenting patient related factors:* absence of contra-stenting factors, high risk of restenosis, high risk of re-interventions.
– *Contra-stenting patient related factors:* anti-platelet drug resistance, known prothrombotic syndromes, poor compliance, metallic allergies, expected major non-cardiac surgeries within six to 12 months.

The presence of a multitude of pro-stenting factors indicates that the interventional strategy should probably be at least primary stenting. The presence of one or more contra-stenting factors indicates that the stenting strategy should probably be less than conditional stenting.

Risk reduction by better target site evaluation and PCI guidance

To maximise benefits of stenting and reducing the stenting-specific risks, a large number of factors related to the target site must be considered. These factors evolve and change throughout the intervention and must be re-assessed repeatedly. The following considerations can help with making good stenting-related decisions:

– *Basic angiographic target lesion assessment criteria:* in addition to the assessment of SYNTAX score[36] or similar criteria to define the complexity of coronary artery disease comprehensive angiographic assessment of relevant aspects of intervention including evaluations of the proximal access, target vessel tortuosity, upstream lesions, presence and degree of proximal calcifications, previous interventional sites, detailed status of the target lesion including surface morphology, eccentricity and plaque distribution in at least two projections, status of the downstream vascular territory including the length of the downstream target vessel, presence of collaterals at risk, status of dependent branches and non-target coronary vessels.
– *Test run:* in target lesions with "hostile" proximal access and tight or highly calcified target lesions a test run is required using a deflated balloon catheter with or without predilatation of the target lesion may provide important information about the stability of the entire interventional system, its proximal tracking ability and the dilatability of the target lesion. In addition, angiographically "hidden" features such as unforeseen endoluminal friction or difficult crossing may be uncovered.
– *Second-look control angiography.* In selected patients with complex target sites and/or highly abnormal coronary vasomotion

despite coronary vasodilatation a second-look angiography, frequently performed the next day, may be helpful to determine the presence of relevant remaining lesions, to exclude dissections and thus to avoid unnecessary stenting.

– *Adjunct diagnostic modalities:* in patients with angiographically ambiguous target sites the use of adjunct modalities should always be considered, despite ambivalent recommendations[37]. In these cases intracoronary ultrasound (IVUS) may be preferred to guide interventions (a) to define lesions, (b) to size instrumentation, and (c) to evaluate intermittent and final outcomes. However, with the current relatively rigid and bulky IVUS probes care must be taken to avoid injuries particularly in delicate interventional sites. Similarly, coronary pressure-wire measurements may be highly effective in strategic decision-making regarding angiographically borderline or ambiguous lesions, multivessel disease with multiple lesions, diffuse disease and other states[38].

Thus, careful, critical and comprehensive angiographic assessment of interventional sites prior and during interventions along with judicious use of IVUS and pressure-wire in selected cases may allow early recognition of otherwise unapparent latent risk thus reducing the actional risk, particularly in complex and escalating procedures.

Risk reduction by improved outcome assessment

Evidence-based medicine's standard manner of reporting PCI outcomes is to count the incidence of angiographic, procedural and clinical endpoints[39].

– *Angiographic success* depends primarily on assessments of the degree of residual or recurrent stenosis and less frequently on assessments of cross-sectional area, antegrade coronary blood flow, and myocardial perfusion.

– *Procedural success* has been defined as angiographic success in absence of any clinically relevant complications, usually within 24 hours or before hospital discharge.

– *Clinical success* relies on absence of symptoms and freedom from major adverse cardiac effects such as cardiac and vascular death; procedure related acute myocardial infarction, repeat target vessel revascularisation (TVR) or target lesion revascularisation (TLR).

Recently, to improve comparability of PCI outcomes between studies, unequivocal definitions of clinical endpoints such as cardiac, vascular and non-cardiovascular death, myocardial infarction, repeat target lesion, target vessel and non-target vessel revascularisation and stent thrombosis have been proposed and, importantly, the use of composite endpoints such as major adverse cardiac events (MACE) has been discouraged[40]. To optimise PCI practice, we need to keep in mind that clinical success is what counts the most and hence comparisons based on the weaker (but more common) procedural or angiographic criteria may be misleading - a fact that we feel has been often overlooked in today's stenting-related discourse and only recently corrected by the recommendations of the Academic Research Consortium. Nevertheless, also procedural outcome criteria should be extended to better reflect clinical outcome and quality of interventions. Examples of extended procedural outcome criteria include:

– *Routine measurements of CKMB before and after all PCI.* The critical importance of measuring indicators of peri-interventional myocardial damage has been extensively discussed in the literature and shall not be repeated here[41,42].

– *Length of each target lesion and corresponding length of stented segments.* It is well known that the length of the stented segments typically exceeds the initial length of the target lesions[43]. Given the average length of stented segments of 31 mm[44], 24-31% of the total length of the epicardial LAD or 39-52% of the epicardial LCx or 22-26% of the RCA would be stented in a single intervention[45] reducing the chances of success of future revascularisation attempts in case of disease progression.

– *Number of stents per lesion:* the number of stents implanted per lesion is typically greater than one, with an average between 1.1 and 1.4 in clinical trials[46,47] and being even greater in real-life settings[44]. Assuming the intention to treat a single lesion with a single stent, the percentage of unplanned extended stenting could thus be as high as 50%. Since the actional risk of any interventional procedure increases with the number of interventional steps, particularly if unplanned[15] and its procedural outcome benefits correspondingly decreases[48] it is plausible that the number of implanted steps should be kept to a minimum[15].

– *Non-target vessels.* The status of any non-target vessel should not change during PCI. To assess for any relevant damage any closure of relevant side-branches (> 2 mm in diameter), pre-existing collateral or other non-target vessels should also be reported.

– *TIMI flow grade.* TIMI flow is a critical predictor of clinical outcome[49], therefore TIMI flow grade in the target vessel assessed on the final angiograms should become a part of standard protocols.

We submit that both, research and standard clinical protocols should report these extended procedural outcome criteria.

In summary, to maximise the benefits of intracoronary stenting and to minimise the stent-related risks and complications, today's highly stenting-inclined PCI practice should be modified by broadening the range of interventional strategies, better case selection, more sophisticated PCI guidance and more stringent evaluation of outcomes.

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