

## The Bailout Stent

### Is a Friend in Need Always a Friend Indeed?

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**W**hen invited to write an editorial on bailout stenting, many titles came to mind—"The Double-Edged Sword," "Friend or Foe," and "Jekyll and Hyde"—to convey the current balance of the efficacy and the risk associated with bailout stent therapy. Rather than consolidating the role of stenting in the emergency management of abrupt or threatened occlusion following coronary interventional procedures, the observational study reported by Hearn and colleagues in this issue of *Circulation*<sup>1</sup> raises further questions over the benefit-to-risk ratio of bailout stenting.

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Abrupt vessel closure occurs during coronary balloon angioplasty in 5.6% of patients, whereas an additional 1.7% of patients develop an occlusion during the following 24-hour period.<sup>2</sup> The mechanisms of abrupt coronary occlusion include a combination of dissection, subintimal hemorrhage, thrombus formation, vasoconstriction, and elastic recoil.<sup>3</sup> When acute coronary occlusion persists, it leads to myocardial infarction in about 40% of cases and death in about 4%.

In the early experience of balloon angioplasty, abrupt occlusion was managed by emergency coronary artery bypass surgery. In contrast to elective surgery, however, emergency surgery was found to convey a high morbidity and mortality risk. As experience with balloon angioplasty grew, the practice of immediate redilatation was developed. While prolonged balloon inflation with or without a perfusion balloon or laser balloon angioplasty offered an alternative to emergency surgical management, they rarely achieved definitive success. Thrombolytic therapy (either intravenous or intracoronary) has been anecdotally successful. However, the overall experience has been disappointing. Moreover, if the patient proceeds to emergency surgery, prior thrombolytic therapy may complicate the operation. Despite these strategies, abrupt closure after coronary intervention continues to result in unacceptable morbidity and mortality. With such room for improvement, stenting with its scaffolding properties opened a new avenue, and while initially viewed by some as a bridge to surgery, it is now heralded by many as the path to avoid surgery.

#### The Paradox

Considerable overlap exists between the lesional characteristics predisposing to abrupt closure following coronary interventional procedures and the relative contraindications to elective stenting (and thus it could be thought that the bailout stent gives coronary stenting a bad reputation): Univariate and multivariate analyses of qualitative and quantitative criteria have shown that severe, long, complex lesions, at a branch or bend point, of ACC/AHA type B, C, containing intracoronary thrombus or dissection and unstable angina lead to an increased likelihood of acute closure following balloon angioplasty. While factors found to predict subacute thrombosis after stent implantation have included bailout indication (odds ratio, 5.4), lesion length, type C lesion, stent size <3.25 mm, residual thrombus, and unstable angina.<sup>4,5</sup>

Unfortunately, in the setting of an abrupt vessel closure attended by acute ischemic consequences, an operator is unable to electively select only those vessels and lesion characteristics that are ideally suited to stent implantation. Thus, vessels containing characteristics that might normally be regarded as relative contraindications to stenting frequently impose themselves on the interventionist who is left with a choice of either stenting under unfavorable conditions or adopting an alternative, less-effective strategy known to carry a higher risk. Stenting in bailout management could be considered the best of a bad lot. In large vessels, subtending a substantial amount of myocardium, which develop a totally occlusive dissection, the case for bailout stenting appears clear (white), whereas for small vessels <2 mm developing a subocclusive thrombosis following intervention, the preference for stenting over alternative nonsurgical strategies is weak (black). Unfortunately, like many aspects of medicine, most cases fall into a "gray" intermediate category.

#### Empty Threats?

Studies of emergency therapy are inherently confounded by terminology and the quality of data acquisition. In the case of bailout stenting, although the term "acute closure" of a vessel appears steadfast and clear, the term "threatened closure" appears soft and open to interpretation by the operator. Indeed, a threatened event such as an "impending myocardial infarction" is a diagnosis that in reality can only be confirmed after the event if intervention is withheld. In the observational study reported by Hearn et al, the definition of threatened occlusion included either static or dynamic elements.<sup>1</sup> A static component such as a large dissection

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will remain subjective, whereas the incorporation of an evolving process such as a recorded decrease in luminal diameter or change in TIMI grade flow over time offers a more rigorous approach. In most reports on bailout stenting, outcome for threatened occlusion has been grouped to include a wide spectrum of angiographic, ECG, or clinical criteria, thus rendering the results difficult to interpret and limiting their direct applicability to clinical practice.

### **The Learning Curve and the Legacy**

The historical series of bailout coronary stenting reported by Hearn et al<sup>1</sup> reflects the early experience of coronary stenting. Between September 1987 and December 1990, Gianturco Roubin stents were implanted in 103 patients. In view of the approximately 3- to 6-year time span from stent implantation to publication of the results, the report is to some extent of limited relevance to the current practice of coronary stenting. The design of the pioneering series necessitated the referral to bypass surgery of all nine patients in the first phase of the study and an additional nine patients in phase II in whom potential closure would have incurred a significant risk of mortality. Their rate of emergency coronary artery bypass surgery for ongoing ischemia after stent implantation was 11 of 98 patients (11%) in whom stenting was attempted and in whom surgery was not mandated by the study protocol. Their rates of in-hospital q wave myocardial infarction and mortality after stenting were 4.9% and 4.0%, respectively. It is not possible to decipher whether their results with bailout stenting improved over the 3-year study period as the sequential breakdown of their results is presented in only two phases, with the first phase containing only the first nine patients as above.

In a second single-center observational series of bailout therapy with Gianturco Roubin stents in 115 patients between October 1989 and June 1991 involving an operator previously experienced with Gianturco Roubin stent implantation, the in-hospital rates for emergency bypass surgery, q-wave myocardial infarction, and mortality were 4.2%, 7%, and 1.7%, respectively.<sup>6</sup> A comparable outcome was subsequently reported in a multicenter study of similar design.<sup>7</sup> These results were favorable considering that in a meta-analysis of nine series of bailout stent therapy incorporating an accumulative experience of five different stent prototypes in 464 patients from 1986 through 1991, mean rates of in-hospital emergency bypass surgery, myocardial infarction, and mortality were 8.4%, 10.6%, and 4.1%, respectively.<sup>8</sup>

### **The Prospects**

Clearly, the results of the above bailout studies compare poorly with those reported for elective stenting from the same era. It would also be envisaged that over recent years the outlook for all stenting has improved due to advances in procedural and postprocedural management. Following the observations that subacute thrombosis and restenosis occur more frequently in stents of smaller size and the quantitative angiographic observations that even during maximal stent inflation the nominal manufacturer's size of a stent is rarely achieved and that recoil immediately after stent implantation is the order of 20%,<sup>9</sup> policies have changed from

matching stent size in the reference vessel diameter to a policy of choosing a stent of slightly larger nominal size than the reference vessel size to compensate for the above limitations. On the basis of a large databank at the Thoraxcenter of balloon angioplasty procedures, only approximately 20% of the population would be able to receive a stent of more than 3.0 mm under a policy of strict matching for vessel size. In the series reported by Hearn et al<sup>1</sup> a stent size of >3.0 mm was chosen in only 16% of patients which compares with the series of Roubin et al where 17% of stents deployed were >3.0 mm.<sup>6</sup> The stent sizing chosen by Hearn et al may, however, have been influenced by their process of patient selection whereby patients were selected if they had "lesions that, if closed after stent placement, would not result in massive myocardial ischemia or hemodynamic instability." It is noteworthy that the recent Benestent I and STRESS trials on elective stenting excluded vessels of <3.0 mm.

A second change in policy is the criterion of procedural success. In the report of Hearn et al,<sup>1</sup> procedural success was defined as <50% residual diameter stenosis. As with other interventional techniques the current aim in coronary stenting is now changing to achieve a "zero" percent residual diameter stenosis. This latter change in policy is likely to have a major effect in both short- and long-term outcome after coronary stenting particularly in patients receiving a stent of small size.

Accurate implementation of both the new stent-sizing policy and the policy of greater luminal gain (the bigger the better) has recently been made possible by the almost ubiquitous presence of on-line computerized quantitative coronary angiography in the interventional suite.

The advent of intracoronary imaging has further improved procedural management. Intracoronary ultrasound can be used to detect asymmetrical stent expansion or residual dissection behind a stent, whereas angiography can provide valuable information on stent deployment with the detection of luminal encroachment at sites of articulation in a mesh stent or protrusion of intima between struts in a coil stent, both of which may be ameliorated by the placement of a second stent or prolonged or high-pressure inflation of a noncompliant balloon within the stent. Furthermore, angiography can detect the development of thrombus within a stent that can be treated with intracoronary urokinase or t-PA. As a reflection of its practical value, angiography altered management in 18 cases in a recent series of 50 stent implantations (unpublished data from the Scripps Clinic and Research Foundation and the Arizona Heart Institute).

The postprocedural hazard of subacute thrombosis continues to curb enthusiasm for coronary stenting. Once solved, the inherent complications of our current approach to its prevention will be obviated, ie, internal hemorrhage and local femoral arterial complications. While the development of material that is less thrombogenic than stainless steel and tantalum has so far been disappointing, local coating of struts with heparin may offer some hope<sup>10</sup> and will be addressed by the ongoing pilot phase of the Benestent II trial. In the meantime, the optimization of anticoagulant control by the use of the coagulant markers. TAT and F<sub>1+2</sub> have helped to drastically reduce the incidence of subacute



thrombosis.<sup>5,11</sup> Furthermore, improved mechanisms of achieving local hemostasis by Vasoseal® and collagen plugs in addition to the use of mechanical devices such as Femostop® and clamping devices, have facilitated uninterrupted anticoagulant therapy following stent implantation. Recently, some investigators have opted to not anticoagulate patients receiving large-diameter stents after optimal deployment has been confirmed by intracoronary imaging.<sup>12</sup> However, the safety of this approach has not been determined.

### The Selection

All series of bailout stenting have reported a high implantation success rate, which is remarkable taking into account the technical difficulties that may be encountered in a bailout situation. Disappearance of angiographic landmarks and spasm of the vessel segment may render stent delivery and correct positioning difficult. The selection of the diameter, length and type of stent, and selection of the guide wire and guiding catheter may all influence deployment success. In the case of acute takeoff and tortuosity, longitudinal flexibility of the stent is desirable.

Stent selection may also be guided by mural tomographic information provided by intracoronary ultrasound. Lesions characterized by excessive elastic recoil may require a "hard" stent with strong circumferential support such a mesh stent with sturdy metallic struts, whereas lesions that have been extensively disrupted may require only a "soft" stent with a lighter architecture and minimal metallic surface area. The precise effect of lesional characteristics and the role of intracoronary ultrasound in the determination of stent requirements are an area of future research.

### 'In Doubt—Let's Randomize'

Are randomized trials of bailout coronary stenting ethical? A fractured radius is currently managed by fixation in a plaster of Paris. Yet the need for a randomized controlled trial of fixation of limb fractures has been deemed to be unnecessary. As we feel confident from observational studies that bailout stenting can be effective in the prevention of myocardial infarction and the preemption of emergency bypass surgery, how can randomized trials of bailout stenting be warranted? Until such time as the thrombotic and hemorrhagic sequelae of coronary stenting can be overcome, randomization of patients to the nonstenting limb of a controlled trial seems ethical. The policy proposed by Andreas Gruntzig and echoed by Spencer King—"in doubt—Let's randomize"—still appears reasonable.

The Gianturco Roubin Stent Acute Closure Evaluation (GRACE) trial will address the immediate and long-term efficacy and safety of urgent stent implantation in the setting of failed balloon angioplasty or other interventional device. The control limb will be randomized to prolonged and/or repeated balloon dilatation. One important aspect of the trial design is the inclusion of a prestudy phase on 200 patients during which investigators must exhibit proficiency at implantation of the Gianturco Roubin stent. Before commencing the formal GRACE trial, the investigator must have a less than 5% rate of subacute closure or thrombosis and less

than 10% rate of hemorrhagic complications during the prestudy. Furthermore, investigators should have enough potential patients to meet the minimum cases per institution criterion. This design concept represents a new direction in interventional trials in keeping with the upcoming directional atherectomy trials EURO-CARE (<20% residual stenosis required) and OARS and BOAT, with emphasis on optimal performance by all investigators at the upper plateau of the learning curve.

### The Showdown

To convincingly evaluate the relative merits and demerits of bailout stenting, large, multicenter randomized trials need to be conducted exclusively by experienced operators at high-volume centers over a short period of time and reported expeditiously to have an impact on current practice.

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