JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 9, NO. 11, 2016
ISSN 1936-8798/$36.00
http://dx.doi.org/10.1016/j.jcin.2016.03.004
PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Coronary Stent Fracture

A New Form of Patient-Prosthesis Mismatch?*

Jay Giri, MD, MPH, Matthew D. Saybolt, MD

Perfection is not attainable, but if we chase perfection we can catch excellence.
—Vince Lombardi (1)

Improvements in technology and technique have been associated with continuous, steady declines in post-percutaneous coronary intervention (PCI) adverse events, including clinically significant in-stent restenosis and thrombosis. However, the prevalence of coronary artery disease and corresponding breadth of clinical investigation into revascularization continue to yield discoveries of rare or previously unrecognized events and pathologies. Thus is the story of coronary stent fracture (SF), an infrequently reported complication first discovered following a venous bypass graft intervention and later in epicardial coronaries treated with drug eluting stents (2,3). Coronary SF is rarely included as an assessed endpoint in stent performance evaluation, likely because it is thought to have a low overall clinical incidence and benign course. Nonetheless, SF has been observationally accompanied by in-stent restenosis (ISR), thrombosis, aneurysm, ischemic events and target lesion revascularization (TLR) (4,5).

SF has been reported in nearly all bare metal stents (BMS) and drug-eluting stents (DES), and the reported rates vary widely by scaffold type, and are contingent upon the rigor with which investigators have sought out this complication. In a meta-analysis of 8 studies (n = 5,321 patients; 108 SF) within <12 months follow-up after DES implantation, the mean reported incidence of SF was 4.0% (95% confidence interval [CI]: 0.4% to 16.3%) (6). Consistent with prior observations, the probability of SF was highest in right coronary arteries, lesions with overlapping stents, and longer stents (average length: 46 mm; 95% CI: 38 to 54 mm). Lesions with stent fractures had a higher rate of ISR (38% vs. 8.2%, respectively; $p < 0.0001$) as well as a higher rate of TLR (17% vs. 5.6%, respectively; $p < 0.0001$). Repeat angiography and procedures were generally clinically driven, creating a bias toward an overestimation of SF when judged as a proportion of only the population of patients who received repeat angiography. However, even in this selected population, all cases of SF may not have been captured due to short follow-up and limited use of invasive coronary imaging. Standard fluoroscopic angiography detection may be insensitive to definite SF, as a 29% rate of SF has been seen at autopsy, using high-contrast film-based radiography of explanted coronaries (7). Given the above evidence, one might reasonably conclude that SF increases ISR, TLR, morbidity, and mortality. However, a reliable association with major adverse cardiac events (MACE) has yet to be published in an unselected population that has been assiduously followed for SF after initial DES implantation. Furthermore, the high incidence of SF, often devoid of associated pathology at autopsy, suggests that SF remains clinically silent in most patients.

SEE PAGE 1115

In this issue of *JACC: Cardiovascular Interventions*, Kan et al. (8) present important insights into the incidence, patterns, and predictors of SF following DES implantation and examined correlations with future adverse events. Data were acquired from an all-comers 4-center registry in Nanjing, China, where practice patterns encouraged all patients to have routine follow-up angiography 9 to 12 months post

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

From the Cardiovascular Medicine Division, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania. Dr. Saybolt has received research support from Infraredx, Inc. Dr. Giri has reported that he has no relationships relevant to the contents of this paper to disclose.

procedure, a very different approach than that routinely used in the United States. Between November 2003 and January 2014, 8,602 patients received 10,077 PCI. After exclusion of the use of BMS, poor quality angiographic images, and those patients who did not return for the recommended repeat angiographic evaluation, a total of 6,555 patients with 16,482 DES implanted into 10,751 diseased vessels were included in the analysis. All index and post PCI procedural and follow-up angiograms were analyzed in a blinded fashion with quantitative coronary angiography (QCA). Follow-up angiograms were screened for SF, and suspected but non-definitive cases were confirmed with intravascular ultrasonography or optical coherence tomography. Using the stent boost technique, Kan et al. (8) confirmed the cases and categorized them as types I to IV according to the classification by Popma et al. (9). The study's primary endpoints were incidence of SF, ISR, clinically driven TLR, and definite or probable ST.

Over a mean angiographic follow-up of 341 days (interquartile range [IQR]: 36 to 3,390 days), 803 patients (12.3%) were found to have SF, and classifications of SF were equally distributed among the classes described by Popma et al. (9). Stent and vessel-level rates of SF were 22.0% and 17.2%, respectively, exceeding all prior published observations and incredibly approaching the incidence observed in the aforementioned autopsy study (7). Stent fracture was more likely to be discovered at progressively later timepoints after the index PCI, implying that continued stress on a stent over time leads to fracture, and at least some fractures occur long after drug elution has completed. In multivariate analysis, seven procedural factors were independently associated with SF: stents in the right coronary artery (odds ratio [OR]: 10.816), stainless steel stents (OR: 2.601), stent length >25 mm (OR: 2.444), hinge motion (OR: 7.447), overlapping stents (OR: 4.037), multiple stents (OR: 5.224), and stent/vessel ratio of <0.8 (OR: 5.289).

Unquestionably, there were significant differences in baseline clinical and lesion characteristics between patients with and without SF. Adding significantly to previous work, the investigators performed propensity score matching (PSM) to ameliorate confounding. According to PSM, 684 pairs with and without SF were matched for all baseline clinical and lesion characteristics. Results of the comparisons of myocardial infarction (MI), TLR, target vessel revascularization (TVR), TVMI, and definite ST were 4.5% vs. 2.0% ($p = 0.014$), 22.2% vs. 9.5% ($p < 0.001$), 23.4% vs. 10.7% ($p < 0.001$), 3.5% vs. 1.6% ($p = 0.027$), and 3.2% vs. 1.3% ($p = 0.020$), respectively. SF was associated with higher rates of MACE, driven primarily by MI, TLR, and definite ST but not death. Currently only expert clinical opinions and anecdotes guide the treatment of clinically apparent SF, and there are limited studies comparing the effects of re-stenting and ballooning focal ISR within a fractured stent. In the authors' practice, focal ISR subtypes were generally treated with angioplasty, whereas diffuse ISR was usually treated with repeat DES. In a novel subgroup analysis, the investigators found that patients with SF requiring TLR had rates of future ISR and repeat TLR similar to those patients without SF requiring TLR, demonstrating that treatment of ISR associated with SF should likely be no different than our current standard approaches.

The investigators are to be commended for their study design and novel observations in a large population treated with DES. The results represent perhaps the most comprehensive and clinically relevant report of coronary SF ever published. Their PMA strongly suggests that stent fracture independently leads to adverse events post PCI and is not just a marker of a "bad vessel." This provides us with a potential additional target for reducing late PCI complications. SF risks include a mixture of factors intrinsic to the stent (compliance, overlap), extrinsic to the stent (angulation, tortuosity, calcification, axial force, cardiac motion), and factors related to the operator (inflation pressure, post dilation). In the short term, we can modify our procedures (i.e., through avoidance of excessive stent/post-dilation balloon oversizing and use of overlapped stents) or choose altogether alternative management strategies such as optimization of medical management, surgical revascularization, or use of isolated drug-eluting balloon angioplasty in vessels that carry a high risk of SF. In the longer term, the current study raises the intriguing possibility that SF is a mechanical phenomenon for which precision medicine and better engineering may lead to a future where this "patient-stent mismatch" can be avoided altogether.

Much time and energy is spent worrying about SF in the superficial femoral artery, which has been shown to be prone to this complication due to its biomechanics. True "hinge-point" vessels such as the common femoral artery and popliteal artery have traditionally been considered "no-stent" zones, but technology and technique have evolved to the point where stenting even in these areas is now an option in patients who are at high-risk for open surgery. The field of endovascular lower-extremity artery intervention has evolved through application of techniques originally applied in the coronary arteries. The case of SF may be one where this pathway could be reversed. For instance, vessels prone to SF may represent an appealing niche for the use of nitinol-based coronary stents. In order to deliver and fully expand these devices, more aggressive pre-stent vessel preparation may be necessary. These are battles which are fought every day in the SFA, and significant innovation and investigation are warranted to ascertain whether lessons learned in the SFA apply to the coronaries.

Finally, the association of SF with ST remains a real concern, particularly as bioresorbable vascular scaffolds (BVS) become more widely used. BVS have already been noted to have higher incidence of ST (10). As BVS slowly lose their structural integrity, might there be malapposition, protrusion, or strut discontinuity events mimicking DES fracture events, thus sharing a common mechanism with SF that at least partially accounts for the observed ST signal? If so, simple technical improvements in BVS such as decreasing strut size may not be enough to reduce ST rates to that which are seen with the latest generation coronary DES.

Investigation and innovation in the coronary stent field have represented one of the truest forms of continuous quality improvement in medicine. Through delving deeply into the overlooked phenomenon of coronary SF, the current study represents another step on this journey. Although perfection may never be realized, there is no question that the operators of 2 decades ago would consider the current state of our field to be excellent.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jay Giri, Hospital of the University of Pennsylvania, Cardiovascular Medicine Division, Gates Pavilion, 9th Floor, 3400 Spruce Street, Philadelphia, Pennsylvania 19104. E-mail: giri.jay@gmail.com.

REFERENCES

1. Chuck Carlson, Game of My Life: 25 Stories of Packers Football (2004), p. 149; Richard Scott, Jay Barker, Legends of Alabama Football (2004), p. 78.

2. Chowdhury PS, Ramos RG. Coronary-stent fracture. N Engl J Med 2002;347:581.

3. Sianos G, Sjoerd H, Ligthart JM, et al. Stent fracture and restenosis in the drug-eluting stent era. Catheter Cardiovasc Interv 2004;61:111–6.

4. Canan T, Lee MS. Drug-eluting stent fracture: incidence, contributing factors, and clinical implications. Catheter Cardiovasc Interv 2010;75(2):237–45.

5. Chinikar M, Sadeghipour P. Coronary stent fracture: a recently appreciated phenomenon with clinical relevance. Curr Cardiol Rev 2014;10. 349–35.

6. Chakravarty T, White AJ, Bunch M, et al. Meta-analysis of incidence, clinical characteristics and implications of stent fracture. Am J Cardiol 2010; 106:1075–80.

7. Nakazawa G, Finn AV, Vorpahl M, et al. Incidence and predictors of drug-eluting stent fracture in human coronary artery. J Am Coll Cardiol 2009;54:1924–31.

8. Kan J, Ge Z, Zhang J-J, et al. Incidence and clinical outcomes of stent fractures on the basis of 6,555 patients and 16,482 drug-eluting stents from 4 centers. J Am Coll Cardiol Intv 2016;9:1115–23.

9. Popma JJ, Tiroch K, Almonacid A, Cohen S, Kandzari DE, Leon MB. A qualitative and quantitative angiographic analysis of stent fracture late following sirolimus-eluting stent implantation. Am J Cardiol 2009;103:923–9.

10. Cassesse S, Kastrati A. Bioresorbable vascular scaffold technology benefits from healthy skepticism. J Am Coll Cardiol 2016;67: 932–5.

KEY WORDS in-stent restenosis, percutaneous coronary intervention, stent, target lesion revascularization