Research Highlights

Highlights from the latest articles in interventional cardiology

Angiographic stent thrombosis at coronary bifurcations: short- and long-term prognosis

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Evaluation of: Armstrong EJ, Yeo KK, Javed U *et al.* Angiographic stent thrombosis at coronary bifurcations: short- and long-term prognosis. *JACC Cardiovasc. Interv.* 5(1), 57–63 (2012).

Stent thombosis is a rare, but potentially fatal complication of percutaneous coronary intervention (PCI). Although premature discontinuation of dual antiplatelet therapy has been identified as the most common cause of angiographic stent thrombosis, technical misadventures also contribute to causation of stent thrombosis (ST) [1]. Inadequate stent apposition, malapposition or stent strut fractures have been associated with stent thrombosis. With the advent of better stent technology, such as thinner struts, easier deliverability, better visibility and more novel drug-coated stents have enabled interventional cardiologists to undertake PCI in patients with higher risk lesions. Bifurcation lesions are a much higher risk lesion subset. As newer drug-coated stents are associated with a lower risk of in-stent restenosis, more patients with coronary bifurcations are undergoing percutaneous interventions. Patients with such high-risk lesions used to be referred for coronary artery bypass graft surgery in the past. Bifurcation PCI causes increased risk of both the acute and late stent thrombosis.

Armstrong *et al.* have analyzed a California multicenter registry from five academic hospitals from 2005 to 2010 [2]. A total of 173 cases of angiographic ST have been identified, of which 20 cases were angiographically determined as definite ST at coronary bifurcations. These were lesions where a stent in the main vessel crossed a side branch of ≥2 mm (provisional single stent approach) or there was a planned double stent bifurcation approach. A total of nine of 20 bifurcation ST (45%) occurred with the double stent approach and eight cases had thrombus in both vessels (both the parent and branch vessels). In-hospital mortality was 20% for bifurcation ST versus 2% with nonbifurcation ST ($p < 0.0001$). Even at 2.3 years follow-up, bifurcation ST caused increases in both the long-term mortality (hazard ratio: 3.3; $p = 0.007$), and increased risk of major adverse cardiovascular events (hazard ratio: 2.2; $p = 0.04$) compared with nonbifurcation ST. Patients with bifurcation ST were younger, less likely to have undergone prior coronary artery bypass graft surgery and less likely to be taking aspirin or a thienopyridine. Rates of late ST were greater than acute ST. Patients with bifurcation ST were more likely to have a drug-eluting stent (DES) ($p = 0.02$, compared with a bare-metal stent). More patients with bifurcation ST presented with ST elevation myocardial infarction (80 vs 64%) and cardiogenic shock (25 vs 20%).

The results from this study further strengthen the concerns that premature discontinuation plays a very important role in causing stent thrombosis. By definition, a bifurcation lesion involves a parent vessel and a branch vessel, thereby subtending a larger area of myocardium. ST at the bifurcation therefore causes larger myocardial infarction that, in turn, leads to worsening of left ventricular dysfunction. This is associated with a higher incidence of congestive heart failure and death. Prevention of ST is therefore crucial. Compliance with dual antiplatelet therapy cannot be overemphasized in

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Future Medicine part of fsg

these patients. If compliance is a concern, bifurcation stenting should therefore be avoided. Current guidelines recommend continuation of dual antiplatelet therapy for at least 12 months. As most of the ST occurred late, this may make a compelling case for continuation of dual antiplatelet therapy beyond the currently recommended duration of 12 months. In addition, routine use of intravascular ultrasound following stent deployment will ensure adequate stent apposition, and detection of stent deformities so that these misadventures could be taken care of if needed. Aggressive use of glycoprotein IIB/IIIA inhibitors, and use of newer antiplatelet agents may lessen the incidence of stent thrombosis. Although bifurcation ST occurred more with DES, this is likely from wider adoption of DES in preference to bare-metal stents for these high-risk lesions.

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The Leipzig prospective vascular ultrasound registry in radial artery catheterization: impact of sheath size on vascular complications

Evaluation of: Uhlemann M, Möbius-Winkler S, Mende M *et al.* The Leipzig prospective vascular ultrasound registry in radial artery catheterization: impact of sheath size on vascular complications. *JACC Cardiovasc. Interv.* 5(1), 36–43 (2012).

Miniaturization in the sizes of catheters and sheaths has heralded a new era in the field of interventional cardiology. Although cardiac catheterization and percutaneous coronary intervention via transradial approach was developed nearly two decades ago, widespread adoption of this approach has been rather limited [1,2]. However, with the demands from the patients for quicker ambulation, and from the payers, for faster discharge of patients following cardiac catheterization rejuvenated the transradial catheterization technique. Vascular access site complications lead to more bleeding, longer hospital stay and more need for blood transfusions. These complications are associated with worse adverse outcomes [3]. Although transradial catheterization has been gaining much wider acceptance in Europe, Asia and Canada, this technique has been met with more reluctance from the USA operators. Admittedly, younger cardiologists are more amenable to explore this approach, compared with their senior colleagues. Conventionally, transradial catheterization has been associated with fewer vascular access site complications, better hemostasis at the access site, earlier discharges and better patient satisfaction. In addition, a recent randomized trial studied patients with acute coronary syndrome undergoing cardiac catheterization, and compared the outcomes at 30 days (composite of death, myocardial infarction, stroke, and noncoronary artery bypass-related bleeding) among the patients with radial versus femoral approach. Radial approach was superior to femoral approach in reducing vascular complications, and also in reducing the primary outcome among patients with ST segment elevation myocardial infarction [4]. Even with all of these benefits of transradial catheterization, complications from this approach are likely to occur. Radial artery occlusion (RAO)

following cannulation of the radial artery is a potentially hazardous complication as this may lead to limb ischemia with a potential for limb loss.

Uhlemann *et al.* from Leipzig, Germany, have published data from their prospective vascular ultrasound registry following radial artery catheterization [5]. Between November 2009 and August 2010, 455 patients had undergone transradial catheterization with a third having access with 5 F sheath, and two thirds with 6 F sheaths. Duplex sonography was perfomed in each of these patients before discharge. Patients who had developed symptomatic RAO, were treated with low molecular weight heparin. A follow-up study was performed after 14 days. They found that the incidences of access site complications were 14.4% with 5 F sheaths, and 33.1% with 6 F sheaths ($p < 0.001$). RAO occurred in 13.7% with 5 F compared with 30.5% with 6 F ($p < 0.001$). Younger age, female sex, presence of peripheral vascular disease and larger sheath sizes were found to be the predictors of RAO in their findings. More than 40% with RAO were symptomatic immediately, and 7% became symptomatic within a mean of 4 days. A total of 59% of RAO patients had received low molecular weight heparin and 55.6% of patients with RAO receiving low molecular weight heparin had successful recanalization on Duplex sonography compared with 14% with conventional treatment after a mean follow-up of 14 days.

This study confirms that smaller sheath sizes lead to lower numbers of vascular access complications. Although diagnostic transradial catheterization could be performed with sheaths as small as 4 F, percutaneous coronary intervention needs to be performed with at least a 5 F sheath. Although most of the inteventionalists use 6 F sheaths as their conventional size, 5 F sheath remains underutilized. Ease of stent delivery, and sense of security with larger sheaths in case of complications mostly drive the intent of the use of larger sheaths. Although most of the postprocedural access site complications are detected following development of symptoms and routine use of Duplex sonography is not a standard practice. In this study, 22 patients with confirmed RAO by Duplex still had palpable radial pulse, thus re-emphasizing the need for Doppler ultrasound in all patients undergoing radial artery canalization. Although use of heparin during radial catheterization is commonly practiced, the dose of heparin administered is variable. Heparin use of 5000 units may cause less RAO compared with lower heparin doses (2000–3000 units). In this study, all diagnostic catheterization patients had received 25,000 units of heparin and for percutaneous coronary intervention, 100 µ/kg heparin were used.

Radial catheterization is gaining popularity among interventional cardiologists across the globe. Thus, while bleeding complications are definitely fewer with transradial access, minimizing the occurrence of RAO is paramount as it will lend further credibility to this approach as the preferred modality in the near future. Early diagnosis is crucial and the use of routine Doppler sonography is a simple and noninvasive tool to detect this potentially reversible complication, as treatment with low molecular weight heparins improves the canalization of RAO. Use of smaller sheaths will also minimize the rate of RAO. In addition, a patent radial artery will keep options open for future vascular access if recatheterization is necessary.

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Improvements in transcatheter aortic valve implantation outcomes in lower surgical risk patients: a glimpse into the future

Evaluation of: Lange R, Bleizifer S, Mazzitelli D *et al.* Improvements in transcatheter aortic valve implantation outcomes in lower surgical risk patients: a glimpse into the future. *J. Am. Coll. Cardiol.* 59(3), 280–287 (2012).

With the development of the transcatheter aortic valve prosthesis, a new horizon has been uncovered in interventional cardiology. Aortic stenosis is a progressive and degenerative disease of the elderly, and is associated with significant mortality once symptomatic. Treatment of these sick patients becomes challenging as surgical aortic valve replacement remains the only hope of survival among patients with severe aortic stenosis, yet that comes with the price of extremely high complications of mortality and morbidity. Transcatheter aortic valves have given some hope to patients who are considered very high risks for surgery or inoperable [1].

The Medtronic Core Valve and Edward Sapien prosthetic devices have been approved in Europe and in Australia since 2007 for the treatment of high risk or inoperable surgical patients with severe symptomatic aortic stenosis. With a recently concluded randomized trial [1], the Edwards Sapien valve has been approved in the USA for use among inoperable surgical risk patients. However, with the increasing experience of the procedural success and with at least 5 years of clinical experience, interventional cardiologists and cardiac surgeons are becoming more comfortable with these devices and are meeting with better success, with fewer adverse outcomes. It is therefore just a matter of time before the realm of these valves will extend beyond its currently approved indications with high risks/inoperable patients.

The study by Lange *et al.* marks such a paradigm shift in treating the patients with severe aortic stenosis [2]. In this single center study in Munich, Germany, patients undergoing transcatheter aortic valve implantation (TAVI) were subcategorized into quartiles (Q1–Q4) defined by enrollment date. Each quartile included 105 patients. Baseline characteristics, and mortality at 30 days and at 6 months were then analyzed based on the quartiles. The relationship between quartiles and mortality was examined using adjusted and unadjusted Cox proportional hazard models. Compared with Q4 patients, Q1 patients were at higher risk of surgical mortality as defined by higher logistic Euroscores (25.4 ± 16.1 vs 17.8 ± 12%; $p < 0.001$) and higher Society of Thoracic Surgeons scores (7.1 ± 5.5 vs 4.8 ± 2.6%; $p < 0.001$). Unadjusted mortality at 30 days and 6 months were much lower among Q4 quartiles versus Q1 (11.4% with Q1 vs 3.8% with Q4 at 30 days; $p = 0.053$ and; 23.5% with Q1 vs 12.4% with Q4 at 6 months; $p = 0.07$). After adjustment for baseline characteristics, there were no significant differences in mortality, both at 30 days and at 6 months between Q1 and Q4. This study raises the hope that better clinical outcomes can be achieved even among lower surgical risk patients with TAVI compared with higher risk groups and can portend to broaden the scope of TAVI, even among lower risk groups, a conventionally surgical aortic valve replacement group.

Although TAVI appears very promising, the durability of these prosthetic devices over longer periods cannot be ascertained at this point and hence caution should be exercised while implanting these devices among younger and lower risk subjects with a much higher life expectancy. Vascular complications and the need

for pacemaker implantation are also potentially hazardous adverse outcomes of TAVI that need to be weighed up against more time-tested aortic valve replacement. While the upcoming trials are going to recruit these lower risk patients, the devices need to be perfected further to provide long-term durability while allowing smaller sheath sizes, and better deliverability as these improvisations will minimize adverse events further.

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