Which stent for diabetic patients: the glass half-full or half-empty?

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This editorial refers to ‘Safety and efficacy of drug-eluting vs. bare metal stents in patients with diabetes mellitus: long-term follow-up in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR)†, by U. Stenestrand et al. on page 177

Diabetes, as we are becoming keenly aware, is growing to epidemic proportions, and it is incumbent on cardiologists to consider the ‘comparative effectiveness’ of our treatments for its cardiovascular complications. The incidence of death or myocardial infarction (MI) has been found to be five times higher in patients with diabetes compared with those without. In 2001, the National Cholesterol Education Program’s Adult Treatment Panel 3 classified diabetes as a risk equivalent to established coronary artery disease.

The relative impact of revascularization strategies for multivessel diabetic patients with ischaemic heart disease has been extensively studied, with evidence favouring more complete revascularization with surgery over percutaneous methods. A meta-analysis of 10 percutaneous coronary intervention (PCI) vs. coronary artery bypass graft (CABG) trials conducted before drug-eluting stents (DESs) were introduced confirmed that in multivessel disease patients with diabetes, survival was better with surgery (Figure 1). The question of revascularization choice is being revisited now that DESs are widely used.

Another pertinent question relates to whether revascularization is needed for stable diabetic patients with ischaemic heart disease. The recently completed BARI 2D Trial showed that there was little to be gained by stenting patients with mild-to-moderate degrees of coronary obstruction and ischaemia. However, for patients requiring revascularization, several trials have been performed and are underway to test the question of whether DESs have levelled the playing field with surgery. The CARDia Trial and the diabetic patients in the SYNTAX Trial had similar survival rates treated with DESs or surgery. The 1-year follow-up is too short to engender confidence, but the early results were encouraging. The FREEDOM Trial, nearing enrolment completion, will be the largest study of diabetic multivessel disease patients randomized to a DES or CABG.

Will the use of DESs in these diabetic patients change the results first seen in the EAST and BARI trials and the meta-analyses of the pre-DES trials favouring CABG? Trials of DESs vs. bare metal stents (BMSs) have not been powered for clinical events, and much of what we know so far has been gleaned from registries. Some registries, including the Swedish Registry, raised a red flag about the long-term safety issues regarding DESs. Fortunately, further experience of that registry and others (NY and Massachusetts) has not shown excess mortality or MI events but has confirmed a significant reduction in revascularization events. As we pointed out 7 years ago, the problem of restenosis, although a significant inconvenience, was not often associated with death or MI. Our prediction of the number needed to treat by using DESs to prevent one revascularization event was >20. This seems borne out by these more recent registries.

Because of the organized health system in Sweden and the ability to carry out near complete follow-up for hard events, this experience is especially instructive. Stenestrand et al. have examined the outcome of diabetic patients treated in the SCAAR/SWEDE-HEART Registry.

All consecutive patients with diabetes who underwent stenting with a BMS or a DES during 2003–2006 were followed from 1 to 4 years (median 2.5). The size of the study provided an opportunity to evaluate important subgroups, especially those with or without ST-segment elevation myocardial infarction (STEMI). The patients receiving a DES or a BMS were enrolled concurrently during a period of increasing use of DESs. This method risks selection bias and the authors have attempted to mitigate that bias with propensity score methods. Nonetheless, other registries have been handicapped by unadjustable selection bias. For example, selecting patients for a BMS who are poorly insured and in whom chronic double antiplatelet therapy compliance is judged to be unreliable presents a problem. This may be less of a problem in the Swedish Registry because of the national health system with universal coverage. Also there seems to be a significant heterogeneity in selection based on geography (apparently related to physician preference rather than patient variables).

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The primary outcome was a composite of death or MI, with those plus restenosis used as a secondary outcome. Similar to previous registries the occurrence of death or MI was not different after risk adjustment. This was true for patients with or without STEMI. The patients receiving only one stent were analysed separately since this could produce a clear comparison of DESs and BMSs. For patients with multiple stents, the use of one or more DESs placed them in the DES group. Approximately 60% of the patients had multivessel disease, and complete revascularization was recorded for 53–57% of the patients for single or multiple stents. The number of multiple stent patients receiving mixed DESs and BMSs is not provided but would be of interest. None of the subgroups showed a difference in the primary outcome of death or MI. The endpoint of restenosis was obviously dependent on how many patients underwent catheterization and were found to have restenosis. The assumption is that repeat angiograms were only done for changes in symptoms or ischaemia during follow-up. The choice of restenosis as an endpoint differs from most other registries and trials which have used target lesion or target vessel revascularization as a measure of stenting success. Although not a defined endpoint, the new revascularization by PCI was 19% for DESs and 19.7% for BMSs. Surgery during follow-up was performed in 2.6% of the DES group and 3.3% of the BMS group. After risk adjustment, there was a statistically significant relative reduction in new revascularization in the one-stent and multiple-stent groups. In the STEMI group there was no reduction in restenosis demonstrated.

Since this registry showed no improvement in death or MI, the most interesting data relate to how helpful the DES selection was for reducing restenosis in various subgroups. Availability of baseline procedural and clinical data enabled calculation of an absolute benefit. The number of patients needed to treat with a DES as compared with a BMS varied in the single stent group from 21 for stent length >20 mm to 47 for short stents, and from 27 for stent diameter <3 mm to 40 for those ≥3 mm. In the multiple stent cohort, the overall number needed to treat was 19. In other words, by using DES exclusively in single stent patients, fewer than three restenoses per 100 patients treated would be avoided, and for multiple stent patients, fewer than five restenoses per 100 patients treated would be avoided. These numbers were predicted after the first DES registry results were reported. The finding that even these modest reductions in restenosis were not seen in the STEMI group may not be surprising given that the STEMI patients’ recurrent symptoms or progressive ischaemia triggering catheterization may be less than that for patients without STEMI.

Another secondary outcome, MI, was less in the DES group. The speculation provided by the authors that the lower incidence was possibly due to a lower restenosis rate seems not to be tenable. The absolute difference in restenosis was small and there are no data presented to suggest that the restenosis events were precipitated by MI. It seems much more likely that the small difference in unadjusted MI incidence (17.1% for BMS vs. 16.1% for DES) and an adjusted risk ratio of 0.80 (0.66–0.96) for the one-stent cohort; and unadjusted MI incidence (20.2% BMS vs. 17.7% DES) and an adjusted risk ratio of 0.81 (0.65–1.00) for the multiple-stent group was due to the well-known protective effect of double antiplatelet therapy. The actual duration of clopidogrel use is not known, but the recommendation was clearly for much longer use in the DES group.

This registry within a system that can capture outcomes consistently and in which roughly half of the patients received a DES has provided important insight into the relative benefit of this therapy in diabetic patients. The results can be considered a glass half-full, i.e., reduction in restenosis with no effect on death and MI, or half-empty since the hard endpoints were not improved. Unfortunately to me this seems to be a glass only 3–5% full (the absolute reduction in restenosis events). We expect more from a technology so advanced and expensive.

Conflict of interest: none declared.

References

Figure 1 Meta-analysis of patients treated with PCI or CABG before the availability of DESs. Adapted from Hlatky et al.3


CARDIOVASCULAR FLASHLIGHT

Aorto-left ventricular tunnel causing severe aortic regurgitation in adult man

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A 30-year-old man with history of patent ductus arteriosus ligation since he was 3 years old was referred for examination. He complained of chest pain and mild dyspnoea on exertion. Physical examination revealed diastolic decrescendo murmur with maximum at left parasternal border, blood pressure was 140/50, heart rate 94 b.p.m., and there were no signs of congestive heart failure. On electrocardiograph, there was sinus tachycardia with left ventricle hypertrophy and a chest X-ray showed moderately enlarged cardiac silhouette. Echocardiogram revealed ejection fraction of 50%, left ventricle dilation and severe aortic regurgitation with effective regurgitant orifice of 0.6 cm², regurgitant volume 73 mL, pressure half-time 320 ms, and diastolic reversal flow in descending aorta. The regurgitation jet was outgoing from area between right and left aortic cusp and eccentrically crossed left ventricular outflow tract in posterior direction. The finding was initially considered to be a sequela of infective aortic endocarditis with periavalvar aorto-ventricular fistulation, but there was no history or evidence of underwent endocarditis and therefore aorto-left ventricular tunnel (ALVT) was diagnosed (Panel A, ALVT is indicated by arrows in all figures). Moreover, a transoesophageal echocardiographic study was performed and confirmed the presence of ALVT. The aortic end of the tunnel was above sinotubular junction and localized in between of left and right coronary cusp (Panel B). The ventricular end vented beneath the aortic valve in interventricular septum (Panel C). Patient was referred to cardiac surgeon and successful closure of ALVT was performed (perioperative finding is in Panel D, ostium of ALVT indicated by arrow).

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