

With FREEDOM Comes Responsibility

Scott W. Murray, BSc (Hons), MB ChB, MRCP

The recent publication and presentation of results from the Future REvascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial¹ has stirred up further controversy in the debate regarding revascularization strategies.

FREEDOM enrolled 1900 patients with diabetes and coronary artery disease, the majority of whom had 3-vessel disease, to treatment with coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI) with first-generation drug-eluting stents (DESs). Of particular note, the trial exclusion criteria included left main stem disease. The final results show a clear benefit for CABG in patients with 2- or 3-vessel disease over PCI.

Overall, the results are not surprising. However, it is important to question if we can generalize these results to our current “real world” practice. If you consider some of the previous trials comparing CABG surgery to PCI, you realize that the results come from a highly selected population. On average, less than 10% of those patients considered were actually randomized. Only the Syntax trial was designed as an “all-comers trial” with 41% of screened patients ending up either in a registry or the trial itself.²

The overwhelming message from these trials over the years is that interventional cardiology can do better. There are areas in our practice where clinical inertia and lack of enthusiasm for new techniques keep us firmly in our place as “second-rate revascularizers.”

The EXCEL trial is ongoing and exploring the role of PCI vs CABG

for the left main stem, an area not covered by the FREEDOM trial, but something that has shown promise in the SYNTAX trial comparisons² and the Le Mans registry.³

The final point I would like to make about these comparison trials is that by the time they are completed, we have moved on to new paradigms. The most recent developments since FREEDOM are:

- (1) Reports from the large SCAAR registry in Sweden (94,384 consecutive stent procedures) suggest that new second-generation DESs appear to show a significant reduction in mortality over the first generation (23% at 2 years).⁴ It is interesting to see the Kaplan-Meier curves for PCI start to worsen after 2 years in FREEDOM. It is possible that this was driven by stent thrombosis occurring due to Cypher and Taxus stent use.
- (2) The angiogram should no longer be used as a tool to decide the functional significance of coronary artery lesions. Due to our reliance on this, we continue to make decisions based upon flawed judgments. Fractional flow reserve (FFR) should be employed to make decisions on which lesions to revascularize.^{5,6} Subsequent plans could be improved by the use of a “functional” SYNTAX score to make the decisions. Hopefully, in the future, non-invasive FFR computed tomography coronary angiography will guide us before a procedure is even contemplated.
- (3) Intravascular ultrasound guided stent implantation has recently been shown in a large meta-analysis

to confer a mortality benefit.⁷ If we are going to put a stent in, we should at least make sure it is well deployed and geographical miss or stent edge issues are minimized.

In summary, it seems that CABG will remain the gold standard treatment for individuals with diabetes and multi-vessel disease and for those without diabetes with complex disease. PCI will never be able to protect the myocardium from future events like a bypass graft can. Multidisciplinary “heart” team meetings mean that as PCI doctors we now have the responsibility to make the right choice for our patients based on the current evidence. However, we also have the responsibility to try and up our game to make sure that when we can do something, we do it to the best of our ability.

References

1. Farkouh ME, Domanski M, Sleep LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med*. 2012 Nov 4 [Epub ahead of print].
2. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360(10):961-972.
3. Buszman PE, Kiesz SR, Bochenek A, et al. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. *J Am Coll Cardiol*. 2008;51(5):538-545.
4. Sarno G, Lagerqvist B, Frober O, et al. Lower risk of stent thrombosis and restenosis with unrestricted use of ‘new-generation’ drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J*. 2012;33(5):606-613.
5. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360(3):213-224.
6. De Bruyne B, Pijls NH, Kalesan B, et al; for the FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367(11):991-1001.
7. Zhang Y, Farooq V, Garcia-Garcia HM, et al. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: a meta-analysis of one randomised trial and ten observational studies involving 19,619 patients. *EuroIntervention*. 2012;8(7):855-865.