Cardiovascular Revascularization Medicine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Transcatheter Therapeutic Conference 2016 — Highlights of Late-breaking Trials

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ARTICLE INFO

Available online xxxx

Keywords:
Coronary
TAVR
Bioresorbable stent
Structural heart intervention

The late-breaking trials presented at the Transcatheter Therapeutic Conference (TCT) 2016 in Washington, DC, covered a wide range of interventional and structural heart technologies and devices, including bioresorbable vascular scaffolds, drug-coated balloons, left atrial appendage closure, neuroprotection, patent foramen ovale closure, and transcatheter aortic valve replacement. In this review, we highlight the major studies presented at the conference that will have a major impact on current clinical practice

1. EXCEL study: Everolimus-eluting stents or bypass surgery for left main coronary artery disease [1]

1.1. Background

Left main coronary artery disease is associated with high morbidity and mortality owing to the large amount of myocardium at risk. European and U.S. guidelines recommend that most patients with left main coronary artery disease (LMCAD) undergo coronary artery bypass grafting (CABG). Previous randomized trials that compared CABG to percutaneous coronary intervention (PCI) for unprotected left main (LM) disease suggested that the rate of a composite of death, stroke, myocardial infarction (MI), or unplanned revascularization at 5 years was similar among patients treated with paclitaxel-eluting stents and those treated with CABG. This equivalent performance was observed only in the patients with coronary artery disease of low or intermediate anatomical complexity. Due to recent advancements in stent design that have improved the safety profile the EXCEL investigators evaluated alternative methods of revascularization for patients with LMCAD.

1.2. Synopsis and main findings

A total of 1905 eligible patients with LMCAD of low or intermediate anatomical complexity (SYNTAX score of 32 or lower) were randomized to undergo either PCI with everolimus-eluting metallic stent (Xience, Abbott Vascular) (PCI group, 948 patients) or CABG (CABG group, 957 patients). The primary end point was the rate of a composite of death from any cause, stroke, or MI at 3 years. The trial was powered for noninferiority testing of the primary end point. At 3 years follow-up, death, stroke, and MI occurred at similar rates between CABG and PCI recipients (14.7% vs 15.4%, HR 1.00, 95% CI 0.79–1.26). The adverse event rate was also less in the PCI-treated patients at 30 days (4.9% vs 7.9% for CABG, HR 0.61, 95% CI 0.42–0.88). More interestingly, rates of MI – especially ST-elevation myocardial infarction – were lower in the PCI-group (0.7% vs 2.3% for CABG, HR 0.32, 95% CI 0.14–0.74). However, ischemia-driven revascularization was more common after PCI (7.5% for CABG vs 12.6%, HR 1.72, 95% CI 1.27–2.33). Definite stent thrombosis was less likely than graft occlusion (5.4% vs 0.7%, HR 0.12, 95% CI 0.05–0.28).

1.3. Conclusion and clinical implications

In patients with LMCAD and low or intermediate SYNTAX scores by site assessment, PCI with everolimus-eluting stents was noninferior to CABG with respect to the rate of the composite end point of death, stroke, or MI at 3 years.

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http://dx.doi.org/10.1016/j.carrev.2016.11.006
1553-8389/

Please cite this article as: Alraies MC, et al, Transcatheter Therapeutic Conference 2016 — Highlights of Late-breaking Trials, Cardiovasc Revasc Med (2016), http://dx.doi.org/10.1016/j.carrev.2016.11.006

2. NOBLE trial: Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis: a prospective, randomized, open-label, non-inferiority trial [2]

2.1. Background

The NOBLE trial was a prospective, randomized, open-label, non-inferiority trial that enrolled patients with LMCAD in 36 centers in northern Europe and randomized them 1:1 to treatment with PCI or CABG.

2.2. Synopsis and main findings

A total of 598 LMCAD patients were randomized to PCI and 603 to CABG. In contrast to EXCEL, the NOBLE results suggested that CABG was actually the better choice for left main disease. After five years of follow-up, the primary composite outcome of death, non-procedural MI, stroke, and repeat revascularization occurred in 29% of PCI patients versus 19% of the CABG group, thus demonstrating inferiority for PCI (HR 1.48, 95% CI 1.11–1.96; $p = 0.007$). However, all-cause mortality rates were no different between PCI and CABG groups (11.6% vs 9.5%, HR 1.07, 95% CI 0.67–1.72). Also, symptomatic graft occlusion from CABG was just as likely as definite stent thrombosis (4% vs 3%, HR 0.59, 95% CI 0.26–1.36).

2.3. Conclusion and clinical implications

The findings suggest that CABG might be better than PCI for treatment of left main stem coronary artery disease, contradicting EXCEL's results. Both trials are rigorous and well-conducted but vary widely in their methodology, follow-up duration, definition used for left main disease, and how revascularization was performed. Given these differences, it may be too early to conclude that PCI is equivalent to CABG for all patients with significant left main CAD and these results will probably not change guidelines. The decision between the two procedures may ultimately rest on patient's characteristics, the operator's experience with LM stenting, and a rigorous evaluation by the heart team. Interventional cardiologists should use these data to engage patients in a dialogue about which approach is most appropriate for their individual circumstances.

3. RESPECT: Final long-term outcomes from a prospective, randomized trial of PFO closure in patients with cryptogenic stroke

3.1. Background

In patients with cryptogenic ischemic stroke and patent foramen ovale (PFO), the presumed cause of stroke is paradoxical emboli from the venous system that cross the PFO to reach the systemic circulation. Furthermore, the prevalence of PFO in patients with cryptogenic stroke is higher than in the general population. Theoretically, closing the PFO should prevent recurrent cryptogenic stroke in these patients.

3.2. Synopsis of main findings

The RESPECT trial was a randomized controlled trial with blinded endpoint adjudication. Patients were randomized 1:1 to PFO closure with the Amplatzer Occluder or medical therapy. A total of 980 patients were enrolled from 2003 to 2011 at 69 sites in the United States and Canada. The results of the RESPECT trial, published in 2013, showed a trend toward reduction in ischemic stroke with PFO closure, but this wasn't statistically significant. Updated results presented to the US Food and Drug Administration (FDA) in May 2016 to support a premarket approval (PMA) application for the Amplatzer PFO Occluder showed no statistically significant difference in the intention-to-treat analysis, but did meet statistical significance in the as-treated and device-in-place analyses. Based on these results, the FDA approved the Amplatzer PFO Occluder in October 2016, against the recommendation of the American Academy of Neurology.

Extended 10-year follow-up presented at TCT 2016 by Dr. David E. Thaler, Tufts Medical Center, Boston, MA, found a significant reduction in the rate of ischemic stroke with PFO closure (HR 0.55 [0.305–0.999] , $p = 0.046$). In further analysis of those patients for whom no other cause of stroke was identified, the effect was greater (HR 0.38 [0.18–0.79], $p = 0.007$). After excluding those patients age > 60 years, the difference was also statistically significant (HR 0.42 [0.21–0.83], $p = 0.01$). The event-free survival curves presented in 2013 continued to separate with time, demonstrating a clear benefit of PFO closure to prevent recurrent cryptogenic strokes over time. However, in older patients (>60 years), other causes of stroke become more prevalent and it is likely that the curves would eventually converge again.

3.3. Conclusion and clinical implication

These findings support PFO closure using the Amplatzer PFO Occluder in younger patients with cryptogenic stroke and PFO. Both the manufacturer and the FDA emphasize the importance of joint decision-making between neurologists and cardiologists to ensure that the correct patient population is targeted with the device. In particular, thorough exclusion of other causes of stroke is warranted before offering patients PFO closure.

4. Watchman US post-approval study: Multicenter, prospective, registry results with a left atrial appendage closure device for stroke prevention in patients with atrial fibrillation [3]

4.1. Background

The US FDA approved the Watchman device (Boston Scientific, Marlborough, MA) in March 2015 for left atrial appendage closure in patients with atrial fibrillation, high risk of ischemic stroke and high bleeding risk with oral anticoagulants. Since then, uptake has been tempered by patient and clinician concerns about procedural complications. Absent a national registry, manufacturer clinical specialists collected procedural details and peri-procedural complications for every device implantation in the US. Dr. David R. Holmes, Mayo Clinic, Rochester, MN, presented the findings at TCT 2016.

4.2. Synopsis of main findings

From March 2015 through May 2016, 3822 consecutive patients underwent device implantation at 169 US institutions. Watchman implantation was successfully accomplished in 3653 of 3822 patients (95.6%). Average procedure duration was approximately 50 min. Operators with no Watchman implantation experience performed half of the procedures. Partial device recapture was required in 23% of cases. Pericardial effusion requiring intervention occurred in 39 patients (1.0%): 24 were successfully drained percutaneously, 12 required surgery, and three did not survive. A total of 11 patients (0.29%) developed smaller pericardial effusions, which were managed conservatively. Three patients suffered strokes (0.08%), of which two had symptoms consistent with ischemic stroke and one had a head CT showing intracerebral hemorrhage. One patient died within 7 days of the procedure from a pulmonary embolism. There were nine (0.24%) device embolizations, of which six required surgical removal and three were removed percutaneously.

4.3. Conclusion and clinical implication

Overall, these results are very reassuring. Procedural success was high despite the large proportion of naive operators. Watchman device implantation appeared safe with pericardial tamponade, procedure-related stroke, and mortality rates of approximately 1%, 0.08%, and 0.08%, respectively. These findings are consistent with European

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