outcomes. In addition, the evidence for complete vs incomplete revascularization is not consistent among the trials. In spite of the above limitations, rSS may help us to identify subset of patients at risk of adverse events following PCI who might benefit from additional revascularization if possible or by aggressive medical treatment and close follow-up.

4. G.G. Stefanini, B. Kalesan, P.W. Serruys, et al. Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents versus durable polymer sirolimus-eluting stents in patients with coronary artery disease (LEADERS): 4 year follow-up of a randomised non-inferiority trial. Lancet 378 (2011) 1940–1948.

Background: The effectiveness of durable polymer drug-eluting stents comes at the expense of delayed arterial healing and subsequent late adverse events such as stent thrombosis (ST). We report the 4-year follow-up of an assessment of biodegradable polymer-based drug-eluting stents, which aim to improve safety by avoiding the persistent inflammatory stimulus of durable polymers.

Methods: We did a multicentre, assessor-masked, non-inferiority trial. Between Nov 27, 2006, and May 18, 2007, patients aged 18 years or older with coronary artery disease were randomly allocated with a computer-generated sequence to receive either biodegradable polymer biolimus-eluting stents (BES) or durable polymer sirolimus-eluting stents (SES; 1:1 ratio). The primary endpoint was a composite of cardiac death, myocardial infarction, or clinically indicated target vessel revascularisation (TVR); patients were followed-up for 4 years. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00389220.

Findings: 1707 patients with 2472 lesions were randomly allocated to receive either biodegradable polymer BES (857 patients, 1257 lesions) or durable polymer SES (850 patients, 1215 lesions). At 4 years, biodegradable polymer BES were non-inferior to durable polymer SES for the primary endpoint: 160 (18.7%) patients versus 192 (22.6%) patients (rate ratios [RR] 0.81, 95% CI 0.66–1.00, p for non-inferiority <0.0001, p for superiority = 0.050). The RR of definite ST was 0.62 (0.35–1.08, $p = 0.09$), which was largely attributable to a lower risk of very late definite ST between years 1 and 4 in the BES group than in the SES group (RR 0.20, 95% CI 0.06–0.67, $p = 0.004$). Conversely, the RR of definite ST during the first year was 0.99 (0.51–1.95; $p = 0.98$) and the test for interaction between RR of definite ST and time was positive ($P_{interaction} = 0.017$). We recorded an interaction with time for events associated with ST but not for other events. For primary endpoint events associated with ST, the RR was 0.86 (0.41–1.80) during the first year and 0.17 (0.04–0.78) during subsequent years ($P_{interaction} = 0.049$).

Interpretation: Biodegradable polymer BES are non-inferior to durable polymer SES and, by reducing the risk of cardiac events associated with very late ST, might improve long-term clinical outcomes for up to 4 years compared with durable polymer SES.

Clinical perspective

Durable polymers in the first generation drug-eluting stents (DES) have been shown to be responsible for persistent vascular inflammatory response and delayed arterial healing with resultant late adverse events. The biodegradable biolimus-eluting stent (BES) is designed in such a way that it offers an attractive combination of controlled drug elusion in parallel with biodegradation of the abluminal polymer into inert monomers within 6–9 months and only a bare-metal stent (BMS) remains thereafter. In the all-comer LEADERS trial, the BES stent met the noninferiority composite endpoint of death, myocardial infarction and target vessel revascularization at 9 months (BES: 9% vs SES: 11%, $p = 0.39$). The study population was followed up further for 3 years for the durability of the safety and efficacy outcomes. At the end of 4 years, BES not only met the primary outcomes and was also associated with lower incidence of very late definite stent thrombosis (0.12%/year vs 0.6%/year). In the subgroup analysis, BES showed a pronounced advantage in patients with ST-elevation myocardial infarction. The notable features of this study are: (1) the safety outcomes were evident only after the first year that is after complete degradation of the polymer – the proof of concept for the biodegradable polymer, (2) long-term durability of the anti-restenotic efficacy (3) higher incidence of definite ST in the presence of long-term dual antiplatelet therapy in the SES cohort – underlining the continued proneness of this stent platform to very late thrombosis (4) even though the TLR, MI, and primary composite endpoint were numerically better, the study was not powered to show the superiority of BES over SES. This was elegantly shown in the pooled analysis of the individual patient data from three studies comparing biodegradable polymer stents and durable polymer SES (Stefanini GG, et al, Eur Heart J 2012). (5) Superior outcomes in patients with STEMI, even though this study was not powered for this outcome. However, the COMFORTABLE AMI trial presented in EuroPCR 2012 has shown excellent safety outcomes for BES when compared to BMS with significantly lower incidence of target vessel reinfarction, TVR, and ST at 1 year. In conclusion, long-term results from the LEADERS and similar trials provide encouraging evidence for the clinical use of biodegradable polymer stent platforms.

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W.S. Weintraub, M.V. Grau-Sepulveda, J.M. Weiss, et al., Comparative effectiveness of revascularization strategies. N. Engl. J. Med. 366 (16) (2012) 1467–1476, doi: 10.1056/NEJMoa1110717.

Effectiveness of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for the treatment of patients with stable multi-vessel coronary artery disease is

a debatable issue. Weintraub and colleagues compared the two strategies from observational registry data of over 180,000 patients from the American College of Cardiology Foundation (ACCF) and the Society of Thoracic Surgeons (STS) Database Collaboration (ASCERT study). This study included medicare patients who were 65 years or older with stable multi-vessel coronary artery disease and underwent a revascularization procedure between January 2004 and December 2007 in U.S.

As expected, two groups had significant differences at baseline. PCI group had more females and older patients while CABG group had more patients with heart failure, diabetes, hypertension, chronic lung disease, cerebrovascular disease, history of smoking, or peripheral arterial disease. PCI group patients had higher ejection fraction despite having history of more acute coronary syndromes. Triple vessel disease was more in CABG group and double vessel disease was more in PCI group. In the PCI group, 78% received drug-eluting stents, 16% received bare metal stent and 6% had procedure without any stent. These groups were adjusted using inverse probability weighting and after adjustment all clinical covariates were well balanced. One year after the procedure, there was no significant difference in the mortality between the CABG and PCI groups (6.2% and 6.8% respectively). At 4 years, however, CABG demonstrated a significantly lower adjusted mortality than PCI (16.4% vs. 20.8%; risk ratio, 0.79; 95% CI, 0.76–0.82). The benefit of CABG was present across all subgroups like age, diabetes, renal dysfunction, etc.

Major limitation of this study, as discussed by authors and the accompanying editorial is the effect of unmeasured confounders. Treatment selection usually involves a careful clinical judgement that goes beyond statistical calculations and a few measured variables. Adequate control of confounders may not be possible in this kind of non-randomized comparison and thus affecting the reliability of the results. Another limitation is bias in the selection of revascularization procedure as evident by the huge difference in the unadjusted baseline characteristics of the two groups. Various important clinical variables were not reported in the databases such as, bleeding risk, stroke rate, drug compliance, angiogram and completeness of revascularization procedure.

Perspective

In various clinical trials comparing the two revascularization strategies, mortality advantage for CABG has been found in some studies for patients with diabetes and complex coronary artery disease. The most contemporary SYNTAX trial provides a comprehensive SYNTAX score to access the extent and complexity of the coronary artery disease and is a useful tool in decision making for the choice of revascularization strategy. More light on this issue is expected from the recently concluded FREEDOM trial that has studied the two strategies in diabetic multi-vessel disease. Results of this trial are expected later this year in the annual AHA meeting. One important aspect that has not been addressed in the ASCERT study is the impact of optimal medical therapy. As shown in the COURAGE trial, optimal medical therapy is at least as good as PCI in mortality reduction for patients with stable coronary artery disease. Scientific advancements has not only resulted in better revascularization strategies over the time but has also contributed significantly to the medical management of coronary artery disease. A more contemporary answer to this debate is expected from the proposed ISCHEMIA trial which will compare angiography and revascularization plus optimal medical therapy with the conservative strategy of optimal medical therapy only in stable coronary artery disease.

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Mathias C. Brandt, Felix Mahfoud, Sara Reda, Stephan H. Schirmer, Erland Erdmann, Michael Böhm, Uta C. Hoppe, Renal sympathetic denervation reduces left ventricular hypertrophy and improves cardiac function in patients with resistant hypertension, Salzburg, Austria; and Cologne and Homburg/Saar, Germany. J. Am. Coll. Cardiol. 59 (2012) 901–909.

Objectives: This study investigated the effect of catheter-based renal sympathetic denervation (RD) on left ventricular hypertrophy (LVH) and systolic and diastolic function in patients with resistant hypertension.

Background: LVH and diastolic dysfunction are associated with elevated sympathetic activity and increased morbidity and mortality. The effect of RD on LVH and LV function is unclear.

Methods: Forty-six patients underwent bilateral RD, and 18 patients served as controls. Transthoracic echocardiography was performed at baseline, and after 1 month and 6 months.

Results: Besides significant reduction of systolic and diastolic blood pressure at 1 month and 6 months, RD significantly reduced mean interventricular septum thickness from 14.1 ± 1.9 mm to 13.4 ± 2.1 mm and 12.5 ± 1.4 mm ($p = 0.007$), and LV mass index from 53.9 ± 15.6 g/m^2 (112.4 ± 33.9 g/m^2) to 47.0 ± 14.2 g/m^2 (103.6 ± 30.5 g/m^2) and 44.7 ± 14.9 g/m^2 (94.9 ± 29.8 g/m^2) ($p < 0.001$) at 1 month and 6 months, respectively. The mitral valve lateral E/E' decreased after RD from 9.9 ± 4.0 to 7.9 ± 2.2 at 1 month and 7.4 ± 2.7 at 6 months ($p < 0.001$), indicating reduction of LV filling pressures. Isovolumic relaxation time shortened (baseline 109.1 ± 21.7 ms vs. 85.6 ± 24.4 ms at 6 months, $p < 0.006$), whereas ejection fraction significantly increased after RD (baseline: $63.1 \pm 8.1\%$ vs. $70.1 \pm 11.5\%$ at 6 months, $p < 0.001$). No significant changes were obtained in control patients.

Conclusions: Besides the known effect on blood pressure, our study showed for the first time that RD significantly reduces LV mass and improves diastolic function, which might have important prognostic implications in patients with resistant hypertension at high cardiovascular risk.

Perspective

Chronic activation of the sympathetic nervous system is involved in the development and maintenance of arterial