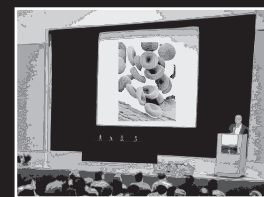


Conference Scene

A congress report



European Society of Cardiology Congress 2009 29 August–2 September 2009, Barcelona, Spain

The European Society of Cardiology/World Heart Federation congress held in Barcelona, Spain, from 29 August to 02 September 2009 brought novelties regarding new devices, tools and drugs of interest for interventional cardiology to the forefront.

The European Society of Cardiology (ESC)/World Heart Federation Congress held in Barcelona 3 years ago in 2006 saw a series of presentations that have influenced more than the beliefs of the cardiological community. The open questions on the safety of drug-eluting stents (DES) posed by the BASKET-LATE trial [1], the Camenzind meta-analysis of the SIRIUS and TAXUS trials [2], the SCAAR registry [3] and the data from the Bern–Rotterdam registry [4] on late thrombosis led to drastic changes in the market penetration of DES, plummeting from more than 80% to less than 20% in Sweden, and triggered public alarm voiced by the general press leading to stormy phone calls and emergency visits from angry patients who were convinced they had been implanted with a ‘time bomb’ and were at high risk of lethal coronary events. The consequence was more than a marked fall in the value of the shares of device companies. It was a major loss of credibility for the interventional community at large who were accused of having given up their integrity and vigilance to follow the dream of a stent without restenosis and the sirens of the industry. Was all this turmoil justified?

In one of the first of the 2009 sessions, some of the protagonists of the initial DES 2006 drama and investigators in major DES trials and registries, such as Dr E Camenzind (Geneva, Switzerland), Dr S James (Uppsala, Sweden), Dr A Kastrati (Munich, Germany) and Dr D Holmes (Rochester, MS, USA), were invited to debate the issue. Camenzind reviewed the experimental data demonstrating the potential for prolonged wall inflammation after DES use, and presented the 3-year data from the BASKET-LATE trial, illustrated in detail by Pfisterer

in a separate session. Starting the assessment 6 months after stent implantation, the annual incidence of death and myocardial infarction (MI) was 3.6% in the DES group versus 1.5% in the bare-metal stent (BMS) group ($p < 0.009$), with a difference entirely attributable to stents implanted in large vessels [5]. This 826-patient trial was dwarfed in size and follow-up duration by the 60,937 patients enrolled in the SCAAR Registry, of which the 6-year follow-up data were presented at ESC for the first time [JAMES S *ET AL.*; FOR THE SWEDISH CORONARY ANGIOGRAPHY AND ANGIOPLASTY REGISTRY (SCAAR) STUDY GROUP. UPPSALA UNIVERSITY HOSPITAL, SWEDEN, UNPUBLISHED DATA]. The adjusted rates of mortality and MI reported for single stents or the overall population were superimposed. These results remain at variance with other large trials reporting a mortality benefit with DES for the most complex off-label indications [6]. Similarly, the 4-year results they presented for 12,535 patients treated after ST elevation MI (STEMI) [NILLSON T *ET AL.*; FOR THE SWEDISH CORONARY ANGIOGRAPHY AND ANGIOPLASTY REGISTRY (SCAAR) STUDY GROUP. UPPSALA UNIVERSITY HOSPITAL, SWEDEN, UNPUBLISHED DATA] showed no mortality difference, a reassuring result after the late mortality increase shown in 5093 patients enrolled in the GRACE Registry [7], but still worse than the mortality benefit reported by Mauri *et al.* in 3379 matched cases from the Massachusetts registry [8].

These data and the results reported in randomized trials presented by Kastrati dispelled the scariest expectations imagined in 2006. Still, all presenters pointed out that both randomized trials and registries indicate a persistent very late stent thrombosis with an incidence of 0.5% observed both in the Bern–Rotterdam [4]

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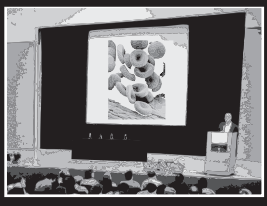
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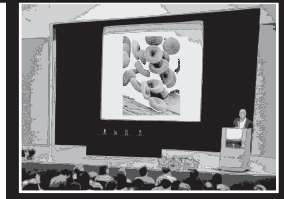


and SCAAR registries [3]. Holmes reported data from the Mayo Clinic registry of the late 1990s, indicating the phenomenon was also present in BMS but the incidence of very late stent thrombosis was lower. The small increase in very late stent thrombosis, despite the extreme severity of this complication resulting in death or MI in most cases, is not enough to make the safety profile of DES worse than BMS, which are also plagued by acute events owing to aggressive restenosis. Still, action is required to manufacture safer devices and test more efficient antiplatelet drugs.

The ESTROFA-2 registry closely followed 4119 patients treated with second-generation stents (the zotarolimus-eluting stent Endeavor™ and the everolimus-eluting stent [EES] Xience/Promus™) enrolled in 32 Spanish centers between 2006 and April 2008 [9]. Definite thrombosis rate at 2 years was low (1.0% for zotarolimus- and 0.9% for EES), with an extremely low incidence in the interval 12 to 24 months (0.1 and 0.2%, respectively). Biodegradable polymers were indicated as a potential solution to the problem of very late thrombosis. The largest randomized comparison of DES with biodegradable and biostable polymers was reported by the ISAR Investigators in the Hot Line session [10]. The stent studied was developed in Munich and elutes sirolimus for 4 to 6 weeks postimplant via a polymer expected to be fully absorbed by the surrounding tissue after 6 to 9 months. The 1299 patients treated with this stent were compared with 1304 patients receiving conventional, commercially available sirolimus-eluting stents (SES; Cypher™) and EES (Xience). At the 6 to 8 months angiographic follow-up, late lumen loss was 0.24 and 0.26 mm for the biodegradable and biostable stents, respectively. The similar restenosis rate explained the nearly identical rate of repeat revascularization at 12 months (13.7 and 13.9%, respectively). Death and MI were also similar in the two groups with a definite stent thrombosis at 1 year of 1.5% for the biostable and 1.0% for the biodegradable stent ($p = 0.29$). The expected follow-up of 5 years may capture a further spread in the incidence of very late stent thrombosis, as suggested by two Japanese studies, both assessing at 9 months the SES (Cypher) and

paclitaxel-eluting stents (PES; TAXUS) [11,12]. Investigators from Toyohashi observed that at 9 months follow-up, full coverage was detected only in 18 and 33% of cases, respectively ($p = 0.03$). Between 10 and 20% of struts remained uncovered in 5 and 17% of the PES and SES, respectively ($p = 0.03$). In a separate study from Kobe, 24 patients received a SES and a PES in the same artery and at 6 months after implantation, 4.6 and 11.1% of the apposed struts were uncovered in the PES and SES groups, and the average neointimal thickness also differed, being greater for the PES group ($150 \pm 163 \mu\text{m}$ vs $94 \pm 103 \mu\text{m}$, respectively; $p < 0.01$) [13].

There was great expectation for the update of the SYNTAX trial [14], which presented its primary 1-year end point in the *New England Journal of Medicine*. The main criticism, particularly from cardiac surgeons, was that the equivalence in major hard end points (death, MI and stroke) at 1 year was not going to hold with time and that the difference in new revascularization, which already drew at 1 year the major adverse cardiac and cerebrovascular event (MACCE) rate in favor of surgery (12.1 vs 17.8%; $p < 0.002$), was due to progressive increase over time. The 2-year results, presented by Kappetein *et al.*, showed no difference in the incidence of additional deaths and strokes [15]. MI after the first year, by contrast, occurred more frequently in the 903 patients treated with TAXUS stents (1.2 vs 0.1%; $p = 0.008$) leading to an overall greater frequency 2 years after treatment in the TAXUS group (3.3 vs 5.9%; $p < 0.01$). Still, there was no overall difference in the combined end point of death/MI/stroke at 2 years (10.8% in the TAXUS group and 9.6% in the coronary artery bypass graft [CABG] group; $p = 0.44$). Unexpectedly, revascularization between 1 and 2 years was not significantly different in the two groups (3.4% for CABG, 4.7% for TAXUS; $p = 0.06$) with most of the absolute difference at 2 years (8.6 vs 17.4%; $p < 0.001$) occurring between 6 and 12 months and relatively flat, nearly parallel, curves between 18 and 24 months. The overall MACCE rate at 2 years remained significantly lower with CABG surgery (16.3 vs 23.4%; $p < 0.001$), but groups with a low and intermediate



SYNTAX score (<33) and patients with left main artery disease showed no significant difference. An update in results (from 12 to 18 months) was also demonstrated by the FAME Investigators [16]. The study randomized patients with multivessel disease to angioplasty of all angiographically significant stenoses versus selective angioplasty only of lesions with a fractional flow reserve of less than 0.80. The significant difference in major adverse cardiac events observed at 1 year in the group with a flow fraction reserve-guided approach (-5.1%) had a further increase in the subsequent 6 months (-5.3%), dispelling criticisms that leaving intermediate lesions untreated creates greater risks of late events.

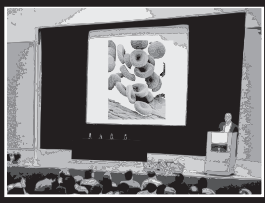
Three studies on acute STEMI were presented at the Hot Line trials session. The TRIANA trial (Primary Angioplasty versus Fibrinolysis in the Very Elderly) was expected to randomize 560 patients older than 75 years to primary angioplasty or thrombolysis [17]. The study was terminated prematurely with only 266 patients enrolled and did not meet the end point of demonstrating a significant reduction of the combined end point of death, reinfarction and disabling stroke with primary percutaneous coronary intervention (PCI; OR: 1.46 in favor of primary PCI; 95% CI: 0.81–82.61; $p = 0.21$). However, all components of the primary end point, as well as major bleeding, were lower in the primary PCI group and it could be argued that a 3.0% incidence of disabling stroke after thrombolysis – versus 0.8% after PCI – can be a more than sufficient argument against the use of lytics in this

high-risk group. The NORDISTEMI trial randomized patients with acute (<6 h) STEMI admitted to district general hospitals in an area of central-eastern Norway remote from primary angioplasty centers [18]. Consequently, tenecteplase was administered to all patients, with half (132 patients) treated conservatively at the center of initial admission and the remaining 134 immediately transported for more than 158 km to the nearest angioplasty center. The primary end point of death, reinfarction, recurrent ischemia and stroke at 12 months was not met (20.9 vs 27.3%; $p = 0.18$), but the secondary end point of death, re-MI and stroke was in favor of an immediate transfer. Verheugt concluded that the NORDISTEMI trial confirms the advantage of a rapid transfer, at least within 24 h, for patients far away from a primary angioplasty center, as indicated in the PCI and STEMI ESC guidelines [19,20]. Finally, 80 patients with cardiogenic shock postacute MI were randomized to receive upfront abciximab at the time of diagnosis versus provisional use of abciximab during angioplasty [21]. The primary end point of death, reinfarction, stroke and renal failure was similar in the two groups (42.5 vs 27.5%; $p = \text{NS}$) with no difference in in-hospital mortality (37.5 vs 32.5%; $p = \text{NS}$) and an excess of bleeding in the thrombolysis arm.

The introduction of newer and safer devices and adjunctive pharmacological treatment holds the promise to decrease long term PCI-related complications and enlarge the indications to angioplasty to our patients.

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