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News from TCT 2006

Latest data on drug-eluting stent controversy

An abundance of new information on the controversy surrounding drug-eluting stents was presented and discussed at the Transcatheter and Therapeutics (TCT) meeting held in Washington DC, US, in October.

The controversy, which dominated the World Congress of Cardiology, in Barcelona, Spain, the previous month, centres around concern about a possible increase in late stent thrombosis leading to death and myocardial infarction (MI) in patients receiving drug-eluting stents.

New information on this phenomenon presented at the TCT meeting, included two new meta-analyses of trials with the first two drug-eluting stents, Cypher® and Taxus®, and new registry data. The meta-analyses both suggested small increases in late stent thrombosis with the drug-eluting stents compared with the bare metal variety but this did not seem to translate into an increase in death/MI, as was suggested in the studies presented in Barcelona. The registry data presented at the TCT meeting showed a 0.4% increased risk of stent thrombosis with drug-eluting stents.

In the meta-analysis of Taxus® trials, there was an increase in late stent thrombosis of 0.5% between one and four years after stent implantation, giving an annual rate of about 0.15% per year (table 1). For the Cypher® trials, the late-stent-thrombosis rate was 0.6% between one and four years – about 0.2% per year (table 2).

These data, showing no increase in death/MI rates with the drug-eluting stents, contrast with other meta-analyses of trials with the same two stents presented at the Barcelona meeting, which did show increased death and MI with the drug-eluting stents. Trying to account for this difference, Drs Gregg Stone and Martin Leon (Columbia University, New York, US) who presented the new studies at the TCT meeting, said they obtained the data for their meta-analyses directly from the manufacturers of the Cypher® and Taxus® stents, whereas the authors of the studies presented in Barcelona obtained their data from mainly published or presented studies.

Table 1. Taxus® meta-analysis

End point	Taxus®	Bare metal stent	P value
Stent thrombosis	1.3%	0.9%	0.290
Late stent thrombosis (1–4 years)	0.7%	0.2%	0.033
Death or myocradical infarction	12.4%	11.8%	0.770

Table 2. Cypher® meta-analysis

End point	Cypher®	Bare metal stent	P value
Stent thrombosis	1.2%	0.6%	0.200
Late stent thrombosis (1–4 years)	0.6%	0%	0.025
Death or myocardial information	11.6%	10.3%	0.390

New registry

The new registry data came from a Spanish study known as ESTROFA, which tracked stent thromboses among 13,500 patients given drug-eluting stents in 17 hospitals between 2002 and 2006. Of these, 1.2% developed stent thrombosis, and 0.48% developed late stent thrombosis (after six months). Presenting the data, Dr de la Torre Hernandez (Santander, Spain) said there was a 0.4% increase in stent thrombosis after six months with both the Cypher® and Taxus® stents compared with bare-metal stents, which he suggested would be outweighed by the reduction in restenosis seen with these stents.

During the discussion period, Dr Stuart Pocock (London University) said he believed the excess risk of stent thrombosis with drug-eluting stents to be small – about one event per 500 patient-years of follow-up. "This is relatively low, and it needs to be seen in the context of the overall benefits," he commented. But others pointed out that these new meta-analyses only referred to low-risk patients in whom these stents were officially licensed, but they did not address the many higher-risk patients who actually receive the stents.

New definition for stent thrombosis

Further complicating the issue, a new definition for stent thrombosis was proposed at the TCT meeting, and new analyses data using this definition suggest that there may actually not be an increase in late stent thrombosis with drug-eluting stents after all.

The new definition, which has been developed by an expert group known as the Academic Research Consortium to eliminate variability in the definitions across various drug-eluting-stent trials, includes patients with definite/confirmed stent thrombosis, probable stent thrombosis, and possible stent thrombosis. Previously called the 'Dublin Definitions', this defines stent thrombosis as definite when confirmed by angiography or when pathologic confirmation of acute thrombosis in acute coronary syndrome (ACS) patients is made. Probable stent thrombosis is defined as any unexplained death within 30 days, or as target vessel MI without angiographic confirmation of thrombosis or other identified culprit lesion. Possible stent thrombosis is defined as unexplained death after 30 days.

Chair of the group, Dr Donald Cutlip (Harvard Clinical

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Research Institute, Boston, US) presented results from four randomised trials of the Cypher® stent – RAVEL, SIR-IUS, E-SIRIUS, and C-SIRIUS – which showed that the risk of stent thrombosis up to four years after stent implantation was not statistically different from that with bare metal stents. A similar analysis of Medtronic's Endeavor I, II, and III studies plus registry data with the Endeavor stent showed higher rates of stent thrombosis with the drug-eluting stent versus bare metal stents with the new definition but higher event rates with the bare metal stent.

Bioabsorbable stent studies encouraging

A new sirolimus-eluting stent with a bioabsorbable polymer, known as Excel®, appears to be safe with no late stent thrombosis observed at six or 12 months, a new registry study suggests. The Medistra Excel Drug-Eluting Stent Trial (MEDISTRA) study, also showed less late loss and less restenosis with the Excel® stent compared with first-generation drug-eluting stents and bare metal stents.

Dr Teguh Santoso (University of Indonesia Medical School, Jakarta, Indonesia) noted that the registry included 277 'all-comer' angioplasty patients who had a total of 771 stents implanted, of which 470 were the Excel® stent. Other stents used included 137 sirolimus-eluting, 66 paclitaxel-eluting, and 46 bare metal stents. There were no in-hospital events in these patients.

By 30 days there had been two cardiac deaths, one case of target vessel revascularisation/target lesion revascularisation (TVR/TLR), and two cases of subacute thrombosis. There were no additional deaths by 12 months, but there were three more cases of TVR/TLR by six months and another two cases at 12 months. The Excel® stent is made in China and is cheaper than other available drug-eluting stents. Dr Santoso suggested the fact that the polymer bioabsorbs after six months may make the stent safer, as it behaves like a bare metal stent after this time. Discussant of this trial, Dr Philip Urban (Latour Hospital, Geneva, Switzerland) said the data were encouraging but preliminary.

Next – a fully bioabsorbable stent

Preliminary data on the first fully bioabsorbable drug-eluting stent was also presented at TCT meeting. The everolimus-coated stent, which is in development by Abbott, is designed to be fully absorbed and slowly metabolised by the coronary artery. It will release drug into the artery and then slowly absorb over time.

Data on the first 30 patients with single *de novo* native coronary lesions enrolled in the ABSORB trial of this stent showed no major adverse cardiac events and no stent thrombosis at 30 days.

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