薬剤溶出ステントの長期リスクが問題にされた

PASSIONおよびDEDICATION：スタディの結果ST上昇MI患者に対する薬剤溶出ステント使用に関する懸念が示唆された

PASSION and DEDICATION: Studies raise concerns about use of drug-eluting stents in patients with ST-segment-elevation MI

ST上昇心筋梗塞患者に対する薬剤溶出ステント（DES）とベアメタルステントを比較した2つのスタディの結果、薬剤溶出ステントに関する疑問が持ち上がった。PASSIONトライアルの5年間の結果、パクリタキセル溶出ステント（Taxus Express2）とベアメタルステント（Express2 or Liberté）の複合一次エンドポイント（心臓死、心筋梗塞再発、標的病変に対する再血行再建術施行）はそれぞれ18.3%と22.0%であり、統計学的に有意ではなかった。個々に比較すると2つのステント群間でいずれの主要な心イベントに関しても有意差は認められなかった。さらに、確実な（definite）ステント血栓発現率はベアメタルステント群と比較しDES群において2倍であった（それぞれ3.6%と1.7%）が、確実なおよびかなり確実と思われる（probable）ステント血栓発現率はそれぞれ3.9%と3.4%であり、同等であった。DEDICATIONトライアルでは、薬剤溶出ステント群において主要な有害心事象は少なかったものの、心死亡率は有意に高かったと報告された。これらのスタディは第59回American College of Cardiology学会で発表された。

Full Text

Long-term results from two studies comparing drug-eluting stents (DES) with bare-metal stents in patients with ST-segment-elevation myocardial infarction (STEMI) have raised some questions about the long-term risks of the drug-eluting devices, according to research presented at the American College of Cardiology's 59th annual scientific session.

In one study, known as the PASSION trial, investigators observed no differences between the two stents in the composite end point of cardiac death, recurrent MI, or target lesion revascularization at five years and no significant differences in the incidence of major adverse cardiac events, but they did observe a trend of very late stent thrombosis in DES-treated patients. In the DEDICATION trial, investigators report an increased risk of cardiac death at three years in patients treated with a DES compared with patients treated with a bare-metal stent. Despite a finding of lower rates of adverse cardiac events than in bare-metal stent patients, cardiac mortality was significantly higher in patients who received drug-eluting stents

In the first randomized, controlled trial to report 5-year data on the safety and benefits of drug-eluting stents compared with bare metal stents in acute myocardial infarction, known as the PASSION trial, researchers found no statistically significant difference in either safety or efficacy between the two groups.

The 5-year findings from the PASSION trial contrasted with the researchers' hypothesis that the paclitaxel-eluting stent would perform significantly better for cardiac death, recurrent myocardial infarction, and target lesion revascularization. The results also failed to show a statistically significant difference between the two stent types in preventing very late stent thrombosis, which has been a primary concern of drug-eluting stent use.

The trial dated from between March 2003 and December 2004 and randomized 619 patients with acute myocardial infarction to receive either the Taxus Express2 (a paclitaxel-eluting stent) or the Express2 or Liberté (bare-metal stents). All stents were manufactured by Boston Scientific.

Specifically, the prospective, single-blind study did not show a statistically significant difference between the paclitaxel-eluting stent and the bare-metal stent for the primary composite endpoint of cardiac death, recurrent myocardial infarction, and target lesion revascularization, at 18.3 percent and 22.0 percent, respectively.

The researchers also did not find a statistically significant difference between the two stent groups for any of the major cardiac events when examined individually.

Furthermore, despite a two-fold increase in the occurrence of definite stent thrombosis in the paclitaxel-eluting stent group compared with the bare-metal stent group - at 3.6 percent and 1.7 percent, respectively - the occurrence of both definite and probable stent thrombosis, (which includes suspected clots that have not been confirmed and which more closely resembles a real-world patient population) was comparable, at 3.9 percent and 3.4 percent, respectively.

"I think we can conclude from the trial that the use of drug-eluting stents in primary angioplasty is safe through several years after implantation," said Maarten Vink, M.D., of the Onze Lieve Vrouwe Gasthuis Hospital in Amsterdam, The Netherlands, one of the study's researchers. "Compared to bare-metal stents, we did not find a difference in the occurrence of the primary composite endpoint of major adverse cardiac must carefully weigh the benefits and drawbacks of using drug-eluting stents for acute myocardial infarction."

The 5-year data follow in line with both PASSION's 1-year data and 2-year data - which also found no statistically significant safety or benefit differences between the two stents - but Vink notes that the 5-year results are especially important to examine in light of data in clinical registries that associate drug eluting stent use with very late stent thrombosis.

While Vink acknowledges that the study provides valuable insight into the debate surrounding this issue, he cautions that because the PASSION trial is the first large, randomized, controlled study to report 5-year data, its findings cannot provide definitive answers on the use of drug-eluting stents in acute myocardial infarction.

"Right now, the clinical guidelines are not conclusive concerning the use of drug-eluting stents in angioplasty for acute myocardial infarction, as the European Society of Cardiology does not define if they should be used, while the American College of Cardiology provides an indication for them," said Vink. "Because the guidelines are not uniform, I think their use will remain an issue-one without a definite answer- until we have data from more large, randomized, long-term studies."

The PASSION study was funded by the Department of Interventional Cardiology at the Onze Lieve Vrouwe Gasthuis Hospital. Dr. Vink has no personal disclosures.

The DEDICATION trial researchers conclude that more research is needed on the relative costs and benefits of using drug-eluting versus bare-metal stents in patients who have experienced a ST-elevation myocardial infarction.

A team of Danish researchers recently completed the three-year DEDICATION trial examining the effectiveness and risks of drug-eluting stents versus bare-metal stents. The team randomly assigned 626 patients who received percutaneous coronary intervention (PCI), also known as coronary angioplasty, within 12 hours of a STEMI to receive either a drug-eluting stent or a bare-metal stent. After three years, patients who had received a bare-metal stent were more likely to have experienced a variety of negative outcomes including target lesion revascularization, target vessel revascularization, and other major adverse cardiac events. All-cause mortality, the rates of a myocardial infarction, re-infarction and stroke were similar in both groups. However, patients in the drug-eluting stents group were more likely to die from cardiac-related problems.

"The key message here," said Peter Clemmensen, M.D., of Copenhagen University Hospital, Denmark, and President of the Danish Heart Foundation, "is that we have shown that, despite a finding of lower major adverse cardiac events, cardiac mortality was significantly higher in the drug-eluting stent group."

Because of this mixed set of results, further study is warranted to determine the long-term effects of drug eluting versus bare-metal stents.
"We encourage other trialists to conduct long-term follow up in their STEMI trials involving drug-eluting stents," Clemmensen said.

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