ステント埋込み後18ヵ月の成績はエンデバーよりサイファの方が優れていた

SORT OUT III：head-to-head比較においてエンデバーステントはサイファステントよりも死亡率、心筋梗塞発症率、標的血管再血行再建術施行率が高かった

SORT OUT III: Endeavor has higher rates of death, myocardial infarction, and target vessel revascularization than Cypher in head-to-head comparison

18ヵ月のhead-to-head比較において、エンデバーステントを埋め込んだ方がサイファステントに比べ心筋梗塞、死亡、および標的血管再血行再建術施行症例が多かったとの研究結果が第59回American College of Cardiology学会で発表され、同時にLancetに掲載された。SORT OUT IIIトライアルは、薬物溶出ステントを埋め込まれた患者ほぼ全員を組み入れ、臨床エンドポイントを評価するように検出力をつけたall-comerトライアルである。冠動脈疾患を有する患者をエンデバー（1,162人）またはサイファ（1,170人）ステントを埋め込む群に無作為に割り付けた。両者ともに薬物溶出ステントであるが、エンデバーは第二世代のzotarolimus溶出ステントであり一方サイファは第一世代のシロリムス溶出ステントである。ステント埋め込みから18ヵ月後の複合一次エンドポイントである心臓死、心筋梗塞または標的血管の血行再建術施行は、エンデバーステントにおいてサイファステントよりも有意に多かった（9.7%と4.5%、P<0.0001）。エンデバーを埋め込まれた患者はまた二次エンドポイント（心筋梗塞、標的血管再血行再建術施行、および総死亡）に関してもサイファーステントを埋め込まれた患者よりも多く認めた（4.4%対2.7%、P=0.035）。

Full Text

In a head-to-head 18-month comparison, researchers found that implantation with the Endeavor stent led to more cases of myocardial infarction, death and target vessel revascularization than the Cypher stent, according to research presented at the American College of Cardiology's 59th annual scientific session. This study is simultaneously published in the Lancet and will appear in the March 2010 print edition and was released online at the time of presentation.

The trial was conducted by researchers from the university hospitals in Denmark under the auspices of the Danish Organization for Randomized Trials with Clinical Outcomes (SORT OUT). The SORT OUT III trial randomized patients with coronary artery disease to either the Endeavor (1,162 patients) or the Cypher (1,170 patients) stent. Both stents are drug eluting, but the Endeavor is a second-generation zotarolimus-eluting stent, while the Cypher is a first-generation sirolimus-eluting stent.

The researchers found that after 18 months, significantly more patients with the Endeavor experienced the primary composite endpoint of cardiac death, myocardial infarction or target vessel revascularization than patients with the Cypher stent, at 9.7 percent and 4.5 percent, respectively. Patients with the Endeavor also experienced the secondary endpoints more frequently than those with the Cypher, including myocardial infarction (2.1 percent versus 0.9 percent); target vessel revascularization (7.9 percent versus 3.3 percent); and all-cause death (4.4 percent versus 2.7 percent).

"Based on the Endeavor III trial findings showing that the Endeavor stent had a more uniform layer of neointimal coverage, we and many others believed it would provide strong protection against general stent thrombosis and myocardial infarction, but we found there is a high risk of early stent thrombosis and early myocardial infarction in the Endeavor, which may be related to the faster elution of the drug," said Dr. Michael Maeng, Ph.D., of the Department of Cardiology at Aarhus University Hospital in Denmark and the lead researcher. "If you have to compare the two stents, the Cypher stent is a better stent." Maeng added that based on the Endeavor III trial's findings, many interventional cardiologists may be surprised by the 18-month outcomes of SORT OUT III, as many had expected the Endeavor to show superior performance in the long-term.

While the inferiority of the Endeavor stent for these outcomes is similar to the trial's 9-month findings, the researchers did find two main differences between the two sets of SORT OUT III data: the outcomes for stent thrombosis and all-cause mortality. In the 9-month findings, a statistically significant difference existed for stent thrombosis between the two stents in favor of the Cypher (13 events compared with 4). However, in the 18-month findings, there was no longer any statistically significant difference (13 events versus 6), although the Cypher still recorded a lower number of stent thrombosis cases. Alternately, the all-cause mortality rates between the two stents were not statistically significant at 9 months (2.2 percent compared with 1.5 percent for the Endeavor and the Cypher, respectively) but the 18-month data showed a statistically significant difference (4.4 percent versus 2.7 percent, respectively).

In addition, both sets of SORT OUT III data differ from the only other large, published trials to compare the two stents: the Endeavor III trial and the ISAR-TEST-2 study. Endeavor III and ISAR-TEST-2 did not find statistically significant differences in safety between the Endeavor and the Cypher at 9 months, although the Endeavor did have significantly higher late lumen loss and binary restenosis rates.

According to Maeng, two main characteristics of the SORT OUT III trial could have caused the difference: the SORT OUT trial was an all-comer trial that accepted nearly all patients receiving a drug eluting stent, and it was powered to assess clinical endpoints.

"If you want to assess clinically relevant differences between the various drug-eluting stents, you have to compare the stents in routine clinical care patients," Maeng said. "The Endeavor III was performed in 436 low-risk patients with a single non-complex lesion and was only powered to assess an angiographic endpoint. SORT OUT III randomized 2,332 all-comers and was powered to assess a clinical endpoint."

The study was supported by unrestricted grants from Cordis and Medtronic. Neither company had access to the clinical trial database. Dr. Maeng has received speaking honoraria from Cordis, consulting fees from Medtronic, and travel grants from both companies.

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