"Real world"スタディの結果、薬剤溶出ステントは安全で有効であることが示された

レジストリのデータから高齢者における薬剤溶出ステントの死亡率に対する有益性が示された

Registry data suggests mortality benefit for drug-eluting stents in elderly

「現実の世界（Real world）」の患者に対するステント留置術を評価した過去最大のスタディの結果、薬剤溶出ステントはベアメタルステントと比較し、重篤な心血管疾患予防の点で優れ、安全性は同等であることが確認されたとのレイトブレイキングクリニカルトライアルの結果が2009年第58回American College of Cardiology学会i2サミットにて発表され、同時にJournal of the American College of Cardiologyオンライン版に掲載された。研究者らは、米国心血管疾患データレジストリ（National Cardiovascular Data Registry）およびMedicare proceduralレジストリの2004～2006年に血行再建術を施行された患者のデータを解析した。そのうち217,675人が薬剤溶出ステントで治療され、45,025人がベアメタルステントで治療を受けた。年齢中央値は薬剤溶出ステント群で74.5歳でありベアメタルステント群で75.3歳であった。30ヵ月間の経過観察期間中の死亡率、非致死性心筋梗塞発症率および血行再建術再施行率は薬剤溶出ステントを使用された患者においてベアメタルステントを使用された患者よりも有意に低かった（ハザード比[HR]はそれぞれ0.75、0.76、0.91）。脳卒中および重大な出血は基本的に差がなかった（HRはそれぞれ0.96および0.91）。さらに、STEMIおよびnon-STEMIに関する長期のハザード比は薬剤溶出ステントの方に良好な値が認められた。

Full Text

The largest-ever study to evaluate stenting in "real-world" patients has confirmed that drug-eluting stents are better than bare-metal stents at protecting patients against serious cardiovascular illness, and are equally safe, according to research presented during the i2 Summit at the American College of Cardiology's 58th annual scientific session.

The study found that during three years of follow-up, drug-eluting stents significantly reduced the risk of myocardial infarction, death and additional heart procedures when compared to bare-metal stents, while provoking no increased risk of stroke or major bleeding.

"Some previous studies have suggested that drug-eluting stents are associated with an excess long-term death rate, whereas others have not," said Pamela S. Douglas, M.D., Geller professor of medicine at Duke University. "The biggest take home message of our study is: Drug-eluting stents are safe."

Several randomized controlled trials have shown that drug-eluting stents are better than bare- metal stents at keeping the coronary artery from constricting with scar tissue, but their findings on long-term safety have been inconsistent. Equally important, randomized controlled trials are very selective about the types of patients they enroll.

"Few patients who currently require stenting would be considered eligible for a randomized controlled trial - only about 20 percent in our population," Douglas said. "Real-world data are required to assess stent safety and performance in the other 80 percent."

For the study, Dr. Douglas and her colleagues analyzed data from the American College of Cardiology's National Cardiovascular Data Registry (ACC-NCDR) on patients over the age of 65 who had a stenting procedure performed from 2004 to 2006. Of these, 217,675 were treated with drug-eluting stents and 45,025 were treated with bare-metal stents. Median age was 74.5 versus 75.3 years in the drug-eluting and bare metal stent groups, respectively. Follow-up information for each patient was obtained from Medicare claims data. The combination of these two data sets created a novel and powerful resource for assessment of post-marketing stent performance in a community setting.

Researchers adjusted the data for 102 patient characteristics such as sex, age and co-existing medical conditions. They found that patients who received drug-eluting stents had significantly lower rates of death (hazard ratio [HR], 0.75), nonfatal heart attack (HR, 0.76) and repeat heart procedures (HR, 0.91) when compared to patients who received bare-metal stents. In addition, there were essentially no differences in rates of stroke (HR, 0.96) or major bleeding (HR 0.91).

The investigators were not able to directly assess rates of stent thrombosis. However, data that Douglas characterized as "suggestive" showed that after one year, the type of heart attack that is associated with stent thrombosis (STEMI) was no more common with drug- eluting stents than bare-metal stents. In addition, the long-term hazard ratio favored drug-eluting stents for both STEMI and non-STEMI heart attacks.

This study was simultaneously published online in the Journal of the American College of Cardiology.

The study was funded by the Cardiovascular Consortium of the Agency for Healthcare Research and Quality (AHRQ), a federal agency in the Department of Health and Human Services, with additional support from ACC-NCDR.

"Today's findings provide important new evidence for decision-making by heart disease patients and their physicians," said AHRQ Director Carolyn M. Clancy, M.D. "These findings should help resolve many lingering questions regarding the safety of drug-eluting stents in recent years."

ACC2009特集

SYNTAXの結果から治療方針を決定するのに役立つ情報が得られる

SYNTAX解析の結果、多くの患者においてPCIに軍配が上がったが、QOLおよび医療経済上、CABGとPCIのバランスには疑問の余地がある

SYNTAX analysis favors PCI in many patients, but quality of life and economics question CABG-PCI balance

重症の冠動脈疾患患者においてはバイパス手術の方がステント留置術よりも臨床上の予後に関して有利な結果であったが、冠動脈が解剖学的に最も複雑な患者においてはバイパス術を選択するのが最良な一方で、QOLや経済的なことを考慮すると真っ直ぐな病変や中等度の複雑性病変では経皮的冠動脈インターベンション（PCI）の方が良いとのレイトブレイキングクリニカルトライアルの結果が、2009年第58回American College of Cardiology学会i2サミットで発表された。Synergy between PCI with Taxus and Cardiac Surgery（SYNTAX）トライアルの1年間の結果から、死亡率、心筋梗塞または脳卒中発症率はPCIとCABG群で同等であったが、再血行再建施行例数に関してはPCIの方が有意に多いことが示された。ステントもCABGも全体のQOLは向上させたが、胸痛の軽減に関してはCABGの方がやや良好であった。費用対効果解析の結果、疾患の複雑性が費用対効果に影響することが示された。真っ直ぐな3枝病変または左主幹冠動脈病変および中等度の複雑性病変の患者においては、質で補正した余命がPCIの方がCABGよりも良好であり医療費も安かった。しかし、複雑性3枝病変の患者においては質で補正した余命がCABGの方が良好であり、全体的なコストはPCIとCABGとでほぼ同等であった。

Full Text

A new report from the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial shows that the advantages of bypass surgery are less obvious once quality of life and economic data are included in the analysis. Instead, the complexity of coronary artery disease becomes a major factor in determining whether stenting or surgery is the preferred treatment according to research presented during the i2 Summit at the American College of Cardiology's 58th annual scientific session.

A new report from the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial shows that the advantages of bypass surgery are less obvious once quality of life and economic data are included in the analysis. Instead, the complexity of coronary artery disease becomes a major factor in determining whether stenting or surgery is the preferred treatment.

"Clinicians, patients, guideline issuers and payers will find this information helpful in making clinical decisions, as well as in setting treatment priorities," said David J. Cohen, M.D., MSc, director of cardiovascular research at Saint-Luke's Mid America Heart Institute and a professor of medicine at the University of Missouri. "From a patient's perspective, quality of life differences are very important to consider. Similarly, given current constraints within the healthcare system, evidence that one approach is less costly could also be incorporated into treatment guidelines."

The main SYNTAX trial enrolled 1,800 patients with a build-up of cholesterol plaque in either three coronary arteries or the critically important left main coronary artery, randomly assigning 897 to coronary artery bypass grafting (CABG) and 903 to PCI with drug-coated stents. At the one-year mark, rates of death, myocardial infarction or stroke were similar for the PCI and CABG groups, while the number of repeat heart procedures was significantly higher in the PCI group.

The new study set out to determine whether there were differences in the quality of life with the two procedures. Researchers measured not only overall quality of life but also the impact of a patient's heart disease on symptoms, physical limitations, pain, vitality and other factors. In addition, they collected economic data throughout the study on cardiovascular procedures, hospitalizations, outpatient testing, physician visits and medications.

They found that both stenting and CABG improved the overall quality of life over one year of follow-up, although angina relief was slightly better with CABG. Under the U.S. healthcare system, surgery was initially about $6,000 (or about 25 percent) more costly than PCI, reflecting higher hospital costs and much higher physician fees. However, PCI added approximately $2,500 in follow-up costs over the next year, mostly because of additional procedures and the need for long-term anticoagulants.

A formal cost-effectiveness analysis found that for the population as a whole, the clinical benefits of CABG did not justify its higher cost at one year. However, the complexity of coronary disease - determined by such factors as where the plaque was located, the number of lesions to treat, the length of lesions and whether they were calcified or layered with fragile blood clots - had a substantial influence on cost-effectiveness. In straightforward three-vessel or left main coronary disease, PCI led to better quality-adjusted life expectancy than CABG and lower healthcare costs. Findings were similar for patients with disease of intermediate complexity. However, for patients with complex three-vessel disease, quality-adjusted life expectancy was better with CABG, while overall costs at one year were nearly identical for the two procedures.

"The most important message is that there is no single answer. The relative cost-effectiveness of PCI and CABG for left main and three-vessel disease depends strongly on the complexity of underlying coronary disease," Cohen said. "It is also important to note that our analysis applies only to the U.S. healthcare system. Given differences in treatment patterns and resource costs, the specific balance of costs and effectiveness may be very different in other countries."

Five-year follow-up is planned for all patients in the SYNTAX trial.

ACC2009特集

健康人の心血管リスクの改善

JUPITER：一次予防としてスタチンを用いてLDLコレステロールおよびC反応性蛋白レベルを低下させることにより心血管リスクが改善する

JUPITER: Lowering LDL and C-reactive protein levels with statins improves cardiovascular risk in primary prevention

スタチン療法開始後に低密度リポ蛋白（LDL）コレステロールおよび高感度C反応性蛋白（hsCRP）が低下した健康な男女は心血管リスクが劇的に低下したとのデータが2009年第58回American College of Cardiology学会で発表され、同時にLancet誌に掲載された。このJUPITERスタディ（一次予防におけるスタチン使用の正当性の証明：ロスバスタチンを評価する介入試験）の解析において研究者らは、LDLおよびhsCRPレベルに関連した心筋梗塞、脳卒中、不安定狭心症による入院、動脈血行再建術、または心血管死発生率に対するロスバスタチン（20mg）とプラセボの効果を評価した。ロスバスタチンを内服しLDLコレステロールレベル70mg/L（1.8mmol/L）未満およびhsCRP2mg/L未満に達した者は心血管リスクが65%低下したのに対し、これらのレベルのいずれか一つを達成した者またはどちらも達成できなかったものにおける低下率は36%に過ぎなかった。無病生存率はLDLコレステロールおよびhsCRPレベルがより強力に低下（LDL<70mg/dLおよびhsCRP<1mg/L）した者においてより高かった；これらの患者は心血管リスクが80%低下した。JUPITERの他の報告によると、ロスバスタチンは静脈血栓塞栓症のリスクを40%以上低下させるとのことである。

Full Text

Healthy men and women who achieved low levels of both low-density lipoprotein (LDL) cholesterol and high sensitivity C-reactive protein (hsCRP) after starting statin therapy dramatically lowered their risk of a future heart attack, stroke, need for bypass surgery, or cardiovascular death, according to new data presented today at the American College of Cardiology's 58th Annual Scientific Session.

The study - the first to prospectively examine clinical benefits of "dual targets" after initiating statin therapy - demonstrates significantly lowered cardiovascular risk of up to 80 percent among patients who achieved more aggressive reductions in on-treatment LDL and hsCRP levels. Researchers suggest that clinicians consider screening for hsCRP, a marker of underlying inflammation, in addition to LDL cholesterol when identifying patients at high risk for heart disease or monitoring the success of treatment among patients starting statin therapy.

"Our data strongly confirms that statins reduce vascular risk by lowering both inflammation and cholesterol, and we found that achieving low levels of both matters for heart health," said Paul Ridker, M.D., Brigham & Women's Hospital, Boston. "Reducing cholesterol is clearly important, but a reduction in hsCRP with statin therapy appears equally important, and patients who lower both simply do better than those who lower only cholesterol or only hsCRP."

In this analysis of 15,548 initially healthy men and women participating in the JUPITER trial, researchers prospectively evaluated the effects of rosuvastatin (20 mg) versus placebo on rates of myocardial infarction, stroke, hospitalization for unstable angina, arterial revascularization, or cardiovascular death according to achieved levels of LDL and hsCRP.

Compared to those given placebo in the JUPITER trial, those taking rosuvastatin who achieved target levels of LDL less than 70mg/L (1.8 mmol/L) and hsCRP less than 2 mg/L experienced a 65 percent reduction in CV risk compared to only a 36 percent reduction among those treated with rosuvastatin who did not achieve one or both of these target levels. Event-free survival was even greater among patients achieving more aggressive LDL and hsCRP levels (LDL less than 70mg/dL and hsCRP less than 1mg/L); these patients had an 80 percent reduction in cardiovascular risk. The effects remained after adjustment for all available baseline characteristics that varied between groups, including pre-randomization levels of both LDL cholesterol and hsCRP.

JUPITER was a randomized, double blind, placebo controlled trial. Study participants were followed for a maximum of five years (median 1.9 years). Enrolled patients had an LDL of less than 130 mg/dL, which meant they did not qualify for statin therapy under current guidelines.

"JUPITER previously showed that statin therapy is highly effective among patients with low cholesterol who are at risk due to increased levels of inflammation as picked up by elevated hsCRP. We now know that the large benefit gained is due not only to reduction in cholesterol, but to reduction in hsCRP as well," Ridker said. "A patient can be at risk for myocardial infarction or stroke even when cholesterol levels are low. Inflammation is a major determinant of CV risk, and statin drugs are 'two-fers' that lower both inflammation and cholesterol."

It is critical to identify new strategies to detect patients at high risk, and then link those strategies to treatment approaches that work and are cost-effective, he added. "For any patient with high cholesterol or a high hsCRP level, the first steps remain diet, exercise, and smoking cessation," Ridker said. "However, for those electing to start drug therapy, both reductions in LDL and hsCRP appear to be indicators of the success of statin therapy."

These results will be simultaneously published in The Lancet.

Another report from JUPITER found that daily therapy with rosuvastatin cut the risk venous thromboembolism (VTE), by more than 40 percent overall.

"The clinical bottom line here is simple," said Ridker. "In addition to reducing risks of myocardial infarction and stroke, we now have hard evidence that aggressive statin therapy reduces life-threatening blood clots in the veins. In contrast to drugs like warfarin and heparin, we got this benefit with no bleeding hazard at all, so the new data are an exciting advance for our patients."

JUPITER was conducted by investigators in 26 countries and was overseen by an academic statistician and an independent Data and Safety Monitoring Board. The study was funded by AstraZeneca.

抗凝固療法の代替療法

PROTECT AF：新たなデバイスは心房細動患者の脳卒中リスクを軽減する

PROTECT AF: Novel device cuts stroke risk in patients with atrial fibrillation

低侵襲技術を用いた心内植込み型デバイスは非弁膜症性心房細動患者の脳卒中予防に最も広く処方されている薬剤に取って代わる可能性があるとの、心房細動患者の塞栓予防(PROTECT AF)トライアルの結果が2009年第58回American College of Cardiology学会i2サミットで発表された。研究者らは現在の標準治療であるワルファリンによる抗凝固療法と、WATCHMANとして知られる、一般的に左心耳（LAA）内に形成される血栓を捕捉する生地で覆われた膨張型ニチノールケージを比較した。707人の非弁膜症性心房細動患者を、WATCHMANデバイスでLAAを閉鎖しその後ワルファリンを中止する群（463人）またはワルファリン長期治療群（244人）に無作為に割り付けた。900超患者／年の経過観察期間中における両脳卒中（虚血および出血）発症率および心血管死－有効性の一次評価項目－はデバイス群で100患者／年当り3.4例であったのに対し、ワルファリン群では100患者／年当り5.0例であり、32%低下した（相対リスク、0.68）。

Full Text

A device implanted in the heart using minimally invasive techniques may replace the most widely prescribed drug for stroke prevention in patients with nonvalvular atrial fibrillation, according to research presented during the i2 Summit at the American College of Cardiology's 58th annual scientific session.

In the Embolic Protection in Patients with Atrial Fibrillation (PROTECT AF) trial, researchers compared the current standard of therapy, anticoagulation with warfarin, to a fabric-covered expandable nitinol cage known as the WATCHMAN, which blocks blood clots that typically form in the left atrial appendage (LAA). They found that the WATCHMAN reduced by some 30 percent the combined risk of cardiovascular death and stroke (both ischemic and hemorrhagic).

"Patients with atrial fibrillation have a six-fold increased risk of stroke and therefore require long-term anticoagulation therapy," said David R. Holmes, Jr., M.D., Scripps Professor of Medicine at the Mayo Graduate School of Medicine, Rochester, MN. "The placement of this device results in excellent long-term outcomes - effective ischemic stroke prevention with the elimination of hemorrhagic strokes and major bleeding often associated with the use of warfarin."

To implant the WATCHMAN, an interventional cardiologist guides the device into the right atrium, then into the left atrium through a puncture in the wall separating the two upper chambers of the heart. Once the catheter is positioned in the opening of LAA, the WATCHMAN is released and left permanently in place to block the formation and release of blood clots.

For the PROTECT AF study, 707 patients with nonvalvular atrial fibrillation were randomly assigned to closure of the LAA with the WATCHMAN device (463 patients), followed by discontinuation of warfarin, or to long-term treatment with warfarin (244 patients). The study found in over 900 patient-years of follow-up that the combined rate of stroke (ischemic and hemorrhagic) and cardiovascular death - the primary measures of effectiveness - was 3.4 per 100 patient-years in the device group vs. 5.0 per 100 patient-years in the warfarin group, a reduction of 32 percent (relative risk [RR], 0.68).

As for the safety of the device, the researchers observed more procedure-related complications in patients treated with the device (8.7 vs. 4.2 per 100 patient-years; RR, 2.08). Most complications were related to device implantation. However, after successful implantation of the WATCHMAN and discontinuation of warfarin therapy, complication rates were significantly lower with device therapy (1.7 vs. 4.2 per 100 patient-years; RR, 0.40).

The researchers concluded that the WATCHMAN is an effective alternative to warfarin therapy for preventing stroke in patients with atrial fibrillation.

"The take-home message is that although there are complications associated with implantation of the device, patients can avoid the need for chronic warfarin therapy, with all its attendant risks," Holmes said.

Eptifibatide使用のタイミングに関する疑問への回答がスタディにより得られた

EARLY-ACS：高リスク患者に対するPCI中の早期eptifibatide使用の有意な有益性は認めない

EARLY-ACS: Insignificant advantage to early Eptifibatide use during PCI in high-risk patients

心筋梗塞の高リスク患者に対する抗凝固薬使用の最良のタイミングに関する10年間に渡る論争が解決した：結論は「どのタイミングで投与しても構わない」である。EARLY ACSスタディ（非ST上昇急性冠症候群に対する早期の糖蛋白IIb/IIIa阻害）の結果が2009年第58回American College of Cardiology学会レイトブレイキングクリニカルトライアルのセッションで発表され、同時にNew England Journal of Medicineに掲載された。EARLY ACSは、標準的な抗血栓療法に加え、早期eptifibatide投与とPCI中のeptifibatide臨時投与を比較した、無作為化二重盲検コントロールスタディであった。計9,492人の患者が組み入れられ、全員が試験薬開始から12～96時間後に侵襲的治療を施行された。有効性の一次エンドポイントは、あらゆる原因による死亡、心筋梗塞、緊急血行再建術を必要とする虚血の再発、または96時間以内のベイルアウトステント施行の総合であった。二次エンドポイントは30日以内の死亡または心筋梗塞であった。その結果、早期のeptifibatide使用は一次エンドポイントも二次エンドポイントも有意に低下させないことが示された。しかし、早期にeptifibatideを使用することにより生命を脅かさない出血は増加することが明らかにされた。

Full Text

In patients with high risk of myocardial infarction, early utilization of eptifibatide is not superior to delayed, provisional use of eptifibatide during percutaneous coronary intervention (PCI), according to research presented at the American College of Cardiology's 58th annual scientific session.

The EARLY ACS study (Early Glycoprotien IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndromes) aimed to clarify the best strategy for eptifibatide use, an antiplatelet drug therapy successfully implemented in clinical practice for 10 years. Two common strategies of eptifibatide utilization were examined in patients with high-risk of myocardial infarction: early intravenous injection upon immediate arrival at the hospital, and delayed, provisional injection during PCI.

"The drivers for our study are the gaps that exist in the practice guidelines for when and how best to use eptifibatide, an already tested and proven treatment, in the context of other modern therapies that have evolved since the drug was first introduced," said L. Kristin Newby, M.D., MHS, associate professor of medicine at Duke University Medical Center, Durham, N.C.

"Guidelines in North America and Europe vary in their recommendations regarding early use vs. delayed provisional treatment with eptifibatide and drugs like it. Individual hospitals and individual clinicians in all regions apply these recommendations differently."

EARLY ACS was a randomized, double-blind, controlled study of early eptifibatide vs. provisional eptifibatide during PCI with standard background antithrombin therapy. A total of 9492 patients were enrolled, all of whom were scheduled to undergo an invasive strategy 12 to 96 hours after starting the study drug.

The primary efficacy endpoint for EARLY ACS was composite all-cause death, myocardial infarction, recurrent ischemia requiring urgent revascularization or thrombotic bailout during the first 96 hours. The secondary endpoint was death or myocardial infarction through 30 days. Safety endpoints included bleeding, transfusions, stroke and serious adverse events. At its final enrollment, EARLY ACS had a 98 percent power to detect a 22.5 percent reduction in the 96-hour primary composite with early eptifibatide vs. delayed, provisional eptifibatide and 81 percent power for a 15 percent reduction in 30-day death or myocardial infarction.

"We set out to determine what is the better strategy when it comes to the treatment of these high- risk patients," said Robert P. Giugliano, M.D. assistant professor of medicine at the Brigham and Women's Hospital, Harvard, M.A. "Many hospitals in the United States routinely start a course of injectable eptifibatide early when a patient arrives at the hospital. However, there are other physicians who prefer to employ a 'wait and see' approach with the drug until after catheterization. Prior to this study, it was not clear which strategy was better. And, according to current practice guidelines, either strategy would be supported."

They found that early use of eptifibatide was not associated with any significant reduction in either the primary or the secondary endpoints. They did find, however, that earlier use of eptifibatide was associated with more non-life-threatening bleeding.

"Our study, although not the final word regarding eptifibatide, has helped shed a light on how to best use eptifibatide among high-risk patients," Newby said. "In general, physicians can feel comfortable with a strategy of delayed, provisional administration after a decision to proceed to PCI is made." As far as patients are concerned, the primary results from EARLY ACS are the key message - an early routine strategy of eptifibatide is not superior to a delayed provisional strategy."

The study was funded by the Schering-Plough Research Institute and Millennium Pharmaceuticals.

Co-authors include Robert Harrington, Robert Califf, Kerry Lee, Jennifer White and Lisa Berdan from Duke, Christoph Bode, from the University of Freiberg; Paul Armstrong, from the University of Alberta; Gilles Montalescot, of Centre Hospitalier Universitaire Pitie-Salpetriere; Frans Van de Werf, Universitair Ziekenhuis Gasthuisberg; Eugene Braunwald, Brigham and Women's Hospital; Steven Hildemann, Essex-Pharma GmbH; and John Strony and Enrico Veltri, Schering-Plough Corporation.

心室再建術の効果は根拠がない

STITCH：心不全患者に対しCABGに加え外科的心室再建を施行してもCABG単独と効果は同等である

STITCH: Surgical ventricular reconstruction plus CABG no better than CABG alone in heart failure patients

虚血性心不全に対する外科治療（STICH）トライアルの結果、冠動脈バイパス術（CABG）に加えて外科的心室再建術（SVR）を施行された患者はCABGのみを施行された患者と比較し状態が良好なわけではない、と2009年第58回American College of Cardiology学会で発表されNew England Journal of Medicineに掲載された。研究者らは左室駆出率≤35%で外科医がCABGを行うことにより管理できると判断した冠動脈疾患を有し、瘢痕化した機能不全組織が前壁ー心尖部にある患者（年齢中央値62歳、男性85%）をCABGのみ（499人）またはCABGに加えSVR（501人）を施行する群に無作為に割り付けた。どちらの手術も症状および運動耐容能を改善した。SVRは左室収縮末期容積指数を20%減少させたのに対し、CABGでは3%の減少であった。しかし、経過観察期間（中央値4年間）の死亡率または心原性の入院率は二群間で差がなかった（CABG群で56%、CABG/SVR群で57%）。またACCで発表されAmerican Heart Journalオンライン版に掲載されたSTICHトライアルサブ解析においては、SVRはQOLの改善もしくは他の臨床上の有益性を生み出すことなく医療費を増やす、と結論付けられた。

Full Text

A surgical procedure that reduces the size of a scarred, enlarged heart did not improve long-term survival or reduce the number of hospitalizations in patients with heart failure, according to research presented at the American College of Cardiology's 58th annual scientific session and simultaneously published in the New England Journal of Medicine.

The first phase of the Surgical Treatment for Ischemic Heart Failure (STICH) trial showed that patients who had surgical ventricular reconstruction (SVR) in addition to coronary artery bypass grafting (CABG) fared no better over an average of four years of follow-up than patients treated with CABG alone.

"Over the last decade, as we have been doing better at managing the myocardial infarctions that cause injury to the heart, these scars have gotten smaller and smaller," said Robert H. Jones, M.D., Mary and Deryl Hart Distinguished Professor of Surgery at Duke University Medical Center, Durham, NC. "Now we know that with good, intensive medical therapy and very good revascularization, there is no intrinsic value to SVR over bypass surgery alone."

Surgical ventricular reconstruction returns the ventricle to a more normal, compact size. At a smaller size, the heart experiences less stress and strain and, like a healthy heart, might regain the ability to temporarily expand to meet the body's demands for increased cardiac output. Previous studies have shown that one of the strongest predictors of survival in patients with heart failure is the size of the heart at the end-systolic volume.

For the study, investigators recruited 1,000 patients from 96 medical centers in 23 countries. Patients were required to have an ejection fraction of≤ 35 percent, coronary artery disease the surgeon felt could be well managed by CABG, and an area of scarred, dysfuctional tissue in the anterior-apical region. About half of patients had moderate-to-severe angina. Heart failure was deemed moderate-to-severe in a similar proportion, and more than 60 percent had triple-vessel disease. The median age was 62, and 85 percent of patients were men.

Patients were randomly assigned to undergo CABG alone (499 patients), or CABG plus SVR (501 patients). All patients received intensive medical therapy. Both surgeries improved symptoms and exercise capacity, and SVR was successful in reducing end-systolic volume index by 20 percent, compared to 3 percent with CABG. However, after a median follow-up of 4 years, there were no differences between the two groups in combined rates of death or hospitalization for cardiac causes (56 percent among patients in the CABG group and 57 percent among patients treated with both CABG and SVR).

"This is the first time that a proposed new heart operation has been tested in this way," Jones said. "Our findings emphasize the importance of taking what appear to be medical breakthroughs and subjecting them to very rigorous comparisons with the best available therapy."

A second report from the STICH trial presented at ACC and published online in the March 30 in the American Heart Journal, concluded that that SVR increases costs without improving quality of life or providing other clinical benefits.

For the quality of life substudy, investigators conducted interviews with patients before and after their surgeries to collect information on physical and social limitations, satisfaction, and other measures of quality of life. Both treatment groups improved their quality of life after surgery but there was no difference between the two groups throughout 3 years of follow-up.

This substudy also looked at the economic consequences in the United States of having surgical ventricular reconstruction including whether the procedure would be cost effective. Information was collected on the length of surgeries, post-operative time in the intensive care unit, total length of hospital stay, rates of rehospitalization, hospital billing data, and physician costs. Costs were assigned using the 2008 Medicare Fee Schedule. Total hospitalization costs were $14,595 higher for bypass combined with the ventricular reconstruction.

"The results of the STICH trial demonstrate that routine use of surgery to reconstruct the left ventricle does not improve survival, hospitalization, quality of life or cost benefit over bypass surgery alone," said George Sopko, M.D., a medical officer at NHLBI and co-author of the mortality paper in NEJM. "There is still much to learn from the rich source of information provided by this trial, and we look forward to additional analysis of the results as patients continue to be followed."

Surgical reconstruction initially showed encouraging results and improvement in heart failure symptoms in some non-randomized studies, according to Sopko. "As with many initially promising procedures, further rigorous scientific testing is needed before full acceptance into medical practice," he added.

Investigators have already enrolled more than 1,200 patients in the next phase of the STICH trial. It will answer an even more crucial question: whether bypass surgery itself is effective in improving long-term survival in patients with heart failure who are already receiving the best possible medical therapy.

ACC2009特集

電気刺激は心不全の予後を改善する

FIX-HF-5：新たなデバイスは心臓のポンプ機能を強化し運動耐容能およびQOLを改善する

FIX-HF-5: Novel device helps heart to pump more forcefully improving exercise capability and quality of life

電気刺激を心臓に送り毎回の収縮力を強化する治験デバイスは心不全患者の治療に有望であることが示された、と2009年第58回American College of Cardiology学会で発表された。FIX-HF-5スタディでは、駆出率35%以下で心電図上QRSの狭いNYHAクラスIIIまたはIVの心不全患者を、最大限の薬物療法単独（213人）または心収縮力調整（CCM）と最大限の薬物療法を組み合わせた群（215人）に無作為に割り付けた。6ヵ月後の時点で安全性は両群ともに等しく良好であったが、Peak VO2およびQOL（スコアが低いほどQOLが高い）はCCM群の方が良好であった(pVO2は0.65mL/kg/min改善し[p=0.024]，QOLスコアは9.7ポイント低下した[p<0.0001])。無酸素性代謝閾値に有意差はなかった。しかし、中等度の心不全（NYHAクラスIII）で駆出率が25%以上の患者185人のみを解析したところ、三つの指標は全てCCM群において有意に改善していた（無酸素性代謝閾値は0.64mL/kg/min多く[p=0.03]，pVO2は1.31mL/kg/min多く[p=0.001]，QOLスコアは10.8ポイント低かった[p=0.003]）。

Full Text

An investigational device that delivers electrical impulses to the heart, thereby strengthening the force of each contraction, is showing promise in patients with heart failure, helping them to exercise more vigorously and promoting a greater sense of well-being, according to research presented today at the American College of Cardiology's 58th annual scientific session.

The FIX-HF-5 study found that cardiac contractility modulation (CCM) significantly improved peak ventilatory oxygen uptake (pVO2) and quality of life in patients with moderate-to-severe heart failure, when compared to the best available medical care. In patients with only moderate heart failure, CCM also improved anaerobic threshold, a new marker being tested as a gauge of treatment effectiveness.

"Cardiac contractility modulation shows great promise for the treatment of heart failure," said William T. Abraham, M.D., a professor of medicine, physiology, and cell biology and director of cardiovascular medicine at The Ohio State University in Columbus. "It has the potential to be a real breakthrough."

The CCM device - known as the Optimizer (Impulse Dynamics, Orangeburg, NY) - looks much like a pacemaker and, like that device, is implanted under the skin in the chest with wires threaded into the right side of the heart. Unlike a pacemaker, which controls the heart rate and rhythm, CCM delivers its electrical impulses precisely when the heart is recharging between beats and will not respond by contracting. Instead, the heart converts the electrical energy into a more forceful contraction the next time it beats.

For the study, researchers recruited 428 patients with NYHA class III or IV heart failure, an ejection fraction of ≤35 percent, and narrow QRS tracings on the electrocardiogram (which would rule out cardiac resynchronization).

Patients were randomly assigned to optimal medical therapy alone (213 patients) or CCM plus optimal medical therapy (215 patients). At baseline and six months after device implantation, researchers tested the effectiveness of CCM by having all patients exercise on a treadmill while wearing a mask that measures the air that is breathed in and out. The investigators evaluated both peak VO2, an indicator of maximum exercise capacity, and a new indicator, anaerobic threshold, which shows how vigorously a patient can exercise before running out of ready energy reserves and switching to a less efficient form of metabolism. Researchers also measured quality of life using the Minnesota Living with Heart Failure Questionnaire. With this questionnaire, a lower score indicates a better quality of life.

At six months, safety was equally good in both groups, while Peak VO2 and quality of life were significantly better among patients treated with CCM, as compared to optimal medical therapy alone. Peak VO2 was better by 0.65 mL/kg/min, p = 0.024; and the quality of life score was 9.7 points lower, p<0.0001. There was no significant difference in anaerobic threshold.

However, when researchers analyzed data only for the 185 patients with moderate heart failure (NYHA class III) and an ejection fraction ≥25 percent, all three indicators improved significantly more in the CCM group (anaerobic threshold was better by 0.64 mL/kg/min, p = 0.03; pVO2 was better by 1.31 mL/kg/min, p = 0.001; and the quality of life score was lower by 10.8 points, p = 0.003).

"It may be that some people are too sick, or their heart is too damaged, to respond to CCM," Abraham said. "This study has provided us with important insight into the 'sweet spot,' where this therapy is most effective."

冠動脈石灰化スコアは中等度リスクの患者を再分類するのに役立つ

Heinz Nixdorf Recall Study：冠動脈石灰化は伝統的なリスクファクターよりも心血管疾患の予知因子して優れている

Heinz Nixdorf Recall Study: Coronary artery calcium better predictor of cardiovascular disease than classic risk factors

冠動脈石灰化（CAC）スコアは標準的な心血管リスクファクター（米国コレステロール教育プログラム[NCEP]の定めた）よりも、中等度リスクの患者のうち誰が心筋梗塞（MI）を起こしやすいかまたは心疾患にて死亡しやすいかの予知因子として優れている、と2009年第58回American College of Cardiology学会で発表された。CACスコアが最も高い4分の1に入る者と最も低い4分の1に入る者を比較すると、心疾患イベントの相対リスクは女性で3.16（p=0.009）であり、男性で11.09（p<0.0001）であった。受信者動作特性曲線（ROCカーブ）を作成し、この曲線の下部領域（AUC）により検査の臨床イベント予知能が計測できた（スコア1.0が最も望ましい）。NECPリスク分類およびCACスコアのAUCはそれぞれ0.667および0.740であり、NECPリスク分類とCACスコアを組み合わせるとAUCは0.754であった。NECPリスク分類とCACスコアの両者を含めた他の解析では、NECPリスクの最も高い者を最も低い者と比較するとMIまたは心臓死のオッズは3.19であった（p<0.0001）。CACスコアのリスク層別能はそれよりも優れ、冠動脈石灰化スコアが最も高い4分の1の者は最も低い4分の1の者と比較しオッズ比が4.26であった。

Full Text

Coronary calcium scoring can help predict who is likely to have a myocardial infarction or die of cardiac disease, according to a late breaking clinical trial presented at the American College of Cardiology's 58th Annual Scientific Session.

To assess a patient's risk for cardiovascular disease, most doctors rely on classical risk factors such as cholesterol levels, blood pressure, family history, age, sex, and diabetes. The Heinz Nixdorf Risk Factors Evaluation of Coronary Calcium and Lifestyle (Heinz Nixdorf Recall) study found that the coronary artery calcium score was a better predictor of cardiovascular disease than classic risk factors at predicting risk over five years. When the two sets of information were added together, predictive strength was better still. The findings were drawn from an observational study in a general population, roughly half of whom were women.

"Our results demonstrate that prediction of coronary events can be improved when calcium scoring is performed, especially in persons in the intermediate-risk category," said Raimund Erbel, M.D., director of cardiology at University Clinic Essen, University Duisburg - Essen, Germany. "This means that persons at intermediate risk with a high coronary calcium score should be recommended intensive lifestyle changes and maybe risk-modifying medication, while persons at intermediate risk with a low coronary calcium score have a more favorable prognosis."

Coronary calcium levels are detectable long before other symptoms of coronary disease. The total coronary calcium burden is considered a measure of the extent of atherosclerotic disease. In addition, it is currently believed that a large amount of coronary calcium indicates a high likelihood of rupture-prone plaque somewhere in the coronary arteries. This may explain the link between the coronary calcium score and increased rates of cardiac events.

For the study, Dr. Erbel and colleagues recruited 4,487 randomly selected subjects without known coronary disease. Study participants ranged in age from 45 to 75 years, and 52 percent were women. Patients were placed into risk categories on the basis of standard cardiovascular risk factors, as defined by the National Cholesterol Education Program (NCEP). Electron-beam CT was used to measure the coronary calcium score.

Of the 4,137 study participants with complete follow-up data, 93 suffered cardiac death or nonfatal heart attack, including 28 women. When coronary calcium scores in the highest one- fourth were compared to those in the lowest one-fourth, the relative risk of a cardiac event was 3.16 (p = 0.009) for women and 11.09 (p<0.0001) for men.

Researchers then developed receiver operating characteristic (ROC) curves, in which true- positive and false-positive results are calculated and plotted in relation to each other. The area under the curve (AUC) measures the ability of a test to predict a clinical event, with a score of 1.0 being ideal. The area under the curve for the NCEP risk categories was 0.667, while the AUC for coronary calcium scoring was 0.740, and the AUC for a combination of NCEP risk categories and coronary calcium scoring was 0.754. In another analysis that included both NCEP risk categories and coronary calcium score, the odds of a heart attack or cardiac death among study participants in the highest NCEP risk category, as compared to the odds in the lowest risk category, was 3.19 (p<0.0001). Coronary calcium scoring did an even better job differentiating risk, with an odds ratio of 4.26 when the highest one-quarter of coronary calcium scores was compared to the lowest (p<0.0001).

"Calcium scoring has now been validated and reached a place in preventive cardiology," Dr. Erbel said.

The research team plans to follow-up on patients for the next five years so they can analyze the 10-year risk prediction capability of coronary calcium scoring and other factors.

ワルファリンより安全な代替療法

ACTIVE-A：大血管イベントの予防に関してクロピドグレル／アスピリンの併用はワルファリンよりも安全な代替療法のようである

ACTIVE-A：Clopidogrel/aspirin combination therapy appears to be a safer alternative to warfarin for prevention of major vascular events

クロピドグレルとアスピリンの併用により大血管イベントが11%減少したとのレイトブレイキングクリニカルトライアルACTIVE-Aの結果が、2009年第58回American College of Cardiology学会で発表された。2006年には、クロピドグレルをアスピリンに追加してもワルファリンよりも有効性が低いとのACTIVE-Wの結果が報告されたが、このスタディに参加した患者の多くはスタディに組み入れられた時点でワルファリンをすでに内服していたため、ワルファリンに好ましいバイアスがかかっていた可能性があり、この結果は解釈が難しかった。ACTIVE-Aでは、心房細動の認められた患者7,554人に対してアスピリンにクロピドグレルを併用投与した効果を、二重盲検プラセボコントロール試験で直接評価した。このトライアルでは全ての患者がアスピリン（推奨用量：一日75～100mg）を内服しており、クロピドグレル（一日75mg）またはプラセボを内服する群に無作為に割り付けられた。主要な血管イベント全体（脳卒中、心筋梗塞、中枢神経系以外の全身性塞栓症または血管死の合計）の発現が11%低下したのに加え、併用療法の結果、脳卒中発現率が28%低下し心筋梗塞発現率が23%低下した。クロピドグレルにより年1.27～2%であった重大な出血のリスクが58%増加した。

Full Text

A combination of clopidogrel and aspirin reduces major vascular events by 11 percent, including a 28 percent reduction in stroke and a 23 percent reduction in myocardial infarction, according to research presented at the American College of Cardiology's 58th annual scientific session.

The results of ACTIVE-A assessed the safety and efficacy of adding clopidogrel to aspirin in high-risk atrial fibrillation (AF) patients who are unsuited to use vitamin K antagonists (VKA) such as warfarin as a treatment therapy for AF.

Oral anticoagulants, such as warfarin and aspirin, are the only proven effective therapies in treatment for AF, and warfarin has proved to be the more effective of the two. However, many patients who are unsuited to use VKA such as warfarin, and they receive aspirin. Warfarin reduces stroke by 38 percent; however, it increases major hemorrhage by 70 percent and intracranial hemorrhage by greater than 100 percent. It is also difficult to tolerate, requiring monitoring and restrictions of lifestyle. Aspirin alone is modestly effective, reducing stroke by 22 percent.

Guidelines recommend warfarin for high-risk patients but many patients do not take it because of bleeding risk or because of their physician does not recommend it.

"The purpose of the ACTIVE-A trial was to determine if the addition of clopidogrel to aspirin would reduce major vascular events and stroke in patients with AF, at an acceptable risk of increased hemorrhage," said Stuart Connolly, M.D. of McMaster University and one of the principle investigators of ACTIVE-A. "If you treated one thousand patients over the course of three years by adding clopidogrel to aspirin, you would prevent 28 strokes, 17 of which would be fatal or disabling, and you would prevent six heart attacks. This would occur at a cost of 20 major hemorrhages."

In 2006, the ACTIVE-W study reported that adding clopidogrel to aspirin was less effective than warfarin, but this result is difficult to interpret because most patients in that study were on warfarin at the time of enrollment, potentially biasing results in favor of warfarin. In ACTIVE-A the effect of adding clopidogrel to aspirin is directly evaluated in a double-blind placebo- controlled clinical trial of 7,554 patients with documented AF and at least one risk factor for stroke.

In ACTIVE-A, all patients were treated with aspirin (75-100 mg/day, recommended) and randomized to receive either clopidogrel (75 mg/day) or matching placebo. The primary outcome was the composite of stroke, myocardial infarction, non-CNS systemic embolus or vascular death; major bleeding was a secondary safety outcome. Clopidogrel increased risk of major hemorrhage by 58 percent from 1.27 percent to 2 percent/year.

"Addition of clopidogrel to aspirin in many patients with AF, unsuitable for warfarin will provide an overall benefit at an acceptable risk," said Salim Yusuf, M.D. of McMaster University and one of the principle investigators "When compared to aspirin alone, warfarin is more effective than clopidogrel plus aspirin against stroke in AF. However clopidogrel provides only about three-quarters of the benefit of warfarin over aspirin, but with only about three- quarters of the increased risk of major and intracranial hemorrhage."

CRTは臨床転帰を改善する

REVERSE：両心室ペーシングを最大限の薬物療法に組み合わせることで軽度心不全患者に有益性がもたらされる

REVERSE: Biventricular pacing combined with optimal medical therapy is beneficial in patients with mild heart failure

心臓再同期療法（CRT）を評価した24ヵ月間のヨーロッパのスタディの結果、心臓の同期不全を有する軽度心不全患者に対し最大限の薬物療法に両心室ペースメーカーを組み合わせることにより、最大限の薬物療法のみを受けたコントロール群と比較し悪化の程度が有意に低下したことが示されたとの研究結果が2009年第58回American College of Cardiology学会で発表された。このスタディは、薬物療法で良好に治療されているが軽度の症状のある患者または過去に心不全を有したwide QRSの無症状の患者に対してCRTの有効性を評価した、左室収縮不全患者における再同期リバースリモデリング（REVERSE）の多国籍コホートスタディである。CRTと最大限の薬物療法の併用（CRT ON）と最大限の薬物療法のみ（CRT OFF）の群における悪化のパーセンテージを比較した一次エンドポイントは経過とともに増加し、疾患の進行は停止しないことが示された。しかし、悪化の程度はCRT OFF群と比較するとCRT ON群において有意に低かった。CRT ON群において、左室機能の改善は著明でありその程度は18ヵ月の間に向上し効果はスタディの最後の6ヵ月間持続した。一方、CRT OFF群では観察期間終了に向かい悪化した。

Full Text

A 24-month European study measuring cardiac resynchronization therapy (CRT) showed that using a biventricular pacemaker combined with drug therapy on patients with mild heart failure and ventricular dyssynchrony showed the magnitude of worsening at measured time points was significantly lower than in the control group who received optimal medical therapy alone, according to research presented at the American College of Cardiology's 58th annual scientific session.

Worsening is defined as either the occurrence of heart failure hospitalizations, death, the need to be programmed to the opposite randomization assignment, worse New York Heart Association (NYHA) functional class or worse wellbeing as judged by the patient.

This study is a multi-national European cohort of the REVERSE trial presented at ACC08 which was a one-year multi-center trial that gauged whether CRT plus optimal medical therapy (CRT ON) can manage the progression of heart failure compared to optimal medical therapy alone (CRT OFF). The results from that earlier one-year study, which included both United States and European patients, failed to show that adding CRT to optimal medical therapy significantly influenced the primary end point, which was percent worsening. However, the data did show that device therapy most likely improved left ventricular function and prevented heart-failure hospitalizations - both secondary endpoints of the study.

"We wanted to assess if CRT in medically well-treated but mildly symptomatic patients or in asymptomatic patients with previous heart failure and with a wide QRS could modify disease progression," said Cecilia Linde, M.D., Ph.D, Karolinska University Hospital, Stockholm, Sweden.

The primary endpoint of comparing the worsening percentage in both CRT ON and CRT OFF increased over time, indicating disease progression did not stop. However, the magnitude of worsening at each time point was significantly lower in the CRT ON when compared to the CRT OFF group.

Improvement in left ventricular function was marked and progressed over 18 months with sustained benefit over the last six months of the study period. In contrast, the disease progression, being worsening ventricular function, in the CRT OFF group was seen towards the end of the observation period.

"We noticed that the 262 European patients improved by CRT, regarding the clinical composite response and in terms of sustained reverse remodeling," Linde said. "This translates into a significant decrease in death and heart failure hospitalizations."

As with the main REVERSE trial, there was no significant benefit in the NYHA functional classification, quality of life or exercise capacity, which is not surprising in mildly symptomatic or asymptomatic patients.

"Optimal heart failure medication, when properly introduced, means that patients who are admitted for heart failure for the first time may revert to an asymptomatic or mildly symptomatic stage," Linde said.

Left ventricular function does not normalize or improve sufficiently by administering drugs in all patients. In these patients, disease progression that results in worsening symptoms or even the need for hospitalization due to heart failure over the following 12 to 24 months is expected.

"Our study demonstrated that CRT in a subset of such patients with wide QRS easily detected with an ordinary ECG and indicating delayed ventricular activation, is an important addition to treatment that achieves substantial reverse modeling, which postpones the time to the next heart failure progression," Linde said.

"Thus, we believe it impacts disease progression."

画像検査により心不全のリスクが見極められる

ADMIRE-HF：新たな核医学検査は心不全患者のリスクを定義付けるのに役立つ

ADMIRE-HF: New nuclear imaging test helps define risk in patients with heart failure

心臓の交感神経の整合性を評価する簡単な核医学検査である心筋シンチグラフィにより予後が不良と考えられる患者を見極めることができるとのADMIRE-HFの結果が2009年第58回American College of Cardiology学会で発表された。この検査は交感神経に取り込まれるノルエピネフリンの生理的アナログである123Iメタヨードベンジルグアニジン（123ImIBG）を 放射性トレーサーとして用いる。日本およびヨーロッパのスタディの結果、123ImIBGの取り込みが少ないと予後不良であることが示された。このトライアルではクラスIIおよびIIIの心不全患者964人に123ImIBGを静脈内注射し核画像検査を施行した。約4分の1の患者（238人）が平均18ヵ月の経過観察期間中に主要な心イベントを来たした。2年間の無病生存率はH/M（心臓／縦隔比：健康人のH/M比は約2）≥1.60の患者で85%であり、H/M比<1.60の患者では63%であった。H/M比が低い群では心臓死が51人に認められたのに対し、H/M比が高い群では2人であり、2年にわたる心臓死に関してH/M比が高いことによる陰性的中率は98.8%であった。

Full Text

A simple nuclear imaging test called myocardial scintigraphy can evaluate the integrity of the sympathetic nerves in the hearts of patients with Class II and III heart failure, according to research presented at the American College of Cardiology's 58th scientific session.

"The Prognostic Significance of 123I-mIBG Myocardial Scintigraphy in Heart Failure Patients: Results From the Prospective Multicenter International ADMIRE-HF Trial" employs myocardial scintigraphy, which enables doctors to examine heart functions at the cellular level to determine if those functions are working properly. Cellular malfunction results in patients at higher risk for deterioration of the heart's pumping ability and possibly even death.

"ADMIRE-HF allows us to get a better understanding and gives us a qualitative measurement of what's happening at the molecular level in the nerves of the heart, which cannot be seen on tests such as echocardiograms and x-rays," said Arnold F. Jacobson, M.D., Ph.D., Head of the Cardiac Center of Excellence, GE Healthcare.

ADMIRE-HF is the integration of two multicenter international Phase 3 trials designed to show the prognostic value of scintigraphy with the norepinephrine analog 123I-mIBG (AdreView) as a risk indicator for major cardiac events among 964 patients with heart failure. The composite endpoint was the time to the first occurrence of NYHA (New York Heart Association) heart failure class progression, potentially life-threatening arrhythmic event, or cardiac death, as determined by an independent adjudication panel. Patients were followed for a maximum of two years.

Roughly one-quarter (238) of the patients experienced major adverse cardiac events during a mean follow-up of 18 months; first events were heart failure progression in 163 subjects, arrhythmic events in 51 and 24 cardiac deaths. An additional 29 cardiac deaths occurred as later events. Two year event-free survival was 85 percent in patients with H/M ≥1.60 (heart/mediastinum ratio) compared with 63 percent for those with H/M <1.60. Fifty-one cardiac deaths occurred in the low H/M group compared to two in the high H/M group and the negative predictive value of a high H/M for cardiac death over two years was 98.8 percent.

The test is easily performed with an IV injection of a radioactive tracer, which enables images of the heart to be taken over several hours using a nuclear medicine imaging device. The tracer is safe, with radiation exposure similar to other nuclear medicine procedures. The agent has been in clinical use for more than 20 years in Japan, Europe and the United States with very few adverse reactions reported.

While the test itself has no effect on the patient's condition, the information it provides may contribute to the development of a more effective management strategy.

"The use of the imaging test is consistent with the current trend toward gaining better and earlier understanding of heart disease at a molecular level in order to institute more effective prevention and management strategies," Jacobson said. "We've known about this testing method for years, but ADMIRE-HF is the first large-scale multicenter prospective validation of its prognostic power and provides data that clinicians may be able to use to improve current practice.

Admire-HF is still investigational in nature and any clinical application of the results will only be possible once the FDA approves the agent for a cardiac indication.

アトルバスタチンによりPCI後のMI率が低下する

NAPLES II：高用量アトルバスタチンは多面的効果によりPCI後の非Q波心筋梗塞発現率を低下させる

NAPLES II: High dose atorvastatin reduces non Q-wave myocardial infarction following PCI through pleiotropic effects

経皮的冠動脈インターベンション（PCI）後24時間以内に80mgのアトルバスタチンを投与することによりPCI後の非Q波心筋梗塞（MI）発現率が低下するとの研究結果が2009年第58回American College of Cardiology学会i2サミットで発表された。過去に施行されたNovel Approaches for Preventing or Limiting Events：NAPLES（イベントを抑制および減少させる新たなアプローチ）Iトライアルの結果、PCIの7日以上前にアトルバスタチン40mgを投与することにより周術期の非Q波MI発現率が低下することが示された。NAPLES IIではインターベンションの24時間以内に高用量のアトルバスタチン投与もまた予防効果があるか否かを調査することが目的であった。このトライアルでは、選択的PCIを予定されているスタチンを内服していない患者668人をアトルバスタチン80mg投与群（338人）またはアトルバスタチン非投与群（330人）に無作為に割り付けた。周術期のMI発現率はアトルバスタチン群で9.5%でありコントロール群で15.8%であった（P=0.014；オッズ比0.56）。トロポニンの正常上限値の3倍以上の上昇発現率はアトルバスタチン群で26.6%でありコントロール群で39.1%であった（P<0.001；オッズ比0.56）。筆者らは、今回の結果からスタチンが周術期の心筋壊死を予防するという概念が支持されると述べている。

Full Text

Giving 80 mg of atorvastatin within 24 hours of a percutaneous coronary intervention (PCI) reduces the incidence of non Q-wave myocardial infarction (MI) after PCI, according to research presented during the i2 Summit at the American College of Cardiology's 58th annual scientific session.

An earlier trial, Novel Approaches for Preventing or Limiting Events (NAPLES) I, showed that 40 mg of atorvastatin administered at least seven days before PCI reduced the rate of periprocedural non Q-wave MI. NAPLES II sought to determine whether a high loading dose of atorvastatin given in the 24 hours before an intervention would also be protective.

"One of the complications after stent implantation is the rise in troponin and CK-MB, which may occur in up to 30 percent of patients, even though their procedure has been completely successful. This rise is associated with worse outcomes after PCI. There are many data to support that statins administered one week before stenting can prevent CK-MB and troponin increase," said Carlo Briguori, M.D., PhD of Clinica Mediterranea, Naples, Italy. "We wanted to learn if giving a high dose of atorvastatin right before stenting would have a similar protective effect."

NAPLES II randomly assigned 668 patients scheduled for elective PCI who were not on statin therapy to atorvastatin 80 mg (n = 338) or no atorvastatin (n = 330). The primary endpoint was the incidence of periprocedural MI as assessed by analysis of creatine kinase myocardial enzyme (CK-MB) and cardiac troponin I before and at intervals of six and 12 hours after the intervention.

Periprocedural MI was defined as a CK-MB elevation greater than three times the upper limit of normal (ULN) alone or associated with chest pain or ST segment or T-wave abnormalities.

The incidence of periprocedural MI was 9.5 percent in the atorvastatin group and 15.8 percent in the control group (P = 0.014; odds ratio, 0.56). The incidence of troponin elevation greater than three times ULN was 26.6 percent in the atorvastatin group and 39.1 percent in the control group (P < 0.001; odds ratio, 0.56).

"These findings support the concept that statins prevent periprocedural necrosis," Dr. Brigouri said.

"The fact that atorvastatin was effective when we started it at a very high dose 24 hours before PCI suggests that the major mechanism by which statins are effective is through their pleiotropic effects - interference with the inflammatory and thrombotic pathways that may be involved in the CK-MB increase following stenting."

ACC2009特集

小型のLVAD代替療法

部分的循環補助により薬物療法の無効な心不全患者の心機能が改善する

Partial circulatory support improves heart function in medically refractory heart failure patients

AAバッテリサイズで重さ25gのポンプにより薬物療法の無効な心不全患者の部分的な循環が補助され血行動態および心機能が改善した、と2009年第58回American College of Cardiology学会で発表された。このスタディでは、たった2.5～3.0L／分の血液を拍出するだけで心機能を補助する循環補助装置を16人の患者（男性13人、平均年齢52歳、ベースラインの平均駆出率20%）に植え込んだ。植え込み前の平均動脈圧は71mmHg、平均肺毛細管楔入圧は29mmHg、心拍出係数は1.9L/min/m^2であった。16人中13人の患者（81%）が3ヵ月後も生存していた。そのうち7人に10.6±6週の時点で右心カテーテルを施行した。平均動脈圧（70±6mmHg対80±10mmHg、P=0.04）および心拍出係数（2.1±0.4対2.9±0.6、P=0.02）の増加と肺毛細管楔入圧の大幅な低下（30±5対16±4、P=0.002）が認められた。peak VO2は3.0±0.5ml/kg/min増加した（10.7±2.2対13.7±2.2、P= 0.008）。

Full Text

A pump the size of an AA battery weighing 25 grams provided partial circulatory support and improved hemodynamics and cardiac function when implanted in patients with medically refractory heart failure, according to research presented at the American College of Cardiology's 58th annual scientific session.

The Synergy™ Pocket Micro-pump may expand the use of circulatory assist devices in a large population of chronic heart failure patients who are not sick enough to justify being implanted with a full support ventricular assist device (VADs) but who have tried all other less invasive options without success. Traditional ventricular assist devices provide full support, taking over the work of the heart's main pumping chamber in end-stage heart failure patients in or near cardiogenic shock. Their use is restricted because the surgery required for their insertion is major, invasive and risky.

"Traditional VADs pump five to seven liters of blood per minute and therefore, just by physical necessity, they have to be large," said Daniel Burkhoff, M.D., Ph.D, adjunct associate professor at Columbia University, New York, and chief medical officer of CircuLite, Inc., developer of the Synergy device. "Synergy, the smallest device being investigated in adults, supports cardiac function by pumping just 2.5 to 3.0 liters of blood per minute."

"This study was done to determine if such partial support would be adequate to provide long-term benefits in NYHA Class IIIb and early Class IV patients."

In the study, 16 patients (13 males), mean age 52 years, with a mean baseline ejection fraction of 20 percent, were implanted with the Synergy™ pump. Before implantation, their mean arterial pressure was 71 mmHg, mean pulmonary capillary wedge pressure was 29 mmHg, and mean cardiac index was 1.9 L/min/m^2. The duration of their partial support was a median 81 days and ranged from six to 213 days.

Thirteen of the 16 patients (81 percent) were alive at three months. Of these, seven patients had right heart catheterization at 10.6 ± 6 weeks. Increases in mean arterial pressure (70 ± 6 mmHg vs 80 ±10 mmHg, p = 0.04) and cardiac index (2.1 ± 0.4 vs. 2.9 ± 0.6, p = 0.02) with large reductions in capillary wedge pressure (30 ± 5 vs. 16 ± 4, p = 0.002) were observed. Peak VO2 increased by 3.0 ± 0.5 ml/kg/min (10.7 ± 2.2 vs. 13.7 ± 2.2, p = 0.008).

"Prior studies have shown that when you implant a full ventricular support device, patients' hemodynamic function and heart function improve. The significance of this research is that we have shown for the first time that with long-term partial circulatory support, patients' hemodynamic condition is significantly improved and these improvements are sustained over time," Burkhoff said. "This is real proof of concept that the use of partial circulatory support is feasible and likely to be clinically meaningful. The ultimate goal is to use partial circulatory support not as a bridge to transplant, but as a long-term therapy. In Europe, the distinction between bridge to transplant and long-term support is blurred because the wait times are so long for a heart that patients can be supported for six to 24 months or more, even in a bridge situation."

ACC2009特集

小児期の中性脂肪により将来の心血管イベントが予測できる

小児期の中性脂肪増加は成人期の心血管イベントのリスクを上昇させる

Elevated triglycerides in childhood increase risk for cardiovascular events in adulthood

血中中性脂肪レベルの上昇している小児は成人期早期の心血管疾患（CVD）イベントのリスクが高い可能性があるとの研究結果が2009年第58回American College of Cardiology学会で発表された。CVDのないコントロール789人と比較し、CVDを発症した者は小児期中性脂肪の平均値（127対76mg/dl、P<0.0001）およびボディマスインデックス（BMI, 24.3対20.0kg/m^2、P=0.012）が上昇していた。中性脂肪およびBMIの差は小児期の年齢、性別および人種でコントロールと症例をマッチングさせた後も依然として有意であった。多変量解析の結果、CVD歴のある者はまた、CVDのない者と比較し、たばこ乱用、過剰体重または肥満があり（BMI33.2対28.6、P=0.0078）、糖尿病を有し（血糖122対90mg/dl、P=0.0001）、中性脂肪が上昇（251対135mg/dl、P=0.0016）している率が有意に高かった。このリスクファクターの差は成人期の年齢、性別および人種で補正してもなお認められた。この若年者を対象としたスタディではCVD症例数は少なかったが、今回のデータから小児期の中性脂肪上昇および肥満は若年期のCVD発症の原因となっていることが示唆された。

Full Text

Children with elevated levels of triglycerides may be at increased risk of cardiovascular disease (CVD) events in early adulthood, according to research presented at ACC09: the American College of Cardiology's 58th annual scientific session.

This finding is based on a 25 to 30 year follow-up study of 808 out of 1756 subjects, first evaluated as school children between 1973 and 1976. Researchers restudied eligible participants to compare childhood and adult CVD risk factors in those who did and did not develop CVD in their 30s and 40s. Of these, 19 reported cardiovascular events as adults, the most common being heart attacks, angioplasties to re-open clogged coronary arteries, and bypass surgeries.

"Pediatric triglycerides are an exceptionally strong, independent predictor of early onset cardiovascular events," said John Morrison, Ph.D., professor emeritus of Preventive Cardiology, Cincinnati Children's Hospital. "Those who developed cardiovascular disease events tended to have higher levels of triglycerides and were more likely to be overweight or obese in childhood."

Compared to the 789 CVD-free controls, participants who developed CVD had higher average childhood triglyceride (127 vs. 76 mg/dl, p < 0.0001) and body mass index (24.3 vs. 20.0 kg/m^2, p = 0.012). The differences in triglycerides and BMI remained significant after matching the controls and cases (15 to 1) by childhood age, sex and race.

In multivariate analyses, those with a history of CVD were also significantly more likely to abuse tobacco, be overweight or obese (BMI 33.2 vs. 28.6, p =0.0078), live with diabetes (blood sugar 122 vs. 90 mg/dl, p =0.0001), and have elevated triglycerides (251 vs. 135 mg/dl, p =0.0016) as adults compared to the CVD-free group. These risk factor differences remained significant even after adjusting for adult age, sex and race. Normal triglyceride levels are less than 150 mg/dl.

In conducting this longitudinal childhood-to-adulthood study, researchers found participants who had moved away by researching family names and birthdates through various search engines.

Participants' blood was drawn at hospitals in their area and sent overnight to Cincinnati Children's Hospital. Comparisons of the original childhood data between participants and non- participants (those who were not followed) indicated that participants had higher BMI as children (p = 0.004). After adjusting for age, sex and BMI, differences in total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels between the participants and non- participants in childhood were not significant, indicating those who were followed did not differ from those who were not followed with respect to lipid profile.

Although there were few cases of CVD in this young study group, the data suggest pediatric triglycerides and obesity play a role in the development of early CVD.

"In the last decade, we have started to appreciate more the role of triglyceride-rich remnant particles in cardiovascular risk, and how they can accelerate the formation of lipid deposits in the arteries," Morrison said.

"While lowering LDL-cholesterol levels remains a primary therapeutic target, pediatric triglycerides and obesity, as well as smoking and early onset type 2 diabetes, remain serious risk factors for early CVD," said Samrat Yeramaneni, M.D., Clinical Research Associate, Jewish Hospital Cholesterol Center. "Based on our findings, we encourage pediatricians and family practitioners to take notice of elevated levels of triglycerides, which are a part of standard lipid profiles, and screen for overweight and obesity as indicators of future risk of CVD and initiate early interventions."

The baseline and follow-up studies were funded by the National Heart Lung and Blood Institute of the National Institutes of Health.