心停止後早期の低体温療法は生存率を上昇させる

PRINCE：心停止後の患者に速やかに低体温療法を施行することで脳損傷を伴わない生存の確率が増大する

PRINCE: Chance of survival without brain damage greater when person in cardiac arrest is cooled quickly

心停止後、迅速に低体温療法を施行することにより脳損傷を伴わない生存の確率が改善するとのPRINCE（Pre-Resuscitation Intra-Nasal Cooling Effectiveness：蘇生前鼻腔内冷却療法の有効性）研究の結果が2009年American Heart Association学会で発表された。ヨーロッパの研究者らは、心肺蘇生（CPR）施行中に脳を冷却するRhinoChillという新たな方法を用いた。彼らは、目撃者のいる心停止成人患者200人を、標準的蘇生法群または心停止直後に低体温療法を開始する蘇生法群に無作為に割り付けた。生存して入院した患者全てがさらに標準的なクライテリアによる低体温療法を施行された。報告された患者182人（平均年齢66歳、男性71%）中、低体温療法群の46.7%が生存して退院したのに対し、標準的蘇生法群におけるその割合は31%であった。さらに、低体温療法群のうち退院時に神経学的状態が良好であったのは36.7%であり、標準的蘇生法群におけるその割合は21.4%であった。心停止後10分以内に蘇生を開始された患者137人中、低体温療法患者の59.1%が生存して退院したのに対し標準的蘇生法患者では29.4%であった。また、これらの患者のうち神経学的に問題がなかったのは低体温療法患者では45.5%であり、標準的蘇生法患者では17.6%であった（p=0.01）。

Full Text

Rapidly cooling a person in cardiac arrest may improve their chance of survival without brain damage, according to research presented at the American Heart Association's Scientific Sessions 2009.

"We now have a method that is safe and can be started within minutes of cardiac arrest to minimize damage during this very critical period," said Maaret Castren, M.D., lead author of the study and professor of emergency medicine at the Karolinska Institute in Stockholm.

For years, people hospitalized after cardiac arrest have been cooled to reduce injury to the brain and other tissues that occurs when the blood supply returns after being temporarily halted. In the PRINCE (Pre-Resuscitation Intra-Nasal Cooling Effectiveness) investigation, Castren and colleagues at 14 other centers across Europe used a new tool, RhinoChill, that cools the brain during ongoing cardiopulmonary resuscitation (CPR).

Researchers randomized 200 adults going into witnessed cardiac arrest to receive either standard resuscitation or resuscitation with cooling started as soon as possible during the arrest, with ongoing CPR. All patients who survived to hospitalization were further cooled according to standard criteria. Eighteen patients were excluded from the analysis because a 'do-not-resuscitate' order was found or there was a non-cardiac reason for their cardiac arrest.

In the 182 patients reported, 83 (average age 66 years, 71 percent male) were randomized to receive nasal cooling (although two were not cooled because of user or device problems) and 99 (average age 64.8, 78 percent male) received standard care.

RhinoChill is a non-invasive device that introduces coolant through nasal prongs. The system is battery-powered and requires no refrigeration, making it suitable for emergency medical technicians in the field to use while a person is receiving CPR.

The patients in each group were similar in their initial heart rhythms, how much time lapsed before CPR was started and whether CPR restored a pulse. The median time between arrest and the initiation of cooling was 23 minutes. On arrival at the hospital, the cooled patients' temperatures (measured at the eardrum) were significantly lower (average 34.2°C, 93.56 F) than those receiving standard care (35.5°C, 95.9 F, p = 0.0001).
In the total group:

- 46.7 percent of those cooled survived to hospital discharge, compared with 31 percent of those receiving standard care;
- 36.7 percent of those cooled were in good neurological condition on hospital discharge, compared with 21.4 percent of those receiving standard care.

In the 137 patients in whom resuscitation efforts began within 10 minutes of cardiac arrest:

- 59.1 percent of those cooled survived to hospital discharge, compared with 29.4 percent of those receiving standard care;
- 45.5 percent of those cooled were neurologically intact at hospital discharge, compared with 17.6 percent of those receiving standard care (p=0.01).
- Our results show that the earlier you can do the cooling, the better," Castren said. "When resuscitation efforts were delayed, there was no significant difference in survival."

In a time analysis, patients who received a combination of early CPR started within six minutes of collapse and cooling had the best outcomes.
Patients with ventricular fibrillation (VF) are the subgroup of cardiac arrest patients most likely to survive. In this study, of the 56 patients who had VF:

- 62.5 percent of those cooled survived to hospital discharge, compared with 47.6 percent of those who received standard care;
- 50 percent of those cooled were neurologically intact at hospital discharge, compared to 28.6 percent of those who received standard care.
- RhinoChill is easy and safe to use during a cardiac arrest outside of the hospital," said Denise Barbut, M.D., senior author of the study and president and chairman of BeneChill, Inc., maker of the device. "Although the study was not powered to look at outcomes, there seemed to be a significant benefit on survival and neurologically intact survival, specifically in those treated within 10 minutes."

Eighteen adverse reactions were reported after the treatment, including three nosebleeds and 13 nasal discolorations. Coloring spontaneously returned to normal in all patients who survived. Serious adverse events, such as seizure or repeat cardiac arrest, occurred in seven cooled patients and 14 controls.

RhinoChill has been approved for marketing in Europe and the company expects to start selling the device there in March 2010.

Other authors are Per Nordberg, M.D.; Didier Desruelles, M.D.; Frank Eichwede, M.D.; Pierre Mols, M.D., Ph.D.; Leif Svensson, M.D., Ph.D.; Fabio Taccone, M.D.; Jean-Louis Vincent, M.D., Ph.D.; Hans-Jorg Busch, M.D.; Michael Vergnion, M.D.; Christian Storm, M.D.; Antonio Pesenti, M.D., Ph.D.; Fabien Guerisse, M.D.; Thomas Elste, M.D.; Markus Roessler, D.E.A.A.; Harald Fritz, M.D.; and Pieterjan Dumez, M.D.
Funding was provided by BeneChill, Inc.

突然死患者の死後遺伝子検査は患者の血縁者において費用対効果に優れる

突然死患者の遺伝子を死後に検査し患者の血縁者のリスクを同定することは費用対効果に優れる

Postmortem genetic tests after sudden death may provide less expensive way to identify risk to surviving relatives

原因不明の突然死(SUD)に関連する遺伝子変異を同定する死後標的検査は、第一度近親者に包括的な循環器系検査を施行するよりも経費が少なく有効な方法であるとの研究結果が2009年American Heart Association学会で発表された。研究者らは146のSUD症例において、心臓突然死(SCD)に関連する2つの遺伝性の心調律異常について死後検査の費用を比較した。突然死した患者の26.7%においてQT延長症候群(LQTS)またはカテコールアミン誘発性多形性心室頻拍(CPVT)に関連した疾患を引き起こす可能性のある変異が認められた。その後、突然死した人の中で変異の認められた者の近親者160人における疾患を標的とした評価の経費およびgenotype-negativeの第一度近親者(424人)の全般的な臨床評価の経費を推算した。死亡した人々の遺伝子検査、およびその検査で変異が陽性であった者の近親者160人の疾患を標的とした循環器的評価、および変異陰性の突然死した者の第一度近親者424人の全般的な臨床評価全てにかかる経費は678万ドルと推定された。一方、現在推奨されているSUD患者の近親者584人全員に対する一次循環器的評価の後に疾患を標的とした遺伝子検査を行う方法では700万ドルを超えるであろうと考えられた。

Full Text

Targeted postmortem testing to identify genetic mutations associated with sudden unexplained death (SUD) is an effective and less expensive way to determine risk to relatives than comprehensive cardiac testing of first degree relatives, according to research presented at the American Heart Association's Scientific Sessions 2009.

Postmortem genetic testing can identify mutations that cause cellular dysfunctions leading to heart rhythm disturbances that can cause sudden cardiac death. Such inherited genetic defects occur in 25 to 30 percent of SUD victims, according to lead researcher Michael J. Ackerman, M.D., Ph.D., pediatric cardiologist and director of the Long QT Syndrome Clinic and the Windland Smith Rice Sudden Death Genomics Laboratory at the Mayo Clinic in Rochester, Minn.

Ackerman and senior research technologist David Tester, B.S., compared the yield and costs of postmortem genetic/molecular autopsy testing in 146 SUD cases. They found that 40 of the victims (26.7 percent) had either a catecholaminergic polymorphic ventricular tachycardia (CPVT) mutation (18) or a long QT syndrome mutation (22), both known contributors to sudden death. Researchers estimated the costs of testing 160 relatives of victims who tested positive for mutations. The tests included genetic tests and either treadmill stress tests or electrocardiograms.

For the 424 relatives of the 106 victims who tested negative for mutations, researchers estimated the cost to do more extensive clinical cardiac testing.

Researchers estimated that the total cost of doing postmortem genetic testing, genetic confirmation testing of relatives of mutation-positive victims, followed by cardiac tests for both relatives of mutation-positive and mutation-negative SUD victims, was $6.78 million.

In contrast, the total cost associated with what is currently recommended - comprehensive cardiac testing for all 584 relatives of the SUD victims, regardless of mutation status, followed by directed genetic testing - would have exceeded $7.7 million.
The researchers' primary endpoint, which they reached, was to see if the postmortem testing model would be less expensive and, if so, how great the savings might be.

"With less than 150 SUD cases, use of a cardiac channel molecular autopsy would be estimated to save almost $1 million dollars indicating a much less expensive way of evaluating those left behind," Tester said. "If you identify a mutation in a sudden unexplained death victim, you can do a simple genetic test in first-degree relatives to assess their risk and perform a disorder-directed clinical evaluation rather than a full clinical evaluation. If a relative is negative for the causative mutation, they may not need to undergo further clinical evaluation at all, and that saves money."

The researchers said that insurance companies pay for comprehensive cardiac testing for family members despite the fact that commercial molecular/genetic testing of the deceased can provide just as accurate a risk profile and in many cases minimize the need for clinical testing.

"We are reporting that there is data available to make such cardiac risk evaluations on both sides of the grave," said Ackerman. "The real question is whether it is more prudent and effective to have sudden unexplained death surveillance in autopsy-negative cases. Some insurers cover postmortem gene testing, but it is the exception, not the rule."

The prevalence of the mutations in the SUD autopsies and first-degree relatives was comparable to rates reported by European researchers.

"Clinical screening can be much more selective if there is postmortem gene testing for the defects that result in sodium and potassium channelopathies," said Ackerman. "Currently, however, evaluations of the surviving family members are insurance-covered medical expenses whereas postmortem genetic testing has generally been denied."

The study had limitations and needs to be corroborated by further research. "The cohort we studied was not a population-based collection of SUD cases but instead involved cases that were referred by coroner's/medical examiner's throughout North America so we don't know what the true yield of postmortem genetic testing for autopsy negative SUD is at this time," said Tester.
Coauthors include Argelia Medeiros-Domingo, M.D., Ph.D.; Carla M. Haglund, B.A.; and Jonathan N. Johnson, M.D.

The study was funded in part by an American Heart Association research grant.

Cardiology特集

AHA2009（第82回米国心臓病協会）

トピックス一覧

スタディの結果HDL増加はLDL降下に勝る

ARBITER 6-HALTS：スタチンを内服している患者においてナイアシンを用いてHDLを増加させることにより、エゼチミブでLDLを低下させるよりも頸動脈内中膜厚が減少することが示された

ARBITER 6-HALTS: In patients on statins, raising HDL with niacin decreases carotid intima-media thickness more effectively than reducing LDL with ezetimibe

スタチンに高密度リポ蛋白（HDL）コレステロール上昇作用のあるナイアシンを併用させることにより、低密度リポ蛋白（LDL）コレステロール低下作用のあるエゼチミブを併用するよりも動脈壁プラーク蓄積の減少および心疾患リスク低下には有効であることが、2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表され、New England Journal of Medicineに掲載された。コレステロール低下の治療効果に関する研究の血管生物学：動脈硬化に対するHDLおよびLDL治療戦略（The Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6: HDL and LDL Treatment Strategies in Atherosclerosis [ARBITER 6-HALTS]）スタディは、動脈硬化性心血管疾患のハイリスク患者363人を組み入れた。対象者は通常のスタチンに加えナイアシンまたはエゼチミブを内服する群に無作為に割り付けられた。一次エンドポイントは頸動脈内中膜厚（IMT）であった。一次エンドポイントが達成されたためスタディは6月に早期終了された。特に、208人の14週間の経過観察データの結果, ナイアシン群においては平均HDLコレステロールが42mg/dLから50mg/dLに上昇し、IMTの有意な減少が認められた。エゼチミブ群においては平均LDLコレステロールレベルが83mg/dLから66mg/dLに低下した。しかし、平均IMTの全般的な変化は認められなかった。

Full Text

In combination with statins, adding a medication that raises high-density lipoprotein (HDL) cholesterol was more effective in reversing artery wall plaque buildup and in reducing heart disease risk than adding a drug that lowers low-density lipoprotein (LDL) cholesterol, researchers reported today at the American Heart Association Scientific Sessions 2009.

In the study titled The Effect of Extended-release Niacin or Ezetimibe Added to Chronic Statin Therapy On Carotid Intima Media Thickness (ARBITER 6-HALTS), researchers found:

- Adding the cholesterol drug niacin to a statin improved HDL cholesterol levels and significantly reduced arterial plaque buildup within 8 months, with further improvement seen at the end of the study (14 months).
- A second approach, adding ezetimibe to a statin, lowered LDL cholesterol to a greater extent, but did not raise HDL. With it, there was no overall effect on arterial build up in the neck arteries.
- With ezetimibe, greater reductions in LDL cholesterol paradoxically were associated with more arterial buildup, a result opposite to that expected.
- The incidence of major cardiovascular events such as fatal and non-fatal heart attack was higher in the ezetimibe group as compared to the niacin group (5 percent vs. 1 percent).

HDL And LDL Treatment Strategies (HALTS) was a prospective, randomized, parallel group, open-label, blinded endpoint study conducted at Walter Reed Army Medical Center in Washington, D.C., and Washington Adventist Hospital in Tacoma Park, Md. It included 363 adults (80 percent male, average age 68 years) with or at high risk for atherosclerotic cardiovascular disease.

All participants were on cholesterol-lowering statin drugs, and their LDL cholesterol was at the treatment goal of under 100 milligrams per deciliter (mg/dL) of blood. Their HDL cholesterol was lower than 50 mg/dL for men and 55 mg/dL for women.

The researchers randomly assigned the subjects to receive either niacin or ezetimibe in addition to their usual statin. The primary endpoint was the change in the wall thickness of the carotid artery in the neck between the two groups of patients. In June, researchers halted the trial early because the primary endpoint was met. Specifically, 14-month follow-up data on 208 patients showed that in the niacin group, average HDL cholesterol rose from 42 mg/dL to 50 mg/dL and there was a significant regression in artery wall thickness. In the ezetimibe group, average LDL cholesterol levels dropped from 83 mg/dL to 66 mg/dL; however no overall change was found in average artery wall thickness.

"These findings for ezetimibe are counter to the prevailing understanding of LDL cholesterol - that lowering LDL cholesterol results in slowing of the atherosclerotic process as has been convincingly shown for other classes of lipid modifying drugs, such as statins and bile acid resins," said Allen J. Taylor, M.D. FAHA, principal investigator of the study and director of Advanced Cardiovascular Imaging and the Lipid/Prevention Clinic in the Department of Medicine (Cardiology) at Washington Hospital Center in Washington, D.C.

In earlier studies demonstrating the protective effects of statins, researchers found strong associations between LDL cholesterol reduction and the prevention of cardiovascular disease. Consequently, many people now view LDL cholesterol reduction as a way to measure whether a treatment will be useful.

But HALTS researchers' findings "challenge the use of LDL reduction as a guaranteed surrogate for clinical performance, particularly for new clinical compounds, and in this particular case, ezetimibe," Taylor said. Patients should know their HDL numbers and, if they are low, ask their doctors if adding a treatment such as niacin is right for them once their LDL is treated to goal with a statin drug, he said.

Co-authors are: Todd C. Villines, M.D.; Patrick J. Devine, M.D.; Mark Turco, M.D.; Len Griffen, M.D.; Michael Miller, M.D.; Eric J Stanek, Pharm. D.; and Neil J Weissman, M.D.

Study sponsor: Abbott Inc. (initially Kos Pharmaceuticals, Inc., Cranbury, N.J.) provided an unrestricted, investigator-initiated research grant administered by the Henry M. Jackson Foundation for the Advancement of Military Medicine in Rockville, Md. The investigators were solely responsible for all aspects of the study and the final decisions on manuscript content.

Disclosures: Dr. Taylor reports receiving lecture fees from Abbott. Dr. Turco reports receiving consulting and lecture fees from Abbott Cardiovascular. Dr. Miller reports receiving lecture fees and grant support from Merck-Schering Plough. Dr. Villines reports receiving lecture fees from Novartis Pharmaceuticals. Dr. Devine reports receiving consulting fees from Medacorp, MDLinx, and Guidpoint Global, equity ownership in Evergreen solar, Openwave, Unifi, Novavax, Genaera Pharm, and Generex Biotech. Dr. Stanek is senior director of research in Personalized Medicine Research and Development at Medco Health Solutions, Inc. (Franklin Lakes, N.J.), but all work performed on this trial was independent of this relationship. No other potential conflict of interest was reported.

血小板機能アッセイ―役立つものもあれば役立たないものもある

POPULAR：検査により血管形成術とステント留置施行後の抗血栓療法に抵抗性の患者が予知できる

POPULAR: Tests predict which patients are resistant to anti-clotting therapy during angioplasty plus stenting

血小板機能検査6つのうち3つは血管形成術（PCI）およびステント留置術を施行された患者の血栓関連の有害事象リスクを予測することができると2009年American Heart Association学会で報告された。POPULARトライアルは抗血栓薬投与中患者における血小板機能検査をhead-to-headで比較した初めてのものである。研究者らはPCIおよびステント留置術を施行された1,069人の連続した患者を対象に、6つの血小板機能検査を比較した。一次エンドポイントは総死亡、心筋梗塞、緊急血行再建術施行、脳卒中またはステント血栓の合計であった。1年間の観察後に3つの検査（Light Transmittance Aggregometry、VerifyNow-P2Y12™カートリッジ、およびPlateletworks™アッセイ）で血小板機能が高かった患者は総一次エンドポイント発現率が高かった（12.1%対6%）。他の3つの検査による評価の予後予知能は不良であった。研究者らは、待機的血管形成術およびステント留置術を施行する患者全てにおいて血小板機能検査を行い血栓関連合併症のハイリスク患者を検出するのは有用であると述べている。

Full Text

Three platelet function tests all identified heart patients who will have high platelet reactivity, increasing heart attack risk, despite being pre-treated with aspirin and clopidogrel before coronary stenting, researchers reported at the American Heart Association's Scientific Sessions 2009.

POPULAR (Do platelet function assays predict clinical outcomes in clopidogrel pre-treated patients undergoing elective PCI) is the first head-to-head comparison of tests for platelet reactivity despite anti-clotting medication.

Specifically, it examines which of the many tests available best predicts thrombotic complications, such as myocardial infarction and stroke, in patients pre-treated with aspirin and clopidogrel who then undergo percutaneous coronary intervention (PCI) with stent implantation, said Jurrien M. ten Berg, M.D., Ph.D., an interventional cardiologist at St. Antonius Hospital, Nieuwegein, the Netherlands, and senior investigator of the study.

"Only a minority of centers routinely uses platelet reactivity testing to guide therapy, but it is used extensively as a research tool," he said. "I think we are on the brink of making platelet reactivity a clinical tool."

Dual antiplatelet therapy with aspirin and clopidogrel is used for its ability to reduce clot-related complications of PCI. But in some studies a significant number (30-40 percent) of patients are resistant to the treatment and are at risk of clot-related complications even after that treatment, said ten Berg.

Researchers haven't conducted a large study comparing the many tests that check platelet reactivity, said Nicoline J. Breet, M.D., presenter of the study and a Ph.D. fellow and cardiologist-in-training at St. Antonius Hospital.

In POPULAR, researchers compared six different tests of platelet reactivity in 1,069 consecutive patients undergoing angioplasty with stent placement and included one-year follow-up. The primary endpoint was a composite of all-cause death, heart attack, urgent revascularization, stroke or stent thrombosis, ten Berg said. Patients who had high platelet reactivity (HPR) on three of the tests -- the Light Transmittance Aggregometry (LTA), the VerifyNow-P2Y12®-cartridge and the Plateletworks® assay - had a significantly greater incidence of the combined primary endpoint (12.1 percent vs. 6 percent) at one year compared to patients who did not, ten Berg said. Three other tests evaluated didn't predict outcomes. Of the three predictive tests, the LTA is the most labor-intensive and can't be performed at bedside, and Plateletworks™ must be done within 10 minutes of drawing blood, ten Berg said. The third test, VerifyNow-P2Y12® does not have those limitations, he said.

In conclusion, it is useful to test the response to antiplatelet therapy in all patients undergoing elective angioplasty plus stent placement to identify those patients at highest risk for clot-related complications," ten Berg said. These results have not yet been extended to demonstrate that basing additional treatment(s) on the test results would improve patient outcomes in those at higher risk.

Study sponsor: The study received no funding. Siemens Healthcare Diagnostics provided the Dade® PFA Collagen/ADP Test Cartridge and the novel INNOVANCE® PFA P2Y* free-of-charge.

Co-authors are: Jochem W. van Werkum M.D., Ph.D.; Heleen J. Bouman MSc; Johannes C. Kelder, M.D.; Henk J.T. Ruven, Ph.D.; Egbert T. Bal, M.D.; Vera H. Deneer, PharmD, Ph.D.; Ankie M. Harmsze, PharmD; Jan A.S. van der Heyden, M.D.; Benno J.W.M. Rensing, M.D., Ph.D.; Maarten J. Suttorp, M.D., Ph.D.; Christian M. Hackeng, Ph.D.; Jurrien M. ten Berg, M.D., Ph.D.

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CABG後の簡単な共同ケアによりうつが減少する

BtB Trial：共同ケアによりバイパス術後うつ病患者のQOLおよび気分が改善する

BtB Trial: Collaborative care improves quality of life and mood of depressed patients after artery bypass graft surgery

冠動脈バイパス術後の回復期にある患者は共同ケアチームの補助により回復が早まると2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表され、同時にJAMAに掲載された。Bypassing the Blues(BtB)Trialにおいては、電話を基本とした共同ケア治療プログラムは通常のケアと比較し、CABG後8ヵ月の患者の精神および身体健康上の予後においてより有効であり術後再入院をも減少させる可能性もあることが示された。8ヵ月間の観察後、身体機能およびうつ病を評価する検査のスコアは、共同ケアを受けた患者において通常のケアを受けた患者と比較し有意に改善していた。うつ病患者はまた、気分障害の症状が50%以上軽減したと報告する率が高く（50%対29.6%、p<0.001）、特に男性において著明であった（60.5%対33.3%、p<0.001）。治療は男性においてより有効であったが、女性においても有効性は認められた。さらに、共同ケアを受けたうつ病男性は通常の治療を受けた男性と比較し術後8ヵ月間の心血管疾患による再入院率が低かった（13%対23%、p=0.07、うつ病のないCABG後患者における13%と同等）。

Full Text

Depressed patients recovering from coronary artery bypass graft (CABG) surgery recover faster with a little help from their collaborative care (CC) team, according to findings reported in a late breaking clinical trial at the American Heart Association's Scientific Sessions 2009 and published simultaneously in JAMA.

In the Bypassing the Blues (BtB) Trial, a telephone-based collaborative care treatment regimen proved more effective than usual care at improving mental and physical health outcomes of patients eight months after CABG and may even reduce the rate of rehospitalization following surgery. BtB is the first effectiveness trial of a collaborative care strategy for treating depression following an acute cardiac event.

"We were able to demonstrate that our intervention significantly improved quality of life and reduced adverse mood symptoms as early as two months following surgery and we found a trend toward reduced rehospitalizations at eight months among depressed men randomized to our intervention" said Bruce L. Rollman, M.D., M.P.H., the study's lead author and associate professor of medicine, psychiatry, and clinical and translational science at the University of Pittsburgh School of Medicine. Study nurses screened 2,485 CABG patients for depression at seven Pittsburgh-area hospitals using the two-item Patient Health Questionnaire (PHQ-2), and confirmed the depression finding using the PHQ-9 administered over the telephone two weeks later. Then, 302 patients were randomized to either their doctors' "usual care" (UC) for depression or to eight months of collaborative care delivered via telephone by study nurses working in partnership with other healthcare professionals. The study also included a group of 151 non-depressed post-CABG patients to facilitate comparisons with depressed study patients (total patients: 453).

Study nurses monitored patients' symptoms and relayed treatment recommendations between the patients and their primary care physicians following evidence-based treatment protocols under weekly supervision of a study primary care physician and psychiatrist. Treatment options included antidepressant pharmacotherapy, a self-help workbook, and/or referral to a community mental health specialist. However, patients were required to obtain medication from their PCP and pay for it, as the study did not dispense any medications.
Researchers used the SF-36 questionnaire to assess patients' mental and physical health, the Duke Activity Status Index (DASI) to assess physical functioning, and the Hamilton Rating Scale for depression to assess mood symptoms. As expected, depressed patients had significantly worse scores than non-depressed patients in all of these areas at baseline. At eight months follow-up, compared with those who received usual care, patients who received collaborative care reported significantly improved scores on the SF-36, DASI, and HRS-D. Depressed patients were also more likely to report a 50 percent or greater decline in their adverse (or negative) mood symptoms (50 percent vs. 29.6 percent; p<0.001), which was particularly notable in men (60.5 percent vs. 33.3 percent; p<0.001). While the intervention was more powerful among men, women in the intervention also reported benefits, said Rollman.

Moreover, depressed men tended to have a lower eight-month incidence of rehospitalizations for cardiovascular causes than depressed UC men (13 percent vs. 23 percent; p=0.07) that was similar to non-depressed post-CABG men (also 13 percent).

"Depression is common following CABG surgery and is associated with worse clinical outcomes," Rollman said. "Unfortunately, it's also overlooked by many clinicians caring for these patients despite the availability of several simple screening instruments such as the PHQ-2 and PHQ-9. Although several treatment trials for depression have been conducted in heart patients, most had generally disappointing results. Collaborative care has been proven effective in dozens of trials conducted in primary care settings, but ours is the first to apply this approach to a population with cardiovascular disease and one of the very few studies to examine the impact of treating post-CABG depression."

Rollman characterized BtB as a real-world trial that could be adopted as part of the "medical home" concept now being discussed by Congress. The findings and telephone mode of intervention delivery have major public health implications, particularly for medically frail individuals, those living in rural settings, and others with physical challenges impeding face-to-face depression treatment.

"Now that we have demonstrated the effectiveness of our approach, we're presently looking at Medicare and other insurance claims data to evaluate the cost-effectiveness and possible cost-savings of our intervention which could speed its adoption into routine clinical care," Rollman said.

Study sponsor: National Heart Lung and Blood Institute.

Co-authors are: Bea Herbeck Belnap, Ph.D.; Sati Mazumadar, M.D.; Patricia R. Houck, M.S.; Peter J. Counihan, M.D.; Wishwa N. Kapoor, M.D., M.P.H.; Herbert C. Schulberg, Ph.D.; Charles F. Reynolds III, M.D. (co-principal investigator).

Disclosures: None.

Cardiology特集

AHA2009（第82回米国心臓病協会）

トピックス一覧

TicagrelorはプライマリPCIにおける心イベントを軽減する

PLATO STEMI：可逆的な新規経口抗血小板薬はSTEMI後のプライマリPCIを受けた患者において心イベントを抑制する

PLATO STEMI: New reversible oral anti-platelet drug reduces cardiac events in primary PCI patients following STEMI

可逆的経口抗血小板薬ticagrelorによりクロピドグレルによる標準的な治療と比較し、ST上昇心筋梗塞（STEMI）患者における心イベントが少なかったと、2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表された。血小板抑制と患者の予後（PLATelet Inhibition and Patient Outcomes：PLATO）トライアルは、ステントを用いたプライマリ冠動脈形成術（PCI）を予定されたSTEMI患者8,430人を、アスピリンに加え治験薬ticagrelorまたはクロピドグレルを内服する群に無作為に割り付けた。この無作為化二重盲検試験において、被験者は2006～2008年の間に43ヵ国862施設から組み入れられた。1年間の経過観察期間中にticagrelor群患者の9.3%が一次エンドポイント（心臓発作、脳卒中または血管死の合計）に合致したのに対し、クロピドグレル群においては11%であった；つまり、治験薬において相対リスクが15%低かった。総死亡率もticagrelorにより、6.0%から4.9%に低下し、相対リスクは18%低下した。同様に、新たな心筋梗塞およびステント血栓のリスクも軽減した。重大な出血の発現率上昇は認められなかった。

Full Text

Acutely ill myocardial infarction patients who received both aspirin and a new reversible oral anti-platelet medication had fewer cardiac events than patients on aspirin and the most commonly used, irreversible anti-platelet drug, researchers reported in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

In the PLATelet Inhibition and Patient Outcomes (PLATO) trial, a subset of 8,430 patients who were in the midst of ST-elevation heart attacks (STEMI) and were scheduled for primary percutaneous coronary intervention (PCI) with stenting received the investigational drug ticagrelor or clopidogrel in addition to aspirin. Participants for the randomized, double blind trial were recruited from 862 sites in 43 countries between 2006 and 2008.

The ticagrelor group suffered fewer cardiovascular events from the onset of the trial, and the benefits continued the longer patients took the drug during the year-long follow-up, said Philippe Gabriel Steg, M.D., lead investigator of the study. "The results are very clear and actually very consistent with the overall trial results of the larger PLATO trial, namely that there's a reduction in the primary endpoint - a composite of incidence of heart attack, stroke or vascular death - with no increase in major bleeding complications compared to clopidogrel," said Steg, professor of cardiology and director of the coronary care unit at H?pital Bichat-Claude Bernard in Paris, France.

Bleeding is usually a concern with new antiplatelet agents. Since ticagrelor is a more potent agent than one of the American Heart Association/American College of Cardiology guidelines recommended medications, clopidogrel, bleeding was a concern. "The good news is that there was no sign of increased major bleeding regardless of how we defined it," he said.

Following up to one year, 9.3 percent of the ticagrelor group met the primary endpoint, compared to 11 percent of the clopidogrel group - a 15 percent relative risk reduction for the investigational group. The patients in Steg's analysis had STEMI and were scheduled to receive primary PCI - also known as angioplasty - and stenting during the acute phase of their heart attacks. The 4,201 patients randomized to the test group received 180 milligrams (mg) of ticagrelor during PCI, followed by 90 mg twice daily for six to 12 months. The other 4,229 patients received 300 mg of clopidogrel with a provision for an additional 300 mg during PCI, followed by 75 mg daily for six to 12 months. All patients in the trial also received daily aspirin therapy.

"STEMI is really the most acute form of coronary disease and represents roughly 40 percent of the patient group enrolled in the larger PLATO trial," Steg said. "It is a common condition, and it is a high-risk condition for which the standard of care, clopidogrel, has clear drawbacks."

"Clopidogrel's drawbacks include a slower onset of effectiveness, which is not suited to the need for rapid effect in STEMI, and a modest and inconsistent anti-platelet effect - many patients respond well, but a sizeable unresponsive group remains at high risk of blood clots despite therapy," Steg said. Clopidogrel also binds permanently to the platelets' P2Y12 receptors, so its effect lasts seven to 10 days after the medication is stopped. In contrast, ticagrelor's effect is direct and reversible, he said.

"With ticagrelor, there is an actual disassociation between the drug and the P2Y12 receptor so that the drug does not bind permanently to the receptor, and the receptor and the platelet can regain function, with normal platelet clotting ability returning in about four days, which may explain the absence of increased bleeding with ticagrelor" Steg said. "However, ticagrelor does have off-target effects, which probably explain a side effect more commonly seen with ticagrelor than clopidogrel: dyspnea, or breathlessness, which affected 12.9 percent of ticagrelor patients and 8.3 percent of the clopidogrel group."

Overall mortality was reduced with ticagrelor - from 6.0 percent to 4.9 percent, a relative reduction of risk of 18 percent. Likewise, the risk of new myocardial infarction and the risk of stent thrombosis were also reduced. "Furthermore, the benefit is not solely achieved during the acute phase, the first 30 days after angioplasty, but the benefit accrues over time so that the longer you treat, the greater the difference in event rates," Steg said. "There is a strong rationale to prefer this new agent both in the acute (first 30 days) and in the late phase after a heart attack."

Study funded by: AstraZeneca (manufacturer of the investigational drug).

Co-authors are: Richard C. Becker, M.D.; Christopher P. Cannon, M.D.; Hakan Emanuelsson, M.D., Ph.D.; Robert A. Harrington, M.D.; Jay Horrow, M.D.; Steen Husted, M.D., D.Sc.; Hugo Katus, M.D.; Robert F. Storey, M.D., D.M.; Lars C. Wallentin, M.D., Ph.D.

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Cangrelorは一次エンドポイントでは有益性を示さなかったがいくつかの二次エンドポイントにおいては有意な結果を示した

CHAMPION PLATFORM：PCI時に使用する新たな抗血小板薬は一次エンドポイントにおいては優れていなかったが死亡およびステント血栓を減少させた

CHAMPION PLATFORM: New antiplatelet agent for PCI not superior for primary endpoint, but did reduce death and stent thrombosis

新たな静注薬P2Y12血小板阻害薬は、複合一次エンドポイント（心筋梗塞、総死亡率および血行再建術の必要性）においては明確な有益性を示さなかったが死亡率およびステント血栓は減少させた、と2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表され、New England Journal of Medicineに掲載された。CHAMPION PLATFORMの第III相試験では、血管形成術およびステント挿入を施行された患者5,362人をプラセボまたは治験薬cangrelorをPCI中に投与する群に無作為に割り付けた。施術後に全ての患者が、通常投与される非可逆的抗血栓薬クロピドグレル600mgを経口投与された。中間解析レビュー委員会がcangrelorはクロピドグレルに対し一次エンドポイント（総死亡率、心筋梗塞および血行再建術の必要性）において上位性を示さないであろうと結論付けたため、トライアルは終了となった。しかし、いくつかの二次エンドポイントは興味深くまた情報の多い結果であった。例えば、総死亡率単独のエンドポイントはcangrelor群において0.7%から0.2%に有意に低下した（67%低下）。さらに、急性ステント血栓は治験薬群において有意に低下した。

Full Text

A new reversible blood thinner for angioplasty patients wasn't superior over placebo for its primary combined endpoint of heart attack, all-cause mortality and need for revascularization, but it reduced mortality and in-stent blood clots, researchers reported in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

CHAMPION PLATFORM, a phase III trial, included 5,362 angioplasty-plus-stent patients randomized to receive either a placebo or the investigational drug cangrelor during procedures to reopen coronary artery blockages. Cangrelor is a potent, fast-acting and reversible anti-clotting drug delivered intravenously.

After their procedures, all patients received 600 milligrams (mg) of the oral, nonreversible anti-clotting drug clopidogrel, which is routinely used in such procedures.

The trial, which enrolled patients beginning in 2006, ended when an interim review committee concluded that cangrelor would fail to show superiority over clopidogrel for its primary endpoint: a composite of all-cause death, heart attack and the need for coronary revascularization procedures.

"There was no statistically significant difference between the two arms of the trial at our 48-hour endpoint," said Deepak L. Bhatt, M.D., M.P.H., chief of cardiology at the VA Boston Healthcare System. "However, a number of secondary endpoints had very interesting and informative findings. For instance, all-cause death as a stand-alone endpoint was reduced significantly from 0.7 percent in controls to 0.2 percent (67% reduction) in the cangrelor group.

"It is intriguing, of course, but it is a secondary endpoint and needs to be interpreted with some caution given that the primary endpoint was not met and the number of deaths overall was low."

Furthermore, acute stent thrombosis was significantly reduced in the test group.

"That's something that interventional cardiologists really worry about because stent thrombosis is often associated with a recurrent heart attack or death," said Bhatt, who is also director of the integrated interventional cardiovascular program at Brigham and Women's Hospital and the VA Boston Healthcare System and a faculty member at Harvard Medical School in Boston, Mass. "Acute stent thrombosis was reduced from 0.6 percent in controls to 0.2 percent in the test group (69% reduction), again a significant benefit. So there seems to be a plausible mechanism by which mortality may have been reduced since stent thrombosis was reduced."

Researchers found no difference in endpoints between test and control groups for severe bleeding and need for blood transfusion. However, less severe bleeding was significantly higher with the new agent, 5.4 percent vs. 3.4 percent in controls, an indication of the investigational drug's potency, Bhatt said. Because it's reversible and is delivered through an intravenous line, bleeding events can be ended quickly after the drug is no longer administered. Clopidogrel is given orally and is irreversible - once it binds to a platelet it remains for the life of that blood cell, usually 7 to 10 days. That puts clopidogrel patients at higher risk of bleeding complications if they need emergency surgery, he said.

"At least in theory, cangrelor has all the attributes that an interventional cardiologist would want: Its onset of action is very quick and it's very potent, but on the back end you can turn it off," Bhatt said.

The Medicines Company funded the study.

Co-authors of the study are the CHAMPION executive committee members.

Disclosure: Dr. Bhatt receives grant support from the study sponsor.

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トピックス一覧

乳児の心臓奇形に対する二つの術式の成績の比較は複雑な結果であった

乳児における重症の中隔欠損に対する新たなシャント術は1年生存率を改善するが合併症が多い

New shunt procedure for correcting severe heart defect in infants improves survival to one year, but has more complications

心臓が重度に未発達な状態で生まれた小児は新たなシャント術を施行されることにより1歳まで生存する確率が上昇するが、この方法は長期において最も安全な方法ではない可能性があると2009年American Heart Association学会で発表された。この初めての手技の新たな方法は、機能している右室を肺動脈へつなぐ右室から肺動脈(RV-to-PA)へのシャントを用いる。従来の方法はBlalock-Taussigシャント(MBTS)変法を用い、大動脈を肺動脈につなぐ。ある15施設のトライアルで555人の小児(男児61%、白人73%)をRV-PAシャントまたはMBTS術を施行する群に無作為に割り付けた。12ヵ月後に心臓手術を必要とせずに生存している乳児は、RV-PAシャント群においてMBTS群と比較し、有意に多かった(74%対64%、p=0.01)。RVからPAへのシャントは合併症が多く、240のインターベンションを必要とした(乳児100人当たり87.6)。MBTS群においては心血管系のインターベンションを必要とする例がはるかに少なかった(183人、乳児100人当たり66.5%、p=0.006)。平均2年後には、MBTSと比較したRV-PAシャント術の移植を必要としない生存率の有益性は消失し、その差は有意ではなくなった(68%対62%、p=0.14)。

Full Text

Infants born with a severely underdeveloped heart are more likely to survive to their first birthday when treated with a new shunt procedure - yet it may not be the safest surgery long term, according to research presented at the American Heart Association's Scientific Sessions 2009.

Babies born with a critically underdeveloped left side of their hearts require three surgeries to correct the problem. A portion of the first operation, the Norwood Procedure, includes a connection to deliver blood from the heart to the pulmonary arteries feeding the lungs so that blood can pick up oxygen. There are currently two ways it can be done:

- The new modification of the Norwood utilizes a right ventricle to pulmonary artery (RV-to-PA) shunt to connect the functioning right ventricle to the pulmonary artery.
- The traditional version uses a modified Blalock-Taussig shunt (MBTS), which connects the aorta (the major blood vessel delivering blood from the heart to the body) to the pulmonary artery.

In a 15-center trial by the Pediatric Heart Network, 555 infants (61 percent male, 73 percent Caucasian) were randomized to receive either the RV-to-PA shunt or MBTS procedure.

In the first results from the study, the researchers reported:

- At 12 months, significantly more babies survived without requiring a heart transplant with the RV-to-PA shunt (74 percent) compared to the MBTS (64 percent, p=0.01).
- The RV-to-PA shunt had more complications, necessitating 240 interventions (87.6 for every 100 babies), for example, to make adjustments to the shunt or use balloons or stents to keep it open. Far fewer cardiovascular interventions were needed (183, or 66.5 for every 100 babies) in the MBTS group (p=0.006).
- At an average of two years, the transplant-free survival advantage of RV-to-PA (68 percent) over MBTS (62 percent) had diminished and was no longer significant (p=0.14).

"Early results seem to favor the RV-PA shunt, but by two years there is no longer any survival advantage," said Richard G. Ohye, M.D., lead author of the study and associate professor of surgery at the University of Michigan Medical School in Ann Arbor. "It is still unknown which will turn out to be better over the long term."

For example, the children still must undergo other stages of surgical repair to increase the amount of oxygen in their blood. Good pulmonary artery growth is important in the success of this procedure. In the results so far, overall pulmonary artery growth was significantly greater after the MBTS.

"Ongoing surveillance as these children grow and undergo the final surgical procedure will be very important to determine the proper roles of the shunts," Ohye said.

Although rare, having a single working ventricle is the most common severe congenital heart defect. "Just 25 to 30 years ago, this defect was uniformly fatal," Ohye said. "Now babies are treated with a series of three surgeries, but many still die, even when treated at experienced centers."

Each shunt procedure has theoretical advantages, but researchers previously didn't have hard evidence about which option to choose. The downside of the MBTS is that it takes blood away from the arteries feeding the heart muscle. The RV-to-PA shunt doesn't do this, but requires an incision into the baby's only working ventricle, creating scarring that might interfere with its later function.

"Roughly 50 percent of surgeons use each type, but we truly don't know which is better because there has never been a study," Ohye said. "In fact, there has never been a multi-center, randomized clinical trial performed in congenital heart surgery. This trial sets a new standard for using evidence-based medicine to evaluate new procedures in congenital heart surgery."

Co-authors are Sarah Tabbutt, M.D., Ph.D.; Lynn A. Sleeper, Sc.D.; Gail D. Pearson, M.D., Sc.D.; Lynn Mahony, M.D.; Jane W. Newburger, M.D., M.P.H.; Minmin Lu, Ph.D.; Peter C. Laussen, M.B.B.S.; Caren S. Goldberg, M.D., M.S.; Nancy W. Ghanayem, M.D.; Peter C. Frommelt, M.D.; Andrew M. Atz, M.D.; Steven Colan, M.D.; Jeffrey P. Jacobs, M.D.; James Jaggers, M.D.; Kirk R. Kanter, M.D.; Catherine Dent Krawczeski, M.D.; Alan B. Lewis, M.D.; Brian W. McCrindle, M.D., M.P.H.; L. LuAnn Minick, M.D.; Seema Mital, M.D.; Christian Pizarro, M.D.; Chitra Ravishankar, M.D.; Ismee A. Williams, M.D.; and J. William Gaynor, M.D.
Author disclosures are on the abstract.

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J-CHF: Tailoring carvedilol dose to heart failure patients' response more effective

患者ごとに合わせた用量の心不全治療薬を使用した方が全ての患者に対し同用量の薬剤を使用するよりも有効性が高いとの研究結果が2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表された。収縮不全におけるβ遮断薬の用量および有効性を最大限にするための無作為化試験：日本における慢性心不全（J-CHF）スタディでは、軽度から中等度の慢性心不全患者364人を組み入れ、3用量（1日用量2.5mg、5mg、または20mg）のβ遮断薬カルベジロールを投与する群に無作為に割り付けた。3年間の経過観察期間中に20%の患者が一次エンドポイント（総死亡または心不全を含む心血管疾患による入院の合計）に到達した。群間に統計学的有意差は認められなかった。しかし、1日20mg内服群に割り付けられた患者の26%は有害事象のため内服中止か用量変更を行ったのに対し、低用量群におけるその割合はわずか2%であり、中等用量群では7%であった。カルベジロール開始後早期に心拍数低下および血漿BNP低下が認められた患者においては、一次エンドポイントに関する予後が良好であった。

Full Text

Tailoring the dose of a heart failure drug to a patient's response is better than the one-size-fits-all approach, according to research presented in a late-breaking clinical trial at the American Heart Association's Scientific Sessions 2009.

The Randomized Trial to Optimize the Dose and Efficacy of Beta-Blocker in Systolic Heart Failure: Japanese Chronic Heart Failure (J-CHF) Study involved 364 patients with mild to moderate heart failure assigned to one of three daily dosages of the beta blocker carvedilol (2.5 mg, 5 mg or 20 mg).

Researchers sought to determine the optimum minimal dose of the drug. They also investigated background factors that could predict the response to beta-blocker treatment, and established a method for individualized treatment with the drug.

During three years of follow-up, 20 percent of the patients reached the primary endpoint -- a composite of all-cause death or hospitalization for cardiovascular disease including heart failure. Researchers found no statistically significant difference between groups. However, 26 percent of the patients assigned to get 20 mg/day had to discontinue or change their dose due to adverse effects, compared to only 2 percent in the low-dose group and 7 percent in the moderate-dose group.

"Beta-blocker therapy has proved to be a very powerful tool in the treatment of patients with heart failure," said Masatsugu Hori, M.D., Ph.D., principal investigator of the study, president of the Osaka Medical Center for Cancer and Cardiovascular Diseases and professor emeritus at Osaka University in Osaka, Japan. "However, the optimum dose of beta-blockers in patients with chronic heart failure is unknown. We found that all three of the doses we tested were equally effective at reducing our primary endpoint."

The target dose is the maximum dose that has shown to be effective in randomized clinical trials. The clinical target dose in the United States and Europe is 50 mg of carvedilol greater than the highest dose of 20 mg used in this study.

In the previous study, MUCHA (Multi-center Carvedilol Heart Failure Dose Assessment trial) conducted in Japan in patients with mild to moderate heart failure, researchers found no significant difference in outcome between 5 mg and 20 mg daily dose of carvedilol, though it remains difficult to determine how individual patients will respond.

"The important point may not be dosage," said Hiroshi Okamoto, M.D., Ph.D., co-author of the study and director of cardiovascular medicine at Nishi Sapporo National Hospital (Hokkaido Medical Center) in Sapporo, Japan. "Our results do not simply indicate that 2.5 mg/day is the optimal dose. Rather, our results indicate that therapeutic response to carvedilol shows a high amount of variability between individuals, and we had better select the dose that can achieve reductions in heart rate and/or plasma BNP beyond dosage."

Change in a patient's heart rate and/or plasma BNP is "one of the very simple markers to predict mortality, and the optimal dose is the lowest one that reduces heart rate and BNP in an individual patient," Hori said.

"We are searching possible genes that may someday help predict individual response. It appears to be related to the responsiveness of heart rate and levels of plasma BNP, a biomarker for heart stress in response to the drug," Okamoto said.

連続流LVADを用いることにより生存率が上昇する

HeartMate II：末期心不全患者において連続流左室補助装置はパルス波タイプのものと比較し生存率を改善する

HeartMate II: Continuous flow left ventricular assist device improves survival more than pulsatile type in end-stage heart failure

重症心不全患者において連続流左室補助装置（LVAD）は、現在使用されているパルス波タイプのものと比較し、2年生存率が良好であると2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表され、New England Journal of Medicineに掲載された。HeartMate II最終的治療トライアルにおいて、末期心不全患者200人が連続流LVAD（HeartMate II）またはパルス流LVAD（HeartMate XVE）を植え込まれた。全ての患者が最大限の薬物治療でもコントロール不良で移植の適応ではなかった。複合一次エンドポイント（2年後に障害を残す脳卒中および再手術を必用とするデバイスの故障のない状態）に到達したのは、連続流LVAD患者においてパルス流LVAD患者と比較しはるかに多かった（46%対11%）。1年および2年生存率も連続流LVAD群において良好であった（1年生存率68%対55%、2年生存率58%対24%）。2年後の障害を残す脳卒中発現の割合は両群で同等であった（連続流群11%対パルス流群12%）。ポンプを修理または交換するために再手術を必用としたのは持続流群で10%であったのに対し、パルス流装置群においては36%であった。

Full Text

A new, continuous flow heart pump, or left ventricular assist device (LVAD), delivered better two-year survival in advanced heart failure patients than the current pulsatile model, researchers reported in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

In the HeartMate II Destination Therapy Trial, researchers tested a new device that helped heart failure patients who weren't responding to optimal medical therapy and weren't eligible for a heart transplant. They found significant improvement in outcomes of patients who received the continuous flow LVAD (HeartMate II) compared to those who received a pulsatile flow LVAD (HeartMate XVE), the only FDA-approved device for treating such patients.

"The results of this trial will alter the manner in which we provide mechanical circulatory support," said Joseph G. Rogers, M.D., co-author of the study and medical director of the Duke Heart Failure Program at Duke University Medical Center in Durham, N.C. "In the past, mechanical pumps delivered blood in a pulsatile manner; in other words, they beat like a human heart.

"The newer pump is smaller, operates quietly and has demonstrated superior durability. Interestingly, it also pumps blood continuously, which reduces the systolic blood pressure. We believe that in the future there will be little need for pulsatile blood pumps."

The study included 200 end-stage heart failure patients implanted at 38 U.S. medical centers between March 2005 and May 2007. All patients had failed optimal medical therapy and were ineligible for a heart transplant.

The primary endpoint was survival free from disabling stroke and device failure requiring re-operation at two years. Secondary endpoints included overall survival, adverse events, quality of life and functional capacity.

A greater proportion of continuous flow LVAD patients successfully reached the primary composite end-point compared to pulsatile flow (46 percent vs. 11 percent) - a highly significant finding, researchers said.

At one-year follow-up, 68 percent of the continuous flow LVAD patients had survived compared to 55 percent in the pulsatile flow group. At two years, survival was 58 percent for the continuous flow device vs. 24 percent with the pulsatile device.

Both groups experienced early and sustained improvements in their quality of life scores and functional capacity. The distance walked in six minutes (a common measure of functional abilities) increased from 182 to 318 meters in the continuous flow patients and from 172 to 306 meters in the pulsatile flow patients at one year, Rogers said.

Over the 24 months of the study, the rate of disabling stroke was similar in both study arms (11 percent for continuous flow LVAD vs. 12 percent for pulsatile flow LVAD).

In addition, 10 percent of the patients who received the continuous flow LVAD needed surgery to repair or replace the pump compared to 36 percent of patients with the pulsatile device.

Furthermore, other adverse events were less common in the continuous flow pump group than in the pulsatile one.

"Severe heart failure is associated with a very poor prognosis," Rogers said. "Patients diagnosed with advanced heart failure treated with optimal medical therapy have a 10 percent to 20 percent survival rate in the ensuing two years. Further, these patients are unlikely to experience significant improvement in their quality of life or functional abilities with routine medical or electrical therapies."

Transplantation is a standard treatment for patients with advanced heart failure. But an estimated 150,000 U.S. patients have advanced heart failure while the number of heart donors each year is about 2,100. "We believe that with improved technology and management strategies, LVADs will fill this important gap," Rogers said.

Thoratec Corporation, in Pleasanton, Calif., funded the study.

Co-authors are: Mark S. Slaughter, M.D.; Carmelo A. Milano, M.D.; Stuart D. Russell, M.D.; John V. Conte, M.D.; David Feldman, M.D., Ph.D.; Benjamin Sun, M.D.; Antone J. Tatooles, M.D.; Reynolds M. Delgado, M.D.; James W. Long, M.D., Ph.D.; Steven C. Horton, M.D.; Thomas C .Wozniak, M.D.; Waqas Ghumann, M.D.; David J. Farrar, Ph.D.; and Howard Frazier, M.D.

Disclosures: Dr. Rogers has served as a consultant for Thoratec.

施設の心臓手術の可否はPCI後の死亡率に影響しない

急性心筋梗塞に対する血管形成術を心臓手術が可能な病院と不可能な病院のいずれで施行されても1年死亡率は同等である

One-year mortality similar in patients undergoing angioplasty for acute myocardial infarction at hospitals with and without cardiac surgery capability

急性心筋梗塞(MI)に対する一次血管形成術(PCI)を心臓手術が可能な病院と不可能な病院のいずれで施行されても1年死亡率は同等であると2009年American Heart Association学会のレイトブレイキング登録研究のセッションで発表された。一次経皮的冠動脈形成術後の予後:施設内で心臓手術が可能な病院と不可能な病院との比較スタディにおいて、一次PCIを施設内での心臓手術の可能な(SOS)病院で行った方が施設内で心臓手術の不可能な(No SOS)病院と比較し予後が良好であるのか否かを調査した。一次PCIを施行されたSTEMI患者3,018人(うち977人はNo SOS病院で施行)の解析が行われた。No SOS病院では診断のための心臓カテーテル検査を施行しているが心臓手術の設備がないためPCIは日常的には施行されていなかった。結果として、一次PCI後の30日および1年死亡率はいずれの施設で施行されても差がなかった(1年死亡率=SOSで9.41%対No SOSで8.58%)。再血行再建術を必要とする率についても両群間で差はほとんどなかった。しかし、MI再発およびさらに血管形成術を必要とする率は心臓手術の設備のない病院で施行された群で多かった。

Full Text

One-year mortality is similar at hospitals with or without on-site cardiac surgery for patients undergoing primary percutaneous coronary intervention (PCI) to treat an on-going heart attack, researchers reported in a late-breaking clinical registry study presentation at the American Heart Association's Scientific Sessions 2009.

In the Outcomes Following Primary Percutaneous Coronary Intervention: A Comparison Between Hospitals With and Without Cardiac Surgery On-Site study, researchers sought to determine whether patients fared better after having primary PCI at hospitals with cardiac surgery on site (SOS) compared to those having PCI at community hospitals without cardiac surgery on site (No SOS).

They found the rate of death at 30 days and one-year follow-up was no different following primary PCI at either type of facility (one year = 9.41 percent with SOS vs. 8.58 percent without SOS).

"Primary PCI, meaning PCI during the acute phase of a heart attack, is the preferred treatment of an ST-elevation myocardial infarction (STEMI), but it is not widely available," said Marc A. Pfeffer, M.D., Ph.D., the study's principal investigator, the Dzau Professor of Medicine at Harvard and a senior physician in cardiovascular medicine at Brigham and Women's Hospital in Boston, Mass. "Performing PCI at community hospitals without cardiac surgery on site could increase the number of STEMI patients with timely access to this lifesaving procedure."

Primary PCI at hospitals without SOS is not routinely done, though many states have approved its use at hospitals that meet certain American College of Cardiology/American Heart Association guidelines for procedure volume.

To increase the number of STEMI patients with timely access to primary PCI, the Massachusetts Department of Health approved a pilot program in 1997 for primary PCI at hospitals without SOS to determine its safety and effectiveness, said Alice K. Jacobs, M.D., senior author of the study and professor of medicine and director of the Cardiac Catheterization Laboratories and Interventional Cardiology at Boston University Medical Center in Massachusetts.

The researchers analyzed 3,018 STEMI patients who underwent primary PCI, including 977 treated at No SOS hospitals, between January 2005 and September 2007, whose data was collected in the Massachusetts Data Analysis Center registry. The No SOS hospitals had the capability of performing cardiac catheterization for diagnostic purposes, but without a cardiothoracic surgery program they would not routinely have done PCI.

The study had four primary endpoints that researchers analyzed separately: all-cause mortality, recurrent heart attack, repeat need for PCI, and target vessel revascularization at 30 days and one year.

As with mortality, researchers found little difference among patients needing a repeat procedure to reopen the originally blocked cardiac vessel.

"However, patients undergoing primary PCI at hospitals without SOS had a slightly higher incidence of recurrent heart attack at 30 days for reasons that are unclear and will require further study," said Anis, a fellow at Boston University Medical Center during the study who is now in practice in Winchester/Northern Virginia.

At one year, the rate of recurrent heart attack was 6.66 percent at hospitals without SOS vs. 5.06 percent (p=0.11) at those with on-site cardiac surgery.

Although target vessel revascularizations were the same between groups, researchers found more revascularizations of other coronary arteries in the No SOS group, which could indicate more staged procedures in patients in the No SOS group with multi-vessel disease.

The study was funded through a contract with the Massachusetts Department of Public Health.

Co-authors are: Sharon-Lise T. Normand, Ph.D.; Robert E. Wolf, M.Sc.; Ann Lovett, R.N., M.A.; Laura Mauri, M.D., M.Sc.; and Neal Patel, M.D.

Disclosures: Four of the authors (Anis, Mauri, Patel and Jacobs) perform PCI at hospitals with SOS.

貧血治療薬のリスクは有益性を凌駕する

ダルベポエチンアルファのリスクは糖尿病および腎疾患を有する患者の心血管疾患の有益性を凌駕する

Risks of Darbepoetin alfa outweigh benefits in cardiovascular disease patients with diabetes and kidney disease

貧血改善薬のリスクは腎疾患を有する2型糖尿病患者において有益性を凌駕するとの、この薬剤の初めての大規模プラセボコントロールスタディの結果が2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表された。2004年に開始されたTREAT試験は24ヵ国4,038人の患者を対象に施行された。患者の半数は女性であり平均年齢は68歳であった。このAranesp治療による心血管イベント減少を目的としたトライアル(TREAT)の早期結果によると、慢性腎臓病および中等度の貧血を有する2型糖尿病患者においてダルベポエチンアルファを用いてヘモグロビンレベルを上昇させると輸血の必要性が軽減することが示された。研究者らは、貧血を治療することにより心血管死亡率および罹患率が低下することを期待していた。しかし、死亡または心血管イベント(非致死性心筋梗塞、うっ血性心不全、脳卒中または心筋虚血による入院)の複合エンドポイントの発現率を低下させなかった。さらに、ダルベポエチン群患者の脳卒中発現率は倍であった(5%対2.6%)。筆者らは、このトライアルはサロゲートマーカーが臨床上の予後に取って代わるものではないことを示した恰好な例であると述べている。

Full Text

Risks from a drug used to correct anemia outweighed its benefits in type 2 diabetic patients with kidney disease and anemia, according to results of the first large, placebo-controlled study of the agent reported in a late-breaking clinical trial at the American Heart Association's Scientific Sessions 2009.

Earlier results of the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT), reported at a recent meeting of the American Society of Nephrology, showed that that use of darbepoetin alfa to raise hemoglobin levels in patients with type 2 diabetes, chronic kidney disease (without dialysis) and moderate anemia lessened the need for blood transfusions.

Researchers said they hoped by treating the anemia it would lessen the cardiovascular mortality and morbitity of patients. However, it failed to reduce the rate of the composite endpoint of death or cardiovascular events (nonfatal heart attack, congestive heart failure, stroke or hospitalization for myocardial ischemia). In addition, almost twice as many patients randomized to the darbepoetin had a stroke (5 percent versus 2.6 percent).

There were two subgroups: the nearly two-thirds of TREAT patients with prior cardiovascular disease and the 11.1 percent of patients with a history of stroke.

In a new analysis, reported at the American Heart Association Scientific Sessions, those stroke patients seemed particularly vulnerable to the adverse events when randomized to darbepoetin, said Marc A. Pfeffer, M.D., Ph.D., the study's principal investigator, the Dzau Professor of Medicine at Harvard and a senior physician in cardiovascular medicine at Brigham and Women's Hospital in Boston, Mass.

Researchers, who looked at a composite endpoint of cardiovascular events, found that 47 percent (109 of 231) of the stroke survivors taking darbepoetin alfa had a cardiac event or died, compared to 37 percent of the placebo group (79 of 216 subjects).

TREAT, started in 2004, was conducted in 24 countries in 4,038 patients, more than half women, average patient age 68.

Darbepoetin alfa belongs to a class of drugs called erythropoiesis-stimulating agents (ESAs) that have been used for more than a quarter century to fight anemia. ESAs effectively raise hemoglobin levels.

"This trial is an excellent example of why surrogate markers, such as increased hemoglobin levels, should not take the place of clinical outcomes data," Pfeffer said.

"TREAT underscores the importance of placebo-controlled trials to assess risks as well as benefits. This new data will help physicians and patients make more informed decisions about the use of ESAS, and we believe for many that the risks will outweighs the benefits."

The research was supported and conducted in collaboration with Amgen.

Co-authors are: Emmanuel A. Burdmann, M.D., Ph.D.; Chao-Yin Chen, Ph.D.; Mark E. Cooper, M.D.; Dick de Zeeuw, M.D., Ph.D.; Kai-Uwe Eckardt, M.D.; Jan M. Feyzi, M.S.; Peter Ivanovich, M.D.; Reshma Kewalramani, M.D.; Andrew S. Levey, M.D.; Eldrin F. Lewis, M.D., M.P.H.; Janet B. McGill, M.D.; John J.V. McMurray, M.D.; Patrick Parfrey, M.D.; Hans-Henrik Parving, M.D.; Giuseppe Remuzzi, M.D.; Ajay K. Singh, M.D.; Scott D. Solomon, M.D.; and Robert Toto, M.D.

Disclosures: Dr. Pfeffer reports receiving consulting fees from Abbott, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Centocor, CVRx, Genentech, Cytokinetics, Daiichi Sankyo, Genzyme, Medtronic, Novartis, Roche, Sanofi-Aventis, Servier and VIA Pharmaceutics; grant support from Amgen, Baxter, Celladon, Novartis and Sanofi-Aventis; and being named co-inventor on a patent for the use of inhibitors of the renin-angiotensin system in selected survivors of myocardial infarction.

心不全患者の鉄欠乏を補正することにより症状が改善する

FAIR-HF：慢性心不全患者において鉄欠乏を治療することにより症状、心機能分類およびQOLが改善する

FAIR-HF: Treatment for iron deficiency improves symptoms, functional capacity and quality of life in chronic heart failure patients

慢性心不全（CHF）患者に鉄剤（ferric carboxymaltose）を静脈内注射し鉄欠乏を改善することにより症状、運動耐容能およびQOLが改善すると2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表され、New England Journal of Medicineに掲載された。研究者らは鉄欠乏を有する心不全患者459人を調査した。3分の2の患者は鉄欠乏が回復するまで鉄剤の静脈内注射を毎週の後月に1回施行され、3分の1はプラセボを投与された。鉄剤を静注された群の患者は、スタディの2つの一次エンドポイント（24時間後の自己申告によるPatient Global Assessment[PGA]、P<0.0001およびNew York Heart Association[NYHA]クラススコア、P<0.0001）の有意な改善を示した。PGAのエンドポイントに関しては、鉄剤に振り分けられた患者の50%が24週後に”非常に改善”または”中等度改善”と報告したのに対し、プラセボ群においてはこの種の改善を示した者は28%に過ぎなかった。トライアルの結果によると、鉄剤群の患者の47%が24週後にNYHAクラスIまたはIIであったのに対し、プラセボ群ではわずか30%であった。PGAとNYHAクラスの結果はあらかじめ定義された全てのサブグループにおいて同等であった。

Full Text

Intravenous (IV) iron treatment with ferric carboxymaltose to reverse iron deficiency can significantly improve symptoms, exercise tolerance and quality of life for chronic heart failure (CHF) patients, researchers said in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

"Our study shows that treating iron deficiency for 24 weeks with iron in the form of I.V. ferric carboxymaltose safely improves symptoms in patients with chronic heart failure with anemia," said Stefan D. Anker, M.D., Ph.D., Professor of Cardiology and Cachexia Research, Department of Cardiology, Charité Medical School in Berlin, Germany. Anker is lead investigator of the FAIR-HF (Ferinject® Assessment in patients with IRon deficiency and chronic Heart Failure) study.

Anker added, "This is the first fully successful phase 3 trial of a drug for chronic heart failure to improve symptoms in many years. Besides symptoms, our treatment also improved functional exercise capacity as measured by the 6-minute walking test and quality of life and it was very well tolerated."

The researchers studied 459 heart failure patients with iron deficiency in 75 study sites, mainly in Europe and Argentina. Researchers randomized two-thirds of the patients to receive weekly I.V. injections of iron until the iron deficiency was reversed, with monthly treatment thereafter. The other one-third received a placebo (saline).

The group treated with I.V. iron showed significant improvements in both of the study's two primary endpoints: 1) self-reported Patient Global Assessment (PGA) score after 24 weeks (P<0.0001) and 2) a measure of CHF severity called New York Heart Association (NYHA) class (P<0.0001). To illustrate the results, for the PGA endpoint, 50 percent of patients assigned to ferric carboxymaltose were either "much improved" or "moderately improved" at week 24 compared to only 28 percent of patients showing this kind of improvement in the placebo group. For NYHA class, the study showed that 47 percent of patients assigned to ferric carboxymaltose were in NYHA class I or II at week 24, compared to only 30 percent of patients on placebo therapy.

The results for PGA and NYHA class were very similar in all predefined subgroups, regardless of whether they were defined by hemoglobin or ferritin level, age, or gender. "It is important that the benefits of I.V. iron were observed in patients regardless of a diagnosis of anemia, suggesting that iron deficiency itself is an important therapeutic target in heart failure patients, independent of presence of anemia." said Anker.

Furthermore, researchers found significant improvements in the secondary endpoints. After 24 weeks, patients receiving I.V. iron injections undergoing the six-minute walk test were able to walk 39.1 meters further than at baseline, compared with just 8.6 meters further in the placebo group.

From as early as week 4 of the study, and throughout the study, I.V. iron improved quality of life assessments compared with placebo (P<0.001). There was no significant difference in mortality or rates of adverse events, including hospitalizations, between the treatment and placebo groups.

Sponsor: Vifor Pharma Ltd., Switzerland.

Authors are: Stefan D. Anker, M.D Ph.D.; Piotr Ponikowski, M.D Ph.D.; Philip A. Poole-Wilson, M.D. (deceased); Josep Comin Colet, M.D.; Gerasimos Filipatos, M.D.; Ronnie Willenheimer, M.D.; Kenneth Dickstein, M.D. Ph.D.; Helmut Drexler (deceased), M.D.; and Thomas L?scher, M.D.; Stuart Pocock, Ph.D; Claudio Mori, M.D.; Barbara von Eisenhart Rothe, M.D.

Disclosures: Stefan D. Anker is a member of the Executive Committee of FAIR-HF and a consultant to Vifor Pharma Ltd. and Amgen Inc. He has received honoraria for speaking for the companies.

Cardiology特集

AHA2009（第82回米国心臓病協会）

トピックス一覧

累積X線線量は急性MIで入院中の患者において高い

急性心筋梗塞で入院した患者は入院中に高線量の電離放射線を被曝する

Patients admitted to hospital for acute myocardial infarction receive high ionizing radiation dose during stay

急性心筋梗塞(MI)患者の入院中の平均電離放射線被曝量が検査による胸部X線撮影の725倍であるとの研究結果が2009年American Heart Association学会で発表された。MI患者の総被曝量を調査した初めての大規模スタディにおいて、研究者らは急性MIの治療を受けた患者64,074人(女性23,394人男性40,680人)のデータを解析した。スタディによると、患者らは電離放射線を使用した検査を合計で276,651件受けた。つまり、患者一人当たり平均7件の検査を受けたことになる。患者らの入院中の累積被曝量は14.52mSv―原子力発電および他の電離放射線を扱う環境で勤務する者に許可されている年間累積線量の約3分の1―であった。解析された9つの検査中、全患者のうち83%が胸部X線撮影を、77%はカテーテル検査を、15%は体部のコンピュータ断層撮影を、12%は頭部CTを施行された。1%～6%の患者が他の3つの核医学検査および胸部CT検査を施行された。

Full Text

Acute myocardial infarction patients received an average total dose of ionizing radiation equal to 725 chest X-rays from medical tests during their hospital stay, according to research presented at the American Heart Association's Scientific Sessions 2009.

In the first large study to examine total radiation dosage in heart attack patients, researchers found those admitted to academic hospitals had a cumulative effective radiation dose of 14.5 millisieverts (mSv) - about one-third the annual maximum accumulation permitted for workers in nuclear power plants and other ionizing radiation environments.

"It's potentially a new way to consider radiation exposure and safety," said Prashant Kaul, M.D., lead author of the study and a fellow in cardiovascular medicine at Duke University Medical Center in Durham, N.C. "We think physicians should not only have a greater awareness of dose accumulation from the tests they are ordering, but also understand the testing patterns they use for common diagnoses."

Total short-term exposure likely counts, he said. A person's lifetime exposure to ionizing radiation can potentially increase the risk of cancer. However, risk estimates vary for developing malignancies at specific exposure levels.

Physicians perform several billion imaging studies annually worldwide, about one-third of them in cardiovascular patients. The collective dose received annually from ionizing radiation medical tests increased an estimated 700 percent between 1980 and 2006, according to the American Heart Association.

Kaul urged increased efforts to better determine the appropriate use of various radiation-based tests when assessing and treating heart attack patients.

"We should not withhold necessary, appropriate tests that involve ionizing radiation - they provide very important information," Kaul said. "What we should do is evaluate and understand the clinical indications for tests that involve ionizing radiation. We need to be sure they are being done appropriately."

Researchers analyzed data from 64,074 patients - 23,394 women and 40,680 men - treated for acute heart attack between 2006 and the second quarter of 2009 at 49 academic hospitals throughout the United States that participate in the University Health System Consortium and subscribe to their resource manager database.

Among the study's findings:

- Patients received 276,651 tests that used ionizing radiation, an average of seven per patient.
- Patients averaged a total accumulation of 14.52 mSv during their hospital stay.
- Among the nine types of tests analyzed, 83 percent of all patients received chest X-rays; 77 percent had catheter procedures; 15 percent underwent body computed tomography (CT) scans; and 12 percent had a head CT.
- Between 1 percent and 6 percent of patients had three other nuclear imaging tests and chest CT.

Physicians tend to focus on the radiation dose of each procedure rather than the cumulative dose a patient will receive, he said. "This makes the risk seem smaller to patients than it actually is. The risk at an individual level is small with one test, but with multiple tests the risk likely increases. Additionally, a small individual risk applied to a growing and aging population could potentially represent a future public health problem, especially if the trend continues to be increased use of cardiac imaging tests involving ionizing radiation."

The study has several limitations. For one, the researchers used estimates of typical effective radiation doses from several sources, including the American Heart Association Committee on Cardiac Imaging. Thus, their reported cumulative and radiation dose per patient is an estimate rather than actual measurement.

Moreover, the researchers selected nine tests used in assessing heart attacks for their study, but physicians may also use others.

Manesh R. Patel, M.D, is co-author of the study.

Author disclosures are on the abstract.

Duke University Division of Cardiovascular Medicine funded the study.

大豆はオメガ3脂肪酸の有益性を増強させる（Abstract# 1404/Poster 2071）

魚の調理法がオメガ3脂肪酸の心保護に関する有益性に影響する

How fish is cooked affects cardioprotective benefits of omega-3 fatty acids

オメガ3脂肪酸による心保護目的で魚を食べる際には、揚げたり塩漬けにしたりまたは乾燥させたりするよりも焼いたり蒸したりするほうが有効であり、減塩しょうゆや豆腐はその有益性を増強させると2009年American Heart Association学会で発表された。スタディの結果から、心保護作用は性別や民族性（おそらく調理法の違い、遺伝子感受性、またはホルモン因子による）の影響も受けることが示唆された。このスタディは、45～75歳の心疾患既往歴を有さない82,243人の男性および103,884人の女性を対象とした。オメガ3脂肪酸摂取量は男性においては心疾患による死亡の全リスクと逆比例した―傾向は主に白人、日系アメリカ人、およびラテン系民族において認められた。全体で、1日3.3gのオメガ3脂肪酸を摂取する男性は1日0.8g摂取する男性と比較し、心臓死のリスクが23%低かった。女性においてはそれぞれの摂取レベルにおいて心保護作用を有していたが、一貫して有意なわけではなかった。塩漬けまたは乾燥の魚は女性においてはリスクファクターであった。しょうゆおよび照り焼きソースを追加すると男性では保護的に作用し、女性では心血管疾患死と逆比例の関係を示した。豆腐は全ての民族において心保護作用を有していた。

Full Text

If you eat fish to gain the heart-healthy benefits of its omega-3 fatty acids, baked or boiled fish is better than fried, salted or dried, according to research presented at the American Heart Association's Scientific Sessions 2009. And, researchers said, adding low-sodium soy sauce or tofu will enhance the benefits.

"It appears that boiling or baking fish with low-sodium soy sauce (shoyu) and tofu is beneficial, while eating fried, salted or dried fish is not," said Lixin Meng, M.S., lead researcher of the study and Ph.D. candidate at the University of Hawaii at Manoa. "In fact, these methods of preparation may contribute to your risk. We did not directly compare boiled or baked fish vs. fried fish, but one can tell from the (risk) ratios, boiled or baked fish is in the protective direction but not fried fish."

The findings also suggest that the cardioprotective benefits vary by gender and ethnicity - perhaps because of the preparation methods, genetic susceptibility or hormonal factors.

Many studies have suggested that eating omega-3 fatty acids reduces the risk of heart disease; however, little is known about which source is most beneficial.

In this study, researchers examined the source, type, amount and frequency of dietary omega-3 ingestion among gender and ethnic groups. Participants were part of the Multiethnic Cohort living in Hawaii and Los Angeles County when they were recruited between 1993 and 1996. The group consisted of 82,243 men and 103,884 women of African-American, Caucasian, Japanese, Native Hawaiian and Latino descent ages 45 to 75 years old with no history of heart disease.

Researchers divided their intake of canned tuna, other canned fish, fish excluding shell fish, or soy products that contain plant omega-3s (soy, tofu and shoyu) into quintiles, quartiles, or tertiles when applicable. They also surveyed the preparation methods: raw, baked, boiled; fried; salted or dried. The initial study did not consider grilled fish.

Those in the highest quintile consumed a median 3.3 grams of omega-3 fatty acids a day. The lowest quintile consumed a median of 0.8 grams a day.

Omega-3 intake was inversely associated with overall risk of death due to heart disease in men - a trend mainly observed in Caucasians, Japanese Americans and Latinos. However, there weren't many blacks or Hawaiians in the study, so the results should be interpreted cautiously, Meng said.
Overall, men who ate about 3.3 grams per day of omega-3 fatty acids had a 23 percent lower risk of cardiac death compared to those who ate 0.8 grams daily.

"Clearly, we are seeing that the higher the dietary omega-3 intake, the lower the risk of dying from heart disease among men," Meng said.

Japanese and Hawaiians eat fish more often compared to whites, blacks and Latinos, and they prepare fish in a variety of methods, Meng noted.

For women, the omega-3 effect was cardioprotective at each level of consumption but not consistently significant, Meng said. Salted and dried fish was a risk factor in women.

In contrast, adding less than 1.1 gram/day shoyu and teriyaki sauce at the dinner table was protective for men but not for greater than 1.1 gram/day. For women, shoyu use showed a clear inverse relationship to death from heart disease. She noted that shoyu that is high in sodium can raise blood pressure, so she stressed low-sodium products. Eating tofu also had a cardioprotective effect in all ethnic groups.

"My guess is that, for women, eating omega-3s from shoyu and tofu that contain other active ingredients such as phytoestrogens, might have a stronger cardioprotective effect than eating just omega-3s," said Meng, noting that further studies are needed to confirm the hypothesis.

During the average 11.9 years of follow-up, 4,516 heart-related deaths occurred in the group, according to state and national death records, which were cross-referenced through the end of 2005.

The study didn't consider possible dietary changes over time; subjects who were diagnosed with heart disease after their baseline food intake surveys might have modified their eating habits. Further, the study didn't account for the possible effects of fish-oil supplementation.

In light of these limitations, the researchers plan to include subjects' dietary patterns over time and a cross-validation of their omega-3 levels through blood analysis.

"Our findings can help educate people on how much fish to eat and how to cook it to prevent heart disease," Meng said. "Alternately, if it is verified that the interactions between fish consumption, risk factors and ethnicity are due to genetic susceptibility, the heart-disease prevention message can be personalized to ethnic groups, and future study could identify susceptibility at the genetic level."

Co-authors are Lynne Wilkens, Dr.P.H., and Laurence Kolonel, M.D., Ph.D.

Author disclosures are on the abstract. An American Heart Association Pacific Mountain Pre-doctoral Fellowship grant funded the study. The data for this research is based on Multiethnic Cohort Study of Diet and Cancer under the NIH grant R37 CA054281.

Cardiology特集
AHA2009（第82回米国心臓病協会）

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アスピリンにクロピドグレルを併用しても有意な有益性は認められない

CASCADE：アスピリン単独と抗血小板薬併用療法のバイパス術後の静脈グラフト疾患予防効果は同等である

CASCADE: Aspirin alone as effective as dual antiplatelet therapy in preventing vein graft disease one year after bypass surgery

冠動脈バイパスグラフトの開存維持率はアスピリン単独とアスピリンとクロピドグレルの併用とでは同等である、と2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表された。冠動脈疾患術後のクロピドグレル（Clopidogrel After Surgery For Coronary Artery DiseasE ：CASCADE）無作為化コントロールトライアルは、クロピドグレルをアスピリンに追加することで冠動脈バイパス術（CABG）後の伏在静脈狭窄およびグラフト閉塞が軽減するか否かを評価した初めての前向き試験である。研究者らは初回の多枝CABGを2本以上の伏在静脈グラフト（SVGs）を用いて施行された患者113人を、アスピリン162mgとクロピドグレル1日75mgまたはアスピリンとプラセボを1年間内服する群に無作為に割り付けた。1年後の静脈グラフトの開存率はアスピリン単独群で93.2%であったのに対し、アスピリンとクロピドグレルを内服した群で94.3%であり統計学的有意差はなかった。二次エンドポイントである静脈グラフトの開存率、主要な心血管イベント、または大出血に関しても有意差はなかった。

Full Text

Aspirin alone is as effective as aspirin and clopidogrel in keeping coronary artery bypass grafts open during the first year after surgery, researchers reported in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

The Clopidogrel After Surgery For Coronary Artery DiseasE (CASCADE) Randomized Controlled Trial is the first prospective randomized study to evaluate whether the addition of clopidogrel to aspirin reduces saphenous vein graft narrowing and graft occlusion after coronary artery bypass grafting (CABG).

"We found no significant difference in the amount of vein graft thickening, or the number of blocked bypasses, cardiovascular events or bleeding events for the 113 CABG surgery patients treated with either aspirin and clopidogrel or aspirin alone," said Alexander Kulik, M.D., M.P.H., lead author of the study and a cardiovascular surgeon at the Boca Raton (Fla.) Community Hospital.

Researchers randomly assigned the patients to one year of 162 milligrams (mg) a day of aspirin plus 75 mg/day of clopidogrel or 162 mg/day of aspirin plus placebo. More than 90 percent of patients in the CASCADE trial were also taking cholesterol-lowering statin drugs.

"I think this study presents both good news and bad news," said Kulik, who was a cardiac surgery resident at the University of Ottawa Heart Institute in Ontario, Canada, where the study was based, during most of CASCADE's May 2006 through July 2008 enrollment period.

"The good news is that patients and their doctors can expect more than 90 percent of vein grafts to remain open one year after surgery with the use of aspirin and statins," Kulik said. "In this study there was no statistical difference in the vein graft patency rate between the 93.2 percent for the aspirin only group vs. 94.3 percent for those who received aspirin plus clopidogrel. However, it is bad news for the advancement of the cardiac surgery field. It has been more than 10 years since the last advance in medical therapy for bypass grafts, which was a study showing that statin therapy helps keep vein grafts open."

Aspirin is the standard antiplatelet therapy for post-CABG patients, while dual antiplatelet therapy with aspirin and clopidogrel is routinely used during and after angioplasty and during acute heart attacks. Some surgeons have recently begun using clopidogrel instead of or in addition to aspirin after bypass surgery, believing that it might improve outcomes. The study didn't validate that belief, Kulik said.

The CASCADE trial was funded by research grants from Physicians' Services Inc. Foundation, Boston Scientific Inc. and the Bristol-Myers Squibb Sanofi Canada Partnership.

Co-authors are: Michel Le May, M.D.; Jean-Claude Tardif, M.D.; Robert De Larocheliere, M.D.; Sarika Naidoo, B.Sc.; George A. Wells, Ph.D.; Thierry G. Mesana, M.D., Ph.D.; Pierre Voisine, M.D.; and Marc Ruel, M.D., M.P.H.

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性別に応じた心臓リハビリテーションはうつ病を改善する（Abstract# 1480）

意欲をかき立てるような「女性のみの」心臓リハビリテーションはうつ症状を軽減する

Motivational "women-only" cardiac rehabilitation program improves symptoms of depression

心血管疾患を有する女性のうつ症状は、意欲をかき立てるような女性限定の心臓リハビリテーションに参加することで改善したとの研究結果が2009年American Heart Association学会で発表された。5年間の無作為化臨床試験の一次目的は、変化ステージをマッチさせた、動機付けを強化された、女性限定12週間の心臓リハビリテーションプログラムに参加した女性と、従来の教育および運動からなる12週間の心臓リハビリテーションプログラムに参加した女性とを、複数の身体的心理社会的予後に関して比較することであった。このトライアルに最後まで参加した女性225人（平均年齢63歳）のうつ症状をリハビリ終了後および6ヵ月の経過観察後に評価した。従来の心臓リハビリテーションに参加した女性のうつ病スコアは12週間のうちに16.5から14.3まで低下したのに対し、強化リハビリ群では17.3から11.0まで低下した。この結果は2群間のうつ症状の経時的な有意差を示している（p=0.13）。6ヵ月間の経過観察期間ののち、従来リハ群の平均スコアは15.2であり女性に特化したリハ群の平均スコアは13であった（p<0.001）。

Full Text

Depressive symptoms improved among women with coronary heart disease who participated in a motivationally-enhanced cardiac rehabilitation program exclusively for women, according to research presented at the American Heart Association's Scientific Sessions 2009.

Depression often co-occurs with heart disease and is found more often in women with heart disease than in men. Depression also interferes with adherence to lifestyle modifications and the willingness to attend rehabilitation.

"Women often don't have the motivation to attend cardiac rehab particularly if they're depressed," said Theresa Beckie, Ph.D., lead investigator and author of the study and professor at the University of South Florida's College of Nursing in Tampa, Florida. "Historically women have not been socialized to exercise and their attendance in cardiac rehabilitation programs has been consistently poor over the last several decades. This poor attendance may be partly due to mismatches in stages of readiness for behavior change with the health professional approaching from an action-oriented perspective and the women merely contemplating change - this is destined to evoke resistance."

Cardiac rehabilitation programs tailored to the needs of women and to their current level of readiness to change may improve adherence to such programs and potentially improve outcomes for women, she said.

The primary goals of the 5-year randomized clinical trial were to compare multiple physiological and psychosocial outcomes of women who participated in a 12-week stage-of-change matched, motivationally enhanced, gender-tailored cardiac rehabilitation program exclusively for women compared to women attending a 12-week traditional cardiac rehabilitation program comprised of education and exercise. Depressive symptoms of 225 women (average age 63) who completed this trial were examined after the interventions as well as after a 6-month follow-up period.

Participants completed the 20-item Center for Epidemiological Studies Depression Scale prior to beginning the intervention, one week after completing the intervention, and again six months later. The questionnaire asked them about how often in the past week they felt depressed, hopeful, lonely, happy and fearful.

Depression scores for the women participating in the traditional cardiac rehab dropped from 16.5 to 14.3 in 12 weeks, while scores in the augmented group dropped from 17.3 to 11.0 - "a significant decline compared to the traditional group," said Beckie.

After a 6-month follow-up, the traditional rehab group had an average score of 15.2 and those in the women-specific program had an average score of 13. Beckie said "we found that improvements in depressive symptoms were sustained at the 6-month follow-up in the augmented group while those in traditional cardiac rehab were essentially unchanged. This intervention also led to significantly better attendance and completion rates than those in the traditional cardiac rehabilitation program."

The intervention was guided by the transtheoretical model of behavior change and was delivered with motivational interviewing clinical methods. The motivationally-enhanced intervention began with an assessment of their stage of motivational readiness to change regarding three behaviors: healthy eating, physical activity, and stress management. The investigators then applied appropriate stage-matched strategies to promote the uptake of health behaviors.

"The stage-matched intervention used in conjunction with motivational interviewing applied the patient-centered principles of expressing empathy, rolling with resistance to change, respecting patient autonomy and supporting self-efficacy for change" Beckie said.

"We didn't push them if they weren't ready to make the changes," Beckie said. "We have found that if some patients receive long lists of behaviors they are expected to change immediately - such as quitting smoking, eating healthier, exercising regularly - they are overwhelmed. Pushing such patients who are not ready can lead them to tune out or drop out. Instead, for these women, we acknowledged their ambivalence about change and gave them strategies to move toward being ready by reinforcing their own motivations for changing. It's unrealistic to expect all patients to change their lifestyle all at once, right now in front of you." The woman-centered program is a more individualized approach to rehabilitation.

"You can't treat everyone the same when it comes to changing health behaviors," she said. Beckie hopes these results will lead to symptoms of depression being assessed more often in women suffering from heart disease and to more motivationally augmented, women-specific rehabilitation options. The participants may not be completely representative of the national population because they all had health insurance.

Beckie's co-author is Jason Beckstead, Ph.D. Author disclosures are on the abstract.

The National Institute of Nursing Research funded the 5-year study.

オフポンプバイパス術はステント術よりも認知機能の結果が良好である

OctoStent Study：ステント留置を伴う血管形成術はオフポンプバイパス術よりも認知機能を低下させる可能性がある

OctoStent Study: Angioplasty plus stenting may be associated with greater cognitive decline than off-pump coronary artery bypass

動脈硬化の低リスク患者において長期の認知機能および運動能力は、オフポンプ冠動脈バイパス術（OPCAB）後の患者の方がステント留置を伴う冠動脈形成術後の患者よりも良好である、と2009年American Heart Association学会のレイトブレイキング臨床試験のセッションで発表された。研究者らはOctopusスタディの一部であるOctoStentトライアルの低リスク患者201人（エントリー時280人）の7.5年間の認知機能の結果を報告した。患者はOPCABまたは低侵襲のベアメタルステント留置を伴う経皮的冠動脈インターベンション（PCI）を受ける群に無作為に割り付けられた。認知機能に関する長期予後をOPCAB群とPCIステント群で比較したこの初めてのスタディでは、死亡率または心筋梗塞発症率に差はなかったが、OPCAB群患者においてPCIステント群患者と比較し、特に学習および言語記憶領域の認知機能が有意に良好であった。認知機能変化は軽微なものであったが、7つ全ての認知機能領域の検査にわたり認められた。このスタディが溶出ステントにおいても確認されれば、医師および患者が血行再建術の方法を選択する際に考慮すべき問題に加わるであろう。

Full Text

Long-term thinking and motor skills were better for low-risk patients with clogged arteries after off-pump coronary artery bypass surgery (OPCAB) compared to angioplasty with coronary stenting, in a study presented at the American Heart Association's Scientific Sessions 2009.

In a late-breaking clinical trial presentation of neurocognitive outcomes from the OctoStent trial, part of the Octopus Study, researchers reported 7.5 year cognitive results for 201 of an initial 280 low-risk patients with blocked coronary arteries.

Researchers randomly assigned patients to either OPCAB or the less-invasive percutaneous coronary intervention (PCI) with implantation of bare metal stents.

"We found that although the patients had similar cardiac outcomes, without significant between-group difference in the composite of death, stroke, heart attack and re-interventions, the OPCAB patients had better long-term cognitive performance than the PCI patients," said Jakub J. Regieli, M.D., PhD executive investigator of the study and a cardiologist in training at the University Medical Center in Utrecht, The Netherlands.

"Although the cognitive differences were subtle, they occurred in all seven cognitive domains we tested, which is remarkable," said Regieli."

Conventional coronary artery bypass graft surgery (CABG) may be associated with cognitive declines postoperatively, and past studies of OPCAB do not show a reduction in these declines, said Regieli. On the other hand, PCI may also be associated with neurological complications, and there is accumulating evidence that procedural micro-embolization occurs more frequently than previously assumed. Comparisons of CABG, OPCAB and PCI have in general been short-term, and have produced inconsistent results. In this first long-term clinical outcome comparison of OPCAB to PCI-stenting regarding cognition, researchers found no difference in mortality or heart attack rates, but significantly better cognitive performance, particularly in the areas of learning and verbal memory, in OPCAB patients compared to PCI patients.

"In addition, we observed a much higher absolute risk of re-intervention in the PCI versus CABG patients (30 percent versus 17 percent)," Regieli said.

"There is no clear-cut explanation for the beneficial cognitive outcome after OPCAB and the mechanisms cannot be deduced from the current study per se," Regieli said. "The avoidance of any aortic manipulation during OPCAB, as pertains to the 85 percent undergoing only arterial revascularization in that patient group, may have resulted in less cerebral micro-embolization. At the same time, in patients treated with stents, and bare metal stents in particular, repeated catheterization and PCI may induce more cerebral micro-emboli than currently assumed."

More research is needed to confirm the findings from this small study, especially whether the findings can be extrapolated to the current era of drug-eluting stents. Also, additional analyses to better define determinants of neurocognitive outcome in these patients are underway, he said.

Study sponsors: UMC Utrecht, The Netherlands.

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