ボーラスでの抗凝固薬投与はSTEMI後の梗塞サイズを減少させる

INFUSE AMI:Abciximabボーラス単回投与は前壁STEMIに対しPCIを施行された患者の心筋障害サイズ軽減に役立つ可能性がある

INFUSE AMI: A bolus dose of abciximab may help reduce size of heart damage in patients undergoing PCI for anterior STEMI

STEMIに対し経皮的冠動脈インターベンション（PCI）を施行される患者に抗凝固薬abciximabをボーラス単回投与することにより30日後の梗塞サイズが減少したとのスタディ結果が2012年American College of Cardiology学会で発表され、同時にJAMAオンライン版に掲載された。INFUSE AMIスタディは左冠動脈近位部または中部の閉塞によるSTEMI発症後4時間以内に来院しプライマリPCIを抗凝固薬bivalirudinを用いて施行された患者452人を対象とした。患者らはボーラスでの梗塞領域冠動脈内abciximab局所投与またはabciximab非投与および手動での血栓吸引施行群または血栓吸引非施行群に無作為に割り付けられた。梗塞サイズは心臓磁気共鳴画像を用いて30日後に評価した。冠動脈内abciximab投与群に割り付けられた患者においてはabciximab非投与患者と比較し、総心筋量に対するパーセンテージとして計測された梗塞サイズ（中央値15.1%対17.9%）および絶対梗塞量(中央値18.7g対24.0g)が有意に小さかったが、異常壁運動スコアはそうではなかった。血栓吸引術施行群に割り付けられた患者は血栓吸引を施行されなかった患者と比較し、梗塞サイズ(中央値17.0%対17.3%)、絶対梗塞量（中央値20.3g対21.0g)、および異常壁運動スコアに有意差はなかった。

Full Text

Administration of a bolus dose of the anticoagulant drug abciximab into the coronary artery among STEMI patients who were undergoing a percutaneous coronary intervention (PCI) and also receiving another anticoagulant resulted in reduction in the size of damage to the heart muscle at 30 days, while a procedure that involved use of a catheter to remove the blood clot blocking that coronary artery did not produce these results, according to a study appearing in JAMA. The study is being published early online to coincide with its presentation at the American College of Cardiology's annual scientific sessions.

"Primary percutaneous coronary intervention (PCI) is widely accepted as the most effective reperfusion modality for ST-segment elevation myocardial infarction (STEMI). However, myocardial recovery after primary PCI is often suboptimal despite restoration of coronary blood flow, in part due to thrombus embolization resulting in impaired microvascular perfusion," according to background information in the article. Two strategies proposed to reduce this complication after PCI include bolus infusion of intracoronary abciximab and manual thrombus aspiration. "However, conflicting results have been reported as to whether intracoronary abciximab and manual aspiration thrombectomy reduce infarct size or improve clinical outcomes, in part because of differences in patient selection, devices, and study methodology."

Gregg W. Stone, M.D., of Columbia University Medical Center and New York–Presbyterian Hospital, New York, and colleague investigated whether bolus intracoronary abciximab, manual aspiration thrombectomy, or both would reduce infarct size in high-risk patients with STEMI. The study, conducted between November 2009 and December 2011, included 452 patients presenting at 37 sites in 6 countries within 4 hours of STEMI due to blockage in the proximal or mid left anterior descending artery occlusion undergoing primary PCI with the anticoagulant bivalirudin. The patients were randomized to bolus intracoronary abciximab delivered locally at the infarct lesion site vs. no abciximab and to manual aspiration thrombectomy vs. no thrombectomy. Infarct size was assessed at 30 days by cardiac magnetic resonance imaging (cMRI).

Evaluable cMRI results at 30 days were present in 181 and 172 patients randomized to intracoronary abciximab vs. no abciximab, respectively, and in 174 and 179 patients randomized to manual aspiration vs. no aspiration, respectively. The researchers found that patients randomized to intracoronary abciximab compared with no abciximab had a significant decrease in infarct size measured as a percentage of total myocardial mass (median, 15.1 percent vs. 17.9 percent) and absolute infarct mass (median, 18.7 g vs. 24.0 g), but not in abnormal wall motion score. Patients randomized to aspiration thrombectomy vs. no aspiration had no significant difference in infarct size (median, 17.0 percent vs. median, 17.3 percent), absolute infarct mass (median, 20.3 g vs. 21.0 g), or abnormal wall motion score.

"The principal findings from this multicenter, prospective, randomized trial in patients presenting early in the course of a large evolving anterior STEMI undergoing primary PCI with bivalirudin anticoagulation are as follows: (1) bolus intracoronary abciximab delivered to the infarct lesion site significantly but modestly reduced the primary end point of infarct size at 30 days; (2) in contrast, manual aspiration thrombectomy did not significantly reduce infarct size; and (3) indices of myocardial reperfusion, ST-segment resolution, and 30-day clinical event rates were not significantly different between the randomized groups," the authors conclude.

This study was sponsored and funded by Atrium Medical. Atrium supplied the local drug delivery catheter. Aspiration catheters were provided at a discount by Medtronic. Bivalirudin was provided at no charge by The Medicines Company. All other study devices and drugs were commercially purchased.

ACC2012特集

骨髄は虚血性心不全治療に有効ではない

FOCUS Trial：骨髄を用いた虚血性心不全の治療はある心機能計測値を改善しなかった

FOCUS Trial: Treatment for chronic ischemic heart failure with bone marrow cells does not show improvement for certain heart function measures

患者の骨髄を用いた慢性虚血性心不全の治療は心機能計測値のほとんどを改善しなかったとのスタディ結果が2012年American College of Cardiology学会で発表され、同時にJAMAオンライン版に掲載された。FOCUSトライアルにおいて研究者らは、5つの米国内心、肺、および血液施設-スポンサーのついた心臓血管細胞療法研究 ネットワーク施設において、慢性虚血性心疾患および左室機能低下を伴う心不全かつ/または狭心症を有し最大限の薬物療法を受けている患者に対し、経心内膜自家骨髄単核球細胞（BMCs）投与の効果を評価するスタディを施行した。患者はBMCsまたはプラセボの経心内膜注入を受ける群に無作為に割り付けられた。データ解析の結果、左室収縮末期容積指数、最大酸素摂取量、および可逆的欠損（reversible defect）の変化から成るエンドポイントは両群間で統計学的な有意差がないことが示された。
パーセント心筋欠損、総欠損サイズ、固定性欠損サイズ、局所壁運動、および臨床上の改善などの二次エンドポイントのいずれにおいても差がなかった。左室駆出率を評価した検査分析では、62歳以下の患者においては統計学的に有意な治療効果が認められた。

Full Text

Use of a patient's bone marrow cells for treating chronic ischemic heart failure did not result in improvement on most measures of heart function, according to a study appearing in JAMA. The study is being published early online to coincide with its presentation at the American College of Cardiology's annual scientific sessions.

Cell therapy has emerged as an innovative approach for treating patients with advanced ischemic heart disease, including those with heart failure. "In patients with ischemic heart disease and heart failure, treatment with autologous bone marrow mononuclear cells (BMCs) has demonstrated safety and has suggested efficacy. None of the clinical trials performed to date, however, have been powered to evaluate specific efficacy measures," according to background information in the article.

Emerson C. Perin, M.D., Ph.D., of the Texas Heart Institute and St. Luke's Episcopal Hospital, Houston and colleagues conducted a study to examine the effect of transendocardial administration of BMCs to patients with chronic ischemic heart disease and left ventricular (LV) dysfunction with heart failure and/or angina. The patients in the phase 2 randomized trial were receiving maximal medical therapy at 5 National Heart, Lung, and Blood Institute–sponsored Cardiovascular Cell Therapy Research Network (CCTRN) sites between April 2009 and April 2011. Patients were randomized to receive transendocardial injection of BMCs or placebo. The primary outcomes measured for the study, assessed at 6 months, were changes in left ventricular end-systolic volume (LVESV) assessed by echocardiography, maximal oxygen consumption, and reversibility of perfusion (blood flow) defect on single-photon emission tomography (SPECT). Of 153 patients who provided consent, a total of 92 (82 men; average age: 63 years) were randomized (n = 61 in BMC group and n = 31 in placebo group).

Analysis of data indicated no statistically significant differences between the groups for the primary end points of changes in LVESV index, maximal oxygen consumption, and reversible defect. There were also no differences in any of the secondary outcomes, including percent myocardial defect, total defect size, fixed defect size, regional wall motion, and clinical improvement.

In an exploratory analysis, the researchers did find that when LVEF was assessed, patients age 62 years or younger showed a statistically significant effect of therapy. Patients in the BMC group demonstrated an average increase in LVEF of 3.1 percent from baseline to 6 months, whereas patients in the placebo group showed a decrease of −1.6 percent.

"In the largest study to date of autologous BMC therapy in patients with chronic ischemic heart disease and LV dysfunction, we found no effect of therapy on prespecified end points. Further exploratory analysis showed a significant improvement in LVEF associated with treatment. Our findings provide evidence for further studies to determine the relationship between the composition and function of bone marrow product and clinical end points. Understanding these relationships will improve the design and interpretation of future studies of cardiac cell therapy," the authors write.

ACC2012特集

患者の生存期間はPCI後よりもCABG後の方が長い

ASCERT Trial：スタディの結果、生存期間は冠動脈形成術よりも冠動脈バイパス術を施行された患者の方が長いことが示唆された

ASCERT Trial: Study suggests better survival in patients undergoing bypass surgery compared to coronary angioplasty

冠動脈バイパス術は低侵襲の経皮的冠動脈インターベンションよりも生存率を上昇させるようであるとの新たなエビデンスが示され、第61回American College of Cardiology学会で発表され、同時にNew England Journal of Medicineに掲載された。過去のいくつかのスタディにより、この2つの治療法の長期予後は同等であることが示唆されたが、バイパス手術の予後の方が良好であることを示したスタディもあった。ASCERTトライアルにおいて研究者らはAmerican College of Cardiology Foundation CathPCIデータベース、Society of Thoracic Surgeons CABGデータベース、およびU.S. Medicare請求データベースから得た患者データを組み合わせ、2004～2008年に治療を受けた冠動脈バイパス術後患者86,000人およびPCI後患者103,000人の生存率を比較した。治療後4年間の死亡率はPCIを施行された患者において冠動脈バイパス術を選択された患者よりも高かった（それぞれ20.8%および16.41%）。この結果は解析した全てのサブグループにおいて同様であった。このスタディは安定虚血性心疾患患者における血行再建術の選択決定の際の情報として役に立つだろう、と筆者らは述べている。

Full Text

Patients with coronary heart disease and their doctors have long been challenged by the decision of whether to pursue bypass surgery or opt for the less-invasive percutaneous coronary intervention (PCI). New evidence reveals bypass surgery appears to carry a higher long-term survival rate, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

The study analyzed health outcomes of 190,000 patients across the United States to compare the results of bypass surgery to those of PCI. The study found that patients who underwent PCI had a higher death rate in the first four years after treatment than those who had opted for bypass surgery (20.8 percent and 16.41 percent, respectively).

"Our study is the most general one ever done because it uses data from across the whole country. It is also much larger than any other study," said William S. Weintraub, M.D., chair of cardiology at Christiana Care Health System and the study's lead investigator. "Combining data from several large databases, we found that survival was better with coronary surgery than percutaneous coronary intervention."

Dr. Weintraub cautioned that the results do not mean bypass surgery is best for every patient. "It does push the needle toward coronary surgery, but not overwhelmingly so," said Dr. Weintraub. "When we're recommending coronary surgery to patients, even though it is a bigger intervention than PCI, we can now have a little more confidence that the decision is a good one."

While some previous studies have suggested the two treatments have similar long-term outcomes, others have also shown better outcomes with bypass surgery. Patients and doctors tend to choose the less-invasive PCI when both treatments are an option.

The study, called the ACCF and STS Database Collaboration on the Comparative Effectiveness of Revascularizaton Strategies (ASCERT), combined patient data from the American College of Cardiology Foundation CathPCI database, the Society of Thoracic Surgeons CABG database and the U.S. Medicare claims database to compare survival rates among 86,000 bypass surgery patients and 103,000 PCI patients who underwent treatment from 2004-2008. Dr. Weintraub says that a major limitation of observational studies, such as this one, is that the groups may not have the same level of risk, and so it is possible that the worse outcomes in the PCI patients were related to these patients being sicker overall. "We used sophisticated statistics to account for different levels of risk, but there may be differences between the two groups that we could not account for," he said.

The large number of cases allowed the researchers to compare results across many subgroups. "What was a surprise to us all was how consistent the data were no matter what analytic approach we used, and how consistent the data were across all subgroups," said Dr. Weintraub. "Survival was better with coronary surgery for all patient subgroups. This study should help inform decision making concerning the choice of revascularization in patients with stable ischemic heart disease."

This study was funded by the National Institutes of Health's National Heart, Lung and Blood Institute.

This study was simultaneously published online in the New England Journal of Medicine.

ACC2012特集

オンポンプバイパス術とオフポンプバイパス術の短期予後は同等である

CORONARY trial：オンポンプバイパス術とオフポンプバイパス術に関する最大のスタディの結果、両者ともに安全に施行できることが証明された

CORONARY trial: Largest study of on-pump and off-pump bypass proves both can be done safely

人工心肺使用（オンポンプ）および人工心肺不使用（オフポンプ）で施行される冠動脈バイパス術を比較した結果、全体の技術に差はなかったが臨床的には明らかな差があったことが示されたとの研究結果が第61回American College of Cardiology学会で発表された。2007年10月以降、CORONARYトライアルでは、冠動脈疾患を有しCABGを予定された患者4,752人（平均年齢67.6歳、80.0%男性）を徹底的に評価し、確実にオフポンプまたはオンポンプ手術いずれもが適応であることを確認したあとでこれらのいずれかの手術に無作為に割り付けた。患者当たりの平均グラフト数は3.1であった。バイパス術後30日以内の死亡、心筋梗塞、腎不全および脳卒中からなる一次総アウトカムに関しては、統計学的に同等であった（オフポンプ患者9.9%およびオンポンプ患者10.3%）。同様に、この総アウトカムの個々のイベントについても差がなかった。オフポンプ手術の方が必要とする血液製剤の量、出血による再手術、肺合併症および急性腎障害が少なかったが、再血行再建術の施行がより多かった。この発現率はまれであった（オフポンプ群で2,375人中16人、あるいは0.7%に対しオンポンプ群で0.2%）。

Full Text

A large randomized trial comparing bypass surgery done with a heart-lung machine (on-pump) and without it (off-pump) found no differences in results between techniques overall but some clinically relevant differences, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Off-pump coronary artery bypass graft (CABG) surgery eliminates the need to insert a cannula into the aorta, to cross-clamp the aorta, connect the patient to the heart-lung machine, and stop and restart the heart, suggesting that patients would do better with this approach. However, small, randomized clinical trials and meta-analyses have not been able to determine conclusively whether one CABG technique has better outcomes than the other. The CORONARY trial, conducted at 79 centers in 19 countries, compared the risks and benefits of off-pump and on-pump bypass in the largest patient population studied to date. While the CORONARY trial was recruiting patients, data from the ROOBY (Randomized On/Off Bypass) trial were published showing poor results for off-pump bypass.

"After ROOBY's results, we looked again at our trial design and decided to continue, with the approbation of the Data Safety Monitoring Board," said André Lamy, MD, Division of Cardiac Surgery at Canada's McMaster University in Hamilton, ON, and one of the study's three lead investigators. "ROOBY was done through the U.S. Veterans Administration at only 18 hospitals. Our trial was international and much larger, it had more women and sicker patients and our surgeons were more experienced in off-pump procedures"

Since October 2007, the CORONARY trial has enrolled 4,752 patients with coronary artery disease who were slated for CABG and randomly assigned to off-pump or on-pump surgery after a complete assessment to make sure they were suitable candidates for both techniques. The mean patient age was 67.6 years, 80.9 percent were men and the average number of grafts was 3.1 per patient.

For the primary composite outcome of death, myocardial infarction, kidney failure and stroke at 30 days post-bypass, the results were statistically neutral: 9.9 percent for off-pump patients and 10.3 percent for the on-pump group. Similarly, no differences were seen for individual events of the composite outcome. These results were a surprise to the researchers. Based on previous meta-analyses, Dr. Lamy and his colleagues expected that off-pump CABG would decrease the rate of stroke and renal failure.

"We found that off-pump did reduce the amount of blood products needed, reoperation for bleeding, pulmonary complications and acute kidney injury, but there was also more revascularization in off-pump patients, meaning that surgery didn't work completely," Dr. Lamy said. This was a rare occurrence (16 of 2,375 patients, or 0.7 percent versus 0.2 percent in the on-pump group), but it is considered a technical failure and requires the patient to return to the operating room for a repeat CABG or for a stent in the cath lab, where imaging systems guide those catheter-based procedures.

"This introduces a new concept in cardiac surgery, allowing patient-specific decisions for bypass surgery," Dr. Lamy said. "Off-pump procedures are trickier and more stressful, and the benefit is for the patient, not the surgeon, so in many places, they're simply not done. My goal is to persuade surgeons to individualize the technique – to do off-pump bypass or on-pump when indicated – so their patients will benefit."

The CORONARY trial will conduct safety and efficacy follow-up at five years and assess total costs and neuro-cognitive results at 30 days and at five years after CABG. The 30-day cost data and neuro-cognitive results are expected within six months.

ACC2012特集

血管形成術後の抗血小板薬3剤併用は有効である

HOST-ASSURE:血管形成術後の血栓予防において抗血小板薬3剤併用は倍用量の2剤併用と同等に有効である

HOST-ASSURE: Three-drug regimen equal to double-dose two-drug approach in preventing clots after angioplasty

血管形成術後血栓予防薬の比較において、アジアで好まれる3剤併用療法は欧米諸国の高リスク患者に対し一般的に使用される倍用量2剤併用療法と同等に安全で有効であることが示されたとの研究結果が第61回American College of Cardiology学会で発表された。アスピリンと倍用量（150mg）クロピドグレルを用いた倍用量2剤併用療法（DDAT）は有望な抗血小板療法である。アジアにおける高リスク患者に対する3剤併用抗血小板療法（TAT）では、2剤併用抗血小板療法（DAT:アスピリンとクロピドグレル75mgの併用）にシロスタゾールを併用する。HOST-ASSUREスタディでは患者をTAT（1,879人）またはDDAT（1,876人）に無作為に割り付けた。一次エンドポイントは、血管形成術後1ヵ月以内の心血管関連死、非致死性心発作、脳卒中および重大な出血のイベント発現であった。これらのイベントの合計がTAT群では23例（1.2%）、DDAT群では27人（1.4%）であり、倍用量2剤併用療法に対する3剤併用療法の非劣性が示された。心筋梗塞はTAT群の方が少なかった（1例対5例）。副作用はDDATの方が少なかった（8例）が、TAT群の34例のうち生命を脅かしたり重篤な有害反応を来したりするものはなかった。

Full Text

In a comparison of drugs to prevent blood clots after angioplasty, a three-drug regimen favored in Asia to increase anti-clotting effect was found to be as safe and effective as a double-dose two-drug treatment commonly used in high-risk patients in Western countries, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Angioplasty comes with a known risk of blood clots. For that reason, treatment with anti-platelet drugs such as clopidogrel is standard after angioplasty. Double-dose dual anti-platelet therapy (DDAT), using aspirin and double-dose (150 mg) clopidogrel, is a potent anti-platelet regimen for high-risk patients undergoing angioplasty. In Asia, cilostazol is added to dual anti-platelet therapy (DAT: aspirin and 75 mg of clopidogrel) in a regimen of triple anti-platelet therapy (TAT) in high-risk patients. Several studies have demonstrated that cilostazol does more than prevent platelet clumping; it also shows activity in preventing restenosis, vasodilation, protecting kidneys, and improving blood levels of cholesterol and triglycerides.

"TAT is widely used in Korea and Japan because we experienced the benefit of cilostazol in terms of major adverse cardiovascular events (MACE) after angioplasty," said Hyo-Soo Kim, MD, PhD, director of cardiac catheterization and coronary intervention at Seoul National University Hospital, Republic of Korea, and the study's principal investigator. "In the numerous clinical studies about angioplasty, we have an impression that the MACE rate is lower in Korean studies than in Western ones."

Although previous studies support the addition of cilostazol to conventional dual anti-platelet therapy, cilostazol is not familiar to many Western physicians because it was developed by a Japanese company that has neither marketed it widely outside Asia nor sponsored a large clinical trial of the drug. "Most clinical evidence supporting cilostazol's benefit comes from investigator-initiated trials like ours," Dr. Kim said. "HOST-ASSURE is the first large-scale randomized trial to directly compare the two treatment strategies and confirm the non-inferiority of TAT compared with DDAT."

The 2 x 2 factorial trial was designed to compare the two anti-platelet regimens and two types of drug-releasing stents (data to be reported in the future). Patients were randomly assigned to TAT (1,879 patients) or to DDAT (1,876 patients). All patients received 300−600 mg of clopidogrel plus 300 mg of aspirin before angioplasty with (TAT) or without (DDAT) a loading dose of 200 mg of cilostazol. In the TAT group, 100 mg of cilostazol twice daily was added to DAT for a month after the procedure; in the DDAT group, the maintenance regimen was 150 mg of clopidogrel with aspirin.

The primary endpoint was the occurrence of events including cardiovascular-related death, non-fatal heart attack, stroke and major bleeding at one month after angioplasty. That total was 23 patients (1.2 percent) in the TAT group and 27 patients (1.4 percent) in the DDAT group, demonstrating non-inferiority of the three-drug regimen compared with the double-dose two-drug treatment. The TAT group had fewer heart attacks (one patient vs. five). The DDAT group had fewer side effects (eight patients), but none of the 34 patients in the TAT group who had side effects developed life-threatening or severe adverse reactions. The most frequent side effects of cilostazol are headache and gastrointestinal trouble, and most of the side effects are reversible, Dr. Kim noted. Patients will be followed for three years.

"This study provides evidence for the already popular adjunctive use of cilostazol in clinical practice in Asia – in particular in Korea and Japan," Dr. Kim said. "If TAT is equivalent to a potent regimen such as DDAT that is used for high-risk patients, TAT would be preferred because it has additional vascular biologic benefit on top of its anti-platelet effect."

HOST-ASSURE was sponsored by the Ministry of Health and Welfare, Republic of Korea, and supported by a grant from the Innovative Research Institute for Cell Therapy, Seoul National University Hospital, and an unrestricted grant from Boston Scientific Korea. The funding sources had no role in study design, data collection or analysis. Dr. Kim has no conflict of interest with the sponsor or funders.

ACC2012特集

新たなクラスの血小板阻害薬は有効であることがphase IIIトライアルで証明された

TRA 2°P-TIMI 50：標準的な抗血小板療法にvorapaxarを加えることにより再発性心血管イベントのリスクが軽減する

TRA 2°P-TIMI 50: Adding vorapaxar to standard antiplatelet therapy reduces risk of recurrent cardiovascular events

治験段階の抗血小板薬vorapaxarを標準的な抗血小板薬に追加することにより、既知の動脈硬化を有する患者の再発性心血管イベントリスクを軽減することができると第61回American College of Cardiology学会において発表され、同時に New England Journal of Medicineに掲載された。この無作為化二重盲検プラセボコントロール多国籍試験では、26,449人の患者において過去の心筋梗塞（17,779例）、脳卒中（4,883例）または下肢動脈の動脈硬化性狭窄（3,787例）などの確定した動脈硬化に対し標準的な抗血小板薬を投与し2年以上追跡した。参加者は標準療法と試験用血小板阻害薬（経口2.5mg1日1回）または標準療法とプラセボのいずれかを内服する群に無作為に割り付けられた。Vorapaxarは心血管死、MIまたは脳卒中をさらに13%（3年後に9.3%対10.5%、p<0.001）低下させた。この新たな心血管イベントの低下はMI既往を有する患者で最大であり、彼らにおいてはこれらのイベントが20%低下した（p<0.001）。

Full Text

Adding vorapaxar, an investigational platelet blocker, to standard antiplatelet therapy significantly reduces the risk of recurrent cardiovascular events in patients with known atherosclerosis according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Doctors routinely prescribe aspirin therapy to help prevent blood clot formation post-myocardial infarction. Other platelet blockers, such as clopidogrel, are often added for as long as a year but it is unclear whether adding any platelet blocker to aspirin beyond this timeframe is useful. Despite such therapies, survivors of myocardial infarction (MI) have an almost 15 percent chance of having another atherosclerosis-related event that brings them to the hospital within a year.

Now, researchers led by the TIMI Study Group at Brigham & Women's Hospital in Boston, Mass. have shown, for the first time, that adding a new antiplatelet agent on top of standard therapy, including aspirin, is effective for long-term secondary prevention in stable patients with a prior MI. When used with aspirin and other standard antiplatelet therapy in a broad group of patients with previous MI, stroke or peripheral arterial disease, vorapaxar reduced the risk of cardiovascular death, heart attack or stroke by an additional 13 percent (9.3 vs. 10.5 percent at three years, p<0.001). This reduction in new cardiovascular events appeared greatest in patients with prior heart attack, among whom there was a 20 percent decline in these events (p<0.001).

Vorapaxar is the first of a new class of investigational Protease Activated Receptor 1 (PAR-1) thrombin receptor antagonists. Unlike other antithrombotic drugs, vorapaxar blocks thrombin from stimulating platelets to stick together and create clots. Blood thinners, like Coumadin, and other antiplatelets like aspirin or clopidogrel, do not directly target these same actions of thrombin.

"In the lab, we have seen very compelling science showing the importance of thrombin's action on platelets causing blood clots in arteries," said David A. Morrow, MD, MPH, senior investigator at the TIMI Study Group, director of the Samuel A. Levine Cardiac Unit at Brigham & Women's Hospital, and the study's lead investigator. "This is the first study to show definitively that blocking this pathway reduces the risk of suffering another cardiovascular event."

This randomized, double blind, placebo-controlled, multinational study followed 26,449 patients for more than two years while receiving standard antiplatelet therapy for established atherosclerosis, including previous MI (n=17,779), stroke (n=4,883), or atherosclerotic narrowing in the arteries of the legs (n=3,787). Participants were randomly assigned to either take the investigational platelet blocker (2.5 mg orally once daily) with standard therapy, or a placebo with standard therapy.

"It's exciting to find clearly that we can reduce the risk of a recurrent thrombotic event by adding another platelet inhibitor to aspirin over the long-term," Dr. Morrow said. "Adding this new class of antiplatelet therapy reduced the risk of new cardiac events in stable patients, especially among the subset of patients with a prior heart attack."

Dr. Morrow commented that if vorapaxar becomes available for clinical use, it does not appear suitable for everyone with atherosclerosis. "Of the groups we studied, the benefit was compelling to us only in patients with a prior MI," said Dr. Morrow. In addition, this new therapy was found to increase the risk of severe bleeding, including intracranial bleeding. The risk of intracranial bleeding was highest among patients who have suffered from previous strokes; vorapaxar would likely not be appropriate for stroke victims or patients at high risk of bleeding. Stroke patients who were enrolled in the study ended their participation early after advice by the study's data and safety monitoring board.

Patients who took vorapaxar had significantly more bleeding events (GUSTO moderate or severe bleeding at three years 4.2 percent with vorapaxar vs. 2.5 percent with placebo, p<0.001). Intracranial hemorrhage was higher with vorapaxar than placebo (1.0 vs. 0.5 percent, p<0.001) with lower overall rates in patients with no history of stroke (3 years: 0.6 percent with vorapaxar vs. 0.4 percent with placebo, p=0.049).

Dr. Morrow and his team look forward to learning more from this very rich dataset to identify the patients who may have the best balance of benefit vs. bleeding risk with this agent.

The study was funded by Merck Research Laboratories. Dr. Morrow has received research grant support and consulting fees from Merck and other manufacturers of antiplatelet and anticoagulant therapies.

This study was simultaneously published in New England Journal of Medicine.

ACC2012特集

テレメディスンは薬物療法管理および患者ケアを改善する

薬物療法、血圧および全体的な心臓リスクは自己モニターおよび報告により改善する

Pharmacotherapy, blood pressure and general cardiac risk improve with self-monitoring and reporting

インターネットベースのテレメディスンシステムは、従来の定期的な受診よりも、より適切で有効な薬物療法、より良好な血圧コントロールおよび全体的な心血管リスク低下に繋がるとの研究結果が第61回American College of Cardiology学会で発表された。2つの大規模病院の患者らが組み入れられ、従来通りの管理または従来の管理にテレメディスンを加えた群に無作為に割り付けられた。テレメディスン群患者は心血管疾患リスク軽減に関する助言を受け、家庭用血圧計を与えられ使用法を教わった。彼等は自身の血圧、心拍、体重、1日の歩数、および喫煙数を週2回6ヵ月間にわたり報告するよう求められた。6ヵ月間の介入終了までにコントロール群の処方薬はほとんど変更されなかったのに対し、テレメディスン群では数は少ないが処方薬数は有意に増加した（2.20±1.20から2.34±1.15, p=0.004）。テレメディスン群において処方薬数が増加したのは過剰治療を意味するのではなく、患者の自己モニターおよび報告に基づき薬剤の増加かつ/または調整をより適切に行ったことを反映している、と筆者らは述べている。

Full Text

Internet-based telemedicine systems appear to lead to more appropriate and effective pharmacotherapy, better blood pressure control and an overall reduction in cardiovascular risk compared to conventional, periodic office visits, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Patients who reported blood pressure readings more frequently via a web-based portal received more timely treatment decisions and medication adjustments from their health care team compared to a control group of hypertensive patients who had routine office visits. These findings have important implications for clinical practice given that – aside from lifestyle changes – antihypertensive medications are the most effective way to help patients lower their blood pressure.

"The ongoing monitoring and reporting of blood pressure levels seems to bring about important changes in physician prescribing habits, which we think ultimately benefit patients," said Val Rakita, M.D., internal medicine resident at Temple University Hospital and the study's co-investigator. "Based on our findings, physicians appear to prescribe more blood pressure medications for those patients who continue to have high blood pressure despite the medications they are on. In fact, in one subset of patients, not only did we find they were prescribed more blood pressure medications, it also actually led to a larger blood pressure reduction compared to all other groups."

In this study, patients from two large medical centers were recruited and randomized to receive either usual care or telemedicine with usual care. Patients in the telemedicine group received counseling on cardiovascular disease risk reduction and were given a home blood pressure cuff and trained on how to use it. They were asked to report their blood pressure, heart rate, weight, steps taken per day, and tobacco use twice weekly for six months. By the end of the six-month intervention, medications prescribed to those in the control group were virtually unchanged, while there was a small, but significant, increase in the number of medications ordered (2.20±1.20 to 2.34±1.15, p=0.004) for patients in the telemedicine group.

Dr. Rakita says that prescribing more medication in the telemedicine group did not signify overtreatment, but was a reflection of more timely decisions to increase and/or adjust medications based on patient self-monitoring and reporting.

Unlike other types of telemedicine, which may include telephone interactions, this study looked at an internet-based system that supported ongoing communication between patients and health care providers.

"This allows for greater convenience for both sides and most likely led to the better results," Dr. Rakita said. "High blood pressure is one of the most important risk factors for cardiovascular disease. Employing an internet-based patient-physician communication system that can help lower blood pressure could make it possible to reduce patients' cardiovascular risk."

This was a secondary analysis of a telemedicine trial of 241 patients with uncontrolled hypertension (BP≥ 150/90 mmHg). More than half of study participants (56.8 percent) were taking one or two blood pressure-lowering medications at the start of the study. The initial average blood pressure was 156/89±14/11 among all patients. All patients had baseline and six-month follow-up visits. Monthly reports on blood pressure and treatment guidelines were provided to both the patient and physician in the telemedicine group.

Although there was no significant difference in the decrease in blood pressure between the two groups overall, the primary group of non-diabetic patients using telemedicine was found to have lower blood pressure compared to all other groups. Dr. Rakita said it is reasonable to believe that the use of additional blood pressure medications in the telemedicine group would have translated to an associated drop in blood pressure in these patients had they been followed for a longer period of time.

"The goal of telemedicine is to reduce disease and the burden on the healthcare system in a cost-effective way," he said. "By showing that a relatively low-cost, internet-based telemedicine system can change physicians' prescribing habits and perhaps [lower] blood pressures, this can lead to obvious benefits to patients and the healthcare system."

This study was funded by the Agency for Healthcare Research and Quality.

ACC2012特集

閉塞血管については、百聞は一見に如かず

自身の冠動脈石灰化を実際に見た患者はスタチン療法や減量プログラムへのアドヒアランスが良好である

Better adherence to statin therapy and weight loss programs in patients who actually view their coronary artery calcification

血管壁内へのカルシウム沈着を単に見ることで患者はスタチン療法および減量勧告の遵守に駆り立てられるようであるとの研究結果が第61回American College of Cardiology学会で発表された。2つの関連したスタディにおいて、心臓コンピュータ断層撮影を用いた冠動脈石灰化（CAC）スコアリングを施行された患者が自身の動脈画像を見せられた。疾患が最も重症で自分の心臓画像を見た患者は、検査を受けた結果疾患が軽度またはなかった患者と比較し、スタチンを指示通り内服する確率が2.5倍高く減量する確率が3倍以上高かった。スタチン調査（患者2,100人）の結果、CACスコアが0の者ではコンプライアンスが最も低く（36%）、CACスコアが上昇するとともに上昇した（1～99、51.8%;100～399、56.5%;>400、59.1%; 傾向分析に関しp<0.001）。減量調査（患者518人）に関しても同様の傾向が認められ、冠動脈石灰化所見のない者では20%しか減量しなかったのに対し最も重症の者（CAC>400）においては40%減量した。

Full Text

It seems a picture is worth more than a thousand words for people who see evidence of coronary artery disease. Simply seeing a build-up of calcium in the walls of the arteries appears to prompt patients to better adhere to both statin therapy and recommendations for weight loss, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

In two related studies, patients undergoing coronary artery calcium (CAC) scoring with cardiac computed tomography were shown images of their arteries. The researchers found the most striking results among patients with increasingly severe disease.

Individuals with the most severe disease, those with a CAC score over 400, who saw images of their heart were 2.5 times more likely to take statins as directed and more than three times more likely to have lost weight compared to those who had a scan and saw little or no evidence of underlying disease. These findings are significant because patient compliance is often a major barrier to effectively preventing and treating heart disease. For instance, compliance to statin therapy has been reported to be as low as 20 to 50 percent.

"Beyond the diagnostic and predictive value of cardiac computed tomography, it is also quite beneficial in terms of motivating people to pursue behaviors that we know result in a reduction in cardiovascular mortality and morbidity," said Nove Kalia, MD, one of the lead investigators for both studies. "Taking medication as directed, as well as adhering to behavioral modification, such as exercise for weight loss, can both have a huge impact on cardiovascular events going forward. What's most interesting is that the higher the person's calcium score, the more likely they were to be compliant."

Dr. Kalia said that while previous studies have investigated the impact that patient-viewed cardiac scans can have on behavior, these are the first large-scale studies to corroborate similar results seen in a previous study looking at a reduction in Framingham risk score; they also found statistically significant findings across all CAC scores. The researchers split groups into quartiles based on their score, which correlates in linear fashion with the severity of their disease.

The statin study included 2,100 individuals who underwent baseline CAC testing and completed a follow-up questionnaire; it found compliance was lowest (36 percent) among those with a CAC score of 0, which is indicative of very little to no disease, and was then found to increase as CAC scores increased. (1 to 99, 51.8 percent; 100 to 399, 56.5 percent; > 400, 59.1 percent; p <0.001 for trend). In logistical regression analysis, those with CAC scores of 1-99, 100-400 and >400, as compared to those with a score of 0, were 2.0- (95 percent CI 2.0-3.5 p<0.001), 2.4- (95 percent CI 2.0-3.5 p<0.001) and 2.6- (95 percent CI 2.0-3.5 p<0.001) fold respectively more likely to adhere to statin therapy when adjusted for age, gender and race.

Similar trends were found in the weight loss study (518 patients) in which behavioral modification resulting in weight loss was also lowest among those who saw the scan and did not have any evidence of coronary artery calcification. These individuals only lost weight 20 percent of the time, whereas those with severe disease (CAC>400) lost weight 40 percent of the time. In logistical regression analysis, those with CAC score of 1-99, 100-400 and >400, as compared to those with a score of 0, were 2.0- (95% CI 1.1.0-3.9 p<0.001), 3.6- (95% CI 1.7-7.3 p<0.001) and 3.3- (95% CI 1.6-6.9 p<0.001) fold respectively more likely to lose weight when adjusted for age, gender and race.

"Seeing a coronary artery calcium scan gives patients a visual picture of how severe their disease is, and this picture seems to have a really big impact," said Dr. Kalia. "With increasing use of noninvasive imaging, it seems we already have a powerful tool in helping to motivate patients to be compliant. While we haven't clarified whether this increased compliance results in reductions in event rates we have extrapolated that this would likely be the case. I think we may find this can also help improve outcomes."

Dr. Kalia said this is an important line of inquiry given that studies showing the benefits of medications and weight loss to prevent or treat heart disease assume fairly high compliance rates that are not sustained in real life. He said he hopes that cardiac images, which are already a routine part of patient evaluation, further motivate patients to take action for their heart health.

Because this was a retrospective study, the reasons for doing the CAC study were varied across patients. All patients underwent baseline CAC testing; those in the statin study then completed a comprehensive follow-up questionnaire and those in the weight loss study returned for a follow-up scan with documented weight taken at visits one and two.

The database Dr. Kalia and his team used went back a decade, meaning the indications for getting scans have changed and expanded since the start of the study. Today, coronary CT scans are most commonly used to risk stratify people who arrive at the hospital with chest pains or suspected coronary disease and are considered to be at intermediate risk.

Additional research is warranted to confirm these findings prospectively and to look at how increased compliance translates to improved outcomes for patients.

Dr. Kalia reports no conflicts of interest.

ACC2012特集

ERにおける心臓CTにより胸痛の原因が迅速に同定できる

ROMICAT II:心筋梗塞の疑いのある患者の評価において心臓CTはより迅速で有効である

ROMICAT II: Cardiac CT is faster, more effective for evaluating patients with suspected myocardial infarction

胸痛の評価において心臓CT冠動脈造影を早期に使用することにより、心筋梗塞治療のために入院させるべき患者と帰宅させても安全な患者とを医師がすぐに鑑別でき、時間と医療費を節約できるとのROMICAT IIスタディの結果が第61回American College of Cardiology学会で発表された。ROMICAT IIスタディは、胸痛を伴い救急外来（ER）を受診し、症状および早期ER評価（血液検査および心電図の結果）に基づくMIリスクが中等度の患者1,000人を組み入れた。患者は、心臓CT検査を初回の診断検査として施行される群または、患者の状態や医師の判断に基づき心臓負荷検査を行う群または全く検査を行わない標準的処置群に無作為に割り付けられた。ERにおいて、CT検査で胸痛患者を評価することにより、患者の平均病院滞在時間は18時間減少した。CT検査を受けた患者の半分が9時間以内に安全に退室したのに対し、標準治療を受けた患者のうち9時間以内に退室したのはわずか15%であった。CTを使用することにより標準治療よりもERのコストが10～20%節約できた。

Full Text

Cardiac computed tomography angiography scans can provide a virtually instant verdict on whether chest pain is from blockage of the coronary arteries. When used early to evaluate chest pain, the scans save patients and hospitals time and money by allowing doctors to quickly determine who should be admitted for treatment for a heart attack and who can be safely sent home, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

The ROMICAT II study involved 1,000 patients at nine hospitals across the United States. The results showed that using CT scans to evaluate patients with chest pain in the emergency room (ER) reduced their average time spent in the hospital by 18 hours. Half of the patients receiving the CT scan were safely discharged within nine hours compared to only 15 percent of patients receiving standard care. The use of CT resulted in 10 percent to 20 percent cost savings to the ER over standard care.

"These data suggest that doing a CT scan early benefits both patients and physicians," said Udo Hoffmann, MD, MPH, director of cardiac imaging at Massachusetts General Hospital and the study's lead investigator. "Physicians benefit because they can discharge many patients from the overcrowded ER very quickly, with solid reassurance that they're not having a heart attack, while the standard evaluation takes much longer to assess whether the symptoms stem from blockages in their arteries. Patients benefit from an earlier diagnosis and can safely go home from the ER earlier."

The study enrolled patients who arrived in the ER with chest pain and who were at intermediate risk for a myocardial infarction based on their symptoms and initial ER evaluation, which included blood tests and electrocardiogram results. Patients were randomly assigned to receive either a CT scan as their first diagnostic test or standard care, which could include a cardiac stress test or no tests at all, depending on the patient's situation and physician preference.

Because healthy patients were discharged much earlier and often needed just a CT scan and a single blood test, their health care costs were lower. "It looks like CT saves time and money for the health care system in those who have no blockages in their coronary arteries. Though only a modest amount of money is saved per patient, it may save a lot of money considering the millions of patients affected across the country," Dr. Hoffmann said. "CT allows you to spend your health care dollars focusing on the people who are actually sick. One could argue that this is a better use of health care resources."

CT scans also provide useful prognostic information that doctors can refer back to if the patient experiences chest pain again. "If their CT scan shows clear heart arteries, we know from our previous ROMICAT I study that their prognosis over the next two years is really good, which can be useful farther down the road," Dr. Hoffmann said.

Other studies have offered somewhat conflicting assessments of the efficiency and effectiveness of using CT scans as the first diagnostic test for chest pain. This trial is unique because the CT scan was done much earlier in the evaluation process compared to other studies and was used in a real-life setting. Moreover, this was the first trial to show that physicians could act on the information from the CT scan in a way that improved a measure of care – safe earlier discharge – after ER presentation for chest pain. "It shows that cardiac CT is ready for use in a pragmatic health care setting, as it is more effective than the standard ER evaluation," said Dr. Hoffmann.

This study was funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

ACC2012特集

肺塞栓症に対するrivaroxabanの効果は標準治療の効果と同等である

EINSTEIN PE:新たな経口抗凝固薬rivaroxabanは肺塞栓症に対する標準的な治療法よりも安全である

EINSTEIN PE: New oral anticoagulant rivaroxaban safer than standard approach to treat pulmonary embolism

肺塞栓症の初回治療および長期治療における重要な安全性指標に関し、新たな経口抗凝固薬は標準的な注射薬治療よりも成績が優れていたとの研究結果が第61回American College of Cardiologyにおいて発表され、New England Journal of Medicineオンライン版に掲載された。EINSTEIN-PEトライアルは2,419人の患者をrivaroxaban群（15mg1日2回内服を3週間の後に20mg1日1回）および2,414人を標準治療群（体重1kg当り1.0mgのenoxaparin1日2回を5日以上継続しINR2.0以上が2日間以上持続し、それに加えビタミンK阻害薬を無作為化後48時間以内に開始しINRを2.0～3.0とするように用量調節した時点でenoxaparinを中止）に無作為に割り付けた。Rivaroxaban群の再発率は2.1%（50件）であったのに対し、標準療法では1.8%（44件）であり、有効性に関する非劣性が有意に認められた。出血に関する安全性評価に関しては、rivaroxabanの方がはるかに良好であった:重大なまたは臨床的に明らかな出血に関する主要な安全性評価では、10.3%であったのに対し標準治療では11.4%であった;重大な出血のみに関しては、1.1%であったのに対し標準治療では2.2%であった。一次エンドポイント発現率は患者背景に関係なく同等であった。

Full Text

A novel oral anti-coagulant outperformed the injected standard therapy on important safety measures for initial and long-term treatment of pulmonary embolism (PE) and showed comparable efficacy, according to data from the EINSTEIN-PE trial presented at the American College of Cardiology's 61st Annual Scientific Session.

Venous thromboembolism (VTE) is the third most common cardiovascular disease, and PE is the third most common cause of hospital-related death. EINSTEIN-PE is one of a series of large international phase III clinical trials of the anti-coagulant rivaroxaban to treat VTE or prevent a recurrence in patients with acute PE or DVT. The Food and Drug Administration has approved rivaroxaban as the only oral anti-coagulant for prevention of VTE in patients who have knee or hip replacement, procedures that carry clotting risks.

The trial compared rivaroxaban with standard therapy – injection of the anti-coagulant enoxaparin, followed by a vitamin K antagonist (VKA; either warfarin or acenocoumarol) chosen by each participating site – to demonstrate that the oral drug as a single agent is equivalent to the complicated two-drug standard therapy. In the standard regimen, enoxaparin must be given as an injection, and the VKA must be monitored with INR testing to make sure the dose is adequate and safe, because common drugs such as antibiotics, alcohol and some foods interact with VKAs: the higher the INR number, the higher the risk of bleeding.

"If you give standard treatment in the right way, it's a perfectly effective drug with almost 90 percent reduction in recurrent thrombosis, but it has to be well controlled," said Harry R. Buller, M.D., Ph.D., professor of vascular medicine at the Academic Medical Center, Amsterdam, The Netherlands, who chairs the program for the three EINSTEIN studies. "The reason people look for alternatives is that it's a nightmare to give. Rivaroxaban makes things easier for everybody – patients and physicians. Our major aim was to show that it's at least as good as standard care."

The study, conducted at 263 sites in 38 countries, randomly assigned 2,419 patients to the rivaroxaban arm and 2,414 to standard treatment. All enrolled patients had a primary diagnosis of PE, and 25 percent in both groups also had DVT. Patients were treated for three, six or 12 months (average, seven) as deemed appropriate by each clinician before randomization. The rivaroxaban group received 15 mg twice a day for three weeks followed by 20 mg once a day. In the standard-therapy arm, the regimen was enoxaparin at 1.0 mg per kg of body weight twice daily, continued at least five days and stopped when the INR was 2.0 or more for two consecutive days, plus a VKA started within 48 hours after randomization with dose adjustment to maintain an INR of 2.0 to 3.0.

Rivaroxaban's efficacy was highly significant for non-inferiority with 2.1 percent recurrences (50 events) vs. 1.8 percent (44 events) in the standard-therapy arm. On safety measures of bleeding, rivaroxaban did much better: principal safety measure of major or clinically relevant bleeding, 10.3 percent vs. 11.4 percent for standard treatment; for major bleeding alone, 1.1 percent vs. 2.2 percent for standard therapy. Rates for primary endpoints were similar in both study arms regardless of patient characteristics.

"Physicians want to know about major bleeding, the most important safety outcome, and rivaroxaban was highly significantly superior. This was our most astonishing finding," Dr. Buller said. "Rivaroxaban is just as good as standard treatment for PE – these data are pretty convincing – and this is an oral-only approach, which makes it very simple. The subcutaneous injections can be hazardous as well."

Researchers also will be doing a subgroup analysis of the 8,200 patients in the EINSTEIN-PE and EINSTEIN-DVT trials to see if they can identify a risk profile for patients who are likely to have bleeding problems on standard treatment or the new drug.

The trial was sponsored by Bayer HealthCare and Janssen Pharmaceuticals. Dr. Buller is reimbursed for patients who participate in the study, travel costs and administrative time, and those funds go to the hospital.

This study was simultaneously published online in the New England Journal of Medicine at the time of presentation and will appear in the April 2012 print edition.

ACC2012特集

妊娠は心筋梗塞のリスクを上昇させる

妊娠中の心筋梗塞は一般の人々よりも重症になる傾向にある

Myocardial infarction during pregnancy tends to be more serious than among general population

妊娠中の心筋梗塞（MI）はより重症になり合併症が多く、また非妊娠集団に一般的に認められる原因とは異なる原因で発症する傾向にあり、一部の症例では標準的な治療法が必ずしも最良ではないとの研究結果が第61回American College of Cardiology学会で発表された。同じ研究グループによる過去の2つの調査を拡大した今回のスタディでは、2005年以降に発症した新規発症妊娠関連MI、150例を解析した。解析の結果、ほとんどの妊婦は、高血圧、糖尿病または高脂血症などの一般的な心血管リスクファクターを有さず、にもかかわらずより重症のMIを有する傾向にあった。実際、これらの女性の死亡率は7%であり、同年代の非妊娠患者において予測される死亡率の2～3倍高かった。さらに、一般集団においては動脈硬化がMIの最も一般的な原因であるが、妊婦においてはこれは原因の3分の1に過ぎなかった。より多い原因が冠動脈解離であった。冠動脈解離は血栓溶解療法のようなガイドラインで推奨されている標準治療を用いると実は悪化する可能性があることも研究者らは明らかにした。

Full Text

Myocardial infarctions (MI) during pregnancy tend to be more severe, lead to more complications, and also occur for different reasons than commonly seen in the non-pregnant general population, suggesting that, in some cases, the standard approach to managing this condition may not always be best, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

The changes brought about by pregnancy, including the dramatic shift in hormones and increased volume of blood being pumped through the body, can increase a woman's risk of MI during pregnancy and in the 12 weeks after delivery. There is limited clinical information about how to optimally treat—and perhaps, more importantly, how not to treat—MI during pregnancy and post partum. This study, which is an extension of two previous surveys by the same research group, analyzed 150 new cases of MI associated with pregnancy occurring since 2005 to better understand how heart attacks occur and are being treated in pregnant women.

The analysis found that most pregnant women did not present with traditional cardiovascular risk factors, such as high blood pressure, diabetes or high cholesterol levels, yet they tended to have more serious MIs. In fact, the death rate in these women was 7 percent, which is two to three times higher than what is expected in non-pregnant patients of the same age. In addition, MIs in most of these women were caused by different mechanisms than those occurring in the non-pregnant general population.

"Despite advances in the management of myocardial infarction, we found that the rate of severe complications including heart failure, cardiogenic shock, and maternal or fetal mortality continues to be high among pregnant women compared to others," said Uri Elkayam, M.D., professor of medicine at the University of Southern California in Los Angeles and the study's lead investigator. "Therefore, every effort should be made for early diagnosis and appropriate treatment of pregnancy-associated acute myocardial infarction. We believe this study provides important information that can help guide clinicians, and hopefully improve the care of these patients."

While atherosclerosis is the most common cause of MI in the general population, this was only the cause in one-third of pregnant women. More common among pregnant women was coronary dissection. This is very rare in non-pregnant patients and is thought to occur during and immediately after pregnancy because of the weakening of the wall of the coronary arteries. Researchers also found that coronary dissection may actually be worsened by blind use of guideline-recommended standard therapies such as thrombolytic therapy.

"We have very clear guidelines for treating myocardial infarction in the general population. These guidelines, however, may not always apply to women with pregnancy-associated MI, and may actually cause more harm than good," said Dr. Elkayam. "It is, therefore, important to identify the cause of heart attack in pregnant women before deciding what therapies to use."

In particular, he said coronary angiography to identify the mechanism of MI and guide therapy is recommended in high-risk patients when urgent treatment is needed. At the same time, however, in several patients coronary dissection was reportedly caused by coronary angiography or angioplasty and led to either death, a need for extensive stenting or coronary bypass surgery. For this reason, Dr. Elkayam advises that stable and low-risk women with pregnancy-associated MI be treated conservatively.

Although the likelihood of having an MI during pregnancy is very low—estimated to occur in 1 in 16,000 deliveries—this risk is still three to four times higher in pregnant women than in non-pregnant women of the same age, according to Dr. Elkayam. As more women postpone having a first baby, the incidence of this condition is expected to grow.

This analysis included 150 cases published in the literature or consulted by the research team since 2005 and builds upon previous analysis of another 228 cases prior to 2005. More positively, maternal mortality has been decreasing steadily since the first survey, dropping from 16 percent prior to 2005 to 7 percent after 2005.

"This study is another step in better understanding the cause of pregnancy-associated heart attacks and their potential management," said Dr. Elkayam. He is hopeful that a national registry will be created to better track MIs in pregnant women and establish optimal protocols that lead to better outcomes.

ACC2012特集

LDL低下療法は早く開始するほどよい

LDL療法は若年で開始した方が高齢で開始するよりも有意に優れている

Lowering LDL early in life is significantly better than treating with statins when older

LDL低下療法を若年で開始した方が遅く開始するよりも冠動脈疾患（CHD）のリスクが3倍低下したとのスタディ結果が、第61回American College of Cardiology学会で発表された。動脈硬化が発現する前の早い時期にLDLコレステロールを低下させた方が当然心筋梗塞（MI）軽減にはより有効であろうと思われるが、この仮説を立証するのは困難であった。この仮説を調査するには、従来の無作為化トライアルであれば非常に大人数の無症状の若年者を何十年も追跡する必要がある。これの替わりとして研究者らは、Mendelian無作為化コントロールトライアル（mRCT）と呼ばれる新たなスタディデザインを用いて、その各々がLDLコレステロールレベル低下と関連する9つの一塩基多型（SNPs)の影響を調査した。その結果、9つのSNPs全てが、生涯におけるLDLコレステロールが1mmol/L（38.67mg/dl）低下するごとに一貫してCHDリスクが50～60%低下するのに関連のあることが示された。LDLを2mmol/L（77.34mg/dl）低下させることにより、CHDリスクはほぼ80%低下させることができた。

Full Text

Coronary atherosclerosis can lead to myocardial infarction and other forms of coronary heart disease (CHD). Lowering low-density lipoprotein (LDL) reduces the risk of CHD, and researchers found that lowering LDL beginning early in life resulted in a three-fold greater reduction in the risk of CHD than treatment with a statin started later in life, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

By the time most people begin treatment to lower LDL, CHD has often been quietly developing for decades. Because coronary atherosclerosis begins early in life, lowering LDL at a younger age may produce even greater reductions in the risk of CHD. Researchers sought to test this hypothesis by using genetic data to conduct a series of "natural" randomized controlled trials involving over one million study participants.

"Our study shows that the benefit of lowering LDL cholesterol depends on both the timing and the magnitude of LDL reduction," said Brian A. Ference, M.D., MPhil, MS.c., FACC, director of the cardiovascular genomic research center at Wayne State University School of Medicine and the study's principal investigator. "The increased benefit of lowering LDL beginning early in life appeared to be independent of how LDL was lowered. This means that diet and exercise are probably as effective as statins or other medications at reducing the risk of CHD when started early in life."

Lowering LDL cholesterol at an early age, before the development of atherosclerosis, would understandably be more effective at reducing heart attacks, but testing this hypothesis has proven difficult. A conventional randomized trial would have to follow a very large number of young, asymptomatic people for several decades to test this hypothesis. As an alternative, researchers used a novel study design called a Mendelian randomized controlled trial (mRCT) to study the effect of nine single-nucleotide polymorphisms (SNPs), or single-letter changes in DNA sequence, each of which is associated with lower levels of LDL cholesterol. Because each of these SNPs is allocated randomly at the time of conception, inheriting one of these SNPs is like being randomly allocated to a treatment that lowers LDL cholesterol beginning at birth. The researchers found that all nine SNPs were associated with a consistent 50-60 percent reduction in the risk of CHD for each 1 mmol/L (38.67 mg/dl) lower lifetime exposure to LDL cholesterol. Lowering LDL by 2 mmol/L (77.34 mg/dl) could reduce the risk of CHD by almost 80 percent.

"The results of our study demonstrate that the clinical benefit of lowering LDL can be substantially improved by initiating therapies to lower LDL cholesterol beginning early in life," Dr. Ference said.

Dr. Ference reports no conflicts of interest.

ACC2012特集

モノクローナル抗体はスタチン療法の有効性に上乗せできる

新たなモノクローナル抗体を注射することによりスタチンのLDL低下の有効性が上乗せされる

Injection of novel monoclonal antibody adds to effectiveness of LDL lowering with statins

新たなモノクローナル抗体は循環LDLコレステロールを40～72%低下させ、現在の標準治療に抵抗性の患者の新たな治療選択となる可能性をもつとの研究結果が第61回American College of Cardiology学会で発表され、Journal of the American College of Cardiologyオンライン版に掲載された。近年の発見により、スタチン療法がLDL受容体の破壊に繋がる酵素であるPCSK9の産生を刺激することが示された。今回のスタディでは、PCSK9に結合しその作用を遮断しLDL受容体の変性を防ぐモノクローナル抗体SAR236553/REGN727の効果を試した。この多施設無作為化トライアルではLDLコレステロール値が100mg/dL以上の患者183人を観察した。循環LDLコレステロールは、50、100、または150mgを2週毎に投与する群に割り付けられた患者において、それぞれ40%、64%、および72%低下した。LDLコレステロールは200または300mgを4週毎に注射された患者において、43%および48%低下した。プラセボ群では循環LDLコレステロールが5%減少した。

Full Text

A novel monoclonal antibody identified in a new study dramatically lowered circulating LDL cholesterol by 40 percent to 72 percent, a development with potential to provide a new option for patients who are resistant to cholesterol-lowering drugs such as statins or to the current standard of care, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

The traditional statin therapy lowers LDL cholesterol by inhibiting the production of cholesterol in liver cells, causing an increase in the number of LDL receptors on the cell surface. These receptors grab LDL circulating in the blood and deliver it into the liver, where it is subsequently processed and flushed out of the body. About one in five people with high low-density lipoprotein (LDL) are resistant to cholesterol-lowering drugs such as statins, and for many others the current standard of care does not lower cholesterol enough.

A recent discovery showed that statin therapy stimulates the production of PCSK9, an enzyme that leads to the destruction of LDL receptors. The present study tested SAR236553/REGN727, a monoclonal antibody that binds to PCSK9, blocking its effects and preventing the degradation of LDL receptors.. More LDL receptors mean more LDL is brought out of the blood into the liver, and circulating levels of LDL cholesterol decrease.

"We've known for 30 years that lowering LDL cholesterol with statins lowers the risk of heart disease and that the more you can lower LDL cholesterol, the greater reduction in that risk," said James McKenney, PharmD, chief executive officer of National Clinical Research, and the study's lead investigator. "However, we know in some cases that even the best statin can't get LDL cholesterol as low as it should be."

This multi-center, randomized trial looked at 183 patients who had an LDL cholesterol reading of 100 mg/dL or higher. The patients had already been treated with atorvastatin for more than six weeks at stable doses of 10, 20 or 40 mg. The participants were divided into six groups: a placebo control; three groups who received a subcutaneous injection of SAR236553/REGN727 every two weeks (Q2W) at doses of either 50, 100, or 150 mg; and two groups who received an injection of SAR236553/REGN727 at 200 or 300 mg every 4 weeks (Q4W), alternating with placebo shots at two weeks. The study's primary endpoint was the percentage LDL cholesterol reduction from baseline to after 12 weeks.

Dr. McKenney reported a remarkable dose-response to SAR236553/REGN727 injections. Circulating LDL cholesterol was lowered by 40 percent, 64 percent, and 72 percent in patients assigned to 50, 100, or 150 mg Q2W doses, respectively. LDL cholesterol was reduced by 43 percent and 48 percent for patients who received 200 or 300 mg Q4W injections. The placebo group reported a 5 percent reduction of circulating LDL cholesterol.

"Our LDL cholesterol treatment goals were less than 100 or 70 mg/dL," Dr. McKenney said. "All of the participants receiving one of our doses met those goals."

Dr. McKenney said the results surprised him, "Statins are good medicines and getting a 70 percent reduction on top of them is remarkable."

The SAR236553/REGN727 antibody was discovered two years ago, and these are the first Phase II results for an anti-PCSK9 antibody to be presented. Dr. McKenney said a longer study is needed to establish the long-term safety of the antibody, but the results from this trial were promising, with only one adverse reaction reported.

"This is a very hopeful step in the treatment of heart disease in this country," said Dr. McKenney.

This study was funded by Sanofi US, Bridgewater, N.J., and Regeneron Pharmaceuticals, Tarrytown, N.Y. Dr. McKenney reports that he is an employee of a research company that has received research funding from Regeneron and Sanofi.

The study was published online in the Journal of the American College of Cardiology at the time of presentation.

ACC2012特集

高血圧の早期発見早期治療の重要性

中年以前の急激な血圧上昇は不可逆的な心障害を来し得る

Rapid rise in blood pressure before midlife may cause irreversible heart damage

若年者の血圧高値に対する現在の“観察および待機”する方法により患者を不可逆的な心障害に向かわせる可能性があるとの研究結果が、第61回American College of Cardiology学会で発表された。このスタディでは生涯の経過における心臓の健康指標を追跡し将来の予後を予測した結果、中年期の、単にある閾値を超えるだけではない急激な血圧上昇は後の心疾患リスクを上昇させる可能性があることが示された。さらに、スタディの結果、降圧薬はたとえ血圧を正常レベルまで回復させたとしても高血圧による心障害を完全には回復させられないことが示された。この結果から、中年期の急激な血圧上昇を早期発見し治療することが必要であることが示唆された。スタディの結果に基づき、30歳代であったとしても、境界または前高血圧（収縮期血圧120～139mmHgまたは拡張期血圧80～89mmHg）はより頻回にモニターし医師らが血圧変化率を観察できるようにすべきである、と筆者らは述べている。

Full Text

The current “watch-and-wait” approach to high blood pressure readings in younger people may set patients on a course for irreversible heart damage, according to research presented at the American College of Cardiology’s 61st Annual Scientific Session.

The study tracked cardiac health indicators over the course of a lifetime to predict future outcomes and found that a sharp rise in blood pressure in midlife, not just crossing a certain threshold, can increase a person’s risk of heart disease later in life. Furthermore, the study showed blood pressure medications do not fully reverse damage to the heart from high blood pressure, even if drugs are successful in returning blood pressure to normal levels. The findings suggest that early detection and treatment of rapidly rising blood pressure in midlife may be required to prevent long-term damage to the heart.

“Just being on blood pressure medication will not completely get your heart back to where it was before you started having high blood pressure,” said Arjun K. Ghosh, MBBS, MRCP (U.K.), clinical research fellow at the International Centre for Circulatory Health of Britain’s National Heart and Lung Institute, Imperial College London and clinical career development fellow at the U.K. Medical Research Council’s Unit for Lifelong Health and Ageing on behalf of the study team.

Based on the study findings, Dr. Ghosh said a borderline or pre-hypertensive blood pressure reading (a systolic pressure of 120 to 139 mm Hg or a diastolic pressure from 80 to 89 mm Hg) – even in your 30s – should warrant more frequent monitoring so doctors can assess the rate of change in blood pressure. Current guidelines are based on a single, one-off measure of blood pressure and doctors rarely prescribe blood pressure-lowering medications for people in their 30s, as the risk of them having a cardiovascular event in the next 10 years is low.

“If people have a rapid rise in blood pressure, early treatment should be considered, because we know from this study that, 30 years down the line, they’re going to have more heart damage than somebody with a slower rise in blood pressure,” Dr. Ghosh said. “We’re potentially talking about a completely new way of assessing and treating blood pressure in younger people.”

The results revealed people who experienced a relatively rapid increase in blood pressure during midlife typically had a larger left ventricle – an independent risk factor for heart disease and other health problems – than those whose blood pressure edged up more slowly or later in life. Those taking medication to manage high blood pressure had a larger left ventricle than those with the same blood pressure who had never taken medication, suggesting that treatment in later life did not reverse the consequences of a rapid rise in blood pressure in earlier years.

Doctors are currently more likely to recommend blood pressure medications for older people who have a higher overall cardiovascular risk, thanks in part to their age, and few monitor patients’ blood pressure frequently enough to track the rate of increase. However, said Dr. Ghosh, “that approach may be fundamentally incorrect, because you’re not taking into account your previous life-course blood pressure. You need to watch more closely, and you need to identify if there is a rapid rise in blood pressure.”

The findings resulted from a study of 1,653 men and women born in Britain in one week in March 1946. Now entering its 66th year, the study represents the longest-running birth cohort in the U.K. and is also one of the longest running in the world. Participants were screened for blood pressure and other health indicators at ages 36, 43 and 53. From age 60-64, participants underwent echocardiography imaging to allow researchers to assess their heart health.

This study is based on data from the Medical Research Council National Survey of Health and Development, a long-term birth cohort study funded by the Medical Research Council of the United Kingdom. Dr. Ghosh has no conflicts of interest to report.

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