血管形成術施行の際の抗凝固薬の比較

ST上昇心筋梗塞の治療として血管形成術を行う際にabciximabおよびtirofibanを使用した場合の成績は同等である

Abciximab and tirofiban produce similar outcomes in patients who have angioplasty as treatment for ST-segment elevation myocardial infarctions

ST上昇心筋梗塞の治療として血管形成術を行う際にabciximabおよびtirofibanを使用した場合の術後成績は同等であるが、シロリムス溶出ステントを使用した方がベアメタルステントを使用するよりも優れているようであるとAmerican College of Cardiology学会で発表された。研究者らは745人の患者における抗凝固療法およびステントにおいて比較した。術後90分の解読可能な心電図のある患者722人（97%）においてST上昇の改善が50%以上認められたのはabciximab投与患者361人中302人（83.6%）であり、tirofiban投与患者361人中308人（85.3%）であった。虚血および出血の成績は同等であった。8ヵ月の時点での主要な有害事象はtirofiban（9.9%）およびabciximab（12.4%）で同等であったが、ベアメタルステント（54人、14.5%）ではシロリムスステント（29人、7.8%）よりも高かった。再血行再建術施行率はベアメタルステントで10.2%、シロリムス溶出ステントでは3.2%であった。

Full Text

Abciximab and tirofiban produce similar post-procedural outcomes in patients who have angioplasty as treatment for ST-segment elevation myocardial infarctions, but use of a sirolimus-eluting stent appears to have advantages over use of an uncoated stent, according to a presentation at the annual meeting of the American College of Cardiology.

The study was designed to compare use of the two anticoagulants in patients receiving uncoated stents, as well as to compare sirolimus-eluting and uncoated stents. Infusion with abciximab and implantation of an uncoated-stent is a common treatment strategy for patients undergoing angioplasty for ST-segment elevation myocardial infarction. It was unclear whether there would be similar benefits in use of tirofiban, which could have clinical and economic implications. Use of drug-releasing stents in this patient population has been discouraged because of conflicting efficacy results and safety concerns.

Marco Valgimigli, MD, PhD, of the cardiovascular Institute, University of Ferrara, Italy, and colleagues evaluated high-dose tirofiban and sirolimus-releasing stents compared with abciximab infusion and uncoated-stent implantation in 745 patients with undergoing angioplasty. The trial was conducted in Italy, Spain, and Argentina between October 2004 and April 2007.

Among the 722 patients (97 percent) who had an interpretable electrocardiogram, at least 50 percent resolution of ST-segment elevation at 90 minutes post-procedure occurred in 302 of 361 patients (83.6 percent) and 308 of 361 patients (85.3 percent) in the abciximab and tirofiban groups, respectively. Ischemic and hemorrhagic outcomes were similar.

At 8 months, the major adverse event rate was similar among patients who received tirofiban (9.9 percent) and those who received abciximab (12.4 percent), but was higher among patients who received uncoated stent (54 patients, 14.5 percent) compared with patients who received sirolimus-releasing stent (29 patients, 7.8 percent).
Revascularization was 10.2 percent for uncoated stents compared with 3.2 percent for sirolimus-releasing stents.

The article was published online by Journal of the American Medical Association on March 30 and will appear in the April 16 print issue.

"In summary, our study provides evidence that in a broad population of largely unselected patients undergoing percutaneous coronary intervention for STEMI, tirofiban therapy is associated with a noninferior resolution from ST-segment elevation at 90 minutes post-intervention compared with abciximab, and at 8-month follow-up, major adverse coronary events are approximately halved by sirolimus-eluting stent implantation compared with uncoated stents," the authors concluded.

ACC2008 特集

ステント血栓症再発の予測

オランダのステント血栓症スタディの結果、ステント血栓症は一般的に認められ、治療のために新たなステントを留置することによりさらなる血栓症再発のリスクを増加させることが明らかになった

Dutch Stent Thrombosis Study finds that stent thrombosis is common and that placement of a new stent during repair increases risk for further recurrence

ステント血栓症は比較的一般的に認められ、他のステントを留置するなどの治療はさらなる血栓症のリスクを増加させるとのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。オランダステント血栓症スタディでは初めてステント血栓症を造影上確認された連続する患者437人を組み入れた。フォローアップ中に74人（16.9%）がステント血栓症を再発した。このグループのうち61人は2回、12人は3回、そして1人は4回ステント血栓を発症した。ステント血栓症再発の3つの予測因子が明らかにされた。初回エピソードに対する緊急治療中の新たなステント留置により再発リスクは4.2倍増加し、心筋梗塞の既往によりリスクは2.6倍、後期血栓によりリスクは2.1倍上昇した。

Full Text

Stent thrombosis is relatively common, and treatment that includes placement of another stent increases the risk for further thrombosis, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

Jochem Wouter van Werkum, MD, a cardiologist at St Antonius Hospital, Nieuwegein, the Netherlands, led the Dutch Stent Thrombosis Study. He and his colleagues enrolled a total of 437 consecutive patients who had stent thrombosis confirmed by angiography between January 2004 and February 2007.

The researchers collected data on clinical characteristics (for example, diabetes, age and duration of antiplatelet therapy), angiographic characteristics (for example, undersizing of the stent, dissection and whether the lesion was located at an arterial branchpoint), and procedural characteristics (for example, whether a drug-eluting or bare-metal stent was used and the length and diameter of the stent).

The researchers found that 74 of the 437 patients (16.9 percent) experienced multiple episodes of stent thrombosis. Of these, 61 patients had two episodes of stent thrombosis, 12 patients had three episodes and one patient had four episodes.

Further analysis revealed three independent predictors of repeat stent thrombosis. Patients who had an additional stent implanted during emergency treatment for the first episode of stent thrombosis were 4.2 times as likely as other patients to experience a repeat episode of stent thrombosis. Patients with a previous myocardial infarction faced 2.6 times the usual risk of repeat stent thrombosis, and patients who developed thrombosis long after stent implantation (late stent thrombosis) faced 2.1 times the usual risk of a repeat episode.

Dr. van Werkum and his colleagues concluded that additional stent placement at the time of emergency treatment for the first stent thrombosis should be avoided.

ACC2008 特集

Aliskirenと左室肥大

ALLAYトライアルの結果、直接的レニン阻害薬aliskirenの高血圧を有する過体重患者における左室肥大軽減作用はロサルタンと同等であることが示された

ALLAY trial finds that direct renin inhibitor aliskiren is as effective as losartan in reducing left ventricular hypertrophy in overweight patients with hypertension

高血圧を有する過体重患者におけるaliskirenの左室肥大軽減作用はロサルタンと同等であることが示された、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiologyで発表された。36週間にわたるALLAYトライアルでは比較的コントロールの良好な高血圧患者でbody mass indexが25kg/m^{2}より大きい患者460人を、aliskiren 1日300mg（154人）、ロサルタン1日100mg（152人）、またはaliskiren 300mgとロサルタン 100mg併用投与群（154人）に無作為に割り付けた。全ての患者は血圧が目標値に達するように治療された。左室心筋量は36週までに全ての群の患者において有意に改善した。心筋重量減少は数の上では併用群で大であったが、その差は統計学的に有意ではなかった。筆者らは、より長期の治療を行うかコントロールの不良な高血圧患者に対して治療を行えば、併用療法により心筋重量軽減効果がより有意に認められる可能性があるが、この仮説を検証するさらなる研究が必要であろう、と述べている。

Full Text

The direct renin inhibitor aliskiren is as effective as losartan in reducing left ventricular hypertrophy in overweight patients with hypertension, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

The ALLAY (The ALiskiren Left Ventricular Assessment of HypertrophY) Trial, conducted at 77 centers in eight countries, examined whether aliskiren, alone or in combination with losartan, was at least as effective as losartan in reducing hypertrophy in this patient population.

After screening 1,086 patients, 460 patients with a body mass index greater than 25 kg/m^2 were randomized to one of three treatment arms: aliskiren 300 mg daily (154 patients), losartan 100 mg daily (152 patients), or aliskiren 300 mg daily plus losartan 100 mg daily (154 patients), with all patients treated to blood pressure targets. Treatment with the study drug was continued for 36 weeks.

Researchers compared changes in left ventricular mass index as assessed by cardiovascular magnetic resonance imaging between baseline and 36 weeks. The researchers also looked at changes in left ventricular volumes, 24-hour ambulatory blood pressure and electrocardiographic voltage during the same 36-week period.

Aliskiren was as effective as losartan in reducing left ventricular mass, which improved significantly in all treatment groups after nine months of therapy. The degree of left ventricular mass reduction was numerically greater in the combination arm, but it failed to reach statistical significance.

Aliskiren, either alone or in combination with losartan, was very well tolerated with no differences in adverse events between groups and a very low level of adverse events. There were no increases in hyperkalemia, hypotension or renal dysfunction in patients receiving aliskiren either alone or in combination.

"Aliskiren inhibits the renin-angiotensin-aldosterone axis at the beginning of the cascade. It is likely that patients would derive many of the same benefits from inhibiting the renin angiotensin system at this step as they do with inhibition at more proximal steps in the system," said Scott Solomon, MD, of Brigham and Women's Hospital and Harvard Medical School, and lead author of the study.

"Moreover, inhibiting the renin-angiotensin-aldosterone (RAAS) system with ACE inhibitors or angiotensin receptor blockers results in reflexive rises in plasma renin activity. This provides a rationale for combining a renin inhibitor with another inhibitor of the renin-angiotensin-aldosterone system, as aliskiren has been shown to reduce plasma renin activity either alone or when combined with other RAAS-blocking drugs. Because treatment of hypertension can be difficult, physicians and patients will benefit from additional agents that can not only lower blood pressure, but can affect the end-organ damage that hypertension causes."

"These data suggest that aliskiren, which is the first orally active direct renin inhibitor and is currently approved for treatment of hypertension, is as effective as an angiotensin receptor blocker for reducing left ventricular mass. Along with other recently reported studies with aliskiren showing incremental benefits in reducing abnormal protein excretion in the urine (proteinuria) in diabetic patients and improvements of indicators of heart function in heart failure patients, these data suggest that aliskiren is efficacious for end-organ protection, beyond just blood pressure reduction."

The patients in this study had relatively well-controlled hypertension and thus the overall degree of blood pressure lowering observed was moderate.

"It is conceivable that treating patients with higher blood pressures or for a longer period of time would have resulted in greater left ventricular mass reduction with the combination of aliskiren plus an angiotensin receptor blocker, but this remains to be determined in future studies," he concluded.

ACC2008 特集

薬剤溶出ステントと心筋梗塞

大規模登録データ解析の結果、薬剤溶出ステントはベアメタルステントと比較し急性心筋梗塞患者の予後を改善することが示唆された

Analysis of data from large registry suggests that drug-eluting stents offer better outcomes for patients with acute myocardial infarction than uncoated stents

薬剤溶出ステントはベアメタルステントと比較し死亡率は同等であるが再狭窄のリスクを軽減し、急性心筋梗塞患者の予後を改善するようであるとのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。研究者らはマサチューセッツ（米国）でステントを挿入された患者7,216人のデータを解析した。ここでは冠動脈インターベンション全例がデータベースに登録されている。薬剤溶出ステントを挿入された患者4,016人とベアメタルステントを挿入された患者3,200人のベースラインのリスクの差を補正するために、患者を最大63個の項目でマッチさせた。2年間のリスクで補正した血行再建術施行率は薬剤溶出ステント治療患者で有意に低く（15.5%対20.8%）、死亡率および再梗塞発症率は同等であった。筆者らはより長期のフォローアップデータを得るためさらに患者をモニターし続けているが、薬剤溶出ステントは抗血小板療法を遵守できる患者においては安全であると考えている。

Full Text

Drug-eluting stents appear to offer better outcomes for patients with acute myocardial infarction than uncoated stents, with similar mortality but significantly reduced risk for restenosis, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

"This study confirms that the same benefits that drug-eluting stents offer other patients in preventing restenosis of the coronary arteries are still there for patients with myocardial infarction, and there doesn't appear to be any trade-off in increased risk of repeat MI or death," said Laura Mauri, MD, MSC, an interventional cardiologist at Brigham and Women's Hospital, an assistant professor of medicine at Harvard Medical School, and chief scientific officer at the Harvard Clinical Research Institute, all in Boston.

To evaluate the long-term safety and effectiveness of drug-eluting stents, Mauri and her colleagues analyzed data from 7,216 patients who underwent stenting for acute MI in Massachusetts, where hospitals are required to submit data on all coronary interventions to a state database. Of these, 4,016 patients were treated with a drug-eluting stent and 3,200 were treated with a bare-metal stent. To adjust for differences in baseline risk, patients in the two groups were matched on up to 63 variables.

Researchers found that the two-year, risk-adjusted rate of revascularization was significantly lower in patients treated with drug-eluting stents when compared with bare-metal stents (15.5 percent versus 20.8 percent). Mortality was 10.4 percent and 13.2 percent, respectively, in the two groups, and repeat MI occurred in 9.5 percent and 11.0 percent, respectively.

"These findings are reassuring," Mauri said. "Although neither bare-metal stents nor drug-eluting stents were originally approved in the setting of acute myocardial infarction, it is probably the most important condition we treat with stents. I would feel comfortable considering drug-eluting stents on the basis of these results--with the caveats that treated patients must be able to take antiplatelet therapy and that we definitely want to see even longer-term follow-up."

The researchers plan to continue follow-up in Massachusetts and re-examine the findings when more data are available.

ACC2008 特集

ピオグリタゾンとグリメピリドの比較

PERISCOPEトライアルの結果、ピオグリタゾン治療により冠動脈プラークは進行しないが、グリメピリド治療では時間とともに有意に進行することが示された

PERISCOPE trial finds no progression of coronary plaque with pioglitazone therapy but significant progression over time with glimepiride

ピオグリタゾンは2型糖尿病患者の冠動脈硬化の進行を抑制することのできる第一の抗糖尿病薬のようである、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。PERISCOPEトライアルでは543人の患者をピオグリタゾン（15～45mg）またはグリメピリド（1～4mg）を18ヵ月間投与する群に無作為に割り付け、忍容性があれば可能な限り最大用量を使用した。組み入れ時および治療18ヵ月後に血管内超音波検査を施行した。その結果、プラーク量はピオグリタゾン群で軽度減少した（マイナス0.16%）がグリメピリド群では有意な進行が認められた（プラス0.73%）。ピオグリタゾンはまた、高密度リポプロテインコレステロール、中性脂肪、およびC反応性蛋白などの生化学マーカーや血圧の改善においても結果が良好であった。グリメピリドに割り付けられた患者の方が低血糖または狭心症の発現を多く認め、ピオグリタゾンに割り付けられた患者の方が浮腫や骨折の発現を多く認めた。

Full Text

Pioglitazone appears to be the first diabetes therapy able to reduce progression of coronary atherosclerosis in patients with type 2 diabetes, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

The PERISCOPE trial (Pioglitazone Effect on Regression of Intravascular Sonographic Coronary Obstruction Prospective Evaluation) compared two approaches to management of diabetes, randomizing 543 patients for 18 months to the thiazolidinedione pioglitazone, which reduces blood glucose level by increasing insulin sensitivity or the sulfonylurea glimepiride, which lowers blood glucose by stimulating insulin release by the pancreas).

The prospective, randomized, multicenter, double-blind trial treated patients with coronary disease and type 2 diabetes for 18 months at 97 academic and community hospitals in North and South America. Patients underwent intravascular ultrasonography to measure the amount of plaque volume at entry. Patients received either glimepiride, 1-to-4 mg, or pioglitazone, 15-to-45 mg, titrated to maximum dosage, if tolerated. After 18 months, a second ultrasound examination was performed to determine the amount of change in coronary plaque volume. The primary endpoint was the rate of progression of coronary plaque as measured by the ultrasound procedure.

The principal finding was an absence of progression of coronary plaque with pioglitazone (negative 0.16 percent) compared with highly significant progression with glimepiride (positive 0.73 percent) as assessed with intravascular ultrasound.

There were also major differences between treatments in biochemical effects including marked differences in levels of high-density lipoprotein cholesterol, triglycerides and C-reactive protein. Other important endpoints included changes in glycohemoglobin levels, insulin levels, other lipid parameters and blood pressure - all more favorable for patients treated with pioglitazone.

There were adverse effects in both treatment groups: More patients assigned to glimepiride experienced episodes of low blood sugar or angina and more patients assigned to pioglitazone experienced edema and fractures.

"Atherosclerosis can be particularly aggressive in patients with diabetes, which is currently increasing at an alarming rate in the developed and developing world," said Steven Nissen, MD, Chairman, Department of Cardiovascular Medicine, Cleveland Clinic and lead author. "By defining the optimal strategy for managing coronary heart disease in this patient population, this study has major implications for how we will treat diabetics with coronary disease in the future."

ACC2008 特集

Abciximabと心筋梗塞

BRAVE-3トライアルの結果、クロピドグレルの初期投与量を高用量にすることによりST上昇心筋梗塞に対し血管形成術を施行される患者におけるabciximabの必要性が軽減されることが示された

BRAVE-3 trial finds that high loading dose of clopidogrel can eliminate need for abciximab in patients with ST-elevation myocardial infarction undergoing angioplasty

クロピドグレルの初期投与量を高用量にすることによりST上昇心筋梗塞に対し血管形成術を施行される患者におけるabciximabの必要性を軽減することができる、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiologyで発表された。BRAVE-3トライアルでは800人の患者にクロピドグレル600mgを前投与し、その後abciximabまたはプラセボを静脈内投与する群に無作為に割り付けた。一次エンドポイントは5～10日後に施行した核医学検査による心筋血流で評価した最終的な梗塞サイズとした。その結果、群間に差はなかった。Abciximab群では心筋損傷は平均10%でありプラセボ群では9%であった。さらに、30日間の死亡、再梗塞、脳卒中、および緊急血行再建術施行からなる複合エンドポイントは両群間で同等であった（abciximabとプラセボで、それぞれ5%および3.8%）。

Full Text

A high loading dose of clopidogrel can eliminate the need for abciximab in patients with acute ST-elevation myocardial infarction undergoing angioplasty, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

The BRAVE-3 study was the first to test the influence of high-dose clopidogrel on the value of abciximab exclusively in this patient population.

"Acute myocardial infarction is a major medical problem, and the present study will help to define the optimal treatment strategy," said Julinda Mehilli, MD, an associate professor and staff cardiologist at Deutsches Herzzentrum, Technical University, Munich, Germany. "Therapy without abciximab would certainly be more cost-effective and reduce the risk of bleeding complications."

The BRAVE-3 researchers enrolled 800 patients with ST-elevation infarctions who were undergoing angioplasty. All were pretreated with 600 mg clopidogrel and then randomized to intravenous abciximab or placebo during the procedure.

The study was designed primarily to compare how the two treatment strategies affected infarct damage as evaluated by myocardial blood flow on a nuclear scan conducted 5 to 10 days later. There was no difference between groups: Damage involved an average 10 percent of the left ventricle with abciximab and 9 percent with placebo. In addition, the 30-day combined rates of death, repeat infarction, stroke and urgent revascularization procedure were similar in the two groups (5 percent and 3.8 percent, respectively).

"For patients with acute ST-elevation myocardial infarction undergoing primary coronary intervention after pre-treatment with a 600-mg loading dose of clopidogrel, the additional use of abciximab is not associated with any measurable benefit after 30 days," Mehilli said.

高齢者の高血圧治療

HYVETトライアルの結果、高齢患者の血圧を低下させることにより心血管イベント発現率および総死亡率の両者が有意に減少することが示された

HYVET trial finds that reducing blood pressure in elderly patients can significantly cut both rate of cardiovascular events and total mortality

高齢患者の血圧を低下させることにより心血管イベント発現率および総死亡率の両者が有意に減少することが示された、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。HYVETスタディでは80歳以上（平均年齢83歳7ヵ月）の患者3,845人をペリンドプリルにインダパミド徐放錠またはプラセボを追加する群に無作為に割り付けた。その結果、インダパミドにより、総死亡率の21%低下、脳卒中死亡率の39%低下、致死性および非致死性心筋梗塞の64%低下、および心血管イベントの34%低下などの有益性が認められ、これらの効果は1年間の経過観察中に明らかとなった。治療による明らかな有益性が認められたため、このスタディは早期に中止されたが、実薬治療の長期の有益性を評価するため、インダパミド投与群患者に関しては延長試験が進行中である。

Full Text

Reducing blood pressure in elderly patients with hypertension can significantly cut both rate of cardiovascular events and total mortality, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

The 3,845-patient Hypertension in the Very Elderly Trial (HYVET), which was coordinated by scientists from Imperial College London, is the largest ever clinical trial to look at the effects of lowering blood pressure solely in patients age 80 years and over. Patients were given either a placebo or the diuretic indapamide slow release 1.5 mg, with the addition of the angiotensin-converting enzyme inhibitor perindopril in tablet form once a day.

Benefits of treatment included a 21 percent reduction in total mortality rate, a 39 percent reduction in stroke mortality rate, a 64 percent reduction in fatal and non-fatal heart failure, and a 34 percent reduction in cardiovascular events, with benefits apparent within the first year of follow-up.

The reduction in overall mortality was a novel and unexpected result. Earlier trials had demonstrated that reducing blood pressure in the under-80 population reduces incidence of stroke and cardiovascular events. However, previous smaller and inconclusive studies also suggested that lowering blood pressure in those aged 80 or over reduced the number of strokes, but did not reduce, and even possibly increased, total mortality.

In July 2007 the trial was stopped early on the recommendation of an independent data monitoring committee after they observed significant reductions in overall mortality and stroke in those receiving treatment. The final results of the trial showed a significant reduction in stroke mortality rate, but the reduction in all strokes of 30 percent did not quite reach statistical significance (p=0.06).

Emeritus Professor Christopher Bulpitt, the lead investigator on the study from the Care of the Elderly Group at Imperial College London, said: "Before our study, doctors were unsure about whether very elderly people with high blood pressure could see the same benefits from treatment to lower their blood pressure as those we see in younger people. Our results clearly show that many patients aged 80 and over could benefit greatly from treatment. Populations are living longer and we have growing numbers of people living well into their 80s and beyond, so this is good news. We are very pleased that cardiovascular events were reduced safely with a reduction in total mortality."

The researchers hope that their findings will clear up uncertainty among clinicians about the benefits of treating patients aged 80 and over for high blood pressure.

Dr Nigel Beckett, the trial coordinator from the Care of the Elderly Group at Imperial College London, added "Many very elderly people with high blood pressure are not being treated for it at the moment, because doctors are unsure about whether or not treatment will help them. We hope that following our study, doctors will be encouraged to treat such patients in accordance with our protocol."

As the trial was stopped early, an extension involving patients receiving active treatment is now underway to assess the longer-term benefits of treatment.

Patients with high blood pressure (defined as a systolic blood pressure between 160-199 mmHg), from thirteen countries across the world, were randomized for the double-blind, placebo-controlled trial, which began in 2001. The mean age of participants was 83 years and 7 months.

Patients were given either placebo or indapamide slow release (SR) with the addition of perindopril, in tablet form once a day as required, to achieve a target blood pressure of 150/80 mmHg. The average follow-up of patients was just over 2 years, by which time 20 percent of placebo subjects and 48 percent of those taking medication had achieved the target blood pressure of 150/80 mmHg. In those patients who were followed up for longer, a larger number of patients receiving active treatment achieved target blood pressure.

ACC2008 特集

高血圧のより良い治療

ACCOMPLISHスタディはアンジオテンシン変換酵素阻害薬とカルシウム拮抗薬が高血圧患者に対し有益性が大きいことが示された後、早期に終了された

ACCOMPLISH study ends early after angiotensin-converting enzyme inhibitor plus calcium channel blocker shows large benefits for patients with hypertension

アンジオテンシン変換酵素（ACE）阻害薬とカルシウム拮抗薬の併用は高血圧患者に対し非常に有効であったためphase IIIトライアルが早期に終了された、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。ACCOMPLISHスタディでは10,700人の患者をベナゼプリルとアムロジピン併用またはベナゼプリルとヒドロクロロチアジド併用群に無作為に割り付けた。対象患者の3分の2はスタディに組み込まれる前の治療では良好な血圧コントロールが得られなかったが、両併用治療ともに高血圧および他の心血管危険因子を有する患者の推奨血圧値を達成するのに有用であった。最も重要なことに、ACE阻害薬／カルシウム拮抗薬を併用した患者は他の併用療法を受けた群と比較し、心血管死、心筋梗塞、脳卒中、不安定狭心症による入院および血行再建術施行率を含む心臓関連イベントが20%少なかった。

Full Text

Combined therapy with an angiotensin-converting enzyme inhibitor plus a calcium channel blocker was so effective for patients with hypertension that a phase III trial was ended early, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

The international ACCOMPLISH study (Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension) compared two single-pill combinations of two medications: either an angiotensin-converting enzyme inhibitor and calcium channel blocker or an enzyme inhibitor and diuretic.

The randomized study of 10,700 adults showed that both drug combinations helped people who had hypertension and other cardiovascular risk factors recommended blood pressure levels despite the fact that two thirds of participants had been unable to achieve good blood pressure control with other medications prior to enrollment in the study.

Most importantly, the study revealed that patients taking the enzyme inhibitor/channel blocker combination had 20 percent fewer cardiac-related events than patients taking the other combination. Those events included cardiovascular deaths, myocardial infarctions, strokes, hospitalizations for unstable angina and revascularization procedures
One treatment arm received benazepril plus amlodipine, whereas the other pill combined benazepril and hydrochlorothiazide.

"These results demonstrate the superiority of an angiotensin-converting enzyme inhibitor/calcium channel blocker pill fixed-dose combination treatment strategy for reducing cardiovascular morbidity and mortality, and provides evidence that should modify future guidelines for the treatment of hypertension," says Kenneth Jamerson, M.D., the leader of ACCOMPLISH. Jamerson is a professor of internal medicine at the University of Michigan Medical School and a member of the Cardiovascular Center.

Results from the ACCOMPLISH trial show that just six months of treatment with either drug combination was enough to bring the blood pressure of 73 percent of patients into an acceptable range. However, by the end of the trial blood pressure control rates were 80 percent, with mean systolic blood pressure less than 130 mm Hg. This represents exceptional blood pressure control when contrasted to the current control rate of approximately 30 percent in the United States.

All patients in the study received no more than 40 milligrams of benazepril in each dose; amlodipine doses began at 5 mg and could be increased to 10 mg, while hydrochlorothiazide doses began at 12.5 mg and could be increased to 25 mg.

"These ACCOMPLISH results shake the foundations of current recommendations and define a new standard which will enhance the achievement of the primary goal and assist clinicians in meeting the daily challenges of hypertension management," said ACCOMPLISH executive committee member Eric J. Velazquez, MD, an Associate Professor of Medicine at Duke University Medical Center.

ACC2008 特集

Prasugrelとクロピドグレル

TRITON-TIMI 38トライアルの結果、急性冠症候群患者においてprasugrelはクロピドグレルよりも、ステント留置のタイミングおよびステントのタイプにかかわらず、優れていることが示された

TRITON-TIMI 38 trial shows that prasugrel is superior to clopidogrel in patients with acute coronary syndrome regardless of stent timing and type

急性冠症候群患者において、血管形成術中に留置したステントのタイプまたはステント留置のタイミングにかかわらず、prasugrelはクロピドグレルよりも優れているようであるとのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。TRITON-TIMI 38スタディにおいて、13,608人の患者を、prasugrelまたはクロピドグレルを用いた術前の導入用量及び1年間のフォローアップ治療による抗血小板療法を行う群に無作為に割り付けた。最終的に1つ以上のステントで治療された12,844人中6,461人はベアメタルステントのみを、5,743人は薬剤溶出ステントのみを挿入された。結果として、prasugrelは30日間のステント血栓および後期ステント血栓を減少させた（それぞれ0.64%対1.56%、0.49%対0.82%）。新たなデータ解析の結果、prasugrelの利点は広範囲の患者および治療にわたり高度に有意に認められることが示された。

Full Text

Prasugrel appears to be superior to clopidogrel as an antiplatelet agent in patients with acute coronary syndrome regardless of type of stent placed during angioplasty or timing of the procedure, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

Prasugrel reduced by more than half the risk of thrombosis inside the stent. Now a new analysis of data from the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel (TRITON-TIMI 38) reveals that the investigational drug maintains its edge over clopidogrel regardless of the type of stent, the amount of time since the stenting procedure, or the way stent thrombosis is defined.

For the main TRITON-TIMI 38 study, researchers recruited 13,608 patients who needed a stent from 707 medical centers in 30 countries. Patients were randomized to anti-platelet therapy consisting of either a 300-mg loading dose of clopidogrel before the procedure, followed by a maintenance dose of 75 mg daily for one year, or to a loading dose of 60 mg of prasugrel, followed by 10 mg daily for one year.

Stephen D. Wiviott, MD, Brigham and Women's Hospital, Boston, led the new stent analysis. Of the 12,844 patients who ultimately were treated with at least one coronary stent, 6,461 patients received only bare-metal stents and 5,743 patients received only drug-eluting stents. Overall, prasugrel reduced both 30-day stent thrombosis when compared with clopidogrel (0.64 percent vs. 1.56 percent) and late stent thrombosis (0.49 percent vs. 0.82 percent).

For bare-metal stents, the respective rates of stent thrombosis with prasugrel and clopidogrel were 1.3 percent vs. 2.4 percent, and for drug-eluting stents, 0.8 percent vs. 2.3 percent. Prasugrel's advantage remained highly statistically significant across a broad array of patient and procedural characteristics.

ACC2008 特集

動脈プラークの進行を停止する

ASTEROIDトライアルの結果、積極的なロスバスタチン療法により冠動脈内の動脈硬化性プラークの縮小を促すことが示された

ASTEROID trial shows that aggressive rosuvastatin therapy can induce regression of atherosclerotic plaque in the coronary arteries

積極的なロスバスタチン療法により冠動脈内の動脈硬化性プラークの縮小を促すことができるとのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。ASTEROIDトライアルでは507人の患者を1日40mgのロスバスタチンで24ヵ月間治療した。これらの患者のうち379人からはベースライン時およびスタディ終了時の評価可能な血管造影写真が得られた。スタディに参加するためにはいずれかの冠動脈に、20%を超えた血管造影上血管内径狭窄が1ヵ所以上あることを条件とした。過去の解析からは、50%未満の血管造影上血管内径狭窄を有する1本の冠動脈の血管内超音波の結果、アテロームの容積が減少したことが示されている。今回の新たな結果から、治療により内径狭窄率が低下し定量的血管造影で計測した最小径が改善することも示された。

Full Text

In a first-of-its-kind finding, aggressive rosuvastatin therapy has been shown to cause regression of atherosclerotic plaque in the coronary arteries, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

"Previous studies have shown that statin therapy can slow the development of plaque in the coronary arteries," said Christie Ballantyne, MD, director of the Center for Cardiovascular Disease Prevention at the Methodist DeBakey Heart & Vascular Center and lead author of the study. "However, no statin monotherapy study has stopped the growth of plaque--- or actually reduced the amount of plaque in the arteries in areas with narrowing or stenosis, as this study shows."

A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden (ASTEROID) was designed to determine effects of treatment with rosuvastatin on progression of coronary atherosclerosis in patients who had a clinically indicated cardiac catheterization that showed angiographic evidence of coronary artery disease. Coronary atherosclerosis was assessed by intravascular ultrasound (IVUS, the primary endpoint) and quantitative coronary angiography (QCA, a secondary endpoint).

A previous report had shown ultrasound assessment of single coronary arteries with less than 50 percent angiographic luminal narrowing showed regression of atheroma volume. The new findings showed that treatment also produced regression by decreasing percent diameter stenosis and improving minimum lumen diameter as measured by angiography.

ASTEROID was a prospective, multi-center, international open-label trial that enrolled men and women 18 years or older with a clinical indication for coronary catheterization and angiographic evidence of coronary disease who met specific angiographic and ultrasound criteria. Inclusion required demonstration of at least one obstruction causing more than 20 percent angiographic luminal diameter narrowing in any coronary vessel.

The left main coronary artery had to have at most 50 percent reduction in lumen diameter by visual estimation, and the target vessel for ultrasound interrogation could not have undergone angioplasty or bypass surgery nor have more than 50 percent luminal narrowing throughout a target segment with a minimum length of 40 mm. Segments for angiographic analysis could not have undergone angioplasty or bypass surgery.

ASTEROID treated 507 coronary disease patients with rosuvastatin 40 mg/day for 24 months. Of these patients, 379 had evaluable angiograms at baseline and at study end. Blinded angiography analysis of percent diameter stenosis and minimum lumen diameter was performed for up to 10 segments of the coronary arteries and their major branches with greater than 25 percent diameter stenosis at baseline. For each patient, the means of all matched lesions at baseline and study end were calculated. There were 292 patients with 613 matched segments that met the criterion of greater than 25 percent stenosis.

Rosuvastatin reduced low-density lipoprotein cholesterol by 53.3 percent to 61.1±20.3 mg/dL; high-density lipoprotein cholesterol increased by 13.8 percent to 48.3±12.4 mg/dL.

Mean±standard deviation percent diameter stenosis decreased from 37.3±8.4 percent (median [minimum-maximum] 35.7 percent [26-73 percent]) to 36.0±10.1 percent (median 34.5 percent [8-74 percent]). minimum lumen diameter increased from 1.65±0.36 mm (median 1.62 [0.56-2.65] mm) to 1.68±0.38 mm (median 1.67 [0.76-2.77] mm; p<0.001).
In summary, ASTEROID data show that patients with heart disease who take the maximum dose of rosuvastatin (40 mg per day) for 24 months and achieve an average low-density lipoprotein cholesterol level below 70 mg/dL and a significant increase in high-density lipoprotein cholesterol had a mean reduction in coronary plaque volume.

ACC2008 特集

抗血小板療法の改善

ARMYDA-RELOADスタディの結果、急性冠症候群患者にはたとえ患者が既にクロピドグレルを内服していたとしても、導入用量のクロピドグレルを投与することにより有益性が認められることが示された

ARMYDA-RELOAD study finds benefit in giving patients with acute coronary syndrome a loading dose of clopidogrel even when they are already taking it

クロピドグレルを既に定期的に内服している急性冠症候群患者は血管形成術前に「再導入」をすることにより有意な有益性が認められる、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。ARMYDA-RELOADの研究者らは血管形成術の10日以上前からクロピドグレルを内服していた患者436人を組み入れた。うち167人（38%）は急性冠症候群の患者であった。患者らは、術前4～8時間に導入用量（600mg）のクロピドグレルまたはプラセボを内服する群に無作為に割り付けられた。30日後、全体の主要な心有害事象発現率は両群間で同等であった。しかし、急性冠症候群患者においては、クロピドグレルの再導入により主要な心有害事象発現率が有意に低下した（それぞれ7%対18%）。出血発現率には差はなかった（両群ともに5%）。

Full Text

Patients with acute coronary syndrome who take clopidogrel achieve significant benefit from a 'reloading' dose prior to angioplasty, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

Patients typically take 75 mg clopidogrel daily; in the Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty-RELOAD (ARMYDA-RELOAD) study, such patients who were about to undergo angioplasty for an acute coronary syndrome event were given a 'reloading' dose of 600 mg.

Researchers found that the extra medication was associated with a nearly two thirds reduction in post procedural major adverse coronary event rate (combination of death, myocardial infarction, or repeat revascularization) without increase in risk for bleeding.

Prior to the current trial, no study has ever specifically examined the effect of clopidogrel reloading on patients with acute coronary syndrome.

"The implications of the study are self-evident: When a patient with acute coronary syndrome is undergoing percutaneous coronary intervention and has been taking clopidogrel before, it is a very good idea to give a further loading dose of 600 mg prior to the procedure. This will protect against ischemic complications, without fear of more bleeding," said Germano Di Sciascio, MD, professor and chairman of cardiology at Campus Biomedico, University of Rome, Italy.

"In patients with stable syndromes, ongoing preexisting clopidogrel may supply sufficient anti-platelet effect to safely undergo the procedure."

Researchers recruited 436 patients who had been taking clopidogrel for more than 10 days before their procedure. Of these, 167 (38 percent) had acute coronary syndrome. Patients were randomized to receive an additional 600-mg loading dose of clopidogrel or placebo four to eight hours before their procedure. Blood tests confirmed that platelet reactivity was significantly lower in the reload group compared with the placebo group in patients with acute coronary syndrome.

After 30 days, the overall rates of major adverse cardiac events were the same in the two groups: 7 percent in patients who received clopidogrel reloading versus 9 percent in the placebo group. A similar finding was observed in patients with stable chest pain (8 percent versus 4 percent, respectively).

However, in patients with acute coronary syndromes, clopidogrel reloading significantly reduced the major adverse cardiac event rate (7 percent versus 18 percent, respectively). There was no difference in the rates of bleeding (5 percent in both groups).

Fundamental differences in the cardiovascular conditions that characterize acute and stable chest pain may explain the effectiveness of clopidogrel reloading in patients with acute coronary syndrome, Dr. Di Sciascio said.

"Patients with acute coronary syndrome have higher platelet reactivity, higher inflammatory status and more intracoronary thrombus," he said. "This may make them more prone to benefit from clopidogrel reloading."

ACC2008 特集

Rimonabantと冠動脈疾患の進行

STRADIVARIUSトライアルの結果からは、冠動脈疾患を有する肥満患者の動脈プラークの進行をリモナバント療法により遅延できると結論付けることはできない

STRADIVARIUS trial is inconclusive regarding ability of rimonabant therapy to slow progression of arterial plaque in obese patients with coronary disease

新たなスタディデータはリモナバント療法が冠動脈疾患を有する肥満患者の動脈プラークの進行を遅延させることができると証明するには不十分である、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。STRADIVARIUSにおいて839人がrimonabant（1日20mg）またはプラセボを、18～20ヵ月投与する群に無作為に割り付けられた。医学的な理由により冠動脈造影を要する患者のみ組み入れ可とした。対象者らは無作為割付後3、6、12、および18ヵ月後に予定受診をした。主な超音波上の評価項目はアテローム容積のパーセント変化であり、二次評価項目は、プラークの負荷を異なる方法で計測した、標準化総アテローム容積であった。Rimonabant群とプラセボ群とで、パーセントアテローム容積はそれぞれ0.25%および0.51%増加したが、二次評価項目ではrimonabantの方が成績が良好で、それぞれ2.2mm^{3}の減少と0.88mm^{3}の増加であった。

Full Text

New study data are inadequate to prove whether rimonabant therapy can slow progression of arterial plaque in obese patients with coronary disease, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

In STRADIVARIUS (the Strategy to Reduce Atherosclerosis Development Involving Administration of Rimonabant -The Intravascular Ultrasound Study), ultrasonographic coronary imaging was used to assess atherosclerotic progression. Steven E. Nissen, MD, of the Cleveland Clinic and colleagues conducted a randomized, double-blinded clinical trial from December 2004 to December 2005 comparing rimonabant with placebo in 839 patients at 112 centers in North America, Europe and Australia.

Patients were randomized to rimonabant (20 mg daily) or matching placebo for 18 to 20 months. Patients were eligible to participate in the study only if they also required coronary angiography for a medical reason. The patients returned for scheduled clinic visits at 3, 6, 12, and 18 months following randomization. The main outcome the researchers were observing was a change in the percent atheroma volume (PAV) and the secondary outcome was a change in normalized total atheroma volume (TAV). PAV and TAV are different measurements of plaque build-up in an artery.

"In the rimonabant versus placebo groups, PAV increased 0.25 percent versus 0.51 percent, respectively, and TAV decreased -2.2mm^3 vs. an increase of 0.88mm^3," the researchers reported.

"Rimonabant-treated patients had a larger reduction in body weight (-4.3kg [-9.5 lbs.] vs. -0.5 kg [-1.1 lbs.]) and greater decrease in waist circumference (-4.5 cm [-1.77 inches] vs. -1.0 cm [- 0.39 inches]). In the rimonabant vs. placebo groups, high-density lipoprotein cholesterol levels increased 5.8mg/dL (22.4 percent) vs. 1.8mg/dL (6.9 percent) and median (midpoint) triglyceride levels decreased -24.8 mg/dL (20.5 percent) vs. -8.9 mg/dL (6.2 percent)." However, LDL-C ("bad" cholesterol) levels and blood pressure changes did not differ significantly between treatment groups.

"Psychiatric adverse effects were more common in the rimonabant group (43.4 percent vs. 28.4 percent)," the researchers note. Anxiety and depression were the most often reported adverse effects. "Administration of rimonabant, 20mg, daily for 18 months did not significantly reduce the rate of progression of coronary disease for the primary IVUS (intravascular ultrasound) end point, the change in PAV," the authors said. "However, the secondary endpoint, change in TAV, showed a statistically significant treatment effect favoring rimonabant."

The authors concluded that because the current study failed to achieve a statistically significant effect for the primary efficacy measure, additional studies will be required to further define the role of rimonabant in the treatment of abdominally obese patients with coronary disease and metabolic risk factors."

ACC2008 特集

血管内僧帽弁修復術の評価

EVERESTトライアルの結果、血管内edge-to-edge repair術により僧帽弁逆流量を減少し心不全症状が軽減することが示された

EVEREST trial finds that endovascular edge-to-edge repair can reduce mitral regurgitation and help relieve symptoms of heart failure

血管内edge-to-edge repair術は僧帽弁逆流量を減少し心不全症状を軽減させることが示されたとのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。新たなサブ解析ではEVEREST Iまたは現在進行中のEVEREST IIスタディの初期に治療を受けた患者23人に焦点を当てた。全ての患者は中等度重症または重症の機能性逆流を有し、83%の患者がクラスIIIまたはIVの心不全を有していた。術後の僧帽弁逆流は、MitraClipで治療された22人中19人（83%）において軽度から中等度であった。1年後、12人の患者が完全にフォローアップされ、ベースラインからフォローアップまでのデータが揃っていた。12人中10人（83%）は引き続き僧帽弁逆流が軽度から中等度であり、12人中9人（75%）は症状および日常機能としてNYHAクラスが少なくとも1度改善したままであった。さらに、拡張期左室内径はベースラインから12ヵ月後までに縮小した。

Full Text

Endovascular edge-to-edge repair can reduce mitral regurgitation and help relieve symptoms of heart failure, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

One-year findings from the EVEREST trial were reported at the meeting. The Endovascular Valve Edge-to-Edge Repair Study (EVEREST) evaluated use of the MitraClip for treatment of mitral regurgitation. The new sub-analysis focused on 23 patients treated at 15 medical centers either during the EVEREST I study or during the "roll-in" phase of the ongoing EVEREST II study, which is comparing MitraClip therapy to open-chest surgery.

All patients in the new analysis had functional regurgitation. Before the procedure, all patients had moderately severe or severe mitral regurgitation, and 83 percent of patients had heart failure ranked as New York Heart Association (NYHA) functional class III or IV.

After the procedure, mitral regurgitation was mild to modest in 19 of 22 patients (83 percent) treated with the MitraClip. After one year, 12 patients had completed follow-up and had matched data from both baseline and follow-up. Ten of the 12 patients (83 percent) continued to have only mild to modest mitral regurgitation and nine of 12 (75 percent) continued to enjoy an improvement in symptoms and daily function of at least one NYHA class.

In addition, heart size was significantly smaller. For example, the left ventricular internal diameter during diastole fell from an average of 6.0 cm at baseline to 5.4 cm at 12 months and left ventricular end-diastolic volume fell from an average of 208 mL at baseline to 178 mL at 12 months.

"This is a small study, but it demonstrates a proof of principle that the MitraClip can reduce mitral regurgitation and improve heart function in patients with functional mitral regurgitation," Hermiller said. "These findings are promising and interesting, but clearly we need a lot more data."

ACC2008 特集

シロリムス溶出ステントとステント内狭窄に対する近接照射療法

SISRトライアルの結果、シロリムス溶出ステントはベアメタルステント内血栓の患者に対し近接照射療法よりも優れていることが示唆された

SISR trial suggests sirolimus-eluting stents are superior to brachytherapy as treatment for patients with thrombosis in a bare metal stent

長期トライアルのデータから、シロリムス溶出ステントはベアメタルステント内血栓の患者に対し近接照射療法よりも優れていることが示唆された、とAmerican College of Cardiology学会で発表された。SISRトライアルにおいて384人の患者がベアメタルステント内血栓に対する血行再建術に対しステントまたは近接照射療法を施行される群に無作為に割り付けられた。3年後に、薬剤溶出ステントを留置された患者は近接照射療法を受けた患者と比較し、さらなる血行再建術を必要とする確率が有意に低かった（追加の施術を必要としなかった率はステント群で81%、近接照射療法群で71.6%であった）。死亡や心筋梗塞などの安全性のエンドポイントは両群間で有意差がなかった。Academic Research Consortiumの定義で「確実」または「かなり確か」とされた血栓再発率は両群間で差がなかった（ステント3.7%、近接照射2.6%）。

Full Text

A new analysis of long-term trial data suggests sirolimus-eluting stents are superior to brachytherapy as treatment for patients with thrombosis in a bare metal stent, according to a presentation at the annual meeting of the American College of Cardiology. The SISR trial had randomized 384 patients to stenting or brachytherapy for revascularization.

At three years, 81 percent of patients who received the stent had not required target lesion revascularization compared with 71.6 percent of patients receiving brachytherapy. Among patients who did require target vessel revascularization, the survival free rates were 78.2 percent for sirolimus-eluting stent and 68.8 percent for brachytherapy.

Stent thrombosis rates, defined as definite and probable per the Academic Research Consortium definitions, were not significantly different (3.7 percent for the stent versus 2.6 percent for brachytherapy).

Differences in three-year rates of target vessel failure (stent, 75.1 percent; brachytherapy, 67.9 percent) and major adverse cardiac events did not reach statistical significance, likely reflecting progression of coronary artery disease at sites other than the original location of bare metal stent restenosis. Rates f major adverse events were 75.5 percent for the stent and 70.5 percent for brachytherapy.

Patients who received the drug-eluting stent were significantly less likely to need target lesion revascularization at three years compared to patients who received brachytherapy. In addition, there were no significant differences in safety endpoints, such as the rates of death, myocardial infarction, or stent thrombosis between the two treatment arms of this study.

The original trial was designed for nine months of follow-up. This longer-term, follow-up analysis focused on pre-specified safety endpoints, namely death, myocardial infarction and stent thrombosis, as well as target lesion revascularization, an efficacy endpoint, to determine whether any new safety issues emerged and whether the major benefit of the drug-eluting stent, reduction in repeat revascularization procedures, was maintained.

"These data continue to favor the CYPHERR Stent compared to radiation therapy in these patients with complex coronary artery disease," said David R. Holmes Jr., MD, Principal Investigator and Professor of Medicine, The Mayo Clinic College of Medicine, Rochester, MN. "Neither treatment modality in this study was associated with any new safety issues or concerns."

ACC2008 特集