心房細動に対しては大まかな心拍コントロールで十分なようである

RACE II：心房細動患者は厳密な心拍コントロールをしなくても健康を維持できるようである

RACE II: Patients with atrial fibrillation stay healthy even without strict control of heart rate

最新のガイドラインに反して、心房細動（AF）患者の心拍コントロールは大まかであっても厳密にコントロールするのと同等のようである、と第59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。慢性心房細動の心拍コントロールの有効性（Rate Control Efficacy in Permanent Atrial Fibrillation：RACE II）スタディではAF患者614人を大まかな心拍コントロール（安静時心拍数<110bpm）または厳密なコントロール（安静時<80bpmおよび中等度の労作時<110bpm）を行う群に無作為に割り付けた。目標心拍数に達するためにβ遮断薬、カルシウム拮抗薬、および/またはジゴキシンが用いられた。追跡観察中に大まかな心拍コントロール群患者のうち38人および厳密な心拍コントロール群患者のうち43人が心血管死または心不全による入院をしたかあるいは脳卒中、血栓、重篤な出血または生命にかかわる不整脈を発現した。これらのイベントの3年間の累積発現率は大まかなコントロール群で12.9%、厳密コントロール群で14.9%であり、大まかなコントロールの「非劣性」が示された。標的心拍数の達成度は厳密コントロール群よりも大まかなコントロール群の方が優れており（98%対67%）診察を必要とする回数も少なかった。

Full Text

Contrary to current guidelines, taking a lenient approach to controlling heart rate in patients with atrial fibrillation appears to be just as good as taking a strict approach and poses no greater risk of death or other serious complications, according to research presented at the American College of Cardiology's 59th annual scientific session.

The Rate Control Efficacy in Permanent Atrial Fibrillation (RACE II) study evaluated whether therapy aimed at achieving a resting heart rate of less than 110 beats per minute in patients with atrial fibrillation was "noninferior" to therapy targeted at a resting heart rate of less than 80 beats per minute. RACE II, the first randomized trial to investigate the best level of heart rate control in patients with atrial fibrillation, found that clinical outcomes were similar with the two approaches, but lenient control was easier and less time-consuming to achieve.

"Guidelines, though not evidence-based, recommend strict rate control in patients with atrial fibrillation to reduce symptoms and the risk of heart failure, bleeding and stroke, and to improve quality of life, exercise tolerance and survival," said Isabelle C. Van Gelder, M.D., a cardiology professor at the University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, and the Interuniversity Cardiology Institute Netherlands, Utrecht, The Netherlands. "Our study suggests that lenient rate control is the first-choice strategy in patients with permanent atrial fibrillation."

Previous studies have shown that patients fare just as well when medications are used to control the heart rate, rather than trying to force the heart back into a normal rhythm. But whether maintaining a near normal heart rate (strict rate control) is necessary to keep patients healthy over the long run has been unknown.

The researchers recruited 614 patients with atrial fibrillation, randomly assigning them to lenient rate control, defined as a heart rate of less than 110 bpm at rest, or to strict rate control, defined as a heart rate of less than 80 bpm at rest and less than 110 bpm during moderate exercise. To achieve the target heart rate, patients were treated with beta-blockers, calcium-channel blockers, and/or digoxin. During a follow up that ranged from two to three years, 38 patients in the lenient-control group and 43 patients in the strict-control group either died of cardiovascular causes, were hospitalized for heart failure, or experienced a stroke, a blood clot, serious bleeding or a life-threatening arrhythmia. The estimated cumulative incidence of these events at 3 years was 12.9 percent in the lenient-control group and 14.9 "noninferiority" of the lenient-control strategy.

Efforts to achieve the target heart rate were more successful with lenient control than with strict control (98 percent vs. 67 percent) and required fewer visits to the doctor (75 vs. 684, with a median of 0 and 2 visits, respectively). Symptoms were comparable in the two groups.

"For both patients and health care providers, lenient rate control is more convenient," Van Gelder said.

The RACE II study was funded by a major grant from the Netherlands Heart Foundation, additional grants from the Interuniversity Cardiology Institute Netherlands and the Working group Cardiology The Netherlands, and by unrestricted educational grants from AstraZeneca, Biotronik, Boehringer Ingelheim, Boston Scientific, Medtronic, Roche and Sanofi Aventis France, which were paid to the Interuniversity Cardiology Institute Netherlands. Dr. Van Gelder has received consulting fees from Sanofi-Aventis, Boehringer Ingelheim and Cardiome, grant support from Medtronic, Biotronik and St. Jude Medical, and lecture fees from Sanofi-Aventis, Boehringer Ingelheim and Medtronic.

This RACE II study will be simultaneously published in the New England Journal of Medicine and was released online at the time of presentation.

ACC2010特集

心房細動に対してアブレーションは薬物よりも優れている

STOP-AF and CABANA：トライアルの結果、心房細動に対しては薬物治療よりもアブレーションの方が有効であることが示された

STOP-AF and CABANA: Trials show effectiveness of ablation techniques over anti-arrhythmic drug therapy for the treatment of atrial fibrillation

第59回American College of Cardiology学会で発表された2つのスタディの結果、心房細動（AF）の治療としてアブレーションは抗不整脈薬治療よりも有効であり安全性は同等であることが示された。26の医療機関の患者245人を組み入れた発作性心房細動の維持治療（The Sustained Treatment of Paroxysmal Atrial Fibrillation：STOP-AF）スタディでは、Arctic Front®心臓クリオアブレーションカテーテルシステムで治療された発作性AF患者の70%近くが施術後1年間洞調律を維持し、一方薬物療法群で洞調律を維持できたのは7%を少し上回っただけであった。クリオアブレーションの初期成功率は98%であった。より実質的な心血管疾患を基礎疾患として有するより進行したAF患者に対するカテーテルアブレーションの有効性を評価した初めてのスタディのひとつである、心房細動に対するカテーテルアブレーションと抗不整脈薬治療の比較（The Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation：CABANA）パイロット研究の結果、カテーテルアブレーションは薬物療法よりも症候性AF再発予防に有効であることが示された。しかし、持続性および長期の持続性AF患者も含むこれらの患者らにおける成功率は他の無作為化臨床試験で認められた成功率よりも低かった。CABANAは大規模無作為化コントロール試験の基礎を築くようにデザインされた。

Full Text

In patients with an intermittent form of atrial fibrillation, use of a cryoablation catheter is nearly 10 times more effective and equally safe as conventional anti-arrhythmic drug therapy for eliminating the irregular heart rhythm, according to research presented at the American College of Cardiology's 59th annual scientific session. Another study, also presented at the ACC2010, showed that using an ablation catheter appears to be more effective than anti-arrhythmic therapy in treating more advanced atrial fibrillation.

The Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP-AF) study found that nearly 70 percent of patients with intermittent, or paroxysmal, atrial fibrillation who were treated with the Arctic Front® Cardiac CryoAblation Catheter System remained free of atrial fibrillation after one year, as compared with just over 7 percent of patients assigned to drug therapy.

For the study, investigators from 26 medical centers in the United States and Canada recruited 245 patients with paroxysmal atrial fibrillation. All patients had already tried treatment with at least one antiarrhythmic drug, but were unsuccessful. Patients were randomly assigned in a 2-to-1 ratio to cryoablation or treatment with an anti-arrhythmic medication that had not previously failed. During the next 90 days data collection was deferred, allowing each patient's doctor to adjust drug therapy or repeat cryoablation, as needed. After that, patients were followed-up in the clinic at 1, 3, 6, 9 and 12 months. They also sent heart-rhythm tracings to their doctor over telephone lines every week and when experiencing symptoms.

Researchers found that the cryoablation procedure was initially successful in about 98 percent of patients.

After one year, nearly 70 percent of patients treated with cryoablation were free of atrial fibrillation and had not required use of a non-study drug or an interventional procedure to treat atrial fibrillation, as compared with just 7 percent of patients in the anti-arrhythmic drug group.

Just over 3 percent of patients treated with cryoablation experienced a serious complication, specifically, narrowing of the pulmonary vein in seven out of 228 patients, one of whom required an interventional procedure to widen the vein. Phrenic nerve palsy was noted after 11 percent of cryoablation procedures, but none of the cases was considered serious, and approximately 98 percent resolved by the 12-month follow up.

Researchers also tracked complications related to atrial fibrillation itself. During the follow-up period, nearly 97 percent of patients in the cryoablation group and nearly 92 percent of patients in the drug therapy group avoided cardiovascular death, myocardial infarction, stroke, or hospitalization for recurrence or ablation of atrial fibrillation, ablation of atrial flutter, complications related to unwanted blood clots, heart failure, hemorrhage, or anti-arrhythmic drug treatment. Less than 1 percent of patients treated with cryoablation were hospitalized for the recurrence of atrial fibrillation, as compared with 6 percent in the anti-arrhythmic drug group.

The Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (CABANA) pilot study-one of the first to evaluate the feasibility of catheter ablation in patients with more advanced atrial fibrillation and substantial underlying cardiovascular disease-was designed to lay the foundation for a large, randomized controlled trial.

"This pilot study establishes the feasibility and importance of conducting an extended pivotal trial critical for establishing long-term outcomes, mortality, quality of life, and cost of ablation and drug therapy for atrial fibrillation," said Douglas L. Packer, M.D., a cardiologist at Mayo Clinic, Rochester, MN and trial principal investigator.

Abnormal electrical impulses cause the upper chambers of the heart to quiver, and stimulate the heart to race at a rapid rate, rather than contract with a slow, steady rhythm. Anti-arrhythmic drugs are successful in eliminating atrial fibrillation in only about half of patients and can have serious side effects. Drug therapy is often aimed at simply controlling the heart rate. Catheter ablation is an alternative treatment in which a catheter is threaded into the left atrium and typically radiofrequency energy is applied to tissue around the entrance to the pulmonary veins, where most abnormal electrical impulses originate, as well as other trouble spots in the heart.

For the study, investigators recruited 60 patients with atrial fibrillation, more than two-thirds of whom had a persistent or long-standing persistent form of the arrhythmia. The study group tended to have multiple additional health problems: 80 percent of patients had high blood pressure, 18 percent had diabetes, 35 percent had coronary artery disease, and 36 percent had mild-to-moderate heart failure. Nearly half (48 percent) already had left atrial enlargement. Some 30 percent of patients had previously tried anti-arrhythmic drug therapy.

Of the 60 patients in the study, 31 were randomly assigned to drug therapy, and were treated with either anti-arrhythmic drugs (87 percent) or medications to control the heart rate only without eliminating the arrhythmia (13 percent). The remaining 29 patients were randomly assigned to catheter ablation. In nearly all patients, radiofrequency energy was applied to tissue around the entrance of the pulmonary veins. In addition, in 13 out of 29 patients (45 percent) electrophysiologists chose to create additional linear lesions to block the spread of electrical impulses in problem areas.

Investigators found that catheter ablation was more effective than drug therapy for preventing recurrent symptomatic atrial fibrillation. However, treatment success rates in these patients, some of whom had persistent and long-standing persistent atrial fibrillation, were lower than observed in other randomized clinical trials. Late recurrent atrial fibrillation may also diminish the overall effectiveness of ablation therapy, according to Dr. Packer. The CABANA pivotal trial, which will further examine these issues, is currently recruiting patients and is aiming for a total enrollment of 3,000.

The STOP-AF study was funded by Medtronic.

The CABANA Pilot study was funded by St. Jude Medical Foundation.

Dr. Packer in the past 12 months has provided consulting services for Biosense Webster, Inc., Boston Scientific, CyberHeart, Medtronic, Inc., nContact, Sanofi-Aventis, St. Jude Medical, and Toray Industries. Dr. Packer received no personal compensation for these consulting activities. Dr. Packer receives research funding from the NIH, Medtronic, Inc., CryoCath, Siemens AG, EP Limited, Minnesota Partnership for Biotechnology and Medical Genomics/ University of Minnesota, Biosense Webster, Inc. and Boston Scientific.

Mayo Clinic and Drs. Packer and Robb have a financial interest in mapping technology that may have been used at some of the 10 centers participating in this pilot research. In accordance with the Bayh-Dole Act, this technology has been licensed to St. Jude Medical, and Mayo Clinic and Drs. Packer and Robb have received annual royalties greater than $10,000, the federal threshold for significant financial interest.

Mayo Clinic and Dr. Robb have a financial interest in Analyze-AVW technology that was used to analyze some of the heart images in this research. In accordance with the Bayh-Dole Act, this technology has been licensed to commercial entities, and both Mayo Clinic and Dr. Robb have received royalties greater than $10,000, the federal threshold for significant financial interest. In addition, Mayo Clinic holds an equity position in the company to which the AVW technology has been licensed.

ACC2010特集

遠隔モニターはイベントから方針決定までの時間を短縮する

CONNECT：植込み型デバイスの遠隔モニターは方針決定に必要な時間を短縮し診療回数を減らす

CONNECT: Remote monitoring of implanted devices reduces time needed for clinical decision-making and results in fewer office visits

植込み型デバイスから循環器専門医の診察室へ自動的に不整脈情報を送信するワイヤレス監視システムは、問題が発生してから治療方針が決定されるまでの時間を有意に削減すると第59回American College of Cardiology学会で報告された。遠隔通知による方針決定時間の短縮に対する臨床評価（The Clinical Evaluation Of Remote Notification to Reduce Time to Clinical Decision：CONNECT）トライアルでは植込み型除細動器または心臓再同期療法除細動器を植え込まれた患者1,997人を組み入れ、遠隔モニターまたは標準的な診察室でのケアを行う群に無作為に割り付けた。ワイヤレス遠隔モニターは、電話回線を用いて診断に必要な情報を自動的に送信し患者側は何もする必要はない。遠隔モニター群患者はデバイス植込み1ヵ月後および15ヵ月後のみ受信した。標準的なケアを受けた患者は一般的には3～6ヵ月ごとの指定されたスケジュールで経過観察された。その結果、臨床上の問題発生からそれを処理する方針決定までの平均所要時間が有意に短縮された（標準的ケア群29.5日に対し遠隔モニター群10.5日）。平均入院期間も有意に短縮し（それぞれ4.0日対3.3日）、遠隔治療群患者において1回入院当たり推定$1,659の経費削減が見込まれた。

Full Text

A wireless monitoring system that automatically sends information about arrhythmias from a device in the patient's chest to the cardiologist's office significantly cuts the time between when a problem arises and a treatment decision is made, according to research presented at the American College of Cardiology's 59th annual scientific session.

The Clinical Evaluation Of Remote Notification to Reduce Time to Clinical Decision (CONNECT) evaluated a wireless remote monitoring and notification system based on Medtronic's Conexus-enabled cardiac resynchronization therapy defibrillators (CRT-Ds) and implantable cardioverter-defibrillators (ICDs). The wireless telemetry system was compared with standard care, in which a cardiologist reviews information from an implanted device during an in-person clinic visit. The study showed that remote monitoring and automatic notification cut by nearly two-thirds the time to clinical decision-making.

"This system allows the clinician to better manage the patient's disease by making critical information immediately available," said George H. Crossley, M.D., president of Mid-State Cardiology, a unit of St. Thomas Heart, and a clinical professor of medicine at the University of Tennessee College of Medicine, both in Nashville, TN. "By learning about clinical events earlier, we have the opportunity to intervene earlier, improve outcome and prevent disease progression."

The use of remote monitoring for follow-up of CRT-D or ICD, has the potential to improve both patient safety and healthcare efficiency. CONNECT is the largest randomized, prospective study designed to quantify these advantages.

For the study, researchers from 136 sites in the United States recruited 1,997 patients with an ICD or CRT-D, randomly assigning them to remote monitoring or standard in-office care. All patients were followed-up for 15 months after device implantation. Those in the remote-monitoring group were given a home monitor capable of receiving a wireless telemetry signal from the implanted device and automatically transmitting diagnostic information to the cardiologist's office over a telephone line, without any action on the patient's part. The devices were programmed to send routine information on a schedule determined by the cardiologist, and to immediately send alerts in the case of a worrisome development. Patients in the remote-monitoring group were seen in the office 1 month and 15 months after device implantation only. Patients receiving standard care were followed-up in the office on a fixed schedule, typically every three to six months, without remote monitoring.

Data from CONNECT showed a significant reduction in the time between the onset of a clinical problem and a clinical decision on how to manage it (29.5 days, on average, in the standard-care group vs. 10.5 days, on average, in the remote-monitoring group). There was also a significant reduction in the average length of hospitalization (4.0 days vs. 3.3 days, respectively), which resulted in an estimated savings of $1,659 per hospitalization, on average, for patients in the remote-monitoring group.

"Although in our current analysis we were not able to determine the direct mechanism of this reduction in the length of stay, this is the first trial to show a correlation between remote management and significant positive changes to healthcare utilization," Dr. Crossley said.

CONNECT was funded by Medtronic. Dr. Crossley reports receiving speaker and research and consulting fees from Medtronic, speaker fees from Guidant, and research support from St. Jude Medical.

ACC2010特集

ステント埋込み後18ヵ月の成績はエンデバーよりサイファの方が優れていた

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

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

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

Full Text

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

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

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

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

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

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

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

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

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

ACC2010特集

糖尿病患者の血圧は低ければよいというわけではない

INVEST：スタディの結果、冠動脈疾患を有する糖尿病患者に対する強力な降圧治療に対し警鐘が鳴らされた

INVEST: Study warns against aggressive blood pressure lowering in diabetic patients with coronary artery disease

心血管疾患を有する糖尿病患者に対する厳密な降圧療法は標準的な降圧療法と比較し、心筋梗塞予防、脳卒中または死亡のリスクをより軽減するということはないようであり、一部の症例では有害な可能性さえあると第59回American College of Cardiology学会で発表された。国際的ベラパミルSR－トランドラプリル（INVEST）スタディは冠動脈疾患（CAD）を有する糖尿病患者6,400人をカルシウム拮抗薬またはβ遮断薬のいずれかとアンジオテンシン変換酵素（ACE）阻害薬および/またはサイアザイド系利尿薬を併用する群に無作為に割り付けた。収縮期血圧が140mmHg以上の者－患者の約3分の1－はコントロール不良と分類した。収縮期血圧が130mmHg未満の患者は厳密コントロールとし、収縮期血圧が中間の者（130mmHg以上140mmHg未満）は標準コントロールとした。コントロール不良群患者は標準治療群と比較し死亡、心筋梗塞、または脳卒中のリスクが50%高かった。しかし、厳密コントロール群患者におけるリスクは標準治療群患者と同等であった。さらに解析を行った結果、収縮期血圧を130mmHg未満にすることにより標準治療と比較し総死亡のリスクが有意に増加することが示された。

Full Text

Tight blood pressure control in patients with diabetes and cardiovascular disease is no more effective in preventing myocardial infarction, stroke or death than standard blood pressure treatment, and in some cases may actually be harmful, according to research presented at the American College of Cardiology's 59th annual scientific session.

The International Verapamil SR-Trandolapril (INVEST) Study showed that in patients with both diabetes and documented coronary artery disease (CAD), keeping systolic blood pressure under 140 mmHg significantly cut cardiovascular risk. However, more intensive treatment to reduce systolic blood pressure to below 130 mmHg did not appear to offer any additional benefit.

"Current guidelines suggest 'lower is better' with regard to blood pressure," said Rhonda M. Cooper-DeHoff, Pharm.D., M.S., an associate professor of pharmacy and medicine at the University of Florida, Gainesville. "Our data suggest that in patients with both diabetes and coronary artery disease, there is a blood pressure threshold below which cardiovascular risk increases."

As many as two out of three adults with diabetes have high blood pressure. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends blood pressure goals of less than 130/80 mmHg in people with diabetes. INVEST is the first study to critically evaluate the effects of systolic blood pressure lowering in patients with both diabetes and documented CAD.

For the study, INVEST randomly assigned 6,400 patients with diabetes and CAD to blood pressure lowering therapy based either on a calcium-channel blocker or a beta-blocker, plus an angiotensin converting-enzyme (ACE) inhibitor and/or a thiazide diuretic. The target was a blood pressure of less than 130/<85 mm Hg. For the analysis, patients were categorized according to the degree of blood pressure control actually achieved. Patients with a systolic blood pressure of 140 mmHg or higher-almost one third of patients-were classified as Not Controlled. Those with a systolic blood pressure below 130 mmHg were classified as Tight Control and those with a systolic blood pressure in between (130 mmHg or greater, but under 140 mmHg) were classified as Usual Control.

During a follow-up period equivalent to more than 16,893 patient-years, researchers found that patients in the Not Controlled group had nearly a 50 percent higher combined risk of death, myocardial infarction, or stroke when compared with the Usual Care group. However, those in the Tight Control group had a similar risk to those in the Usual Control group. Further analysis showed that lowering systolic blood pressure below 130 mmHg significantly increased the risk of all-cause death when compared to Usual Care, an increase that became apparent about 30 months into the study and persisted for an additional five years of follow up.

When researchers then analyzed blood pressure in 5mmHg increments in the Tight Control group, they discovered that a systolic blood pressure below 115 mmHg was associated with increased mortality.

"Diabetic patients with CAD in whom blood pressure is not controlled have an increased risk for unfavorable cardiovascular outcomes, so the message to lower systolic blood pressure below 140 mmHg is still important," Cooper-DeHoff said. "However, it is not necessary to lower systolic blood pressure below 130 mmHg to reduce that risk. Most importantly, reducing systolic blood pressure below 115 mmHg may be associated with increased mortality."

Abbott Laboratories provided funding for INVEST. Dr. Cooper-DeHoff also received support from an NIH career development award.

ACC2010特集

糖尿病における心血管リスクに対する薬物研究の結果は残念なものであった

NAVIGATOR：スタディの結果、糖尿病および心血管疾患の予防に対して疑問が生じた

NAVIGATOR: Study raises questions on prevention of diabetes and cardiovascular disease

糖尿病および心血管疾患の高リスク患者においてアンジオテンシン受容体遮断薬バルサルタンは、心血管系の健康状態維持には効果がなく糖尿病発症を軽度減少させたのみであり、一方糖尿病治療薬ナテグリニドにおいては糖尿病または心疾患進行に対し有意な効果が認められなかったと第59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。心血管リスクファクターまたは心血管疾患を有する耐糖能異常患者9,306人を解析した。二重無作為化デザインを用いて、患者らはナテグリニド（最高60mgを1日3回食直前に内服）またはプラセボ、およびバルサルタン（最高1日160mg）またはプラセボのいずれかを内服する群に割り付けられた。全ての患者が5%の減量維持、週5日平均30分の運動、および低脂肪食を目標とした生活習慣改善プログラムに参加した。その結果、バルサルタンはプラセボと比較し、糖尿病発症リスクを14%減少させたが、心血管死、非致死性心筋梗塞、非致死性脳卒中、心不全による入院、不安定狭心症、または血行再建術の複合リスクは軽減しなかった。ナテグリニドは糖尿病発症および心血管リスクのいずれも減少させなかった。

Full Text

In patients at high risk for diabetes and cardiovascular disease, a drug used for treating the heart and blood vessels had no effect on cardiovascular health but modestly reduced progression to diabetes, while a drug for controlling blood sugar levels had no significant effect on progression of either diabetes or heart disease, according to research presented at the American College of Cardiology's 59th annual scientific session and published simultaneously in the New England Journal of Medicine.

The Nateglinide And Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) study was a large, international, randomized trial involving patients at high risk for diabetes and cardiovascular disease. The study found that, when added to a program to promote a healthy lifestyle, valsartan reduced progression to diabetes by 14 percent in high-risk patients, but nateglinide had no effect on diabetes progression. Neither medication reduced the risk of cardiovascular illness, such as myocardial infarction or stroke. "Most experts believed that nateglinide would prevent diabetes and that valsartan would reduce cardiovascular events in this population," said Robert M. Califf, M.D., Vice Chancellor for Clinical.

Research at Duke University Medical Center, Durham, NC and the lead investigator. "Interestingly, with respect to nateglidine, we found the opposite. The results with valsartan confirmed previous studies that showed a reduction in diabetes. It was disappointing that there was no reduction in cardiovascular events, but in such a large study, with patients on other therapies that are known to impact cardiovascular disease, this lack of event reduction is consistent with other studies."

Nateglinide is a diabetes medication that minimizes spikes in blood sugar after meals by stimulating the pancreas to produce more insulin. Researchers had hypothesized that nateglinide would reduce progression to diabetes by restoring a more normal insulin response after meals. It was hoped the drug would reduce the risk of cardiovascular disease.

Valsartan is an angiotensin-receptor blocker (ARB) that is used to treat high blood pressure, heart failure, and the long-term consequences of a myocardial infarction. Some studies have suggested that medications that block the renin-angiotensin system may not only help the cardiovascular system, but may also delay or prevent the development of diabetes.

For the study, researchers at 806 medical centers in 40 countries analyzed 9,306 patients with glucose intolerance and either cardiovascular risk factors or established cardiovascular disease. Using a double randomization design, patients were assigned to receive either nateglinide (up to 60 mg three times a day before meals) or a matching placebo, and valsartan (up to 160 mg daily) or a matching placebo. All patients were required to participate in a lifestyle program, with the goal of maintaining a 5 percent weight loss, increasing physical activity to an average of 30 minutes five days a week, and to follow a low-fat diet.

"Lifestyle modification remains the best choice for preventing diabetes in high-risk patients," said Rury R. Holman, MB, ChB, FRCP, professor of Diabetic Medicine, and Diabetes Trials Unit Director, University of Oxford, UK. "Eating a healthy diet, exercising regularly, and maintaining a normal body weight are critical for long-term health in patients at risk for diabetes and vascular disease."

Patients were followed for 5 years, on average, for development of diabetes and 6.5 years, on average, for cardiovascular disease. Researchers found that valsartan reduced the risk of progression to diabetes by 14 percent. When compared with the placebo, valsartan did not reduce the risk of a combination of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, hospitalization for heart failure, unstable chest pain, or the need for a surgical or catheter-based procedure to restore blood flow through clogged arteries, nor did the ARB reduce the risk of key cardiovascular outcomes, which excluded unstable chest pain or vascular procedures. Nateglinide failed to reduce both progression to diabetes and cardiovascular risk.

Investigators speculated that the study's results may have been influenced by how effective the lifestyle program was in reducing both diabetes progression and cardiovascular risk. By the end of the study, a large number of patients were taking medications prescribed by their personal physician to inhibit the rennin angiotensin system or to treat abnormal lipid levels or high blood pressure, and this may have lowered overall risk.

The trial was sponsored by Novartis. Prof. Holman reports receiving grant support from Asahi Kasei Pharma, Bayer Healthcare, Bayer Schering Pharma, Bristol-Myers Squibb, GlaxoSmithKline, Merck, Merck Serono, Novartis, Novo Nordisk, Pfizer and Sanofi-Aventis; consulting fees from Amylin, Eli Lilly, GlaxoSmithKline, Merck and Novartis; and lecture fees from Astella, Bayer, GlaxoSmithKline, King Pharmaceuticals, Eli Lilly, Merck, Merck Serono, Novo Nordisk, Takeda and Sanofi-Aventis. Dr. Califf reports receiving research grant support from Novartis Pharmaceuticals, Johnson & Johnson/Scios, Lilly, Merck, and Schering Plough, and consulting fees from Annenberg, Aterovax, Bayer/Ortho McNeil, BMS, Boehringer Ingelheim, GSK, WebMd/theheart.org, Johnson and Johnson/Scios, Kowa Research Institute, McKinsey & Company, Medtronic, Merck, Novartis Pharmaceuticals, Sanofi Aventis, and Schering Plough, and an equity position with NITROX, LLC. All personal income from industry relations is donated to non-profit entities.

ACC2010特集

ワルファリンに関するgenotypeにより入院が減少する

MM-WES：遺伝子検査により最も有効な抗凝固療法用量が決定でき入院が3分の1近く減少する

MM-WES: Genetic testing helps determine most effective dose for anticoagulant therapy, cutting hospitalizations by nearly one-third

各々の患者に対する最も安全で有効な抗凝固療法用量を医師が決定するのに役立つある簡便な遺伝子検査により、一般的に用量を試したり失敗したりして調整する重要な開始時期の入院数を有意に減少させるとの研究結果が第59回American College of Cardiology学会で発表された。Medco-Mayoワルファリン有効性スタディ（Medco-Mayo Warfarin Effectiveness Study：MM-WES）ではワルファリン療法を開始する患者896人を組み入れた。医師は患者から血液検体または頬粘膜のスワブを採取し、2つの遺伝子（CYP2C9およびVKORC1）の発現に関するレポートおよびこの結果を解釈するための臨床情報を得た。例えば、genotypeに基づきワルファリン感受性が高いと分類された患者の主治医はワルファリン投与量を減量し血液検査をより頻回に行った。6ヵ月後、全ての理由による入院および出血または血栓塞栓症による入院は遺伝子検査を受けた者において遺伝子検査を受けずに従来通りにコントロールされた者と比較し、それぞれ31%および29%少なかった。Genotype決定後の入院のみを対象とした解析では、遺伝子検査をされた患者の全ての原因による入院のリスクは33%低く、出血または血栓塞栓症による入院は43%低かった。

Full Text

A simple genetic test that helps physicians determine for each patient the safest and most effective dose of an anticoagulant significantly reduces the number of hospitalizations during the critical start-up phase when dosing is typically adjusted by trial and error, according to research presented at the American College of Cardiology's 59th annual scientific session.

The Medco-Mayo Warfarin Effectiveness Study (MM-WES) found that hospital admissions for any cause could be cut by nearly one-third, as could hospitalizations for either excess bleeding or unwanted blood clotting simply by testing for variations in two genes that strongly influence a patient's sensitivity to the blood thinner warfarin.

"Genetic testing is a tool clinicians can use to more accurately predict the best warfarin dose early on," said Robert S. Epstein, M.D., chief medical officer and president of the Medco Research Institute in Franklin Lakes, N.J. "Patients may get to a stable dose more quickly and, therefore, have a lower risk of negative outcomes."

Warfarin sensitivity varies widely, however, and it can take weeks or even months of repeated blood tests and dose adjustments to determine the right dose for each patient. During that time, patients are at high risk for either thromboembolism from too little warfarin, or dangerous bleeding from too much warfarin. The MM-WES study is the first national, prospective, comparative effectiveness study to evaluate the role of genetic testing in assisting physicians to gauge the best warfarin dose and monitoring intensity during the early dose-adjustment phase of treatment.

For the study, researchers recruited 896 patients who were beginning warfarin therapy. All study participants were members of a prescription benefits plan managed by Medco Health Solutions. They came from 49 of 50 states and a variety of practice settings.

Shortly after starting warfarin therapy, patients gave a blood sample or a cheek swab, which was analyzed at the Mayo Clinic in Rochester, M.N. For each patient, the ordering physician received a report on the genetic expression of two genes, CYP2C9 and VKORC1, as well as clinical information on how to interpret the findings. For example, a patient might be classified as having a high sensitivity to warfarin based on genotype. In this case, the physician would be advised to reduce the warfarin dose and monitor blood tests more frequently. If a patient were found to have a low sensitivity to warfarin, the report would recommend an increase in warfarin dose. Each physician was free to decide how to respond to the report and what action to take.

The researchers found that, during the first six months of warfarin therapy, patients who had genetic testing were 31 percent less likely to be hospitalized for any cause, when compared to an historical control group that did not undergo genetic testing. Patients in the gene-testing group were also 29 percent less likely to be hospitalized for bleeding or thromboembolism. The study's findings were even stronger when the analysis included only hospitalizations that occurred after genotyping. In this per-protocol analysis, patients who underwent genetic testing had a 33 percent lower risk of all-cause hospitalization and a 43 percent lower risk of hospitalization for bleeding or thromboembolism.

The cost of genetic testing - approximately $250 to $400, depending on the laboratory - is justified by the savings, according to Epstein. "If we reduce just two hospitalizations per 100 patients tested, that more than compensates for the cost of genotyping," he said.

Medco provided funding for genotyping and data collection. Researchers from the Mayo Clinic and Washington University donated their time.

ACC2010特集

ステント留置前の血栓除去術により予後が改善する

JETSTENT：ステント留置前のレオリティック血栓除去はステント留置単独よりも再灌流および短期臨床エンドポイントの成績が良好である

JETSTENT: Rheolytic thrombectomy before stenting leads to better reperfusion and short-term clinical end points than stenting alone

急性ST上昇心筋梗塞に対するダイレクトステント留置術前にレオリティック血栓除去術を施行する方がステント留置術単独よりも臨床成績が良好であるとのリサーチ結果が第59回American College of Cardiology学会で発表された。JETSTENTトライアルでは501人の患者をダイレクトステント留置術または血栓除去術とダイレクトステント留置術を行う群に無作為に割り付けた。一次エンドポイントは、早期ST回復（30分後の50%以上のST上昇軽減）および30日後の梗塞サイズであった。ダイレクトステント留置術に加え血栓除去術を施行された群において、ステント留置術単独群と比べ、有意に多くの患者が指定時間内にST上昇の回復を示した（それぞれ85.8%と78.8%、P=0.43）。1ヵ月後のシンチグラフィーで評価した梗塞サイズには、両群間で有意差はなかった。臨床上のエンドポイントに関しては、1および6ヵ月後の主要な心血管有害事象が血栓除去術群で有意に少なかった（それぞれ3.1%対6.9%、P=0.05および11.9%対20.6%、P=0.012）。このスタディにおける他のサロゲートエンドポイント（myocardial blush gradeおよびcorrected TIMI frame countなど）について有意差は認めなかった。施術時間は血栓除去術を施行した群において有意に長かった（約15分）が成功率は両群間で同等であった。

Full Text

Conducting rheolytic thrombectomy before direct infarct-related artery stenting in patients with acute ST-segment elevation myocardial infarction produced better clinical results than performing direct stenting alone, according to research presented at the American College of Cardiology's 59th annual scientific session.

The randomized, prospective JETSTENT trial enrolled 501 patients at eight sites across Europe and South America between December 2005 and September 2009 to determine how use of a rheolytic thrombectomy system would affect myocardial reperfusion and clinical outcomes for patients with acute ST-segment elevation myocardial infarction. The trial's primary endpoints were ST-segment resolution at 30 to 45 minutes post-procedure and final infarct size at 30 days. The trial's clinical endpoints included a composite of death, myocardial infarction, target vessel revascularization, and stroke at one, six, and 12 months, as well as a composite of death and readmission for congestive heart failure at 12 months.

The study found that significantly more patients receiving rheolytic thrombectomy in addition to direct stenting experienced resolution of their ST-segment elevation in the designated time frame than those patients receiving stenting alone, at 85.8 percent and 78.8 percent, respectively. Additionally, while no significant differences were revealed in infarct size as assessed by 1-month scintigraphy (median infarct size was 11), the researchers found a value of 6 percent in the thrombectomy arm and 12.6 percent in the direct stenting alone arm. The researchers also found a significant decrease in major cardiovascular adverse events both at 1 month and at 6 months for patients randomized to receive rheolytic thrombectomy than patients in the direct stenting alone arm (3.1 percent versus 6.9 percent and 11.9 percent versus 20.6 percent, respectively). The researchers did not find a significant difference between the study's other surrogate endpoints, including myocardial blush grade and the corrected TIMI frame count.

Procedural times were significantly longer (about 15 minutes) for those treated with thrombectomy but procedural success rates were similar in both treatment groups.

"These study results support the routine use of thrombectomy in patients with acute ST-segment elevation myocardial infarction and evidence of thrombus," said David Antoniucci, M.D., head of the Division of Cardiology at Careggi Hospital in Florence, Italy, and the study's lead researcher.

The JETSTENT data contrast with the outcomes of Possis Medical's previous study, the AngioJet rheolytic thrombectomy in patients undergoing PCI for acute myocardial infarction (AiMI) trial.

Specifically, AiMI found that in a sample of 480 patients, rheolytic thrombectomy did not lead to better reperfusion and was associated with a significantly higher mortality rate at 30 days and 6 months postprocedure.

According to Antoniucci, the JETSTENT study - which was designed also to address questions raised by the AiMI findings - differs from the AiMI study in three key ways. First, it includes only patients with angiographically visible thrombus. Second, it uses a "single-pass antegrade" technique in which the thrombectomy device is activated before crossing the lesion and moved in a proximal-to-distal approach in order to cut the risk of embolization. Third, it has a narrow temporal definition of ST-segment elevation resolution (defined as more than 50 percent resolution within 30-45 minutes from the procedure) which allows for greater sensitivity than the 90-minute time frame that was used in the AiMI study.

"Early ST-segment resolution was inversely related to the occurrence of major adverse events, suggesting that it is a reliable marker of reperfusion." Antoniucci said. "Also, multivariable analysis showed that randomization to rheolytic thrombectomy is independently related both to early ST-segment resolution and to the occurrence of major adverse cardiovascular events." Medrad Interventional/Possis funded the study. The funding company was not involved in the management, collection, and analysis of data. Dr. Antoniucci has no personal financial relation with the sponsor.

ACC2010特集

薬剤溶出ステントの長期リスクが問題にされた

PASSIONおよびDEDICATION：スタディの結果ST上昇MI患者に対する薬剤溶出ステント使用に関する懸念が示唆された

PASSION and DEDICATION: Studies raise concerns about use of drug-eluting stents in patients with ST-segment-elevation MI

ST上昇心筋梗塞患者に対する薬剤溶出ステント（DES）とベアメタルステントを比較した2つのスタディの結果、薬剤溶出ステントに関する疑問が持ち上がった。PASSIONトライアルの5年間の結果、パクリタキセル溶出ステント（Taxus Express2）とベアメタルステント（Express2 or Liberté）の複合一次エンドポイント（心臓死、心筋梗塞再発、標的病変に対する再血行再建術施行）はそれぞれ18.3%と22.0%であり、統計学的に有意ではなかった。個々に比較すると2つのステント群間でいずれの主要な心イベントに関しても有意差は認められなかった。さらに、確実な（definite）ステント血栓発現率はベアメタルステント群と比較しDES群において2倍であった（それぞれ3.6%と1.7%）が、確実なおよびかなり確実と思われる（probable）ステント血栓発現率はそれぞれ3.9%と3.4%であり、同等であった。DEDICATIONトライアルでは、薬剤溶出ステント群において主要な有害心事象は少なかったものの、心死亡率は有意に高かったと報告された。これらのスタディは第59回American College of Cardiology学会で発表された。

Full Text

Long-term results from two studies comparing drug-eluting stents (DES) with bare-metal stents in patients with ST-segment-elevation myocardial infarction (STEMI) have raised some questions about the long-term risks of the drug-eluting devices, according to research presented at the American College of Cardiology's 59th annual scientific session.

In one study, known as the PASSION trial, investigators observed no differences between the two stents in the composite end point of cardiac death, recurrent MI, or target lesion revascularization at five years and no significant differences in the incidence of major adverse cardiac events, but they did observe a trend of very late stent thrombosis in DES-treated patients. In the DEDICATION trial, investigators report an increased risk of cardiac death at three years in patients treated with a DES compared with patients treated with a bare-metal stent. Despite a finding of lower rates of adverse cardiac events than in bare-metal stent patients, cardiac mortality was significantly higher in patients who received drug-eluting stents

In the first randomized, controlled trial to report 5-year data on the safety and benefits of drug-eluting stents compared with bare metal stents in acute myocardial infarction, known as the PASSION trial, researchers found no statistically significant difference in either safety or efficacy between the two groups.

The 5-year findings from the PASSION trial contrasted with the researchers' hypothesis that the paclitaxel-eluting stent would perform significantly better for cardiac death, recurrent myocardial infarction, and target lesion revascularization. The results also failed to show a statistically significant difference between the two stent types in preventing very late stent thrombosis, which has been a primary concern of drug-eluting stent use.

The trial dated from between March 2003 and December 2004 and randomized 619 patients with acute myocardial infarction to receive either the Taxus Express2 (a paclitaxel-eluting stent) or the Express2 or Liberté (bare-metal stents). All stents were manufactured by Boston Scientific.

Specifically, the prospective, single-blind study did not show a statistically significant difference between the paclitaxel-eluting stent and the bare-metal stent for the primary composite endpoint of cardiac death, recurrent myocardial infarction, and target lesion revascularization, at 18.3 percent and 22.0 percent, respectively.

The researchers also did not find a statistically significant difference between the two stent groups for any of the major cardiac events when examined individually.

Furthermore, despite a two-fold increase in the occurrence of definite stent thrombosis in the paclitaxel-eluting stent group compared with the bare-metal stent group - at 3.6 percent and 1.7 percent, respectively - the occurrence of both definite and probable stent thrombosis, (which includes suspected clots that have not been confirmed and which more closely resembles a real-world patient population) was comparable, at 3.9 percent and 3.4 percent, respectively.

"I think we can conclude from the trial that the use of drug-eluting stents in primary angioplasty is safe through several years after implantation," said Maarten Vink, M.D., of the Onze Lieve Vrouwe Gasthuis Hospital in Amsterdam, The Netherlands, one of the study's researchers. "Compared to bare-metal stents, we did not find a difference in the occurrence of the primary composite endpoint of major adverse cardiac must carefully weigh the benefits and drawbacks of using drug-eluting stents for acute myocardial infarction."

The 5-year data follow in line with both PASSION's 1-year data and 2-year data - which also found no statistically significant safety or benefit differences between the two stents - but Vink notes that the 5-year results are especially important to examine in light of data in clinical registries that associate drug eluting stent use with very late stent thrombosis.

While Vink acknowledges that the study provides valuable insight into the debate surrounding this issue, he cautions that because the PASSION trial is the first large, randomized, controlled study to report 5-year data, its findings cannot provide definitive answers on the use of drug-eluting stents in acute myocardial infarction.

"Right now, the clinical guidelines are not conclusive concerning the use of drug-eluting stents in angioplasty for acute myocardial infarction, as the European Society of Cardiology does not define if they should be used, while the American College of Cardiology provides an indication for them," said Vink. "Because the guidelines are not uniform, I think their use will remain an issue-one without a definite answer- until we have data from more large, randomized, long-term studies."

The PASSION study was funded by the Department of Interventional Cardiology at the Onze Lieve Vrouwe Gasthuis Hospital. Dr. Vink has no personal disclosures.

The DEDICATION trial researchers conclude that more research is needed on the relative costs and benefits of using drug-eluting versus bare-metal stents in patients who have experienced a ST-elevation myocardial infarction.

A team of Danish researchers recently completed the three-year DEDICATION trial examining the effectiveness and risks of drug-eluting stents versus bare-metal stents. The team randomly assigned 626 patients who received percutaneous coronary intervention (PCI), also known as coronary angioplasty, within 12 hours of a STEMI to receive either a drug-eluting stent or a bare-metal stent. After three years, patients who had received a bare-metal stent were more likely to have experienced a variety of negative outcomes including target lesion revascularization, target vessel revascularization, and other major adverse cardiac events. All-cause mortality, the rates of a myocardial infarction, re-infarction and stroke were similar in both groups. However, patients in the drug-eluting stents group were more likely to die from cardiac-related problems.

"The key message here," said Peter Clemmensen, M.D., of Copenhagen University Hospital, Denmark, and President of the Danish Heart Foundation, "is that we have shown that, despite a finding of lower major adverse cardiac events, cardiac mortality was significantly higher in the drug-eluting stent group."

Because of this mixed set of results, further study is warranted to determine the long-term effects of drug eluting versus bare-metal stents.
"We encourage other trialists to conduct long-term follow up in their STEMI trials involving drug-eluting stents," Clemmensen said.

The DEDICATION study received unrestricted grants from Johnson & Johnson, Medtronic, Abbott, and Boston Scientific.

ACC2010特集

高リスク患者はACSに対する積極的な治療の恩恵を被る

FIR Collaboration：非ST上昇急性冠症候群に対しては選択的な侵襲治療よりもルーチンの侵襲治療の方が良い

FIR Collaboration: Routine invasive strategy better than selective invasive care for non-ST acute coronary syndrome

非ST上昇急性冠症候群患者に対するより積極的な治療により保存的治療よりも長期予後が改善すると第59回American College of Cardiology学会で発表、Journal of the American College of Cardiologyに掲載された。FIR共同トライアル（FRISC-II、RITA-3およびICTUSスタディのメタ解析）では個々の患者のデータを解析し、重度の症状または虚血の徴候を有する患者に対するより積極的なルーチンの侵襲的（RI）治療（全患者に早期の冠動脈造影を施行し適応の場合には血行再建術を施行する）または保存的な選択侵襲的（SI）治療（標準的な薬物療法と特異的な症例にのみ冠動脈造影を施行）の長期予後を明らかにした。5年後の心血管死および非致死性心筋梗塞（MI）発現率はRI治療群の方が低かった。特に、RI群に割り付けられた患者2,721人中14.7%が心血管死または非致死性MIを発現したのに対し、SI群患者2,746人におけるその割合は17.9%であった。治療効果が最も著明に認められたのは非致死性MI単独であり、RI群の10%に認められたのに対しSI群におけるその割合は12.9%であった。心血管死単独および総死亡もRI群において少なかった。

Full Text

A more aggressive treatment approach to patients with non-ST elevation acute coronary syndrome (ACS) leads to better long-term outcomes than more conservative care, according to research presented at the American College of Cardiology's 59th annual scientific session.

The FIR Trial Collaboration is the first meta-analysis of all relevant studies containing five-year data. The lead investigators from each of the studies (FRISC-II, RITA-3 and ICTUS) collaboratively analyzed the individual patient data to determine the long-term outcomes of using either a more aggressive routine invasive (RI) strategy - consisting of early coronary angiography for every patient followed by revascularization, if indicated - or a more conservative selective invasive (SI) strategy-consisting of standard medical treatment and coronary angiography only for specific cases-in patients with severe symptoms or signs of ischemia.

At the five-year mark, patients receiving the RI strategy had lower incidences of cardiovascular death and non-fatal myocardial infarction. Specifically, 14.7 percent of the 2,721 patients randomized to the RI group experienced either cardiovascular death or non-fatal myocardial infarction, compared with 17.9 percent of the 2,746 patients in the SI group. The most marked treatment effect was seen for non-fatal myocardial infarction alone, which occurred in 10 percent of the RI cohort and 12.9 percent of the SI cohort, but the researchers also saw both a lower number of cardiovascular deaths alone and a lower number of deaths from any cause in the RI group.

"The reason why we need this combined 'meta-analysis' of all the trials, and based on individual patient data, is that there is inconsistency in the findings of the individual studies," said Dr. Keith A. Fox, the British Heart Foundation Professor of Cardiology at the Centre for Cardiovascular Science at the University of Edinburgh, United Kingdom, and the study's lead researcher. "It is only with this combined analysis that we can get a conclusive result. The study has demonstrated that there is a clear impact on reduced CV death and myocardial infarction."

In addition to discovering that an RI strategy produced better long-term results than a SI strategy, the team also uncovered an unexpected finding: not all patients benefited equally. Those in the highest risk group - based on a number of variables including age, diabetes, and previous myocardial infarction, among others - benefitted the most from undergoing the RI strategy. The researchers note that risk can be estimated at the bedside using a simple scale based upon the patient's characteristics (age, diabetes, ECG signs of ischemia, hypertension, prior myocardial infarction and Body Mass Index).

While Fox notes that this finding highlights a common paradox in medical treatment - that the majority of patients who receive interventions are low risk - he adds that the study lends support to the idea of systematically risk-stratifying patients in order to determine who should receive an intervention.

"If patients are high risk and without contraindication but they are not going for an invasive strategy, we need to ask 'why,'" Fox said.

The need for risk stratification is supported by guidelines including the American College of Cardiology/American Heart Association Guidelines.

The meta-analysis was conducted using resources from each of the host institutions for their respective studies. The original studies were supported as disclosed in the original publications.

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

ACC2010特集

橈骨動脈グラフトの開存率は伏在静脈と同等である

冠動脈バイパス術後1年間の開存率は伏在静脈グラフトと橈骨動脈グラフトとで同等である

Saphenous vein and radial artery have same graft patency one year after coronary artery bypass graft surgery

伏在静脈グラフトと橈骨動脈グラフトを比較したスタディの結果、1年後のグラフト開存率は同等であったとの研究結果が第59回American College of Cardiologyで発表された。このスタディでは待機的冠動脈バイパスグラフト術（CABG）を施行される患者733人を橈骨動脈または伏在静脈グラフト（366人を橈骨動脈グラフト群、367人を伏在静脈グラフト群）を用いる群に無作為に割り付けた。1年後にグラフト造影を行った結果これらの2つのグラフト群間で開存率に差はなかった。手術の合併症、心筋梗塞、脳卒中、再血行再建術、および死亡からなる二次エンドポイントに有意差はなかった。可能性のある合併症を明らかにするため、研究者らは術後1週にもグラフト造影を行った。その結果、2つのグラフトの開存率はそれぞれ橈骨動脈99%および伏在静脈97%であり、同等の成績であった。しかし、橈骨動脈グラフトの方が疾患の早期徴候が多く認められた（びまん性狭窄［string sign］は橈骨動脈グラフトの8%において認められたのに対し伏在静脈においては1%であった）。

Full Text

A study comparing saphenous vein grafts and radial artery grafts found that they both resulted in equal graft opening at one year, according to research presented at the American College of Cardiology's 59th annual scientific session.

Conducted at 11 Veterans Affairs medical centers between 2003 and 2008, the prospective study randomized patients undergoing elective coronary artery bypass graft surgery (CABG) to receive either the radial artery or the saphenous vein graft. In the final analysis, 733 patients were included (366 with the radial artery, 367 with the saphenous vein).

The study found that at one year, graft angiography revealed no difference in graft opening between the two conduits, with the radial artery leading to 89 percent, and the saphenous vein leading to 89 percent.

No significant differences were noted for the secondary endpoints either, which included surgical complications, myocardial infarction, stroke, repeated revascularization, and death. In order to determine when potential complications would occur, the researchers also performed graft angiography at one week after surgery, for which they found the two grafts also performed equally, at 99 percent for the radial artery and 97 percent for the saphenous vein.

"In the United States alone, there were 165,000 CABG procedures performed in 2008, according to the Society of Thoracic Surgeons database, and over 10,000 of these cases used the radial artery graft," said Steven Goldman, M.D., Chief of Cardiology at the Tucson VA, Southern Arizona VA Health Care System, and the study's lead researcher. "That tells us that surgeons today are using radial artery grafts, but the answer to whether or not they are better than vein grafts is still unclear."

According to Goldman, many surgeons believe the radial artery is superior to the saphenous vein, because arterial grafts develop less disease than vein grafts and are better able to withstand aortic pressure. In addition, the left internal mammary artery is commonly used in CABG procedures and has shown positive results in published studies. However, Goldman said that a procedure using the left internal mammary artery is actually very different - and can be much more complicated - than a procedure using the radial artery, because the former requires reattaching only one end of the artery, while the latter requires total transplantation.

"While the study findings raise new questions from the surgical perspective regarding graft durability in the short term, we need to see the data from our study of long-term graft patency - which analyzes 5-year outcomes - before making substantive judgments on the performance of the radial artery graft," Goldman said.

Only one other study has thus far pitted the radial artery against the saphenous vein, but its outcomes were different than the current trial, finding that the radial artery had significantly more graft patency than the saphenous vein at one year. That study's 5-year findings have yet to be published.

The study was funded by The Department of Veterans Affairs Cooperative Studies program.

ACC2010特集

急性心不全に対する利尿薬の用量調節

DOSE：体液貯留に対しループ利尿薬は持続投与でもボーラス投与でも結果は同等であるが高用量フロセミド投与の方が有効である可能性がある

DOSE: Loop diuretics have similar results whether given by continuous infusion or bolus, but high-dose furosemide may be better for fluid overload

急性心不全で入院した患者に対し、高用量または低用量の利尿薬を持続的または間歇的に投与しても総合的な症状改善または腎機能変化には有意な差がないとの研究結果が第59回American College of Cardiologyで発表された。利尿薬の最適な使用法の評価（Diuretic Optimization Strategies Evaluation：DOSE）スタディにおいて、急性非代償性心不全および体液貯留を有する患者308人を高用量または低用量フロセミド静脈内注射（それぞれ常用経口投与量の2.5倍または常用経口投与量と同用量）を投与する群に無作為に割り付けた。二重無作為化アプローチにより患者らはまた、静脈内投与を12時間ごとあるいは持続的に投与する群に無作為に割り付けられた。その結果、高用量フロセミドを72時間投与することにより全体の徴候の改善がより認められる傾向にあった。高用量のフロセミド投与による腎機能の有意な悪化（ベースラインから72時間後までの血清クレアチニンレベルの変化の中央値で計測）はみられなかった（高用量群で0.06mg/dLに対し低用量群で0.01mg/dL）。全体の体液量減少および体重変化のような体液量オーバーロード改善に対するフロセミドの有効性などいくつかの二次計測項目に関しても高用量フロセミド群で良好な傾向にあった。

Full Text

In patients hospitalized with acute heart failure, there is no significant difference in overall symptom relief or change in kidney function whether a diuretic is delivered at high or low doses or by continuous or intermittent infusion, according to research presented at the American College of Cardiology's 59th annual scientific session.

The Diuretic Optimization Strategies Evaluation (DOSE) Study did suggest, however, that high-dose furosemide may be more effective than low-dose furosemide at improving several individual measures of fluid overload and symptom severity. Furthermore, significant deterioration in kidney function, although more common with high furosemide doses, tended to be transient. DOSE is the largest randomized controlled trial of diuretic strategies ever conducted in patients hospitalized for sudden worsening of heart failure. It is the first clinical trial completed by the National Heart, Lung, and Blood Institute's Heart Failure Clinical Research Network, which was established to promote innovative clinical research in heart failure.

"Despite decades of clinical experience, high-quality data supporting the safety and effectiveness of furosemide in acute heart failure are sparse," said G. Michael Felker, M.D., MHS, a co-principal investigator and an associate professor of medicine in the Divisions of Cardiology and Clinical Pharmacology at Duke University Medical Center, Durham, NC. "DOSE was an attempt to take the principles of evidence-based medicine-prospective, randomized, controlled trials-that we use to evaluate new drugs and apply them to old drugs like furosemide that we prescribe every day. These results give us a more precise understanding of the trade-off between relief of congestion and the risks of renal dysfunction."

Diuretics such as furosemide are used to treat more than 90 percent of patients who are hospitalized for acute decompensated heart failure (ADHF), to reduce fluid overload and make it easier to breathe. However, because high-quality data are not available to guide the use of furosemide, there is a great deal of variation among clinicians and hospitals in both the total dose and the way the intravenous drug is administered. Observational data have suggested that higher doses of furosemide may be associated with worsening kidney function, abnormal concentrations of sodium and potassium in the blood, low blood pressure, and death. In addition, some small studies have suggested that giving furosemide as a continuous infusion may be the safest and most effective approach, but most clinicians still use intermittent "bolus" dosing.

For the study, researchers recruited 308 patients with ADHF and fluid overload from nine regional medical centers and their referring hospitals in the U. S. and Canada. Patients were randomly assigned to treatment with either high- or low-dose intravenous furosemide (delivered at 2.5 times their usual daily oral dose or at the same level as their usual daily oral dose, respectively). In a double-randomization approach, patients were also assigned to intravenous dosing either every 12 hours or to a continuous infusion.

Researchers observed a trend suggesting greater global symptom resolution with high-dose furosemide over 72 hours. This was not associated with significant deterioration in renal function as measured by the median change in serum creatinine level from baseline to 72 hours (0.06 mg/dL for high-dose furosemide vs. 0.01 mg/dL for low-dose). Several secondary measures of the effectiveness of furosemide in relieving fluid overload, such a net volume loss and change in body weight, also tended to favor high-dose furosemide.
"These findings suggest that high-dose furosemide may be preferable to low-dose," Felker said. "The price seems to be a transient and relatively small deterioration in kidney function."

The infusion strategy used for delivering furosemide (intermittent vs. continuous) made no difference in the global measure of symptom resolution or in the change in serum creatinine level (0.04 mg/dL for both groups).

"Given that there has been no adequately sized clinical trial of diuretic dose or route of administration to date-and because of the encouraging trends in the high-dose group-these results may have an immediate impact on the care of hospitalized heart failure patients," said Christopher O'Connor, M.D., the study's senior co-principal investigator, a professor of medicine and director of the Duke Heart Center.

"We will change our standard of care today, and the results may be reflected in future guidelines."

DOSE was sponsored by the National Heart Lung, and Blood Institute. Drs. Felker and O'Connor have no potential conflicts of interest to report.

ACC2010特集

マラソンランナーは心疾患のリスクが高い可能性がある

過度の長期間持久運動は動脈スティフネスを増加させ心血管系の健康状態に影響する可能性がある

Too much long-term endurance exercise increases aortic stiffness and may impact cardiovascular health

新たなデータにより定期的に走っているマラソンランナーは動脈のスティフネスが増加していることが示され、一部の高強度の運動は心血管系の健康状態に悪影響を及ぼす可能性があることが示唆されたと、第59回American College of Cardiologyで発表された。研究者らは、定期的にマラソンをして鍛えている健常人49人と持久運動をしていないコントロール46人の血圧および動脈の弾力性を比較した。マラソンランナーは定期的に週2～9時間走り30ヵ月から21年間継続していた。研究者らは脈波伝搬速度を用いて動脈のスティフネスを計測した。全ての検査は被検者が安静にしている時に行われた。マラソンランナーは上腕の上腕動脈で計測した収縮期血圧がコントロール群よりも有意に高かった（126±15対115±12）。上腕動脈の拡張期血圧（78±10対71±9）および平均血圧（94±12対86±10）もまたコントロールと比較し高かった。脈波伝搬速度もまたマラソンランナーにおいて高く（6.9±1対6.3±1）、マラソンランナーは動脈のスティフネスが上昇していることが示唆された。運動強度と動脈のスティフネスは正の相関関係にあり、より強度の運動により大きな動脈のスティフネスが上昇する可能性が考えられた。

Full Text

New data show regular marathon runners have increased stiffness of the aorta, suggesting that some types of higher intensity exercise may negatively impact heart health, according to research presented at the American College of Cardiology's 59th annual scientific session.

The study - the first to investigate the chronic effect of intense long-term endurance training on the elastic properties of the large arteries - found that male marathon athletes (females were not included in the study) had significantly increased stiffness of the aorta when compared with subjects of similar health status performing recreational exercise.

"Our data suggest that exercise may have an inverted U-shape relation with arterial stiffness. In other words, when you do not exercise you have higher risk of cardiovascular events, but the same also happens when you exercise too much," said Despina Kardara, M.D., Athens Medical School, Hippokration Hospital, Athens, Greece, and lead investigator of the study. "Regular long-term endurance training is generally beneficial for heart health, but it seems that the cardiovascular system is like a sports car engine. If you do not use it, it will decay, but if you run it too fast for too long, you might burn it out."

Researchers evaluated blood pressure and artery elasticity in 49 healthy men who regularly trained to run marathons and 46 control subjects who were not endurance athletes. Marathon runners had regular training times ranging from two to nine hours per week over periods ranging from 30 months to 21 years.

Control participants were matched for age, height and cardiovascular risk factors. To estimate stiffness of the aorta, researchers used an index called pulse wave velocity that measures the speed at which blood travels through the aorta. All tests were performed when participants were at rest prior to the marathon race.

Marathon runners had significantly higher systolic blood pressure than controls when measured at the brachial artery in the upper arm (126±15 vs. 115±12). Brachial diastolic blood pressure (78±10 vs.71±9) and mean blood pressure (94±12 vs. 86±10) were also increased compared to controls. Pulse wave velocity was also higher in athletes (6.9±1 vs. 6.3±1), indicating that marathon runners had increased aortic stiffness. The intensity of participants' exercise regimens was positively related to arterial stiffness, suggesting that more vigorous exercise may result in increased stiffness of the large arteries.

"This is important because stiff arteries lead to high blood pressure and can impair the heart, keeping it from performing properly," Dr. Kardara said. "Overall, aortic stiffness is an indicator of cardiovascular disease and hardening of the arteries, and a predictor of heart attack and related death."

Researchers say there may be several explanations for arterial stiffening in marathon runners. One plausible theory is that extreme exercise may place repeated and excessive stress on the artery wall leading to its fatigue, according to Charalambos Vlachopoulos, M.D., Athens Medical School, Hippokration Hospital, a co-investigator of the study.

"Endurance athletes should be cautious about the amount and volume of their training programs, trying not to wear themselves out, and always work in close collaboration with their physicians, especially before participating in an intense endeavor like marathon running," said Dr. Kardara.

This study was supported by the 1st Cardiology Department of Hippokration Hospital, the Athens Medical School and the Athens Classic Marathon Organizing Committee.

ACC2010特集

一般的な皮膚疾患により冠動脈疾患のリスクが上昇する

乾癬は心房細動や脳卒中などの広範な心血管イベントのリスクファクターである

Psoriasis is a risk factor for a wide range of negative cardiovascular events including atrial fibrillation and stroke

乾癬は広範な心血管イベントのリスクファクターであると第59回American College of Cardiologyで発表された。乾癬は軽症例および中等度/重度症例いずれも心房細動のリスクを上昇させた（それぞれ相対リスク[RR]1.22と1.51）。軽症の乾癬および中等度/重度の乾癬はまた脳卒中のリスクも増加させた（それぞれ[RR]1.19と1.45）。心房細動および脳卒中のリスク上昇は年齢依存性であり、スタディ開始時の1997年に50歳未満であった患者における相対リスクはそれぞれ2.28および1.92であった。軽症の乾癬は総死亡のリスクは上昇させなかった（[RR]1.04）が、中等度/重度の乾癬は死亡リスクを上昇させた（[RR]1.67）。心筋梗塞のリスクは軽症の乾癬では上昇しなかった（[RR]1.10）が、中等度/重度の乾癬では上昇した（[RR]1.24）。軽症および中等度/重度の乾癬により血管形成術施行のリスクは上昇した（それぞれ[RR]1.29および1.59）。これらの新たな発見から、乾癬患者に対しては皮膚疾患症状のみを治療するのではなく心血管疾患に関しても監視し予防する必要があることが示唆された。

Full Text

Psoriasis is a risk factor for a range of negative cardiovascular events, according to research presented at the American College of Cardiology's 59th annual scientific session.

The study - the first to ever link psoriasis with coronary problems on a nationwide scale - tracked rates of psoriasis, atrial fibrillation, stroke, heart attack, angioplasty and death in the entire adolescent and adult population of Denmark over a decade. Using a nationwide register of hospital visits and prescriptions, researchers tracked 40,262 patients with mild to severe psoriasis from the start of 1997 until the end of 2006. The researchers believed that psoriasis could be associated with coronary disease because both disorders are associated with excess inflammation.

Their hypothesis proved to be correct. Patients with severe psoriasis were more likely to experience all of the adverse cardiac events the researchers tracked and patients with mild psoriasis were more likely to experience atrial fibrillation, stroke and angioplasty.

"Although the association of psoriasis to myocardial infarction and stroke has been reported previously, the results have been ambiguous, debated, and the clinical relevance doubted," said Ole Ahlehoff, M.D., Copenhagen University Hospital Gentofte and the study's lead researcher. "Our results establish psoriasis as a clinically significant and independent risk factor for a range of cardiovascular adverse events."

Psoriasis was associated with increased risk of atrial fibrillation for both mild cases (relative risk 1.22) and moderate/severe cases (relative risk 1.51). Mild psoriasis (relative risk 1.19) and moderate/severe psoriasis (relative risk 1.45) were also associated with increased risk of stroke. The increased risks of atrial fibrillation and stroke were age-dependent, with a relative risk of 2.28 and a relative risk of 1.92, respectively, in patients with moderate/severe psoriasis who were younger than 50 years old at the beginning of the study in 1997.

Mild psoriasis did not confer increased risk of all-cause mortality (relative risk 1.04), but moderate/severe psoriasis was associated with an increased risk of death (relative risk 1.67). The risk of myocardial infarction was not raised in mild psoriasis (relative risk 1.10) but was in moderate/severe psoriasis (relative risk 1.24).

Psoriasis conferred increased risk of angioplasty for both mild cases (relative risk 1.29) and moderate/severe cases (relative risk 1.59).

The researchers adjusted for a wide range of possible confounding factors and the association between psoriasis and cardiac troubles remained.

These novel findings, including the higher risk for younger patients, indicate that psoriasis patients should not only be treated for the symptoms of that disorder, but should also take steps to monitor and prevent cardiovascular problems, according to the researchers.

"I believe that our results call for increased awareness of psoriasis as a contributor to cardiovascular disease and for a discussion of future medical management," Ahlehoff said. "For example, should patients with psoriasis receive statin therapy earlier than predicted by traditional risk-scores? Since psoriasis is a common disease, affecting two to three percent of people world-wide, reducing cardiovascular risk in this large group of patients could have a considerable impact."

This study was funded by the Department of Cardiology at Copenhagen University Hospital Gentofte.

ACC2010特集