職務ストレスが心疾患リスクを上昇させる（Abstract＃18520）

職務ストレスが高い女性は心血管疾患リスクが40%高い

Women with high job strain have 40 percent increased risk of cardiovascular disease

職務ストレスが高いと訴える女性は、職務ストレスの少ない女性と比較し、心筋梗塞(MI)や血行再建術を受けるなどの心血管疾患リスクが40%高い、と2010年American Heart Association学会で発表された。さらに、仕事の不安定さ―仕事を失う怖れ―は高血圧、高脂血症や過剰体重などの心血管疾患リスクファクターと関連があったが、MI、脳卒中、侵襲的な循環器系の処置または心血管死とは直接的な関連はなかった。ランドマーク研究であるWomen's Health Studyに参加した健常女性17,415人の職務ストレスを解析した。この女性たちは平均年齢57歳で主に白人の医療従事者であり、心疾患リスクファクター、職務ストレスおよび仕事の不安定さに関する情報を提供した。彼女らは10年間以上、心血管疾患の発症に関して追跡調査された。職務ストレスが高いと報告した女性はMI、虚血性脳卒中、冠動脈バイパス術またはカテーテルによる血管形成術および死亡リスクが40%高かった。MIリスクは約88%高く、一方バイパス術または侵襲的な処置を受けるリスクは43%高かった。過去に男性に対し行った職務ストレスに関する調査でも同様の結果が得られている。

Full Text

Women who report having high job strain have a 40 percent increased risk of cardiovascular disease, including myocardial infarctions and the need for revascularization procedures, compared to those with low job strain, according to research presented at the American Heart Association's Scientific Sessions 2010.

In addition, job insecurity - fear of losing one's job - was associated with risk factors for cardiovascular disease such as high blood pressure, increased cholesterol and excess body weight. However, it's not directly associated with heart attacks, stroke, invasive heart procedures or cardiovascular death, researchers said.

Job strain, a form of psychological stress, is defined as having a demanding job, but little to no decision-making authority or opportunities to use one's creative or individual skills.

"Our study indicates that there are both immediate and long-term clinically documented cardiovascular health effects of job strain in women," said Michelle A. Albert, M.D., M.P.H., the study's senior author and associate physician at Brigham and Women's Hospital, Boston, Mass. "Your job can positively and negatively affect health, making it important to pay attention to the stresses of your job as part of your total health package."

Researchers analyzed job strain in 17,415 healthy women who participated in the landmark Women's Health Study. The women were primarily Caucasian health professionals, average age 57 who provided information about heart disease risk factors, job strain and job insecurity. They were followed for more than 10 years to track the development of cardiovascular disease. Researchers used a standard questionnaire to evaluate job strain and job insecurity with statements such as: "My job requires working very fast." "My job requires working very hard." "I am free from competing demands that others make."

The 40 percent higher risks for women who reported high job strain included heart attacks, ischemic strokes, coronary artery bypass surgery or balloon angioplasty and death. The increased risk of heart attack was about 88 percent, while the risk of bypass surgery or invasive procedure was about 43 percent.

"Women in jobs characterized by high demands and low control, as well as jobs with high demands but a high sense of control are at higher risk for heart disease long term," said Natalie Slopen, Sc.D., lead researcher and a postdoctoral research fellow at Harvard University Center on the Developing Child in Boston.

Previous research on the effects of job strain has focused on men and had a more restricted set of cardiovascular conditions. "From a public health perspective, it's crucial for employers, potential patients, as well as government and hospitals entities to monitor perceived employee job strain and initiate programs to alleviate job strain and perhaps positively impact prevention of heart disease," Albert said.

Co-authors are Robert G. Glynn, Ph.D., and Julie Buring, Sc.D. Author disclosures are on the abstract.
The National Institutes of Health funded the Women's Health Study.

Cardiology特集

AHA2010（第83回米国心臓病協会）

トピックス一覧

アルコール摂取量はバイパス術後の心臓に関する問題と関連がある（Abstruct＃14440）

バイパス術を受けた男性患者において少量から中等量の飲酒と心血管系合併症が少ないことには関連がある

Light to moderate drinking linked to fewer cardiovascular complications in male bypass patients

冠動脈バイパス術を受けた男性患者のうち少量から中等量（1日2～3杯）の飲酒をする者は非飲酒者と比較し、その後の心臓血管手術、心筋梗塞（MI）、脳卒中および死亡が25%低かった、と2010年American Heart Association学会で発表された。しかし、中等量から大量（1日6杯以上）の飲酒をする左室機能低下を伴うバイパス患者は非飲酒者と比較し、その後の心血管死の確率が倍であった。研究者らは冠動脈バイパス術を施行された患者1,021人に標準的なアンケートを行い、その後3.5年間のバイパス術施行、MI、脳卒中および心血管死に関して調査した。毎日約2杯飲酒する患者は禁酒家と比較し心血管イベントが少なかった。一方、中等量から大量（1日約4杯）の飲酒をする左室機能に問題のある男女は、術後に追加処置を必要としたりMIまたは脳卒中を発現する確率が高かった。少量から中等量のアルコール消費は1日5～30gのアルコールで定義され、中等量から大量は1日60g以上で定義された。

Full Text

Light to moderate alcohol consumption (about two to three drinks daily) among male coronary artery bypass patients was associated with 25 percent fewer subsequent cardiovascular procedures, myocardial infarction (MI), strokes and death compared to non-drinkers, in a study presented at the American Heart Association's Scientific Sessions 2010.

However, bypass patients with left ventricular dysfunction who were moderate to heavy drinkers (more than six drinks daily) were twice as likely to have subsequent cardiovascular deaths compared to non-drinkers.

"The benefit of light amounts of alcohol consumption has been documented in healthy individuals, but our analysis showed a benefit from light alcohol intake in post-coronary bypass patients," said Umberto Benedetto, M.D., Ph.D. at the University of Rome La Sapienza in Italy. "However, our analysis indicated that alcohol consumption is not advisable in patients with left ventricular dysfunction and heart failure. No adverse correlation was found between moderate alcohol consumption and any medication."

Light to moderate alcohol consumption was defined as five to 30 grams of alcohol daily; moderate to heavy was defined as more than 60 grams daily.

Researchers used a standard questionnaire to compare alcohol consumption in 1,021 patients who underwent heart bypass and reviewed subsequent bypass procedures, heart attacks, strokes and cardiac deaths during the following 3 1/2 years. Patients consuming about two drinks daily had fewer cardiovascular events when compared to abstainers.

Moreover, moderate to heavy alcohol consumption (about four drinks daily) by patients with left ventricular problems was associated with significantly greater risk of dying.

Results of the study need to be confirmed over a longer follow-up period, with more patients and controls, Benedetto said.

The American Heart Association does not recommend people start consuming alcohol to prevent heart disease because too much alcohol can raise blood pressure and have other negative effects. For those who already drink alcohol, the association recommends women limit themselves to a drink a day and men limit themselves to two drinks per day.

Co-authors are: Giovanni Melina, M.D., Ph.D.; Davide Sansone, M.D.; Roberta Di Bartolomeo, M.D.; Emiliano Angeloni, M.D.; Simone Refice, M.D.; Ivan Stigliano, M.D.; Antonino Roscitano, M.D.; Tommaso Hinna Danesi, M.D.; and Riccardo Sinatra, M.D.

キサントーマにより心血管疾患が予測される（Abstract # 14027/P2049）

眼瞼へのコレステロール沈着は心筋梗塞、冠動脈疾患および死亡リスクが高いことを予測する

Cholesterol deposits on eyelids predict higher risk of myocardial infarction, coronary artery disease and death

キサントーマと呼ばれる眼瞼へのコレステロール沈着は心筋梗塞（MI）、虚血性心疾患および早期死亡を予測するとのポスタープレゼンテーションがデンマークの研究者により2010年American Heart Association学会で発表された。研究者らは12,939人のベースライン時におけるキサントーマの有無を調査した。これらの人々のうち1,903人がMIを発症、3,761人が虚血性心疾患を発症し、8,663人が最長33年の追跡期間中に死亡した。年代別の虚血性心疾患およびMIの累積発生率はキサントーマを有する者において高く、生存率は低かった。キサントーマはMIリスクの51%上昇および虚血性心疾患リスクの40%上昇を予測した。キサントーマを有する者は、血中コレステロールレベルなどのよく知られた心血管リスクファクターで補正した後の死亡リスクも17%高かった。このコレステロール沈着を有する人々の半分で血中コレステロールレベルが正常であることから、研究者らはこの病変が潜在的な動脈性疾患の独立したマーカーである可能性があると述べている。

Full Text

Cholesterol deposits on eyelids, "xanthelasmata," predict risk for myocardial infarction (MI), artery disease and early death, according to Danish researchers presenting at the American Heart Association 2010 Scientific Sessions.

Because half of the people with the deposits have normal blood cholesterol levels, scientists said the lesions may be an important independent marker of underlying artery disease.

Copenhagen researchers established the presence or absence of xanthelasmata at baseline in 12,939 people. Of these, 1,903 developed MIs, 3,761 developed ischemic heart disease and 8,663 died during up to 33 years of follow-up. Cumulative incidence of ischemic heart disease and heart attack as a function of age increased in those with xanthelasmata, and the proportion surviving decreased.

Xanthelasmata predicted 51 percent increased risk of MI and 40 percent increased risk of ischemic heart disease. Those with xanthelasmata also had a 17 percent increased risk of death after adjustments for well-known cardiovascular risk factors including blood cholesterol levels.

The results suggest that other factors besides cholesterol levels - including capillary leakage, characteristics of macrophages or intercellular matrix components - "may predispose certain individuals to both xanthelasmata and to atherosclerotic disease and early death," researchers said.

"In societies where other cardiovascular disease risk factors can't be readily measured, presence of xanthelasmata may be a useful predictor of underlying atherosclerotic disease," researchers said.

10代での塩分摂取量を少なくすることにより成人期の心臓の健康状態が改善する可能性がある（Abstract＃18899/P2039）

コンピュータモデル解析により10代での食塩摂取量を減少させることによる長期の心血管系の有益性が推定された

Computer modeling analysis projects long-term cardiovascular benefits of reducing dietary salt intake as teenagers

10代で日々の食塩摂取量を減少させることにより成人期の高血圧、心疾患および脳卒中を軽減する可能性がある、と2010年American Heart Association学会で発表された。最新のコンピュータモデル解析を行うことにより、米国の研究者らは青少年期の加工品からの食事性食塩摂取量を3g減少させることによる健康への影響を国内レベルで予想した。研究者らはモデルから、10代で日々の食塩摂食量を3g減らすことにより10代の高血圧患者数が44%～63%（380,000～550,000人）減少すると予想した。また、35～50歳時の高血圧患者数が30～43%（270～390万人）減少すると推定した。10代から50歳になった時の健康上の有益性で予測できたのは、冠動脈疾患の7～12%の減少、心筋梗塞の8～14%の減少、脳卒中の5～8%の減少および総死亡の5～9%減少などであった。摂取食塩の約80%が加工食品または調理済み食品由来であった。

Full Text

By reducing the salt teenagers eat each day by 3 grams, researchers projected through modeling a 44 percent to 63 percent (380,000 to 550,000) decrease in the number of hypertensive teenagers and young adults. They estimated a 30 percent to 43 percent decrease (2.7 to 3.9 million) in the number of hypertensives at ages 35 to 50.

"Reducing the amount of salt that is already added to the food that we eat could mean that teenagers live many more years free of hypertension," said Kirsten Bibbins-Domingo, Ph.D., M.D., lead author of the study and associate professor of medicine and epidemiology at the University of California, San Francisco. "The additional benefit of lowering salt consumption early is that we can hopefully change the expectations of how food should taste, ideally to something slightly less salty."

A one-gram-per-day reduction in salt consumption results in a small drop of systolic blood pressure of 0.8 mm Hg, she said. "Reducing the salt in the teenage diet from an average of 9 grams to 6 grams would get teenage boys and girls to appropriate levels of salt intake."

Measurable health benefits over time as teenagers reach age 50 would include:

- 7 percent to 12 percent reduction in coronary heart disease (120,000 to 210,000)
- 8 percent to14 percent reduction in heart attacks (36,000 to 64,000)
- 5 percent to 8 percent reduction in stroke (16,000 to 28,000)
- 5 percent to 9 percent reduction in death from any cause (69,000 to 120,000)

About 80 percent of salt comes from processed or prepared foods - 35 percent of that in cereals, breads and pastries.

"The hidden places of salt in our diet are in breads and cereals, canned foods and condiments, and of course fast foods," said Bibbins-Domingo, also co-director of the UCSF Center for Vulnerable Populations. "Most of the salt that we eat is not from our salt shaker, but salt that is already added in food that we eat."

Pizza is the biggest culprit of salt for teens in the United States according to data from the National Center for Health Statistics.

Manufacturers should continue to reduce salt in their foods in cooperation with local, state, and federal regulatory agencies, she said. Many major companies have already joined the National Sodium Reduction initiative and have voluntarily agreed to work to lower the salt content that is already added to processed and prepared foods.

Co-authors are: Pamela Coxson, Ph.D.; Tekeshe Mekonnen, M.S.; David Guzman, M.S.; and Lee Goldman, M.D., M.P.H. Author disclosures are on the abstract.

The American Heart Association funded the study.

軽度心不全においてアルドステロン拮抗薬は多大な有益性を示した

EMPHASIS-HF：エプレレノンは軽度症状を有する収縮期心不全患者の生存率を有意に改善する

EMPHASIS-HF: Eplerenone significantly improves survival in systolic heart failure patients with mild symptoms

収縮期心不全及び軽度症状を有する患者にアルドステロン拮抗薬エプレレノンを投与したところ、プラセボを投与された患者と比較し死亡および入院のリスクが37%低下したとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表され、New England Journal of Medicineオンライン版 に掲載された。軽症心不全患者にエプレレノンを投与した際の入院および生存率に関するスタディ（Eplerenone in Mild Patients Hospitalization And Survival Study in Heart Failure：EMPHASIS-HF）において、軽症心不全患者2,737人（平均年齢69歳、男性78%、白人82%）を、標準的な心不全治療法に加えエプレレノン（25～50mg）またはプラセボを投与する群に無作為に割り付けた。対象となった患者のほとんどが心不全を数年間（平均5年間近く）患っていた。平均追跡期間は21ヵ月であった。3分の2の患者が動脈硬化歴を有していた。エプレレノンを投与された患者のうち死亡または入院したのは249人であったのに対しプラセボ群では356人であった―統計学的に有意な差であった。エプレレノンはまた、プラセボと比較し、総死亡率と入院を3分の1以上減少させた。心不全死および入院減少におけるエプレレノンの有益性が圧倒的であったため、被検者の組み入れは予定された2010年5月よりも前に終了された。

Full Text

Patients with systolic heart failure and mild symptoms given eplerenone had a 37 percent reduced combined risk of death and hospitalization than patients who received a placebo, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

In the Eplerenone in Mild Patients Hospitalization And Survival Study in Heart Failure (EMPHASIS-HF), 2,737 patients with mild heart failure were randomized to receive eplerenone (25-50 milligrams) or placebo, as well as standard heart failure therapy. Among patients taking eplerenone, 249 deaths or hospitalizations occurred, compared to 356 in the placebo group - a statistically significant difference.

Eplerenone is in an aldosterone antagonist. These medications improve the remodeling of the failing heart by blocking the action of aldosterone, a naturally occurring hormone that was initially found to help maintain appropriate amounts of salt and water in the body. However, aldosterone can also have a number of direct harmful effects on the cardiovascular system. Aldosterone concentrations are abnormally high in people with heart failure.

Under current guidelines, aldosterone antagonists, including eplerenone and the older spironolactone, are recommended only for patients with moderate to severe heart failure and reduced heart function or for patients with heart failure following a recent heart attack. Until this study, their effects in patients with mild disease were unclear.

"This treatment is certainly going to change the guidelines for mild heart failure," said Faiez Zannad, M.D., Ph.D., the study's lead author and professor of therapeutics and director of the Clinical Investigation Center at the Nancy University Hospital Center in Nancy, France. "Now patients with all kinds of severity of systolic heart failure, whether it is post-myocardial infarction, with mild or severe symptoms, are potentially eligible for some kind of aldosterone blockade, and, certainly, for eplerenone."

In the study, eplerenone also decreased the rate of a number of other complications. It's also important that eplerenone reduced the number of deaths due to any cause and hospitalizations for any reason, by one-third compared to placebo, Zannad said.

"What was impressive was that we also hit all the secondary endpoints, including mortality from all causes," he said.

Study participants' average age was 69 years, 78 percent were male, and 82 percent were white. Most had suffered from heart failure for several years, with an average duration of nearly five years. Two-thirds had a history of atherosclerosis.

Patient enrollment began in March 2006 at 270 centers in 29 countries. Average follow-up was 21 months. Enrollment ended before the scheduled end of the study, in May 2010, because eplerenone showed an overwhelming benefit in reducing heart-failure deaths and hospitalizations.

Co-authors are John J.V. McMurray, M.D.; Henry Krum, Ph.D.; Dirk J. van Veldhuisen, M.D., Ph.D.; Karl Swedberg, M.D., Ph.D.; Harry Shi, M.S.; John Vincent, M.B., Ph.D.; Stuart J Pocock, Ph.D.; and Bertram Pitt, M.D. Author disclosures are on the abstract.
Pfizer, Inc. funded the study.

トピックス一覧

魚油は心房細動再発を軽減しなかった

高用量オメガ3は心房細動再発を軽減しないようである

High-dose omega-3 does not appear to reduce recurrence of atrial fibrillation

魚油など由来のオメガ3脂肪酸のサプリメントにより心房細動(AF)治療が改善する可能性があるとのいくつかのデータが示されていたが、600人以上の患者を対象とした無作為化トライアルにおいて高用量の処方オメガ3は6ヵ月間のAF再発を減少させなかったことが示されたとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表され、JAMA 12月1日号に掲載される。このスタディでは、実質的な器質的心疾患を有さない確認された有症状の発作性または持続性AF外来患者(それぞれ542人および121人)計663人を対象とした。対象者は処方薬オメガ-3(1日8mg)またはプラセボを最初の7日間、次いで処方薬オメガ-3(1日4mg)またはプラセボを第24週まで投与された。その後6ヵ月間に発作性心房細動患者群に認められた有症状のAFまたは心房粗動イベントはプラセボ群で129件(48%)であり実薬群で135件(52%)であった。持続性AF患者群では有症状のAFまたは心房粗動がプラセボ群で18件(33%)、実薬群で32件(50%)認められ、発作性、持続性群を合計するとプラセボ群で147イベント(46%)であり実薬群で167件(52%)であった。

Full Text

Although some data have suggested that omega-3 fatty acid supplements, such as from fish oil, may improve treatment of atrial fibrillation, a randomized trial with more than 600 patients finds that treatment with high-dose prescription omega-3 did not reduce the recurrence of atrial fibrillation over six months, according to a study that will appear in the December 1 issue of JAMA. The study is being released early online because it was presented as a Late Breaking Clinical Trial at the American Heart Association's 2010 annual meeting.

"Atrial fibrillation (AF) is a highly prevalent disease that is responsible for reduced quality of life, costly hospitalizations, heart failure, stroke, and death. No current therapy, drug, device, or ablation is uniformly effective, and several available therapies have the potential to cause harm. Consequently, useful alternatives are being sought," the authors write. "Limited data from small trials suggest omega-3 polyunsaturated fatty acids may provide a safe, effective treatment option for AF participants."

Peter R. Kowey, M.D., of the Lankenau Institute for Medical Research, Wynnewood, Pa., and colleagues conducted a randomized clinical trial to assess the efficacy of a pure prescription formulation of omega-3 fatty acids (prescription omega-3), at a dose considerably higher than what has been tested in previous trials, for preventing recurrent atrial fibrillation. The study included 663 U.S. outpatient participants with confirmed symptomatic paroxysmal (sudden attacks) (n = 542) or persistent (n = 121) AF, with no substantial structural heart disease, who were recruited from November 2006 to July 2009 (final follow-up was January 2010). Participants received prescription omega-3 (8 grams/day) or placebo for the first 7 days; prescription omega-3 (4 grams/day) or placebo thereafter through week 24.

After 6 months of follow-up, the researchers found that in the paroxysmal group, there were 129 documented symptomatic AF or flutter (abnormal, rapid heart beat) events (48 percent) in the placebo group and 135 (52 percent) in the prescription group. In the persistent AF group, there were 18 documented symptomatic AF or flutter events (33 percent) in the placebo group and 32 (50 percent) in the prescription group, while in the 2 groups combined there were 147 events (46 percent) in the placebo group and 167 (52 percent) in the prescription group.

None of the secondary efficacy end points, including first recurrence of AF or flutter in the persistent group and both groups combined, reached statistical significance. Sixteen participants (5 percent) taking placebo, and 12 (4 percent) taking prescription omega-3 discontinued study medication due to an adverse event.

"In this population of patients with symptomatic paroxysmal AF or persistent AF, and no evidence of substantial structural heart disease, prescription omega-3 did not show evidence of reducing the recurrence of symptomatic atrial fibrillation," the authors write.

They add that several factors might contribute to the discordance between their findings and those of other studies. "Either the positive results reported in some trials represent a chance effect of small sample sizes or the differences are real. If the latter, there are several possibilities, including differences in the study populations, in population-specific AF mechanisms, in dosing regimens and product formulations, or in concomitant therapies. In our study, nearly half the events occurred during the first 2 weeks of follow-up, suggesting that fish oil may not have rapid effects, even with high-loading doses."

新たな心ポンプが目標を達成した（Abstract＃21723）

ADVANCE：新たな定常流ポンプは心臓移植を待機している心不全患者に対し承認されているデバイスと同等の効果を有する

ADVANCE: New continuous-flow pump works as well as approved devices in heart failure patients waiting for transplant

第三世代の定常流ポンプHeartWare®左心室補助装置（HVAD）は承認されているデバイスと同等に有効であるとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表された。研究者らは、重度心不全治療としてのHVADの非無作為化評価（non-randomized Evaluation of the HVAD for the Treatment of Advanced Heart Failure：ADVANCE）スタディに140人の患者を組み入れた。ほとんどの患者（82%）が心不全を1年以上患っていた。コントロール群は市販されている左心室補助ポンプを同じ期間に使用した比較患者499人であった。HVAD患者のうち92%がこのポンプを装着した状態で180日間生存し、心臓移植を受けたかまたはデバイスから離脱できるまで回復した―全てが治療に成功したと考えられた。同様に、承認済みのポンプを装着した心臓移植を待機しているコントロール群患者の90%の治療が成功した。心臓移植からほぼ1年（360日）後に、HVAD群患者の91%およびコントロール群患者の86%が生存しておりこの差は統計学的に有意ではなかった。ポンプ埋め込み3ヵ月後の心機能分類およびQOLは、承認されたポンプ同様改善した。この新たなデバイスの1つの長所は心嚢内に埋め込めるほどサイズが小さいことである、と研究者らは述べている。

Full Text

A third-generation experimental pump implanted to assist the heart in patients with advanced heart failure waiting for a heart transplant works as well as approved devices, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

In the non-randomized Evaluation of the HeartWare® HVAD Left Ventricular Assist Device System for the Treatment of Advanced Heart Failure (ADVANCE) study, researchers found that the HeartWare® left ventricular assist device (HVAD) met its primary endpoint, producing outcomes comparable to already approved bridge-to-transplant pumps.

Among HVAD patients, 92 percent survived for 180 days with the pump, received a transplant or had recovered enough to have the device removed - all considered successful treatment. Similarly, 90 percent of control patients waiting for heart transplants on approved pumps were treated successfully. Nearly one year (360 days) after implantation, 91 percent of HVAD patients and 86 percent of controls had survived, a difference that was not statistically significant.

From March 2009 to February 2010, investigators enrolled 140 patients from the United Network for Organ Sharing's heart-transplant waiting list to receive an HVAD at one of 30 centers. Their average age was 53 years, 72 percent were male and most (82 percent) had suffered from heart failure for at least a year.

The control group included 499 comparable patients from a nationwide listing of all heart failure patients who received commercially available left ventricular assist pumps during the same period. Researchers compared survival and success rates between the HVAD and control patients 180 and 360 days after implantation. They also evaluated the HVAD patients' functional capacity and quality of life, as well as adverse effects of the HVAD pump.

HVAD patients were able to walk 113 meters, about 371 feet, farther in six minutes than at baseline when tested three months after surgery, and had very large improvements on two heart failure-specific and two generalized quality of life measures.

"With this success rate, doctors and patients should have increased comfort with a ventricular-assist device as a bridge to transplant," said Keith Aaronson, M.D., M.S., lead author of the study and associate professor of internal medicine and medical director of the Heart Transplant and Mechanical Circulatory Support Programs at the University of Michigan Medical Center in Ann Arbor. "These patients don't just survive to a transplant, they feel better and can be much more active."

Two types of these surgically implanted devices are approved for use. First generation devices are known as pulsatile-flow because they pause between pumps to fill with blood, creating a pulsing rhythm similar to the heart's beat. The newer, more durable, continuous-flow pumps continually propel blood outwards and, therefore, flow is less pulsatile.

"The results of ventricular assist device therapy have improved dramatically in recent years with the advent of continuous-flow pumps," Aaronson said. "The commercially available continuous-flow pump is an excellent pump, but all would agree that there is room for improvement."

The HVAD is also a continuous-flow pump, but is smaller in size. This allows part of it to be implanted directly into the heart's main pumping chamber, the left ventricle, with the remainder of the device positioned within the space surrounding the heart. In contrast, other continuous-flow devices are placed in the abdomen within a surgically created pocket.

Another key difference is that the HVAD, a centrifugal device, propels blood outward from the center of a spinning disc, which is suspended only by magnetics and the blood itself. In comparison to axial devices that propel blood in the direction of flow, centrifugal flow devices may provide greater pulsatility, which is proposed to reduce the incidence of internal bleeding often associated with continuous-flow devices. It may also reduce arrhythmias.

Researchers didn't compare complication rates in this study. However, Aaronson noted that bleeding and infection rates in this study were lower than have been found in studies investigating other ventricular assist devices. He said only a head-to-head comparison can confirm whether these differences are valid and significant.

Co-authors are Mark S. Slaughter, M.D.; Edwin McGee, M.D.; William G. Cotts, M.D.; Michael A. Acker, M.D.; Mariell L. Jessup, M.D.; Igor D. Gregoric, M.D.; Pranav Loyalka, M.D.; Valluvan Jeevanandam, M.D.; Allen S. Anderson, M.D.; Robert L. Kormos, M.D.; Jeffrey J. Teuteberg, M.D.; Francis D. Pagani, M.D. Ph.D.; Steven Boyce, M.D.; David Hathaway, M.D.; Leslie W. Miller, M.D.; and Michael A. Acker, M.D. Author disclosures are on the abstract.

HeartWare, Inc., of Framingham, Mass., funded the study.

トピックス一覧

心臓再同期療法は軽度心不全患者において有用である（Abstract＃21768）

RAFT：軽度－中等度の症状を有する心不全患者において心臓再同期療法を追加することにより死亡および心不全による入院が減少する

RAFT: Adding cardiac-resynchronization therapy reduces deaths, heart failure hospitalizations in patients with mild-to-moderate symptoms

薬物療法および埋め込み型除細動器で治療されている軽度－中等度の症状を有する心不全患者に心臓再同期療法（ICD）を追加することにより死亡および心不全による入院が有意に減少する、とのレイトブレイキング臨床試験の結果が2010年AHA学会で発表され、New England Journal of Medicineオンライン版に掲載された。外来心不全患者に対する再同期/除細動トライアル（Resynchronization/defibrillation for Ambulatory heart-Failure Trial：RAFT）において研究者らは、軽度から中等度の心不全および左室機能低下を有する患者1,798人（平均年齢66歳、男性82%）をICDまたはCRT機能も備えたICDを受ける群に無作為に割り付けた。両群ともに薬物療法も受けた。平均追跡期間は40ヵ月であり、この種のスタディでは最長のスタディの1つであった。統計学的に有意な結果として、ICD/CRT併用群はCRTを受けない群と比較し死亡または心不全による入院率が25%低いことが示された。ICD/CRT併用群患者はまたCRTを受けない患者と比較し総死亡率も25%低かった。これらの結果から、ICD/CRTは軽度から中等度の心不全患者において価値のある治療であることが示されたと研究者らは述べている。

Full Text

Adding cardiac-resynchronization therapy (CRT) significantly reduces deaths and heart failure hospitalizations among heart failure patients with mild-to-moderate symptoms being treated with medication and an implantable cardioverter defibrillator (ICD), according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

In the Resynchronization/defibrillation for Ambulatory heart-Failure Trial (RAFT), investigators randomized patients with mild to moderate heart failure to receive either an ICD or an ICD equipped to provide cardiac-resynchronization therapy (CRT). With CRT, special leads from the ICD pace the heart's main chambers to beat in synchronization. Both groups also received standard medical treatment.

Previous studies have shown that resynchronization therapy combined with ICD treatment can reduce symptoms and hospitalizations among patients with severe heart failure. Before results of RAFT, the therapy's effects on patients with milder symptoms and on death rates weren't clear.

In a statistically significant finding, patients on the combined ICD/CRT regimen were 25 percent less likely to die or be hospitalized for heart failure, compared to patients who didn't receive CRT. Patients on the combined ICD/CRT treatment were also 25 percent less likely to die of any cause, compared to patients who didn't receive CRT.

"This study conclusively demonstrated that this particular therapy, in addition to an ICD, will save lives," said Anthony Tang, M.D., the study's lead author and an electrophysiologist at Royal Jubilee Hospital in Victoria, B.C., Canada. "For patients, and for the physicians who treat them, this definitely showed that we can reduce hospitalization, suffering and dying."

Although complications were minimal among all participants, the wires connecting the device to the heart were more likely to become dislodged among ICD/CRT patients than among those with ICD alone (6.9 versus 2.2 percent and a statistically significant difference).

Investigators enrolled 1,798 patients with mild to moderate heart failure and left ventricular dysfunction in a prospective study at 34 sites in Canada, Europe, Australia and Turkey between January 2003 and February 2009. The patients' average age was 66 years, and 82 percent were male. Two-thirds of participants had heart failure related coronary artery disease, and one-third had heart failure of undetermined origin.

Researchers compared death rates and heart failure hospitalizations lasting longer than 24 hours between the ICD-only group and the ICD/CRT group. Average follow-up was 40 months, one of the longest for a study of this kind.

"CRT alone, without a defibrillator, has been demonstrated to save lives," said Tang, who is CIHR Research Chair and professor of medicine at the University of British Columbia and adjunct professor of medicine at the University of Ottawa. "The defibrillator also has been shown to save lives. The big question is, when the two are added together does it still make sense?"

To further resolve the issue, the investigators are analyzing the cost-effectiveness of ICD/CRT compared with ICD only and quality-of-life data from the study.

Co-authors are George A. Wells, Ph.D.; Mario Talajic, M.D.; J. Malcolm O. Arnold, M.D.; Robert Sheldon, M.D.; Stefan H. Hohnloser, M.D.; Stuart Connolly, M.D.; Graham Nichol, M.D.; Jean L. Rouleau, M.D.; David H. Birnie, M.D.; Raymond Yee, M.D.; and John Sapp, M.D. Author disclosures are on the abstract.

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Cardiology特集
AHA2010（第83回米国心臓病協会）

トピックス一覧

[News01]
職務ストレスが心疾患リスクを上昇させる

[News02]
アルコール摂取量はバイパス術後の心臓に関する問題と関連がある

[News03]
キサントーマにより心血管疾患が予測される

[News04]
10代での塩分摂取量を少なくすることにより成人期の心臓の健康状態が改善する可能性がある

[News05]
軽度心不全においてアルドステロン拮抗薬は多大な有益性を示した

[News06]
魚油は心房細動再発を軽減しなかった

[News07]
新たな心ポンプが目標を達成した

[News08]
心臓再同期療法は軽度心不全患者において有用である

[News09]
Nesiritideは安全だが有益性は乏しいことが示された

[News10]
バイオマーカーにより心不全および死亡リスクが予測できる

[News11]
新薬はHDLを有意に上昇させLDLをほぼ半分に低下させる

[News12]
CRPスクリーニングは従来の心臓リスク評価を改善しない

[News13]
糖尿病患者に対する薬物療法と迅速な血行再建術の併用は有益である

[News14]
腎除神経療法による高血圧治療

[News15]
家族性心房細動

[News16]
重篤な下肢虚血に関するトライアルで遺伝子治療は不成功に終わった

Nesiritideは安全だが有益性は乏しいことが示された（Abstract＃21828）

ASCEND-HF：重症心不全患者を対象とした大規模スタディの結果、nesiritideは安全であるが症状または死亡率に対する有意な有益性はないことが示された

ASCEND-HF: Large study of patients with severe heart failure confirms nesiritide safe, but shows no significant benefit on symptoms or mortality

大規模臨床試験において、急性非代償性心不全患者に対し薬剤nesiritideは安全であることが証明されたが、呼吸困難に対しては有効性がわずかであり、再入院または死亡率に対する有意な効果はないことが示されたとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表された。急性非代償性心不全におけるnesiritideの臨床上の有効性に関する試験（Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial：ASCEND-HF）において研究者らは急性重症心不全患者7,141人（平均年齢67歳、女性34%）を静脈内nesiritide持続投与またはプラセボ投与のいずれかを標準的な治療法に加えて投与する群に無作為に割り付けた。半数以上（60%）が冠動脈疾患を有していた。治療6時間後に nesiritideはプラセボと比較し息切れをやや改善させ、有意な改善はnesiritide群患者の947人（15.0%）に、プラセボ群では874人（13.4%）に認められた。同様に、治療24時間後に呼吸機能が著明に改善した患者はプラセボよりもnesiritide群において多かった－nesiritide群患者のうち1,063人（30.4%）であったのに対しプラセボ群患者では966人（27.5%）であった。しかし、呼吸困難に関する事前に特定していたエンドポイントに関しての有意差はなかった。この薬剤は30日間の再入院または死亡（nesiritide群9.4%対プラセボ10.1%）に関しても有意差は示さなかった。

Full Text

In a large clinical trial, the drug nesiritide proved to be safe but had little effect on dyspnea, and no significant effect on hospital readmission or death rates among patients with acutely decompensated heart failure, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

In the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial (ASCEND-HF), researchers randomized 7,141 patients with acute, severe heart failure to receive either continuous intravenous nesiritide or a placebo, both added to standard therapy, which includes diuretics, morphine and other medications.

Six hours after treatment, nesiritide slightly improved shortness of breath compared with placebo, with significant improvement occurring in 947 nesiritide patients (15.0 percent) and 874 placebo patients (13.4 percent). Similarly, 24 hours after treatment, more patients on nesiritide displayed markedly improved breathing function compared to placebo - 1,063 nesiritide patients (30.4 percent) compared to 966 placebo patients (27.5 percent). However, there was no significant difference in the pre-specified endpoint for dyspnea. At 30 days post-treatment, the rates of death from any cause and hospital readmission for heart failure were slightly lower with nesiritide compared to placebo. At 9.4 percent versus 10.1 percent, however, the difference in these rates was not statistically significant either.

Nesiritide is a manufactured drug derived from a naturally occurring protein known as human B-type natriuretic peptide. The drug helps to relax the blood vessels, which can improve circulation, and increase the body's output of excess salt and water.

"Nesiritide was marketed and widely used in the U.S. because of a perception that it had a major effect on dyspnea and then largely abandoned in clinical use because of concerns that it might increase rates of death and renal failure, said Robert M. Califf, M.D., study chair and vice chancellor for clinical research at Duke University School of Medicine in Durham, N.C. "Now that we finally have a proper clinical trial we know that both perceptions were incorrect; nesiritide is safe but has only a modest effect on dyspnea. This is a major signal that we must do a better job defining the biological effects of drugs early in development and conduct adequately powered outcomes trials much earlier to give doctors and patients the necessary information to enable appropriate use of the treatment in practice."

ASCEND-HF, a randomized double-blind trial, included participants from 400 international centers in 30 countries. Average age of patients studies was 67 years, 34 percent were female and 15 percent were African American. More than half (60 percent) had blockages or narrowing of the blood vessels supplying the heart. Treatment began within 24 hours of hospitalization for worsening symptoms and continued for between one to seven days. The study ran from May 2007 to September 2010; patients were followed for 30 days.

Previous studies have shown that nesiritide can relieve shortness of breath if given within three hours of the onset of worsening heart failure, but it was unclear whether this improvement persisted. Also unknown was whether nesiritide caused renal impairment or increased the risk of death, which previous, much smaller studies have indicated. An important finding from this trial is that the drug did not increase these risks.

"I think the main message is that we need to do adequately powered studies to really understand the balance of safety and effectiveness," said Adrian F. Hernandez, M.D., co-investigator of the trial and associate professor of medicine at Duke University School of Medicine. "Now that we've done an adequate trial, we know that nesiritide can be used safely, but there is no mandate to use it because of its modest effects."

"ASCEND-HF represents an important milestone in our understanding of acute heart failure care as this is the first robust drug safety study completed in this difficult to treat patient population," said Christopher M. O'Connor, M.D., the study's co-principal investigator and director of the Duke Heart Center. "Given the complexities of heart failure, there is a significant need for better medications for use in treatment," said Randall C. Starling, M.D., study co-investigator and head of the section of Heart Failure and Cardiac Transplant Medicine and vice chairman of Cardiovascular Medicine at Cleveland Clinic. "With the safety questions related to nesiritide having now been addressed, it could be an option for physicians depending on their interpretation of clinical benefit."

The trial was led by an international executive committee which also included Paul W. Armstrong, M.D.; Kenneth Dickstein, M.D.; Daniel Gennevois, M.D.; Vic Hasselblad, Ph. D.; Michael Komajda, M.D.; Barry Massie, M.D.; John J.V. McMurray, M.D.; Markku Nieminen, M.D.; Jean L. Rouleau, M.D.; and Karl Swedburg, M.D. ASCEND-HF was coordinated by the Duke Clinical Research Institute led by Craig J. Reist, Ph.D. Author disclosures are on the abstract.

Johnson & Johnson funded the study.

Cardiology特集
AHA2010（第83回米国心臓病協会）

トピックス一覧

[News01]
職務ストレスが心疾患リスクを上昇させる

[News02]
アルコール摂取量はバイパス術後の心臓に関する問題と関連がある

[News03]
キサントーマにより心血管疾患が予測される

[News04]
10代での塩分摂取量を少なくすることにより成人期の心臓の健康状態が改善する可能性がある

[News05]
軽度心不全においてアルドステロン拮抗薬は多大な有益性を示した

[News06]
魚油は心房細動再発を軽減しなかった

[News07]
新たな心ポンプが目標を達成した

[News08]
心臓再同期療法は軽度心不全患者において有用である

[News09]
Nesiritideは安全だが有益性は乏しいことが示された

[News10]
バイオマーカーにより心不全および死亡リスクが予測できる

[News11]
新薬はHDLを有意に上昇させLDLをほぼ半分に低下させる

[News12]
CRPスクリーニングは従来の心臓リスク評価を改善しない

[News13]
糖尿病患者に対する薬物療法と迅速な血行再建術の併用は有益である

[News14]
腎除神経療法による高血圧治療

[News15]
家族性心房細動

[News16]
重篤な下肢虚血に関するトライアルで遺伝子治療は不成功に終わった

バイオマーカーにより心不全および死亡リスクが予測できる（Abstract＃18591）

バイオマーカーである心臓トロポニンTは心不全および心血管死のリスク予測に役立つ

Cardiac troponin T biomarker may help predict risk of heart failure, and cardiovascular death

血液バイオマーカーの1つである心臓トロポニンT(cTnT)は高齢者において心不全(HF)発症または心血管死と関連があると2010年AHA学会で発表され、JAMA 12月8日号に掲載される。研究者らは心不全の既往のない65歳以上の4,221人を対象にスタディ開始時、および2～3年後(2,918人)にcTnTを計測した。cTnT濃度は2,794人(66.2%)の患者において検出限度以上であった。追跡期間中央値11.8年の間に1,279人が新規のHFを発症し、1,103件の心血管死が発現したが、いずれのエンドポイントもcTnT高濃度と関連があった。HFおよび心血管死のリスクはcTnTのベースライン時点でのレベルに関係なく、フォローアップ時点での値が検出可能な者において検出不可の者よりも高かった。ベースライン時点でのcTnTが検出可能であった者はHFおよびリスクファクターで補正後の心血管死のリスクが50%高かった。一方、cTnTが50%以上低いとリスクファクターで補正後のHFリスクおよび心血管死リスクが低かった。

Full Text

Certain measures of the blood biomarker cardiac troponin T (cTnT), a cardiac-specific protein, using a highly sensitive test, are associated with the development of heart failure or cardiovascular death in older adults, according to a study that will appear in the December 8 issue of JAMA. The study is being released early online because it was presented at the American Heart Association's 2010 annual meeting.

"Older adults comprise the majority of new-onset heart failure (HF) diagnoses, but traditional risk-factor prediction models have limited accuracy in this population to identify those at highest risk for hospitalization or death," according to background information in the article. Blood-based biomarkers, including troponins, have been advocated for use as supplemental to clinical risk factors to identify older adults at high risk for adverse cardiovascular outcomes, but studies examining the prognostic value of these markers have reported inconsistent results.

Prior studies have used standard troponin assays that are only able to detect circulating troponin levels in a small proportion of individuals. Recently, a highly sensitive cardiac troponin T assay has been developed, designed to improve accuracy. "This assay has detected circulating cTnT in almost all patients with chronic HF or ischemic heart disease and provides independent prognostic information with respect to HF admission and cardiovascular death in these patients," the authors write.

Christopher R. deFilippi, M.D., of the University of Maryland School of Medicine, Baltimore, and colleagues examined the ability to detect a measurable cTnT concentration in older adults using the highly sensitive cTnT assay and whether higher concentrations would be associated with a greater risk of new-onset HF and cardiovascular death. The researchers analyzed data from the Cardiovascular Health study and included 4,221 community-dwelling adults ages 65 years or older without prior HF who had cTnT measured using the highly sensitive assay at the beginning of the study (1989-1990) and repeated after 2 to 3 years (n = 2,918). Concentrations of cTnT were equal to or more than the limit of detection in 2,794 participants (66.2 percent).

During a median follow-up of 11.8 years from the initial cTnT measurement, 1,279 participants experienced new-onset HF and 1,103 cardiovascular deaths occurred, with a greater risk of both end points associated with higher cTnT concentrations. Also, the risks of HF and cardiovascular death were higher among those participants with detectable compared with undetectable levels at follow-up, irrespective of the baseline level.

Analysis indicated that for participants with measurable cTnT levels at the beginning of the study, an increase of more than 50 percent was associated with an increased risk of HF and a greater risk of cardiovascular death, adjusting for baseline cTnT and risk factors. In contrast, a decrease of more than 50 percent was associated with a risk factor adjusted lower risk of HF and lower risk of cardiovascular death compared with those participants with 50 percent or less change.

For the prediction of both outcomes, the addition of baseline cTnT measurements to clinical risk factor models only modestly but statistically significantly improved classification.

"Detectable cTnT levels as measured by a highly sensitive assay were present in the majority of community-dwelling older adults in this cohort, and higher concentrations-within a normal range established for a younger general population-reflect a greater burden of cardiovascular risk factors and imaging evidence of cardiac disease. Independent of these comorbidities, cTnT concentrations were associated with risk of new-onset HF and cardiovascular death. Furthermore, longitudinal changes in cTnT concentrations were common in this cohort and correspond with a dynamic change in risk levels over time," the authors conclude.

新薬はHDLを有意に上昇させLDLをほぼ半分に低下させる（Abstract＃21824）

DEFINE：CETP阻害剤anacetrapibはLDLおよびHDLコレステロールに多大な効果を有する

DEFINE: CETP inhibitor anacetrapib has large effect on LDL and HDL cholesterol

ある治験薬はこのクラスの他の薬剤で認められた血圧上昇がなく高密度リポ蛋白(HDL)コレステロールレベルを2倍以上に上昇させ低密度リポ蛋白(LDL)コレステロールを半分近く低下させたとのレイトブレイキング臨床試験結果が2010年AHA学会で発表され同時にNew England Journal of Medicine 2010年11月17日号に掲載された。AnacetrapibによるCETP阻害の効果および忍容性の評価(Determining the EFficacy and Tolerability of CETP INhibition with AnacEtrapib：DEFINE)は20ヵ国153施設において1,623人の患者(平均年齢62.5歳；女性23%；アジア人、黒人または多人種17%、ヒスパニック15%)にコレステロールエステル輸送蛋白(CETP)阻害剤anacetrapib 100mgまたはプラセボを18ヵ月間内服させた無作為化二重盲検試験である。患者は既にスタチンおよび/または他の脂質低下薬で治療されており、LDLコレステロールレベルの目標を達成していた。AnacetrapibはLDLを811mg/dLから49mg/dLへと40%低下させた。またHDLレベルは40mg/dLから101mg/dLに上昇した。参加者の血圧や電解質に変化はなかった。

Full Text

An experimental drug more than doubles the level of high-density lipoprotein cholesterol (HDL) and cuts low-density lipoprotein (LDL) cholesterol nearly in half without the blood pressure increase linked to another agent in its class, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

Determining the EFficacy and Tolerability of CETP INhibition with AnacEtrapib (DEFINE) is a randomized, double-blind trial of 1,623 patients who took either 100 mg of the cholesterylester transfer protein (CETP) inhibitor anacetrapib, or a placebo for 18 months at 153 centers in 20 countries. The patients were already being treated with a statin and/or other lipid-lowering medicine and had achieved their goal level of LDL cholesterol.

The study's primary endpoints were the percent change in LDL and safety as measured by a number of clinical and laboratory measures as well as cardiovascular (CV) events.

Anacetrapib reduced LDL by 40 percent - from 81 mg/dL to 49 mg/dL. It also more than doubled the level of HDL from 40 mg/dL to 101 mg/dL without raising blood pressure.

"Anacetrapib has a knock-your-socks-off effect on HDL and a jaw-dropping effect on LDL," said Christopher P. Cannon, M.D., senior investigator of the TIMI Study Group in the cardiovascular division of Brigham and Women's Hospital in Boston, Mass. "These changes are striking because virtually all the patients in the study were already taking cholesterol-lowering drugs and achieved previously unattainable levels of good and bad cholesterol."

The experimental drug is one of a new class that blocks the ability of the CETP enzyme to transfer cholesterol particles from HDL to LDL.

Elevated LDL and low levels of HDL are both risk factors for cardiovascular disease. Statins reduce LDL and lessen cardiovascular risk. Despite statin therapy, many patients still have a high risk of cardiovascular disease.

High natural levels of HDL are associated with lower cardiovascular risk, which is why researchers have been looking for ways to increase HDL levels, said Cannon, an associate professor of medicine at Harvard Medical School.

"No treatments raise HDL levels as substantially as seen here (more than doubling of the levels)," said Cannon.

Patients in DEFINE were 62.5 years old on average; 23 percent were women; 17 percent were Asian, black or multiracial and 15 percent were Hispanic. The study included interim safety analyses at six and 12 months, and researchers found no change in blood pressure or electrolytes among participants.

Levels of aldosterone, a hormone produced in the adrenal gland that affects kidney function and blood pressure, didn't change. The researchers also found no increase in muscle problems or liver function abnormalities between groups - a side effect occasionally associated with statins.

Although the study was not designed or powered to assess the effects of anacetrapib on cardiovascular events, fewer cardiovascular events occurred in the anacetrapib group than in the statin-only group. The full efficacy and safety of anacetrapib will be evaluated in a larger Phase III trial, Cannon said.

"This agent provides us a very strong add-on treatment to statins that dramatically increases the good cholesterol and dramatically further decreases the bad cholesterol," he said. "If the cardiovascular effects are borne out by future research, it would be a very promising approach to reducing cardiovascular events in patients with or prone to atherosclerosis."

Co-authors are Sukrut Shah, R.Ph., Ph.D.; Hayes M. Dansky, M.D.; Michael Davidson, M.D.; Eliot A. Brinton, M.D.; Antonio M. Gotto Jr., M.D., D.Phil.; Michael Stepanavage, M.S.; Sherry Xueyu Liu, M.S.; Patrice Gibbons, M.S.; Tanya B. Ashraf, B.A.; Jennifer Zafarino, M.S.; Yale Mitchel, M.D. and Philip Barter, M.D., Ph.D. Author disclosures are on the abstract.

Merck Research Laboratories, Rahway, N.J., funded the study.

トピックス一覧

CRPスクリーニングは従来の心臓リスク評価を改善しない（Abstract＃21685）

ASCOT：ASCOTの結果がCRPをスタチン処方の指標とすることに関する論争をあおり立てる

ASCOT: Results from ASCOT fuels debate over using CRP as an indication for prescribing statins

高感度C反応性蛋白スクリーニングは伝統的な心血管疾患リスクファクターを有する中年患者のリスク評価をほんのわずかしか改善しない、とのレイトブレイキング臨床試験結果が2010年AHA学会で発表された。研究者らは、プラセボを対照としたアトロバスタチンのコレステロール低下効果を比較したAnglo-Scandinavian Cardiac Outcomes Trial（ASCOT）に参加した英国およびアイルランドの患者4,853人を解析した。その結果、参加者のベースライン時の低密度リポ蛋白（LDL）コレステロールおよびC反応性蛋白（CRP）は両者ともに心血管イベント予測能を有することが示された。しかし、スタディ開始時点の患者の他のリスクファクターまたはトライアル中のLDLの変化を考慮した後では、CRPは心血管イベントとの相関を失った。筆者らは、JUPITERトライアルなどの近年のスタディを考慮すると、これらの患者においてCRP計測のさらなる価値が認められなかったことは驚きであると述べている。JUPITERにおいて研究者らは、元のコレステロールレベルが正常でCRP上昇以外に他のリスクファクターを有さない人々にコレステロール低下薬スタチンを投与することにより、初回の心血管イベントが37%減少したことを示した。JUPITERと異なりASCOTではCRPが心血管リスク予測を改善するまたはスタチンによるCRP低下効果により心血管イベントが減少するとの仮説を支持しなかった。

Full Text

High-sensitivity C-reactive protein screening only minimally improved risk assessment in middle-aged patients with traditional cardiovascular disease risk factors, according to late-breaking clinical trial research presented at the American Heart Association's Scientific Sessions 2010.

Researchers analyzed 4,853 patients in the United Kingdom and Ireland who were part of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), which compared the cholesterol-lowering effects of the drug atorvastatin to a placebo.

They found that participants' baseline levels of low-density lipoprotein (LDL) cholesterol and levels of C-reactive protein (CRP) were both predictive of cardiovascular events. However, after the researchers considered other risk factors at the start of the study, or in-trial changes in LDL, the changes in CRP were no longer linked to cardiovascular events.

"Our key findings are that if you measure CRP at baseline in a population of middle-aged and elderly people with high blood pressure, and with a few additional risk factors for cardiovascular disease, it does independently predict cardiovascular events over the course of our trial," said Peter S. Sever, F.R.C.P., principal investigator of ASCOT and professor of clinical pharmacology and therapeutics at Imperial College London. "But when you add screening CRP values to a conventional risk model used by doctors, such as the Framingham Risk Score, CRP really has a very small additive effect."

Participants in the analysis were 65 years old on average, predominantly male, with total cholesterol levels under 250 milligrams per deciliter (mg/dL) of blood, including levels considered normal to moderately elevated. In the treatment group, the statin drug reduced LDL by 40 percent and reduced median CRP by 27 percent over six months.

During 5.5 years of follow-up, 485 cardiovascular events occurred in ASCOT particpants. Those cases were age and sex-matched with 1,367 controls from within the group who hadn't had a cardiovascular event. The researchers then used statistical models to evaluate the association between cardiovascular events and patients' cholesterol and CRP levels.

In those taking atorvastatin, LDL below the median while on treatment was associated with a reduction in cardiovascular events compared with those taking placebo or with those with LDL above the median. This risk reduction was unchanged after the researchers adjusted for the participants' other baseline risk factors.

However, in those taking atorvastatin, CRP below the median was not associated with reduced cardiovascular events compared with those with CRP above the median after adjusting for other risk factors and the changes in LDL.

The lack of added value of CRP measurement in the patients "was surprising in light of recent studies such as the randomized, placebo-controlled JUPITER trial," Sever said.

In JUPITER, researchers found that taking a cholesterol-lowering statin reduced first cardiovascular events by 37 percent in people who primarily had normal cholesterol levels and no other risk factors except elevated CRP.

"The message coming out of the JUPITER study was that we should be screening people for CRP irrespective of their other risk factors," Sever said. "That's very, very expensive and almost certainly not a cost-effective intervention, particularly given these findings that measurement of CRP doesn't add anything in a much more widely representative population."

ASCOT doesn't support the hypothesis that CRP improves cardiovascular risk prediction or that the CRP-lowering effect of statins reduces cardiovascular events, Sever said.

Co-authors are Neil R. Poulter, F.R.C.P.; Choon-Lan Chang, Ph.D.; Simon A. M. Thom, M.D., F.R.C.P.; Alun D. Hughes, M.B.B.S., Ph.D.; Paul Welsh, Ph.D. and Naveed Sattar, Ph.D.

Author disclosures are on the abstract.

Pfizer, Inc. funded the study.

糖尿病患者に対する薬物療法と迅速な血行再建術の併用は有益である（Abstract＃12697）

心疾患を有する糖尿病患者において血行再建術を含む治療は血流改善に繋がる

Treatment that includes revascularization results in better blood flow in patients with diabetes and heart disease

心疾患を有する糖尿病患者において早期の血行再建術は強力な薬物療法単独と比較し心臓への血流をより改善するとのスタディ結果が2010年AHA学会で発表された。以前、BARI 2D（2型糖尿病におけるバイパス/血管形成術による血行再建術に関する調査[Bypass Angioplasty Revascularization Investigation 2 Diabetes]）において、薬物療法に加え血行再建術を施行された患者は血糖、血圧およびコレステロールコントロール（病状が悪化した場合にのみ後に手術を施行）の強化治療のみを受けた患者と比較し、死亡および心筋梗塞（MI）が少なくはなかったことが示された。今回のサブスタディでは、1,505人の対象者にストレス心筋潅流SPECTを施行し血流が十分な心筋領域を同定し計測した。試験開始後1年間に、薬物誘発性虚血が認められず異常なしとの結果であったのが血行再建術群患者の59%であり薬物療法群患者の49%であった。血流減少は血行再建術群患者の心筋組織の3%、薬物療法群患者の心筋の9%に認められた。虚血が多いほど死亡およびMIのリスクが高かった。この結果から、薬物療法および生活習慣介入で管理されている心疾患を有する糖尿病患者のスクリーニングの重要性が示唆された。

Full Text

Treatment that included early surgical procedures to open blocked arteries resulted in better blood flow to the heart than aggressive medical treatment alone in patients with both diabetes and heart disease, according to a study presented at the American Heart Association's Scientific Sessions 2010.

Previously, researchers in BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) found that over five years there were no fewer deaths and myocardial infarctions (MI) in people who had medical treatment along with prompt revascularization than in those who received only intensive treatment to manage blood sugar, blood pressure and cholesterol levels (with surgery performed later only if their condition worsened).

"Even though the main trial showed no difference in clinical outcomes, this study revealed that revascularization had a greater benefit in reducing the extent of ischemia which is often important in controlling symptoms," said Leslee J. Shaw, Ph.D., lead author of the study and professor of medicine at Emory University School of Medicine in Atlanta, Ga.

In the current sub-study of BARI 2D, 1,505 participants underwent stress myocardial perfusion SPECT to locate and measure areas of myocardium receiving sufficient blood flow. One year into the trial, researchers found:

- Fifty-nine percent of revascularization patients and 49 percent of medical patients had normal results with no drug-induced ischemia.
- Reductions in blood flow involved 3 percent of the heart tissue in revascularization patients and 9 percent of heart muscle in medical patients.
- More ischemia was associated with a greater risk of death or MI.

The results indicate the value of scanning patients with diabetes and heart disease who are being managed with medication and lifestyle interventions.

"The benefits of lifestyle and medication take several months, so scanning after a year can provide a barometer of how effective your treatment has been at reducing ischemia," Shaw said. "Because nerves can be damaged by high blood sugar levels, people with diabetes don't always get chest pain when blood flow is reduced. This test can show reductions in blood flow whether or not you have symptoms, and a normal test can be very reassuring."

The BARI 2D trial compared various treatment strategies for patients with both type 2 diabetes and heart disease.

Co-authors are: Manuel Cerqueira, M.D.; Maria M. Brooks, Ph.D.; Veronica V. Sansing, M.S.; George A. Beller, M.D.; Rodica Pop-Busui, M.D.; Raymond Taillefer, M.D.; Bernard R. Chaitman, M.D.; Raymond J. Gibbons, M.D.; and Ami E. Iskandrian, M.D. Author disclosures are on the abstract.

The National Heart, Lung, and Blood Institute funded the study.

トピックス一覧

腎除神経療法による高血圧治療（Abstract＃21826）

Symplicity HTN-2：ラジオ波を用いた腎神経焼灼は難治性高血圧患者の血圧低下に役立つ

Symplicity HTN-2: Blasting kidney nerves with radio waves helps lower blood pressure for those with stubborn hypertension

腎近傍の神経を沈静化する非薬物治療は、平均5種類の薬剤を内服しても血圧がコントロールできない患者の血圧を安全かつ有意に低下させたとのレイトブレイキング臨床試験の結果が2010年AHAで発表されLancetに掲載された。Symplicity HTN-2トライアルは降圧療法を目的とした血管内選択的腎交感神経除神経術に関する国際多施設前向き無作為化コントロールトライアルであり、カテーテル治療と薬物療法の併用群52人と薬物療法のみを受けたコントロール54人を比較した。スタディ開始時に二群の平均血圧はほぼ同等であった（治療群178/98mmHg対コントロール群178/97mmHg）。参加者の平均年齢は58歳であり、35%が女性で97%が白人であった。6ヵ月後の治療群の収縮期血圧は平均33.4mmHg低下し、拡張期血圧は平均12.5mmHg低下した。一方、コントロール群の平均収縮期血圧はやや（0.9mmHg）上昇し、平均拡張期血圧はやや（0.3mmHg）低下した。血圧が140/90mmHg未満に低下したのは腎除神経術で治療された患者では39%であり、それに比べコントロール群では6%であった。

Full Text

A non-drug treatment that silences nerves near the kidneys safely and significantly reduced blood pressure in patients unable to control their hypertension despite taking an average of five medications, according to late breaking clinical trial research presented at the American Heart Association's Scientific Sessions 2010.

This is the first human randomized controlled trial of therapeutic renal denervation (RDN), a procedure using a catheter-based probe inserted into the renal artery emitting high-frequency energy to deactivate nerves near both kidneys that are linked to high blood pressure. This approach is considered minimally invasive since the kidney nerves are nearby and the energy can be delivered via this catheter-based approach.

The trial, Symplicity HTN-2: International, Multicenter, Prospective, Randomized, Controlled Trial of Endovascular Selective Renal Sympathetic Denervation for the Treatment of Hypertension, compared 52 participants who were randomly assigned to catheter treatment plus medication to 54 controls who received medication alone.

"The procedure safely and successfully silences the nerves for six months, and perhaps permanently," said Murray Esler, M.D., principal investigator of the trial and associate director of the Baker IDI Heart and Diabetes Institute in Melbourne, Australia.

"This procedure provides a revolutionary, non-drug method for controlling high blood pressure in patients who are unresponsive to multiple antihypertensive drugs," he said. "Resistant hypertension is common, occurring in perhaps 15 percent to 20 percent of patients. This procedure is likely to have very wide application."

At the start of the study, the two groups had nearly identical average blood pressures: 178/98 mm Hg for the treatment group versus 178/97 mm Hg for controls. Participants were average age 58, 35 percent were female and 97 percent were Caucasian.

Data at six months showed the treatment group's systolic pressure fell an average 33.4 mm Hg while diastolic pressure dropped an average 12.5 mmHg. In contrast, controls' average systolic pressure rose slightly (0.9 mmHg) and their average diastolic pressure fell slightly (0.3 mm Hg).

"In a small minority of patients in the study, some high blood pressure medication could be stopped or reduced," Esler said.

In addition, of the 48 RDN patients for whom the researchers had complete data when the news release was written, 93.8 percent had at least a 5 mm Hg reduction in systolic blood pressure and 87.5 percent had at least a 10 mm Hg drop in systolic blood pressure, Esler said.

In approximately 39 percent of those who received RDN, compared to six percent of the control group, blood pressure was reduced to less than 140/90 mm Hg. Pressure below 140/90 mm Hg is considered controlled to target despite being higher than the120/80 mmHg considered ideal for adults.

"Target blood pressure is usually unattainable with drug therapy in patients with severely resistant hypertension," Esler said.

The study found no serious device or procedure-related events, no cardiovascular complications and no kidney-related complications.

Esler said the results are significant from a public health standpoint because of high blood pressure's well-documented link to the development of myocardial infarction and stroke, and because hyperactivity of the renal nerves is seen in chronic kidney disease, heart failure and high blood pressure. Future studies will evaluate the effects of the new treatment on those conditions.

While the study population was not ethnically diverse, Esler said he expected the findings to extend across all groups.

Co-authors include members of the Symplicity HTN-2 study group. Author disclosures are on the abstract.

Ardian Inc., funded the study (maker of the SymplicityR Catheter System™).

トピックス一覧

家族性心房細動（Abstract＃12286）

心房細動を有する第一度近親者がいることで、この疾患の発症リスクは上昇する

Having a first-degree relative with atrial fibrillation associated with increased risk for this disorder

Framingham Heart Studyの参加者4,000人余りの心房細動（AF）遺伝性に関する調査の結果、第一度近親者におけるAF発症は確立されたAFリスクファクターおよびAF関連遺伝子亜型で補正後のAFリスクであることが示された、と2010年AHA学会で発表されJAMA 11月24日号に掲載される。当初の参加者およびその子供は30歳以上であり、スタディ開始時にAFを有さず、親または兄弟の少なくとも一人がスタディに参加した。この解析の対象者4,421人（平均年齢54歳；女性54%）中、440人がAFを発症した。家族性AFは1,185人（26.8%）に発現し、早期家族性AF（発症年齢が65歳以下）は351人（7.9%）に発現した。ベースラインの調査時にAFの家族が存在する2,393人のうち、AFを有するのが父親であったのが1,163人、母親が1,068人、兄弟が404人であった。AF発症頻度はAF家族歴を有する者において家族歴のない者より高かった（それぞれ絶対イベント率が5.8%と3.1%であり、約40%リスク上昇）。

Full Text

An examination of the heritability of atrial fibrillation (AF) among more than 4,000 participants in the Framingham Heart Study finds the occurrence of AF in first-degree relatives was associated with AF risk after adjustment for established AF risk factors and AF-related genetic variants, according to a study presented at the 2010 AHA Scientific Sessions and appears in the November 24 issue of JAMA.

"A heritable component underlying atrial fibrillation has been well demonstrated, and it is now evident that genetic variants are associated with AF risk," the investigators write. However, the contribution of familial AF (defined in this study as the occurrence of AF in a first-degree relative prior to an examination commencing an 8-year follow-up period) to predicting new-onset AF remains unknown.

Steven A. Lubitz, M.D., M.P.H., of the Cardiovascular Research Center, Massachusetts General Hospital, Charlestown, Mass., and colleagues examined the association between AF occurrence in a first-degree relative and AF risk and hypothesized that considering familial AF would improve prediction of new-onset AF. Participants were from the Framingham Heart Study, a prospective community-based cohort study started in 1948. Original and offspring participants were at least 30 years of age, free of AF at the beginning of the study, and had at least 1 parent or sibling enrolled in the study. The 4,421 participants in this analysis (average age, 54 years; 54 percent women) were followed up through December 2007.

During the period 1968-2007, 440 participants developed AF. Familial AF occurred among 1,185 participants (26.8 percent) and premature familial AF (onset 65 years of age or younger) occurred among 351 participants (7.9 percent). Of the 2,393 baseline examinations at which familial AF was present, sources included fathers (n = 1,163), mothers (n = 1,068), and siblings (n = 404). Among participants with familial AF, the number of affected relatives ranged from 1 to 5.

The researchers found that AF occurred more frequently (approximately 40 percent increased risk) among participants with familial AF than without familial AF (unadjusted absolute event rates of 5.8 percent and 3.1 percent, respectively). The association was not weakened by adjustment for AF risk factors or reported AF-related genetic variants. Atrial fibrillation risk was associated with increasing number of affected first-degree relatives.

Assessment of premature familial AF was associated with a very slight increase in predictive accuracy compared with traditional risk factors.

"Future efforts should attempt to discern the factors that mediate the association between familial AF and AF risk, further explore the relationships between premature familial AF and risk prediction, and determine whether incorporating genetic variants into an AF prediction model enhances its performance," the authors conclude.

重篤な下肢虚血に関するトライアルで遺伝子治療は不成功に終わった（Abstract＃21790）

TAMARIS：実験的遺伝子治療は末梢血管疾患患者の下肢切断または死亡を防止しなかった

TAMARIS: Experimental gene therapy did not prevent amputation or death in patients with peripheral vascular disease

遺伝子治療は重篤な末梢血管疾患(PAD)により足潰瘍を来した患者の下肢切断または死亡を防止しなかったとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表された。過去のphase 2トライアルの勇気づけられる結果に反して、NV1FGF遺伝子治療の重篤下肢虚血における下肢切断回避率に関するトライアル（NV1FGF Gene Therapy Trial on Amputation-Free Survival in Critical Limb Ischemia）−phase 3無作為化二重盲検プラセボコントロールトライアルにおいて、NV1FGFとして知られる細胞増殖因子による実験的遺伝子治療を受けた患者はプラセボを投与された患者と比較して結果が良好ではなかった。この12ヵ月間のスタディにおいて、研究者らは重症PAD患者259人（男性70%、平均年齢70歳）をプラセボ治療群に無作為に割り付け、一方266人の患者は遺伝子治療細胞増殖因子を投与された。プラセボを投与された患者のうちトライアル中に下肢切断に至ったのは21%であったのに対し、遺伝子治療を施行された患者におけるその割合は26%であった。プラセボ群の15%が死亡し、一方遺伝子治療群では 18%が死亡した。これらの結果に有意差はなかった。

Full Text

Gene therapy did not prevent amputations or death among patients with severe peripheral vascular disease and resulting foot ulcers, according to a late-breaking clinical trial presented at the American Heart Association's Scientific Sessions 2010.

Despite encouraging data from the Phase 2 trial, patients treated with the experimental gene therapy growth factor known as NV1FGF did not fare better than those given placebo among participants in the NV1FGF Gene Therapy Trial on Amputation-Free Survival in Critical Limb Ischemia - Phase 3 Randomized Double-Blind Placebo-Controlled Trial (TAMARIS).

Scientists designed NV1FGF to stimulate new blood vessel growth to increase blood flow to save the legs and prolong the lives of patients with peripheral artery disease (PAD).

"Overall, it's a very disappointing result," said William R. Hiatt, M.D., a co-author of the study. "Patients with peripheral artery disease are very sick and at high risk of limb loss and death. We desperately need new medical advances to treat this population."

The trial's patients, who suffered from critical limb ischemia, had exhausted available options and were highly likely to have a leg amputated or die from their disease. Because of the severe lack of blood flow in their legs, many patients had severe leg and foot pain and painful foot ulcers.

Researchers conducted the study after an earlier, smaller study showed "quite positive" results for ulcer healing. "It's troublesome after having a quite remarkable Phase 2 trial," said Hiatt, professor of medicine and cardiology at the University of Colorado School of Medicine and president of CPC Clinical Research, a non-profit cardiovascular and clinical trials research organization affiliated with the University of Colorado in Aurora, Colo.

"There was a lot of promise for gene therapy to treat coronary and peripheral artery disease over the last decade," he said. "We hope that the next phase of stem cell based therapy will have better results."

In the 12-month study, researchers randomly assigned 259 patients to receive an inactive placebo treatment, while 266 patients received the gene therapy growth factor. The patients, who came from 30 countries, were at high risk of losing a leg because of severe PAD. The patients had foot ulcers as well as low blood pressure in the ankle or foot and were not good candidates for surgical revascularization, a procedure to restore blood flow.

More than half the patients had diabetes - far higher than the rate of diabetes in the general population, which is about 10 percent. "Diabetes predisposes you to ulcers, so this is not unexpected," Hiatt said.

The patients and their doctors didn't know if the eight injections they received contained placebo or NV1FGF, which is still an experimental therapy in the United States. They received injections in leg muscles on days one, 15, 29 and 43 of the study.

Of patients on placebo, 21 percent suffered a major amputation during the trial, compared to 26 percent of those on the gene therapy regimen. Fifteen percent of the placebo group died, compared to 18 percent of the gene therapy group. These results were not significantly different.

Seventy percent of the participants were men, the average age was 70. Sixty-one percent had a history of smoking and 54 percent had a history of coronary artery disease.

In future studies, researchers should focus on stem cell-based therapy and stem cell lines that promote angiogenesis, growth of new blood vessels, Hiatt said. "That's the next step in my mind. Angiogenesis remains a viable treatment option to study."

Co-authors are Eric Van Belle, M.D., Ph.D.; Sigrid Nikol, M.D., Ph.D.; Lars Norgren, M.D., Ph.D.; Iris Baumgartner, M.D., Ph.D.; Vickie Driver, M.D., Ph.D. and Jill Belch, M.D. Professor Belch was the chair of the steering committee and will be the primary author on the study results. Author disclosures are on the abstract.

Sanofi-Aventis funded the study.

Cardiology特集
AHA2010（第83回米国心臓病協会）

トピックス一覧

[News01]
職務ストレスが心疾患リスクを上昇させる

[News02]
アルコール摂取量はバイパス術後の心臓に関する問題と関連がある

[News03]
キサントーマにより心血管疾患が予測される

[News04]
10代での塩分摂取量を少なくすることにより成人期の心臓の健康状態が改善する可能性がある

[News05]
軽度心不全においてアルドステロン拮抗薬は多大な有益性を示した

[News06]
魚油は心房細動再発を軽減しなかった

[News07]
新たな心ポンプが目標を達成した

[News08]
心臓再同期療法は軽度心不全患者において有用である

[News09]
Nesiritideは安全だが有益性は乏しいことが示された

[News10]
バイオマーカーにより心不全および死亡リスクが予測できる

[News11]
新薬はHDLを有意に上昇させLDLをほぼ半分に低下させる

[News12]
CRPスクリーニングは従来の心臓リスク評価を改善しない

[News13]
糖尿病患者に対する薬物療法と迅速な血行再建術の併用は有益である

[News14]
腎除神経療法による高血圧治療

[News15]
家族性心房細動

[News16]
重篤な下肢虚血に関するトライアルで遺伝子治療は不成功に終わった