エボロクマブは心血管イベントを有意に低下させた (Abstract 17-LB-15607)

FOURIER：PCSK9阻害薬は一貫した抑制効果とLDL-Cの著明な低下を示した

FOURIER: First outcomes trial of PCSK9 inhibitor shows consistent benefits and confirms marked drops in LDL-C

新規PCSK9阻害薬の1つであるエボロクマブは、低比重リポ蛋白（LDL）コレステロール値を劇的に低下させることは示されているが、心血管疾患歴を有しスタチン治療を受けている患者の心血管イベントリスクも有意に低下させることが、American College of Cardiology's 66th Annual Scientific Sessionで発表された。エボロクマブはLDLコレステロール中央値を92 mg/dLから30 mg/dLに、59%低下させた。心血管死亡率単独への影響は認められなかったが、心筋梗塞および脳卒中において、それぞれ27%と21%の統計学的に有意な低下が認められた。FOURIER試験の結果は同時に、*New England Journal of Medicine* に掲載された。

Full Text

Evolocumab, one of the new targeted PCSK9 inhibitor drugs that has been shown to dramatically lower levels of low-density lipoprotein (LDL), also significantly lowers the risk of cardiovascular events in patients with existing heart or vascular disease already on statin therapy, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

Evolocumab reduced by 15 percent the risk of the trial's primary endpoint — a composite of myocardial infarction (MI), stroke, hospitalization for angina, revascularization, or cardiovascular death — compared with placebo during the study duration, a median of 26 months. Researchers also saw a 25 percent reduction in the study's more serious secondary endpoint — cardiovascular death, MI or stroke — after the first year. The trial confirms trends observed in earlier open-label studies.

"With this trial, we now have definitive data that by adding evolocumab to a background of statin therapy, we can significantly improve cardiovascular outcomes and do so safely," said Marc S. Sabatine, MD, the Lewis Dexter, MD, Distinguished Chair in Cardiovascular Medicine at Brigham and Women's Hospital in Boston, chair of the Thrombolysis in Myocardial Infarction (TIMI) study group and the study's lead author. "I think these results are very good news for patients with atherosclerotic disease, who remain at high risk for these events."

Results of FOURIER (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) are highly anticipated as the first large, long-term randomized clinical trial designed to rigorously assess whether evolocumab, given along with statin therapy, can improve outcomes among high-risk patients. Evolocumab is a fully human monoclonal antibody that works by blocking proprotein convertase subtilisin-kexin 9 (PCSK9), a protein that reduces the liver's ability to remove LDL cholesterol from the blood.

This protein became an intriguing target when scientists discovered that people with genetically lower levels of PCSK9 activity had lower rates of MIs.

In this trial, researchers enrolled 27,564 patients with pre-existing cardiovascular disease between February 2013 and June 2015 at 1,272 sites in 49 countries. Most patients (81 percent) had a history of MI, 19 percent had suffered an ischemic stroke, and 13 percent had symptomatic peripheral artery disease. Patients' average age was 63 years and ranged from 40 to 85 years of age. The majority (75 percent) were men. The median baseline LDL cholesterol was 92 mg/dL.

To be included, patients had to have an LDL-C ≥70 mg/dL or a non–high density lipoprotein cholesterol ≥100 mg/dL (total cholesterol minus high-density lipoprotein cholesterol to accommodate for other sized cholesterol particles) and be on optimized statin therapy. Patients who had had an acute MI or stroke within the previous four weeks and those with advanced heart failure, uncontrolled heart rhythm disorders, upcoming cardiac surgery and end-stage kidney disease were excluded.

Patients on a moderate-to-high intensity statin regimen were randomly assigned 1:1 to receive subcutaneous injections of evolocumab (either 140 mg every two weeks or 420 mg every month based on patient preference) or matching placebo. Sixty-nine percent of patients were on a high-intensity statin and 30 percent were on moderate-intensity statin. Patients were followed every 12 weeks for routine health assessments, lab work and a resupply of the study drug.

In terms of lipid-lowering, evolocumab reduced LDL cholesterol by 59 percent from a median of 92 to 30 mg/dL, which remained steady throughout the duration of the study, and is in line with previous trial results. The primary endpoint occurred in 11.3 percent of the placebo group and 9.8 percent of the evolocumab group, which translates to a 15 percent reduction. The composite of MI, stroke or cardiovascular death occurred in 7.4 percent of the placebo group and was reduced by 20 percent to 5.9 percent in the evolocumab group. When examining individual outcomes, there was no effect on cardiovascular mortality by itself, but there was a statistically significant 27 percent reduction in MI and a 21 percent reduction in stroke.

Data also showed greater benefit over time; the secondary endpoint was significantly reduced by 16 percent in the first year and 25 percent beyond the first year.

"Consistent with data from statin trials, it takes time for LDL lowering to translate to healthier arteries," Sabatine said.

Reductions in the primary and key secondary endpoints were consistent across all the key subgroups, including age, sex, different types of cardiovascular disease, intensity of statin therapy, dosing regimen of evolocumab and baseline LDL cholesterol levels, including those with the lowest quartile of LDL cholesterol—starting at 74 mg/dL—in whom evolocumab reduced LDL down to 22 mg/dL.

"We've never been able to plumb these depths before. These data strongly suggest that patients benefit from lowering LDL cholesterol well below current targets," Sabatine said.

The rate of adverse events, including allergic reactions, neurocognitive, new-onset diabetes and muscle-related problems, were the same in both study arms. Rates of injection site reactions were slightly more common with evolocumab (2.1 vs. 1.6 percent), but the vast majority were mild, and the overall rates of stopping the study drug due to suspected treatment-related adverse events were low and similar in both groups (1.6 and 1.5 percent). Researchers also looked at whether patients receiving evolocumab generated an undesired immune response to the treatment; only 0.3 percent developed antibodies that could bind evolocumab and none interfered with the drug.

This study is limited by its relatively short follow up and that it only studied patients with known cardiovascular disease. Sabatine said future studies would need to examine PCSK9 inhibitors in other high-risk populations not addressed in this study (for example, in patients with diabetes but without known cardiovascular disease).

"We need to treat LDL cholesterol more aggressively, and now we have a new validated means to do so," Sabatine said. "People with atherosclerotic disease should discuss their LDL cholesterol with their physician and consider whether they need to lower it further."

The trial was funded by Amgen.

The EBBINGHAUS study will examine evolocumab's effect on cognitive function from a subset of patients in FOURIER.

This study was simultaneously published online in the *New England Journal of Medicine* at the time of presentation.

ACC2017特集

自己拡張型経カテーテル的大動脈弁置換術（TAVR）は中等度リスクの患者に適している(Abstract 17-LB-16607)

SURTAVI：TAVRは重症の大動脈弁狭窄を有する中等度リスク患者において安全かつ有効な手術である

SURTAVI: TAVR is as safe and effective as surgery in intermediate-risk patients with severe aortic stenosis

2年間のデータにより、重症の大動脈弁狭窄を有する中等度リスク患者において、自己拡張型経カテーテル的大動脈弁置換術（TAVR）と標準的な開胸手術を比べた場合、脳卒中と全死亡を合わせた率に差がないことが明らかになった、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。全体として、30日、1年および2年間のデータにより、全死亡はTAVR群とSAVR群で同様であることが示された。さらに、主要な後遺障害を伴う脳卒中の割合において、統計学的に有意な差はなかった。SURTAVI試験の結果は同時に、*New England Journal of Medicine* に掲載された。

Full Text

Two-year data reveal no difference in the combined rate of stroke and death from any cause when comparing the use of self-expanding transcatheter aortic valve replacement (TAVR) with standard open-heart surgery in intermediate risk patients with severe aortic stenosis, according to research presented at the American College of Cardiology's 66th Annual Scientific Session. Researchers say these results suggest TAVR is at least as safe and effective as surgery in these patients.

Aortic stenosis forces the heart to work harder to pump blood and is life-threatening over time. If untreated, the risk of death is 25 percent the first year after symptoms appear. This risk rises to 50 percent the second year. TAVR, which was approved in 2011 for use in patients with severe aortic valve stenosis who were considered at high risk for death and complications associated with surgical aortic valve replacement (SAVR), now holds promise for intermediate-risk patients. In August 2016, data from an earlier trial prompted the FDA to expand the use of the Sapien XT and Sapien 3 transcatheter heart valves in this group.

The SURTAVI trial, which included 1,746 patients at 87 centers in the United States, Europe and Canada, is the second randomized controlled trial to compare TAVR and SAVR in intermediate-risk surgical patients. It is the first to look at outcomes using the self-expanding CoreValve and Evolut-R bioprosthesis valves. Overall, the primary endpoint of all-cause death and disabling stroke was comparable at two years, 14 percent for surgery and 12.6 percent for TAVR.

"TAVR was just as good as surgery, but it was not statistically superior to it," said Michael J. Reardon, MD, professor of cardiothoracic surgery and Allison Family Distinguished Chair of Cardiovascular Research at Houston Methodist Hospital, and the study's lead author, adding that because mortality in the surgical group was so low, it was difficult to meet superiority. "We saw the best surgical outcomes we've seen yet and TAVR did just as well. This is now the second randomized trial that has met its non-inferiority endpoint and should lead to changes in clinical guidelines that will move the field forward and also benefit our patients," he said.

Patients, who averaged nearly 80 years of age, were enrolled in the trial if they had symptomatic, severe aortic stenosis defined by standard parameters (a valve area less than or equal to one, a valve index less than 0.6, and a median gradient over 40 or peak velocity over four) and were considered at intermediate risk for open-heart surgery based on a combination of the Society of Thoracic Surgeons (STS) predicted risk operative of mortality (PROM) score, as well as a series of frailty, disability and other measures that, when considered by the heart team, led to an estimated mortality of 3 to 15 percent. STS PROM scores were 4.4±1.5 in the TAVR group and 4.5±1.6 in the SAVR group. There were no major differences in key baseline characteristics such as age, sex, frailty, disability and other medical conditions.

Patients were randomized 1:1 to receive TAVR or SAVR. Surgeons performing SAVR were allowed to choose any biologic valve or whether to enlarge the annulus or base of the valve if needed so that TAVR would be evaluated against real-world surgery. While the TAVR arm of the trial started with the original CoreValve, which was used in 84 percent of cases, the new Evolut-R system was introduced toward the end of the trial in U.S. centers only and was implanted in 16 percent of patients enrolled. Patients had clinical visits, echocardiograms, electrocardiograms, and/or assessments of quality of life at one, three, six, 12 and 24 months.

Overall, 30-day, one-year and two-year data showed that deaths from any cause were similar for TAVR and SAVR: occurring in 2.2 vs. 1.7 percent of patients at 30 days, 6.7 vs 6.8 percent at one year, and in 11.4 vs 11.6 percent at two years. Moreover, there was no statistically significant difference in the rate of major disabling stroke at two years, 4.5 percent for surgery and 2.6 percent for TAVR. Although not a primary outcome of the study, researchers noted that the risk of any type of stroke at 30 days was statistically superior for TAVR, 3.4 percent compared with 5.6 percent for SAVR.

Based on an analysis of echocardiograms, Reardon said there was some indication that the TAVR valve worked better; TAVR had a statistically superior valve orifice and lower mean gradients than surgery at all time points in the trial.

One of the differences in the trial, Reardon said, is that unlike the earlier PARTNER trial that stratified patients by how the surgeon routed the catheter (via transfemoral or transapial access), SURTAVI stratified patients by need for revascularization. Data showed no difference in outcomes based on whether someone needed the procedure to open blocked arteries, which Reardon said would usually indicate a sicker patient because they also have coronary heart disease.

Similar with earlier studies, researchers report more moderate-to-severe paravalvular leakage in the TAVR versus surgical valves, occurring in5.4 vs. 0.4 percent of patients, respectively. This group also had a higher use of pacemakers. In the surgery arm, there were more transfusions, strokes, acute kidney injury and atrial fibrillation at 30 days.

Researchers also performed quality of life assessments at baseline, one and six months, and yearly thereafter. Patients receiving TAVR reported significantly better quality of life one month after their procedure, but by six months the two groups were similar. Patients in both groups reported markedly better quality of life after receiving a new aortic valve compared with before either intervention.

A potential limitation of the study is the higher dropout rate (8.2 percent) for patients randomly assigned to surgery, which has been a consistent trend across other studies. Reardon said longer follow-up is needed to attain more complete information about the life cycle of the device and how it works, especially as only16 percent of patients received the newer EVOLUT-R system. Patients in the SURTAVI trial will be followed for a total of five years. Reardon and his team are currently enrolling patients in an ongoing randomized controlled trial to evaluate TAVR in low risk patients. Although not all patients would be candidates for TAVR, low risk patients are estimated to comprise 80 percent of patients with aortic stenosis; intermediate-and high-risk patients make up 12 and 8 percent, respectively.

"We found exceeding low mortality at one and two years, which should give us great confidence as we move into lower risk that these outcomes are very good," he said.

Medtronic, the maker of the self-expanding TAVR devices, sponsored the trial.

This study was simultaneously published online in the *New England Journal of Medicine* at the time of presentation.

ACC2017特集

NSAIDに加えてミソプロストールを服用することにより心血管系リスクが低下する(Abstract 17-A-9724)

ミソプロストールを非ステロイド性抗炎症薬と併用することでNSAID単独服用に比べ安全な可能性がある

Combining misoprostol with non-steroidal anti-inflammatory drugs could be safer than NSAIDs alone

胃潰瘍に対して、ミソプロストールを非ステロイド性抗炎症薬（NSAID）とともに服用した人は、NSAID単独服用した人に比べ、重篤な心血管イベント、脳卒中および腎不全のリスクが有意に低かった、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。NSAIDをミソプロストールとともに服用している人は、心筋梗塞、心停止、または心室細動の発現リスクが44%低かった。両薬剤服用者は、NSAID単独服用者に比べ、脳卒中または一過性脳虚血発作のリスクが25%低く、急性腎不全のリスクが34%低かった。

Full Text

People who took the drug misoprostol for stomach ulcers along with non-steroidal anti-inflammatory (NSAID) drugs had a significantly lower risk of serious cardiovascular events, stroke and kidney failure than those who took NSAIDs alone, according to a study presented at the American College of Cardiology's 66th Annual Scientific Session.

NSAIDs, a large category of drugs that includes ibuprofen, celecoxib and dozens of others, are commonly used to treat pain, inflammation and fever and are available by prescription and over the counter. They are one of the most commonly used medications worldwide. They have been linked with rare but life-threatening side effects including myocardial infarction, cardiac arrest, stroke and acute kidney failure, collectively referred to as cardio-renal complications. Because stomach ulcers are a common side effect of many NSAIDs, misoprostol and NSAIDs are sometimes prescribed together in people at high risk for ulcers.

"Right now, clinicians have no direct treatment options to reduce the risk for these NSAID-induced cardio-renal complications, other than to advise against NSAID use, reduce the duration of use or recommend alternative pain management agents, so we set out to discover a treatment to reduce the risk of these effects," said Mark Munger, PharmD, professor of pharmacotherapy at the University of Utah College of Pharmacy and the study's lead author. "Our data, from a large and well-characterized health care system, support a potentially safer NSAID alternative when NSAIDs are combined with misoprostol."

The researchers analyzed the health records of more than 1.6 million people in the U.S. Veterans Affairs health system who took prescription doses of NSAIDs and/or misoprostol between 2005 and 2013. Eleven different NSAID drugs were represented in the sample. After accounting for dozens of baseline characteristics and health conditions, they identified 1,875 people who took NSAIDs alone who were "matched," in terms of baseline health status, with 1,875 people who took NSAIDs plus misoprostol. They then compared health outcomes in the two groups based on their health records over a five-year period.

People taking NSAIDs and misoprostol together had a 44 percent lower risk of having a myocardial infarction, suffering cardiac arrest, or having ventricular fibrillation. Those taking both drugs also had a 25 percent lower risk of strokes or transient ischemic attacks (TIA, "ministroke") and a 34 percent lower risk of acute kidney failure compared to people taking NSAIDs alone.

The study results suggest that combining NSAIDs with misoprostol, either by prescribing them together or by developing a combination pill, could help reduce the risk of cardio-renal NSAID-induced side effects.

Drug labels currently warn of cardio-renal complications for any NSAID dose, whether prescription or over the counter. Studies have shown the highest risk of these complications is seen in people who have recently started NSAID treatment, in those prescribed higher doses and in those who take them for long periods of time.

NSAIDs reduce the levels prostaglandins circulating in the body. This helps to reduce inflammation and thus relieve pain, but it also can have harmful effects in other parts of the body. Misoprostol is thought to counter these harmful effects by potentially replacing some of the reduced prostaglandins. Previous studies have shown misoprostol can lower blood pressure and improve measures of kidney function.

"Hopefully we can reduce the incidence of NSAID-induced cardio-renal adverse effects, which could be especially important in an era in which pain management is in flux," Munger said. He noted that sharp increases in opioid abuse and addiction have fueled a growing emphasis on non-opioid pain management options, such as NSAIDs.

An unrelated recent study suggested some NSAIDs increase the risk of heart failure. Heart failure was not included among the outcomes tracked in this study.
A key limitation of the study is that it was a retrospective analysis based on health records, rather than a prospective or randomized trial.

The study was funded by the Salt Lake City Veterans Affairs Health Services Research and Development (HSR&D) Informatics, Decision-Enhancement and Analytic Sciences (IDEAS) Center with grant support from Veterans Affairs Informatics and Computing Infrastructure (VINCI) and the University of Utah Clinical Cardiovascular Research Fund.

ACC2017特集

手首装着型心拍計は胸部装着型よりも正確さに欠ける (Abstract 17-A-10265)

心拍計の正確さはデバイス、活動のタイプおよび運動強度により異なる

Accuracy of heart rate monitors varies by device, activity type and exercise intensity

研究者らは5つの一般的な手首装着型フィットネストラッカー（アップルウォッチ、Fitbitなど）を試し、様々なタイプの運動や運動強度においてどの程度正確に心拍を計測できるかを調査した。その結果に基づくと、特に活動中の心拍モニターが必要な人においては、旧式の胸帯モニターが最良であった。手首に装着するフィットネストラッカーは、心拍数を過大および過小評価した。誤差は、活動のタイプにより1分当たり±34拍から±15拍の範囲であった。このスタディ結果は、American College of Cardiology's 66th Annual Scientific Sessionで発表された。

Full Text

Researchers at Cleveland Clinic put five popular wrist-worn fitness trackers to the test to find out how accurately they gauge heart rate across several types of exercise and intensity levels. Based on their findings, the old-fashioned chest strap monitor is best, particularly for people who need to monitor their heart rate during activity, according to the study team. The standard chest strap was the most accurate regardless of the intensity of the workout or whether someone was using the treadmill, elliptical or stationery bike.

The results were presented at the American College of Ca rdiology's 66th Annual Scientific Session. This study builds on earlier research by the same team that assessed a different set of heart rate monitors and was limited only to walking or jogging on a treadmill.

Heart rate is often used as part of a formula to calculate how many calories are being burned during exercise. However, for people with heart problems, an accurate heart rate reading is important.

"If you need to know your heart rate with accuracy when exercising — either because you are training for a marathon or have safe heart rate limits set by your doctor, perhaps due to coronary artery disease, heart failure or other heart conditions — wrist-worn monitors are less accurate than the standard chest strap," said Marc Gillinov, MD, The Judith Dion Pyle Chair in Heart Valve Research, Thoracic and Cardiovascular Surgery at the Cleveland Clinic, Ohio and the study's lead author. "We found these devices can equally over-and underestimate heart rate. The error ranged from +/- 34 beats per minute to +/- 15 beats per minute, depending on the type of activity."

This single-center study included 50 volunteers, mostly Cleveland Clinic employees, who responded to internet notices and flyers. They were 38 years old on average (±12 years), 43 percent female and generally healthy. Each participant was fitted with a continuous 4-lead electrocardiogram (EKG), a chest monitor and an armband (Scosche Rhythm+). They were then randomly fitted with two of four different wearable heart rate monitors (one on each wrist). The devices chosen for testing (Apple Watch, Fitbit Blaze, Garmin Forerunner 235, and TomTom Spark Cardio) were based on their popularity and sales figures. Researchers then recorded volunteers' heart rates at rest and after light, moderate and vigorous exercise across three types of activities, including the treadmill, stationary bike and elliptical (with and without hand levers). Measurements on the wearable devices were compared to readings from the chest strap and EKG. Participants exercised for a total of 18 minutes; one dropped off at the final stage due to fatigue.

The chest strap monitor closely matched readings from the electrocardiogram (EKG), which is the gold standard for measuring the heart's activity (level of agreement with EKG, rc=.996; 1 being perfect agreement); however, the wrist-worn devices were less accurate on average (level of agreement with EKG, rc =.67-.92). While the watch-style heart rate monitors may accurately report heart rate at rest, and most were acceptable on the treadmill, they were fairly inaccurate while bicycling or using the elliptical. Of the wrist-worn heart rate monitors, only the Apple Watch provided accurate heart rate readings when participants switched to the elliptical trainer without arm levers; none gave correct measurements when they used arm levers. The wrist and forearm monitors also became less accurate the more intense the activity levels, with the exception of the Apple Watch.

"Even though all these wrist-worn monitors work by the same general principles, there is considerable variation among them," Gillinov said. "Overall, they were most accurate when someone was using the treadmill at low intensity and worst when exercising on the elliptical at high intensity."

What's behind the discrepancies? Unlike the chest strap, which like the EKG measures electrical activity of the heart, wrist-worn monitors use optical sensing or light to measure blood flow.

"It's not measuring what the heart does, but rather [downstream] blood flow — basically the volume of blood in the tissue," Gillinov said, adding that these devices also introduce many more variables that can result in incorrect readings (e.g., insufficient contact with the skin because of sweating or poor fit, skin pigmentation).

The bottom line, Gillinov said, is that the wrist-worn devices don't provide the full picture; nor are they intended to be medical devices.

"We are just at the beginning of a revolution in personal management of health by virtue of wearable physiological monitoring," Gillinov said. "As people take more control of their health and record their own physiological data, they need to know how accurate it is; this is especially concerning for people with heart conditions that can be exacerbated [with activity]. Cardiologists can use this data and decide which monitor they would recommend and help educate patients about their limitations."

This study is limited due to its small size. Researchers say larger studies are needed and should also evaluate how these devices perform in measuring heart rate in people who have heart failure, diabetes, are recovering from heart attack or are obese.

ACC2017特集

ホルモン補充療法は死亡率が低いことと関連がある (Abstract 17-A-12199)

更年期障害の症状緩和のためのホルモン補充療法は動脈硬化を抑制し生存率を改善した

Using hormone replacement therapy to relieve menopause symptoms lowered atherosclerosis and improved survival

更年期障害の症状緩和のためのホルモン補充療法を行っている女性は、ホルモン補充療法を行っていない女性に比べ、死亡リスクが低く動脈硬化度が低かった、との単施設研究がAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。ホルモン補充療法を行っている女性はこれを行っていない女性に比べ、死亡する確率が全体で30%低く、冠動脈石灰化スコアがゼロ（計測可能な最小値）である確率も20%高く、冠動脈石灰化スコアが399超（重度の動脈硬化を示唆）である確率が36%低かった。

Full Text

Women using hormone replacement therapy to relieve the symptoms of menopause faced a lower risk of death and showed lower levels of atherosclerosis compared to women not using hormone therapy, according to a single-center study presented at the American College of Cardiology's 66th Annual Scientific Session.

Hormone replacement therapy has been controversial over the past few decades as studies have associated it with both health benefits — lowering the risk of osteoporosis and improving some measures of heart health, for example —and risks, including links to cancer and stroke. Fear over potential cancer and other risks has fueled a dramatic decrease in the number of women using hormone replacement therapy over the past 15 years. The new study bolsters evidence that the therapy, which involves the use of supplemental estrogen, sometimes along with progesterone or similar hormones, may help improve heart health and overall survival in some women.

"With proper screening and proper follow-up, from a cardiovascular standpoint I believe it is beneficial to take hormone replacement therapy," said Yoav Arnson, MD, a postdoctoral scientist at Cedars-Sinai Medical Center, and the study's lead author. "Our results confirm and enhance previous work in terms of showing lower atherosclerosis. In addition, we've shown very clear survival benefits of using hormone replacement therapy."

The researchers retrospectively analyzed the health records of more than 4,200 women who received a coronary calcium scan at Cedars-Sinai Medical Center between 1998 and 2012. Having higher levels of calcium is a marker for the buildup of plaque, which increases the risk of having a myocardial infarction or stroke.

Forty-one percent of the women reported taking hormone replacement therapy at the time of their calcium scan. Use of hormone therapy was highest between 1998-2002 and gradually decreased during the study period from more than60 percent of women in 1998 to 23 percent of women in 2012. Just over 6 percent of the women died during an average follow-up period of eight years.

Those using hormone replacement therapy were significantly older than those not on the therapy, with an average age of 60 years in the non-therapy group compared to an average age of 64 years in the group taking the therapy. To account for this difference in their analysis, the researchers performed statistical adjustments and also assessed outcomes for separate age groups, divided into five-year intervals.

After accounting for age, coronary calcium score and cardiovascular risk factors including diabetes, high blood pressure and high cholesterol, women using hormone replacement therapy were overall 30 percent less likely to die than those not on hormone therapy. Women using hormone replacement therapy were also 20 percent more likely to have a coronary calcium score of zero (the lowest possible score, indicating a low likelihood of myocardial infarction) and 36 percent less likely to have a coronary calcium score above 399 (indicative of severe atherosclerosis and high myocardial infarction risk).

"Hormone replacement therapy resulted in lower atherosclerosis and improved survival for all age groups and for all levels of coronary calcium," Arnson said. "From this we do think it is beneficial, but we would need prospective or randomized studies to determine which groups might not benefit or even be harmed by this therapy."

Estrogen is thought to be protective of heart health through its beneficial effects on cholesterol and because it increases the flexibility of blood vessels and arteries, allowing them to accommodate blood flow. Studies show that pre-menopausal women, who produce high levels of estrogen, typically have the cardiovascular health of men 10 to 20 years younger than them, but rates of heart disease increase dramatically after menopause, when estrogen levels plummet. By replacing the natural estrogen lost during menopause, hormone replacement therapy could be one way for women to regain the cardiovascular benefits of estrogen, Arnson said.

Women and their doctors weigh many factors when deciding whether or not to use hormone replacement therapy. This study involved a larger number of patients and a longer follow-up time than most other recent studies, and it offers new evidence on potential cardiovascular and survival benefits. It does not, however, offer definitive insights on which groups are likely to benefit most or weigh in on cancer-related or other potential risks. Women who have already had a heart attack, have known heart disease or have a history of blood clots are advised against taking hormone replacement therapy.

ACC2017特集

MI後の睡眠時無呼吸スクリーニングに最適な時期が調査された(Abstract 17-A-9822)

心筋梗塞直後の睡眠時無呼吸のスクリーニング検査はやや信頼性に欠ける

Tests that screen for sleep apnea shortly after a myocardial infarction are somewhat unreliable

心筋梗塞直後に施行された検査の睡眠時無呼吸陽性の診断はやや信頼性に欠ける、との単施設研究がAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。患者はMI直後、および6か月後にスクリーニング検査を受けた。初回に閉塞性睡眠時無呼吸と診断された患者のうち、46%は6か月後の時点では睡眠時無呼吸ではなくなっていた。初回に中枢性睡眠時無呼吸と診断された患者のうち、83%が6か月後に閉塞性睡眠時無呼吸を有していることが明らかになった。初回の検査で睡眠時無呼吸がないと判断された患者の大多数(93%)は、6か月後も睡眠時無呼吸を有さないままであった。

Full Text

Conducting a diagnostic sleep test shortly after a heart attack can help doctors rule out sleep apnea, a form of disordered breathing during sleep, in patients, but tests conducted in the immediate aftermath of a myocardial infarction are somewhat unreliable for positively diagnosing sleep apnea, according to results from a single-center study presented at the American College of Cardiology's 66th Annual Scientific Session. As a result, it may be best to repeat the test after a few months or to delay initial testing before making a definitive diagnosis and initiating treatment.

Sleep apnea is often undiagnosed and untreated. Common signs include daytime sleepiness, heavy snoring and pauses in breathing during sleep. The disorder increases cardiovascular risk, and in people who have had a heart attack, sleep apnea is associated with increased risk for high blood pressure, subsequent heart attack, stroke, heart failure and death.

"In view of the strong association between sleep disordered breathing and heart attack and the established negative prognostic implications of untreated sleep apnea in these patients, cardiologists are becoming increasingly aware of the importance of screening for sleep disorders in their daily practice," said Jeanette Ting, MB, ChB, senior resident at National University Heart Centre, Singapore, and the study's lead author. "Our aim was to determine if the screening should be performed during the acute phase soon after a heart attack or after a period of stabilization."

Sleep apnea is thought to contribute to cardiovascular disease by increasing stress on the heart and blood vessels, causing inflammation, reducing available oxygen and affecting hormones. Doctors can use questionnaires to identify patients who might have sleep apnea, but the only definitive test is an overnight sleep study, in which a specialist uses electrodes and sensors to monitor how often the patient stops breathing during sleep and the length of each pause.

For the study, researchers performed an overnight sleep test in 397 patients treated for heart attack at Singapore's National University Heart Center. This initial test was conducted within five days of hospital admission. A subgroup of 102 patients underwent a second sleep test at home six months later. A total of 52percent of patients tested positive for sleep apnea in the initial test. Forty-two percent had obstructive sleep apnea, the most common form of the disorder, in which the airway is blocked for brief periods by the tongue or throat muscles. Ten percent had central sleep apnea, a less common form in which the brain fails to properly signal the muscles that control breathing.

About a quarter of the patients underwent a second sleep study after six months. A majority of the patients initially found to have sleep apnea showed a change of status in the follow-up sleep study.

Among those initially diagnosed with obstructive sleep apnea, 46 percent no longer had sleep apnea at the 6-month test. Among those initially diagnosed with central sleep apnea, 83 percent were found to have obstructive sleep apnea at the 6-month test. The vast majority (93 percent) of those initially found to have no sleep apnea remained apnea-free at six months.

Overall, patients with sleep apnea were older, had a higher body mass index and more often had high blood pressure compared to those without sleep apnea. Patients showed no significant change in body mass index between the first and second sleep tests.

Mild sleep apnea can sometimes be resolved with weight loss, exercise, smoking cessation, management of allergies or asthma, or a change of sleeping position. For moderate to severe sleep apnea, many patients need to use a continuous positive airway pressure (CPAP) machine. Other treatment options include night-time mouthpieces and, as a last resort, surgery to remove bulky tissues obstructing the airway during sleep. These treatments have been shown to reduce the cardiovascular risk associated with sleep apnea.

The study bolsters evidence from previous smaller studies suggesting sleep apnea diagnosed immediately after a heart attack may resolve naturally over time. In addition, because different types of sleep apnea may require different treatments, the change in apnea type observed in this study underscores the need for repeated or delayed testing after the initial hospitalization for a myocardial infarction. Finding the optimal timing to screen for sleep apnea is important because of the need to avoid unnecessary treatment in people whose sleep apnea may resolve over time, while identifying those who truly need to receive treatment to reduce their cardiovascular risk. Making accurate sleep apnea diagnoses also has a bearing on health care costs.

"It is important to determine if the patient truly has underlying sleep disordered breathing," Ting said. "A repeat sleep study six months later on those found to have obstructive sleep apnea or central sleep apnea should be considered before commencing therapy. Alternatively, deferring the sleep study to six months' follow-up may be considered."

The study was limited by a small sample size. In addition, the baseline sleep study was conducted at the hospital while the second sleep study was performed at the patients' home, which could have influenced the findings. The researchers plan to further analyze the data to assess how sleep apnea might affect measures of heart function.

ACC2017特集

運動歴は乳がん後の心疾患予防に役立つ (Abstract 17-A-12505)

運動は乳がん治療後の心血管疾患を予防するようである

Exercise appears to protect against cardiovascular disease after breast cancer treatment

定期的な運動は心臓の健康習慣の一部として全ての人々に推奨されるが、乳がんの治療を受けた女性が直面する心血管系リスク上昇の軽減にも役立つようである、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。このスタディの結果、診断前に週5時間の中等度の運動に匹敵する運動を行っていた乳がん患者は、診断前の運動レベルが低かった者に比べ、心血管系イベントを発現する確率が40%低く、冠動脈疾患により死亡するリスクが60%低かった。

Full Text

While regular exercise is recommended as part of a heart-healthy lifestyle for any person, it also appears to help mitigate the increased cardiovascular risk faced by women treated for breast cancer, according to a study presented at the American College of Cardiology's 66th Annual Scientific Session.

The study found that women with breast cancer who engaged in the equivalent of five hours of moderate exercise per week before their diagnosis were 40 percent less likely to have a cardiovascular event and 60 percent less likely to die from coronary heart disease compared to those with a low pre-diagnosis level of exercise.

Researchers said this study is the first to examine the long-term impact of exercise before a cancer diagnosis and the cardiovascular benefits of exercise across all types of cancer treatments.

Women who have been diagnosed with early-stage breast cancer face a markedly increased risk of heart disease compared to the general population. This increased risk, which reduces long-term survival, is attributed, in part, to cardiovascular damage from cancer therapies.

"Next to a second or recurrent cancer, heart disease is the second leading killer in cancer patients and survivors, so anything we can do to prevent cancer survivors from developing heart disease is very important," said Tochi Okwuosa, DO, a cardiovascular disease specialist at Rush University Medical Center and the study's lead author. "We found that with exercise, even before one is diagnosed with cancer, you can lower the risk of cardiovascular problems that are caused by chemotherapy and radiation therapy."

The research is based on data from the Women's Health Initiative, a large, nationwide observational study and clinical trial conducted by the National Institutes of Health from 1991-2006.

Researchers extracted data from 4,015 study participants who were diagnosed with non-metastatic breast cancer. Based on physical activity questionnaires participants completed periodically throughout the study, participants were grouped into quartiles of exercise according to metabolic equivalent task (MET) hours per week, a standardized metric that reflects both the amount and intensity of exercise: low (fewer than 2.5 MET hours per week), intermediate (2.5-8.6 MET hours per week), moderate (8.6-18 MET hours per week) and high (more than 18 MET hours per week, which translates to roughly five hours of moderate exercise per week). The researchers then analyzed cardiovascular events during an average of 12 years following participants' breast cancer diagnosis.

After adjusting for age, they found that women reporting intermediate, moderate and high levels of exercise before their cancer diagnosis were 23 percent, 25 percent and 41 percent less likely to experience a cardiovascular event, respectively, compared to women reporting the lowest level of physical activity. Cardiovascular events included cardiovascular death, heart failure, myocardial infarction, angina, stroke or transient ischemic attack (TIA), buildup of plaque in the carotid or peripheral arteries, and revascularization procedures such as angioplasty or bypass surgery.

The results also showed women reporting intermediate, moderate and high levels of exercise before their cancer diagnosis were 41 percent, 55 percent and 60 percent less likely, respectively, to be diagnosed with coronary heart disease compared to women reporting low physical activity. Similar patterns were observed for all types of cancer treatment and after adjusting for a range of cardiovascular risk factors, demographic factors and medical conditions.

Radiation therapy, which in breast cancer is administered relatively close to the heart (particularly with older techniques), damages heart muscle cells and can lead to persistent inflammation many years later. This inflammation is thought to contribute to problems with the heart valves, buildup of plaque in the arteries, faulty heart rhythms and fluid buildup around the heart. Chemotherapy drugs including doxorubicin paclitaxel and others have been associated with an increased risk for heart failure and heart rhythm disorders, Okwuosa said. Even targeted therapies such as trastuzumab, now standard of care in certain types of breast cancers, can increase the risk of heart failure, while other newer therapies can cause significant hypertension, she said.

"Some of the chemotherapies can cause heart problems because the heart has very limited ability to regenerate, unlike hair can regenerate, for example, so the risk of cardiovascular issues can persist for many years," Okwuosa said. "Exercise provides a level of conditioning within our bodies which, even when we're under cardiovascular stress (such as with cancer treatments) at some later point, helps us tolerate that stress better. Exercise performed throughout one's life or even close to the time of cancer diagnosis seems to help the patient down the line with respect to the cardiovascular problems and side effects of the cancer therapy."

The study is limited by its reliance on self-reported exercise behavior rather than more objective measures. In addition, although the results suggested that women who exercised more had a lower risk of having a heart attack or being diagnosed with heart failure, those results were not statistically significant, most likely because those outcomes did not occur in large enough numbers, Okwuosasaid.

ACC2017特集

うつ病はMIまたは狭心症後の死亡リスクを倍増させる (Abstract 17-A-11375)

うつ病は冠動脈疾患の診断後数年間の最大の死亡予測因子である

Depression is strongest predictor of death for years following a diagnosis of coronary heart disease

うつ病は冠動脈疾患の診断後10年間の最大の死亡予測因子である、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。このスタディの結果、うつ病と診断された冠動脈疾患患者はうつ病と診断されていない者に比べ、死亡する確率が約2倍であった。これらの結果は年齢、性別、うつ病発症のタイミング、うつ病歴または心筋梗塞既往歴の有無とは関係なく、一貫して認められた。この影響は数年間持続することから、メンタルヘルスのスクリーニングおよび治療が必要であることが強調される。

Full Text

Depression is the strongest predictor of death in the first decade following a diagnosis of coronary heart disease, according to a study presented at the American College of Cardiology's 66th Annual Scientific Session. The study found people with coronary heart disease who are diagnosed with depression are about twice as likely to die compared with those who are not diagnosed with depression.

"This study shows that it doesn't matter if depression emerges in the short term or a few years down the road — it's a risk factor that continually needs to be assessed," said Heidi May, PhD, a cardiovascular epidemiologist at the Intermountain Medical Center Heart Institute in Salt Lake City and the study's lead author. "I think the take-home message is that patients with coronary disease need to be continuously screened for depression, and if found to be depressed, they need to receive adequate treatment and continued follow-up."

Researchers have long understood heart disease and depression to have a two-way relationship, with depression increasing the likelihood of heart disease and vice versa. Whereas previous studies have investigated depression occurring within a few months of a coronary heart disease diagnosis, the new study is the first to shed light on the effects of depression over the long term.

The researchers analyzed health records from almost 25,000 Intermountain Health System patients tracked for an average of nearly 10 years following a diagnosis of coronary heart disease. About 15 percent of patients received a follow-up diagnosis of depression, a substantially larger proportion than the estimated rate of 7.5 to 10 percent in the general population.

Out of 3,646 people with a follow-up diagnosis of depression, half died during the study period, compared to 38 percent of the 20,491 people who did not have a depression diagnosis. This means people with depression were twice as likely to die compared to those without depression.

After adjusting for age, gender, risk factors, other diseases, myocardial infarction (MI) or chest pain, medications and follow-up complications, the results showed depression was the strongest predictor of death in this patient group. These results were consistent regardless of age, gender, the timing of depression onset, history of depression or whether or not the patient had an MI.

Given the significant impact of depression on long-term survival, the researchers said clinicians should seek ways to better identify depression in patients with coronary heart disease, either by using patient questionnaires designed to screen for depression or by actively watching for signs of depression during follow-up examinations.

"It can be devastating to be diagnosed with coronary artery disease," May said. "Clinicians need to pay attention to the things their patients are expressing, in terms of both physical symptoms as well as emotional and nonverbal factors."

The study did not evaluate the impact of depression treatment on the risk of death.

ACC2017特集

MI直後にすべての閉塞動脈を治療することによる有益性 (Abstract 17-LB-16019)

COMPARE-ACUTE：スタディの結果、心筋梗塞の直後にすべての閉塞した動脈を治療することの有益性が示された

COMPARE-ACUTE: Study shows benefits to treating all blocked arteries at once after myocardial infarction

ST上昇型心筋梗塞（STEMI）後に評価し妥当であれば、すべての閉塞した動脈を治療することにより患者の予後が改善しその後の侵襲的施術の必要性を軽減でき得る、とAmerican College of Cardiology's 66th Annual Scientific Session で発表された。主治医がMI責任病変の狭窄のみを治療した患者に比べ、FFRガイド下評価を受けすべての動脈を治療された患者は、この臨床試験の一次エンドポイントである総死亡、非致死性MI、脳卒中およびその後12か月間の血行再建術から成る複合エンドポイントを発現する確率が、65％低かった。このCOMPARE-ACUTE試験の結果は、ACCにおける発表と同時に*New England Journal of Medicine* に掲載された。

Full Text

Patients experiencing an ST-elevated myocardial infarction (STEMI) often have more than one clogged artery, but under current guidelines doctors typically only clear the blockage responsible for the heart attack. Assessing and, when warranted, treating the additional blockages can improve patient outcomes and reduce the need for subsequent invasive procedures, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

The study's findings are in line with previous studies pointing to benefits of a more comprehensive treatment approach after a STEMI, but it is the first randomized clinical trial in which doctors have used the newer diagnostic tool fractional flow reserve (FFR) to precisely assess secondary blockages. Compared with patients in whom doctors treated only the blockage that caused the MI, patients who received FFR-guided evaluation and treatment of all arteries were 65 percent less likely to experience the trial's primary endpoint, a composite of all-cause mortality, non-fatal heart attack, stroke and subsequent revascularization at 12 months.

"Our study shows you can optimize treatment with this approach and potentially also have economic benefits by reducing the need for extra procedures," said Pieter Smits, MD, a cardiologist at Maasstad Ziekenhuis, Rotterdam, the Netherlands, and the study's lead author. "For the patient, it's a tremendous advantage to know that you have been treated for the artery that brought you to the hospital but also that any other issues have already been investigated and treated if needed. This way the patient won't need to be brought back to the hospital later on and again be put at risk with an invasive procedure or additional diagnostics."

Medical guidelines currently recommend performing PCI on the infarct-related artery after STEMI and leaving the other arteries alone, treating them later if subsequent tests or symptoms indicate they are substantially blocked by atherosclerotic lesions. Smits and his colleagues sought to investigate whether FFR could offer an opportunity to improve outcomes by refining doctors' ability to identify problematic lesions immediately after successful initial PCI. Because it is based on precise measures of blood pressure near lesions, FFR provides a much more accurate assessment of blockages than was previously possible with angiogram alone.

The researchers enrolled 885 STEMI patients at 24 sites in 12 countries in Europe and Asia. Immediately after the infarct-related artery was cleared using PCI, stable patients were randomly assigned to receive FFR-guided assessment of other arteries but no additional PCI (infarct-only revascularization, performed in 590 patients) or FFR-guided assessment and, when indicated by an FFR score of 0.80 or lower, PCI to clear additional lesions (complete revascularization, performed in 295 patients).

The primary composite endpoint occurred in 20.5 percent of patients receiving infarct-only revascularization and 7.8 percent of patients receiving FFR-guided complete revascularization, a difference that was statistically significant. When the components of the composite primary endpoint were analyzed separately, there was no significant difference in the rates of all-cause mortality, non-fatal heart attack or stroke; however, there was a significant reduction in the incidence of subsequent revascularization procedures among patients randomized to receive complete revascularization. All non- urgent revascularization procedures performed within the first 45 days after the initial PCI based on symptoms or stress tests were excluded from this analysis to avoid biasing the results in favor of complete revascularization.

When assessing the lesions other than the one responsible for the STEMI, the researchers found that only about half of these lesions were constricted enough to require treatment. Together, these results suggest that treating non-infarct related lesions is beneficial and that FFR can help clinicians to precisely identify those lesions in need of treatment.

"The results show that using FFR in the acute phase of STEMI, which was never done before, is feasible and safe," Smits said. "Furthermore, FFR-guided complete revascularization allows you to fine-tune the treatment and get better outcome results."

One downside of performing complete revascularization after initial PCI is that doing so increases the complexity of the procedure. However, the results showed that procedures in the complete revascularization arm were on average just six minutes longer than the procedures in the infarct-only revascularization arm, a difference Smits said is relatively minor and likely outweighed by the increased need for subsequent revascularization among those receiving infarct-only revascularization in the initial procedure.

One limitation is that the study struggled with slow enrollment, in part because some participating centers were only able to enroll patients during certain hours of the day or week and because the trial excluded patients who were in shock or unstable, a relatively frequent occurrence with STEMI. The study enrolled patients from 2011 through 2015.

Another limitation is that the study was not large enough to reveal statistically significant differences in all-cause mortality or subsequent heart attacks. A larger study, currently underway, is expected to shed light on these outcomes. In addition, Smits and his colleagues plan to conduct a further analysis of the cost implications of performing infarct-only revascularization versus complete revascularization after STEMI.

The trial, called COMPARE-ACUTE, was funded by two unrestricted grants from Abbott Vascular and St. Jude Medical.

This study was simultaneously published online in the *New England Journal of Medicine* at the time of presentation.

ACC2017特集

リバーロキサバンはアスピリンに比べVTE再発を軽減する (Abstract 17-LB-16118)

経口薬リバーロキサバンはアスピリンに比べ静脈血栓塞栓症の再発リスクを3倍以上軽減する

Oral rivaroxaban reduces risk of recurrent venous thromboembolism more than three-fold compared to aspirin

静脈血栓塞栓症（VTE）リスクの高い患者において、低用量経口リバーロキサバンはアスピリンに比べ、静脈血栓塞栓症の再発を3倍以上軽減し、有意な出血性副作用増加は認めなかった、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。追跡期間中央値351日後、VTE再発を来したのはリバーロキサバン10 mg服用患者では1.2%、20 mg服用患者では1.5%であったのに対し、アスピリン服用患者では4.4%であった。この差は、両リバーロキサバン群でアスピリン群に比べ、統計学的に有意であった。

Full Text

In patients at elevated risk for a recurrence of potentially life- threatening blood clots, a low dose of the oral blood-thinning medication rivaroxaban reduced recurrences more than three-fold compared with aspirin, with no significant increase in bleeding side effects, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

"We have shown that practitioners can safely prescribe rivaroxaban for patients at risk for a recurrent venous thromboembolism (VTE) without being concerned that doing so will increase risk for bleeding side effects," said Philip S. Wells, MD, chief of the department of medicine at the University of Ottawa and Ottawa Hospital in Canada and a co-investigator on the study.

Patients who have had a VTE generally are treated with a blood-thinning medication, or anticoagulant, for six to 12 months after the event. However, some patients remain at elevated risk for another blood clot, as well as for a heart attack or stroke, if anticoagulant therapy is stopped, Wells said. The most common risk factors for VTE are cancer and immobility due to surgery or illness, he said. In addition, some patients develop what are known as "unprovoked" VTEs — that is, VTEs that occur in the absence of known risk factors.

Previous studies have suggested that extended treatment with an anticoagulant such as warfarin or rivaroxaban reduced risk for a recurrent VTE, while other studies have shown that aspirin also reduced risk for a recurrent VTE and might present a lower risk for bleeding side effects than extended treatment with an anticoagulant. This study was the first to directly compare the safety and effectiveness of rivaroxaban and aspirin in patients at risk for a recurrent VTE, Wells said.

The international multicenter study enrolled 3,396 patients who had completed six to 12 months of anticoagulant therapy for a VTE. Patients' average age was 59, and 55 percent were men. Patients were 77 percent Caucasian, 14 percent Asian and 4 percent African-American. Patients were randomly assigned to receive 10 mg of rivaroxaban, 20 mg of rivaroxaban or 100 mg of aspirin once daily for up to 12 months.

The study's primary efficacy endpoint was recurrence of VTE. Secondary efficacy endpoints were deaths due to VTE and unexplained deaths for which VTE could not be excluded as a cause. The primary safety endpoint was major bleeding. The secondary safety endpoint was non-major bleeding that caused an interruption in treatment, a minor medical intervention, physician visit or disruption to daily quality of life.

After a median follow-up of 351 days, 1.2 percent of patients receiving 10 mg of rivaroxaban and 1.5 percent of those receiving 20 mg of rivaroxaban had had a recurrence of VTE, compared with 4.4 percent of patients receiving aspirin. The difference was statistically significant for both rivaroxaban groups compared with aspirin. There were no statistically significant differences on the secondary efficacy endpoints.

Major bleeding occurred in 0.3 percent of patients receiving aspirin, 0.4 percent of those receiving 10 mg of rivaroxaban, and 0.5 percent of those receiving 20 mg of rivaroxaban — differences that were not statistically significant. There were no statistically significant differences on the secondary safety endpoint.

"Rivaroxaban had significantly greater efficacy in preventing VTE recurrence without significantly increasing risk for major bleeding," Wells said. "Our findings show that it's [a safe option] and appears to be highly protective against potentially life-threatening recurrent VTE."

A limitation of the study is that the results may not be generalizable to other patients at risk for recurrent VTE, Wells said. For example, study participants were younger than the typical patient with a VTE. The investigators plan to conduct a follow-up study to examine whether low-dose rivaroxaban is equally effective in other patient populations, he said.

The study was funded by the German pharmaceutical company Bayer AG.

The study was simultaneously published online in the *New England Journal of Medicine* at the time of presentation.

ACC2017特集

CTスキャンは大動脈弁置換術後の弁尖の動きの低下を可視化する(Abstract 17-LB-16234)

抗血小板薬ではなく経口抗凝固薬は無症候性の弁尖血栓症を減少させる

Oral anticoagulants, but not anti-platelet therapy associated with reduced subclinical leaflet thrombosis

大動脈弁置換術を施行された患者の約12%が、弁の動きの低下する無症候性の弁尖血栓症を発症したとの観察研究が、American College of Cardiology's 66th Annual Scientific Session で発表され、同時に*Lancet* に掲載された。CTスキャンの解析の結果、経カテーテル大動脈弁置換術（TAVR）施行患者の13.6%および外科的大動脈弁置換術（SAVR）施行患者の3.8%において、無症候性弁尖血栓が認められ、全体では12.1%に認められた。血栓はTAVR患者においてSAVR患者よりも有意に高率に認められたが、この差はSAVR施行患者の方が若年であり全体的な健康状態が良好であることによると考えられる。

Full Text

About 12 percent of patients undergoing aortic valve replacement developed non-symptomatic subclinical leaflet thrombosis that reduced the motion of the valves, according to an observational study presented at the American College of Cardiology's 66th Annual Scientific Session.

The study is the largest to date investigating thrombosis as a potential cause of reduced valve motion after aortic valve replacement. It confirms a previous, smaller study that suggested blood clots that are detectable with computed tomography (CT) scans but not with more commonly-used echocardiogram scans can develop around the valve and constrain the valve's motion. In the new study, the CT-detected valve-associated clots were found to increase the risk of transient ischemic attacks, also called "mini-strokes," but were not associated with an increased risk of death, heart attack or stroke. Anticoagulant therapy, but not anti-platelet therapy, was associated with a significantly lower risk of developing valve-associated clots.

"This phenomenon of subclinical leaflet thrombosis can be missed if you just use transthoracic echocardiogram," said Raj Makkar, MD, associate director of Cedars-Sinai Heart Institute in Los Angeles, and the study's lead author. "Based on our study, CT is clearly a more sensitive and appropriate technique to actually make a diagnosis of subclinical leaflet thrombosis. This suggests clinicians might want to have a lower threshold to do a CT scan if there is suspicion of reduced motion in the valve, such as from slightly elevated mean gradients on echocardiogram."

CT scans expose patients to more radiation than echocardiogram alone.

The researchers analyzed CT scans and other health records from 850 patients enrolled in two single- center medical registries, known as RESOLVE (which includes patients treated at Cedars-Sinai Heart Institute) and SAVORY (which includes patients treated at Rigshospitalet hospital in Copenhagen, Denmark). The patients had undergone CT scans an average of three months after transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR), two procedures used to replace a patient's faulty aortic valve with an artificial valve. In TAVR, clinicians thread the new valve to the heart through a catheter in the groin or chest; this procedure is generally used for patients at intermediate to high cardiovascular risk, which typically includes older patients and those who have multiple health problems. SAVR is an open-heart procedure used in lower-risk patients.

A total of 720 patients in the two registries had undergone TAVR and 130 had undergone SAVR. Analysis of CT scans revealed subclinical leaflet thrombosis in 13.6 percent of TAVR patients and 3.8 percent of SAVR patients, for an overall rate of 12.1 percent among all patients combined. Although thrombosis was observed in a significantly greater proportion of TAVR patients than SAVR patients, this difference may be attributable to the younger average age and better overall health of patients undergoing SAVR, Makkar said.

The results also showed that subclinical leaflet thrombosis was significantly more common in patients on antiplatelet therapy (typically aspirin plus a P2Y12 inhibitor) compared to those taking anticoagulants. A total of 14.8 percent of patients on antiplatelet therapy had thromboses compared to 4 percent among patients taking warfarin and 3 percent among patients taking non-vitamin K antagonist anticoagulants, or NOACs. There was no significant difference in risk observed among those taking warfarin versus NOACs.

"We need to further study whether routine anticoagulation may be useful for this patient population," Makkar said. "Dual antiplatelet therapy was not effective in preventing and treating subclinical leaflet thrombosis, and it does have a small risk of bleeding, particularly in older patients. There is an impetus to study the risks and benefits of dual antiplatelet therapy further in randomized clinical trials."

An analysis of a small group of patients (58) who underwent a second CT scan showed subclinical leaflet thrombosis resolved over time in the vast majority of patients who were started on oral anticoagulant therapy after the first CT scan and that thromboses resolved in only a small portion of patients who were not started on anticoagulants.

The study also showed that subclinical leaflet thromboses detected with CT scans were reflected in significantly higher mean gradients, a measure used to assess functioning of the aortic valve using echocardiogram. However, Makkar said this difference was not large enough to enable clinicians to diagnose subclinical leaflet thrombosis using echocardiogram alone.

As an observational study, the results do not directly assess cause and effect. Makkar said ongoing randomized clinical trials that include CT scans as part of the protocol should help to further elucidate the factors that contribute to subclinical leaflet thrombosis after aortic valve replacement.

"Our study findings can help optimize the use of different blood thinning medications in patients undergoing aortic valve replacement, which might potentially result in further improvements in valve hemodynamics and clinical outcomes," Makkar said.

This study was simultaneously published online in The *Lancet* at the time of presentation.

ACC2017特集

BococizumabによるPCSK9阻害による結果は様々である (Abstract 17-LB-15353)

PCSK9阻害はベースラインのLDLコレステロール値の高い高リスク患者において心血管系転帰を改善する

PCSK9 inhibition improves cardiovascular outcomes in high risk patients with higher LDL-cholesterol at baseline

早期に終了された臨床試験プログラムにおいて、治験薬PCSK9 阻害薬bococizumabを有効なスタチン療法に加え投与した場合、LDLコレステロール値に対する効果は様々であり、LDLコレステロール値が100 mg/dL未満の患者では心血管イベントに対する有益性はなかった。しかし、ベースラインのLDLコレステロール値が100 mg/dLを超える心血管系リスクの高い患者において、bococizumabはプラセボに比べ心血管系イベントリスクを有意に21%減少させた、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表され、同時に*New England Journal of Medicine* に掲載された。

Full Text

In a clinical program that was terminated early, the experimental PCSK9 inhibitor bococizumab, when given on top of effective statin therapy, had widely varying effects on LDL cholesterol levels and had no benefit on cardiovascular events among those with LDL lower than 100 mg/dL. However, in patients at high cardiovascular risk who had baseline LDL of greater than 100 mg/dL, bococizumab significantly reduced the risk of cardiovascular events by 21 percent compared with placebo, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

Pfizer, the trials' sponsor, announced on Nov. 1, 2016, that the company would discontinue development of bococizumab, citing an unanticipated attenuation of LDL lowering over time, as well as evidence of an immune response in some patients. At that point, all ongoing trials were terminated. The final results of the terminated trials suggest the drug is safe but show mixed results on efficacy.

"These results support the general idea that further reduction in LDL, beyond what you can achieve with a statin, further lowers cardiovascular event rates," said Paul M. Ridker, MD, a cardiologist at Brigham and Women's Hospital, and the study's lead author. "The findings add to what we know about PCSK9 inhibitors, and it is encouraging that we found a statistically significant reduction in events among the highest-risk patients who had the highest LDL levels."

Bococizumab, which will not be available for clinical use, is part of a new class of drugs known as PCSK9 inhibitors. By binding to and inhibiting PCSK9, these drugs prolong the lifespan of LDL receptors in the liver, thus allowing the liver to remove LDL cholesterol from the blood more effectively. LDL, or "bad," cholesterol is the main source of plaque buildup in the arteries.

The research included eight parallel bococizumab trials. Six trials, which together enrolled 4,449 patients, focused on bococizumab's effects on LDL levels over the course of up to one year in patients with various baseline risk factors for high cholesterol and heart disease. The two largest trials, which together enrolled 27,438 patients, focused on cardiovascular outcomes.

The trials enrolled patients with a range of risk factors for heart disease; participants had known cardiovascular disease or had a combination of diabetes, chronic kidney disease or peripheral vascular disease with additional cardiovascular risk factors. The vast majority of participants also took high-dose statin therapy to lower LDL cholesterol. Patients were randomly assigned to receive either bococizumab 150 mg as a subcutaneous injection or a matching placebo injection every two weeks.

In the six trials focused on LDL levels, bococizumab significantly reduced LDL cholesterol by an average of 55 percent at week 12. However, this effect attenuated over time in about 10 to 15 percent of patients.

Furthermore, even among patients in whom LDL reduction was sustained, the trials showed wide variation in the level of LDL reduction achieved, with some patients showing only a 15 percent reduction and others showing an 80 percent reduction.

Ridker said the attenuation of LDL reduction over time was likely due to the development of anti-drug antibodies, which could lower the amount of bococizumab in the bloodstream and, in some patients, markedly reduce its effects on LDL cholesterol. Bococizumab is a monoclonal antibody, which is a type of biologic drug produced by engineered immune cells. Like other existing drugs but unlike some other PCSK9 inhibitors being developed, bococizumab is a humanized monoclonal antibody, meaning that a fraction (in this case about 3 percent) of its biological components is non-human. These components might have triggered the development of antidrug antibodies in a subset of patients, Ridker said.

The two largest studies focused on cardiovascular outcomes. The first, called SPIRE-1, enrolled 16,817 people with LDL cholesterol greater than or equal to 70 mg/dL. The second, called SPIRE-2, enrolled 10,621 people with LDL cholesterol greater than or equal to 100 mg/dL, a level indicating higher cardiovascular risk. Patients in SPIRE-1 and SPIRE-2 were followed for an average of seven and 12 months, respectively, before the trials were terminated.

The primary endpoint for both SPIRE-1 and SPIRE-2 was a composite of nonfatal heart attack, nonfatal stroke, hospitalization for unstable angina requiring urgent revascularization, or cardiovascular death. SPIRE-1 showed no difference in this endpoint between patients receiving bococizumab and patients receiving placebo. In SPIRE-2, the primary endpoint occurred in 224 patients randomized to receive placebo and 179 patients randomized to receive bococizumab, which translated to a statistically significant 21 percent reduction in risk among those taking bococizumab over an average follow-up of 12 months.

Analyses of the combined results for SPIRE-1 and SPIRE-2 revealed that a larger reduction in LDL cholesterol and a longer duration of treatment were both associated with significantly better outcomes. Patients with higher-than-average reduction in LDL levels were 25 percent less likely to experience the primary endpoint than those with lower-than-average LDL reduction. Patients treated with bococizumab for longer periods of time showed a significantly lower risk of the primary endpoint compared with those treated for shorter periods.

Safety outcomes were not significantly different for bococizumab versus placebo with the exception of injection site reactions, which occurred significantly more frequently in patients receiving bococizumab. This finding further bolsters evidence that the drug may have triggered an immune response in some patients.

"In addition to supporting the general hypothesis that PCSK9 inhibitors can lower cardiovascular event rates, differences in this medication class between fully human and humanized therapeutic monoclonal antibodies may be important to consider," Ridker said. "We believe genetic analyses could be very helpful to determine who does and does not develop antidrug antibodies to bococizumab."

The results are limited by the fact that follow-up for SPIRE-1 and SPIRE-2 was terminated early. The study was funded by Pfizer.

The SPIRE Lipid Lowering trials and the SPIRE 1 and SPIRE 2 Cardiovascular Outcomes trials were simultaneously published online in the *New England Journal of Medicine* at the time of presentation.

ACC2017特集

TAVRは微小出血および神経学的障害と関連がある (Abstract 17-LB-16053)

TAVRは高齢者において微小出血のリスクを増加させ神経学的障害と関連する

TAVR increases risk of microbleeds and related neurological impairment in older patients

経カテーテル大動脈弁置換術（TAVR）を施行された高齢患者84人中4分の1近くが、施行後に新たな微小出血を来したとの単施設研究の結果が、American College of Cardiology's 66th Annual Scientific Sessionで発表された。TAVR前に施行されたMRI画像検査において、26%の患者に少なくとも1個の微小出血が認められた。施行3日後に、計40%の患者に微小出血が認められ、23%はTAVR施行前には存在しなかった新たな微小出血であった。TAVRの前後ともに観察された微小出血は、質問票ベースの神経認知機能評価における思考や記憶の障害と関連があった。

Full Text

Small brain microbleeds increase with age and are associated with cognitive decline. Of 84 older patients undergoing transcatheter aortic valve replacement (TAVR), nearly a quarter developed new microbleeds after their procedure, according to results of a single-center study presented at the American College of Cardiology's 66th Annual Scientific Session.

Microbleeds can be observed using MRI scans of the brain and are detrimental to thinking and memory. Previous studies of MRI scans in patients age 80 and older have shown evidence of microbleeds in up to 30 percent of elderly patients. This study revealed increased risks of microbleeding among patients who had undergone a previous cardiovascular intervention and among those with more prolonged exposure to anticoagulant medications, which are used to prevent blood clots that cause strokes and mini-strokes in patients undergoing cardiac procedures. It is the first study to link microbleeding with TAVR and the first to investigate microbleeding as a side effect of any cardiac procedure.

"We are all aware of the potential for silent ischemic strokes after these endovascular procedures, but our study points to the opposite risk—microbleeding—that we have not previously been aware of," said Eric Van Belle, MD, PhD, a cardiologist at the Centre Hospitalier Regional in Lille, France and the study's lead author. "With more and more endovascular procedures, which require anticoagulants, it could be that these procedures are one of the main triggers of microbleeding seen in the older population. It raises the concern that we may be increasing the risk of this microbleeding with each intervention we perform."

To shed light on microbleeds and their possible connection to endovascular procedures such as TAVR or anticoagulant use associated with these procedures, researchers performed MRI scans and questionnaire- based neurological tests in 84 patients before and after the patients underwent TAVR at Centre Hospitalier Regional in Lille, France. Patients underwent MRI scans one day before TAVR and three days after TAVR. Questionnaire-based neurological tests were conducted prior to TAVR, followed by three days after and six months after the procedure.

Before TAVR, MRI scans revealed at least one microbleed in 26 percent of patients. At three days after the procedure, a total of 40 percent of patients had microbleeds and 23 percent had new microbleeds that were not present before TAVR.

Microbleeds observed both before and after TAVR were associated with deficiencies in thinking and memory in the questionnaire-based neurocognitive assessments. Factors that were associated with a significantly higher risk of microbleeds included having a previous cardiovascular intervention, prolonged exposure to anticoagulation, history of bleeding, longer exposure to fluoroscopy during TAVR, and balloon post-dilation, a procedure sometimes used in conjunction with TAVR to reduce leakage of blood across the new valve.

Van Belle said the results strongly suggest that further research is needed to elucidate the causes of microbleeds and determine whether changes in anticoagulation management can help to reduce the risk. He said that the results suggest systematic MRI investigation should be conducted in studies investigating new anticoagulation regimen for patients undergoing TAVR. Currently, he said, MRI scans of the brain are rarely used to assess safety outcomes in cardiovascular studies, in part because MRI cannot be used in patients with a pacemaker or other types of implanted devices.

"It is difficult to do this kind of MRI study in this older population, but based on our results I would say that it is worth it to do so when investigating a new treatment or treatment modification," Van Belle said. "Both mini-strokes and microbleeds likely play a role in cognitive decline. It is possible that using too much anticoagulation therapy could be as bad as using too little."

The study was limited primarily by its small size. In addition, it was not able to definitively show whether new microbleeds observed after TAVR were actually caused by TAVR, the use of anticoagulants or other factors. Further research could be conducted to include a larger study population, involve younger patients or potentially investigate microbleeding after surgical aortic valve replacement or other cardiac procedures, Van Belle said.

ACC2017特集

スタチン服用患者においてエボロクマブは認知機能に影響しない(Abstract 17-LB-16161)

EBBINGHAUS：エボロクマブをスタチン療法に追加することの認知面に関するエビデンスはない

EBBINGHAUS: No evidence of cognitive issues when evolocumab is added to statin therapy

新たなコレステロール低下薬をスタチン治療に追加することにより、記憶力低下や他の認知面や思考に関する新たな問題が引き起こされるとのエビデンスはないと、この問題に取り組む過去最大の最も厳密にデザインされたEBBINGHAUSスタディの結果が示された。研究者らは、エボロクマブ服用患者とプラセボ服用患者とで、患者に対する質問票または医師の報告による認知面での副作用における4つの認知機能検査値のいずれに関しても、重要な差がなかったことを明らかにした。この研究結果は、American College of Cardiology's 66th Annual Scientific Session で発表された。

Full Text

There is no evidence that adding a new cholesterol-lowering drug to treatment with a statin causes memory loss or other problems with cognition or thinking, according to findings from the EBBINGHAUS study, the largest, most rigorously designed study to address this issue to date. The research was presented at the American College of Cardiology's 66th Annual Scientific Session.

Some previous studies had suggested a possible link between high doses of statins and memory difficulties in some patients. In 2012, the U.S. Food and Drug Administration added a safety alert to the labeling for statins, noting that some patients had experienced memory loss and confusion. In 2014, however, a medical expert panel concluded that the evidence that statins cause cognitive side effects was weak to nonexistent.

The question resurfaced in 2015 in two studies with new non-statin drugs known as proprotein convertase subtilisin-kexin 9 (PCSK9) inhibitors, which help the body clear LDL cholesterol from the blood by blocking the protein PCSK9. The two studies reported cognitive side effects that were infrequent (occurring in fewer than 1 percent of patients) but occurred more frequently in patients taking a PCSK9 inhibitor (evolocumab or alirocumab) than in patients who received a placebo. Cholesterol is important for normal memory and brain functioning, but the brain should be able to make all the cholesterol it needs. Nonetheless, there was some concern that the use of medications to reduce LDL-cholesterol in the blood to extremely low levels could deprive the brain of needed cholesterol.

"Ours is the first prospectively designed study to evaluate the relationship between a PCSK9 inhibitor and changes in cognition, including memory, attention and reaction time" said Robert P. Giugliano, MD, SM, a senior investigator in the TIMI Study Group, an associate professor at Harvard Medical School, staff physician at Brigham and Women's Hospital in Boston, and lead author of the study. "Our findings are reassuring in that we found no apparent effect on any of these cognitive domains despite achieving very low blood levels of LDL cholesterol."

The study, known as EBBINGHAUS, enrolled 1,974 patients who were taking part in FOURIER, a large double-blind randomized trial conducted in 30 countries to test the effectiveness of adding evolocumab or a placebo to statin therapy to reduce LDL cholesterol in high-risk patients with heart or blood-vessel disease. The patients in EBBINGHAUS were 63 years old on average; 75 percent had had a heart attack, 20 percent had had an ischemic stroke, and 19 percent had peripheral arterial disease. All were receiving moderate- or high-intensity statin therapy. Patients were excluded from EBBINGHAUS if they had a diagnosis of dementia, cognitive impairment or another significant mental or neurological disorder.

Patients completed a set of validated neurocognitive tests, the Cambridge Neuropsychological Test Automated Battery, when they enrolled in the study, and after 24, 48 and 96 weeks, and at the end of the study. The median follow-up time was about 19 months. The tests, performed on a tablet computer, assessed executive function (ability to pay attention, manage time, plan, organize and remember details) as well as working memory, memory function and reaction time. The primary endpoint was a measure of executive function known as the Spatial Working Memory strategy index. Patients also completed a questionnaire assessing their everyday cognition before, during and at the end of the study.

"We found no important differences between patients taking evolocumab and those on placebo on any of the four measures of cognitive functioning, in the patient questionnaires, or in the physician-report of adverse cognitive events," Giugliano said. "We also looked at patients according to how low their levels of LDL cholesterol went. Patients who reached very low LDL values – less than 25 mg/dL – had cognitive function that was similar to those with higher LDL values."

He added that these findings should "enable physicians to feel more secure about adding evolocumab to a statin to achieve very low levels of LDL cholesterol without worrying that patients' memory or cognitive functioning will be affected."

A limitation of the study is that patients were followed for less than two years on average, Giugliano said. However, long-term follow-up in a subset of the EBBINGHAUS patients is ongoing. A further limitation, he said, is the possibility that patients were experiencing cognitive problems that were not picked up by the tests used in the study. However, he explained the tests have been validated in more than 160 clinical trials over the past 30 years, in both cognitively normal subjects and people with disorders such as schizophrenia and Alzheimer's disease, and are sensitive to both the positive and negative effects that drugs may have on cognition.

The study was funded by Amgen, which manufactures evolocumab.

ACC2017特集

左心耳閉鎖術は脳卒中リスクを低下させる (Abstract 17-LB-16216)

外科的LAA閉鎖術は心房細動患者の血栓塞栓症を減少させる

Surgical LAA occlusion reduces thromboembolism among patients with atrial fibrillation

心房細動患者に対する心臓手術中の追加施術としての左心耳（LAA）閉鎖術は、血栓塞栓症リスクを40%低下させたとの観察研究の結果が、American College of Cardiology's 66th Annual Scientific Sessionで発表された。外科的LAA閉鎖術施行患者のうち、12か月以内に血栓塞栓症により入院したのは1.6%、LAA閉鎖術非施行患者においては2.5%であり（p=0.0016）、リスクは40%軽減された。LAA閉鎖術は死亡を15%減少させ、血栓塞栓症、出血性脳卒中および死亡のリスクを21%減少させた。

Full Text

For patients with atrial fibrillation (AFib), closing the left atrial appendage (LAA) as an add-on procedure during cardiac surgery was associated with a 40 percent reduction in the risk of thromboembolism according to an observational study presented at the American College of Cardiology's 66th Annual Scientific Session.

Reducing stroke risk is paramount in patients with AFib, who are five times more likely to experience a stroke compared to the general population. The study, which is the largest to assess the effects of closing the left atrial appendage, suggests the approach may be a good option, particularly for people with AFib who are at high risk for stroke but cannot take or tolerate anticoagulant medications, according to researchers.

"There's currently a wide variation in the use of this procedure at the time of cardiac surgery, largely due to the fact that there's not good data on the safety or the efficacy of the procedure," said Daniel J. Friedman, MD, a cardiology fellow at Duke Clinical Research Institute in Durham, North Carolina, and the study's lead author. "While our study was not a randomized trial, it does demonstrate strong support for the benefits of closing the left atrial appendage at the time of cardiac surgery in patients with atrial fibrillation."

Research suggests that about 50 percent of patients with AFib who are eligible for anticoagulation therapy actually take anticoagulants.

About 90 percent of strokes in people with AFib result from clots that form in the left atrial appendage. Some cardiac surgeons attempt to reduce the risk of stroke with surgical LAA occlusion, either by placing a small clip over it or by amputating it and then sewing the atrial wall closed. Because its benefits have been largely unknown and open-heart surgery carries significant risks, surgical LAA occlusion is typically performed as an add-on procedure in patients who are undergoing other types of cardiac surgery, such as bypass grafting or valve replacement surgery. The left atrial appendage can also be closed using a procedure performed through a catheter, rather than through open-heart surgery, but this trial investigated only surgical occlusion.

To assess the safety and efficacy of closing the left atrial appendage, the researchers analyzed the health records of 10,524 patients in The Society of Thoracic Surgeons Adult Cardiac Surgery Database, a nationally-representative data set that includes 90 percent of cardiac surgery centers in the United States. They extracted data for Medicare patients with AFib who underwent coronary artery bypass grafting, aortic valve surgery or mitral valve surgery in 2011 or 2012.
About 37 percent of the patients had their left atrial appendage closed during their surgery. Of these, 1.6 percent were hospitalized for thromboembolism within 12 months (the study's primary endpoint), significantly fewer than the 2.5 percent of patients experiencing thromboembolism who did not have their left atrial appendage closed. This translates to a 40 percent reduction in risk over 12 months, Friedman said, noting that this reduction would likely grow more impactful as it accumulates over time.

In addition, closing the left atrial appendage was associated with a 15 percent reduction in the rate of death and a 21 percent reduction in a composite of thromboembolism, hemorrhagic stroke and death. There was no significant difference in the rate of hemorrhagic stroke, a type of stroke caused when a blood vessel in the brain ruptures.

Friedman said the results suggest closing the left atrial appendage is safe and effective for AFib patients undergoing cardiac surgery.

"Intuitively, surgical left atrial appendage occlusion should work; however, there have been concerns that incomplete occlusion actually could lead to increased risk for thromboembolism because it could result in small communications between the appendage and the left atrium," Friedman said. "The fact that we saw such a dramatic association between the procedure and a reduction in thromboembolism was reassuring that, at least in a more contemporary cohort of patients, left atrial appendage occlusion is able to be done in a much more effective way than initial reports had suggested may be the case."

Further analysis revealed the greatest reduction in thromboembolism after left atrial appendage occlusion among patients who were not taking anticoagulant medications at discharge. There was no difference in thromboembolism rates for those who were taking anticoagulants at discharge. Whether left atrial appendage occlusion is effective enough to allow patients to safely stop taking anticoagulants is one potential area for future investigation, Friedman said.

The study is limited by the fact that it is an observational analysis. A prospective, randomized controlled trial would provide more robust evidence to support clinical decision making. The study also was not able to compare different techniques used to close the left atrial appendage, another aspect that could be investigated in future studies, Friedman said.

The study was funded by grants from the Burroughs Wellcome Fund and the U.S. Food and Drug Administration. Friedman receives funding from the National Institutes of Health T 32 training grant HL069749.

ACC2017特集

ペースメーカープログラムは意識消失発作を減少させる (Abstract 17-LB-15773)

SPAIN：再発性の意識消失発作はクローズドループ刺激と呼ばれるペーシングプログラムにより減少する

SPAIN: Recurrent syncope reduced with pacing program called Closed Loop Stimulation

再発性の意識消失発作患者で、意識消失発作に先立つ異常心調律を検出および停止させるようにデザインされたペーシングプログラムを実行するペースメーカーを挿入された患者は、失神が7倍減少したとAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。最初にクローズドループ刺激（DDD-CLS）ペーシングに組み入れられた患者のうち、72.2%において1年間の意識消失発作が50%減少したが、彼らがプラセボ群にクロスオーバーした後に意識消失発作が再発した。初回意識消失発作までの推定時間は、DDD-CLSを植え込まれた患者において長かった（29か月対プラセボ群9.3か月、p=0.0158）。

Full Text

Patients with recurrent syncope who received a pacemaker delivering a pacing program designed to detect and stop the abnormal heart rhythms that precede syncope had a seven-fold reduction in fainting compared with patients in a placebo pacing group, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

The study—the first prospective double-blind placebo-controlled trial to show robustly positive results for the pacing program, known as Closed Loop Stimulation (DDD-CLS), in patients with recurrent syncope—met its primary endpoint of a significant reduction in fainting episodes with DDD-CLS compared to placebo pacing.

"Our study showed up to a seven-fold reduction in recurrences of syncope" in patients who used the DDD-CLS program, said Gonzalo Baron-Esquivias, MD, PhD, FESC, associate professor, chief of the clinical cardiology section and head of studies in the cardiology department at Virgen del Rocio University Hospital in Seville, Spain, and the study's lead author.

This study is important, he said, because of the lack of available treatments for recurrent syncope. "Now a door is open and we have a new possible treatment for these patients," he said.

Syncope is triggered by a sudden drop in blood pressure and heart rate, which in turn reduces blood flow to the brain. While episodes of syncope are not fatal, they can be very dangerous due to loss of consciousness and can severely affect patients' quality of life. About half of all women and one-third of men will experience syncope in their lifetime. The real concern, Baron-Esquivias said, is that for many, these episodes will recur and they aren't predictable.

Pacemakers are widely used to treat other heart-rhythm disorders, particularly bradycardia. In DDD-CLS pacing for recurrent syncope, the pacemaker detects contractions or spasms in the heart muscle that typically occur before an episode of syncope and releases an electrical signal that calms the heart down, preventing sudden dips in heart rate and blood pressure. Earlier small trials of DDD-CLS had shown mixed results in preventing fainting episodes.

In the SPAIN trial, Baron-Esquivias and his colleagues recruited 54 patients aged 40 or older from 12 medical centers in Spain and Canada. All had experienced more than five episodes of syncope in their lifetimes, with more than two in the past year. To be eligible, participants had to have normal results on an electrocardiogram, echocardiogram, 24-hour Holter test, carotid sinus massage and orthostatic test. They also had to show a drop in blood pressure and heart rate on a test in which the head rapidly changes position.

All participants were implanted with a pacemaker. The researchers randomly assigned half to receive DDD-CLS pacing for 12 months and the other half to a pacing program called DDI, which does not respond to the contractions in the heart that precede syncope and, therefore, functioned in the SPAIN trial as a placebo program. After 12 months, the two programs were switched so that the patients who had received DDD-CLS during the first year received DDI for the next 12 months, and vice versa. If a patient in either group had more than three episodes of syncope in one month, their pacing assignment was switched. Patients and their doctors were blinded at all times to their group assignment.

Forty-six patients completed the trial, which lasted two years. The patients' average age was 56, and 48 percent of them were men. During the trial, four patients experienced syncope while receiving DDD-CLS pacing, compared with 21 patients who fainted during DDI pacing, a statistically significant difference.

Among patients initially assigned to DDD-CLS, 72.2 percent saw a reduction of more than 50 percent in syncope episodes within the first year, but fainting recurred after they crossed over to the DDI group. Patients who crossed over to DDD-CLS after a year of placebo pacing saw a reduction of more than 50 percent in syncope episodes during the second year. Nine patients who initially received DDI pacing met the criterion for early crossover to DDD-CLS during the first year. The estimated time to a first fainting episode was longer among patients receiving DDD-CLS—29 months compared with just over nine months for patients receiving DDI, a statistically significant difference.

Limitations of the study are its small size and short duration of follow-up (two years), Baron-Esquivias said.

Baron-Esquivias, who currently uses DDD-CLS pacing to treat patients with recurrent syncope in his own practice, said that if these findings are confirmed by larger, ongoing studies, such as the ongoing BioSync CLS trial sponsored by Biotronic, he expects that international guidelines will be changed to recommend DDD-CLS pacing in these patients.

The trial was funded by the Investigation Agency of the Spanish Society of Cardiology, which received an unrestricted grant from Biotronic Spain. Biotronic is the developer of the DDD-CLS program.

ACC2017特集

心房細動患者においてジゴキシンにより死亡リスクは上昇する(Abstract 17-LB-16129)

ARISTOTLE：ジゴキシンを服用している心房細動患者における死亡リスク上昇に関する新たな懸念

ARISTOTLE: New concerns about heighted risk of death for patients with atrial fibrillation taking digoxin

症状コントロール目的でジゴキシンを投与されている心房細動患者は、心不全の有無にかかわらず死亡リスクが高く、このリスクはジゴキシン血中濃度上昇に伴い上昇する、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。既にジゴキシンを投与されている患者において、全体的なジゴキシン使用と死亡との相関は有意ではなかった。しかし、このコホートであっても、死亡リスクはジゴキシン血中濃度と相関があった：ジゴキシン血中濃度が0.5 ng/mL上昇するごとに、死亡リスクは19%上昇した。

Full Text

Patients with atrial fibrillation (AFib) who are given digoxin to control their symptoms have an increased risk of death, whether or not they have a diagnosis of heart failure, compared with patients not taking the drug, and this risk increases with higher levels of digoxin in the bloodstream, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

An increased risk of death from any cause—the study's primary endpoint—was found in both patients with and without heart failure who started on digoxin. Researchers report the study is one of the largest and most comprehensive analyses of the risk of digoxin use in patients with AFib performed to date.

"Based on our study, digoxin should be avoided in patients with AFib, particularly if symptoms can be alleviated with other treatments," said Renato Lopes, MD, PhD, professor of medicine in the division of cardiology at Duke University Medical Center and lead author of the study. "We showed that starting digoxin was associated with increased risk of death and sudden death, regardless of the presence of heart failure. Thus, based on our findings, avoiding digoxin in patients with AFib—irrespective of the presence of heart failure—seems to be the right approach."

Around 30 percent of patients with AFib worldwide take digoxin, Lopes said. The drug is one of the oldest medications used in cardiology and is very inexpensive. However, its safety for patients with AFib has come under scrutiny, he said.

"A number of recent publications have questioned the safety of this drug, and different analyses looking at different questions have shown conflicting results. There are no randomized data assessing the efficacy and safety of digoxin in patients with AFib," Lopes said.

To get a more definitive answer about digoxin's safety, Lopes and his colleagues analyzed data collected in the ARISTOTLE trial, which compared apixaban with warfarin for the prevention of blood clots, strokes and death in patients with AFib. Of the 18,201 patients enrolled in ARISTOTLE, 17,897 had data available on heart failure status and digoxin use during the trial. Of those patients, 5,824 were on digoxin at the start of the trial; 4,434 of these participants had their blood levels of digoxin measured at baseline. A total of 6,693 patients had heart failure at the time of trial enrollment.

To try to compensate for patients not being randomly assigned to digoxin use, the researchers performed a propensity score analysis—a statistical technique that attempts to estimate the effect of a treatment by accounting for the factors, or covariates, that differ between treated and untreated patients. In this case, those factors included patients' demographic characteristics; medical history; measurements of organ function; other medications used, including antiarrhythmic agents; region of the world; clinical setting, where digoxin was initiated; heart failure status; and biomarkers in the blood that can help predict the risk of death. Each patient taking digoxin was compared with three matched control patients from ARISTOTLE who were not taking the drug.

The researchers found that in patients already receiving digoxin and, therefore more likely to tolerate it, the overall relationship between digoxin use and death was non-significant. However, even in this cohort, the risk of death was related to digoxin concentration in the blood: for every 0.5 ng/mL increase in the blood level of digoxin, the risk of death rose by 19 percent. Among patients whose digoxin levels were greater than 1.2 ng/mL, the death rate increased by a highly significant 56 percent.

The risk of death was even higher for patients who were not taking digoxin before the trial but were started on the drug over the course of ARISTOTLE. These patients had a 78 percent increase in the risk of death from any cause and a fourfold increased risk of sudden death after starting digoxin use.

"Most sudden deaths occurred within six months after digoxin was started," Lopes said.

This hints at cause and effect, he said, though the fact that patients were not randomized to digoxin prevents a definitive determination of causality.

The lack of randomization and the potential for unmeasured confounding factors are the main limitations of the study, he said. In addition, for patients who were on digoxin at study entry, researchers did not know how long they had taken the drug before entering the study. Despite these limitations, the study is one of the most comprehensive in the field to date, incorporating clinical variables, biomarker adjustments and blood digoxin levels, Lopes said.

"To definitively determine the efficacy and safety of digoxin in AFib patients would require a large and well-powered randomized trial," he said. "Until then, our finding that digoxin may be causing more harm than good in patients with AFib is important and may help guide physicians in their clinical decisions when managing these patients."

In the main ARISTOTLE trial, apixaban was found to be statistically significantly superior to warfarin for preventing blood clots, strokes, major bleeding events and death, whether or not patients were taking digoxin at the time of study entry. Therefore, Lopes said that for stroke prevention in AFib patients, apixaban is a better option than warfarin, irrespective of digoxin use.

The digoxin safety study was funded by the Bristol-Myers Squibb and Pfizer Alliance in conjunction with the Duke Clinical Research Institute.

ACC2017特集

新規抗凝固薬は心房細動に対するアブレーション中の大出血を軽減する(Abstract 17-LB-16165)

RE-CIRCUIT：非ビタミンK拮抗経口抗凝固薬の継続投与はアブレーション中のワルファリンの代替薬として優れている

RE-CIRCUIT: Uninterrupted non-vitamin K antagonist oral anticoagulant is good alternative to warfarin during ablation

心房細動治療目的のアブレーション周術期における非ビタミンK拮抗経口抗凝固薬ダビガトランの継続投与により、ワルファリンの継続投与に比べ大出血発現率が有意に低下した、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表され、同時に*New England Journal of Medicine* に掲載された。このRE-CIRCUITトライアルにおいて、一次エンドポイントであるアブレーション中または施術後2か月以内の大出血は、ダビガトラン投与患者で1.6%、ワルファリン投与患者では6.9%であり（相対リスク低下＝77.2%）、5.3%減少した（p=0.0009）。

Full Text

Uninterrupted treatment with dabigatran, a non-vitamin K antagonist oral anticoagulant (NOACs), before, during and after ablation to treat atrial fibrillation significantly reduced the incidence of major bleeding events compared with uninterrupted use of the more established anticoagulant warfarin, according to research presented at the American College of Cardiology's 66th Annual Scientific Session with simultaneous publication in the *New England Journal of Medicine*.

The findings offer evidence that dabigatran is a safe and effective alternative to warfarin in the context of atrial fibrillation ablation. The trial showed a 5.3 percent reduction in its primary endpoint, major bleeding events during ablation or in the first two months after the procedure, with major bleeds occurring in 1.6 percent of study participants who received dabigatran and 6.9 percent of patients receiving warfarin.

"I think it's great news for the field," said Hugh Calkins, MD, professor of cardiology at Johns Hopkins Medicine and the study's lead author. "There have been very few randomized studies focused on doing ablation procedures in fully anticoagulated patients, and the use of NOACs has been increasing dramatically. I expect these findings will encourage clinicians to quickly shift to doing this procedure with uninterrupted use of NOACs."

People with atrial fibrillation are five-times more likely to experience a stroke compared with the general population, and many patients take anticoagulants, or anti-clotting medications, to reduce this risk. However, taking anticoagulants during any kind of surgery can increase the risk of uncontrolled bleeding, raising concerns over how to appropriately weigh the risks and benefits of anticoagulants during ablation.

"Anticoagulation management at the time of atrial fibrillation ablation is critically important because stroke and bleeding are both major complications of the procedure," Calkins said.

Most physicians advise patients to use warfarin continuously before, during and after ablation to reduce the risk of stroke. However, warfarin has some downsides; for example, it requires dietary changes and frequent monitoring of blood coagulation markers, and ablation procedures must be canceled at the last minute if a patient's blood coagulation levels are off-target, creating logistical challenges. In addition, following this guidance can require patients who normally use NOACs to switch temporarily to warfarin around the time of ablation and then switch back, which is cumbersome and sometimes impractical.

The trial is the largest to compare the uninterrupted use of NOACs to uninterrupted use of warfarin in the context of ablation. The researchers prospectively enrolled 704 patients scheduled for atrial fibrillation ablation at 104 sites in 11 countries and randomly assigned patients to receive either dabigatran or warfarin. Patients started anticoagulant therapy four to eight weeks before ablation and used it continuously for up to eight weeks after the procedure.

After excluding patients who did not go through with ablation or failed to meet the study protocol for other reasons, the researchers analyzed outcomes from 317 patients receiving dabigatran and 318 patients receiving warfarin. Dabigatran showed significant improvement over warfarin for the study's primary endpoint, major bleeding events, and equaled warfarin with regard to secondary safety and efficacy endpoints, which included minor bleeding events, stroke, a composite of major bleeding and stroke, and a composite of all serious adverse events. Only one stroke occurred during the study, and it occurred in a patient assigned to receive warfarin.

Calkins noted that there is an approved reversal agent for dabigatran, which gives clinicians an additional tool to control major bleeding if it should occur during a procedure.

The findings confirm and enhance the results of previous, smaller studies suggesting NOACs present a lower risk of major bleeding events compared with warfarin, though this study contradicts the findings of one previous, smaller study comparing dabigatran to warfarin.

The Uninterrupted Dabigatran Etexilate in Comparison to Uninterrupted Warfarin in Pulmonary Vein Ablation (RE-CIRCUIT) trial was funded by Boehringer Ingelheim.

ACC2017特集

血液検査により非心臓手術後の心損傷が検出できる (Abstract 17-LB-16217)

非心臓手術後1か月以内の死亡リスクが高感度トロポニンTアッセイを用いることにより検出される

Risk of death within one month of non-cardiac surgery detected using high-sensitivity troponin T assay

高感度トロポニンTの血液検査は、迅速な治療により命を救える可能性のある非心臓手術後の心損傷を有する患者を検出できる、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。研究者らは、血液アッセイを用いることにより、ピークトロポニンT値が5 ng/L未満の患者の30日以内の死亡リスクは、わずか0.1%であると決定付けた。対照的に、ピークトロポニン値が20～64 ng/Lの者はトロポニンT値が低い者に比べ、術後30日以内の死亡リスクが3倍であり、30日間の絶対リスクは3%であった。

Full Text

A blood test for a protein called high-sensitivity troponin T, which is released into the bloodstream when injury to the heart occurs, can identify patients with heart damage after non-cardiac surgery whose lives could potentially be saved with timely treatment, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

The prospective cohort study met both its primary endpoints: to determine the association between troponin T levels measured by a high-sensitivity troponin T assay and the risk of death within a month of non-cardiac surgery, and to identify diagnostic criteria for myocardial injury after non-cardiac surgery that defines whether or not serious injury to the heart has occurred.

"We found that approximately 18 percent of patients will sustain a heart injury after non-cardiac surgery, but without monitoring troponins, 93 percent of these will be missed," said P.J. Devereaux, MD, PhD, director of cardiology at McMaster University in Hamilton, Canada, and lead author of the study. "Our data show that unrecognized heart injuries may account for about 1 in 4 of the deaths that happen in the first 30 days after surgery."

The effects of surgery anywhere in the body create a "perfect milieu" for damage to heart tissue, Devereaux said, including bleeding, blood clot formation and long periods of inflammation. He said most cases of damage to the heart occur during the first 24 to 36 hours after surgery, when patients usually receive narcotic painkillers that can mask cardiac symptoms.

"This creates a risk that if you don't look for cardiac events, you might miss them," he said, adding that this is the first large international study to establish thresholds of high-sensitivity troponin T that are independently associated with death within 30 days after non-cardiac surgery.

The researchers enrolled 21,842 patients aged 45 years or older (41 percent were 65 years or older) from 23 hospitals in 13 countries in the study. Participants included patients with and without known heart or blood vessel disease. To obtain a broad sample of patients undergoing non-cardiac inpatient procedures, such as hip or knee replacements, researchers examined elective, urgent and emergency surgeries as well as procedures performed during the day, at night, on weekdays and on weekends.

Measurements of high-sensitivity troponin T were taken in the first six to 12 hours after surgery and on the following three days. Halfway through the study, the researchers began measuring levels of the protein immediately before surgical procedures as well as post-surgery. They followed patients for up to 30 days after surgery and recorded all major complications, including stroke, pulmonary embolism, sepsis and bleeding. They adjusted the data for pre-operative and surgical variables previously shown to be associated with 30-day mortality, including active cancer, general surgery, urgent/emergent surgery, history of peripheral vascular disease, history of chronic obstructive pulmonary disease, age, recent high- risk coronary artery disease, history of stroke and neurosurgery.

Overall, 1.4 percent of patients died during the first 30 days after surgery. Using data from the blood assays, the researchers determined that patients with peak troponin T levels less than 5 ng/L had only a 0.1 percent risk of death within 30 days. By contrast, patients with peak troponin T levels between 20 and 64 ng/L had three-times the risk of death within 30 days than patients with lower troponin T measurements as well as a 3 percent absolute risk of 30-day mortality.

The risk of death after surgery rose with higher peak troponin T levels. Patients with peak levels between ≥65 and <1000 ng/L had a 9.1 percent risk of dying within 30 days, while those with peak levels at or above 1000 ng/L had a 29.6 percent risk of 30-day mortality.

In patients whose troponin T levels were measured both before and after surgery, only 13.8 percent experienced peak levels before their procedure, suggesting that taking a baseline measurement is important to rule out a false indication of injury during or after surgery, Devereaux said.

Data from 3,904 patients who sustained myocardial injury after non-cardiac surgery suggested that ischemic injury (i.e., an injury caused by a lack of oxygen) to heart tissue after non-cardiac surgery explained 24 percent of deaths in the first 30 days after surgery. The vast majority of these patients experienced no symptoms of heart damage.

Observational data suggest that drugs such as aspirin or statins can decrease the risk of death in patients with ischemic heart damage after non-cardiac surgery.

"Data also suggest that only a minority of patients who get these injuries receive these drugs, [because they don't show symptoms of heart injury]," Devereaux said, adding that better management of ischemic injury to the heart detected by high-sensitivity troponin T has the potential to prevent many of the deaths after non-cardiac surgery.

"Where we're letting patients down is in post-operative management," Devereaux said. "That requires physicians to get more involved in post-operative care to make sure that patients benefit from these important surgical interventions. Although the vast majority of patients undergoing surgery do well, if even a small proportion of patients are dying, that's a big deal because so many people have surgery."

A limitation of the study was that the researchers did not have pre-operative troponin measurements for about 60 percent of patients, Devereaux said. The absence of this information could have led to an overestimation of ischemic heart injury after surgery, because some patients' highest troponin levels may have occurred before surgery. Devereaux said this meant they could not clearly distinguish between patients with high pre-operative troponin T levels who developed ischemic injuries and those whose injuries were associated with high post-operative levels of troponin T.

The researchers have begun an international randomized controlled trial testing whether starting an anticoagulant based on troponin T levels after non-cardiac surgery can help prevent these post-operative cardiovascular deaths.

The trial received the troponin T assay from Roche Diagnostics; the company was not involved with the study data collection or analyses.

ACC2017特集

ウェブベースのカウンセリングは血圧を低下させる (Abstract 17-LB-16110)

REACH：ライフスタイル介入は収縮期血圧を10 mmHg低下させる

REACH: Lifestyle intervention leads to 10-point drop in systolic blood pressure

高血圧に対するオンラインライフスタイル介入に関する初めてのランダム化二重盲検試験において、ウェブベースのライフスタイルカウンセリング（e-カウンセリング）は対象者の収縮期血圧を10 mmHg低下させ、それに対しウェブベースのコントロール介入に参加した患者における低下は6 mmHgであり、統計学的に有意であった。E-カウンセリング群はまた、脈圧が平均4 mmHg低下したのに対し、コントロール群では1.5 mmHgであった。筆者らは、e-カウンセリングによる介入は、降圧薬をさらに追加したのと同様の効果を示したと述べている。このREACHスタディはAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。

Full Text

In the first randomized, double-blinded trial of an online behavioral intervention for hypertension, participants in web-based lifestyle counseling reduced their systolic blood pressure by 10 mmHg, compared with a 6 mmHg reduction for those taking part in a web-based control intervention, a statistically significant difference. The research was presented at the American College of Cardiology's 66th Annual Scientific Session.

"The electronic counseling (e-Counseling) intervention had an effect similar to that of adding an additional blood-pressure-lowering medication," said Robert P. Nolan, PhD, a senior scientist at the Peter Munk Cardiac Centre, University Health Network, associate professor at the University of Toronto and lead author of the study. "We think this lifestyle counseling intervention can complement and optimize the effectiveness of medical therapy to reduce high blood pressure."

The trial involved 264 participants aged 57.5 years on average, 58 percent of whom were women. Average blood pressure at study entry was about 140/90 mmHg (the cutoff for Stage 1 high blood pressure, or hypertension). A small group of 39 participants (15 percent) had Stage 2 hypertension (blood pressure of at least 160/100 mmHg). Eighty-three percent of participants were taking at least one medication to reduce their blood pressure. All participants received regular medical care throughout the study.

Study participants enrolled through the website of the Heart and Stroke Association of Canada and were randomly assigned to e-Counseling or a control group. Both groups received emails weekly for four months, every other week for another four months and monthly for the last four months of the 12-month trial. The emails to the e-Counseling group provided links to online multimedia and interactive tools to increase motivation and skills to begin and sustain a heart-healthy lifestyle. These included video clips featuring characters discussing their own high blood pressure diagnosis and efforts to make lifestyle changes, as well as tools for tracking diet and level of physical activity. The emails to the control group linked to generic information about heart-healthy living and reducing high blood pressure.

"In the e-Counseling intervention we tried to replicate the experience of going through face-to-face lifestyle counseling for a year," Nolan said. "We made use of what we know from 60 years of research on the effective features of motivational interviewing and cognitive behavioral therapy, and we applied those features using the technology that was available to our team."

Participants were assessed in person three times—at study entry, four months and 12 months—at one of five study centers across Canada. The primary endpoints were changes in systolic and diastolic blood pressure and pulse pressure.

Changes in non-HDL cholesterol and Framingham risk score, which estimates the risk of developing heart disease or stroke over the next 10 years, were also measured. Secondary endpoints were change in physical activity, consumption of fruit and vegetables and smoking cessation.

After 12 months, in addition to the average reduction of 10 mmHg in systolic blood pressure in the e- Counseling group compared with 6 mmHg in the control group, the e-Counseling group also saw a statistically significant average reduction of 4 mmHg in pulse pressure compared with 1.5 mmHg in the control group. These results were similar for all participants, and the therapeutic benefit was not affected by the relative level of blood pressure (Stage 1 or 2 hypertension) at study entry.

Some results differed in men compared with women. For example, men in the e-Counseling group saw an average reduction of 4 mmHg in diastolic blood pressure compared with 1.5 mmHg for controls. Among women, however, both the e-Counseling and control groups saw reductions in diastolic blood pressure of 6 mmHg on average.

At 12 months, the four-day step count increased significantly among e-Counseling participants and declined significantly among controls, resulting in a difference of 1,200 steps per day in favor of the e- Counseling group. No significant changes were seen in fruit and vegetable consumption as both groups reported eating a recommended amount of about eight servings a day at study entry.

"Self-reported dietary data can reflect idealistic views of eating behavior, and it's possible that this may have been an influence in our study," Nolan said.

Because only 9 percent of trial participants reported smoking at study entry, data were insufficient to measure smoking cessation.

In exit interviews, e-Counseling participants spoke of becoming attached to the characters they saw in the video clips, which helped motivate them to achieve their behavior change goals, Nolan said.

"We believe this dynamic way of engaging patients can be a very powerful tool to promote behavior change," he said.

The study has limitations, he said. The participants were all highly motivated individuals who had gone to a website in search of health information. In addition, participants were relatively well-educated, with most having at least some post-secondary education. Finally, because a majority (73 percent) of participants were Caucasian, the results may not generalize to more racially diverse groups.

The study was funded by the Canadian Institutes of Health Research, a government agency.

ACC2017特集