気候変動は心筋梗塞リスクを上昇させる可能性がある (Abstract 18-A-14071-ACC)

心筋梗塞は屋外温度の劇的な変化の後にしばしば増加する

Increase in myocardial infarctions often follows dramatic changes in outdoor temperature

日々の大きな温度変化は心筋梗塞（MI）を有意に増加させたとのスタディ結果が、American College of Cardiology's 67th Annual Scientific Session において3月10日に発表される。MIリスクは温度差が摂氏5度急変する毎に約5% 増加した。摂氏25度を超える温度変化は、摂氏10～25度の温度変化よりもMI率をより上昇させた。一部の気候モデルが地球温暖化と極端な気候イベントとを関連付けていることから、これらの結果は気候変動がMI発症増加に繋がり得ることを示唆している。

Full Text

Large day-to-day swings in temperature were associated with significantly more myocardial infarctions (MI) in a study being presented March 10 at the American College of Cardiology's 67th Annual Scientific Session. Given that some climate models link extreme weather events with global warming, the new findings suggest climate change could, in turn, lead to an uptick in the occurrence of MIs, researchers said.

"Global warming is expected to cause extreme weather events, which may, in turn, result in large day-to-day fluctuations in temperature," said Hedvig Andersson, MD, a cardiology researcher at the University of Michigan and the study's lead author. "Our study suggests that such fluctuations in outdoor temperature could potentially lead to an increased number of heart attacks and affect global cardiac health in the future."

There is a large body of evidence showing that outdoor temperature affects the rate of MIs, with cold weather bringing the highest risk, but most previous studies have focused on overall daily temperatures. This new study is among the first to examine associations with sudden temperature changes.

"While the body has effective systems for responding to changes in temperature, it might be that more rapid and extreme fluctuations create more stress on those systems, which could contribute to health problems," Andersson said, noting that the underlying mechanism for this association remains unknown.

Along with an overall warming trend, climate change is projected to lead to more extreme events, such as heat waves and cold snaps, depending on where someone lives, the researchers explained.

The research is based on data from more than 30,000 patients treated at 45 Michigan hospitals between 2010-2016. All patients had received percutaneous coronary intervention after being diagnosed with ST-elevated myocardial infarction (STEMI).

The researchers calculated the temperature fluctuation preceding each STEMI based on weather records for the hospital's ZIP code. Daily temperature fluctuation was defined as the difference between the highest and lowest temperature recorded on the day of the heart attack.

Overall, the results showed the risk of an MI increased by about 5 percent for every five-degree jump in temperature differential, in degrees Celsius (9 degrees Fahrenheit). Swings of more than 25 degrees Celsius (45 degrees Fahrenheit) were associated with a greater increase in MI rates compared to a smaller increase with temperature swings of 10 to 25 degrees Celsius (18-45 degrees Fahrenheit). The effect was more pronounced on days with a higher average temperature; in other words, a sudden temperature swing seemed to have a greater impact on warmer days. At the far end of the spectrum, on a hot summer day, nearly twice as many MIs were predicted on days with a temperature fluctuation of 35-40 degrees Celsius (63-72 degrees Fahrenheit) than on days with no fluctuation.

"Generally, we think of heart attack risk factors as those that apply to individual patients and we have, consequently, identified lifestyle changes or medications to modify them. Population-level risk factors need a similar approach," said Hitinder Gurm, MD, professor of medicine and associate chief clinical officer at Michigan Medicine and the study's senior author. "Temperature fluctuations are common and [often] predictable. More research is needed to better understand the underlying mechanisms for how temperature fluctuations increase the risk of MIs, which would allow us to perhaps devise a successful prevention approach."

In their analysis, the researchers adjusted for precipitation totals, day of the week and seasonal trends to isolate the effects of daily temperature fluctuations from other potential environmental factors.

Gurm cautioned that the association does not necessarily prove that sudden temperature swings are the cause of the increase in MIs; other factors may have contributed to the results. He noted that it remains important to focus on modifiable cardiovascular risk factors such as smoking, high blood pressure and high cholesterol.

ACC2018特集

炎症性腸疾患はMIリスクを上昇させる (Abstract 18-A-17421-ACC)

心筋梗塞リスクは特に若年の炎症性腸疾患患者において上昇する

Risk of myocardial infarction raised in patients with inflammatory bowel disease especially in young

炎症性腸疾患（IBD）患者は、高コレステロール、高血圧および喫煙など従来の心疾患リスクファクターの有無にかかわらず心筋梗塞（MI）リスクが高い、との研究結果がAmerican College of Cardiology's 67th Annual Scientific Session において3月11日に発表される。IBD患者はMI発症リスクが約23% 高かった。40歳未満の女性IBD患者は、同年代の男性IBD患者に比べMIリスクが高かった。リスクは、18～24歳の患者において最大であった。

Full Text

An analysis of medical-record data from more than 17.5 million patients found that people with inflammatory bowel disease (IBD) are at elevated risk for a myocardial infarction (MI), regardless of whether or not they have traditional risk factors for heart disease such as high cholesterol, hypertension and smoking. People between the ages of 18 and 24 are at the highest risk, according to research to be presented March 11 at the American College of Cardiology's 67th Annual Scientific Session.

"Younger patients had about nine times the risk of a heart attack compared to their peers in the same age group [who didn't have IBD], and this risk continued to decline with age," said Muhammad S. Panhwar, MD, a resident in internal medicine at Case Western Reserve University/University Hospitals Cleveland Medical Center in Cleveland and lead author of the study, one of the largest to date to investigate the link between IBD and heart disease risk. "Our findings suggest that IBD should be considered an independent risk factor for heart disease."

IBD is an umbrella term for two chronic inflammatory conditions, Crohn's disease and ulcerative colitis. While different studies have shown that people with other chronic inflammatory conditions, such as lupus and rheumatoid arthritis, are at increased risk for heart disease, a link between IBD and heart disease has been under debate.

To investigate a possible link between IBD and heart disease risk, Panhwar and his colleagues used IBM Explorys, a large database of de-identified data from electronic medical records for patients of 26 nationwide health care systems in the U.S. They identified adult patients ages 18 to 65 with a diagnosis of IBD between 2014 and 2017 and looked at how many patients with and without IBD had heart attacks. Among more than 17.5 million patients in the database, 211,870 (1.2 percent) had IBD, which is comparable to numbers reported by the CDC.

People with IBD were also more likely to have diabetes, high blood pressure, high cholesterol and smoking — traditional risk factors for heart disease — than people without IBD.

Compared with patients who did not have IBD, myocardial infarctions (MIs) occurred roughly twice as often in those with IBD. After adjusting for age, race, sex and traditional heart disease risk factors, Panhwar and his colleagues found that the patients with IBD had about a 23 percent higher risk of having an MI. Women under the age of 40 with IBD were at higher risk for MI than men with IBD in the same age group. In patients over the age of 40, MI risk was similar for men and women with IBD.

IBD is usually diagnosed between the ages of 15 and 30 years old, and younger patients and females with this condition are known to have more aggressive and disabling disease with more frequent flares, suggesting increased levels of inflammation. Panhwar said this disproportionate amount of inflammation in younger patients with IBD — who often don't have traditional cardiovascular risk factors — and women may explain why they had such a markedly higher risk of MIs.

"Our study adds considerably to a growing set of literature highlighting the importance of chronic inflammation in IBD as having a role in the development of heart disease," Panhwar said. He suggested that physicians who have patients with IBD should be aggressively screening them for heart disease and focusing on risk reduction strategies. "The results suggest clinicians should take seriously any symptoms suggestive of heart disease, such as chest pain, in patients with IBD, especially in younger patients," he said.

Even though this was a very large study, there are some limitations. The database lacks granularity regarding the type of heart attack and did not enable the researchers to exclude from the analysis people who had had previous MIs and may have, therefore, been at higher risk for another MI. Also, the database did not provide information about how individual patients fared over time.

Panhwar said the findings of this study open the field for more research into the link between IBD and heart disease, including the benefit of using anti-inflammatory drugs for the management of cardiovascular risk in patients with IBD. In addition, he expressed hope that the findings will empower people with IBD, especially those under 40 years of age, to have conversations with their doctor about their personal risk of cardiovascular disease.

ACC2018特集

前向きな態度は狭心症患者の転帰を改善する (Abstract 18-A-17200-ACC)

RIVER-PCI：慢性狭心症の見通しを楽観的にとらえていることはその後の転帰が良好なことに繋がる

RIVER-PCI: Optimistic outlook about chronic angina leads to improved outcomes over time

慢性狭心症を対処するに当たって、前向きな態度がその後の転帰を改善するのに役立つ可能性があるとのRIVER-PCIトライアルの結果が、American College of Cardiology's 67th Annual Scientific Session において3月10日に発表される。あまり楽観的でない対照群に比べ、最も楽観的な群では、概して狭心症が少なく心筋梗塞、心不全、糖尿病および慢性腎臓病歴を有する割合が低かった。研究者らは、最も楽観的な群は全体的に健康であることを自覚し自重するよう促しているが、それでも彼らは病院へ行ったり血行再建術を施行されたりする割合が30% 低かった。

Full Text

When it comes to coping with chronic angina, a positive outlook may help improve outcomes over time, according to a study to be presented on March 10 at the American College of Cardiology's 67th Annual Scientific Session.

Researchers at the Duke Clinical Research Institute and Columbia University sought to determine whether people with heart-related chest pain who say they are optimistic about their disease and future health would have fewer episodes of heart-related hospital stays or revascularizations.

"Feeling better about your disease process and ability to reengage in usual activities may actually make chronic angina easier to deal with," said Alexander Fanaroff, MD, a fellow in the department of cardiology at Duke University Medical Center and the study's lead author. "Our findings suggest that if we can identify patients who are less optimistic for whatever reason — whether it's because their disease has made them despair for the future, they have uncertainty about their diagnosis, or they have multiple comorbidities — and help them feel more hopeful by focusing on what they can do, we may be able to positively affect outcomes."

While there has been a lot of attention to the association between depression and heart health, this is the first study to assess whether hope and confidence in one's future health might be protective for people with heart disease and chronic angina symptoms.

Chronic angina is among the most common complaints made by patients visiting the emergency department and it can greatly impair someone's quality of life, Fanaroff said. A less optimistic view of their health may also trigger more visits to the doctor's office, contributing to more evaluation and hospital admissions. "People will often cut back on or stop activities they like to do — tennis, playing with grandchildren, job-related tasks — either because of the pain itself or because they worry that the activity prompting the pain is dangerous [to their heart]," he said.

In this study, those who were self-described as more optimistic were 40 percent less likely to be hospitalized with angina or have a revascularization procedure compared with those who were not. While researchers cautioned that the most optimistic group of patients also tended to be healthier overall, they were still 30 percent less likely to go to the hospital or have a revascularization even after accounting for this fact.

The study analyzed data from nearly 2,400 people with chronic angina undergoing percutaneous coronary intervention (PCI) to open at least one blocked coronary artery who were enrolled in RIVER-PCI, a multi-center, randomized, double-blinded, controlled trial. RIVER-PCI tested whether taking ranolazine in addition to usual care could reduce hospitalizations and revascularization procedures related to angina compared with placebo and found no benefit.

As part of this trial, patients completed a questionnaire about their overall quality of life, how frequently they had angina and how much they agreed or disagreed with the statement, "I am optimistic about my future and returning to a normal lifestyle." These same questions were asked again at one, six and 12 months.

For the present study, Fanaroff and his team grouped patients based on how optimistic they were at the start of the RIVER-PCI trial, regardless of what treatment they received, to see whether perceived optimism had any effect on hospitalizations and revascularizations during the median 643 days of follow up.

Of the patients surveyed, 782 (33.2 percent) were most optimistic ("strongly agree"), 1,000 (42.4 percent) were somewhat optimistic ("agree"), 451 (19.1 percent) were undecided, and 123 (5.2 percent) were not optimistic ("disagree" or "strongly disagree"). The level of optimism reported by patients remained fairly stable over time.

Compared with their less optimistic peers, those who were most optimistic reported having less angina overall and were also less likely to have had a history of myocardial infarction, heart failure, diabetes and chronic kidney disease.

The rate of the primary outcome was higher in undecided (32.8 percent) and not optimistic (35 percent) patients compared with the most optimistic patients (24.4 percent); this finding persisted after adjusting for comorbidities and baseline angina frequency.

Still unanswered, researchers noted, is whether patients who were less optimistic felt that way due to the burden of their disease(s) or general uncertainty about the future living with their disease.

Still, there seems to be a link, Fanaroff said. He added that there is no downside to instilling hope and equipping patients with skills for self-care. "As a clinician, it doesn't cost anything to help patients with chronic angina focus on what they can do, letting them know that there are medications and procedures that can help them return to a normal life and continue to do the things they like to do," he said. "Bottom line: there's reason to be optimistic for patients with chronic angina, and it's important that clinicians relay that to them."

Fanaroff said a reasonable next step would be to test strategies that might encourage someone to adopt a more glass-half-full, positive outlook and track outcomes.

ACC2018特集

アリロクマブは急性冠症候群後の心血管イベントを軽減する(Abstract 18-LB-18859-ACC)

ODYSSEY：PCSK9阻害薬は特に高コレステロール血症患者においてベネフィットがある

ODYSSEY: Benefits of PCSK9 inhibitor especially pronounced in patients with highest cholesterol levels

高強度のスタチン治療にもかかわらず高コレステロール血症が持続する患者群において、PCSK9阻害薬アリロクマブはプラセボに比べ、主要心血管イベント（MACE）を15% 軽減した、とのODYSSEY Outcomes 試験の結果がAmerican College of Cardiology's 67th Annual Scientific Session で発表された。薬剤の効果は、LDLコレステロール値100mg/dL以上の高リスク群でさらに大きく、プラセボに比べ心筋梗塞、脳卒中などの心血管イベントにおいて24%の減少を示した。患者は少なくとも2年間追跡され、そのうち44% は3年以上追跡された。

Full Text

Among patients with persistently high cholesterol despite high-intensity statin therapy, the proprotein convertase subtilisin-kexin 9 (PCSK9) inhibitor alirocumab reduced rates of major adverse cardiovascular events (MACE) by 15 percent compared with placebo, in a study presented at the American College of Cardiology's 67th Annual Scientific Session. The drug's effect was even greater for patients at highest risk —those who started the study with LDL of 100 mg/dL or higher — who saw a 24 percent reduction in cardiovascular events, including myocardial infarction (MI) and stroke, compared with placebo.

The trial, called ODYSSEY Outcomes, was conducted in patients who had recently had an acute coronary syndrome (ACS). Such patients face a substantial risk of further cardiovascular problems and related death, particularly if their cholesterol level is not adequately controlled. Alirocumab is a fully human monoclonal antibody that works by blocking PCSK9. This action of the drug allows the liver to remove more LDL from the blood and lowers the concentration of LDL cholesterol in the blood.

Previous research has shown that PCSK9 inhibitors reduce LDL levels by about half — but ODYSSEY Outcomes is only the second large, randomized trial to investigate whether this LDL reduction translates into improved cardiovascular outcomes. It's the first study with a PCSK9 inhibitor to show an associated mortality benefit, researchers said.

FOURIER, the first outcomes trial, presented at ACC.17, similarly reported that evolocumab, a different PCSK9 inhibitor, reduced the risk of death, MI, stroke, hospitalization for angina or revascularization procedures to clear blocked arteries by 15 percent.

Compared with FOURIER, the ODYSSEY Outcomes trial enrolled a higher-risk group of patients, had a longer duration of follow-up (ranging from two to five years), involved a different dosing strategy and had a slightly different primary endpoint. In addition to significantly reducing the primary endpoint — a combined rate of MI, stroke, hospitalization for unstable angina or death from coronary heart disease — alirocumab was also associated with a 15 percent reduction in death from any cause among the full patient population and a 29 percent reduction in death from any cause among those who started the trial with LDL cholesterol above 100 mg/dL. The study did not raise any major safety concerns for alirocumab.

"We were really pleased to see the treatment was effective and associated with a reduction in mortality. It is remarkable that such a potent intervention is also so safe," said Philippe Gabriel Steg, MD, chief of cardiology at Hôpital Bichat in Paris and co-chair of the study. "Because the treatment effect was so much more marked in the patients with the highest LDL cholesterol, we believe that these patients are the optimal candidates for therapy."

Researchers enrolled nearly 19,000 patients at more than 1,300 centers in 57 countries. All patients had ACS within one month to one year before enrolling in the study. The trial included those whose LDL cholesterol remained70 mg/dL or above, non-HDL cholesterol 100 mg/dL or above, or apolipoprotein B 80 mg/dL or above despite treatment with a high or maximum-tolerated dose of a high-potency statin (atorvastatin or rosuvastatin).

Patients were randomly assigned to receive injections of either alirocumab or placebo every two weeks. Neither patients nor doctors knew who received the drug. To mimic the adjustments a doctor might make when using the drug, those patients randomized to receive alirocumab had their doses adjusted in a blinded fashion (neither patients nor doctors were aware of the adjustments) in efforts to reach LDL cholesterol levels of 25-50 mg/dL. If LDL cholesterol levels dropped consistently below 15 mg/dL, the patient was switched to placebo, again in a blinded fashion.

Patients were tracked for at least two years, with 44 percent tracked for three years or more. Overall, the primary endpoint occurred in 9.5 percent of those receiving alirocumab and 11.1 percent of those receiving placebo, while 3.5 percent of those receiving alirocumab and 4.1 percent of those receiving placebo died.

When researchers looked at causes of death separately, there was no significant difference between the two groups in terms of coronary heart disease and cardiovascular disease deaths. However, Steg noted there may not have been enough events in each subcategory to show a definite difference.

Patients starting the trial with LDL cholesterol levels above 100 mg/dL saw improvements in all outcomes that were assessed, including rates of MI, stroke, unstable angina requiring hospitalization, coronary heart disease death, cardiovascular death and death from any cause. Among these patients, the primary endpoint occurred in 11.5 percent of those receiving alirocumab and 14.9 percent of those receiving placebo, while 4.1 percent of those receiving alirocumab and 5.7 percent of those receiving placebo died.

In terms of safety and tolerability, the only significant difference between the two study groups was minor local site reactions (mild itching, redness or swelling) at the injection site, which occurred in 3.1 percent of those receiving alirocumab and 2.1 percent of those receiving placebo.

Researchers will use the trial data to evaluate the cost-effectiveness of alirocumab. PCSK9 inhibitors cost tens of thousands of dollars per year and are often not covered by insurers.

"Now that we have two trials that consistently show benefits from PCSK9 inhibitors, and given the mortality benefit that we are reporting here for the first time, I think these results may change the equation for these drugs" Steg said. "We're not just talking about preventing nonfatal events such as MIs but actually preserving life."

Researchers will continue to track patient outcomes for up to 10 years to determine whether the benefits continue after stopping the drug.

The trial was funded by Sanofi and Regeneron Pharmaceuticals.

ACC2018特集

着用型自動除細動器は全死亡を減らすが突然死には影響しない(Abstract 18-LB-17834-ACC)

VEST：着用型自動除細動器は全死亡率を軽減するが心筋梗塞後の突然死には影響しない

VEST: Wearable defibrillator reduces overall mortality but not sudden deaths after myocardial infarction

推奨薬剤の投与に加え、心臓の異常なリズムを検出する除細動器を装備した軽量のベストを着用することで、駆出率が低下した患者における心筋梗塞後最初の90日間の死亡確率を低下させる、とのVEST試験の結果が American College of Cardiology's 67th Annual Scientific Session で発表された。主要評価項目である心臓突然死に関しては顕著なベネフィットはなかったが、着用型自動除細動器を着用した患者は全死亡率が35% 減少した。

Full Text

Wearing a lightweight vest equipped with a cardioverter defibrillator that detects abnormal heart rhythms in addition to taking recommended medications is associated with a reduction in the likelihood of dying during the first 90 days following a myocardial infarction (MI) in people whose heart function was also impaired, according to a study presented at the American College of Cardiology's 67th Annual Scientific Session.

People who wore the wearable cardioverter defibrillator (WCD) during the study timeframe were 35 percent less likely to die for any reason compared with those who received medications alone. While the study did not find a significant benefit in terms of reducing sudden cardiac death, the primary endpoint, the study did find that the wearable defibrillator was associated with fewer overall deaths.

"It is possible that sudden deaths were misclassified as it's difficult to define sudden death with accuracy when a death is unwitnessed and there is little documentation," said Jeffrey E. Olgin, MD, professor and chief of cardiology, University of California San Francisco and lead author of the study. "But the cause of death is irrelevant if we can prevent it. This study found that the device was associated with fewer deaths among people recovering from an MI with low ejection fraction. It's also the first therapy associated with a mortality benefit above and beyond standard medical therapy immediately after MI."

The Vest Prevention of Early Sudden Death Trial (VEST) is the first randomized, controlled, multi-center trial of the wearable cardioverter defibrillator. It was designed to test whether this device could effectively reduce sudden death in patients who had recently suffered an MI and had reduced heart function (defined as a low ejection fraction of 35 percent or less), which is indicative of a sizable MI.

Generally, the three-month mortality rate for people recovering from an MI who also have reduced heart function is around 5 percent, Olgin said, and that is with optimal medical management. Similarly, in VEST, 4.9 percent of participants in the control group died compared with only 3.2 percent of those wearing the WCD — an absolute difference of 1.7 percent.

"There is a very high risk of death immediately after an MI that tails off after about three months," Olgin said. "The challenge is that we don't currently have a good way of preventing deaths during this very vulnerable period."

Despite the high rate of sudden death in the months following an MI, implantable cardioverter defibrillators (ICDs) placed in the chest aren't currently indicated for this patient population before 40-90 days for several reasons. First, large studies have failed to show that implanting an ICD during this period results in long-term reductions in mortality.

Second, in many cases someone's ejection fraction will improve in the ensuing months post-MI. In VEST, for example, 60 percent of people with low ejection fraction in the first three months after MI recovered and no longer met the criteria for an ICD at 90 days.

Lastly, there is competing risk of death from other causes not preventable with a defibrillator — for example, another MI or cardiac rupture.

According to Olgin, these new findings suggest WCDs could fill the gap in cardiac therapy until patients can be evaluated for an ICD.

Current guidelines recommend the WCD as a potential tool that practitioners can use, but the researchers believe findings from this large randomized trial will add important data to further inform these guideline recommendations.

The LifeVest WCD is worn under clothing, directly against the skin. It works by continuously monitoring a patient's heart and sounding alarms and/or giving verbal commands to encourage people to seek medical care, if needed. If a life-threatening heart rhythm is detected, the device delivers a shock to restore a normal heart rhythm.

"What's nice about the wearable defibrillator is that it's non-invasive and it's not permanent," Olgin said. "Based on our results, I think we'll see more widespread use of this device in these patients."

The trial enrolled 2,300 adult patients admitted to the hospital for MI with an ejection fraction of ≤35 percent across more than 100 trial sites in four countries. Upon discharge, patients were randomized 2 to 1 to either receive the WCD plus guideline-directed medical therapy or guideline-directed medical therapy alone for 90 days to determine the potential mortality benefit of the WCD. Patients were advised and reminded to wear the WCD as much as possible and only take it off for bathing; participants who wore the WCD did so for an average of 21 hours a day.

The primary outcome was sudden death at three months and secondary outcomes were total and cause-specific mortality, non-fatal ventricular arrhythmias and hospitalizations.

Participants and sites were not blinded to the treatment arm, but they were blinded to any arrhythmia detections during the follow-up. Un-blinding could be requested if a participant had a shock, cardiac arrest or syncopal event.

Outcomes were adjudicated by an independent, blinded panel. The vast majority of patients in both groups — upwards of 85 percent — received appropriate guideline-directed treatment for post-MI management, as well as heart failure management given patients' reduced ejection fraction.

At the end of the study, researchers searched the National Death Index for participants lost to follow up. The rate of cardiovascular-related re-hospitalizations was 25 percent and was similar in both groups.
The study was originally designed with a primary outcome of total mortality. However, because of enrollment difficulties early in the study, the estimated sample size of 4,500 participants became infeasible. After the first 213 participants were enrolled in 2010, the primary outcome was changed to sudden death with a pre- specified secondary outcome of total mortality, Olgin said. He and his team are working on a number of additional analyses from this study. They also plan on transitioning patients into a registry for longer-term follow up.

This study was funded, in part, by the National Institutes of Health and Zoll Medical Corporation, which makes the LifeVest WCD.

ACC2018特集

心不全患者にとってインフルエンザワクチンは有益である (Abstract 18-A-13676-ACC)

季節毎のインフルエンザワクチンは心不全患者の死亡リスクを半減する

Seasonal Flu vaccine cuts risk of death in half for people with heart failure

心不全患者において、季節毎のインフルエンザ(flu)ワクチン接種を受けることにより、接種を受けた年のインフルエンザ流行期の全死亡リスクが50% 低下し、その後の年の死亡リスクが20% 低下した、とAmerican College of Cardiology's 67th Annual Scientific Sessionで発表された。心不全患者78,000人超を対象としたこのメタ解析は、fluワクチン接種により心血管系の原因により入院するリスクを22% 低下させることも示した。

Full Text

For people with heart failure, getting a seasonal influenza (flu) vaccine in a given year was associated with a 50 percent drop in the risk of death during flu season and a 20 percent drop in the risk of death during the rest of the year, according to research presented at the American College of Cardiology's 67th Annual Scientific Session.

The study comes amid a flu season that has brought higher than normal rates of infection and death. Influenza and flu-related complications can cause death even in otherwise healthy people. This is the first study to examine the relationship between influenza vaccination and death or hospitalization in heart failure patients through meta-analysis.

"It is well known that influenza infection is associated with increased risk for mortality in heart failure patients," said Hidekatsu Fukuta, MD, a cardiologist at Nagoya City University Graduate School of Medical Sciences in Nagoya, Japan, and the study's lead author. "Given the high mortality rate and the relatively low influenza vaccination rates in heart failure patients worldwide, our study supports a wider use of influenza vaccination in heart failure patients."

Researchers analyzed six studies conducted in the U.S., Europe and Asia that together included data for more than 78,000 patients with heart failure. Five of the studies were observational and one was a retrospective analysis of results from a clinical trial. The researchers found no randomized control trials designed specifically to investigate influenza vaccination in patients with heart failure.

Taken together, the studies showed that getting the flu vaccine reduced the risk of dying (from any cause) by about half during flu season and by about one-fifth during the rest of the year. Vaccination was also associated with a 22 percent reduction in the risk of being hospitalized for cardiovascular problems.

In the studies, the proportion of heart failure patients receiving the flu vaccine ranged from 26 to 86 percent, reflecting wide variability in vaccination rates among these patients. Researchers suggested this variability may be due to limited guideline recommendations for influenza vaccination in heart failure patients. While the Heart Failure Society of America recommends annual influenza vaccination in all heart failure patients who do not have known contraindications, the ACC/AHA and European Society of Cardiology guidelines do not make such specific recommendations for heart failure patients. The Centers for Disease Control and Prevention recommends that everyone age 6 months and older get a flu shot each year and encourages people with heart disease to stay current on immunizations and talk with their doctor.

The findings suggest influenza vaccination is beneficial for patients with heart failure, although researchers cautioned that while observational studies can show associations, they do not necessarily prove cause and effect.

"Randomized controlled studies should be planned to confirm our observed potential survival benefit of influenza vaccination in these patients," Fukuta said.

ACC2018特集

音楽は運動負荷試験中の運動時間を増加させる (Abstract 18-A-17200-ACC)

運動負荷試験中にアップビートの音楽を聴くことにより運動耐容能が増加する可能性がある

Listening to upbeat music may help improve exercise tolerance during cardiac stress test

通常の運動負荷試験中に音楽を聴くことにより、運動時間が延長し患者の心血管系の健康状態や運動耐容能の重要な情報が得られる可能性がある、とAmerican College of Cardiology's 67th Annual Scientific Sessionで発表された。今回の単一施設ランダム化研究において、音楽群ではコントロール群に比べ、有意に運動時間が長かった(505.8 vs. 455.2秒)－差の絶対値は約50.6秒。さらに、非音楽群に比べ有意ではないが代謝等量(METs)が大きい傾向にあった。

Full Text

If you exercise while listening to music, you may have noticed it can help boost your energy and make your workout seem quicker. Similarly, a study being presented at the American College of Cardiology's 67th Annual Scientific Session suggests listening to music during a standard cardiac stress test can help extend the time someone is able to perform the test, yielding important information about an individual's cardiovascular health and capacity for exercise.

Music can have a powerful impact on our mood, signaling the brain to release feel-good and energy-boosting chemicals. While earlier studies have looked at how music might influence specific markers of heart health, this study is the first to evaluate its impact on exercise tolerance during cardiac stress testing—widely used to measure the effects of exercise on the heart. On average, people who listened to music during the test were able to exercise for almost one minute longer than those who didn't have tunes playing in their ears.

"At least on a small scale, this study provides some evidence that music may help serve as an extra tool to help motivate someone to exercise more, which is critical to heart health," said Waseem Shami, MD, a cardiology fellow at Texas Tech University Health Sciences in El Paso, Texas, and the study's lead author. "I think it's something we intuitively knew, but we found [to be true]. I suspect if it had been a larger study, we'd see a bigger difference."

In this single-center, randomized study, patients scheduled for a routine electrocardiogram (ECG) treadmill stress test were informed about the study and asked if they would participate. A total of 127 patients (53 years of age on average) were randomly assigned to either listen to up-tempo music (mostly Latin-inspired music) or have no music playing during their stress tests. To "blind" the staff and clinicians, all participants wore headphones during their test. Individuals had similar medical histories, including diabetes and hypertension. The majority of participants were Hispanic, reflecting their patient population. There were more females than males in both groups (61.2 and 66.7 percent in the music and control groups, respectively).

Aside from introducing headphones to the test environment, the stress test was conducted as usual in the clinic. Researchers collected and analyzed demographic data (e.g., age, gender, medical history, social history), vital signs (e.g., blood pressure, heart rate) and treadmill end points (e.g., exercise time, maximum heart rate achieved, symptoms, etc.).

Shami explained that stress tests can be challenging—even painful—for some people because the treadmill speed and incline is increased every three minutes. In the standard Bruce protocol, the starting point (i.e., stage 1) is 1.7 mph at a 10 percent grade (5 METs). Stage 2 is 2.5 mph at a 12 percent grade (7 METs). Stage 3 is 3.4 mph at a 14 percent grade (9 METs). This protocol includes three-minute periods to allow achievement of a steady state before workload is increased.
"After six minutes, you feel like you are running up a mountain, so even being able to go 50 seconds longer means a lot," he said. Although the maximum duration for a stress test is 20 minutes, Shami said most healthy people usually last for seven to eight minutes.

Exercise time was significantly longer in the music group compared with the control group, 505.8 versus 455.2 seconds, respectively—an absolute difference of about 50.6 seconds. In addition, there was a (non-significant) trend toward longer metabolic equivalent of task (METs) when compared with the non-music group. A MET is a ratio of the rate of energy expended during an activity to the rate of energy used at rest. Generally, the higher the number, the more energy used and the harder someone worked.

There were no differences in how often patients were able to reach their maximal target heart rate goal between the two groups, which was one of the reasons Shami and team designed the pilot study.

Although the study involved people undergoing cardiac stress testing, Shami said he believes the findings could apply to a wider population and help motivate people to follow recommendations for regular exercise for heart health. Being inactive or not exercising ranks alongside high blood pressure, high cholesterol, smoking and obesity as one of the five major risk factors for cardiovascular disease.

"Our findings reinforce the idea that upbeat music has a synergistic effect in terms of making you want to exercise longer and stick with a daily exercise routine," he said. "When doctors are recommending exercise, they might suggest listening to music too."

Shami said a larger study with greater diversity is needed to be able to determine whether offering music during stress testing can help people achieve their target heart rate and if it should be recommended as a tool to help people.

ACC2018特集

がん治療は心不全リスクを上昇させる (Abstract 18-A-16407-ACC)

乳がんおよびリンパ腫の治療は生命を救うが心不全のリスクを上昇させる可能性がある

Breast cancer and lymphoma treatments save lives but may increase likelihood of heart failure

乳がんまたはリンパ腫の既往を有する患者は、がんを有さない同様の患者群に比べ、心不全発症リスクが3倍以上高かったとのデータが、American College of Cardiology's 67th Annual Scientific Session で発表された。この心不全リスク上昇は、がんの診断後1年ほどの早期に既に発現しており、がん治療終了後20年間持続する。がんを有する者のうち、糖尿病を有する者、または高用量のドキソルビシンを投与されている者は特に、将来の心臓の健康においてリスクが高いことが明らかにされた。

Full Text

Patients with a history of breast cancer or lymphoma were more than three times as likely to develop heart failure compared with a similar group of patients who did not have cancer, according to data being presented at the American College of Cardiology's 67th Annual Scientific Session.

A team of researchers at Mayo Clinic found the elevated risk of heart failure occurred as early as one year after cancer diagnosis and persisted 20 years after patients completed cancer therapy. Among those with cancer, having diabetes or receiving high doses of doxorubicin were found to be especially risky for future heart health.

The study, part of Mayo Clinic's Rochester Epidemiological Project, is one of the first to the researchers' knowledge to directly compare the rate of heart failure in cancer versus non-cancer patients who were well-matched for age, gender and heart disease risk factors, such as diabetes and high blood pressure. Researchers tracked heart failure cases in 1,550 people without cancer and in 900 breast cancer and lymphoma patients in Olmsted County, Minnesota, from 1985 to 2010. About 7 out of every 100 cancer patients developed heart failure during the median follow-up of 8.5 years. People with breast cancer or lymphoma were three times as likely to develop heart failure within five years of their cancer diagnosis, and 20 years following cancer treatment were still nearly twice as likely to have been diagnosed with heart failure compared to similar patients who didn't undergo cancer therapy.

"The risk of heart failure doesn't go away after a couple of years. It's a long-term issue that patients need to discuss with their doctors and use as motivation to stay heart healthy," said Carolyn Larsen, MD, assistant professor of medicine at Mayo Clinic and the study's lead author. "Cancer patients need to have good primary care and cardiology follow-up to make sure all of their risk factors for heart disease are optimally controlled. They should also be assessed for signs and symptoms of heart failure every year so that they can be diagnosed and started on appropriate medical treatment early on."

Among those who had cancer, some had a higher likelihood of facing a heart failure diagnosis than others. For example, when controlling for multiple heart disease risk factors (e.g., age, diabetes, high blood pressure), receiving higher doses of doxorubicin (≥ 300 mg/m^2) and diabetes emerged as the greatest risk factors in the studied population of cancer patients, more than doubling a patient's risk of heart failure. Larsen said additional research is needed to determine why diabetes carries a greater risk than other traditional risk factors, such as high blood pressure, in this group.

Anthracycline drugs, such as doxorubicin, are known to cause heart failure because they cause changes in the DNA structure of the heart muscle cells, leading to irreversible cardiac damage. The damage is related to the cumulative dose of these drugs patients receive over the course of their treatment. In order to reduce the risk of heart damage, clinicians today use the lowest effective dose of anthracyclines or avoid anthracyclines all together when other equally effective treatment options are available.

Still, Larsen said the findings raise important questions about what the appropriate surveillance should be for heart problems post-cancer treatment and suggested that more frequent cardiac imaging may be warranted in some patients to detect signs of heart failure earlier.

"It's an area that needs to be better defined. An echocardiogram is usually done six to 12 months after cancer treatment with an anthracycline, but how often should it be done after that?" she said, explaining there are many differing expert recommendations on the subject with opinions ranging from annually to only if signs or symptoms of heart failure develop. "We need to be more vigilant in making sure we try to prevent or control heart issues post-cancer care, especially in light of the growing appreciation of the connection between some cancer treatments and heart disease."

Larsen emphasized that heart failure is by no means inevitable in patients receiving chemotherapy treatment. One in 10 cancer patients were diagnosed with heart failure in the 20 years following their cancer diagnosis. Additionally, even with heightened risk, a heart healthy lifestyle—maintaining a normal body weight, regular exercise and controlling other risk factors such as high blood pressure, diabetes and high cholesterol—can help lower the risk of heart disease and heart failure.

"If patients know they have received a drug treatment that might increase their risk of heart failure, it's even more important to take care of the aspects of their life that they can control to reduce their risk as much as possible and to work with their medical care team to detect issues as early as possible," Larsen said.

This was a retrospective study and some patients moved away from Olmsted County during the study period, which may have led to underestimated rates of heart failure in cancer patients and non-cancer patients alike.

ACC2018特集

遺伝子型解析はPCI後の薬物選択において有益である (Abstract 18-LB-18910-ACC)

PHARMCLO：個別化遺伝子アプローチを用いた抗血小板薬選択は転帰を改善する

PHARMCLO: Personalized genetic approach to selecting antiplatelet drugs improves outcomes

抗血小板薬選択に遺伝情報を用いた急性冠症候群患者は、12か月後の心筋梗塞（MI）、脳卒中、心血管疾患による死亡および大出血の発現率が大幅に低かった、とAmerican College of Cardiology's 67th Annual Scientific Session で発表され、同時に*Journal of the American College of Cardiology* オンライン版に掲載された。12か月後、複合エンドポイントの発現率は標準治療群で25.9% であり、遺伝子検査を受けた群では15.8% であった（イベント42% 減）。遺伝子検査はまた、異なる処方パターンをもたらした。

Full Text

Patients with acute coronary syndrome experienced a substantially lower rate of myocardial infarction (MI), stroke, death from cardiovascular causes and major bleeding at 12 months if genetic information was used to inform the selection of their antiplatelet medication in a study presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Journal of the American College of Cardiology*.

To reduce the risk of future ischemic events caused by thrombosis, patients with acute coronary syndrome are prescribed a daily aspirin and one of several P2Y12 receptor antagonists. Three main P2Y12 receptor antagonists are available: clopidogrel, ticagrelor and prasugrel. Previous research has indicated that patients' genes can affect how well these different drugs work in individual patients.

The study, called PHARMCLO, is the first to combine clinical characteristics with genetic information to inform the choice of P2Y12 receptor antagonist in patients with acute coronary syndrome.

At 12 months, patients who received a genetic test to inform the choice of medication were 42 percent less likely to experience MI stroke or death from cardiovascular causes, or major bleeding (the trial's composite primary endpoint) compared with patients who did not receive the genetic test.

"Selecting treatment on the basis of genetic data in addition to considerations concerning the patients' clinical characteristics may lead to a more personalized, and therefore more efficient, antiplatelet therapy, thus reducing both ischemic and bleeding risk," said Diego Ardissino, MD, cardiologist at Azienda Ospedaliero-Universitaria di Parma, Italy, and the study's lead author. "PHARMCLO is the first step of a new approach that will see a shift in emphasis away from trying to discover ever more potent antithrombotic drugs and toward ensuring that the right therapy is given to each individual patient."

Researchers enrolled 888 patients hospitalized for acute coronary syndrome in Italy. Half were randomly assigned to receive standard clinical care, in which doctors prescribed clopidogrel, ticagrelor or prasugrel based on the patient's clinical characteristics alone. The other half were assigned to receive a genetic test, the results of which doctors considered, along with clinical characteristics, when prescribing antiplatelet therapy.

At 12 months, the trial's composite primary endpoint had occurred in 25.9 percent of patients receiving standard care and 15.8 percent of patients receiving the genetic test. Genetic testing also resulted in different prescribing patterns. While prasugrel was prescribed at similar rates in both groups, clopidogrel was prescribed significantly more frequently among those who did not receive a genetic test and ticagrelor was prescribed significantly more frequently among those who did receive a genetic test.

Previous studies have shown prasugrel and ticagrelor to be superior to clopidogrel at preventing ischemic events. However, prasugrel and ticagrelor, which are more potent, are also known to increase the risk of bleeding. The findings suggest that having more information about a specific patient's likely response to clopidogrel can help doctors weigh this trade-off.

Several genes have been shown to affect enzymes that make clopidogrel more or less effective in preventing platelet aggregation. For this study, researchers developed an easy-to-use genetic screening tool, ST Q3, that provides information about these genes from a blood sample in just 70 minutes.

"As genotyping to select P2Y12 receptor antagonists in the setting of acute coronary syndromes cannot be delegated to centralized genetic laboratories for reasons of time, we designed the ST Q3 instrument for bedside genotyping as a low-cost, portable system for foolproof use by unskilled personnel," Ardissinosaid.

Researchers suggest the study findings offer a proof of concept that personalized genetic information can be used to inform treatment decisions and improve outcomes for people with acute coronary syndrome.

Further research would be needed to confirm the findings and incorporate genotyping into clinical practice for this patient population.

The PHARMCLO study stopped recruiting patients early after the Ethics Committee of Modena (Italy) required the trial to be prematurely stopped due to the lack of in vitro diagnosis (IVD) certification for the ST Q3 instrument. All of the patients were followed up as planned.

The study was supported by Programma di Ricerca Regione-Università, Regione Emilia-Romagna, bando 2010 – 2012 Area 2 Ricerca per il Governo clinico, a program affiliated with Italy's regional health service.

ACC2018特集

3種の低用量内服は高血圧管理に成功した (Abstract 18-LB-18854-ACC)

TRIUMPH：3種の低用量内服は標準治療よりも血圧を低下させる

TRIUMPH: Triple low-dose pill lowers blood pressure more than usual care

3種の降圧薬の配合剤は標準治療よりも降圧目標を達成した患者数を有意に増加させた、とAmerican College of Cardiology's 67th Annual Scientific Session で発表された。TRIUMPHトライアルにおいて、6か月後の血圧低下は3種配合剤で平均8.7 mmHgであったのに対し、標準治療群では4.5 mmHgであった。3種配合剤群において、有意な副作用増加はなかった。この配合剤はテルミサルタン（20 mg）、アムロジピン（2.5 mg）およびchlorthalidone（12.5 mg）で構成される。

Full Text

A pill combining low doses of three blood pressure-lowering medications significantly increased the number of patients reaching blood pressure targets compared with usual care, researchers reported at the American College of Cardiology's 67th Annual Scientific Session. There was also no significant increase in adverse effects with the "Triple Pill."

"Most people — 70 percent —reached blood pressure targets with the Triple Pill. The benefits were seen straight away and maintained until six months, whereas with usual care control rates were 55 percent at six months and even lower earlier in the trial," said Ruth Webster, MBBS, of The George Institute for Global Health at the University of New South Wales in Sydney, Australia, and lead author of the study. "Based on our findings, we conclude that this new method of using blood pressure-lowering drugs was more effective and just as safe as current approaches."

Despite the availability of effective blood pressure-lowering drugs, hypertension remains a major problem around the world, Webster said. Effectively treating hypertension can help to prevent myocardial infarctions (MI), strokes and kidney problems. Globally, however, many people with high blood pressure receive no treatment, and only about a third of those who are treated achieve recommended reductions in blood pressure. Achieving desired reductions in blood pressure often requires treatment with more than one medication, which increases the complexity of treatment, and patients often have difficulty adhering to regimens that involve taking multiple pills every day.

This study was the first large trial designed to test the theory that starting treatment with low doses of three drugs could achieve better blood pressure control compared with usual care and that combining these drugs in a single pill would make it easier both for doctors to prescribe treatment and for patients to adhere to it, Webster said.

The TRIUMPH trial, which was conducted in Sri Lanka, enrolled 700 patients whose average age was 56 years, 58 percent of whom were women. Trial participants had an average blood pressure of 154/90 mmHg. Over half (59 percent) were receiving no treatment for high blood pressure before they enrolled in the trial. In addition to hypertension, 32 percent of participants had diabetes or chronic kidney disease.

Patients were randomly assigned to receive either the combination pill or usual care. The combination pill, or Triple Pill, consisted of the blood pressure medications telmisartan (20 mg), amlodipine (2.5 mg) and chlorthalidone (12.5 mg). These medications use different mechanisms to reduce blood pressure by relaxing the blood vessels, so the heart does not need to pump as hard to send blood throughout the body. Usual care meant that patients received their doctor's choice of blood pressure-lowering medication.

The trial's primary endpoint was the proportion of patients who achieved a blood pressure target of 140/90 mmHg or less (130/80 mm Hg or less in those with diabetes or chronic kidney disease) at six months.

Compared with patients receiving usual care, a significantly higher proportion of patients receiving the Triple Pill achieved their target blood pressure at six months. The average reduction in blood pressure was 8.7 mm Hg for participants receiving the Triple Pill and 4.5 mm Hg for those receiving usual care. At six months, 83 percent of participants in the Triple Pill group were still receiving the combination pill and one-third of those in the usual-care group were receiving at least two blood pressure-lowering drugs.

The maximum difference between the two groups of patients was observed at six weeks after starting treatment, when 68 percent of those receiving the Triple Pill had achieved a blood pressure within their target range, compared with 44 percent of those receiving usual care. This represented a 53 percent reduction in the risk for high blood pressure for patients receiving the Triple Pill, Webster said.

Rates of participants having to change treatment due to side effects were not significantly different in the two groups (6.6 percent for the Triple Pill, 6.8 percent for usual care). This should allay concerns that use of the three-drug combination pill could lead to an unacceptable increase in adverse medication side effects, Webster said.

Each of the drugs used in the Triple Pill has been shown to be highly effective in reducing blood pressure and preventing deaths and illness due to heart disease and strokes, she said. Each drug represents a different class of blood pressure medication and previous studies have shown that combining such drugs results in synergistic effects.

"The most urgent need for innovative strategies to control blood pressure is in low-and middle-income countries," Webster said. "The Triple Pill approach is an opportunity to 'leap frog' over traditional approaches to care and adopt an innovative approach that has been shown to be effective."

The study's findings are also important for high-income countries, she said. "A control rate of 70 percent would be a considerable improvement even in high-income settings. Most hypertension guidelines in these countries do not recommend combination blood pressure-lowering therapy for initial treatment in all people," she said. "Our findings should prompt reconsideration of recommendations around the use of combination therapy."

An inevitable consequence of a necessarily unblinded study is that doctors might manage patients differently depending on the assigned treatment. However, it is important to note this trial was designed to evaluate a new strategy of care in a real-world setting, Webster said.

To minimize the risk of bias in measuring the main outcomes, the number of patient visits was identical in both groups and all outcomes were standardized and objectively documented, she said.

The researchers are now conducting a follow-up qualitative study to find out what participants and their doctors thought about using the Triple Pill. And they are conducting a cost effectiveness evaluation to determine whether the Triple Pill is a cost-effective solution for blood pressure control.

The study was funded by the National Health and Medical Research Council of Australia as part of a Global Alliance for Chronic Disease.

ACC2018特集

ACSにおけるスタチンのローディングドーズ投与は臨床イベントリスクを減少させない(Abstract 18-LB-17893-ACC)

SECURE PCI：ACSを発症しPCIが予定されている患者に対する高用量スタチンローディングドーズ投与はMACEを減少させない

SECURE PCI: Large loading dose of statin does not reduce MACE in patients with ACS and planned PCI

経皮的冠動脈インターベンション（PCI）を予定されている広範な患者群に対する高用量スタチン投与は、主要心血管イベントに影響を及ぼさなかった、とAmerican College of Cardiology's 67th Annual Scientific Session で発表され、同時に*JAMA* オンライン版に掲載された。すべての患者における主要評価項目発現率は、スタチン内服群で6.2%、プラセボ内服群で7.1% であり、統計学的に有意差はなかった。しかし、実際にPCIを施行されたサブセットにおいて、スタチンはそれらイベント発現率を有意に低下させた（6.0 vs. 8.2%）。

Full Text

Getting a large dose of a statin did not have an impact on major adverse cardiac events among a broad population of patients slated to undergo percutaneous coronary intervention (PCI) in a trial presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Journal of the American Medical Association* (*JAMA*). However, statins did significantly reduce the rates of such events among the subset of trial participants who actually underwent PCI.

In this trial, patients were randomized to receive either a placebo or a "loading dose" of a statin, consisting of two double-doses administered the day before and the day after a scheduled PCI, followed by a daily low-dose of a statin for 30 days.

The trial is the largest study to date aimed at testing the hypothesis that statins could help reduce cardiovascular events around the time of PCI. More than 4,100 patients were enrolled in the trial at 58 centers in Brazil. All patients had acute coronary syndrome for which doctors planned to perform PCI within seven days. However, about one-third of the study participants ultimately did not receive PCI because doctors opted to perform other treatments, such as coronary artery bypass grafting.

Participants in this study were reflective of the broader population of people with acute coronary syndrome, and the study protocols were reflective of common hospital practices, said Otavio Berwanger, MD, PhD, cardiologist and clinical epidemiologist at the Brazilian Clinical Research Institute, Sao Paulo, Brazil, and the study's lead author. He suggested that the results would likely be applicable in many countries and health care environments.

About 70 percent of the patients had never taken statins and about 30 percent had taken them previously or were on low-dose statins when they enrolled in the study. Patients who were already taking a maximum tolerated dose of statins were excluded. In addition to their long-term preventive benefits, basic research suggests statins also may affect processes involved in inflammation and the formation of blood clots.

In this blinded study, half of the participants were randomly assigned to receive two double (80 milligram) doses of atorvastatin — one shortly before the procedure and one within a day afterward. The other half received two doses of a placebo. All patients then took 40 milligrams of atorvastatin daily for 30 days, which is standard practice after acute coronary syndrome. For 30 days, researchers tracked rates of major adverse cardiac events (the trial's primary endpoint), which included death, heart attack, stroke or urgent procedures to clear blocked arteries.

Among all patients, the primary endpoint occurred in 6.2 percent of those taking the statin and 7.1 percent of those taking the placebo, a difference that was not statistically significant. Among patients who received PCI, the primary endpoint occurred in 6 percent of those taking the statin and 8.2 percent of those taking the placebo, a reduction that was statistically significant.

"Although the trial is negative for our primary endpoint in the full study population, the findings of our prespecified analysis are very consistent with smaller trials and observational studies that suggest a reduction in events in the PCI population," Berwanger said. "Viewed in the context of the literature, our study helps to confirm what has been shown before and suggests that it can be beneficial to consider giving a loading dose of a statin to patients who undergo PCI."

Overall, patients who underwent PCI and received a loading dose of statins were 28 percent less likely to experience a major adverse cardiac event and 32 percent less likely to have a heart attack compared with those taking the placebo.

"This study adds another piece to the puzzle," Berwanger said. "I think it also opens the stage for testing other lipid-lowering agents that may have effects beyond lowering lipids."

Researchers will continue to track outcomes for 12 months. In addition, the team is planning another trial focused on assessing potential benefits of statins and other drugs in patients undergoing PCI.

The study was supported by a grant from the Brazilian Ministry of Health.

ACC2018特集

卵円孔開存患者においてデバイスが転帰を改善する (Abstract 18-LB-18898-ACC)

DEFENSE-PFO：デバイスによる閉鎖は潜在性脳卒中後の再発を予防する

DEFENSE-PFO: Device closure prevents secondary strokes after cryptogenic stroke

卵円孔開存（PFO）患者のうち、脳卒中後に開存閉鎖デバイスを植え込まれた者は、薬物療法のみの患者に比べ転帰が良好であった。この結果はAmerican College of Cardiology's 67th Annual Scientific Session で発表され、*Journal of the American College of Cardiology* に掲載された。オープンラベルトライアルであるDEFENSE-PFOにおいて、PFO患者120人がカテーテルによる経皮的PFO閉鎖術と薬物療法の併用、または薬物療法単独群にランダムに割り付けられた。2年間の追跡調査中に、主要評価項目を発現した者は閉鎖術併用群ではいなかったが、薬物療法単独群では6人（13.0%）であった（p=0.013）。

Full Text

Among people with a patent foramen ovale (PFO), those who received a medical device to close this opening after a stroke fared better after two years compared with those who received stroke-preventing medications alone. These findings from a study presented at the American College of Cardiology's 67th Annual Scientific Session and support the results of several similar trials in recent years and suggest patients with a high-risk PFO are likely to benefit most from the device. This study was simultaneously published online in the *Journal of the American College of Cardiology* at the time of presentation.

An estimated 1 in 4 people have a PFO, though many are undiagnosed. The condition does not typically cause symptoms but may increase the risk of stroke.

Among patients younger than 55 years of age who experience a cryptogenic stroke the prevalence of PFOs has been found to be around 46 percent, much higher than the rate of PFOs in the general population. The new findings add to a growing body of evidence that closing the PFO after this type of stroke can help prevent subsequent strokes and related problems, particularly in those with a high-risk PFO.

Researchers stopped enrollment for the trial early after determining, based on the results of several recent trials, that it would be unethical to continue assigning some patients to not receive the PFO closure device in light of mounting evidence of its clear benefits. Despite the smaller-than-expected number of participants, researchers said the new trial helps clarify which patients are likely to benefit most from the medical device based on the physical characteristics of their PFO.

"Considering the high prevalence of PFO in the general population and cryptogenic stroke patients, the key to appropriate use of this medical device is determining how to select optimal candidates for the procedure," said Jae Kwan Song, MD, a cardiologist at Asan Medical Center in Seoul, South Korea and the study's lead author. "Our study showed that the potential benefit from closure can be determined on the basis of the size of the PFO and the movement of the heart wall around the PFO."

In the open label, DEFENSE-PFO trial, 120 patients with PFO were randomized to receive transcatheter PFO device closure plus medical therapy (n=60) or medical therapy alone (n = 60). High-risk PFO was defined as PFO with atrial septal aneurysm, hypermobility or PFO size ≥2 mm. Medical therapy included anticoagulants or antiplatelet drugs as determined by the patients' physicians. No direct oral anticoagulants were used in the study. The primary endpoint was a composite of stroke, vascular death or TIMI-defined major bleeding during the two-year follow-up.

Researchers followed patient outcomes for two years. The study's primary endpoint was a composite of stroke, major bleeding events and death from vascular causes.

No primary endpoint events occurred in the device closure group during follow-up, compared with six events (2-year event rate, 13.0 percent; standard error, 5.0) in the medical therapy alone group (log-rank p = 0.013). Transient ischemic attack was reported in one patient receiving medical therapy alone. Procedural complications in the device closure group included atrial fibrillation (n=2), pericardial effusion (n=1) and puncture site reaction (n=1).

"We believe that PFO closure should be done in selected patients with cryptogenic stroke and PFO," Song said. "With our study and other recent trials, the criteria for selecting patients for the procedure are becoming clearer; in particular, the results suggest that closure is beneficial for those with high-risk PFO."

There are several available medications to prevent blood clots in people who have experienced a stroke, including antiplatelet drugs, direct oral anticoagulants and traditional anticoagulants such as warfarin. Because trials for PFO closure devices have been inconsistent in their selection of medications, Song said additional studies are needed to clarify the potential benefits of different medications when used post-stroke in patients with PFO.

The trial was supported by a research grant from the Cardiovascular Research Foundation (CVRF) in Seoul, South Korea.

ACC2018特集

ダビガトランは非心臓手術後の心筋障害を軽減する (Abstract 18-LB-18909-ACC)

MANAGE：非心臓手術後にダビガトランを投与された患者において死亡率および心血管イベント発現率は低下する

MANAGE: Reduced mortality and cardiovascular events in patients receiving dabigatran after noncardiac surgery

死亡、心筋梗塞（MI）、脳卒中およびその他の心臓または血管合併症の高リスク患者において、抗凝固薬ダビガトランによる治療は非心臓大手術後に発現する心損傷によるこれらのリスクを有意に軽減させた、とAmerican College of Cardiology's 67th Annual Scientific Session で発表された。平均追跡期間16か月後、1つ以上の主要評価項目を発現した患者は、ダビガトラン投与患者の11.1% に対し、プラセボ投与患者では15.2% であった。この結果は、ダビガトラン投与患者においてリスクが28% 低下したと解釈される。

Full Text

Treatment with the anticoagulant dabigatran significantly reduced the risk of death, myocardial infarction (MI), stroke and other heart or blood-vessel complications among patients who were at elevated risk for these events because of heart damage that occurred after major noncardiac surgery, according to research presented at the American College of Cardiology's 67th Annual Scientific Session.

In the first randomized controlled trial to evaluate a treatment for a condition dubbed myocardial injury after noncardiac surgery (MINS), researchers found that patients treated with dabigatran twice daily were 28 percent less likely to die, have a myocardial infarction or stroke, develop blood clots or need an amputation due to cardiovascular disease, compared with patients who received a placebo.

"We have shown for the first time that dabigatran reduces the risk of major cardiovascular complications and offers an option for improving outcomes in a large at-risk population who have MINS," said P.J. Devereaux, MD, PhD, director of cardiology at McMaster University in Hamilton, Canada, and lead author of the study.

Approximately 8 million people every year develop MINS after undergoing surgery such as a hip or knee replacement, bowel resection or abdominal aortic aneurysm repair. This study builds on research that Devereaux and his colleagues presented at the American College of Cardiology's 66th Annual Scientific Session in 2017 showing that MINS may account for about 1 in 4 deaths during the first 30 days after surgery. That research also showed a blood test for high-sensitivity troponin T, which is released into the bloodstream when injury to the heart occurs, can identify patients with MINS whose lives could potentially be saved with timely treatment.

MANAGE was a large international, double-blind study, in which 1,754 patients with MINS were randomized to receive dabigatran 110 mg twice daily or matching placebo. The patients received dabigatran for a maximum of two years and a minimum of four months. The primary efficacy endpoint was a major vascular complication – a composite of vascular mortality and MI, nonhemorrhagic stroke, peripheral arterial thrombosis, amputation and symptomatic venous thromboembolism. The primary safety endpoint was a composite of life-threatening bleeding, major bleeding and critical organ bleeding.

Most cases of MINS currently go undetected, Devereaux said, because at present it is not standard practice in most centers to monitor blood levels of troponin in patients who had major noncardiac surgery. Devereaux said he is hopeful this will change now that this study has shown treatment with dabigatran can improve outcomes for patients with MINS. "Our findings reaffirm that patients who develop MINS are at high risk for bad outcomes," he said. "We owe it to our patients to identify this risk and do what we can to reduce it."

The study enrolled 1,754 patients in 19 countries, 51percent of whom were men, with an average age of 70 years. The primary efficacy outcome was the combined rate of death from a cardiovascular cause, myocardial infarction (MI), stroke due to inadequate blood supply, blood clots or amputation due to cardiovascular disease. The primary safety outcome was the combined rate of life-threatening, major and critical organ bleeding.

During the study, patients, health care providers and research staff were blinded to which group received dabigatran and which received a placebo. After an average follow-up of 16 months, 11.1 percent of patients treated with dabigatran experienced one or more of the primary efficacy outcome events, compared with 15.2 percent of patients who received a placebo. This translates to a 28 percent reduction in risk for patients receiving dabigatran.

When researchers analyzed occurrence rates for the events comprising the primary efficacy outcome, they found trends of benefit for each component. For example, patients treated with dabigatran were 20 percent less likely to die of a cardiovascular cause, 20 percent less likely to have an MI, 30 percent less likely to have an amputation and 53percent less likely to have a venous blood clot than patients who received a placebo.

The result for nonhemorrhagic stroke also demonstrated a benefit with an 80 percent reduction in risk, a difference that was statistically significant compared with patients who were randomized to placebo. There were no statistically significant differences between the two groups in life-threatening, major or critical organ bleeding.

Compared with the placebo group, however, more patients in the dabigatran group experienced bleeding in the lower gastrointestinal tract and minor bleeding.

"It's encouraging that we did not see an increase in major or life-threatening bleeding in patients on dabigatran," Devereaux said.

Researchers noted that while nearly all patients (98.9 percent) completed follow-up, 45.3 percent of those on dabigatran had discontinued the study drug. The most common reason for drug discontinuation was patient request; however, 14percent of these patients had a major complication (e.g., MI, stroke, bleeding).

According to Devereaux, analyses that counted patients up to seven days after they discontinued the study drug showed even larger treatment effects, with 46 percent reductions in major cardiovascular complications with dabigatran and no excess of life-threatening, major or critical organ bleeding.

Devereaux said that future research is needed to evaluate other treatment options for this high-risk group of patients.

The study was funded by grants from Boehringer Ingelheim and the Canadian Institutes of Health Research.

ACC2018特集

短期抗血小板薬2剤併用療法はMIリスクを上昇させる (Abstract 18-LB-18938-ACC)

SMART-DATE：6か月間の抗血小板薬2剤併用療法により心筋梗塞が増加する

SMART-DATE: Myocardial infarction increases with six-month dual antiplatelet therapy

薬剤溶出性ステント植え込み後、6か月または最低12か月の抗血小板薬2剤併用療法（DAPT）にランダムに割り付けされた急性冠症候群（ACS）患者において、18か月以内の総死亡、心筋梗塞（MI）または脳卒中の複合発現率には有意差がなかった。しかし、DAPTを6か月しか施行されなかった患者は、12か月以上継続した患者に比べMIリスクが2倍以上高かった、とAmerican College of Cardiology's 67th Annual Scientific Session で発表され、同時に*Lancet* に掲載された。

Full Text

The combined rate of death from any cause, myocardial infarction (MI) or stroke within 18 months was not significantly different in patients with acute coronary syndrome (ACS) who were randomly assigned to receive dual antiplatelet therapy (DAPT) for either six months or at least 12 months after receiving a drug-eluting stent. Patients who were given DAPT for only six months, however, had more than double the risk of an MI compared with those treated for at least 12 months, according to research presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Lancet*.

"Based on our findings, we can't say that short-term DAPT is safe in patients with ACS who have received drug-eluting stents," said Hyeon Cheol Gwon, MD, a professor in the Division of Cardiology at Sungkyunkwan University, director of the cardiac center at Samsung Medical Center in Seoul, South Korea, and principal investigator of the study. "We conclude that current guidelines that recommend prolonged DAPT in patients with ACS who are not at excessive risk for bleeding should continue to be followed."

Current guidelines published by the American College of Cardiology and the American Heart Association recommend that ACS patients not at excessive risk for bleeding should be treated with DAPT — aspirin plus clopidogrel or a similar drug such as ticagrelor — for at least 12 months after the implantation of a drug-eluting stent. However, there is limited evidence that12 months or more is the optimal duration for DAPT, Gwon said.

Two recently reported studies suggested that six months of DAPT might offer similar benefits in terms of reducing patients' risk for death, myocardial infarction (MI) or stroke, bleeding or other adverse events. These studies, however, had too few participants to provide definitive answers, he said. "This is the largest trial to address the optimal duration of DAPT in patients with ACS," Gwon said.

The SMART-DATE trial enrolled a total of 2,712 Korean patients with ACS who were undergoing angioplasty. Their median age was 63 years, and 75 percent were male. Patients were randomly assigned to receive either DAPT for at least 12 months (DAPT-12) or DAPT for six months followed by aspirin alone for at least another six months (DAPT-6). The primary endpoint was the combined rate of death from any cause, MI or stroke within 18 months after stent insertion.

At 18 months, 63 patients (4.7 percent) in the DAPT-6 group and 56 patients (4.2 percent) in the DAPT-12 group had experienced at least one of the primary endpoint events. Thus, over the entire 18-month follow-up period, DAPT-6 was significantly not worse (or non-inferior) than DAPT-12, Gwon said.

Rates of death from any cause were not significantly different in the two groups (2.6 percent in the DAPT-6 group vs 2.9 percent in the DAPT-12 group). However, the risk of heart attack was 2.4-fold higher in the DAPT-6 group, with MIs occurring in 1.8 percent of DAPT-6 patients vs. 0.8 percent of DAPT-12 patients.

Moreover, during the period between six and 18 months after stent insertion when patients in the DAPT-6 group were being treated with aspirin only, there was a 5.1-foldrisk of having an MI in DAPT-6 patients compared with DAPT-12 patients.

During this period, patients in the DAPT-6 group also had a 69 percent higher risk of dying from any cause or having an MI or stroke.

Limitations of the study, Gwon said, include the absence of blinding — that is, both patients and doctors knew whether a patient was in the DAPT-6 or the DAPT-12 group — and the absence of a group that was randomly assigned to receive a placebo. However, study statisticians and those whose role was to assess outcomes worked independently from those overseeing the trial, he said.

Patients in the trial will be followed for an additional 18 months, for a total of three years of follow-up, Gwon said.

The study was funded by Abbott Vascular Korea, Medtronic Vascular Korea, Biosensors Korea and Dong-A ST, a Korean pharmaceutical company.

ACC2018特集

薬剤が第Xa因子阻害効果をリバースする (Abstract 18-LB-19397-ACC)

ANNEXA-4：Andexanetは第Xa因子阻害薬内服患者の止血を達成する

ANNEXA-4: Andexanet achieves hemostasis in patients taking Factor Xa inhibitors

治験薬andexanetが第Xa因子阻害薬として知られる一般的な抗凝固薬を内服している患者の重篤な出血を制御できた、とAmerican College of Cardiology's 67th Annual Scientific Session で発表された。中間解析の結果、第Xa因子阻害活性中央値がリバーロキサバン内服患者で88%、アピキサバン内服患者で91%、およびエノキサバン内服患者で75%、それぞれ低下したことが示された。エドキサバン内服患者は、今回のスタディでは非常に少数であった。臨床的に非常に良好、あるいは良好に止血が達成できたのは、患者全体の83% であった。承認されれば、andexanetは出血時に第Xa因子の効果を直接リバースできる初めての薬剤となるであろう。

Full Text

The experimental drug andexanet was associated with control of serious bleeding in patients taking a common class of anticoagulants known as Factor Xa inhibitors, according to interim clinical trial results presented at the American College of Cardiology's 67th Annual Scientific Session.

Millions of patients take Factor Xa inhibitors, which elevate the risk of serious bleeding. If approved, andexanet would be the first agent available to directly reverse the effects of Factor Xa inhibition if bleeding occurs.

Factor Xa inhibitors, which inhibit a protein involved in the formation of blood clots, are commonly prescribed for patients who are at high risk for stroke and venous thrombosis. Because Factor Xa inhibitors and other anticoagulants reduce the body's ability to form a blood clot, these drugs can also increase the risk of uncontrolled bleeding. When this happens, it can be challenging for doctors to stop the bleeding and can ultimately lead to death. For example, about 25 percent of patients who experience bleeding in the brain while taking a Factor Xa inhibitor die.

"Unlike for some other anticoagulants, there is currently no approved reversal agent for Factor Xa inhibitors," said Stuart Connolly, MD, professor of medicine at McMaster University in Canada and the study's lead author. "Factor Xa inhibitors are already widely used because of their excellent efficacy and safety profile. However, some physicians and patients may choose to use other anticoagulant drugs because they have a reversal agent rather than using one of the Factor Xa inhibitors. Having a safe and effective reversal agent available will benefit patients with acute bleeding."

Of the people currently taking Factor Xa inhibitors, most are older and have illnesses, such as heart failure, that put them at high risk for cardiovascular problems. According to a recent analysis of the MarketScan Commercial and Medicare databases, roughly 84,000 patients taking Factor Xa inhibitors are hospitalized for major bleeding each year. The most common types of major bleeds include bleeding in the brain, sometimes resulting from a fall, and gastrointestinal bleeding. Andexanet is a recombinant modified Factor Xa molecule designed to bind to and disable Factor Xa inhibitors, thereby allowing Factor Xa produced by the body to play its normal role in the formation of blood clots.

In earlier trials performed in healthy volunteers, andexanet was shown to rapidly reverse the anticoagulant effect of Factor Xa inhibitors without any significant safety problems. ANNEXA-4 is an ongoing clinical trial that uses andexanet to help treat patients experiencing major bleeding while taking Factor Xa inhibitors.

The interim analysis being reported at ACC.18 includes data on safety outcomes for 227 patients and adjudicated efficacy outcomes for 132 patients enrolled at centers in the U.S., Canada and Europe. All trial participants presented with acute major bleeding within 18 hours of taking one of four Factor Xa inhibitors (apixaban, rivaroxaban, edoxaban or enoxaparin).

Patients received an injection of andexanet followed by a two-hour infusion of the drug, with the dosage determined based on the specific Factor Xa inhibitor the patient was taking and how long it had been since the last dose.

The trial assesses the drug's efficacy in terms of two co-primary endpoints: reduction in anti-Factor Xa inhibitor activity and achievement of clinical hemostasis by 12 hours after administration. The interim results show that median anti-Factor Xa inhibitor activity was reduced by 88 percent for patients taking rivaroxaban, 91 percent for patients taking apixaban and 75 percent for patients taking enoxaparin. Very few patients in the study had received edoxaban.
Excellent or good clinical hemostasis was achieved in 83 percent of patients overall.

Safety of andexanet was assessed in all 227 patients. At 30 days, 12 percent of patients had died and 11percent had a thrombotic event (stroke, myocardial infarction or peripheral blood clot).

According to Connolly, these rates of adverse events are in line with what would be expected given the underlying medical condition of the patients in the trial and the fact that many had not resumed anticoagulant treatment during the 30 days after receiving andexanet.

"This study is only focused on patients who are acutely bleeding, but there is also great interest in using a drug like andexanet for patients who come into a medical center on a Factor Xa inhibitor and require urgent surgery," Connolly said. "We hope to study that patient population in the future."

ANNEXA-4 is a single-arm study and does not include any patients who were not given andexanet. Although a randomized controlled trial offers potentially stronger evidence than a single-arm study design, this method was deemed to be impractical because the drug is intended to be used during crisis situations, demanding a speed of response that could be difficult to achieve with randomization protocols.

The trial was funded by Portola Pharmaceuticals Inc., maker of andexanet.

ACC2018特集

Canakinumabは糖尿病への進行を予防しない (Abstract 18-LB-18790-ACC)

CANTOS：心血管系には有益であるものの、抗炎症薬は糖尿病発症予防には効果がない

CANTOS: Despite cardiovascular benefits, anti-inflammatory drug does not impact onset of diabetes

前糖尿病の人々において抗炎症薬は糖尿病の新規診断率には効果がない、とAmerican College of Cardiology's 67th Annual Scientific Session で発表され、同時に*Journal of the American College of Cardiology* オンライン版に掲載された。糖尿病の進行予防には効果はなかったが、抗炎症薬を内服した前糖尿病の人々においては、高感度C反応性蛋白（hsCRP）およびインターロイキン6などの主要な炎症マーカーの有意な低下が認められた。この研究は、心筋梗塞歴を有しhsCRP上昇を認める患者において、canakinumabが主要な心血管イベントを有意に減少させたことを報告した大規模トライアルであるCANTOSスタディの、重要な副次的評価項目である。

Full Text

The anti-inflammatory drug canakinumab had no effect on rates of newly diagnosed diabetes in people who had prediabetes according to research presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Journal of the American College of Cardiology*. The research is a key secondary endpoint from the CANTOS study, a large trial that last year reported canakinumab significantly reduced major adverse cardiovascular outcomes (the trial's primary endpoint) in patients with a history of myocardial infarction and elevations in the inflammatory marker high-sensitivity C-reactive protein (hsCRP).

Since diabetes is thought to be related to inflammatory processes like those involved in heart disease, researchers hypothesized that the drug may help slow or prevent the progression from prediabetes to diabetes.

Patients with prediabetes at the start of the study initially showed a reduction in blood sugar levels (as indicated by a drop from 5.8 to 5.6 in median hemoglobin A1c, a measure of average blood sugar over the previous three months) after six months of taking canakinumab. However, this effect disappeared after about nine months and these patients were ultimately diagnosed with diabetes at a rate comparable to those who received a placebo.

"The results were surprising, because we demonstrated there was an effect on blood glucose that didn't translate into a reduced rate of Type 2 diabetes diagnosis," said Brendan Everett, MD, a cardiologist at Brigham and Women's Hospital, assistant professor of medicine at Harvard Medical School and the study's lead author. "It suggests that alternative inflammatory pathways may be more critical to the development of diabetes than inhibition of interleukin-1 beta, which was the specific mechanism we tested in this study."

Canakinumab is designed to disable interleukin-1 beta, a protein that plays a role in inflammation. The drug is approved for several autoimmune disorders and is being investigated for the management of heart disease.

The CANTOS trial enrolled more than 10,000 patients. Of those, about 4,000 had diabetes at the start of the trial and 1,000 had normal blood glucose levels. The new analysis focuses on the remaining 4,960 patients, who had prediabetes at the start of the trial. In general, people with prediabetes are likely to progress to diabetes unless they adopt substantial lifestyle changes such as losing weight and getting more exercise.

Participants were randomly assigned to receive either a placebo or canakinumab in one of three dosing levels (50, 150 or 300 milligrams per dose). Patients were given injections of the drug (or placebo) every three months for a median of more than 3.5 years. After the study ended and all participants stopped receiving injections, researchers continued to follow those who had prediabetes at baseline for an additional six months.

While there was no effect on diabetes progression, patients with prediabetes showed significant reductions in two major markers of inflammation, hsCRP and interleukin-6. They derived the same benefits from canakinumab as other patients in the study in terms of cardiovascular outcomes, including reduced rates of myocardial infarction, stroke and death from cardiovascular causes.

"Canakinumab is an effective therapy to prevent major cardiovascular events in patients with and without diabetes," Everett said. "It seems to prevent cardiovascular events without increasing the development of Type 2 diabetes among patients who are at risk for the disorder."

In a secondary analysis, the investigators examined the effect of canakinumab on blood glucose in patients with diabetes at the start of the study. In these patients, canakinumab led to similar changes in glucose levels as was seen in patients with prediabetes. However, patients assigned to take canakinumab still required a similar number of diabetes medications, including insulin, as the patients taking the placebo.

One potential area for future research could be to investigate whether canakinumab may contribute to glucose management among people who already have Type 2 diabetes.

The trial was funded by Novartis Pharmaceuticals, maker of canakinumab.

ACC2018特集

MI後のチカグレロル使用の安全性はクロピドグレルと同等である(Abstract 18-LB-17918-ACC)

TREAT：効果的で即効性のある抗血小板薬は線溶療法を施行された患者の出血リスクを上昇させない

TREAT: Potent, fast acting anticoagulant does not raise risk of bleeding in those taking fibrinolytic therapy

心筋梗塞治療目的で線溶療法を施行された75歳未満の患者において、より効果的な抗血小板薬チカグレロルは標準的な抗血小板薬クロピドグレルと比較し、大出血（主要評価項目）のリスクを上昇させなかった、とAmerican College of Cardiology's 67th Annual Scientific Sessionで発表され、同時に*JAMA Cardiology* オンライン版に掲載された。TIMI出血基準の大出血は両群ともに約0.7% の患者に発現し、二群間に統計学的有意差はなかった。今回の新たなスタディと過去のスタディとの大きな違いは、患者が線溶療法を受けていたことである。

Full Text

Among people younger than 75 years who were given fibrinolytic agents to treat a myocardial infarction (MI), taking the more potent blood thinner ticagrelor did not increase the risk of major bleeding (the primary endpoint) compared with the standard blood thinner clopidogrel, in a trial presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in *JAMA Cardiology*.

The results align with those of previous studies assessing ticagrelor's safety. However, a key difference between the new study and earlier ones is that participants were taking fibrinolytic therapy. These new findings suggest ticagrelor, which reduces clotting by preventing platelet aggregation, is safe to use in combination with fibrinolytics, at least in patients younger than 75, researchers said.

The trial was conducted in 10 countries on five continents: Australia, New Zealand, Argentina, Russia, China, Canada, Peru, Brazil, Colombia and Ukraine.

"This is the first large, international trial of ticagrelor in STEMI patients taking fibrinolytic therapy," said Otavio Berwanger, MD, PhD, cardiologist and clinical epidemiologist at Brazilian Clinical Research Institute, Sao Paulo, and the study's lead author. "I think doctors, some of whom are already using ticagrelor off-label, will find the results reassuring because they suggest that you can use ticagrelor in this population without causing more major bleeding or fatal bleeding than clopidogrel."

The trial enrolled 3,800 patients treated for STEMI at more than 180 centers. All patients had received fibrinolytic therapy within 24 hours of their MI. Half of the participants were randomly assigned to take ticagrelor and half took clopidogrel. Patients were given an initial loading dose of their assigned drug and then continued taking the drug for 12 months. After 30 days, the researchers assessed rates of major bleeding events in both study groups using the criteria defined by the Thrombolysis in Myocardial Infarction (TIMI) score, the standard tool used to score bleeding severity.

TIMI-scored major bleeding occurred in roughly 0.7 percent of patients in each group, with no statistically significant difference between the two groups. Thus, the trial met its primary endpoint indicating that ticagrelor is not inferior to clopidogrel in terms of major bleeding at 30 days.

The researchers also found no difference between the study groups in terms of rates of major bleeding according to two other sets of criteria, BARC (Bleeding Academic Research Consortium) and PLATO (Study of Platelet Inhibition and Platelet Outcomes), as well as rates of fatal bleeding and bleeding in the brain. They did observe a significantly higher rate of minor bleeding among patients receiving ticagrelor, which was expected because ticagrelor is a more potent blood thinner.

Researchers will track cardiovascular outcomes for 12 months and plan to report in 2019 on how well each drug performs in preventing major adverse cardiovascular outcomes.

"For patients who may be resistant to clopidogrel, or for those in whom it may be desirable to use the more potent drug, at least from our results doctors can know it is safe to do so," Berwanger said. "However, we will have to wait until next year to assess efficacy."

The risk of bleeding increases with age. Because the new trial was restricted to patients younger than 75 years, Berwanger noted that the findings may not apply to older adults.

The trial was funded by AstraZeneca, maker of ticagrelor.

ACC2018特集

積極的なモニタリングはAFibの診断率を3倍に上昇させる (Abstract LB-18937-ACC)

mSToPS：自己装着胸部パッチは一般的な不整脈を従来の方法よりもより迅速に捕捉できる

mSToPS: Self-applied chest patch catches common irregular heartbeat more quickly than usual care

心房細動（AFib）が高リスクの人々において、心調律を記録する着用型自己装着胸部パッチは、従来の方法に頼るよりも不整脈の検出に優れより迅速な治療を促進する可能性があるとの1年間のデータが、American College of Cardiology's 67th Annual Scientific Session で発表された。mHealth Screening to Prevent Strokes (mSToPS) トライアルの対象患者は心電図を持続的に記録するパッチを装着し、その結果研究者らは連続14日間のデータを得ることができた。AFibは、装着型パッチ群の6.3% およびコントロール群の2.3% において新たに診断された。パッチを用いた積極的なモニタリングにより、抗凝固薬開始率が有意に高まった（5.4% vs. 3.4%）。

Full Text

For people at heightened risk for atrial fibrillation (AFib), wearing a self-adhering chest patch that records heart patterns may better detect the condition and facilitate more timely treatment than relying on usual care, according to one-year data presented at the American College of Cardiology's 67th Annual Scientific Session.

The study, called the mHealth Screening to Prevent Strokes (mSToPS) trial, is one of the first completely digital, nationwide, direct-to-participant and site-less clinical research programs, according to researchers. Patients consented and enrolled exclusively via a web-based platform to undergo active monitoring at home using the iRhythm Zio patch. The patch–about the size of a large Band-Aid – continuously records an electrocardiogram (ECG), the gold standard for detecting AFib. But instead of only providing a brief snapshot of someone's heart rhythm – which is often the case with an ECG in the clinic – this technology allowed researchers to collect 14 consecutive days of data capturing the electrical activity of an individual's heart.

"At one year, people who wore the chest monitor had nearly three times the likelihood of being diagnosed with AFib appropriately. A significantly higher proportion of these patients were started on anticoagulant therapy to lower their stroke risk compared with those who received usual care," said Steven R. Steinhubl, MD, director of digital medicine, Scripps Translational Science Institute, La Jolla, California and lead author of the study. "The data also provide a first glimpse into how this type of ECG screening might influence heart care utilization."

People with AFib have a fivefold greater chance of having a stroke than the general population. New estimates suggest that 37 percent of adults over 55 years of age will develop AFib. But Steinhubl said as many as 1 out of 3 patients may be undiagnosed and, therefore, remain susceptible to stroke.

"A stroke is a very devastating cardiovascular complication of AFib; it can be tragic for patients and costly for payers," Steinhubl said. "If we identify and get these people on a blood thinner, we can reduce their risk of stroke by about 70 percent, which is powerful."

The mSToPS trial enrolled and monitored a total of 1,732 eligible Aetna patients with no heart rhythm issues but who were at moderate risk for AFib (median CHA2DS2-VASc score of 3) and matched them (2:1) to 3,646 observational controls of similar age, sex and risk profiles who received usual care only; all were included in the analysis. The average patient age was 73.7 years.

Once enrolled, participants in the active monitoring group received the wearable chest patch by mail and were given clear written and video instructions on how to use and place the wearable patch. Participants wore it for an average of 12 days and then returned it with a prepaid shipping envelope. The data collected from the patch, currently only U.S. Food and Drug Administration-approved for clinical use, are first analyzed with an algorithm that reads the ECG and preliminarily identifies all rhythm abnormalities, including AFib. In the trial analyses, a clinician and a clinical events committee read all potential diagnoses of AFib in a blinded fashion and either agreed or disagreed. All participants received their ECG study report. Researchers also collected and analyzed use of AFib-related medications, doctor and emergency department (ED) visits, and cases of blood clots and stroke.

The primary endpoint was the incidence of AFib at one year. AFib was newly diagnosed in 6.3 percent of those wearing the patch and 2.3 percent of controls. Compared with controls, participants who wore the chest patch had significantly more primary care physician visits (78.7 vs. 75 percent,) and cardiology outpatient visits (31.6 vs. 23.6 percent), but no difference in ED visits or hospitalizations. Relative to controls, active monitoring with the patch was associated with significantly greater initiation of anticoagulation (5.4 vs. 3.4 percent) and small but statistically significant increases in antiarrhythmic therapy (0.8 vs. 0.3 percent) and pacemaker or implantable cardioverter-defibrillator placement (0.7 vs. zero percent). Researchers were unable to show that the intervention had an impact on clinical outcomes, including blood clots or stroke, given the short follow-up (eight months on average). Study participants will be followed for another two years to track these events.

Still, Steinhubl said the findings demonstrate a feasible, scalable and clinically valuable way of screening for undiagnosed AFib in an at-risk, nationwide population.

"The quality of data collected through the patch is as good as what we see clinically," he said. "What was fascinating is that for the people with AFib, the burden of AFib (the amount of time a person was in AFib relative to their entire monitoring time) was quite low – approximately 1 percent of the time on average." This finding that suggests the prevalence of undiagnosed AFib is likely higher than clinicians might suspect, since it can be easy to miss, which could have important implications for how we should ideally screen for the condition.

"In most cases, the only currently recommended method is to feel someone's pulse or check an ECG for 30 seconds during a routine doctor's visit," Steinhubl said. "Based on our data, individuals have very short episodes of AFib that would make it very difficult to catch in the way we routinely look for it today."

Increasing age is by far the biggest risk factor for AFib, but heart failure, prior stroke and sleep apnea are all additional important risk factors. Steinhubl stressed that one of the most unique and valuable aspects of the study is how it was designed and conducted, including an emphasis on being more participant-centric. Using digital technology, the study was brought directly to the participants, even participants who were 74 years old on average.

"Currently, most people who are able to take part in clinical research live close to academic medical centers," he said. "In a way, mSToPS is proof of principle that site-less trials are possible and might open up clinical research to anybody, anywhere who is interested in taking part."

Researchers will continue to follow participants for another two years to assess any differences in reports of strokes or other systemic thromboemboli.

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ACC2018特集

化学療法による心毒性の軽減 (Abstract 18-LB-18940-ACC)

一部の乳がん患者に対しハーセプチンによる心血管系障害を一般的な心臓治療薬で予防できる

Popular heart medications can prevent Herceptin-induced cardiovascular issues for certain patients with breast cancer

心血管障害と関連があるとされている分子標的薬トラスツズマブの内服開始と同時に、よく知られる2つの心臓治療薬のうちの1つを内服し始めた乳がん患者は、心機能低下予防の面では恩恵がなかった、とAmerican College of Cardiology's 67th Annual Scientific Session で発表された。しかし、トラスツズマブにアントラサイクリン系薬剤ベースの化学療法を同時併用された患者では、ACE阻害薬リシノプリルまたはβ遮断薬カルベジロールを内服している患者においてプラセボ内服患者に比べ2年後の追跡時の心障害発現が半分であった。

Full Text

Breast cancer patients who started taking one of two well-known heart medications at the same time they initiated trastuzumab — a targeted cancer therapy that has been linked to cardiotoxicity — received no benefit in terms of preventing declines in heart function, according to research presented at the American College of Cardiology's 67th Annual Scientific Session. However, in patients who had received or were concurrently receiving anthracycline-based chemotherapy in addition to trastuzumab, the occurrence of heart damage was halved among those taking either the angiotensin converting enzyme inhibitor (ACE-inhibitor) lisinopril or beta-blocker carvedilol, compared with placebo after two years of follow-up.

"Our findings suggest that among women who are only on a standard course of trastuzumab neither carvedilol nor lisinopril seem to make a difference, but for those who had a history of being on anthracycline, these medications can be cardioprotective and should be considered," said Maya E. Guglin, MD, professor of medicine in the Division of Cardiovascular Disease, University of Kentucky, and lead author of the study.

This study comes amid growing awareness that certain cancer therapies can contribute to heart failure or other heart problems. While smaller studies have looked at the utility of these commonly used heart medications in guarding against anthracycline-induced cardiotoxicity, this trial is one of the first and the largest to date to test whether these drugs can prevent trastuzumab-related heart damage and prevent the need to discontinue a potentially life-saving treatment.

"We wanted to see if the cardiopreventive effects apply to trastuzumab," Guglin said. Trastuzumab (Herceptin) has been lauded as a breakthrough treatment for HER2-positive breast cancer, an especially aggressive type of cancer. However, Guglin said some studies have shown that up to 1 in 4 women who receive this therapy experience cardiac effects, including symptomatic heart failure, a condition in which the heart becomes too weak to pump enough blood to meet the body's needs. This has led to stricter clinical guidelines requiring women to be screened via echocardiogram or other imaging modality before starting trastuzumab to assess their ejection fraction — the percent of blood volume that is ejected from the left ventricle, the main pumping chamber of the heart, with each heartbeat. If the ejection fraction is less than 50 percent (low limit of normal), they are not eligible for trastuzumab based on current practice standards.

"It's a very difficult scenario, because we don't want to damage their heart, but at the same time we certainly don't want to compromise the chances of [a] cure from cancer," she said. "Because of this initial screening process, we deny [some of] them potentially life-saving medication."

Guglin explained that while anthracycline chemotherapy can cause long-lasting, potentially irreversible damage to the heart muscle, trastuzumab therapy has been associated with milder and often temporary declines in cardiac function.

"Our data affirm that anthracyclines are aggressive agents that can cause damage to the heart muscle on a much greater scale than trastuzumab," she said, adding that the damage may already be done from prior exposure to this type of chemotherapy. So, while their ejection fraction is normal, making them eligible to start on trastuzumab, their heart may already be compromised.

This prospective, randomized, controlled trial enrolled 468 patients at more than 165 centers in North America who were diagnosed with breast cancer and for whom trastuzumab was clinically indicated. All study participants had normal heart function measured by ejection fraction and were not already taking an ACE-inhibitor or beta-blocker for other medical reasons. Half were receiving or had received anthracycline-based chemotherapy. Patients were randomly assigned to receive once daily lisinopril (10 mg), carvedilol (10 mg Coreg CR) or placebo and were followed for two years (the year of active treatment with trastuzumab and the year that followed). The groups were comparable in terms of age (average of 51 years) and cardiovascular risk factors.

Researchers assessed heart function and any declines with echocardiograms every three months. Neither lisinopril nor carvedilol were statistically different from placebo in terms of preventing cardiotoxicity caused by trastuzumab or preventing related disruptions in therapy. However, in patients who were treated with anthracyclines, these heart medications were effective in preserving left ventricular ejection fraction. Carvedilol and lisinopril reduced declines in heart function by half, which was a statistically significant difference (odds ratio of 0.49 and 0.53, respectively, compared with placebo).

Adverse cardiac effects were similar across the three groups, occurring in 32 percent of patients on placebo, 29 percent of those on carvedilol and 30 percent on lisinopril. Common adverse events were low blood pressure and dizziness, which were milder in the carvedilol group.

"Our study indicates that carvedilol is tolerated better," Guglin said. "But based on our study, if you have breast cancer and your oncologist wants to start you on Herceptin and you've been on an anthracycline, you have a better chance of avoiding decline in cardiac function and taking Herceptin without damaging your heart if you are pretreated with lisinopril or carvedilol, whichever is tolerated better." She is quick to stress that not all cancer treatment therapies cause heart problems and, for those that do, there may be ways to potentially minimize the risk of related heart damage.

Pamela Munster, MD, an oncologist and senior study author said this trial gives important data for clinicians to use when planning cancer treatments for high-risk patients. "This study is of great importance as it provides the oncologist the option to use an anthracycline in HER2 positive, early-stage breast cancer patients," she said. "Anthracycline-based regimens are more effective for high-risk patients, but the increased cardiotoxicity has limited its use."

The researchers will continue to analyze the data and evaluate how taking heart medications alongside targeted cancer therapy affects the magnitude of cardiac dysfunction, how long it lasted and whether or not it can be reversed.

The study was co-sponsored by the University of South Florida and the National Cancer Institute.

ACC2018特集

カルベジロールは乳がん女性の心臓を保護する (Abstract 18-LB-17722-ACC)

化学療法による心障害に対するβ遮断薬の心保護に関する結果は様々である

Beta-blocker shows mixed results in protecting against chemotherapy-induced heart damage

新たに乳がんと診断され化学療法施行中に心毒性保護目的でβ遮断薬カルベジロールを投与された患者を6か月追跡した結果、心機能低下についてはプラセボ群と差がなかった。しかし、カルベジロールを内服した患者は血漿トロポニンI上昇を来す確率が有意に低かった（41.6% vs. 26%）と、American College of Cardiology's 67th Annual Scientific Session で発表され、同時に*Journal of the American College of Cardiology* オンライン版に掲載された。

Full Text

After six months of follow up, women newly diagnosed with breast cancer who were given the beta blocker carvedilol to prevent heart issues while undergoing chemotherapy showed no difference in declines in heart function compared with those taking a placebo. Patients who took carvedilol, however, were significantly less likely to have an elevated plasma levels of troponin I, according to a study presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Journal of the American College of Cardiology*.

The study enrolled 200 patients diagnosed with breast cancer who had normal left ventricular ejection fraction and who, as part of their cancer treatment, were scheduled to receive anthracycline (ANT).

Patients were randomly assigned to receive either carvedilol (median daily dose of 18.4 mg/day) or placebo when starting ANT chemotherapy (240 mg/m^2) until completing it. ANT is a type of chemotherapy that at certain cumulative doses has been shown to cause heart damage by weakening the heart muscles. Carvedilol works by slowing the heart rate, opening blood vessels and improving blood flow, which also lowers blood pressure.

"This is the largest randomized clinical trial of a beta blocker to prevent the toxic effects of contemporary doses of anthracycline [ANT] on the heart," said Mônica Samuel Avila, MD, assistant doctor in the Heart Failure and Heart Transplant Department in Heart Institute, Clinical Hospital of Medical School of São Paulo, and the study's lead author. "This is only short-term follow up, but we found that carvedilol seems to prevent myocardial injury, but it did not have an impact on left ventricular ejection fraction."

Avila also said the study findings further reinforce the need for cardiologists and oncologists to work together to define the best treatment strategies for individual cancer patients that minimize other negative effects, especially to the heart. Neither the patients nor those administering the treatment knew which patients received carvedilol versus the placebo.

Researchers assessed cardiotoxicity by measuring heart function with periodic echocardiograms and blood test to check for high-sensitivity troponin T, which is released into the bloodstream when injury to the heart occurs. These measures were tracked at baseline and after each cycle of ANT chemotherapy (three, six, nine and 12 weeks) and after the end of all chemotherapy (around 24 weeks).
Patients in the carvedilol and placebo groups were an average of 51 and 53 years of age, respectively. All had finished chemotherapy treatment.

For the study's primary endpoint, prevention of greater than a 10 percent reduction in left ventricular ejection fraction at six months, researchers found no significant difference between the carvedilol and placebo groups, 14.5 vs. 13.5 percent, respectively.

Overall, declines in ejection fraction were minimal in both groups and were not statistically significant (from baseline to 24 weeks the average drop in ejection fraction was 65.2 to 63.9 percent in the placebo group and 64.8 to 63.9 percent in the carvedilol group).

Secondary outcomes included carvedilol's effects on two biomarkers, troponin I and B-type natriuretic peptide (BNP), and diastolic dysfunction. Of the 65 (33.8 percent) patients with higher plasma levels of troponin I that are known to be suggestive of heart damage, many more were in the placebo group — 41.6 percent vs. 26 percent. There was no difference in levels of BNP. While not significant, patients in the placebo group tended to have enlarged hearts, compared to patients in the carvedilol group.

Avila said this could indicate that carvedilol may help prevent remodeling or changes in the structure of the heart. According to Avila, the reason why patients taking carvedilol had lower troponin levels, but no differences in changes in ejection fraction, is difficult to explain. She noted that the six-month follow-up may not have been sufficient to see changes in heart function. In addition, any heart damage may not have been severe enough to lead to heart failure. There was only one case of overt heart failure with reduced ejection fraction, which was in the placebo group.

"Previous studies have shown that higher troponin levels can predict cardiovascular events and so we could imagine that carvedilol may be able to prevent these events, but we did not see this finding in our study," she said, adding that she and her team will continue to follow these patients and report data at one and two years.

In the meantime, researchers did find the prevalence of cardiotoxicity in this study to be lower than in previously reported data from other studies — a finding that could be attributed to lower doses of anthracyclines and lower overall cardiovascular risk in the study population. It could be that the beneficial effect of carvedilol might be more pronounced among higher risk patients, Avila said.

In recent years, lower doses of anthracyclines are used to help reduce the risk of heart damage from treatment.

ACC2018特集