活動性の喘息は心筋梗塞のリスクを上昇させる可能性がある(Abstract 15991 and 16110)

活動性の喘息症状を有し長期管理薬使用中でも喘息症状のある人々はMIおよび脳卒中リスクが高い

People with active asthma symptoms and asthmatics on controller medications have elevated risk of MI and stroke

最近の喘息症状や毎日薬物を必要とする喘息は心筋梗塞(MI)リスクを有意に上昇させる可能性があるとの2つの研究論文が2014年American Heart Association年次集会で発表された。1つ目のスタディは、心疾患発症の初期徴候を追跡する地域研究の参加者6,792人(平均年齢62歳、男性47%)を対象とした。心血管リスクファクターで補正した結果、毎日の薬物療法を必要とする喘息患者は喘息を有さない人々と比較し、10年間の追跡期間中にMI、脳卒中またはそれらの関連疾患のようなイベントを来す確率が60%高かった。長期管理薬使用中でも喘息症状を有するとC反応性蛋白やフィブリノーゲンなどの炎症マーカーレベルが有意に高かった。2つ目のスタディは、MIを発症した543人と、同じ年代および性別(平均年齢67歳、女性44%)のMI歴のない患者543人を比較した。喘息と診断された患者は、喘息を有さない者と比較しMIリスクが70%高かった。過去1年間に喘息症状、薬物使用または喘息治療のために受診したことが明らかな"活動性喘息"患者は、最近の喘息症状がない喘息患者と比較しMI発症リスクが2倍であった。

Full Text

Recent asthma symptoms or asthma that requires daily medication may significantly raise the risk of myocardial infarction (MI), according to two research papers presented at the American Heart Association's Scientific Sessions 2014.

"Physicians should do all they can to control every other modifiable cardiovascular risk factor in patients with asthma," said Matthew C. Tattersall, D.O., M.S., study author and an assistant professor of medicine in the Division of Cardiology at the University of Wisconsin-Madison School of Medicine and Public Health in Madison, Wisconsin.

Tattersall's study (Abstract 15991) involved 6,792 participants in the six-community Multi-Ethnic Study of Atherosclerosis (MESA), which tracks early signs of developing heart disease. Patients were an average 62 years old, 47 percent male, 28.4 percent Caucasian, 28 percent African-American, 22 percent Hispanic and 12 percent Chinese-American.

After adjustment for heart disease risk factors, researchers found that people with asthma who required daily medications were 60 percent more likely to have a cardiovascular event such as an MI, stroke or related condition during a 10-year follow-up than people without asthma.

In the MESA study, asthmatics on controller medications, compared to non-asthmatics, had significantly higher levels of inflammatory markers including C-reactive protein and fibrinogen. Patients with a history of asthma but not currently requiring daily medication had intermediate levels of these markers.

In a study (Abstract 16110) in Olmstead County, Minnesota, researchers compared 543 patients who had a heart attack with 543 non-heart attack patients the same age and gender. The average age of patients was 67, 44 percent were women and 95 percent of the participants were Caucasian.

After controlling for traditional heart disease risk factors such as obesity, hypertension, smoking, diabetes and high cholesterol, researchers found that patients diagnosed with asthma had about a 70 percent higher risk of MI than those without asthma.

Patients with "active asthma" who had documented symptoms, medication use or visits to healthcare providers for asthma treatment within the previous year were twice as likely to have an MI than asthma patients with no recent symptoms.

"Chest discomfort or pain can be confused as a symptom of asthma, but because asthma increases the risk of heart attack and treatments for each are quite different, patients need to take chest pain and other symptoms of heart attack seriously and seek prompt treatment," said Young J. Juhn, M.D., M.P.H., senior author of the Olmstead County study and professor of pediatrics and adolescent medicine at the Mayo Clinic in Rochester, Minnesota.

Co-authors of the University of Wisconsin study are Mengye Guo, Ph.D.; Claudia E. Korcarz, D.V.M.; Adam D. Gepner, M.D.; R. Graham Barr, M.D., Dr.P.H.; Kathleen M. Donohue, M.D.; Robyn L. McClelland, Ph.D.; Joseph A. Delaney, Ph.D.; and senior author James H. Stein, M.D.

The Ruth L. Kirschstein National Research Service Award from the National Institutes of Health funded part of the study.

Co-authors of the Olmstead County study are Duk Won Bang, M.D., Ph.D.; Eun Na Kim, M.D.; Chung-il Wi, M.D.; John Hagan, M.D.; Veronique Roger, M.D., M.P.H.; Sheila Manemann, M.P.H.; and Brian Lahr, M.S.

The Scholarly Clinician Award from the Mayo Foundation funded the study.

電子監視は減塩に役立つ可能性がある (Abstract 16922)

電子監視機器の使用により減塩食への良好な適応が得られる

Successful adaptation to a lower sodium diet improves with use of an electronic monitoring device

電子監視機器の使用は心不全患者およびその家族が減塩食を遵守するのに役立つ可能性があるとの研究結果が2014年American Heart Association年次集会で発表された。Family Sodium Watcher Program（Family SWAP）では、減塩食の味付けに適応するための心不全患者と介護者／家族との協力関係に焦点を当て、食品内の塩分含有を検出する電子監視機器を使用し適応期間中には塩分の多い食事を避けた。患者ー介護者のペア15組の3か月間トライアルにおいて、患者8人の介入群は、塩分摂取量を徐々に適応させる方法および電子監視機器を用いた12週間の心不全セルフケア教育を受けた。3か月後に、介入群では24時間の尿中ナトリウム排泄量が有意に減少した（患者3,894mg対3,604mg、p=0.02；介護者4,123mg対3,380mg、p<0.05）。一部の人々は電子監視機器を用いることで減塩食がより楽しくなったと言い、90%の人々が食品中の塩分を味わう能力が変化した、と述べた。介護者らは、このプログラムによる負担の増加はなかった、と報告した。通常管理／コントロール群患者7人は、行動や塩分レベルに変化がなかった。

Full Text

Using an electronic monitoring device may help heart failure patients and their families stick to a low-salt diet, according to research presented at the American Heart Association's Scientific Sessions 2014.

The Family Sodium Watcher Program (Family SWAP) focuses on a partnership between the heart failure patient and a caregiver/member of the family to adapt to the taste of a low-sodium diet and includes using an electronic monitoring device to detect salt content in food and avoid high-salt food during the adaptation period.
In the three-month trial of 15 patient-caregiver pairs, the intervention group of eight patients received 12 weeks of self-care education for heart failure with gradual adaptive strategies in salt intake and use of the electronic monitor. At three months, the intervention group had a significant reduction in 24 hour sodium secretion (Patients 3894mg vs. 3604mg, p=0.02; caregivers 4123mg vs. 3380mg, p<0.05).

Participants said the device was easy to use and helped them maintain a low-sodium diet. Some said they enjoyed their low-salt diets more and 90 percent noticed a change in their ability to taste salt in their food. Caregivers reported no increased burden due to the program. The usual care/control group of seven patients didn't change behavior.

The study team members were Misook L Chung, Debra K Moser, and Terry A Lennie from the University of Kentucky in Lexington, Kentucky, USA. They say that The Family SWAP may help the entire family improve their lifestyles.

The pilot study was funded by the American Heart Association and the University of Kentucky.

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急性大動脈解離はインフルエンザの流行時期と関連がある(Abstract 19298)

急性大動脈解離による入院が多いこととインフルエンザ流行時期のピークは一致する

High hospital admissions for acute aortic dissection coincide with peak flu season

急性大動脈解離（AAD）による入院はインフルエンザ流行時期のピーク（11～3月）に最も多い、との研究結果が2014年American Heart Association年次集会で発表された。研究者らは、2001～2013年の米国疾病管理予防センター（CDC）でのインフルエンザの流行状況とセンターにおける1か月毎のAADによる入院とを比較した。この期間に869件のAAD症例が治療を受けた。AADによる入院は11～3月に最も多かった（この期間内の件数月3.1に対し他の期間の月平均2.1）。インフルエンザ活動性（インフルエンザ様疾患による受診者の割合）はAADのピーク期間は2.6%であったのに対し、他の月では1.1%であった（p<0.001）。特に、A型解離（上行大動脈および／または大動脈弓を含み下行大動脈を巻き込むこともある）はインフルエンザ流行時期のピークと関連があったが、B型はそうではなかった。A型解離とインフルエンザ活動性は周期的に移動し、概して期間中同期していた。インフルエンザが炎症反応を引き起こしそれにより罹患しやすい人々の解離の危険性が上昇するのであろう、と研究者らは仮説を立てている。彼らはハイリスク患者に対する季節毎のワクチン接種を推奨している。

Full Text

Hospital admissions for acute aortic dissection (AAD) were highest during peak flu season November-March, according to research presented at the American Heart Association's Scientific Sessions 2014.

Researchers at the University of Texas Health Science Center at Houston compared national flu activity from the U.S. Centers for Disease Control to monthly admissions for AAD at their center for 2001-13. Doctors treated 869 AAD patients at UT-Houston during the period.

Admissions for AAD were highest in November-March (3.1 per month during this period compared to 2.1 per month for the remaining months). Flu activity (percent of office visits for flu-like illness) averaged 2.6 percent during the peak AAD period (November-March) compared to 1.1 percent in the remaining months (p<0.001).

A mathematical model showed statistically significant seasonality (p<0.001) and showed type A dissection and flu activity moving cyclically and generally in synchrony throughout the period. Type A dissection was significantly linked with peak flu activity while Type B did not.

Type A dissection, the most devastating type of AAD dissection, involves the ascending aorta and/or aortic arch and possibly the descending aorta. Type A generally requires surgery.

"We suspect that flu creates an inflammatory reaction that could theoretically increase chances of dissection in susceptible individuals," said Harleen K. Sandhu, M.D., M.P.H., study senior researcher. "While more research is needed to further explore this association, we suggest at-risk patients, such as older Americans, should get seasonal flu shots."

マリファナの二次吸引は血管を傷害する (Abstract 19538)

マリファナの二次吸引はタバコと同様に血管内皮機能を障害させるがTHCは原因ではない可能性がある

Secondhand marijuana smoke impairs vascular endothelial function as much as tobacco but THC may not be the culprit

マリファナの二次吸引はタバコの受動喫煙と同様に心臓や血管に障害を与え得る、との予備研究の結果が2014年American Heart Association年次集会で発表された。このスタディにおいて、研究者らは改良した喫煙器具を用いてラットをマリファナの煙に曝露させた。高解像度超音波装置を用いて、主要な下肢動脈の機能が計測された。研究者らは煙への曝露前および曝露後10分と40分における大腿動脈拡張度を記録した。マリファナの煙を30分間二次吸引した実験室用ラットは、血管内皮機能が70%低下した。彼らはまた、THCを含有しないマリファナおよび通常の空気を用いて別の検査を行った。ラットが通常の空気に曝露された時に、血管機能の変化はなかった。THCを含有しないマリファナによる血管内皮機能低下は、この化合物が作用の原因ではないことを示唆している。同様に、このスタディから、喫煙の血管内皮機能障害にニコチンは必要ないことが確認された。過去のタバコのスタディにおいて、血管内皮機能は曝露から30分以内に正常範囲内に復する傾向にあった。しかし、マリファナの研究では、曝露から40分経過して計測した血管内皮機能は正常には戻らなかった。

Full Text

Breathing secondhand marijuana smoke could damage your heart and blood vessels as much as secondhand cigarette smoke, according to preliminary research presented at the American Heart Association's Scientific Sessions 2014.

In the study, blood vessel function in lab rats dropped 70 percent after 30 minutes of exposure to secondhand marijuana smoke. Even when the marijuana contained no tetrahydrocannabinol (THC) — a compound in marijuana that produces intoxication — blood vessel function was still impaired.

"Most people know secondhand cigarette smoke is bad for you, but many don't realize that secondhand marijuana smoke may also be harmful," said Matthew Springer, Ph.D., senior author of the study and cardiovascular researcher and associate professor of Medicine at the University of California, San Francisco's Cardiology Division.

Marijuana and tobacco smoke are chemically and physically alike, aside from their active ingredients.

The drop in vascular endothelial function from THC-free marijuana suggests that the compound isn't responsible for the effect. Similarly, this study confirms that nicotine is not required for smoke to interfere with blood vessel function.

In the study, researchers used a modified cigarette smoking machine to expose rats to marijuana smoke. A high-resolution ultrasound machine measured how well the main leg artery functioned. Researchers recorded femoral artery dilation before smoke exposure and 10 minutes and 40 minutes after smoke exposure.

They also conducted separate tests with THC-free marijuana and plain air. There was no difference in blood vessel function when the rats were exposed to plain air. The drop in vascular endothelial function from THC-free marijuana suggests that the compound isn't responsible for the effect. Similarly, this study confirms that nicotine is not required for smoke to interfere with vascular endothelial function.

In previous tobacco studies, blood vessel function tended to go back to normal within 30 minutes of exposure. However, in the marijuana study, blood vessel function didn't return to normal when measured 40 minutes after exposure.

"If you're hanging out in a room where people are smoking a lot of marijuana, you may be harming your blood vessels," he said. "There's no reason to think marijuana smoke is better than tobacco smoke. Avoid them both."

More research is needed to determine if secondhand marijuana smoke has other similar effects to secondhand cigarette smoke in humans.

Co-authors are Xiaoyin Wang, M.D.; Ronak Derakhshandeh, M.S.; Shilpa Narayan, B.S.; Emmy Luu, B.S.; Stephenie Le, B.A.; Olivia Danforth, B.S.; Hilda Rodriguez; Richard Sievers, B.S.; Suzaynn Schick, Ph.D.; and Stanton Glantz, Ph.D. Author disclosures are on the manuscript.

The National Institute on Drug Abuse and the Elfenworks Foundation funded the study.

心房細動に対する治療が認知症リスクを上昇させる(Abstract 13426)

抗凝固／抗血小板療法併用による長期の過剰治療は心房細動患者の認知症リスクを上昇させる可能性がある

Long-term overtreatment with anticoagulant/antiplatelet combination may raise risk of dementia in people with atrial fibrillation

抗凝固薬ワルファリンとアスピリンやクロピドグレルを用いた抗血小板薬の併用による脳卒中予防目的の長期過剰治療は心房細動（AF）患者の認知症リスクを上昇させる可能性がある、との研究結果が2014年American Heart Association年次集会で発表された。研究者らは脳卒中歴または認知症のない患者1,031人が薬物を併用している間、最長10年間調査した。一般的な脳卒中および出血のリスクファクターで補正した結果、凝固能モニター検査の25%以上においてINRが3.0を超えていた患者は、検査上過剰治療の回数が10%未満であった患者よりも認知症と診断される確率が2倍以上であった（HR 2.40、p=0.04）。この増加率は、彼らが過去にワルファリン単独で調査した時よりも高かった。INRの治療域を超えた回数の割合が高い患者においてはまた、弁膜症、腎不全（Cr>2.0）、CHADSスコア3～6および出血歴を有する割合が高かった。これらのデータから、AFと認知症の関連の基となるメカニズムとして微小出血による慢性脳損傷の可能性が示唆される、と筆者らは述べている。

Full Text

Long-term overtreatment with the anti-clotting drug warfarin, combined with antiplatelet therapy with aspirin or clopidigrel to prevent stroke, may raise the risk of dementia in people with atrial fibrillation, according to research presented at the American Heart Association's Scientific Sessions 2014.

Atrial fibrillation raises the risk of stroke and all common forms of dementia. The mechanisms behind the association of atrial fibrillation and dementia are unknown.

"The dual drug regimen is often used to prevent strokes in people with coronary artery disease or peripheral vascular disease, but we have to consider that long-term exposure to anti-clotting drugs such as warfarin, if not well controlled, can significantly increase bleeding risk," said T. Jared Bunch, M.D., lead author of the study and director of electrophysiology at the Intermountain Heart Institute in Murray, Utah. "This may result in micro bleeds in the brain that don't cause symptoms right away, but accumulate over time raising the risk of dementia."

Researchers studied 1,031 patients with no previous history of stroke or dementia for up to 10 years while on the drug combination. After adjusting for traditional stroke and bleeding risk factors, patients with an International Normalized Ratio (INR) greater than 3.0 on 25 percent or more of their monitoring tests were more than twice as likely to be diagnosed with dementia than patients whose tests showed overtreatment less than 10 percent of the time (HR 2.40, p=0.04). The increase is higher than what researchers found in a previous study of warfarin alone. Patients with a higher percent of time with supratherapeutic INRs were also more likely to have valvular heart disease, renal failure (Cr>2.0), a higher percent of CHADS 3-6 scores, and a prior bleed.

Patients who had abnormally slow clotting times were considered to be receiving too much medication.

Researchers previously found that atrial fibrillation patients taking warfarin were more likely to develop dementia if lab measurements of their clotting time were frequently too slow (raising the risk of bleeding) or too fast (raising the risk of blood clots). From those results they concluded that brain injury from both small bleeds and clots was important in the development of dementia in atrial fibrillation patients.

"Even at skilled centers, it's very common to have INR outside the ideal range up to 40 percent of the time, and over the years there may be an accumulative negative impact on cognitive ability," Bunch said.

"If your INRs are consistently too high, for stroke prevention your doctor may want to consider switching you to one of the newer anti-clotting drugs that is easier to regulate or a device placed into the heart that prevents clots from forming or exiting the area in the heart chamber where most clots develop in people with atrial fibrillation," he said.

Most patients in the study were Caucasian; so researchers aren't sure results would apply to other ethnic groups.

Co-authors are Heidi T. May, Ph.D.; Tami L. Bair, R.N.; Victoria Jacobs, N.P.; Brian G. Crandall, M.D.; J. Peter Weiss, M.D.; Jeffrey S. Osborn, M.D.; Charles Mallendar, M.D.; John D. Day, M.D.; Jeffrey L. Anderson, M.D.; Jeffrey L. Olson, M.D.; Katie Johanning; Yenh Long, Pharm.D.; Scott M. Stevens, M.D.; and Scott C. Woller, M.D.

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女性における精神的ストレスの心血管系への有害な作用(Abstract 14860)

心疾患を有する若年女性は感情的ストレスの心血管系への影響を過剰に受けやすい

Young women with heart disease are disproportionally vulnerable to cardiovascular effects of emotional stress

安定冠動脈疾患（CHD）を有する若年女性は、感情的ストレス下に置かれると、男性よりも心筋虚血を生じやすいが身体的ストレスではそうではない、との研究結果が2014年American Heart Association年次集会で発表された。研究者らは安定CHD患者534人に、標準的な精神ストレス検査を施行し、別の日に従来の身体ストレス検査（運動または薬物）を施行した。ストレスと安静時との差から、総虚血性灌流欠損（IPD）の定量的計測が得られた。精神的ストレスに関しては、年齢による性別への有意な影響があった（p=0.001）。55歳以下の女性は精神的ストレスにより同年代の男性と比較し、IPDが3倍以上生じた。55歳以下の女性では心臓への血流が3倍以上減少し、56～64歳では心臓への血流が2倍減少し、65歳以上では心臓への血流には差がなかった。精神的ストレスにより血流に大きな差が生じたのとは対照的に、身体的ストレス下での血流に関しての男女差はなかった。

Full Text

Young women with stable coronary heart disease (CHD) are more likely than men to develop myocardial ischemia if they're under emotional stress, but not physical stress, according to research presented at the American Heart Association's Scientific Sessions 2014.

"Women who develop heart disease at a younger age make up a special high-risk group because they are disproportionally vulnerable to emotional stress," said Viola Vaccarino, M.D., Ph.D., study author and chairwoman of Cardiovascular Research and Epidemiology at Emory University's Rollins School of Public Health in Atlanta, Georgia.

Women generally develop heart disease later in life than men. However, younger women who have premature heart attacks are more likely to die than men of similar age. Risk factors, such as diabetes or high blood pressure, don't explain these mortality differences.

In the study, researchers gave a standardized mental stress test and, on a separate day, a traditional physical stress test (exercise treadmill test or pharmacological stress test) to 534 patients with stable coronary heart disease. For the mental stress protocol, patients were asked to imagine a stressful life situation and deliver a speech about this story in front of a small audience.

Researchers used nuclear imaging to take pictures of the heart while undergoing each of the two stress tests and while at rest. They also monitored heart rate and blood pressure during both mental and physical tests. Then, they analyzed the differences in coronary blood flow based on gender and age. In this manner, the difference between stress and rest provided a quantitative measure of total ischemic perfusion deficit (IPD).

For mental stress there was a significant sex by age interaction (p=0.001). Women ≤55 years had more than threefold IPD with mental stress than men of similar age. Women age 55 and younger had three times greater reduction in blood flow to the heart; age 56-64 had double the reduction in blood flow to the heart; and age 65 and older had no difference in blood flow to the heart. In contrast to the large differences in blood flow observed with mental stress, there was no IPD with physical stress between women and men.

Young and middle-age women may be more vulnerable to emotional stress because they face considerable burden of stressors in everyday life such as managing kids, marriage, jobs and caring for parents, Vaccarino said. Biology may also play a role -- for example, a greater propensity towards abnormal blood vessel function during emotional stress, such as exaggerated constriction of coronary or peripheral blood vessels.

Healthcare providers should be aware of young and middle-age women's special vulnerability to stress and "ask the questions about psychological stress that often don't get asked," Vaccarino said.

"If they note that their patient is under psychological stress or is depressed, they should advise the woman to get relevant help or support from mental health providers, stress reduction programs or other means."

Co-authors are Pratik Pimple, M.B.B.S., M.P.H.; Ernest Garcia, Ph.D.; Jonathon Nye, Ph.D.; Ibhar Al Mheid, M.D.; Kobina Wilmot, M.D.; Ronnie Ramadan, M.D.; Amit Shah, M.D., M.S.C.R.; Paolo Raggi, M.D.; Fabio Esteves, M.D.; Michael Kutner, Ph.D.; Qi Long, Ph.D.; J.D. Bremner, M.D.; and Arshed Quyyumi, M.D.

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ステント留置後の長期抗血小板薬2剤併用療法 (Abstract 19168)

DAPT：抗血小板薬2剤併用療法を薬剤溶出ステント留置後1年以上継続することにより冠動脈血栓のリスクが低下する

DAPT: Continuing dual antiplatelet therapy beyond 1-year after placement of drug-eluting stent reduces risk of coronary thrombosis

チエノピリジン系薬剤（クロピドグレルまたはプラスグレル）およびアスピリンをステント留置後標準的な12か月を超えて内服した患者は標準的な12か月のプロトコールに従って治療された患者よりも、ステント血栓および重大な心血管有害事象のリスクが低い、とのlate-breaking clinical trialの結果が2014年American Heart Association年次集会で発表され、同時に*New England Journal of Medicine*に掲載された。DAPT（抗血小板薬2剤併用療法）スタディは5年間の国際スタディであり、薬剤溶出ステントを留置された患者9,961人（平均年齢62歳、約25%が女性、ほとんどが米国出身）をランダム化し一次解析した。ステント留置後アスピリンとクロピドグレルまたはプラスグレルを12か月ではなく30か月内服した患者は、12か月内服しその後アスピリンとプラセボを18か月間内服した患者（プラセボ群）よりもステント内血栓を発症する確率が0.5倍少なかった。彼らはまたプラセボ群と比較し新たな心筋梗塞を発症するリスクが約半分であった。また、チエノピリジン系薬剤治療中止がいつであってもその後3か月間は虚血イベントが著明に増加することも示され、2剤併用療法はさらに長期にわたり継続すべきであり生涯にわたり継続する必要性さえある可能性が示唆された。

Full Text

Patients who took a thienopyridine drug (clopidogrel or prasugrel) and aspirin beyond the standard 12 months after stent placement reduced the risks of stent thrombosis and major adverse cardiovascular and cerebrovascular events than those whose treatment followed the standard 12 month protocol, according to late-breaking clinical trial research presented at the American Heart Association's Scientific Sessions 2014 and simultaneously published in *New England Journal of Medicine*.

"We know that dual antiplatelet therapy is essential for all patients receiving coronary stents to prevent blood clots within the stents (in-stent thrombosis). This study showed that the preventive benefit continues when the medications can be taken for more than one year," said the study's principal investigator and lead author, Laurel for 30 rather than 12 months after stent placement were 0.5 times less likely to develop in-stent thrombosis than patients who received dual therapy for 12 months, followed by aspirin plus placebo for 18 months (placebo group) and had about half the risk of having new myocardial infarctions compared to the placebo group.

"Overall the benefits of longer therapy were very consistent throughout the types of patients we studied, and outweighed the risks," she said.

"The DAPT (Dual Antiplatelet Therapy) Study was the first and only study comparing durations of treatment with antiplatelet therapy that was adequately powered to detect a benefit on stent-related heart attacks," said Mauri, who is an interventional cardiologist at Brigham and Women's Hospital, associate professor of medicine at Harvard Medical School and Chief Scientific Adviser at the Harvard Clinical Research Institute in Boston, Massachusetts.

To prevent blood clots, standard post-stent treatment involves dual treatment with aspirin and another anti-clotting medication. European guidelines call for six to 12 months of this treatment and U.S. guidelines recommend it for 12 months after the procedure. What was unclear until now was whether extending this combined treatment for longer than 12 months could decrease the risk of in-stent thrombosis or whether it would prevent heart attack or stroke. The safety of longer-term treatment was also assessed in this trial.

Although moderate to severe bleeding was more common among the medication group than the placebo group in the study, fatal bleeding was rare among both groups of patients.

Of particular interest, it was found that ischemic-event rates increased markedly in the 3-month period after discontinuing thienopyridine treatment regardless of when that occurred, leading to suggestions that treatment should maybe continue longer, even for life. While overall stroke rates and death rates were not reduced by extending the combined treatment, the investigators noted in a secondary analysis, including data beyond the time point after all patients had stopped the study drug (to 33 months), that death from any cause was 0.8 percent higher (2.3 percent vs. 1.5 percent) among the medication group compared to those on placebo. The study results were tracked during the study by a data safety monitoring committee, but this difference in risk was not evident until the end of the study, Mauri said.

A secondary analysis revealed that the higher death rate was attributable to trauma and cancer.

"However, there was no difference in the occurrence of new cancers," Mauri said. "In retrospect, it appears that there may have been an imbalance between the groups in the number of patients with known cancer before enrollment in the study. Taken together with results from many other large studies of these medications, enrolling over 60,000 subjects worldwide, that show no difference in mortality, it seems likely that this finding was related to a chance imbalance between the groups studied in the trial."

Prevention of heart attack and blood clots in stents with longer antiplatelet therapy was consistent in all patient groups, drug and stent types studied, Mauri noted, but "physicians should consider individual patient risks in prescribing dual anti-clotting therapy. In particular, the trial excluded patients with a history of major bleeding either before the stent procedure or within the first year of treatment."

DAPT was a five-year, international study of 25,682 patients. 22,866 received drug-eluting stents, and of these 9,961 patients (average age 62, about 25 percent female, and mostly from the United States) were randomized in the primary analysis. The investigators randomly assigned patients to one of the two groups, and neither investigators nor patients knew who was receiving medication versus placebo. The study took place from August 2009, to June 2014, at more than 450 sites in the United States, Canada, Europe, Australia, and New Zealand.

Limitations of the study include the fact that it only included patients who were known to have tolerated anti-clotting medication for a year; and follow-up ended after 33 months, even though the study data suggest that a longer course of treatment may provide additional benefit.

The Harvard Clinical Research Institute and the following stent and pharmaceutical companies supported the study: Abbott; Boston Scientific Corporation; Cordis Corporation; Medtronic, Inc.; Bristol-Myers Squibb Company/Sanofi Pharmaceuticals Partnership; Eli Lilly and Company; and Daiichi Sankyo Company Limited.

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スタチン療法にエゼチミブを併用することで臨床上の有益性が得られる (Abstract 20742)

IMPROVE-IT：異なる作用のコレステロール低下療法はスタチンの心血管リスク低下を増強する

IMPROVE-IT : Cholesterol-lowering drug with different action adds to statin's reduction of cardiovascular risk

高リスクの急性冠症候群（ACS）患者においてスタチン療法に他のタイプのコレステロール低下薬を併用することにより心筋梗塞（MI）および脳卒中がより予防できる、との大規模長期スタディが2014年American Heart Association年次集会で発表された。IMPROVE-IT（IMProved Reduction of Outcomes: Vytorin Efficacy International Trial）スタディは、低比重リポ蛋白（LDL）コレステロールレベルが125mg/dL以下、または既にスタチン内服中であれば100mg/dL以下の50歳以上のACS患者18,144人を組み入れた。患者は平均約6年間追跡され、長期の者では8.5年であった。シンバスタチンとプラセボを投与された患者と比較し、シンバスタチンと非スタチン系薬剤エゼチミブの両者を投与された患者は、全ての心血管イベントリスクが6.4%、MIリスクが14%、脳卒中リスクが14%、および虚血性脳卒中リスクが21%低かった。心血管疾患死は両群ともに統計学的に同等であった。IMPROVE-ITはスタチン療法に非スタチン系薬剤を併用した際の著明な臨床上の有益性を示した初めてのスタディである。

Full Text

Adding another type of cholesterol-lowering drug to statin therapy can better prevent myocardial infarction (MI) and strokes in high-risk patients with acute coronary syndrome (ACS), according to a large, long-term study presented at the American Heart Association's Scientific Sessions 2014.

Compared to patients with coronary heart disease given the drug simvastatin plus a placebo, those given both simvastatin and the non-statin drug, ezetimibe, had a 6.4 percent lower risk of all cardiovascular events, a 14 percent lower risk of all heart attacks, a 14 percent lower risk of stroke, and a 21 percent lower risk of ischemic stroke. Deaths from cardiovascular disease were statistically the same in both groups. Patients were followed an average of approximately six years, and some as long as 8.5 years. Approximately 2 patients out of every 100 patients treated for 7 years avoided a heart attack or stroke. (Number Needed to Treat (NNT) = 50).

"The study is the first to show that adding another non-statin drug to a statin to improve cholesterol levels can help patients with specific heart problems do better," said Christopher P. Cannon, M.D., lead author and a professor of medicine at Harvard Medical School and physician at Brigham and Women's Hospital.

The study, called IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial), was done at 1,158 centers in 39 countries. It enrolled 18,144 patients with ACS 50 years or older with low-density lipoprotein (LDL) cholesterol levels at or less than 125 mg/dL, or at or less than 100 mg/dL if they were already using a statin.

"The patients, enrolled within 10 days of hospitalization for a heart attack or unstable angina, were high risk," Cannon said. About 5,000 of them had suffered a ST-segment elevation myocardial infarction, or STEMI. The remaining 13,000 had suffered a non-STEMI heart attack or had unstable angina. Patients also had at least one feature putting them at high risk for a further cardiovascular event, including a previous MI, diabetes, peripheral artery or cerebrovascular disease, coronary disease in multiple arteries, or bypass surgery in the past.

Statins, such as simvastatin, block cholesterol production in the liver, while ezetimibe, a cholesterol absorption inhibitor, reduces the body's absorption of cholesterol in the intestine. In the study, the dual therapy reduced patients LDL to an average of 54 mg/dL, compared with 69 for those treated with the statin and placebo.

"We took those patients from a clinically appropriate target LDL-C to even lower. We now have solid evidence that lower is good, and even lower can be even better," he said.

The addition of ezetimibe did not raise patients risk of ill effects, such as liver or muscle problems, or cancer, Cannon said.
Over a decade ago, researchers from the TIMI Study Group, based at Brigham and Women's Hospital demonstrated that a high dose statin, which lowered cholesterol further than a regular dose statin, provided better clinical outcomes. But questions remained about whether further reducing cholesterol would be even more effective in reducing cardiovascular-related events. And now, researchers have an answer from the results of the IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT).

Co-authors include study chairmen Eugene Braunwald, M.D., and Robert Califf, M.D., on behalf of the IMPROVE-IT investigators.

"These study results will help expand our treatment options for high-risk ACS patients, especially among those who are intolerant of or who do not achieve desired results with intense statin therapy," said Lori Mosca, M.D., M.P.H., Ph.D., and Professor of Medicine at Columbia University Medical Center and Director of Preventive Cardiology at New York-Presbyterian Hospital. "These results are consistent with decades of research in high-risk ACS patients affirming the central role of aggressive LDL reduction in the prevention of recurrent heart disease. They further suggest that we should consider setting the LDL bar even lower among our high-risk patients to achieve maximum benefit to prevent recurrent heart disease and stroke," Mosca continued.

"Science by nature is evolutionary. Each piece of new data advances our understanding of how to prevent, detect, diagnose and treat heart disease," said Elliott Antman, M.D., President of the American Heart Association. "We are learning more about the biology of cardiovascular disease, and we are making progress."

The IMPROVE-IT study was funded by a research grant from Merck & Co.

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PCSK9阻害薬はスタチン不耐性患者に対する可能性を有している(Abstract 20758)

ODYSSEY ALTERNATIVE：Alirocumabはベースラインレベルが非常に高いスタチン不耐性患者のLDL-Cを低下させる

ODYSSEY ALTERNATIVE : Alirocumab reduced LDL-C in statin intolerant patients with very high baseline levels

PCSK9を標的として阻害するモノクローナル抗体alirocumabは、ベースラインLDL-Cレベルが非常に高いスタチン不耐性患者において、エゼチミブおよびアトルバスタチンと比較し、LDL-C低下作用が有意に大きかった、との研究結果が2014年American Heart Association年次集会で発表された。ODYSSEY ALTERNATIVEスタディでは、ベースラインLDL-Cが非常に高い（～190mg/dL）患者計314人を、2週間毎のalirocumab 75mg自己注射またはエゼチミブ1日10 mg、またはアトルバスタチン1日20mgを24週間内服する群にランダムに割り付けた。Alirocumabの用量は心血管リスクおよび第8週のLDL-C値に応じて12週後に最大150mgまで増加された。50%は第12週の時点で用量増加が不要であった。24週の時点でalirocumabはエゼチミブよりも有意にLDL-Cを低下させた（エゼチミブ群154mg/dL対alirocumab群96mg/dL、p<0.0001）。Alirocumab群患者の42%が第24週の時点でLDL-Cの目標値を達成した。LDL-C目標値を達成したのはalirocumab群患者の方がスタチン群患者よりも有意に多かった（p<0.0001）。さらに、骨関連有害事象は、アトルバスタチンまたはエゼチミブ群よりもalirocumab群の方で少なかった。スタチン不耐性歴を有する患者においてalirocumabは優れた代替療法となり得る、と筆者らは結論付けている。

Full Text

The investigational drug alirocumab produced significantly greater LDL-C reductions in statin-intolerant patients with very high baseline LDL-C levels compared with ezetimibe and atorvastatin according to research presented at the American Heart Association's Scientific Sessions 2014.

Statin intolerance limits many patients from taking cholesterol-lowering statins to lower LDL-C. The drug ezetimibe is often recommended for those who cannot tolerate statins. In this trial, researchers compared the PCSK9 monoclonal antibody alirocumab to ezetimibe in patients with a history of statin intolerance. Statin intolerant patients were unable to tolerate at least two different statins, including one at the lowest dose, due to muscle related symptoms.

In the ODYSSEY ALTERNATIVE study a total of 314 patients with very high baseline LDL-C levels (~190 mg/dL) were randomized to receive either alirocumab as a 75 mg self-administered injection every 2 weeks, or 10 mg/day of ezetimibe, or 20 mg/day of atorvastatin for 24 weeks. Alirocumab dose was increased to 150 mg at week 12 depending on cardiovascular risk and week 8 LDL-C level.

The primary endpoint was percent change in LDL-C from baseline to week 24.

Researchers found that alirocumab produced significantly greater LDL-C reduction than ezetimibe. At 24 weeks, LDL-C for the ezetimibe arm was 154 mg/dL vs. 96 mg/dL for patients on alirocumab (p<0.0001). Fifty percent did not need a dose increase at week 12. Forty two percent of alirocumab patients achieved their LDL-C goals at week 24. Significantly more alirocumab patients achieved LDL-C goals (p<0.0001) than patients on statins. Similar reductions were found in secondary lipid parameters at week 24.

In addition, there were fewer skeletal- related adverse events with alirocumab compared to atorvastatin or ezetimibe.

Patrick Moriarty, M.D., lead author on the study and professor of medicine at the University of Kansas Medical Center in Kansas City, Kansas concluded that alirocumab may be a good alternative therapy in patients with a history of statin intolerance.

高齢者においてアスピリンは一次予防に役立たなかった (Abstract 20753)

JPPP：複数の動脈硬化リスクファクターを有する高齢者において低用量アスピリンは心血管イベントを低下させない

JPPP: Low-dose aspirin does not reduce cardiovascular events in elderly patients with multiple atherosclerotic risk factors

複数の心血管リスクファクターを有する高齢患者において低用量アスピリンは総心血管イベントを有意に低下させなかった、とのlate-breaking clinical trialの結果が2014年American Heart Association年次集会で発表された。Japanese Primary Prevention Project（JPPP）スタディでは、高血圧、脂質異常症および／または糖尿病を有し心血管疾患歴のない60～85歳の患者14,466人を組み入れ、アスピリン腸溶錠1日100mgを内服する群またはアスピリンを内服しない群にランダムに割り付け、リスクファクターのコントロールは継続した。一次エンドポイントは、心血管系の原因による死亡、非致死性脳卒中および非致死性MIの合計であった。追跡期間中央値5.02年の時点で、一次エンドポイント数またはイベントリスクは2群間で差がなかった。TIA率はアスピリン群において有意に少なかった（43%低下、p=0.044）。逆に、アスピリン群では重篤な頭蓋外出血が有意に多かった—ハザード比からそれらのイベントが85%高いことが示された（p=0.004）。TIA減少に関するアスピリンのいかなる有益性も重篤な頭蓋外出血リスクの有意な上昇を考慮しバランスをとるべきである、と筆者らは警告している。

Full Text

Low-dose aspirin was not associated with significant reduction in total cardiovascular events in elderly patients with multiple cardiovascular risk factors according to late-breaking clinical trial research presented at the American Heart Association's Scientific Sessions 2014.

The role of aspirin in the primary prevention of cardiovascular (CV) disease has been hotly debated for several years. Meta-analyses indicate benefits as well as risks. Recently, the US Food and Drug Administration cautioned against the general use of aspirin for the primary prevention of heart attacks and strokes. The Japanese Primary Prevention Project (JPPP) study, prospectively evaluated daily, low-dose aspirin in the primary prevention of cardiovascular events in elderly Japanese patients with one or more risk factors for cardiovascular events but no history of atherosclerotic disease.

A total of 14,466 individuals aged 60 to 85 years with hypertension, dyslipidemia and/or diabetes mellitus who did not have a history of CV disease were randomly assigned to receive enteric-coated aspirin, 100 mg/day or no aspirin, while continuing treatment to control their risk factors. Patients were enrolled from 1007 clinics in Japan between March 20115 and June 2007. Throughout the study, 10.5% of the study population was lost to follow-up.

At a median follow-up of 5.02 years, there was no significant difference between the two groups in the number of primary events or the risk of event. The 5-year cumulative event rates were 2.772 percent for the aspirin treated group compared to 2.960 percent, for the no-aspirin group.

The primary endpoint was a composite of death from CV causes, non-fatal stroke and non-fatal MI. At 5 years there was an insignificant 6% reduction in the risk of a primary endpoint event in the aspirin group vs. the no aspirin group (p = 0.544). No statistically significant interaction between any risk factor and treatment was observed.

When evaluating secondary endpoints, the researchers found that the rate of TIA was significantly reduced in the aspirin group (a 43% reduction, p=0.044). Conversely, there was a significant increase in serious extracranial hemorrhage in the aspirin group − the hazard ratio indicates an 85% increase in such events (p=0.004). Therefore, the authors caution that any benefits of aspirin in terms of the reduced risk of TIA must be counterbalanced with consideration of the significantly increased risk of serious extracranial hemorrhage.

The authors conclude that aspirin was not associated with significant reduction in total cardiovascular events in elderly patients with multiple cardiovascular risk factors.

The JPPP was sponsored by the Japanese Ministry of Health, Labor, and Welfare and the Waksman Foundation of Japan. Enteric coated 100-mg aspirin tablets were provided free of charge by Bayer Yakuhin.

ジルコニウム環状珪酸塩による高カリウム血症治療 (Abstract 20737)

HARMONIZE：致死的な心臓不整脈に関連する可能性のある高カリウムレベルの低下に薬物が役立つ

HARMONIZE: Drug helps reduce high potassium levels associated with potentially lethal cardiac arrhythmias

ジルコニウム環状珪酸塩はカリウムレベルを急速に正常範囲内に低下させ、様々な程度の高カリウム血症患者の正常カリウムレベルを最長4週間維持することができる、との研究結果が2014年American Heart Association年次集会で発表され、同時に*JAMA*に掲載された。ナトリウムジルコニウム環状珪酸塩（ZS9）は、腸内のカリウムに選択的に結合する非吸収性薬剤である。第III相HARMONIZE臨床試験において、高カリウム血症患者（258人）が初回の48時間オープンラベル相にZS9を1日3回投与された。正常カリウムレベルを達成した患者（237人）がその後、5 g（45人）、10 g（51人）、または15 g（56人）のZS9またはプラセボ（85人）を毎日28日間投与される群にランダムに割り付けられた。ZS9のカリウム低下作用は全ての患者サブグループにおいて一貫しており、迅速に認められた（初回投与後1時間）。84%の患者において24時間以内に、98%の患者において48時間以内に、正常カリウムレベルに達した。プラセボと比較し、3用量全てのZS9の方が、最長28日間にわたり正常カリウム値患者の割合が高かった（全ての比較でp=0.0001）。

Full Text

Mikhail Kosiborod, M.D., of Saint Luke's Mid America Heart Institute, Kansas City, and colleagues evaluated the efficacy and safety of the drug zirconium cyclosilicate in patients with hyperkalemia. They reported that the drug was effective both in rapidly lowering potassium to normal range and maintaining normal potassium levels for up to 4 weeks in patients with various degrees of hyperkalemia. The study appears in *JAMA* and is being released to coincide with its presentation at the American Heart Association's Scientific Sessions 2014.

Hyperkalemia is a common electrolyte disorder that can cause potentially life-threatening cardiac arrhythmias and is associated with chronic kidney disease, heart failure, and diabetes mellitus. There is a lack of effective and safe therapies for the management of this disorder in the outpatient setting. Sodium zirconium cyclosilicate (ZS9) is a non-absorbable agent that selectively binds potassium in the intestine, according to background information in the article. In previous studies, this drug was well tolerated and effective in lowering potassium within 48 hours of administration; for this study, outcomes for 28 days were evaluated.

In the phase III, HyperkAlemia RandoMized interventiON multI-dose ZS-9 maintEnance (HARMONIZE) clinical trial, ambulatory patients with hyperkalemia (n = 258) received zirconium cyclosilicate three times daily in the initial 48-hour open-label phase. Patients (n = 237) achieving normal potassium levels were then randomized to receive ZS9, 5 g (n = 45 patients), 10 g (n = 51), or 15 g (n = 56), or placebo (n = 85) daily for 28 days. Patients were recruited from 44 sites in the United States, Australia, and South Africa.

The researchers found that ZS9 was effective both in rapidly lowering potassium to normal range and maintaining normal potassium levels for up to 4 weeks in patients with various degrees of hyperkalemia. The potassium-lowering effect of ZS9 was consistent across all patient subgroups and observed immediately (after 1 hour of the first dose), and normal levels of potassium was achieved in 84 percent of the patients within 24 hours and 98 percent within 48 hours of treatment initiation (P =0.0001 for all comparisons). Compared with placebo, all three doses of ZS9 resulted in significantly higher proportions of patients with normal potassium levels for up to 28 days. These outcomes occurred with a tolerability profile that was comparable with that of placebo.

"Further studies are needed to evaluate the efficacy and safety of zirconium cyclosilicate beyond 4 weeks and to assess long-term clinical outcomes," the authors write.

Bradley S. Dixon, M.D., of the Veterans Administration Medical Center and the University of Iowa, Iowa City, comments on the findings of this study in an accompanying editorial.

"The findings reported by Kosiborod et al suggest that zirconium cyclosilicate may represent a promising new therapy for the acute and short-term (i.e., 28-day) treatment of outpatients with mild hyperkalemia. However, longer-term studies are needed to assess the clinical benefits and risks that may be related to more extended use of this product, especially among hospitalized patients, as well as those with more severe hyperkalemia, other medical conditions, and other medications that affect potassium [levels]."

The study was sponsored and funded by ZS Pharma.

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機械的CPRは用手的CPRと比較し利点がない (Abstract 22737)

PARAMEDIC：機械的CPR装置は用手的胸骨圧迫と比較し生存率を改善しない

PARAMEDIC: Mechanical CPR device does not improve survival compared to manual chest compressions

院外で心停止を来した患者に蘇生を行う際に、機械的装置を用いた持続的な胸骨圧迫が用手的胸骨圧迫よりも生存率を改善することはないとのlate-breaking resuscitation researchの結果が2014年American Heart Association年次集会で発表され、同時に*Lancet*に掲載された。このPARAMEDIC（pre-hospital randomized assessment of a mechanical compression device in cardiac arrest）トライアルでは、院外で非外傷性心停止を経験し、用手的胸骨圧迫または軽量携帯型電動式装置LUCAS-2を介した胸骨圧迫を受ける群にランダム割り付けられた患者の30日生存率を比較した。スタディの結果、英国の4つの救急サービスにより治療を受け、組み入れ条件に合致した患者4,471人（1,652人はLUCAS-2、2,819人は用手的胸骨圧迫）において、30日生存率は機械的群（6.3%）および手動的群（6.9%）とで同等であることが示された。もう1つの所見として、LUCAS-2は、脈拍および呼吸が再開したか、またはイベント後の脳機能が自立して生活できる程度に良好である患者が病院に到着するまで生存する割合を上昇させなかった。これらの結果に基づき、研究者らは用手的胸骨圧迫の代替法としてLUCAS-2を日常的に使用することを推奨していない。

Full Text

Using mechanical devices to perform consistent chest compressions during resuscitation efforts does not improve survival compared to manual chest compressions in people who have a cardiac arrest outside of a hospital, according to late-breaking resuscitation research presented at the American Heart Association's Scientific Sessions 2014 and simultaneously published in *Lancet*.

Using mechanical devices could overcome problems such as differing levels of skill among rescuers and deteriorating quality of compressions as fatigue sets in. However, until this study there had been little evidence of whether or not the devices are effective in saving lives.

The pre-hospital randomized assessment of a mechanical compression device in cardiac arrest (PARAMEDIC) trial compared 30-day survival rates in patients who experienced non-trauma-related cardiac arrest outside of a hospital and were randomly assigned to receive manual chest compressions or compressions delivered via the LUCAS-2, a lightweight, portable, electrically-powered device.

The primary outcome was survival at 30 days following cardiac arrest and was analyzed by intention to treat. Ambulance dispatch staff and those collecting the primary outcome were masked to treatment allocation. Masking of the ambulance staff who delivered the interventions and reported initial response to treatment was not possible.

The study found that 30-day survival was similar after mechanical (6.3 percent) and manual (6.9 percent) compressions among 4,471 eligible patients treated by four ambulance services in the United Kingdom (1,652 randomized to LUCAS-2 and 2,819 to manual compressions).

In secondary findings, LUCAS-2 did not improve the percentage of patients who survived to reach the hospital (22.8 percent LUCAS-2 vs. 23.3 percent manual), in whom pulse and breathing was restored (31.6 percent LUCAS-2 vs. 31.4 percent manual), and whose brain function after the event was good enough to allow them to live independently (4.7 percent LUCAS-2 vs. 6.0 percent manual).

"On the basis of ours and other recent randomized trials . . . the evidence available suggests this does not improve survival," lead author Dr. Gavin D. Perkins, Warwick Clinical Trials Unit, University of Warwick, Coventry, UK, concluded. However, Dr. Perkins noted that use of a mechanical CPR device retains practical advantages such as safety and quality of CPR in the back of a moving vehicle and when transferring a patient to the emergency department.

Based on these results, the researchers do not recommend the routine use of LUCAS-2 as a substitute for manual chest compression.

Funding for the study was received from National Institute for Health Research.

Marfan症候群に対する新たな治療戦略（Abstract 61361）

Marfan症候群の小児においてロサルタンの大動脈拡大速度低下効果はアテノロールと同等である

Losartan equally as effective as atenolol for slowing rate of aortic enlargement in children with Marfan Syndrome

Marfan症候群の小児の大動脈拡大速度を低下させる治療の選択肢が広がったと、American Heart Association年次集会で発表された。Marfan症候群患者におけるアテノロール治療とロサルタン治療とを比較したスタディの結果、大動脈拡大速度は2つの治療群間で有意差がなかった。研究者らは、Marfan症候群患者608人（生後6か月から25歳）においてアテノロール（Marfan症候群患者で最も一般的に用いられる薬剤）とロサルタン（一部の研究においてアテノロールよりも有効である可能性が示唆されている薬剤）を比較した。両薬剤ともに体格で指標化した大動脈根部の経時的な低下をもたらした。3年間の大動脈拡大速度は2群間で有意差がなく、特に若年者において両群ともに大動脈拡大重症度は時間とともに低下した。この結果の原因は不明である。研究者らは薬物の用量設定が重要であると強調している。アテノロールの用量は患者の心拍数で調整され、日常診療においてMarfan症候群患者に使用されているよりも高用量であった。このスタディ結果は同時に*New England Journal of Medicine*に掲載された。

Full Text

Between 70 and 80 percent of patients with the connective tissue condition Marfan syndrome have aortic-root dilation. This condition can result in serious illness and sometimes death. A National Institutes of Health-funded study comparing treatment with widely used blood pressure medications atenolol or losartan in patients with Marfan syndrome who had an enlarged aortic root found no significant difference in the rate of aortic-root dilation between the two treatment groups over three years.

The results of the Atenolol versus Losartan in Children and Young Adults with Marfan Syndrome study, supported by NIH's National Heart, Lung, and Blood Institute (NHLBI), were presented at the American Heart Association (AHA) Scientific Sessions in Chicago. The study was published simultaneously in the *New England Journal of Medicine*.

Marfan syndrome is a genetic disorder that affects connective tissue. Standard care includes frequent cardiac imaging, exercise restriction, administration of a beta-blocker such as atenolol or other medications that may decrease the rate of aortic enlargement, and elective aortic-root replacement when the aortic root becomes too large. Although early diagnosis and refined medical and surgical management have improved survival, patients with Marfan syndrome continue to have high rates of complications and death from heart problems, even at a young age.

This randomized trial, which was conducted by the NHLBI's Pediatric Heart Network, ran from 2007-2011 at 21 clinical centers in the United States, Canada and Belgium and included 608 patients aged 6 months to 25 years. The two drugs work in different ways. Atenolol works by relaxing blood vessels and slowing heart rate to improve blood flow and decrease blood pressure. Losartan blocks the action of certain natural substances that tighten the blood vessels, allowing the blood to flow more smoothly and the heart to pump more efficiently.

Researchers compared atenolol (the drug most commonly used in patients with Marfan syndrome) to losartan (a drug that some research studies suggested might work better than atenolol) in 608 patients (aged 6 months to 25 years) with Marfan syndrome. They found no significant difference in the rate of aortic enlargement between the two groups who were studied over three years.

They noted that drug dosing is important. The dose of atenolol was adjusted to the patient's heart rate and was higher than the dose used in other studies and in routine clinical care of patients with Marfan syndrome. The dose of losartan was the highest FDA-approved dose at the start of the study. However, a higher dose of losartan might have shown a different effect on aortic growth rate. The beneficial effects of each drug seemed to be greater when given to younger children.

Few bothersome symptoms or major side effects occurred with either drug. Researchers conclude that both drugs are well tolerated and safe, therefore therapy can be chosen based on individual patient and health provider preference.

Previous small studies had suggested that losartan might be more effective in slowing aortic-root enlargement than atenolol, which is the most common current therapy. The NIH-funded study, the largest study to date, showed that there is no important difference between the two drugs when used for this purpose.

"These study results are very valuable for clinical practice," said Dr. Gary H. Gibbons, director, NHLBI. "Both drugs were well-tolerated by study participants, and losartan may be another treatment option for patients with Marfan syndrome. Furthermore, evaluating the effect of therapies in children is essential to ensuring evidence-based pediatric care."

Although the rate of change in the aortic root did not differ between treatment groups, the severity of aortic-root enlargement decreased over time in both groups, particularly in young subjects. The cause of this outcome is unknown. Further research is necessary to evaluate the magnitude of this benefit.

"This finding suggests that there is merit in starting therapy at a younger age and at an earlier stage of the disease," said the study's principal investigator, Dr. Ronald V. Lacro, director of the Cardiovascular Genetics Clinic and Marfan Syndrome Program, Boston Children's Hospital. "We have to remember that although this study did not show one drug to be more effective than the other, it still helped us greatly expand our knowledge of Marfan syndrome and the effects of atenolol and losartan."

The Marfan Foundation helped recruit participants and raised funds to support some trial costs. "The Marfan Foundation greatly appreciated the opportunity to partner with the NHLBI and Pediatric Heart Network on this trial, which was critically important to our Marfan community," said Josephine Grima, Ph.D., senior vice president of research and legislative affairs, The Marfan Foundation. "Their commitment to this large pediatric study opened the door to additional research on therapeutics for Marfan syndrome around the world, with scientists in nine other countries conducting trials."

"Public-private partnerships were a hallmark of this trial," said Gail Pearson, M.D., Sc.D., associate director, Division of Cardiovascular Sciences, and director, Office of Clinical Research at NHLBI. "Through the Pediatric Heart Network, we were able to bring together government, industry and patient communities to answer important questions in a population with a rare condition. This is a model that we hope will become more common."

The trial was supported by the by U01 grants from the NHLBI (HL068269, HL068270, HL068279, HL068281, HL068285, HL068292, HL068290, HL068288, HL085057) and the FDA Office of Orphan Products Development. Additional support provided by The Marfan Foundation, Merck & Co., Inc., and Teva Canada Limited.

無症状の糖尿病患者に対するCCTAは支持されない（Abstract 20773）

FACTOR-64：糖尿病患者の冠動脈疾患検出目的でのCT血管造影を用いたルーチンのスクリーニングは不要である

FACTOR-64: Routine screening of patients with diabetes for coronary artery disease with CT angiography not necessary

冠動脈コンピュータ断層血管造影（CCTA）を用いた糖尿病患者のスクリーニングの結果、少数において血行再建術が必要となり、スタチン使用が増加し、血圧およびLDL-Cが低下したが、4年後の心血管イベントは有意に低下させなかった。トライアルは*JAMA*に掲載され、2014年American Heart Association年次集会における発表と同時に公表された。研究者らは、少なくとも罹病期間が3～5年の1型または2型糖尿病で冠動脈疾患症状のない患者900人をCCTAを用いたスクリーニング（452人）または標準的な国内ガイドラインに基づいた糖尿病管理（448人）を行う群にランダムに割り付けた。標準的または強化療法（脂質、血圧および血糖値の治療に対して）は、CCTA所見に基づき推奨値を決定された。平均追跡期間4年後に、一次アウトカムイベント率（死亡、非致死性MI、または入院を要する不安定狭心症の合計）はCCTAとコントロール群とで有意差がなかった（6.2% 対7.6%、p=0.38）。虚血性主要有害心イベントである二次複合エンドポイントもまた2群間で差がなかった（4.4%対3.8% 、p=0.68）。これらの結果はこれらの患者群におけるCCTAスクリーニングを支持しないものであった。

Full Text

Joseph B. Muhlestein, M.D., of the Intermountain Medical Center Heart Institute, Murray, Utah, and colleagues examined whether screening patients with diabetes deemed to be at high cardiac risk with coronary computed tomographic angiography (CCTA) would result in a significant long-term reduction in death, heart attack, or hospitalization for unstable angina. The study appears in *JAMA* and is being released to coincide with its presentation at the American Heart Association's Scientific Sessions 2014.

Diabetes mellitus is the most important coronary artery disease (CAD) risk factor; patients with diabetes often develop severe but asymptomatic CAD. The combination of aggressive, asymptomatic CAD has made it the most common cause of death in patients with diabetes. The development of cardiac imaging with high-resolution CCTA now provides the opportunity to evaluate the actual coronary anatomy noninvasively and ascertain the overall extent and severity of coronary atherosclerosis. However, whether routine CCTA screening in high-risk populations can effect changes in treatment (such as preemptive coronary revascularization or more aggressive medical therapy), leading to a reduction in cardiac events, remains unproven, according to background information in the article.

The FACTOR-64 trial randomly assigned 900 patients with types 1 or 2 diabetes of at least 3 to 5 years' duration and without symptoms of CAD to CAD screening with CCTA (n = 452) or to standard national guidelines-based optimal diabetic care (n = 448). Patients were recruited from 45 clinics and practices of a single health system (Intermountain Healthcare, Utah). Standard or aggressive therapy (for treating abnormal lipid, blood pressure and glucose levels) was recommended based on CCTA findings.

At an average follow-up time of 4 years, the primary outcome event rates (composite of all-cause death, nonfatal heart attack, or unstable angina requiring hospitalization) were not significantly different between the CCTA and the control groups (6.2 percent [28 events] vs. 7.6 percent [34 events], p=0.38). The incidence of the composite secondary end point of ischemic major adverse cardiac events (CAD death, nonfatal heart attack, or unstable angina) also did not differ between groups (4.4 percent [20 events] vs. 3.8 percent [17 events], p=0.68).

"Coronary computed tomographic angiography involves significant expense and radiation exposure, so that justification of routine screening requires demonstration of net benefit in an appropriately high-risk population," the authors write. "These findings do not support CCTA screening in this population."

"What are the take-home messages from this randomized trial," asks Raymond J. Gibbons, M.D., of the Mayo Clinic, Rochester, Minn., in an accompanying editorial.

"Although studies like this are often characterized as 'negative,' there are several important messages. As suggested by the authors, future randomized trials of cardiac imaging in asymptomatic patients with diabetes should be larger and focused on an enriched study population at higher risk. Such a strategy would certainly enhance the chances of success. A more important and more currently applicable message is that guideline-directed medical therapy for hypertension and hyperlipidemia is effective in asymptomatic patients with diabetes and should be implemented more consistently. The data in this study suggest that Intermountain Healthcare has set a new published standard for what is achievable in patients with diabetes with respect to blood pressure control and lipid-lowering therapy and that, when therapy is applied this effectively, patients with diabetes are no longer at high risk for major cardiovascular events."

FACTOR-64 is an Investigator Initiated Study funded by the Intermountain Research and Medical Foundation, the Intermountain Heart Institute Department of Cardiovascular Research, Toshiba Corporation, and Bracco Corporation.

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AHA2014 (第87回米国心臓病協会)

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MI後の僧帽弁修復による有益性はほとんどまたは全くない（Abstract 20772）

虚血性僧帽弁逆流症患者においてCABGに加え僧帽弁修復を施行することによる利益はない

No gain seen to adding mitral valve repair to CABG in patients with ischemic mitral regurgitation

心筋梗塞後の中等度の僧帽弁傷害患者において冠動脈バイパス術（CABG）後にルーチンに僧帽弁修復術を追加することは是認されない可能性がある、とのスタディ結果が2014年American Heart Association年次集会で発表され、同時に*New England Journal of Medicine*に掲載された。このスタディは中等度の虚血性僧帽弁逆流（MR）に対し片方または両方の手術を施行された患者301人を対象とした。研究者らは、心収縮後の左室内残存血液量を6か月後および12か月後に計測することにより各々の患者の状態を評価した。両方の手術を受けた患者とCABG単独治療を施行された患者とで1年後の左心室の器質的障害からの回復、および心不全、脳卒中、機能的状態またはQOLなどの二次計測値には差が認められなかった。しかし、僧帽弁修復術の追加は神経学的イベント増加、クロスクランプや心肺バイパス時間増加、およびICU在室時間や入院期間が長いことと関連があった。さらに長期の追跡調査が現在行われている。

Full Text

Routinely adding mitral valve repair to coronary artery bypass graft surgery for myocardial infarction (MI) patients may not be warranted in patients with moderate mitral valve damage, according to an NIH-funded study. Patients treated with both procedures versus the bypass graft alone showed no differences at one year in recovery from structural damage to the heart's left ventricle, nor in secondary measures such as heart failure, stroke, functional status or quality of life.

The results of the Surgical Interventions for Moderate Ischemic Mitral Regurgitation (IMR) study, supported by NIH's National Heart, Lung, and Blood Institute (NHLBI), were presented at the American Heart Association Scientific Sessions in Chicago and published simultaneously in the *New England Journal of Medicine*.

Of patient suffering a myocardial infarction, about half are left with functional damage to the mitral valve due to the injury and changes to the heart muscle. This damage can result ischemic mitral regurgitation.

Doctors typically treat MI patients with this condition by performing coronary artery bypass graft surgery, sometimes adding mitral valve repair to fix the leaky mitral valve. The study is the first large-scale randomized clinical trial to assess whether adding the repair procedure leads to a measurable benefit for patients.

The study included 301 patients with moderate IMR who had been treated with one or both surgical procedures. Researchers assessed each patient's condition at six and 12 months by measuring the amount of blood remaining in the left ventricle after a heart contraction. Both patient groups showed similar rates of improvement at the 12-month assessment.

At 1 year, when compared with CABG alone, the addition of mitral valve repair to CABG did not result in a greater degree of left ventricular reverse remodeling or an improvement in mortality, MACE, hospital readmission or quality of life. However the addition of MV repair was associated with more neurologic events, increased cross clamp and cardiopulmonary bypass times, and longer ICU and hospital lengths of stay. Longer-term follow-up is ongoing.

This research was conducted as part of NHLBI's Cardiothoracic Surgical Trials Network and was co-funded by the National Institute for Neurological Diseases and Stroke and the Canadian Institutes for Health Research.

心臓の3Dプリントモデルは手術のプランニングに役立つ（Abstract 20614）

外科医らは複雑な障害を有する患者を心臓の3Dプリントモデルを用いて治療する

Surgeons use 3D printed model of heart to treat patients with complicated disorders

心臓の実験的3次元プリントモデルと標準的な医用画像との組み合わせは、外科医が複雑な先天性心奇形を有する患者を治療するのに有用である可能性がある、との研究結果が2014年American Heart Association年次集会で発表された。ほとんどの心臓外科医は手術のプランニングに際してX線、超音波およびMRIを用いて撮影された2D画像を用いる。しかし、これらの画像は複雑な先天性心奇形を現しきれていない可能性がある。しかし今や、医師は標準的な2D画像をガイドとし、最も複雑な構造異常ですら心臓の詳細な3Dモデルを石膏やセラミックなどの様々な素材で作成し示すことができるようになった。研究者らは安価な石膏複合材料を用いて、複雑な先天性心奇形を有する生後9か月女児、3歳男児および20歳代女性の心臓モデルを作成した。モデルと従来の画像を研究した結果、外科医は重度の心奇形患者3人全ての治療に成功した。このモデルは予後に有益であり得る妥協点を外科医らが見極めるのに役立った。今回のスタディは小規模のもので3Dプリントは今の時点ではまだ未承認の開発中の技術であることを研究者らは警告している。

Full Text

An experimental 3-dimensional printed model of the heart, combined with standard medical images, may help surgeons treat patients born with complicated heart disorders, according to research presented at the American Heart Association's Scientific Sessions 2014.

Most cardiac surgeons use 2D images taken by X-ray, ultrasound and MRI for surgical planning. However, these images may not reveal complex congenital heart defects, as opposed to those developing later in life within a structurally normal heart.

But with standard 2D images as a guide, doctors now can build a detailed 3D model of the heart from various materials, such as plaster or ceramic, to reveal even the most complicated structural abnormalities.

"With 3D printing, surgeons can make better decisions before they go into the operating room," said Matthew Bramlet, M.D., study lead author and assistant professor of pediatric cardiology and director of the Congenital Heart Disease MRI Program at the University of Illinois College of Medicine in Peoria. "The more prepared they are, the better decisions they make, and the fewer surprises that they encounter."

"When you're holding the heart model in your hands, it provides a new dimension of understanding that cannot be attained by 2D or even 3D images. What once was used to build trucks, we're using now to build models of hearts."

Researchers used an inexpensive plaster composite material to create heart models of a 9-month-old girl, 3-year-old boy and a woman in her 20s all of whom had complex congenital heart defects. After studying the models and traditional images, surgeons successfully repaired severe heart abnormalities in all three patients.

"You could see that if you make this compromise here, you could fix this problem, and go from a single-ventricle to a two-ventricle repair," Bramlet said. "That is the difference, potentially, between a life expectancy of two to three decades, to four, five or six decades."

Researchers caution that this was a small study and 3D printing is still an emerging technology that is not approved by the Food and Drug Administration. The University's collaborator, the Jump Trading Simulation and Education Center in Peoria, made the printer available for the study.

Co-authors are Randall Fortuna, M.D., and Welke Karl, M.D. Author disclosures are on the manuscript.

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