大気汚染は血管形成術の施行率を上昇させる (Abstract 2072)

大気汚染と冬は心筋梗塞治療率上昇と関連がある

Air pollution and winter linked with rise in treatment for myocardial infarction

寒い月の重度の大気汚染地域は空気の汚染されていない地域に比べ血管形成術施行率が高い、とESC Congress 2019 together with the World Congress of Cardiology で発表された。研究者らは、PM10 を用いて汚染されていない6都市および汚染された5都市を選択した。その結果、汚染地域および非汚染地域いずれにおいても、PM10 濃度の上昇は経皮的冠動脈インターベンション（PCI）の高い施行率と関連があった。空気のきれいな地域の患者は、汚染の悪化により敏感であった。PCI 施行は、1年で最も大気が汚染される冬に多くみられた。

Full Text

Heavily polluted areas have a higher rate of angioplasty procedures than areas with clean air, according to research presented at ESC Congress 2019 together with the World Congress of Cardiology. Procedures are even more common in winter, the most polluted time of year.

Study author Dr. Rafal Januszek of the University Hospital in Krakow, Poland said: "Epidemiological studies have reported negative impacts of pollution on the cardiovascular system but the effects on specific diseases were unclear. We also show for the first time that patients from areas with cleaner air are more sensitive to changes in pollution, while those from more polluted cities can adapt to fluctuations."

Using particulate matter (PM) 10 levels published by the Chief Inspectorate for Environmental Protection in Poland, six unpolluted cities and five polluted cities were selected for the study. PM10 are particles ten micrometres or less in diameter. Sources include industrial processes like iron making and quarrying, lawn mowing, wood and coal stoves, bushfires, dust storms, and vehicle exhaust emissions.

The study enrolled 5,648 patients from unpolluted cities and 10,239 patients from polluted cities. All patients underwent percutaneous coronary intervention (PCI) to open arteries blocked due to acute coronary syndromes. PCI data were obtained from the ORPKI Polish National PCI Registry.

Dates of PCI procedures were matched with air quality on the same day during a 52-week period. Analyses were also performed to compare winter versus non-winter weeks because pollution levels rise during winter.

The annual average PM10 concentration was significantly higher in polluted cities (50.95 µg/m3) compared to unpolluted cities (26.62 µg/m3). In both polluted and unpolluted areas, a rise in PM10 concentration was significantly associated with a greater frequency of PCI.

Patients in cities with clean air were more sensitive to pollution rises, with each 1 µg/m3 increase in PM10 concentration linked to 0.22 additional PCIs per week. While in polluted cities, the same rise in PM10 was linked with just 0.18 additional PCIs per week.

Regarding the seasonal effect, the PCI rate was significantly lower in non-winter, compared to winter, weeks in both polluted and clean cities. "The higher incidence of PCI in winter is related to greater air pollution during this period," said Dr. Januszek. "This is due to several factors such as artificial heating and the resulting smog."

He concluded: "The study shows that the incidence of acute coronary syndromes treated with PCI was higher in winter and rose along with increasing pollution, and this rise was higher in regions with initially cleaner air, if taking the same increment in pollution into account. This is further evidence that more needs to be done to lower pollution levels and protect the public's health."

The authors report no conflicts or sources of funding for this study.

Conference News

糖尿病患者におけるチカグレロルの臨床的有用性

THEMIS試験：チカグレロルとアスピリンの併用は糖尿病を有する安定冠動脈疾患患者の虚血イベントを減少させる

THEMIS: Ticagrelor plus aspirin reduce ischemic events in stable coronary patients with diabetes

チカグレロルとアスピリンの併用は、アスピリン単剤との比較で、糖尿病を有する安定冠動脈疾患患者の虚血イベントを減少させる、とのTHEMIS試験のレイトブレイキングの結果が *New England Journal of Medicine* に掲載され、ESC Congress 2019のHot Line Session で発表された。有効性主要評価項目（心血管死、心筋梗塞または脳卒中の複合）発現率は、チカグレロル群においてプラセボ群よりも低かった（7.7% vs. 8.5%、p=0.038）。TIMI大出血発現率は、チカグレロル群で高かった（2.2% vs. 1.0%、p<0.001）。チカグレロルはまた、*Lancet* に掲載された事前に規定されたサブグループ解析（THEMIS-PCI）において、PCI歴を有する糖尿病患者における虚血性イベントを減少させた。

Full Text

The combination of ticagrelor and aspirin reduces ischemic events compared with aspirin alone in patients with stable coronary artery disease and diabetes according to late breaking results of the THEMIS trial published in the *New England Journal of Medicine*. In addition, ticagrelor reduced ischemic events in patients with diabetes and previous percutaneous coronary intervention (PCI), according to results from the THEMIS-PCI study published in The *Lancet*. Both trials were presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology.

THEMIS Senior author Professor Deepak L. Bhatt of Brigham and Women's Hospital and Harvard Medical School, Boston, US said: "In the overall population studied in THEMIS, the reduction in important ischemic events was somewhat counterbalanced by the increase in bleeding. Therefore, it remains critical to identify which patients are at high ischemic risk, but low bleeding risk, who could benefit from ticagrelor and aspirin."

Patients with diabetes often develop coronary artery disease, with millions of such patients worldwide. Given the global obesity epidemic, rates of diabetes are increasing – rapidly so, in certain parts of the world. Those with both conditions are at high risk of myocardial infarction (MI), stroke, and amputations, in part due to an excess tendency for the blood to clot. Aspirin is generally used to decrease this risk, but cardiovascular events still occur at a high rate.

The THEMIS trial examined whether adding the antiplatelet drug ticagrelor to aspirin would reduce the risk of thrombotic events in these patients. The study enrolled 19,220 patients at 1,315 sites across 42 countries in North America, South America, Asia, Africa, Australia, and Europe. Patients were 50 years or older, had type 2 diabetes, and had stable coronary artery disease (defined as a history of percutaneous coronary intervention, bypass grafting, or angiographic stenosis of 50% or more in at least one coronary artery). Patients with known prior myocardial infarction or stroke were excluded.

Participants were randomly allocated to ticagrelor versus placebo, both on top of aspirin. The primary efficacy outcome was the composite of cardiovascular death, MI, or stroke. The primary safety outcome was Thrombolysis in Myocardial Infarction (TIMI) major bleeding. The median follow-up was 39.9 months.

The incidence of the primary efficacy outcome was lower in the ticagrelor group than in the placebo group (7.7% versus 8.5%; hazard ratio [HR] 0.90; 95% confidence interval [CI] 0.81–0.99; p = 0.038). The incidence of TIMI major bleeding was higher in the ticagrelor versus placebo group (2.2% versus 1.0%; HR 2.32; 95% CI 1.82–2.94; p<0.001).

Prof. Bhatt said: "There was a significant reduction in the primary endpoint of cardiovascular death, MI, and stroke with ticagrelor versus placebo. In addition to heart attack and stroke, acute limb ischemia and major amputations were also reduced with ticagrelor. Major bleeding was significantly increased."

Pinpointing subgroups of patients who could benefit from ticagrelor plus aspirin is crucial, said Prof Bhatt. "These are the patients at high ischemic risk, but low bleeding risk. In particular, those who have previously tolerated dual antiplatelet therapy without any bleeding complications seem to be the best candidates for prolonged therapy with ticagrelor and aspirin."

He noted that THEMIS-PCI, a prespecified subgroup analysis also presented at ESC Congress today and published in The Lancet, identified patients with the best balance of benefit versus bleeding risk. Prof Bhatt said: "In patients with diabetes and stable coronary artery disease with a history of previous coronary artery stenting who have tolerated dual antiplatelet therapy previously without any bleeding, prolonged therapy with ticagrelor and aspirin provides substantial gains in reducing the full spectrum of coronary, cerebral, and peripheral ischemic events."

Senior author of the THEMIS-PCI trial, Professor Philippe Gabriel Steg of Hospital Bichat, Paris, France said: "Treatment with ticagrelor and aspirin also increased major bleeding relative to aspirin alone, but there was a net clinical benefit with dual antiplatelet therapy."

Patients with diabetes represent 25–35% of those undergoing PCI, making it a sizeable population. Dual antiplatelet therapy is administered immediately following PCI, but in the long-term, patients are generally treated with a single antiplatelet agent (usually aspirin).

THEMIS-PCI is a prespecified subgroup analysis of the THEMIS trial, also presented at ESC Congress. THEMIS enrolled 19,220 patients at 1,315 sites across 42 countries in North America, South America, Asia, Africa, Australia, and Europe. Of those, 11,154 patients (58%) had undergone PCI and were included in the THEMIS-PCI study.

"We hypothesized that the efficacy, safety and net clinical benefit of ticagrelor may be different in the subgroup of patients with a history of PCI, who have previously been exposed to dual antiplatelet therapy with aspirin and a P2Y12 inhibitor such as ticagrelor, prasugrel or clopidogrel," noted Prof Steg.

Ticagrelor added to aspirin reduced cardiovascular death, MI, and stroke, (the relative reduction was 15% in patients with prior PCI, p = 0.013) although with a doubling of major bleeding (p<0.0001). The net clinical benefit appeared more favorable in patients with previous PCI than in patients without previous PCI, when evaluated as the composite of efficacy events and bleedings (15% relative risk reduction versus 6% relative risk increase, significant interaction, p = 0.012).

Prof Steg said: "The results suggest that long-term therapy with ticagrelor in addition to aspirin may be considered in patients with diabetes and a history of PCI who have tolerated antiplatelet therapy and have high ischemic risk and low bleeding risk. This is a novel therapeutic option for a large and easy to identify patient population."

AstraZeneca funded THEMIS and THEMIS-PCI. Disclosures: Professor Bhatt received research funding from AstraZeneca to Brigham and Women's Hospital for THEMIS and THEMIS-PCI. Professor Philippe Gabriel Steg discloses the following relationships: Research grant from Amarin, Bayer, Sanofi, and Servier; speaking or consulting fees from Amarin, Amgen, AstraZeneca, Bayer/Janssen, Boehringer-Ingelheim, Bristol-Myers-Squibb, Idorsia, Novartis, Novo-Nordisk, Pfizer, Regeneron, Sanofi, Servier.

Conference News

STEMI後の非責任病変におけるPCIで予後を改善

COMPLETE試験：STEMI後の完全血行再建は責任病変のみの血行再建よりも優れている

COMPLETE: Complete revascularization is superior to culprit-lesion only intervention following STEMI

ST上昇型心筋梗塞（STEMI）後患者において、完全血行再建は責任病変のみに対する経皮的冠動脈形成術（PCI）に比べ主要心血管イベントを減少させる。最初のコプライマリーエンドポイント（心血管死または心筋梗塞）は、完全血行再建術群の7.8% に発現したのに対し、責任病変のみの群では10.5% であった（p=0.004）。2番目のコプライマリーエンドポイント（心血管死、心筋梗塞、または虚血に対する血行再建術施行）は、完全血行再建術群で8.9% であったのに対し、責任病変のみの群では16.7% であった（p<0.001）。このCOMPLETE試験の結果はESC Congress 2019 のHot Line Session で発表され、*New England Journal of Medicine* に掲載された。

Full Text

An international randomized trial has shown that complete revascularization reduces major cardiovascular events compared to culprit-lesion only percutaneous coronary intervention (PCI). Late breaking results of the COMPLETE trial are presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in the *New England Journal of Medicine*.

Up to 50% of patients with ST-segment elevation myocardial infarction (STEMI) have multivessel coronary artery disease. In STEMI patients, opening the culprit artery with PCI reduces cardiovascular death or myocardial infarction. It is unclear whether additional PCI of non-culprit lesions also prevents these events.

"The question of whether to routinely revascularize non-culprit lesions or manage them conservatively with guideline-directed medical therapy alone is a common dilemma," said principal investigator Professor Shamir R. Mehta of the Population Health Research Institute, McMaster University, Hamilton, Canada.

Observational studies suggest a reduction in clinical events with staged, non-culprit lesion PCI, but are limited by selection bias and confounding. Prior randomized trials found declines in composite outcomes with non-culprit lesion PCI but were not powered to detect improvements in hard, irreversible clinical outcomes such as cardiovascular death or new myocardial infarction. While meta-analyses indicate a decline in cardiovascular death or myocardial infarction with non-culprit lesion PCI, there has been no single, large trial showing benefit on this clinically important outcome. The COMPLETE trial was designed to address this evidence gap.

A total of 4,041 patients with STEMI and multivessel coronary artery disease were enrolled from 140 centers in 31 countries. Patients were randomly allocated to complete revascularization with additional PCI of angiographically significant non-culprit lesions, or to no further revascularization. Randomization was stratified by the intended timing of non-culprit lesion PCI: either during or after the index hospitalization.

The first co-primary outcome was the composite of cardiovascular death or myocardial infarction; the second co-primary outcome also included ischemia-driven revascularization.

At a median follow-up of three years, the first co-primary outcome of cardiovascular death or myocardial infarction occurred in 158 patients (7.8%) in the complete revascularization group compared to 213 (10.5%) in the culprit-lesion only group (hazard ratio [HR] 0.74; 95% confidence interval [CI] 0.60–0.91; p=0.004).

The second co-primary outcome of cardiovascular death, myocardial infarction, or ischemia-driven revascularization occurred in 179 patients (8.9%) in the complete revascularization group compared to 399 (16.7%) in the culprit-lesion only group (HR 0.51; 95% CI 0.43–0.61; p<0.001).

There were no significant differences between groups in the occurrence of stroke (p=0.27) or major bleeding (p=0.15).

Regarding the timing of non-culprit lesion PCI, complete revascularization consistently reduced the first co-primary outcome in those stratified to receive non-culprit lesion PCI during the index hospitalization (HR 0.77; 95% CI 0.59–1.00) and after hospital discharge (HR 0.69; 95% CI 0.49–0.97; interaction p=0.62).

Prof Mehta said: "COMPLETE is the first randomized trial to show that complete revascularization reduces hard cardiovascular events compared to culprit-lesion only PCI in patients with STEMI and multivessel coronary artery disease. The benefits emerged over the long term and were observed regardless of whether non-culprit lesion PCI was performed early, during the initial hospitalization or shortly after hospital discharge. These findings are likely to have a large impact on clinical practice and prevent many thousands of recurrent heart attacks globally every year."

The Canadian Institutes of Health Research, AstraZeneca, and Boston Scientific funded the study. The authors received research grants AstraZeneca and Boston Scientific.

Conference News

ダパグリフロジンは糖尿病だけでなく心不全も治療する

DAPA-HF試験：ダパグリフロジンは心不全患者の死亡および入院を減少させる

DAPA-HF: Dapagliflozin reduces death and hospitalization in patients with heart failure

ダパグリフロジンは、糖尿病の有無にかかわらず駆出率の低下した心不全患者の死亡および入院を減少させた、とのDAPA-HF試験のレイトブレイキングの結果がESC Congress 2019 のHot Line Session で発表された。追跡期間中央値18.2か月の間に、一次エンドポイントを発現したのはダパグリフロジン群で16.3% であり、プラセボ群では21.2% であった（p<0.00001）。一次エンドポイントの構成要素はさらに、個別に解析された。ダパグリフロジン投与群の10% およびプラセボ投与群の13.7% が初回の心不全増悪を経験した（p<0.00004）。心血管系が原因で死亡したのは、それぞれ9.6% および11.5% であった（p=0.029）。

Full Text

Dapagliflozin reduces death and hospitalization in patients with heart failure and reduced ejection fraction with and without diabetes. The late breaking results of the DAPA-HF trial are presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology.

Principal investigator Professor John McMurray of the University of Glasgow, UK said: "The most important finding of all is the benefit in patients without diabetes. This is truly a treatment for heart failure and not just a drug for diabetes."

Sodium-glucose cotransporter 2 (SGLT2) inhibitors including dapagliflozin reduce the risk of developing heart failure in patients with type 2 diabetes. The DAPA-HF trial investigated whether dapagliflozin was also useful in treating established heart failure, even in patients without diabetes.

The trial enrolled 4,744 patients with heart failure and reduced ejection fraction in 20 countries and randomly allocated them to either dapagliflozin 10 mg once daily or matching placebo. The primary endpoint was the composite of a first episode of worsening heart failure (hospitalization for heart failure or an urgent heart failure visit requiring intravenous therapy) or death from cardiovascular causes.

The allocated treatments were given on top of standard care: 94% received an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker or angiotensin receptor–neprilysin inhibitor; 96% took a beta-blocker; and 71% took a mineralocorticoid receptor antagonist.

Over a median follow-up of 18.2 months, the primary outcome occurred in 386 of 2,373 patients (16.3%) in the dapagliflozin group and in 502 of 2,371 patients (21.2%) in the placebo group (hazard ratio [HR] 0.74; 95% confidence interval [CI] 0.65–0.85; p<0.00001).

The components of the primary outcome were also analyzed separately. A total of 237 patients (10.0%) receiving dapagliflozin and 326 patients (13.7%) receiving placebo experienced a first episode of worsening heart failure (HR 0.70; 95% CI 0.59–0.83; p<0.00004) and 227 (9.6%) and 273 (11.5%), respectively, died from cardiovascular causes (HR 0.82; 95% CI 0.69–0.98; p=0.029).

Regarding side effects, 178 patients (7.5%) in the dapagliflozin group had an adverse event related to volume depletion compared to 162 (6.8%) in the placebo group, with no significant difference between groups. Adverse events related to renal dysfunction occurred in 153 patients (6.5%) in the dapagliflozin group versus 170 patients (7.2%) in the placebo group, with no significant difference between groups. Major hypoglycemia and lower limb amputation and fracture were infrequent and occurred at similar rates in the two treatment groups.

Prof McMurray said: "Adverse events rarely required the discontinuation of treatment. There was no notable excess of any serious adverse event in the dapagliflozin group."

He concluded: "The trial shows that dapagliflozin reduces death and hospitalization, and improves health- related quality of life, in patients with heart failure and reduced ejection fraction, with and without diabetes. The clinical implications are potentially huge – few drugs achieve these results in heart failure and dapagliflozin does even when added to excellent standard therapy."

The DAPA-HF trial was funded by AstraZeneca. Professor McMurray's employer, Glasgow University, was paid by AstraZeneca for his role as Principal Investigator in the DAPA-HF trial with dapagliflozin.

Conference News

ACSにおいてプラスグレルはチカグレロルに勝る

ISAR-REACT 5試験：プラスグレルはPCIが予定されている急性冠症候群患者の虚血性イベントを減少させる

ISAR-REACT 5: Prasugrel cuts ischemic events in acute coronary syndrome patients headed to PCI

急性冠症候群を有し侵襲的治療を予定されている患者の虚血イベントを低下させるにあたり、プラスグレルはチカグレロルよりも優れている、とのISAR-REACT 5試験の結果が ESC Congress 2019で発表され、*New England Journal of Medicine* に掲載された。一次複合エンドポイント（12か月以内の死亡、心筋梗塞、脳卒中）は、チカグレロル群で9.3% に発現したのに対し、プラスグレル群では6.9% であった（p=0.006）。一次エンドポイントそれぞれの発現は、チカグレロル群とプラスグレル群とで、死亡は4.5% vs. 3.7%、心筋梗塞は4.8% vs. 3.0%、脳卒中は1.1% vs. 1.0% であった。

Full Text

Prasugrel is superior to ticagrelor for reducing ischemic events in patients with acute coronary syndrome and a planned invasive strategy. The late breaking results of the ISAR-REACT 5 trial are presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in the *New England Journal of Medicine*. There was no increase in the rate of major bleeding with prasugrel.

In acute coronary syndromes, a dual antiplatelet regimen with a P2Y12 receptor antagonist plus aspirin is the cornerstone of treatment. Prasugrel and ticagrelor provide greater, more rapid, and consistent platelet inhibition compared to their predecessor clopidogrel. Both drugs are recommended over clopidogrel for 12 months after percutaneous coronary intervention (PCI) in acute coronary syndrome patients with and without ST-segment elevation (STEMI and NSTE-ACS, respectively). Until now, the relative merits of ticagrelor versus prasugrel for the one-year treatment of acute coronary syndrome patients were unknown.

The ISAR-REACT 5 trial tested the hypothesis that ticagrelor is superior to prasugrel in reducing the primary composite endpoint of death, myocardial infarction, or stroke within 12 months in acute coronary syndrome patients intended for an invasive strategy. A total of 4,018 patients were enrolled from 23 centers in Germany and Italy and randomly allocated to prasugrel or ticagrelor.

Patients assigned to ticagrelor received a loading dose as soon as possible after randomization. In other words, the timing of study drug administration was irrespective of clinical presentation and knowledge of coronary anatomy. In the prasugrel group, the timing of study drug initiation depended on clinical presentation. STEMI patients received prasugrel as soon as possible after randomization (i.e. they were pretreated). In patients with NSTE-ACS, administration of the prasugrel loading dose required knowledge of the coronary anatomy.

The primary composite endpoint of death, myocardial infarction, or stroke at 12 months occurred in 9.3% of patients in the ticagrelor group and 6.9% in the prasugrel group (hazard ratio [HR] 1.36; 95% confidence interval [CI] 1.09–1.70; p = 0.006).

The incidence of the individual components of the primary endpoint in the ticagrelor and prasugrel groups was 4.5% versus 3.7% for death, 4.8% versus 3.0% for myocardial infarction, and 1.1% versus 1.0% for stroke. Definite or probable stent thrombosis occurred in 1.3% of patients assigned to ticagrelor and 1.0% assigned to prasugrel and definite stent thrombosis in 1.1% versus 0.6% of patients, respectively.

The increase in anti-ischemic efficacy with prasugrel was not accompanied by a raised bleeding risk. Bleeding (BARC class 3 to 5) was observed in 5.4% of patients in the ticagrelor group and 4.8% of patients in the prasugrel group (HR 1.1; 95% CI 0.8–1.5; p = 0.46).

Principal investigator Professor Stefanie Schuepke of the German Heart Centre Munich said: "In this investigator-initiated, multicenter, randomized clinical trial of invasively treated acute coronary syndrome patients, prasugrel significantly reduced the composite rate of death, myocardial infarction, or stroke compared to ticagrelor with no rise in the rate of major bleeding."

This trial was supported by the DZHK (German Centre for Cardiovascular Research) and the Deutsches Herzzentrum München. Prof. Schüpke reports grants from the DZHK (German Centre for Cardiovascular Research), the Else-Kröner-Memorial Stipendium from the Else Kröner-Fresenius-Stiftung and consulting fees from Bayer Vital GmbH.

Conference News

駆出率の保たれた心不全は依然として治療が困難である

PARAGON-HF試験では駆出率の保たれた心不全におけるエンドポイントは達成できなかったが、一部の患者で有益性が認められた

PARAGON-HF misses endpoint in heart failure with preserved ejection fraction, but benefit noted in some patients

アンジオテンシン受容体-ネプリライシン阻害薬sacubitril/バルサルタンは、駆出率の保たれた心不全患者（HFpEF）における全入院および心血管死減少からなる一次エンドポイントは達成できなかったが、データから一部の患者群において有益である可能性が示された。一次エンドポイント率比は0.87（95% 信頼区間 [CI] 0.75-1.01；p=0.059）であった。駆出率中央値57%未満の患者において有益性が高く、一次エンドポイントが22% 低下し、さらに女性では28% 低下した。このPARAGON-HF試験の結果は、ESC Congress 2019のHot Line Session で発表され、*New England Journal of Medicine* に掲載された。

Full Text

The angiotensin neprilysin inhibitor sacubitril/valsartan missed its primary endpoint of reducing total hospitalization and cardiovascular death in patients with heart failure with preserved ejection fraction (HFpEF), but the data suggest there may be benefit in some patient groups. The late breaking results of the PARAGON-HF trial were presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in the *New England Journal of Medicine*.

The PARAGON-HF trial showed evidence of a heterogeneous response to treatment, with potential benefit in certain subgroups, such as women and patients with an ejection fraction below the median. "Our data strongly imply that one size might not fit all in HFpEF," said co-principal investigator Professor Scott D. Solomon of Brigham and Women's Hospital, Harvard Medical School, Boston, US.
Up to 64 million worldwide have heart failure – of these approximately half have left ventricular ejection fraction of 40% or greater. This encompasses heart failure with mid-range ejection fraction (HFmrEF; ejection fraction 40–49%), and HFpEF (ejection fraction 50% or greater). Evidence- based therapies exist only for heart failure with reduced ejection fraction (HFrEF; ejection fraction 40% or less).

Sacubitril/valsartan, which combines the neprilysin inhibitor sacubitril and the angiotensin receptor blocker valsartan, simultaneously inhibits the renin-angiotensin system and augments endogenous vasoactive peptide systems. The drug reduced morbidity and mortality in patients with HFrEF in the PARADIGM-HF trial. It has a class I guideline recommendation for the treatment of HFrEF.

PARAGON-HF was designed to test the hypothesis that sacubitril/valsartan would improve outcomes in HFpEF. A total of 4,822 patients were randomly assigned to sacubitril/valsartan or valsartan. The comparator was valsartan because most HFpEF patients already take a renin-angiotensin system inhibitor. Patients were required to have signs and symptoms of heart failure, a left ventricular ejection fraction of 45% or greater, evidence of natriuretic peptide elevation, and structural heart disease. The median follow-up was 34 months. The primary endpoint was a composite of total (first and recurrent) heart failure hospitalizations and cardiovascular death.

The rate ratio for the primary endpoint was 0.87 (95% confidence interval [CI] 0.75–1.01; p = 0.059). This reduction was just short of statistical significance and was driven by a decline in heart failure hospitalization with no effect on cardiovascular death or all-cause mortality.

A number of sensitivity analyses, including assessment of investigator-reported outcomes, favored sacubitril/valsartan. Several secondary endpoints, such as quality of life, change in New York Heart Association (NYHA) class, and percentage of patients with worsening renal function, favored sacubitril/valsartan. Prof Solomon said: "The reduction in total hospitalizations for heart failure was smaller than anticipated and not statistically significant. However, some secondary endpoints suggested a modest overall benefit with sacubitril/valsartan."

Sacubitril/valsartan was associated with more hypotension, but less hyperkalemia and less renal dysfunction compared with valsartan, findings similar to those seen in the PARADIGM-HF trial.

Importantly, there was heterogeneity in the population with respect to treatment response. In particular, there was greater benefit in patients with ejection fraction below the median of 57%, with a 22% reduction (rate ratio 0.78; 95% CI 0.64–0.95) and in women, with a 28% reduction (rate ratio 0.73; 95% CI 0.59–0.90) in the primary endpoint. "Our data suggest that there may be differential benefit, with some patients, including those in the lower range of ejection fraction and women responding to a greater degree than others," said Prof Solomon.

He noted that the results at the lower end of the ejection fraction range should be considered in light of the PARADIGM-HF trial which showed substantial benefit in those with heart failure and ejection fraction below 40%. Aside from ejection fraction, the entry criteria for PARADIGM-HF and PARAGON-HF were nearly identical. "Our findings indicate that the benefit of sacubitril/valsartan observed in PARADIGM-HF could extend to heart failure patients with ejection fraction below the normal range, including those designated HFmrEF," he said.

As for the observations in women, Prof Solomon said: "The potential differential benefit in women is intriguing as women make up a much greater proportion of patients with HFpEF compared to HFrEF. Further analyses will explore these subgroup findings in detail and help determine which patients with heart failure across a broad range of ejection fraction might benefit the most from sacubitril/valsartan."

The study was funded by Novartis. Dr. Solomon has received research grants through his institution from Novartis for the conduct of the PARAGON-HF trial and has consulted for Novartis.

Conference News

高感度トロポニンを用いた単回の検査でMIを除外する

HiSTORIC試験：心筋梗塞疑いに対する迅速検査により健康な患者を早期に帰宅させることが可能になる

HiSTORIC: Rapid pathway for suspected myocardial infarction enables healthy patients to go home earlier

心筋梗塞の早期除外診断は、心有害事象を増加させることなく病院滞在時間および入院を減少させる、とのHiSTORIC試験のレイトブレイキングの結果がESC Congress 2019のHot Line Sessionで発表され、*Circulation*に掲載された。この試験では高感度トロポニン検査を用いて、診察時の心筋梗塞を除外する迅速な方法の有効性および安全性を、標準的な方法と比較し調査した。この検査を実地臨床でルーチンに導入することにより、救急外来滞在時間が3時間以上短縮し、救急外来から帰宅する患者の割合は追加リスクなく50%以上増加した。

Full Text

An early rule-out pathway for myocardial infarction (MI) reduces length of stay and hospital admissions without increasing adverse cardiac events, according to late breaking results from the HiSTORIC trial presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in *Circulation*.

Principal investigator Professor Nicholas Mills of the University of Edinburgh, UK said: "This is the first randomized controlled trial to evaluate the efficacy and safety of an early rule-out pathway. Introducing the pathway into routine clinical practice reduced length of stay by more than three hours and increased the proportion of patients discharged from the emergency department by over 50%."

Suspected MIs account for up to 10% of all hospital attendances and 40% of unscheduled admissions. Most of these patients have not had and MI, and effective and safe pathways are needed to rule out this diagnosis in the emergency department.

The diagnosis of myocardial infarction includes measuring the concentration of cardiac troponin, a protein released into the blood when the heart muscle is injured. Guidelines recommend serial testing at presentation and 6 to 12 hours later to coincide with the peak in troponin concentration (standard care). In most hospitals, myocardial infarction is ruled out when the cardiac troponin concentration is less than the upper reference limit or 99th percentile on serial testing.

The HiSTORIC trial examined the efficacy and safety of an expedited pathway, where high-sensitivity cardiac troponin testing is used to rule out myocardial infarction at presentation, compared to standard care. Myocardial infarction is ruled out at presentation with a single test using a lower threshold of 5 ng/L. The scientific basis for this approach to risk stratification is published simultaneously in Circulation. If the troponin concentration is above this risk stratification threshold, cardiac troponin is measured again at three hours; myocardial infarction is ruled out if the concentration is unchanged and remains below the 99th percentile.

This was a stepped-wedge cluster randomized controlled trial in 31,492 consecutive patients with suspected acute coronary syndrome presenting to seven hospitals in Scotland. The hospital was the unit of randomization. The primary efficacy outcome was length of stay, defined as the length of time from initial presentation to the emergency department until final discharge from hospital. The primary safety outcome was myocardial infarction or cardiac death after discharge and was evaluated at 30 days and one year.

Length of stay was 10.1 hours and 6.8 hours before and after implementation of the early rule-out pathway, respectively (adjusted geometric mean ratio 0.78; 95% confidence interval [CI] 0.73–0.83; p<0.001). The proportion of patients discharged from the emergency department without hospital admission increased from 53% to 74% (adjusted risk ratio 1.57; 95% CI 1.34–1.83; p<0.001) after introducing the early rule-out pathway.

At 30 days, the primary safety outcome occurred in 57/14,700 (0.4%) and 56/16,792 (0.3%) patients before and after implementation of the early rule-out pathway, respectively. At one year, the primary safety outcome occurred in 396/14,700 (2.6%) and 307/16,792 (1.8%) of patients before and after introducing the early rule-out pathway, respectively.

"These results show that the use of an early rule-out pathway can be very effective, and earlier discharge is not associated with adverse cardiac event," said Prof Mills. "Most guidelines recommend ruling in and ruling out MI using a single threshold (99th percentile). Our trial demonstrates that using separate risk stratification and diagnostic thresholds allows MI to be ruled out at presentation in more patients without additional risk."

Prof Mills said the potential benefits for patients and healthcare systems are considerable. "We observed substantial reductions in length of stay and increases in the number of patients avoiding hospital admission. In the US alone, more than 20 million patients attend emergency departments with suspected acute coronary syndrome every year. Reducing length of stay by three hours could save more than $3.6 billion annually on bed occupancy alone," he said.

This trial was funded by the British Heart Foundation (BHF) with support from a BHF Research Excellence Award. NLM reports research grants awarded to the University of Edinburgh from Abbott Diagnostics and Siemens Healthineers outside the submitted work, and honoraria from Abbott Diagnostics, Siemens Healthineers, Roche Diagnostics, Singulex and LumiraDx.

Conference News

16年経過してもPCIは未だ血栓溶解療法に勝る

DANAMI-2試験：冠動脈ステント留置により死亡または再梗塞を1年以上遅らせることができる

DANAMI-2: Death or reinfarction delayed by more than one year with coronary stenting

転院を含むプライマリ経皮的冠動脈インターベンション（PCI）治療により、血栓溶解療法に比べ死亡または再梗塞を1年以上遅らせることができる、との DANAMI-2試験の結果が ESC Congress 2019 の Hot Line Session で発表され、*European Heart Journal* に掲載された。プライマリPCIを施行された患者は、16年間の総死亡または再梗塞からなる複合エンドポイント発現率が持続的かつ有意に低かった。これはコホート全体（PCI 58.7% vs. 血栓溶解療法 62.3%、ハザード比 [HR] 0.87）および紹介病院からPCI可能な高度医療センターに転送された患者（PCI 58.7% vs. 血栓溶解療法 64.1%、HR 0.84）、いずれにおいても明らかであった。

Full Text

Death or reinfarction is delayed by more than one year with a primary percutaneous coronary intervention (PCI) strategy that includes hospital transfer, compared to fibrinolysis, to late breaking results from the DANAMI-2 trial presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in *European Heart Journal*.

"In the longest follow-up to date, the analysis confirms that primary PCI should be offered to ST-segment elevation myocardial infarction (STEMI) patients if transfer to a PCI center can be achieved within 120 minutes," said first author Pernille Thrane of Aarhus University, Denmark.

The DANish Acute Myocardial Infarction 2 (DANAMI-2) trial was the first to show that a reperfusion strategy with interhospital transport for primary PCI is superior to fibrinolysis at the local hospital in patients with STEMI at 30 days. Follow-up studies found sustained benefit at three and eight years.

"Very long-term outcomes are important to understand the full clinical impact of primary PCI versus fibrinolysis in STEMI patients," said principal investigator Dr. Michael Maeng of Aarhus University Hospital and Aarhus University. "But high costs and logistical challenges often limit the follow-up period in randomized trials."

This analysis of the trial investigated cardiovascular outcomes and mortality after 16 years of follow-up. A total of 1,572 STEMI patients were enrolled at 24 referral hospitals and five invasive centers in Denmark. Patients were randomly allocated to primary PCI or fibrinolysis. Patients randomized to primary PCI at referral hospitals were immediately transported to the nearest invasive center. For the first three years patients were followed- up with visits at the randomizing hospital. Afterwards, outcome data was obtained from Danish registries. The primary endpoint for this analysis was a composite of all-cause death or reinfarction.

Patients treated with primary PCI had a sustained and significantly lower rate of the composite endpoint of all- cause mortality or reinfarction at 16 years compared to patients treated with fibrinolysis. This was evident in both the entire cohort (PCI 58.7% versus fibrinolysis 62.3%) and in patients transported from a referral hospital to a PCI-capable tertiary hospital (PCI 58.7% versus fibrinolysis 64.1%).

Hazard ratios (HRs) for the benefit of primary PCI over fibrinolysis were 0.87 for the entire cohort and 0.84 for the transferred subgroup. The difference was primarily driven by a consistently reduced rate of reinfarction with primary PCI compared to fibrinolysis (PCI 17.5% versus fibrinolysis 21.8%; HR 0.78).

The average time to the composite endpoint was 10.6 years in the primary PCI group, leading to an average event postponement of 12.3 months compared to fibrinolysis. Furthermore, primary PCI reduced cardiac mortality by an absolute 4.4% (PCI 18.3% versus fibrinolysis 22.7%; HR 0.78), which is the first time that a single study has been able to demonstrate this benefit.

ESC guidelines recommend that STEMI patients are immediately transferred for primary PCI if the time from first medical contact to reperfusion is within 120 minutes. "This timeframe is based on the initial DANAMI-2 results and the long-term benefits are confirmed by this 16-year follow-up," said Ms. Thrane.

Funding for the study was received from Novo Nordic Foundation and Cardiology Research Unit at Aarhus University Hospital, Denmark. Ms. Thrane is the recipient of a research scholarship from Novo Nordic Foundation. Dr. Maeng reports lecture and advisory board fees from Astra-Zeneca, Bayer, Boehringer-Ingelheim, Boston Scientific, Bristol-Myers Squibb, and Novo Nordisk

Conference News

β遮断薬は腎機能障害を有する患者であっても死亡率を低下させる

BB-meta HF試験：心不全および中等度腎機能障害を有する患者においてベータ遮断薬は死亡を減らす

BB-meta HF: Beta-blockers reduce death in patients with heart failure and moderate renal impairment

駆出率の低下した洞調律の心不全（HFrEF）において、β遮断薬はたとえ腎機能障害を有していても死亡を予防するために有効である、と ESC Congress 2019 の Hot Line Session で発表された。追跡期間中央値1.3年の間、腎機能障害は高死亡率と独立して関連があり、腎機能障害が重度であるほど心不全の進行が死亡原因である頻度が高かった。洞調律の患者13,861人において、中等度から中等度-重度の腎障害を有する患者であっても、β遮断薬は死亡率を有意に低下させた。補正後、β遮断薬はプラセボと比較し、死亡リスクをそれぞれ27%および29% 低下させた。

Full Text

Beta-blockers remain effective for preventing death in heart failure with reduced ejection fraction (HFrEF) and sinus rhythm, even in patients with moderate or moderately-severe kidney dysfunction, according to late breaking research presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology.

It is estimated that up to half of heart failure patents have renal impairment according to their estimated glomerular filtration rate (eGFR). ESC 2016 heart failure guidelines state that "there is lack of evidence-based therapies" in patients with kidney dysfunction. In almost every section of the guidelines, clinicians are warned that caution should be exercised when heart failure drugs are used in patients with impaired renal function.

Principal investigator of the study, Dr. Dipak Kotecha of the University of Birmingham, UK said: "Although there is no clear contraindication for most patients, it is not surprising that treatment initiation or uptitration of life- saving heart failure therapies is quite low in patients with coexisting renal dysfunction. Ironically, heart failure patients with impaired kidney function are at the highest risk of adverse outcomes and have potentially the most to gain from therapy."

The efficacy and safety of HFrEF treatment is unknown in those with moderate renal dysfunction (eGFR 45–59 mL/min/1.73m2) or moderately-severe renal dysfunction (30–44 mL/min/1.73m2). Prior analyses have not had sufficient power, and randomized trials tend to exclude these patients (either actively or subconsciously).

In this analysis, individual patient data were meticulously combined from landmark, double-blind, placebo- controlled randomized trials to answer key clinical questions: 1) do beta-blockers reduce mortality in patients with moderate or moderately-severe kidney dysfunction, and 2) does therapy lead to reduction in renal function over time or higher rates of adverse events that could limit clinical value? The analysis was conducted by the multinational Beta-blockers in Heart Failure Collaborative Group (BB-meta-HF).

The primary endpoint was all-cause mortality. Beta-blocker efficacy in patients with left ventricular ejection fraction less than 50% was determined according to eGFR at baseline. Results were stratified by heart rhythm since BB-meta-HF previously found a significant interaction comparing sinus rhythm and atrial fibrillation.

A total of 16,740 patients with HFrEF were included from ten trials. The median age was 65 years and 23% were women. During a median follow-up of 1.3 years, renal dysfunction was independently associated with higher mortality, and cause of death was more often due to progressive heart failure in patients with more severe renal impairment.

In 13,861 patients in sinus rhythm, beta-blockers significantly reduced mortality, even in those with moderate or moderately-severe kidney dysfunction. After adjustment, beta-blockers were associated with a 27% and 29% lower risk of death, respectively, compared to placebo. In those with eGFR 30–44 mL/min/1.73m2, the lowest range tested in large placebo-controlled trials, the absolute risk reduction from beta-blockers for all-cause mortality was 4.7%, with only 21 patients requiring treatment for a year to save a life. In patients with renal impairment, beta-blockers did not lead to any deterioration in eGFR, there was no increase in adverse events compared to placebo, and most achieved reasonable doses in these blinded trials.

Dr. Kotecha said: "In patients with HFrEF and sinus rhythm, these drugs work as effectively at an eGFR of 40 as they do at an eGFR of 90. We show conclusively that moderate or moderately-severe kidney dysfunction should not be a barrier to beta-blocker initiation or uptitration. Unfortunately, data is lacking on patients with severe kidney disease (eGFR less than 30) and we were unable to make any definitive statements on the efficacy or safety of beta-blockers in this group."

In the 2,879 patients with atrial fibrillation at baseline, there was no significant reduction in mortality associated with beta-blockers in any category of eGFR, but also no harm identified. Dr. Kotecha said: "Patients with HFrEF and atrial fibrillation are another high-risk group and we know treatments are less effective when these conditions are combined. Prevention of atrial fibrillation in HFrEF is always best – using guideline- recommended heart failure therapy at appropriate dosages in all patients can substantially reduce the risk of developing atrial fibrillation."

Worsening renal function of 20% or greater during follow-up was associated with a 28% increase in subsequent death overall, and a 46% increase in patients with moderate or moderately-severe renal impairment. "In our study, worsening renal function did not appear to be caused by beta-blocker therapy and all patients were already on ACE inhibitors. Nonetheless, worsening renal function was linked to poor outcomes and this highlights the importance of preserving kidney function by working with renal specialists," said Dr. Kotecha.

Regarding the implications for clinical practice, Dr. Kotecha said HFrEF patients in sinus rhythm with moderate or moderately-severe renal dysfunction should not be restricted from receiving beta-blockers. "This will save lives," he said. "Aim for good doses and inform patients that in blinded trials there was no difference in withdrawal of therapy due to adverse events compared to placebo."

BB-meta-HF received an unrestricted research grant for administrative costs from Menarini, data extraction support from GlaxoSmithKline, consent for data extraction from Merck, AstraZeneca and the National Heart Lung and Blood Institute BioLINCC, and a collaborative research grant from IRCCS San Raffaele Italy. Dr. Kotecha is funded by a National Institute for Health Research (NIHR) Career Development Fellowship.

In addition to the study funding above, Dr. Kotecha reports personal fees from Bayer (advisory board), Chief Investigator for the RAte control Therapy Evaluation in permanent Atrial Fibrillation trial, British Heart Foundation Project Grant and EU Innovative Medicines Initiative Collaboration Grant.

Conference News

PCIとCABGには10年後の死亡率に差はない

SYNTAX試験：バイパス手術と冠動脈ステント留置術とでは10年後の予後は同等である

SYNTAX: Bypass surgery and coronary stenting yield comparable 10-year survival

新規発症3枝病変および左冠動脈主幹部病変を有する患者において、冠動脈バイパス術（CABG）と薬剤溶出性ステント留置術とでは10年生存率は同等である、とのSYNTAX Extended Survival 試験の結果が ESC Congress 2019 で発表され、*Lancet* に掲載された。10年間の追跡調査の結果、患者群全体における生存率は薬剤溶出性ステントを用いたPCIとCABG とで差がなかった（p=0.092）。事前に規定されたサブグループについてさらに解析した結果、3枝病変および進行した複雑な冠動脈病変を有する患者において、CABG は10年生存率において改善を認めた。糖尿病の有無で10年生存率に差はなかった。

Full Text

Ten-year survival rates are similar for bypass surgery and coronary stenting with drug-eluting stents in randomized patients with de novo three-vessel and left main coronary artery disease, according to late breaking results from the SYNTAX Extended Survival study presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in The *Lancet*.

Prespecified subgroup analyses showed that surgery provided a survival benefit in patients with three-vessel disease and more complex coronary artery disease, while no treatment differences were found in patients with left main disease.

Ischemic heart disease is the top cause of death globally. Percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) are options for patients requiring revascularization. European guidelines advise discussing these patients in a multidisciplinary Heart Team.

Individual randomized trials comparing PCI with drug-eluting stents and CABG have not shown a survival benefit for either therapy at mid-term follow-up (e.g. up to five years). The SYNTAX trial was the first large- scale multicenter, randomized study in patients with de novo three-vessel and left main coronary artery disease that underwent PCI with drug-eluting stents or CABG. When clinical equipoise between PCI and CABG was presumed by the Heart Team, 1,800 patients were randomly assigned to PCI with paclitaxel-eluting stents (n=903) or CABG (n=897). Survival curves started to diverge after one-year follow-up and continued to diverge up to five years, but without reaching statistical significance.

The SYNTAX Extended Survival (SYNTAXES) study examined 10-year all-cause death rates in patients with de novo three-vessel and left main coronary artery disease randomized to PCI with drug-eluting stents or CABG in the SYNTAX trial. All 85 SYNTAX sites from 18 North American and European countries were contacted to provide survival data, which was obtained from healthcare records and national death registries. Completeness of follow-up was achieved in 94% of patients and was well-balanced between the CABG and PCI arms.

At 10-year follow-up, there was no survival difference between PCI with drug-eluting stents and CABG in the overall cohort of patients. There were 244 deaths after PCI and 211 after CABG (hazard ratio [HR] 1.17; 95% confidence interval [CI] 0.97–1.41; p=0.092).

When analyses were conducted according to prespecified subgroups, CABG provided a 10-year survival benefit over PCI in patients with three-vessel disease (151 deaths after PCI versus 113 after CABG; HR 1.41; 95% CI 1.10–1.80; p=0.006). CABG also provided a survival benefit in patients with increasingly complex coronary artery disease (defined by higher SYNTAX scores) – this was observed in the overall cohort and in those with three-vessel disease. In the subgroup of patients with left main coronary artery disease, no survival differences existed between PCI and CABG (93 patients died after PCI versus 98 after CABG; HR 0.90; 95% CI 0.68–1.20; p=0.47). This resulted in a treatment-by-subgroup interaction according to the presence or absence of left main coronary artery disease (p for interaction=0.019). Furthermore, CABG and PCI resulted in comparable 10- year survival in patients with and without diabetes.

First author Dr. Daniel Thuijs of the Erasmus University Medical Center, Rotterdam, the Netherlands said: "The SYNTAX Extended Survival study presents robust, clinically relevant, and complete 10-year randomized survival data and can aid a multidisciplinary Heart Team discussion in the process of deciding on the optimal treatment strategy for a patient with coronary artery disease requiring revascularization."

The SYNTAXES study was supported by the German Foundation of Heart Research. The SYNTAX trial (0-5 year follow-up) was supported by Boston Scientific Corporation.

Conference News

2年後の時点で経皮的僧帽弁修復術の有益性は認められなかった

MITRA-FR試験：心不全患者における二次性僧帽弁閉鎖不全症は2年後の転帰を改善しない

MITRA-FR: Reducing secondary mitral regurgitation in heart failure does not improve two-year outcomes

心不全患者における二次性僧帽弁閉鎖不全症に対する経皮的修復術は、標準的な医療と比較し、2年後の時点で死亡および入院を減少させない、との MITRA-FR 試験の結果が ESC Congress 2019 で発表され、*European Journal of Heart Failure* に掲載された。総死亡および心不全による予定外入院は、弁修復術を施行された患者の63.8% および弁修復術を施行されなかった患者の67.1% に発現し、2群間で有意差はなかった。これらの転帰を別々に解析しても、有意差は認められなかった。

Full Text

Percutaneous reduction of secondary mitral regurgitation in patients with heart failure does not lower death and hospitalization at two years compared to standard medical care, according to late breaking results from the MITRA-FR study presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in the *European Journal of Heart Failure*.

The benefits of percutaneous correction of secondary mitral regurgitation in patients with heart failure is controversial. One-year results of MITRA-FR, first reported at ESC Congress 2018 and published in the New England Journal of Medicine, showed no significant impact of mitral valve repair on death and heart failure hospitalization compared to standard medical treatment. In contrast, the COAPT study found that valve repair significantly reduced heart failure rehospitalization and death after two years of follow-up.

"Many hypotheses have been suggested to explain the different outcomes between the two randomized trials," said MITRA-FR principal investigator Professor Jean-Francois Obadia of Civil Hospices of Lyon, France. "One theory is the longer duration of COAPT. We therefore conducted a two-year follow-up of patients in MITRA-FR."

The two-year results show that the combined outcome of all-cause death and unplanned hospitalization for heart failure occurred in 63.8% of patients who underwent valve repair and 67.1% in those who did not, with no significant difference between groups. There were no significant differences between groups when each outcome was analyzed separately. Rates of all-cause mortality were 34.9% and 34.2% in the intervention and control groups, respectively. Rates of unplanned hospitalization for heart failure were 55.9% and 61.8% in the intervention and control groups, respectively.

"This analysis confirms the absence of a significant difference in the rate of the composite outcome of death from any cause or unplanned hospitalization for heart failure in symptomatic patients with severe secondary mitral regurgitation treated by percutaneous mitral valve repair plus medical treatment as compared with those receiving medical treatment alone," said Prof. Obadia. "Percutaneous repair remained safe – there was a very small number of prespecified serious adverse events."

An exploratory analysis of events occurring between 12 and 24 months suggested a lower rate of first hospitalization for heart failure in the intervention group. This was consistent with a divergence in the curves of recurrent hospitalizations for heart failure for each group.

"This repeat event analysis was used as the main endpoint in the COAPT trial and tends to amplify differences compared to the analysis of time to first event, which was the main endpoint in MITRA-FR," said Prof Obadia. "As for any exploratory analysis of secondary endpoints, the interpretation of such an isolated finding should be viewed cautiously and only considered hypothesis generating."

Regarding the differing results between the two trials, Prof Obadia said: "In our view, one of the main reasons is patient selection. Differences in inclusion criteria led to more severe mitral regurgitation, less pronounced left ventricular remodeling, lower pulmonary pressure, and better right ventricular function in COAPT compared to MITRA-FR. In addition, the run-in period assessed by a central eligibility committee was likely to result in more optimized guideline-directed medical therapy in COAPT than in MITRA-FR. However, this set-up may be difficult to implement in everyday practice which rarely achieves optimized therapy."

Prof Obadia said that medical treatment should remain the first line of treatment for heart failure patients with secondary mitral regurgitation. "MITRA-FR and COAPT provide answers but also more questions," he said. "The definition of secondary mitral regurgitation has to be revisited taking into account the dynamic function of the heart. More studies are needed to clarify understanding of this complex disease."

This was an academic study supported by the French Ministry of Health.

Conference News

コレステロールおよび血圧の穏やかな低下の効果

血圧およびコレステロールの穏やかな低下により多くの心血管イベントが回避できる

Most cardiovascular events avoidable with modest blood pressure and cholesterol reductions

心筋梗塞(MI)、脳卒中、および心疾患死の大部分が血圧およびコレステロールの穏やかで持続的な低下により予防可能である、とESC Congress 2019のHot Line Sessionで発表され、*Journal of the American Medical Association*に掲載された。長期にわたり低比重リポ蛋白コレステロール(LDL-C)がより低値で収縮期血圧(SBP)が低いことは、生涯における心血管疾患リスクの独立した更なる軽減と関連があった。健康な食事(DASH食や類似の食事療法)により達成できるLDL-CおよびSBPの軽度の低下であっても、将来の心血管疾患の可能性が低下した。

Full Text

The majority of myocardial infarctions (MI), strokes, and deaths from heart disease can be prevented with modest and sustained decreases in blood pressure and cholesterol. The late breaking results were presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in the *Journal of the American Medical Association*.

Principal investigator Professor Brian Ference of the University of Cambridge, UK said: "Healthy eating and physical activity are effective ways to improve cardiovascular health. The best diet or exercise program differs for each person. It is the one that produces the greatest reductions in both blood pressure and cholesterol for that person AND to which he or she can adhere because the benefits of the reductions accrue overtime."

The study found that long-term exposure to the combination of both lower low-density lipoprotein cholesterol (LDL-C) and lower systolic blood pressure (SBP) was linked with independent and additive reductions in the lifetime risk of cardiovascular disease. The relationship was dose-dependent.

The study shows that even small declines in LDL-C and SBP can substantially diminish the likelihood of ever having a heart attack or stroke. For example, the combination of 0.3 mmol/L (14 mg/dL) lower LDL-C and 5 mmHg lower SBP was associated with a 50% lower lifetime risk of cardiovascular disease.

Prof. Ference said: "These small modifications in LDL-C and SBP are the kind of changes that can be achieved by eating healthily such as the DASH diet or similar diets."

Larger reductions in LDL-C and SBP with more aggressive lifestyle changes or other therapies to achieve the combination of 1 mmol/L (38.67 mg/dL) lower LDL-C and 10 mmHg lower SBP can reduce lifetime risk of cardiovascular disease by 80% and reduce lifetime risk of cardiovascular death by more than two-thirds (68%).
The study included 438,952 participants of the UK Biobank who experienced a total of 24,980 major coronary events (defined as the first occurrence of non-fatal heart attack, ischemic stroke, or coronary death). The average age was 65.2 years (range: 40.4 to 80.0) and 54% were female.

The researchers used genetic variants linked with lower LDL-C and SBP as instruments to randomly divide participants into groups with lifetime exposure to lower LDL-C, lower SBP, or both as compared to a reference group using a 2x2 factorial design. They then compared the differences in plasma LDL-C, SBP and cardiovascular event rates between the groups to estimate associations with lifetime risk of cardiovascular disease.

Prof. Ference said: "It is important to encourage patients and populations to invest in their future health. Maintaining even small reductions in both LDL-C and SBP for prolonged periods of time can pay very big health dividends by dramatically reducing the lifetime risk of cardiovascular disease."

Professor Ference's research is supported by the National Institute for Health Research Cambridge Biomedical Research Center at the Cambridge University Hospitals NHS Foundation Trust. Additional funding was provided by the British Heart Foundation and U.K. Medical Research Council (MRC).

Conference News

地域住民を対象とした塩分置換プログラムは血圧を低下させる

地域レベルで高ナトリウム塩を置換することにより血圧が低下し新たな高血圧発現率が半減する

Replacing high-sodium salt at the community level lowers blood pressure and halves incidence of new hypertension

ペルーにおける地域住民を対象とした塩分置換プログラムは、血圧を低下させ新たな高血圧症例を減少させた、と ESC Congress 2019 の Hot Line Session で発表された。この試験では、ナトリウム75% およびカリウム25% を含み著しい味の違いのない食塩代用品を用いた。対象住民全体において、食塩代用品は収縮期血圧を平均1.23 mmHg、拡張期血圧を0.72 mmHg 低下させ、高血圧発症率を55% 低下させた（p<0.001）。ベースラインで高血圧を有さなかった者において、食塩代用品は高血圧発症率を51% 低下させた。

Full Text

A community-based salt substitution program in Peru lowered blood pressure and cut new cases of hypertension. The late breaking research is presented in a Hot Line Session today at ESC Congress 2019 together with the World Congress of Cardiology.

Senior author Dr. Jaime Miranda from the CRONICAS Centre of Excellence in Chronic Diseases at Universidad Peruana Cayetano Heredia (Cayetano Heredia Peruvian University), Lima, Peru said: "Across the world many societies consume more than the recommended amount of salt. Our sodium reduction intervention lowered blood pressure across communities, with particular benefits in people with hypertension, and reduced the occurrence of new hypertension."

The study used a salt substitute containing 75% sodium and 25% potassium. It was made by mixing equal parts of normal salt (100% sodium) and a commercially available low-sodium product (50% sodium, 50% potassium). Prior research by the group found that the sodium content of salt could be reduced by up to 35% without a noticeable difference in taste.

A stepped wedge cluster randomized trial was conducted between 2014 and 2017 in six villages in Tumbes, a region with high levels of sodium consumption and hypertension. Blood pressure was measured at the beginning of the study and every five months, for a total of seven measurements. Every five months, a village was randomly selected to join the intervention, so that in the final period of the study all villages were in the intervention group.

Prior research showed that Tumbes residents did not make a connection between sodium intake and blood pressure and found dietary change difficult. The study therefore used an innovative social marketing campaign to introduce a new product called Salt-Liz, a name chosen and approved by locals. Salt-Liz was provided to households, grocery shops, community kitchens and street vendors.

When it was a village's turn to join the intervention, households, shops, and vendors choosing to participate were given Salt-Liz in exchange for their own salt. When they ran out, they were given more.

A total of 2,376 individuals were involved in the study. Half were females and the average age was 43 years. In the overall population, the salt substitute reduced systolic blood pressure by an average of 1.23 mmHg and diastolic blood pressure by an average of 0.72 mmHg. Blood pressure reductions were even greater in individuals with hypertension at baseline: average reductions in systolic and diastolic blood pressures were 1.74 mmHg and 1.25 mmHg, respectively.

Among the 1,865 participants (79%) without hypertension at baseline, the salt substitute significantly reduced the likelihood of developing hypertension by 51% compared to using normal salt (hazard ratio 0.49; 95% confidence interval 0.34–0.71; p<0.001).

Dr. Miranda said: "This study was designed to generate small decreases in blood pressure at the population level; it was not a drug trial. This was achieved with the intervention, which also had two additional benefits. First, it lowered blood pressure even more in people with hypertension. Second, it stopped many people without hypertension from getting it. These gains can be sustained over time if people continue using the salt substitute."

To test adherence to the intervention, urine samples were taken in a subset of 600 participants at baseline and three years. Potassium levels increased while sodium levels did not change.

"People may have replaced their sodium intake with other products, but the rise in potassium suggests they did use the salt substitute," said Dr. Miranda. "We also collected qualitative information showing that people liked using the product. Some women told us they switched to the new salt and their families hadn't noticed."

The study demonstrates that population-wide changes in sodium intake and blood pressure are feasible, noted Dr. Miranda. "The intervention was simple, highly acceptable, and low cost. Rather than pushing a healthy behavior change, we engaged people by marketing a new product. Palates adapt, and it is possible that we could return to those villages and reduce sodium even more without a recognizable change in taste."

Regarding roll out of the intervention to other settings and countries, Dr. Miranda said the results provide the basis for different population strategies to reduce sodium consumption. He said: "The reality is that we, as individuals, do not regularly check our sodium or potassium intake, nor should we be doing so. Given the alarming rates of non-adherence to drug therapy of hypertension globally, we urgently require non- pharmacological measures at the population level to improve blood pressure control."

"Hence, innovative approaches like this marketing campaign we used to introduce a salt substitute prove that changes can be introduced and sustained. The salt substitute can be used at the community level, as in our study. But it could also be adopted by food manufacturers and larger shops to nudge behavior change in a healthy direction," he said.

This study was supported by the National Heart, Lung, and Blood Institute, United States, under The Global Alliance for Chronic Diseases (GACD) hypertension programme.

Conference News

心不全における一次予防としてのICDは死亡リスクを低下させる

SwedeHF試験：植込み型除細動器は心不全の死亡率を低下させる

SwedeHF: Implantable cardioverter-defibrillator linked with lower mortality in heart failure

一次予防としての植込み型除細動器（ICD）使用は最新の治療を受けている心不全患者の短期および長期死亡率を低下させる、との late breaking の結果が ESC Congress 2019 で発表され、*Circulation* に掲載された。ICDの使用は1年全死亡の相対リスクを26% 低下させ（p<0.01）、5年全死亡の相対リスクを13% 低下させた（p=0.04）。短期および長期死亡率の低下は、サブグループいずれにおいても一貫して認められた。これらの結果は現在の推奨を支持し、実地臨床におけるより適切なICD植込みの実施を呼びかけるものである。

Full Text

Implantable cardioverter-defibrillator (ICD) use is associated with reduced short- and long-term mortality in patients with heart failure, according to late breaking research presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology and published in *Circulation*.

Patients with heart failure are at increased risk of potentially lethal ventricular arrhythmias and sudden cardiac death. ICDs are used to correct these arrhythmias and prevent sudden death.

ESC guidelines recommend an ICD for primary prevention in symptomatic patients with heart failure with reduced ejection fraction (HFrEF), provided they are expected to survive substantially longer than one year with good functional status.

Principal investigator Dr. Benedikt Schrage of the Karolinska Institutet in Stockholm, Sweden said: "Most randomized trials on ICD use for primary prevention of sudden cardiac death in HFrEF enrolled patients more than 20 years ago. However, characteristics and management of HFrEF have substantially changed since then and it is not known whether ICD improves outcome on top of contemporary treatments. Furthermore, it is unclear whether ICD use is equally beneficial in subgroups such as both women and men or older and younger patients."

This study investigated the association between ICD use and all-cause mortality in a contemporary HFrEF cohort with a focus on subgroups. The study population was compiled from patients in the Swedish Heart Failure Registry (SwedeHF) fulfilling ESC criteria for primary prevention ICD use. Propensity score matching was used to account for differences at baseline.

Of 16,702 eligible patients in SwedeHF, 1,599 (9.6%) had an ICD. Dr. Schrage said "Among patients from SwedeHF fulfilling ESC criteria for primary prevention ICD use, less than 10% had the device. ICD use in Sweden is known to be lower than in other European countries (e.g. Germany or Italy). This could be because most heart failure patients are seen by primary care physicians and geriatricians who could be less inclined to accept device therapy and have a higher perception of contraindications compared to cardiologists."

The propensity matched population consisted of 1,296 ICD users and 1,296 patients without an ICD. The researchers found that ICD use was associated with a 26% relative reduction in the risk of all-cause mortality at one year (p<0.01) and a 13% relative reduction in the risk of all-cause mortality at five years (p=0.04). The five-year absolute risk reduction with ICD use was 3.1% leading to 33 patients needing to be treated to prevent one death in five years.

The short-term and long-term mortality benefit was consistent across subgroups, such as patients with or without ischemic heart disease, males and females, patients under 75 and 75 and older, those enrolled earlier versus later in SwedeHF and thus receiving less or more contemporary treatment, and also for patients with or without cardiac resynchronization therapy.

Dr. Schrage said: "The study found that primary prevention ICD was associated with reduced short-term and long-term all-cause mortality in HFrEF overall and in several subgroups. Our findings support the current recommendations and call for better implementation of ICD use in clinical practice."

This study received support from Boston Scientific and the EU/EFPIA Innovative Medicines Initiative 2 Joint Undertaking BigData@Heart grant. Benedikt Schrage reports no conflict of interest in regard to this study.

Conference News

PCI後予防的ICDの長期の有益性

DAPA試験：早期除細動器植え込みは冠動脈ステント留置後の生存期間を延長する

DAPA: Early implantable cardioverter-defibrillator use prolongs survival after coronary stenting

プライマリ冠動脈インターベンション後の植込み型除細動器（ICD）早期使用は、ST上昇型心筋梗塞（STEMI）後の死亡リスクの高い患者の生存期間を延長する、との late breaking の結果が ESC Congress 2019 で発表された。DAPA 試験の9年追跡において、全死亡はICD 群の24.4%、コントロール群の35.5% に発現し、ハザード比（HR）は0.58であった（95% 信頼区間 [CI]0.37-0.91）。心臓死はICD 群で11.4% であり、コントロール群では18.5% であった（HR 0.52；95% CI 0.28-0.99）。心臓突然死の割合は、両群間で有意差がなかった。

Full Text

Early use of an implantable cardioverter-defibrillator (ICD) after primary coronary intervention lengthens survival in patients at high risk of death after ST-segment elevation myocardial infarction (STEMI). The late breaking results from the DAPA trial were presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology.

First author Dr. Danielle Haanschoten of Isala Hospital, Zwolle, the Netherlands said: "The results of the DAPA trial indicate that certain high-risk patients may benefit from early ICD implantation after primary percutaneous coronary intervention (PCI). However, the study was stopped prematurely. Therefore, more research is needed to support these findings."

ESC guidelines recommend prophylactic ICD implantation at least six weeks after myocardial infarction in ischemic etiology. American guidelines recommend prophylactic ICD implantation at least 40 days after myocardial infarction and at least 90 days after revascularization.

Dr. Haanschoten said: "Advice to delay ICD use is based on the fact that implantation within 40 days was not studied in MADIT II and SCD-HeFT and did not show a survival benefit in two primary prevention trials (DINAMIT and IRIS). It has been unclear which patients might gain from a prophylactic ICD to reduce sudden cardiac death after primary PCI."

The aim of the DAPA trial was to examine whether ICD implantation between 30 and 60 days after primary angioplasty for STEMI would provide a survival benefit in patients at high risk of death. High risk was defined as at least one of the following: primary ventricular fibrillation, left ventricular ejection fraction below 30%, Killip class 2 or higher, or TIMI flow less than 3 after primary PCI.

Patients were randomly allocated to prophylactic ICD implantation or optimal medical therapy. The primary endpoint was all-cause mortality after at least three years of follow-up for each patient. Secondary endpoints were cardiac death and sudden cardiac death.

The trial was halted prematurely in 2013 on advice of the data safety monitoring board due to a slow inclusion rate. A total of 266 patients were randomized and followed-up for a median of nine years.

ICD implantation significantly lowered the risk of all-cause and cardiac mortality. All-cause mortality occurred in 24.4% of the ICD group versus 35.5% in the control group, with a hazard ratio (HR) of 0.58 (95% confidence interval [CI] 0.37–0.91). The rate of cardiac death was 11.4% in the ICD group and 18.5% in the control group (HR 0.52; 95% CI 0.28–0.99). Rates of sudden cardiac death were not significantly different between groups.

Dr. Haanschoten said: "The all-cause mortality curves started to diverge before the first year and the beneficial effects of prophylactic ICD use were preserved throughout the nine-year follow-up. The survival advantage of ICD implantation was mainly driven by a reduction in cardiac mortality."

She concluded: "Together with results of previous trials, the DAPA trial may contribute to early selection of high-risk patients who will profit from an ICD after primary PCI for STEMI. The unexpected ending of the study is an important limitation and further studies are needed before any change in practice can be considered."

Medtronic Inc. was the sponsor of the study and provided financial and technical support. The firm had no interference with the design of the study protocol, data collection or data analysis.

Conference News

末梢動脈疾患に対してスタチンを開始するのに遅すぎることはない(Abstract 80087)

EUROASPIRE試験：研究の結果、PADに対する薬物療法の開始と生涯にわたり遵守することの重要性が示された

EUROASPIRE: Research shows importance of starting and adhering to lifelong medication for PAD

末梢動脈疾患（PAD）患者において、スタチン系薬剤は診断後に遅れて開始された場合でも死亡率を低下させた、とESC Congress 2019で発表された。EUROASPIRE試験において、スタチン内服を中止した患者の死亡率（33%）は、一度も内服したことのない患者と同等（34%）であった。試験期間50か月にわたりスタチン内服を遵守することは、20%の死亡率と関連があった。試験期間中の高用量スタチンの内服は、最も低い死亡率（10%）と関連し、同じ期間中の用量減量は最も高い死亡率と関連した。

Full Text

Statins are linked with reduced mortality in patients with peripheral arterial disease, even when started late after diagnosis, reports a study presented at ESC Congress 2019 together with the World Congress of Cardiology. Patients who stop the drug are at similar risk to those who never start. The research shows the importance of starting and adhering to lifelong medication, preferably at a high dose.

Around 200 million people worldwide have peripheral arterial disease (PAD). Statins are recommended for all patients with PAD, together with smoking cessation, exercise, healthy diet, and weight loss.

But adherence to statins is low: over the past five years, just 57% of patients in Europe took the medication as directed. In 2016 to 2017, only one-third of patients on statins reached the LDL cholesterol target of below 1.8 mmol/L (70 mg/ dl).

This study examined whether adherence to statin therapy influenced survival in patients with symptomatic PAD. The study enrolled 691 patients admitted to hospital between 2010 and 2017 and followed-up for a median of 50 months.

At the beginning of the study, 73% of patients were on statins, increasing to 81% at the 50-month follow-up. The dose of drug also increased between the two time periods, which was paralleled by a significant drop in LDL cholesterol from 97 to 82 mg/dL.

Patients who stopped taking a statin had a similar mortality rate (33%) to those who never took the drug (34%). Adhering to statins throughout the 50 months was linked with a 20% rate of death.

Taking high-dose statins throughout the study was linked with the lowest mortality rate (10%), while reducing the dosage during the study was related to the highest death rate (43%).

Study author Dr. Jörn Dopheide of Bern University Hospital, Switzerland said: "The study shows that adherence to statins is essential for the best prognosis. We also show that it is never too late to start medication and benefit from it. On top of that, it is crucial not to reduce the dose because LDL cholesterol levels rise again, thus increasing the overall risk on top of the residual risk for further events."

He concluded: "All PAD patients should take statins, preferably very potent statins, like rosuvastatin 40 mg or atorvastatin 80 mg, or at the highest tolerable dose. In the rare case of statin intolerance, which was around 2% in our study, alternative lipid lowering therapies must be considered."

No funding was received for this study.

Conference News

心不全および脳卒中患者において白質病変は一般的である(Abstract 89078)

LIFE-Adult試験：心不全患者は脳卒中患者と同様の認知症型脳病変の可能性がある

LIFE-Adult: Heart failure patients have similar odds of dementia-type brain lesions as stroke patients

認知症および認知機能障害と関連のある脳損傷の型は、心不全患者において脳卒中歴を有する患者同様に多く認められる、との LIFE-Adult-Study の結果が ESC Congress 2019 で発表された。心不全患者は、心不全を有さない患者よりも白質領域病変（WML）率が2.5倍高かった。同様に、脳卒中患者は、脳卒中歴を有さない者よりもWHL率が2倍高かった。WHL 率は心不全期間が長いほど増加した（診断から3年以内の1.3から、診断後6年以上2.9へ）。

Full Text

A type of brain damage linked with dementia and cognitive impairment is as common in heart failure patients as it is in patients with a history of stroke, according to findings from the LIFE-Adult-Study presented at ESC Congress 2019 together with the World Congress of Cardiology.

The probability of this damage, called white matter lesions (WML), was also linked to the duration of heart failure. Patients with a long-standing diagnosis had more WML compared to those more recently diagnosed.

"Up to 50% of older patients with heart failure have cognitive impairment and heart failure is associated with an increased risk for dementia," said study author Dr. Tina Stegmann of Leipzig University Hospital, Germany. "However, it is still unclear what the pathological pathways are. Some investigators have identified changes in brain structure in patients with heart failure and cognitive dysfunction, but the findings are inconsistent."

LIFE-Adult is a population-based cohort study conducted in Leipzig. Between 2011 and 2014, 10,000 residents aged 18 to 80 were randomly selected for inclusion in the study. Participants underwent assessments such as a physical examination and medical history during which information on health conditions – for example heart failure and stroke – was collected.

This subgroup analysis included the 2,490 participants who additionally underwent magnetic resonance imaging (MRI) of the brain. The purpose of the analysis was to determine the frequency and associated risk factors for WML in a population cohort and potentially discover a connection with heart failure.

Most participants in the subgroup analysis had no or mild WML (87%), and 13% had moderate or severe WML. Mild WML are common and increase with age. In contrast, moderate or severe WML are associated with cognitive impairment and dementia.

There were significant independent associations between WML and age, high blood pressure, stroke and heart failure. Patients with heart failure had a 2.5 greater probability of WML than those without heart failure. Similarly, stroke patients had a two times higher likelihood of WML than those with no stroke history.

The odds of WML increased as the period with heart failure lengthened: from 1.3 for a diagnosis less than three years, to 1.7 for a diagnosis of four to six years, and 2.9 for a diagnosis longer than six years.

Dr. Stegmann said the connections between heart failure, stroke, and WML could be due to shared risk factors such as age and high blood pressure. In addition, there may be a causal link between heart failure and stroke. It is well known, for instance, that the risk of stroke is higher in patients with heart failure than without.
"The role of dementia and its prevention is of growing interest in heart failure research as the overall heart failure population is ageing and suffering from numerous comorbidities," she added. "Studies are needed to see if WML could be a therapeutic target for treating cognitive decline in patients with heart failure."

Dr. Stegmann concluded: "After cancer, dementia is the most feared disease by patients. But there is currently no clear indication to screen for WML in heart failure patients using brain MRI."

The LIFE-Adult study is supported by the University of Leipzig. LIFE was funded by means of the European Union, by the European Regional Development Fund (ERDF) and by funds of the Free State of Saxony within the framework of the excellence initiative.

Conference News

うつ病は介護者の身体的健康と関連がある (Abstract 81211)

脳卒中既往患者の介護者におけるうつ症状は将来の健康問題を予測する

Symptoms of depression in caregivers of stroke survivors may predict future health problems

うつ徴候を示す脳卒中既往患者の介護者は、将来的に自身の健康面の課題を有するリスクが高い可能性がある、とESC Congress 2019で発表された。慢性的なうつ症状を有する人々の精神的健康状態は、身体的健康状態と密接に関連があった。試験に参加した介護者の3分の1は、1年後の身体の健康状態はまずまず、または不良であると報告し、43%は健康状態が悪化したと報告した。うつ徴候のない介護者に比べ、うつ状態が続いている介護者は、脳卒中既往患者の介護開始1年後の体調不良を訴える確率が7倍高かった。

Full Text

Caregivers of stroke survivors who show signs of depression may have a higher risk of suffering their own health challenges in the future, according to research presented at ESC Congress 2019 together with the World Congress of Cardiology.

The findings highlight the importance of attending to the mental health of caregivers and bring to mind the airline-safety metaphor: 'Secure your own oxygen mask before helping someone else.

"Caregiving is becoming more common and more demanding," says study first author Professor Misook L. Chung of the University of Kentucky College of Nursing in the United States. "More attention needs to be paid, especially early on, to managing depressive symptoms in caregivers. They must realize that self-care is not selfish."

Stroke is a leading cause of long-term disability around the world and often exerts a heavy toll on those in a supporting position. Providing assistance to patients, including helping the survivor with eating, dressing, going to the bathroom and showering, not to mention taking care of meals, organizing a home and supervising medical care, can become a full-time job with a deep emotional component.

The current project is the first longitudinal study to address the issue of persistent depressive symptoms and their effect on physical health as well as changes in health during the first year of stroke caregiving.

The research team enrolled 102 caregivers with a mean age of 58. Two-thirds were female and about 70% were spouses. The rest consisted of other family members, although two or three were family friends, says study senior author Rosemarie King, a retired research professor at Northwestern University School of Medicine in Chicago, Illinois, USA.

Participants answered questionnaires at two points in time: six to ten weeks after the patient was discharged from the hospital and again one year later.

The overall proportion of individuals reporting symptoms of depression like poor appetite or trouble focusing, declined slightly over the course of the study: 32.4% versus 30.4 More than half the participants (57.8%) said they had no issues of mental distress at all, but 20.6% (or one in five) suffered persistent depressive symptoms in the first year of caregiving.

The mental health of people with chronic signs of depression was closely associated with their physical health. One-third of caregivers in the study reported their physical health as fair or poor after one year, while 43% said they felt their health had deteriorated. Compared to caregivers who did not have signs of depression, those with ongoing challenges were seven times more likely to report problems with their health after one-year of caregiving for stroke survivors.

Individuals with persistent symptoms of depression during the first year of caregiving reported heavier caregiving duties, poor family functioning and low interpersonal support.

One limitation of the study is that the researchers did not track primary health outcomes such as diagnoses of physical illness. Instead, they relied on self-reports of caregivers' health status and changes in health status. There was also a high attrition rate, with a third of study participants dropping out. Longer-term studies, with objective measures of caregiver health status, are required.

The conclusions suggest the need for earlier interventions and long-term follow-up of caregivers. "We haven't paid enough attention to caregivers' health," stresses Prof Chung. "Self-care intervention programs should include depressive symptom management for caregivers."

A pilot study conducted by Prof Chung found benefits in a more holistic approach incorporating stress management and self-care management for caregivers. "Cognitive behavioral therapy has shown promise, as have interventions that teach caregivers how to better manage patients' and their own emotions", she concluded.

Conference News

MI後の内出血はがんを疑うきっかけとなる (Abstract 83231)

急性冠症候群患者において、退院後の出血とその後がんと診断されることには関連があることが明らかにされた

Link found between bleeding after hospital discharge and subsequent cancer diagnosis in patients with acute coronary syndrome

心筋梗塞後の退院から6か月以内の出血はその後にがんと診断されることと関連がある、とESC Congress 2019で発表された。研究者らは、退院後抗血小板薬2剤併用療法を施行された急性冠症候群患者3,644人のカルテを、後ろ向きにレビューした。退院後の出血は、新たにがんと診断されるリスクを3倍にした。明らかな原因のない自然出血は、がんと診断されるリスクが4倍高いことと関連があった。このがんとの関連は、出血重症度が高いほど増大した。出血とがんとの関連性は、2剤併用療法の継続の有無に関係なく認められた。

Full Text

Bleeding during the first six months after discharge from hospital for a myocardial infarction (MI) is linked with a subsequent cancer diagnosis, according to research presented at ESC Congress 2019 together with the World Congress of Cardiology.

"Our results suggest that patients should seek medical advice if they experience bleeding after discharge for a heart attack," said study author Isabel Muñoz Pousa of Álvaro Cunqueiro Hospital, Pontevedra, Spain. "Particularly if the bleeding is of gastrointestinal, pulmonary or genitourinary origin, without any obvious reason, and occurs in the first six months. If the cause is cancer, early detection can improve prognosis."

Following discharge for an acute coronary syndrome, patients are typically treated with dual antiplatelet therapy for around one year. This treatment inhibits the formation of blood clots but raises the risk of bleeding. Previous research has suggested that post-discharge bleeding may have negative consequences. This study examined its association with a new diagnosis of cancer.

The researchers retrospectively reviewed the hospital records of 3,644 acute coronary syndrome patients discharged with dual antiplatelet therapy from Álvaro Cunqueiro Hospital. Patients were followed-up for a median of 56.2 months for bleeding events and cancer. The researchers analyzed associations between bleeding and the absolute risk of a new cancer diagnosis.

Bleeding occurred in 1,215 patients (33%) during follow-up and 227 patients (6%) had a new diagnosis of cancer. After adjustment for factors known to influence bleeding or cancer, post-discharge bleeding was associated with a threefold higher risk of new cancer diagnosis. The median time from bleeding to cancer was 4.6 months. The link with cancer increased as the severity of bleeding worsened.

Spontaneous bleeding with no apparent cause was linked with a four times higher risk of cancer diagnosis while there was no relation with bleeding due to trauma such as injury or bladder catheterization.

Regarding the location, blood in the feces was associated with a nearly fourfold risk of cancer diagnosis, while coughing up blood or blood in the urine were linked with four and eight-times greater risks, respectively.

There was a relationship between bleeding and cancer regardless of whether patients were still on dual antiplatelet therapy or not.

Ms. Muñoz Pousa said: "Most of the bleeding episodes in the study were mild. The bleeding events more strongly related with a new cancer diagnosis were severe hemorrhages of unknown cause requiring surgery – for example digestive bleeding needing endoscopic treatment. We found a higher incidence of cancer in the first six months after discharge regardless of whether patients were taking dual antiplatelet therapy or not."

She added: "A possible explanation is that there is a pre-existing subclinical lesion in an organ that is triggered to become cancer by antiplatelet drugs or a stressful situation such as heart attack. This hypothesis needs to be tested and patients should ensure they take antiplatelets as prescribed to avoid having another heart attack."

No funding source was reported for this study.

Conference News