急性心不全の管理に関する知見

EuroHeart Survey on Heart Failure（ヨーロッパにおける心不全に関する調査）によると、いくつかの修正可能な因子は心不全患者の予後を予測し、ケアのガイドに使用できることが示された

EuroHeart Survey on Heart Failure shows that several modifiable factors predict outcome for patients with acute heart failure and can be used to guide care

急性心不全患者のリスク層別化は、EuroHeart Survey on Heart Failure（ヨーロッパにおける心不全に関する調査）で得られたデータを用いて、いくつかの予測因子と修正可能な因子が同定された後に改善するであろう、とEuropean Society of Cardiology学会で発表された。新規発症または急性の非代償性心不全で入院した患者3,441人（心原性ショックを伴う患者は除外）のデータを解析した。平均院内総死亡率5.3%のうち、臨床所見の有無に基づいた死亡リスクは1%未満から50%超と多様であった。急性の非代償性心不全および新規発症の心不全患者の両者において最も強力な独立した短期の総死亡率予測因子は、加齢、低収縮期血圧、腎機能障害、末梢循環不全、および心不全の増悪因子である急性冠症候群であった。年齢を除き、他の全ての因子はモニターすることができ、院内管理のガイドとして使用できる。

Full Text

Risk stratification of patients with acutely decompensated heart failure should improve after a number of predictive, modifiable variables were identified during analysis of data from the EuroHeart Survey on Heart Failure, according to a presentation at the annual meeting of the European Society of Cardiology.

The EuroHeart Survey on Heart Failure collected data on 3,579 patients admitted acutely for heart failure by 133 centers in 30 countries. Patients with cardiogenic shock were excluded from analysis because their short-term mortality is so high that specific models for risk stratification are less useful: All patients require intensive management.

The database of the remaining 3,441 patients included in the EuroHeart Survey on Heart Failure showed that in-hospital all-cause mortality of patients with acute decompensation of already known heart failure condition was 5.3 percent (116/2202 patients), while total in-hospital mortality of patients with de nôvo acute heart failure was 5.4 percent (67/1239 patients).

Within the average mortality rate of 5.3 percent, risk for death greatly varied from less than 1 percent to more than 50 percent according to the presence or absence of clinical variables that significantly influence in-hospital death.

In both situations (worsening or de novo heart failure), the strongest independent predictors of short-term, all-cause mortality were the following: advanced age, low systolic blood pressure, renal dysfunction, signs of peripheral hypoperfusion, and an acute coronary syndrome as precipitating factor for heart failure. With the exception of age, all of these clinical conditions can be appropriately managed in a timely way to reduce in-hospital mortality.

These simple variables, easy to detect in any clinical setting, can be used immediately by physicians to predict which patients need care in an intensive or coronary care unit and can personalize treatment strategy accordingly.

遅れて施行する血管形成術の価値

CARESSスタディの結果、緊急の血栓溶解療法施行後に転送し血管形成術を施行することにより急性心筋梗塞患者の生存率が改善することが示された

CARESS study shows that immediate thrombolysis followed by transfer for emergent angioplasty improves survival of patients with acute myocardial infarction

CARESSスタディの結果、血管形成術の設備のない施設に収容された急性心筋梗塞患者は緊急の血栓溶解療法を施行した後に転送させるべきである、とEuropean Society of Cardiologyで発表された。患者らはabciximabおよび低用量のreteplaseを投与された後、転送される群または同じ病院で継続して治療を受ける群に無作為に割り付けられた。その結果、転送され冠動脈形成術を受けた患者（最初の病院で改善が得られず後に転送された保存的治療群の36%を含む）は、30日後の主要な有害事象を発生しない確率が高かった（4.1%対11.1%）。血栓溶解療法から血管形成術施行までの時間はほとんどの患者において120分を超えており（中央値136分）、つまり彼らはprimary血管形成術の候補ではなかった。これらの結果および出血の合併症が少ない（3.7%で群間差なし）ことから、大規模医療施設の近くに住んでいない多くの患者に対して血栓溶解療法後の血管形成術は有用である可能性が示唆された。

Full Text

The CARESS study shows that patients with acute myocardial infarction admitted to a facility unable to perform angioplasty have better outcomes if transferred to an appropriate facility immediately after receiving thrombolytic therapy, according to a presentation at the annual meeting of the European Society of Cardiology.

The trial, conducted in Italy, Poland and France, involved various networks of community hospitals referring to a larger hospital for direct angioplasty of acute myocardial infarction. Patients were randomized with telephone allocation at the time of admission with all adverse events blindly reviewed by an independent Committee for adjudication and all electrocardiograms and angiograms analyzed by an independent Core Laboratory unaware of the treatment received.

The interval between administration of the thrombolytic drug and angioplasty was greater than 120 minutes in more than half of the patients (median, 136 minutes), which meant they were not candidates for primary angioplasty under current guidelines that require an interval of less than 90 minutes between first qualified medical contact and direct angioplasty.

The concern regarding thrombolysis before angioplasty was challenged by our finding of a low incidence of bleeding (0.8 percent intracranial hemorrhages and 2.9 percent bleeding episodes requiring 1 or more transfusions, with no difference between patients transferred for immediate angioplasty and patients who remained in the hospital of initial admission).

In our view, the lower rate of bleeding complications was due to the inclusion of patients at low risk of bleeding (patients less than 75 years old and well screened for contraindications to thrombolytics). We excluded older patients or patients with high bleeding risk from this trial because we believed in those cases it was more reasonable to pursue a less aggressive pharmacological strategy (for instance using only abciximab) or primary angioplasty.

Patients who were transferred and received angioplasty immediately after thrombolytics were much more likely (4.1 percent vs. 11.1 percent at 30 days) to be free from adverse events such as death, new myocardial infarction, new acute episode of chest pain, and electrocardiographic changes requiring urgent angioplasty.

This advantage was present despite the fact that all patients (36 percent of the entire conservative group) randomized to the group of more conservative treatment (no immediate transfer) were also promptly referred during the first hours post-treatment if there was no evidence that the lytic drugs had opened the occluded artery.

CARESS used a combination of the powerful intravenous anti-platelet agent abciximab and a reduced dose of the fibrin-specific lytic drug reteplase. This combination is very powerful and rapid in its action, with a synergistic effect demonstrated in previous trials and in in-vitro models, and achieved restoration of flow in the occluded artery in 85 percent of cases by the time patients reached the hospital where angioplasty was performed. Its main advantage is, however, the ability to inactivate platelets during the subsequent angioplasty, the opposite of the result observed when only lytics are given, which tend to activate platelets instead.

The authors conclude that the results should lead to a more liberal use of a strategy of facilitated angioplasty (that is, thrombolytics before angioplasty) when there is no certainty that the angioplasty can be performed within 90 minutes.

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糖尿病患者における心血管リスクの管理

ADVANCEトライアルの結果、ペリンドプリルとインダパミドの併用は糖尿病患者における心血管疾患および死亡のリスクを有意に減少させることが示された

ADVANCE trial shows that combination perindopril-indapamide can significantly reduce risk for cardiovascular disease and death in patients with diabetes

ADVANCEトライアルの結果、ペリンドプリルとインダパミドの併用は糖尿病患者における心血管疾患およびそれに関連した死亡のリスクを有意に減少させることが示された、とEuropean Society of Cardiology学会で発表された。20ヵ国の糖尿病患者計11,140人を4.3年間にわたるスタディに組み入れ、合剤またはプラセボ投与群に無作為に割り付けた。既に降圧薬を内服している患者も組み入れ可能とした。既存の治療に合剤を加えることにより総死亡リスクが14%、心血管死亡リスクが18%減少した。冠動脈性心疾患イベントのリスクは14%、腎疾患の新規発症または増悪のリスクは21%減少した。

Full Text

The ADVANCE trial shows that the combination of perindopril and indapamide can reduce risk for cardiovascular disease and related mortality in patients with diabetes, according to a presentation at the annual meeting of the European Society of Cardiology.

ADVANCE (Action in Diabetes and Vascular Disease), the largest-ever study of treatments for diabetes, also found that the fixed-dose drug therapy reduced risk for development or progression of kidney disease.

One of the study leaders, Professor Stephen MacMahon from The George Institute for International Health in Australia, said "these results represent an important step forward in health care for the millions of people with diabetes worldwide. This treatment reduced the likelihood of dying from the complications of diabetes by almost one-fifth, with virtually no side-effects."

A total of 11,140 patients with diabetes from 20 countries worldwide participated in the 4.3 year project. Half received daily treatment with a single tablet containing a fixed combination of perindopril and indapamide), whereas the other half were randomized to matching inactive placebo.

Dr. Anushka Patel, Study Director from The George Institute, said "the participants in ADVANCE were already receiving most of the usual treatments provided to patients with diabetes, including other drugs to lower blood pressure. However, addition of the fixed combination of perindopril and indapamide reduced the risk of death from any cause by 14 percent and the risk of death from cardiovascular disease by 18 percent. In absolute terms, one death would be avoided for every 79 patients treated with the fixed combination of perindopril and indapamide for 5 years. The risk of coronary heart disease events was reduced by 14 percent and the risk of new or worsening kidney disease was reduced by 21 percent."

Professor John Chalmers, the author of previous international guidelines for the treatment of hypertension and chairman of the study management group, said, "the results clearly demonstrate that we have the tools to blunt the impact of the global diabetes epidemic facing rich and poor countries alike. But concerted action is urgently required to ensure that patients with diabetes are identified and provided with treatments proven to improve important outcomes like survival."

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末梢動脈の動脈硬化と心血管死亡率

GetABIトライアルの結果、たとえ軽度の末梢動脈の動脈硬化であっても総死亡率および心血管死亡率の上昇と関連があることが示された

The getABI trial shows that even mild peripheral atherosclerosis is associated with substantial increase in all-cause and cardiovascular mortality

German epidemiological study on Ankle Brachial Index (getABI)トライアルの結果、たとえ軽度の末梢動脈の動脈硬化であっても総死亡率および心血管死亡率の上昇と関連があることが示された、とESCで発表された。無選別のプライマリケアの患者計6,880人（平均年齢72.5歳）をスクリーニングしたところ、女性の方が多く（58%）、さらに46%が過去または現在の喫煙者であり、74%が高血圧、24%が糖尿病、52%が脂質異常を有していた。全ての患者の中で18%に病理学的な異常所見が認められたが、彼らの多くは臨床徴候や訴えがなかった。5年後の総死亡率は症候性末梢血管疾患患者では24%、無症候性末梢血管疾患患者では19%、疾患を有さない者では9%であった。既知の心血管死リスクファクターで補正したところ、末梢血管疾患は、将来の死亡、脳卒中、および心筋梗塞の予測能が最も高かった。

Full Text

The getABI trial shows that even mild peripheral atherosclerosis is associated with substantial increase in all-cause and cardiovascular mortality, according to a presentation at the annual meeting of the European Society of Cardiology.

The German epidemiological study on Ankle Brachial Index (getABI) was initiated in 2001 to answer questions about whether a simple screening test for atherosclerosis can identify it at an early stage, and if so, estimate what risk such patients carry in the future.

Professor Curt Diehm from the Clinic Karlsbad-Langensteinbach, an affiliated teaching hospital of the University in Heidelberg, and his co-workers from various renowned medical institutions in Germany presented a five-year study follow-up.

Professor Diehm explained: "We used the ankle brachial-index (ABI), which is simple to understand and to apply by physicians and nurses. In an individual in the supine position, the blood pressure in the leg arteries is equal to or a little higher than in the arm arteries. If atherosclerotic stenoses in the legs manifests, blood flow after the obstruction decreases, and the pressure in the leg artery is lower than in the arm. This sign is almost as reliable as angiography to identify your atherosclerotic risk patient."

The study included a total of 6,880 unselected patients in primary care, which underwent ABI testing by their primary care physician. Mean age of the patients was 72.5 years, 58 percent were women, 46 percent were past or current smokers, 74 percent had hypertension, 24 percent had diabetes mellitus and 52 percent had lipid disorders.

Of all patients, 18.0 percent had a pathological ABI test, but the majority of these patients had no clinical signs or complaints.

After a five-year observation period, all-cause mortality was 24 percent in patients with symptomatic peripheral atherosclerosis, 19 percent with asymptomatic peripheral atherosclerosis, and 9 percent in patients without peripheral disease. Even when all other known risk factors for cardiovascular death were accounted for by statistical means, peripheral disease had the best ability to predict future death, stroke or myocardial infarction.

Professor Diehm said, "The bad news is we showed that in primary care every fifth patient aged 65 years or older has atherosclerosis in the leg arteries. Because atherosclerosis is not a local process but at the same time progresses in the heart and brain vessels, such patients usually die from heart attacks or stroke. The good news is that the ABI test is not limited to expert use but can be performed in general practice. Thus, family physicians can identify high risk patients and initiate and maintain effective treatment in this large group."

The study also showed that the extent of the blood pressure difference between legs and arms matters: The higher the spread between both pressures is (in other words, the lower the ankle brachial index), the higher was the mortality of patients.

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直接的なレニン阻害と心不全

ALOFTスタディの結果、臨床的に使用可能な初めての経口直接的レニン阻害薬は既存の薬剤で最適に治療されている心不全患者に有望であることが示唆された

ALOFT study suggests that the first clinically available oral direct renin inhibitor has promise for patients with heart failure treated optimally with current drugs

臨床的に使用可能な初めての経口直接的レニン阻害薬aliskirenの有効性、忍容性、および安全性を評価したALOFT（ALiskiren Observation of heart Failure Treatment）スタディの結果、この薬剤が、アンジオテンシン変換酵素阻害薬またはアンジオテンシン受容体拮抗薬およびβ遮断薬で最適に治療されている心不全患者に有望であることが示された、とESCで発表された。この3ヵ月のスタディでは、現在または過去に高血圧を有し血漿中のBNPが100pg/mLを超えているクラスII-IVの心不全患者302人を組み入れた。患者は既に最適の治療をされているかまたは、禁忌のため前述の薬剤を使用していない者に限られた。プラセボと比較しaliskirenは3つの有効性の指標：血漿NT-pro BNP、血漿BNP、尿中アルドステロンをそれぞれ25%、25%、21%低下させた。Aliskirenは過剰な血圧低下や腎障害を引き起こさず、忍容性は良好であった。

Full Text

The ALOFT (ALiskiren Observation of heart Failure Treatment) study, which evaluated tolerability and safety of the first clinically available oral direct renin inhibitor, shows the drug may benefit patients with heart failure who are already optimally treated with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker and beta-blocker, according to a presentation at the annual meeting of the European Society of Cardiology.

Direct renin inhibitors block the renin-angiotensin-aldosterone system at its first and rate-limiting step. As a result, all downstream products in the cascade are suppressed; additionally, the direct inhibitors are specific for the system. Both properties differentiate these new medications from angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

In the ALiskiren Observation of heart Failure Treatment study (ALOFT), 302 patients with New York Heart Association class II-IV heart failure with current or prior hypertension and plasma B-type natriuretic peptide concentration > 100 pg/mL were enrolled in nine countries. Patients had to be optimally treated with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker and beta-blocker, unless contraindicated or not tolerated. Patients were studied for three months.

Although primarily a safety and tolerability study, a variety of efficacy measurements were made. The first three of these were to study the effect of aliskiren compared with that of placebo, on N terminal pro BNP, BNP and aldosterone.

Compared with placebo, aliskiren reduced three parameters significantly: plasma NT-pro BNP by 25 percent, plasma BNP by 25 percent, and urinary aldosterone by 21percent.

There was also a favorable change in Doppler-echocardiographic measure of left ventricular filling pressure. Aliskiren was well tolerated and there was no significant excess of hypotension or renal dysfunction.

Thus, this first sizeable, placebo-controlled trial with aliskiren, showed favorable neurohumoral and other effects in otherwise optimally treated patients with heart failure.

冠動脈造影前の抗凝固療法

血管形成術施行予定の患者に冠動脈造影後にクロピドグレルを内服させた方が冠動脈造影前に非選択的にクロピドグレルを内服させるよりもよい

Post-angiography use of clopidogrel for patients going to angioplasty is superior to nonselective use of clopidogrel before elective coronary angiography

チェコ共和国のスタディの結果、クロピドグレルは待機的な冠動脈造影前の患者に非選択的に内服させるよりも、冠動脈造影後に冠動脈形成術施行予定の患者に内服させた方がよいことが示唆された、とESCで発表された。冠動脈造影の前日に1,028人の患者を、冠動脈造影前にクロピドグレル600mgを内服する群、または冠動脈造影後に冠動脈形成術を施行することになった患者のみに同用量を投与する群に無作為に割り分けた。複合一次エンドポイント（死亡／冠動脈形成術に関連した心筋梗塞、脳卒中または一過性脳虚血発作／7日以内の冠動脈形成術再施行）は両群ともに0.8%に発現した。一方、出血の合併症は非選択的投与群で3.5%に発現したのに対し血管形成術施行患者のみの群におけるその割合は1.2%であった。冠動脈形成術を施行された患者のみを解析すると一次エンドポイント発現率に有意差はなかった（非選択的使用群で1.3%、血管形成術施行患者のみで2.2%）。

Full Text

A multi-center Czech study suggests it is better to give clopidogrel after elective coronary angiography to patients who will undergo angioplasty than to use medication nonselectively prior to elective angiography, according to a presentation at the annual meeting of the European Society of Cardiology.

The current study was designed to address the question whether clopidogrel should be administered as pre-treatment to all patients undergoing elective coronary angiography with the aim to ensure therapeutic levels at the time of possible ad-hoc angioplasty.

The randomized trial enrolled 1,028 patients in five participating hospitals in the Czech Republic. All patients underwent elective angiography. On the day before their procedure, patients were randomized to group A ("nonselective" - clopidogrel 600 mg to all patients more than 6 hours before angiography, 513 patients) or group B ("selective" - clopidogrel 600 mg in the cath-lab after angiography only to patients undergoing subsequent angioplasty; 515 patients).

The combined primary end-point was death / periprocedural myocardial infarction / stroke or transient ischemic attack / re-intervention within seven days. Secondary end-points were troponin elevation, TIMI-flow after angioplasty, and bleeding complications.

Angioplasty immediately following angiography was performed in 29 percent of study patients. Bypass surgery was performed later in 12 percent of patients (mostly after more than seven days). Medical therapy was indicated in 59 percent of patients. Primary end-point occurred in 0.8 percent in both groups (a nonsignificant difference).

Bleeding complications occurred in 3.5 percent of group A patients versus 1.2 percent of group B (a significant difference). Periprocedural troponin elevation was detected in 2.7 percent of group A versus 3.0 percent of group B (nonsignificant difference).

When only the subgroup of patients who underwent angioplasty was analyzed, primary end-point occurred in 1.3 percent of group A versus 2.2 percent of group B (nonsignificant). Periprocedural troponin elevation was detected in 8.6 percent of group A versus 11.1 percent of group B (nonsignificant). Bleeding complications occurred in 7.2 percent of group A versus 0.7 percent of group B and reintervention within seven days in 0.7 percent of group A versus 1.5 percent group B (nonsignificant).

The authors concluded that clopidogrel pretreatment before elective angiography is not justified because it increases the risk of bleeding complications, while the benefit on periprocedural infarction is not significant. Use of Clopidogrel only for patients who will undergo angioplasty after angiography can be done safely in the catheterization laboratory between the two procedures.

急性心原性肺水腫における非侵襲的呼吸補助

3CPOトライアルの結果、急性心原性肺水腫患者への非侵襲的呼吸補助は回復時期を早めるが死亡率は変化させないことが示唆された

The 3CPO trial suggests that noninvasive ventilation of patients with acute cardiogenic pulmonary edema shortens recovery period but does not change mortality

3CPOトライアルの結果、急性心原性肺水腫患者への非侵襲的呼吸補助は初期回復時期を早めるが死亡率は変化させないことが示唆された、とESCで発表された。3年間にわたり英国の患者1,069人が登録され、標準的な酸素投与（367人）、非侵襲的持続的気道内陽圧呼換気（346人）、または非侵襲的間歇的陽圧換気（356人）のいずれかを受けた。標準的な酸素投与と比較し非侵襲的陽圧換気はいずれも、呼吸数および心拍数の低下およびアシドーシスの改善が早かった。患者の苦痛は少なかったが、死亡率は標準的な治療を受けた患者と同等であった。2つの非侵襲的な換気法の結果に差はなかった。

Full Text

The 3CPO trial suggests that noninvasive ventilation of patients with acute cardiogenic pulmonary edema shortens the initial recovery period but does not change mortality, according to a presentation at the annual meeting of the European Society of Cardiology.

Numerous small studies of 20 to 50 patients have suggested that increasing oxygen pressure may help improve outcome. Noninvasive ventilation can be performed by using continuous positive pressure ventilation or intermittent positive pressure ventilation. The trial was designed to see whether noninvasive ventilation can improve survival and which method should be used. Since the study started, several papers have suggested that the total evidence to date indicates noninvasive ventilation should halve the death rate.

The 3CPO trial, led by Dr Alasdair Gray, was undertaken over three years in 26 Emergency Departments across the UK and recruited over 1,000 patients. At the close of the trial, 1,069 patients had been enrolled and received standard oxygen (367 patients), continuous positive airway pressure (346 patients) or noninvasive intermittent positive pressure ventilation (356 patients).

Compared with standard oxygen treatment, both forms of noninvasive ventilation produced better rates of recovery with a more rapid fall in respiration and heart rate as well as a quicker resolution of acidosis. However, the death rate did not differ. Method of noninvasive ventilation did not change responses.

This first major large-scale clinical trial demonstrated that noninvasive ventilation is a useful treatment to alleviate distress and improve breathing, but it does not improve subsequent chances of survival.

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経皮的僧帽弁修復術の可能性

プレリミナリーなEVOLUTIONスタディの結果、経皮的僧帽弁修復術は一部の選択された僧帽弁閉鎖不全患者に実用的となる可能性がある

Preliminary EVOLUTION study results suggest that percutaneous mitral valve repair may become practical for selected patients with mitral regurgitation

スタディの結果、経皮的僧帽弁修復術の改良により一部の選択された僧帽弁閉鎖不全患者に有益で安全となる可能性があることが示唆された、とESCで発表された。EuroHeart Surveyにより、僧帽弁閉鎖不全は多く認められるが（自己弁疾患症例の30%）、患者の50%しか外科的形成術を施行されていないことが確認された。今回の研究は、2つの経皮的アプローチ法（edge-to-edge techniqueおよび僧帽弁輪形成術）が更なる評価に値することを示した。開発中のデバイスは冠動脈洞の遠位部および近位部に固定部位がありこの固定部分の間にブリッジを有する。弁輪形成術の方が冠動脈洞のカテーテル挿入のみでよいため、簡単である。EVOLUTIONのプレリミナリーな結果（患者60人）によると、施行可能率は高く（90%）安全性も優れていた。約80%の患者が90日後の時点で合併症を有さなかった。非常にプレリミナリーな結果からは、逆流の程度が軽減したことが示唆された。

Full Text

Preliminary results from studies such as EVOLUTION suggest that percutaneous mitral repair may be beneficial and safe for selected patients with mitral regurgitation who are not currently being treated surgically, according to a presentation at the annual meeting of the European Society of Cardiology.

Based on EuroHeart Survey results, mitral regurgitation represents the second most important native valve disease in Europe (30 percent). The same survey suggests that mitral valve repair is performed only 50 percent of the time. This shortfall is mostly due to a lack of expertise in performing the procedure. Finally, survey data highlight the fact that half of the patients, despite the presence of severe symptoms and severe mitral regurgitation, are not considered for surgery by their physicians. Thus, there is a need for treatment other than surgery for high-risk patients or those denied surgery.

Percutaneous mitral valve repair was introduced only a few years ago. There are two different approaches to percutaneous mitral valve repair.

The first approach is the edge-to-edge technique, which creates a double mitral valve orifice replicating the surgical intervention pioneered by Professor Alfieri. This technique is very demanding because it requires trans-septal catheterization and sophisticated collaboration between the echocardiographist and interventionist to catch the valve at the appropriate moment and location.

Preliminary clinical results obtained in over 100 patients suggest that in expert hands the feasibility of the technique is high (80-90 percent) and the degree of mitral regurgitation can be reduced to mild in two thirds of cases. In addition, the risk is low, once again, in experienced centers. In patients where the procedure was successful, two thirds remained event free after three years. Thus these data, even if only preliminary, are encouraging.

The second possible approach is mitral annuloplasty, which is achieved by introducing a constraining device in the coronary sinus located in the vicinity of the mitral annulus. The rationale here is that ring annuloplasty is almost always combined with other procedures during surgical interventions on the mitral valve. More than ten devices have been designed and three are currently being studied. They share common technical features: distal fixation and proximal fixation in the coronary sinus and a bridge between the two fixating elements.

Annuloplasty is easier because it only requires catheterization of the coronary sinus. Preliminary results from the EVOLUTION study in 60 patients show high feasibility (90 percent) and good safety profiles: Almost 80 percent of patients experienced no complications within 90 days. Very preliminary efficacy data suggest a reduction in the degree of regurgitation.

Clearly at the present stage these two approaches do not yet reach the standard of the multiple surgical techniques that make the success of surgical mitral valve repair.

The annuloplasty technique could be potentially used in patients with functional mitral regurgitation, while the edge-to-edge technique could be used in selected patients with degenerative mitral regurgitation. The potential clinical indications of the new percutaneous techniques are represented by the vast group of patients with contraindications or judged to be at very high risk for surgery.

Many devices are currently being studied or are at the experimental stage: suture-based direct annuloplasty, percutaneous mitral valve replacement, or transpericardial left ventricular remodeling.

Further research should be carefully evaluated in comparison with surgery and standard contemporary medical treatment including cardiac resynchronization. Trials such as EVEREST II, EVOLUTION II, and AMADEUS are underway.

Development of such new techniques will require close collaboration between engineers, interventionalists, imaging specialists, and surgeons.

薬剤溶出ステントと急性冠症候群

GRACE登録データ解析によると、急性冠症候群患者に対し薬剤溶出ステントはベアメタルステントと比較し慎重に使用すべきであることが示唆された

GRACE registry data analysis suggests that drug-eluting versus bare metal stents should be used with caution in patients with acute coronary syndrome

GRACE登録データ解析によると、急性冠症候群患者に対する薬剤溶出ステント使用はベアメタルステントと比較し2年後の総死亡率が高いため慎重に使用すべきであることが示唆された、とESCで発表された。Global Registry of Acute Coronary syndromEs (GRACE)では、米国、ヨーロッパ、およびオーストラリア／ニュージーランドの14ヵ国のデータを収集した。この解析ではベアメタルステントまたは1つ以上の薬剤溶出ステントを挿入された患者の2年後までの生存率を比較した。生存率は退院6ヵ月後の時点では同等であったが、その後死亡率は薬剤溶出ステント群で高かった。この差はほとんどが急性心筋梗塞に対しステントを挿入された患者によるものであり、後期の再梗塞のリスクが高く、潜在的な差が後期のステント内血栓に関連したことを示唆している。生存率の差は、患者群間のベースラインでの患者背景で補正してもなお認められた。

Full Text

Analysis of GRACE registry data suggests that drug-eluting stents should be used with caution in patients with acute coronary syndrome due to increased all-cause mortality at two years compared with bare metal stents, according to a presentation at the annual meeting of the European Society of Cardiology.

Although drug-eluting stents are extremely effective in preventing restenosis following angioplasty, there has been increasing uncertainty regarding their long-term safety. Specifically, there is concern that some stents may occlude abruptly more than one year after placement due to late stent thrombosis.

Although such thrombosis is rare, probably in the range of less than 1 percent per year, it is extremely severe, with up to 45 percent mortality. Thus, the question is raised whether this rare but life-threatening event may offset the benefit achieved by drug-eluting stents in preventing restenosis.

The risk of late stent thrombosis may be greater in the context of acute coronary syndromes and, in fact, little information is available so far from rigorous randomized clinical trials comparing drug-eluting stents with bare metal stents in these patients, particularly those with acute myocardial infarction. Randomized clinical trials that have compared drug-eluting stents and bare metal stents in the context of acute myocardial infarction are relatively small (totaling fewer than 1,000 patients with drug-eluting stents) and most have only reported one year of follow-up.

The current analysis used the database from the Global Registry of Acute Coronary syndromEs (GRACE), collected in 94 hospitals in 14 countries across 4 continents (Americas, Europe, Australia/NZ) to compare survival at up to two years of patients treated with bare metal stents only or with at least one drug-eluting stent.

Survival appeared similar in at six months after discharge, but thereafter mortality was greater in patients treated with drug-eluting stents. This difference was entirely related to patients treated for acute myocardial infarction and was associated with an increased risk of late reinfarction, suggesting that it may indeed be related to late stent thrombosis.

Although caution should always be exercised when analyzing an observational study such as GRACE (in which patients who received drug-eluting stents and bare metal stents were not similar), this survival difference (which persisted after statistical adjustment for differences in baseline characteristics between the two types of patients) suggests that drug-eluting stents should be used with caution in patients with acute myocardial infarction, at least until more evidence is accumulated of long-term safety from large studies with long-term follow up.

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心室性不整脈の軽減

MERLIN TIMI-36トライアルの結果、ranolazineは急性非ST上昇心筋梗塞患者の心室性および心房性不整脈を減少させることが示された

MERLIN TIMI-36 Trial shows ranolazine reduces ventricular and atrial arrhythmias in patients with acute non-ST elevation infarctions

MERLIN TIMI-36トライアルの結果、標準的な治療を受けている急性非ST上昇心筋梗塞または不安定狭心症の患者にranolazineを投与することにより、心室性および心房性不整脈が減少することが示された、とESCで発表された。このトライアルでは6,560人の患者を、実薬またはプラセボを静脈内投与しその後外来で徐放性薬剤またはプラセボを長期投与する群に無作為に割り付けた（ranolazine 3,279人，プラセボ3,281人）。全ての患者は入院中および外来で、アスピリン、β遮断薬、およびスタチンなどの標準治療も受けた。その結果、ranolazineはプラセボと比較し、8連発以上の心室頻拍の相対リスクを37%低下させ、心臓突然死を減少させた（56対65）。組み入れ後最初の7日間にホルター心電図を施行し、患者全員で計100万拍以上の解析用のデータが得られた。この数はクリニカルトライアルの一部として得られた中で最も多いと考えられた。

Full Text

MERLIN TIMI-36 data show that extended-release ranolazine reduces ventricular and atrial arrhythmias in patients with acute non-ST elevation myocardial infarctions or unstable angina who are already receiving standard therapy, according to a presentation at the annual meeting of the European Society of Cardiology.

MERLIN TIMI-36 (Metabolic Efficiency with Ranolazine for Less Ischemia in Non-ST Elevation Acute Coronary Syndromes) was a multi-national, double-blind, randomized, placebo-controlled, parallel-group clinical trial designed to evaluate the efficacy and safety of the extended-release drug formulation during acute and long-term treatment in 6,560 patients (3,279 received ranolazine, 3,281 received placebo) with non-ST elevation acute coronary syndrome treated with standard therapy.

Within 48 hours of onset of angina, eligible hospitalized patients were enrolled in the study and randomized to intravenous drug or placebo, followed by long-term outpatient treatment with extended-release drug or placebo. All patients also received standard therapy during both hospital-based and outpatient treatment. The doses of ranolazine extended-release tablets used in MERLIN TIMI-36 have been studied in previous Phase III clinical trials.

Participants in the MERLIN TIMI-36 study received modern therapy, with approximately 96 percent of patients on aspirin, approximately 89 percent on beta blockers and approximately 82 percent on statins. Approximately 59 percent of study participants received coronary angiography during their initial hospitalization.

The ranolazine group had a 37-percent reduction in relative risk of ventricular tachycardia lasting eight beats or more and fewer episodes of sudden cardiac death (56 deaths) compared with placebo patients (65 deaths).

As part of the MERLIN TIMI-36 safety assessment, Holter monitors recorded continuous electrocardiographic (ECG) recordings for the first seven days after patients were admitted to the study with an episode of non-ST elevation myocardial infarction or unstable angina. The more than 1,000,000 hours of Holter monitor data from 6,351 study participants are believed to represent the largest Holter monitor database ever collected in a clinical trial.

"The significant reductions in ventricular arrhythmias observed in ranolazine patients in the MERLIN TIMI-36 study provide important and reassuring data regarding the long-term safety of ranolazine and suggest that ranolazine could have potential as a new anti-arrhythmic agent in treating ventricular arrhythmias," said Benjamin Scirica, a cardiologist at Brigham and Women's hospital, an investigator at the TIMI Study group and lead author of the study.

These data represent the first clinical report of the effect of ranolazine to reduce the incidence of cardiac arrhythmias and support the findings of many prior preclinical studies that suggested ranolazine has potential anti-arrhythmic properties due to its action as an inhibitor of the late sodium current.

Extended release ranolazine is currently indicated in the USA for treatment of chronic angina in patients who have not achieved an adequate response with other antianginal drugs, and should be used in combination with amlodipine, beta-blockers or nitrates.

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ステント血栓症に関するさらなる情報

OPTIMISTトライアルの結果、ステント血栓症に対する緊急経皮的冠動脈形成術の成績は期待に反する結果であったことが示された

OPTIMIST trial shows that emergency percutaneous coronary intervention for stent thrombosis is associated with disappointing outcomes

ステント血栓症に対する緊急経皮的冠動脈形成術の成績は、熟練した施設においてもなお成績が不良のようである、とESCで発表された。2年間にわたりOPTIMISTトライアルでは110人の患者を組み入れたが、患者は急性心筋梗塞に対し緊急経皮的冠動脈形成術を施行された者の3.6%を占め、一連のこれらの患者を集めた中では今までで最も多い数である。6ヵ月間の追跡調査による予後解析の結果は、死亡率が17%、主要な冠動脈または脳血管イベント発症率が29%と、期待に反する結果であった。死亡率は、ステント血栓症がステント植え込み1年後に発現した場合、インターベンションを試みた結果が最善ではなかった場合、および施術中にステントを追加で植え込んだ場合に、有意に高かった。塞栓予防デバイスを用いて血栓除去術を施行された心原性ショックのない患者は最大の冠動脈血流回復率が5倍高かった。

Full Text

Emergency percutaneous coronary intervention for stent thrombosis appears to be associated with disappointing outcomes, according to a presentation at the annual meeting of the European Society of Cardiology.

The OPTIMIST (Outcome of PCI for stent-ThrombosIs MultIcentre Study) trial was a non-sponsored, independent, large-scale, multi-center study conducted by 11 hospitals located in around Rome, Italy. During a period of 2 years (2005-2006) all patients who were admitted to participating hospitals with stent thrombosis and treated by percutaneous coronary intervention were enrolled.

Clinical and procedural data was recorded on a detailed questionnaire and clinical outcome up to 6 month after intervention was assessed by ambulatory visit or phone contact. Moreover, procedure efficacy to reestablish optimal coronary blood flow was assessed by performing detailed analyses in an independent core laboratory.

During the study, 110 patients were recruited, constituting the largest series of patients with stent thrombosis collected to date. A first original observation arising from the study was that stent thrombosis, even if it is a rare event, accounted for 3.6 percent of emergency procedures performed in patients with acute myocardial infarction. These data reinforce the perception that stent thrombosis has more than a negligible impact on the contemporary health system and further investigations on its causes and management are merited

The data collected in the OPTIMIST study did not allow for clarification of whether risk of thrombosis is higher after drug-eluting or bare metal stent implantation. However, the data support the hypothesis that stent thrombosis may have different mechanisms of occurrence in different types of stents.

Indeed drug-eluting stent thrombosis, compared with thrombosis in bare metal stents, happened more often after 30 days of implantation or after 15 days post-withdrawal of antiplatelet drug therapy. On the other hand, once stent thrombosis has occurred, clinical manifestations, procedural and clinical outcomes did not appear to be influenced by the type of stent.

Clinical outcome during the six-month follow-up, despite good utilization of all of the best pharmacological and technical resources, was a disappointing 17 percent mortality rate and 29 percent rate of major adverse coronary or cerebral events (death or myocardial infarction or stroke or necessity of a new interventional procedure). These results show that stent thrombosis is not a benign disease and emergency interventions in this setting are still associated with unsatisfactory outcome.

As the individuation of factors associated with worse case outcome may be useful in clinical practice, a series of analyses of independent predictors of bad outcome was performed in OPTIMIST. Such analyses showed that mortality was significantly higher when stent thrombosis occurred one year after stent implantation (i.e. "very late" thrombosis), when the attempted intervention result was not optimal, and when an additional stent was implanted during the procedure.

The first point suggests that clinical surveillance after successful intervention should not be reduced after one year and that the possible value of long-term anti-thrombotic drug administration should be investigated. The other two factors may together provide some interesting suggestions to the interventional cardiologists who perform emergency procedures in patients with stent thrombosis. Indeed, it seems they should aim to reestablish optimal coronary blood flow and not to eliminate any residual coronary vessel narrowing by further stent implantations.

The OPTIMIST study also evaluated the efficacy of novel techniques in the high-risk scenario of stent thrombosis. Previous studies have suggested that thrombectomy using new, specifically-designed devices may facilitate restoration of coronary blood flow in thrombotic lesions by reducing distal embolization of thrombotic debris. In the OPTIMIST study, 1 in every 4 patients was treated using thrombectomy devices as a first strategy. Despite the fact that patients treated by thrombectomy were sicker than the others, no excess adverse clinical events were observed, supporting the safety of this novel approach.

Patients without shock treated by thrombectomy had a five-fold improved rate of optimal coronary flow restoration. This suggests that the role of distal embolization and its prevention may be important only before advanced heart damage has been established.

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薬剤溶出ステントに関する性特異的な情報

TAXUS WOMANスタディの結果、これらの女性患者はリスクが高かったにもかかわらず、薬剤溶出ステント植え込み後の臨床転帰は男性におけるそれと同等であったと報告された

TAXUS WOMAN study reports post-implantation clinical outcomes comparable with those for men despite the higher risk profiles of women patients

TAXUS II、IV、VおよびVIトライアル（TAXUS WOMANスタディ）の結果、パクリタキセル溶出ステントを植え込まれた女性はリスクプロファイルが不良であったにもかかわらず、臨床転帰は男性と同等であった、とESCで発表された。4つのトライアルに組み込まれた患者3,445人のうち955人（27.7%）が女性であった。これらの女性のうち480人が薬剤溶出ステントを植え込まれ475人がベアメタルステントを植え込まれていた。男性と比較し、女性はより高齢であり（平均年齢65.4歳対61.0歳）、対表面積が小さく、糖尿病および高血圧有病率が高く（それぞれ30.4%対21.0%、78.0%対65.1%）、血管径が小さかった（施術前対象血管径2.63mm対2.78mm）。しかし、1および3年後の血管形成術再施行率および主要な有害事象発現率は男女間で差はなかった。

Full Text

Gender-specific analysis of data from the TAXUS II, IV, V, and VI Trials (the TAXUS WOMAN study) suggests that women implanted with paclitaxel-eluting coronary stents have outcomes comparable with those of men despite having poorer risk profiles, according to a presentation at the annual meeting of the European Society of Cardiology.

"This study of data from the TAXUS trials offers encouraging news for women with coronary artery disease," said Ghada Mikhail, MD, Consultant Cardiologist, St Mary's Hospital Trust, London, UK. "Previous trials and registries have demonstrated a less favorable clinical outcome in women compared to men when undergoing coronary revascularization with bare-metal stents. That difference has been previously explained by the smaller vessels and higher risk profile seen in women. These data show, however, that the TAXUS paclitaxel-eluting coronary stent works equally well in women, maintaining its anti-restenotic efficacy advantages and positive safety profile relative to bare-metal stents."

The TAXUS II, IV, V and VI trials evaluated performance of the paclitaxel-eluting stent compared with a bare-metal stent control in patients with coronary artery disease. The TAXUS WOMAN study analyzed pooled results of the women enrolled in these TAXUS trials and compared them with the corresponding endpoints in men.

Of the 3,445 patients enrolled in the TAXUS trials between June 2001 and March 2004, 955 (27.7 percent) were women. Of these women, 480 received drug-eluting stents and 475 received base metal stents. Of the 2,490 men enrolled, 1,238 received drug-eluting stents and 1,252 received base metal stents.

Compared with men, women were older (mean age 65.4 +/- 10.9 years versus 61.0 +/- 10.4 years), had smaller body surface area (1.80 +/- 0.19m^2 versus 2.05 +/- 0.20m^2), had more diabetes (30.4 percent versus 21.0 percent), had more hypertension (78.0 percent versus 65.1 percent), had smaller vessels (pre-procedure reference vessel diameter 2.63 +/- 0.46mm versus 2.78 +/- 0.52mm), and had more history of coronary artery disease (62.2 percent versus 54.7 percent). There were no other significant differences in baseline demographics, lesion or procedural characteristics between the drug-eluting and bare metal stent groups in both genders.

Results show that the drug-eluting stent maintained its advantage in preventing repeat procedures compared to the bare-metal stent control, while showing no significant differences in outcomes based on gender. At one year, the unadjusted rate of target lesion revascularization drug-eluting stent group was 8.1 percent in women versus 6.7 percent in men, while in the bare metal stent group, the unadjusted revascularization rate at one year was 17.5 percent in women versus 16.4 percent in men. At three years, there were continued low revascularization rates in both women and men treated with drug-eluting stents (10.7 percent in women versus 8.8 percent in men, with no difference between men and women).

Comparable results in safety outcomes were seen for women, showing no differences in major adverse cardiac event rates at one year. Adverse event rates in the drug-eluting stent group were 15.6 percent for women versus 13.2 percent for men, while the rate in the bare metal stent group were 24.0 percent for women versus 21.7 percent for men.

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遅発性ステント血栓症に関する死体解剖から得られた情報

薬剤溶出ステントを植え込まれた患者の死体解剖の結果、遅発性ステント血栓症には同定可能なリスクファクターがあることが示唆された

Autopsy series on patients with drug-eluting stents suggests there are identifiable risk factors for late stent thrombosis

死体解剖の研究から遅発性ステント血栓症に関する知見が得られた、とESCで発表された。研究者らは、死亡から30日以上前に薬剤溶出ステントを植え込まれた患者83人（117部位）の死体解剖を行った。計33部位が壁在血栓（25部位）または器質化血栓（8部位）であった。5人の患者（うち3人は突然死し、2人は心筋梗塞を発症）はステント周囲に過敏性反応を起こしていた（ステント植え込み期間112～940日）。ステント血栓症のリスクを上昇させる因子は、不完全密着（8人）、分岐部へのステント留置（7人）、急性心筋梗塞（8人）、およびステントのオーバーラップ（4人）であった。CypherおよびTaxusステントのいずれも遅発性治癒による内膜形成を軽減した。しかし、それぞれのステントに対する反応には違いがあった。フィブリンの沈着はTaxusステントでより高頻度であり、炎症（特に抗酸球浸潤および巨細胞反応）はCypherステントでより多かった。

Full Text

An autopsy series of patients with drug-eluting stents gives new insight into late stent thrombosis, including possible identification of risk factors, according to a presentation at the annual meeting of the European Society of Cardiology.
The stents currently approved in the USA (CYPHER and TAXUS) have been associated with late stent thrombosis (thrombosis more than 30days following implantation). Then current autopsy study was designed to analyze morphologic changes occurring after placement of drug-eluting stents to determine the causes of late stent thrombosis.

Researchers autopsied 83 patients (117 lesions) with coronary artery disease who had drug-eluting stents in place for more than 30 days prior to death. A total of 33 lesions showed either luminal thrombus (25 lesions) or organized thrombus (8 lesions).

Of the 117 total lesions, 6 (in five patients) showed a hypersensitivity reaction (5 Cypher, 1 Taxus).The six stents had been in place from 112 to 940 days; three patients died suddenly and two presented with acute myocardial infarction. From these data it appears that response is limited to the area of the stent, and there is extensive eosinophilic and T-cell infiltration. There may or may not be a granulomatous reaction.

Other morphologic changes that predisposed to stent thrombosis were malapposition (8 patients), stenting of bifurcation lesions (7 patients), acute myocardial infarction (8 patients), and overlapping stents (4 patients). All showed delayed healing, which was further exaggerated either from turbulent flow at malapposition or bifurcation sites or poor healing at sites of plaque rupture or overlapping stents.

Excessive length (more than 30 mm) was a correlate of late thrombosis as well as presence of uncovered stent struts. Uniformly, all cases with thrombi had the presence of fibrin, poor stent coverage by neointima, and less endothelialization.

All 78 lesions that were patent (and drug-eluting stent was not the cause of death) and had been in place for more than 30 days showed less neointima compared with bare metal stents, suggesting that drug-eluting stents are effective in reducing neointimal thickness. A parameter uniformly observed in bare metal stents is that neointimal formation around the circumference of the stent tends to be uniform in distribution. In drug-eluting stents, there is heterogeneity of healing with areas showing excessive fibrin and others with smooth muscle cells within matrix and uneven luminal endothelialization.

Both Cypher and Taxus stents reduced neointimal formation from delayed healing. However, there were inherent differences in the response to each stent, with fibrin deposition more frequent in Taxus stents and inflammation, especially eosinophilic infiltrate and giant cell reaction, greater in Cypher stents.