Press release from the Cardiprogress Foundation

Most important clinical trials presented at the HOT LINE sessions of the European Society of Cardiology Congress 2026

From 28 to 31 August 2026, Munich (Germany) hosted the annual Congress of the European Society of Cardiology. The motto of this year's event was "Research. Innovation. Inspiration."

Congress participants reviewed four new clinical practice guidelines on:

- Cardiac rehabilitation;
- Cardiovascular disease and chronic kidney disease;
- Heart failure (HF);
- The Fifth Universal Definition of Myocardial Infarction (MI).

The full texts of these documents are available online at https://www.escardio.org/guidelines/.

At 12 HOT LINE scientific sessions, the results of 55 specially selected clinical trials were presented for the first time. The studies addressed various fields of cardiology, new principles and methods of diagnosis, and pharmacological and non-pharmacological treatment of cardiovascular pathology, including acute coronary syndromes (ACS), cardiac arrhythmias, HF, atherosclerosis, valvular heart disease, arterial hypertension, cardiomyopathies, and thromboembolism.

The most noteworthy studies are summarised below.

According to current clinical guidelines, oral anticoagulant therapy has a class IIa indication in patients with atrial fibrillation (AF) and an intermediate risk of stroke (1 point in men and 2 points in women on the CHA_2DS_2-VASc score). Such patients were enrolled in the SINGLE-AF trial to receive either direct oral anticoagulants (DOACs) (n = 902) or no anticoagulant therapy (n = 901). At 24 months, the primary composite endpoint, including stroke, systemic embolism, major bleeding, or cardiovascular death, occurred in 0.5% of patients in the DOAC group and in 1.5% in the no-anticoagulation group ($p = 0.03$). The rates of serious adverse events did not differ significantly between the groups. These results support the benefit of DOAC treatment in AF patients with intermediate stroke risk.

According to current guidelines, implantable cardioverter-defibrillators (ICDs) are not indicated for primary prevention if the left ventricular ejection fraction (LVEF) is above 35%. However,

many cases of sudden cardiac death occur in patients with LVEF between 36% and 50%, presumably due to the presence of myocardial scar tissue – a substrate for arrhythmias – which can be detected by late gadolinium enhancement on cardiac magnetic resonance imaging. In the CMR GUIDE trial, such patients were randomised to ICD implantation for primary prevention (n = 180) or to implantation of an implantable loop recorder (n = 173). At a median follow-up of 6.3 years, the primary composite endpoint (sudden cardiac death or haemodynamically significant ventricular tachyarrhythmia) occurred in 7.8% of the ICD group versus 9.2% in the no-ICD group (relative risk [RR] 0.76, 95% confidence interval [CI] 0.37–1.58). These events were less frequent in the ICD group among patients younger than 70 years (RR 0.28, 95% CI 0.09–0.89), but not in those aged 70 years or older (RR 2.33, 95% CI 0.75–7.26; p = 0.01 for interaction). The authors concluded that in patients with LVEF 36–50% and myocardial scar, ICD does not reduce the risk of sudden cardiac death or haemodynamically significant ventricular tachyarrhythmia.

The efficacy and safety of statins for primary prevention of cardiovascular events and for prolonging disability-free survival in older adults remain uncertain. In the STAREE trial, people aged 70 years and older without cardiovascular disease, diabetes, or dementia were randomised to atorvastatin 40 mg/day (n = 4984) or placebo (n = 4987). At a median follow-up of 5.9 years, the composite primary cardiovascular outcome (cardiovascular death, non-fatal MI or stroke, coronary revascularisation) occurred less frequently in the statin group (RR 0.70, 95% CI 0.61–0.82; p < 0.001), whereas the composite measure of disability-free survival (death from any cause, dementia, or persistent physical disability) did not differ between groups (RR 0.94, 95% CI 0.84–1.05; p = 0.25). Serious adverse events occurred with equal frequency in both groups – 2.7%.

Subclinical atherosclerosis is associated with cardiovascular events and death, but its prevalence by age and sex, distribution across vascular territories, and plaque burden across adult life remain insufficiently studied. In the REACT trial, subclinical atherosclerosis was assessed in 16,808 individuals aged 18 to 70 years using three-dimensional ultrasound scanning of carotid and femoral arteries and coronary computed tomography angiography. In the youngest age group (18–29 years), atherosclerosis was detected in 8.7% of men and 6.7% of women; at age 40, in 50% of men and 30% of women; and at age 70, in approximately 90% of participants regardless of sex, due to late and rapid progression of arterial lesions in women. Among younger participants, atherosclerosis was most often peripheral and limited to a single vascular territory. With increasing age, plaque volume increased exponentially, and the prevalence of multifocal disease rose.

The A-CLOSE trial enrolled patients at high ischaemic risk who had undergone drug-eluting stent implantation for ST-segment elevation MI, non-ST-segment elevation MI, or unstable angina at least 12 months earlier. After randomisation, they received either clopidogrel monotherapy (n = 1601) or extended dual antiplatelet therapy (DAPT) (clopidogrel plus aspirin; n = 1602) for one year. The composite rate of adverse clinical events of the primary endpoint (death from any cause, MI, stent thrombosis, stroke, or bleeding type 2, 3, or 5 according to the Bleeding Academic Research Consortium [BARC] classification) was 5.0% in the monotherapy group and 5.1% in the DAPT group (p = 0.001 for non-inferiority). Ischaemic events (death from any cause, MI, stent thrombosis, or stroke) occurred in 3.7% versus 1.6% (RR 2.33, 95% CI 1.47–3.69; p < 0.001), and bleeding in 1.8% versus 4.1% (RR 0.43, 95% CI 0.27–0.67; p < 0.001) in the monotherapy and DAPT groups, respectively. At 12 months after drug-eluting stent implantation, among patients at high ischaemic risk, clopidogrel monotherapy was non-inferior to extended DAPT regarding net clinical benefit up to 24 months.

In the LIBREXIA ACS trial, the efficacy and safety of the oral factor XIa inhibitor milvexian at 25 mg twice daily (n = 7100) were compared with placebo (n = 7094) added to standard antiplatelet therapy within 7 days after ACS. The trial was stopped early due to futility of milvexian. At a median follow-up of 12.2 months, the primary efficacy endpoint (cardiovascular death, MI, or ischaemic stroke) occurred in 5.4% of participants in the milvexian group and 5.1% in the placebo

group (RR 1.05, 95% CI 0.91–1.21; p = 0.50). The primary safety endpoint – bleeding type 3c or 5 according to BARC (intracranial or intraocular bleeding with vision impairment, fatal bleeding) – occurred in 0.3% of patients in both groups (p = 0.88).

The possibility of safely withdrawing aspirin at the initial stage of primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation MI was assessed in the PREMIUM trial. Participants were randomised to low-dose prasugrel monotherapy (20 mg, then 3.75 mg/day; n = 1109) or to DAPT with aspirin and low-dose prasugrel (n = 1107) for 12 months. The primary endpoint (death from any cause, stroke, or MI at 1 year) occurred in 11.0% versus 8.5% of patients (RR 1.34, 95% CI 1.02–1.75; p = 0.40 for non-inferiority), and type 3 (non-fatal major) or type 5 (fatal) bleeding by BARC occurred in 5.6% versus 8.4% (RR 0.66, 95% CI 0.47–0.91) in the prasugrel monotherapy and DAPT groups, respectively. No differences were observed in the rate of definite or probable stent thrombosis between the groups. The hypothesis that low-dose prasugrel monotherapy initiated before PCI is non-inferior to DAPT in terms of efficacy over 12 months could not be confirmed.

The question of which $P2Y_{12}$ inhibitor – prasugrel or ticagrelor – is preferred for patients with ACS remains unresolved. In the SWITCH-SWEDEHEART trial, patients who underwent PCI for ACS and in whom prasugrel was used instead of default ticagrelor in the treatment regimen (n = 7651) were compared with those receiving ticagrelor (n = 9444) based on national registry data. The primary composite endpoint (death from any cause, fatal or non-fatal MI, fatal or non-fatal stroke at 1 year) occurred in 11.8% of the ticagrelor group versus 11.1% of the prasugrel group (RR 0.90, 95% CI 0.77–1.06), while major bleeding occurred in 4.4% and 4.2%, respectively (RR 0.80, 95% CI 0.64–0.99).

For patients with ST-segment elevation MI and multivessel disease, complete revascularisation is recommended, but the preferred strategy for identifying non-infarct-related lesions requiring intervention remains uncertain. In the AIR-STEMI trial, patients with successfully opened infarct-related arteries via PCI were randomised to revascularisation guided by fractional flow reserve (FFR) (n = 913; physiology-guided group) or by conventional angiography (n = 910; angiography-guided group). At a median follow-up of 17.9 months, the primary composite efficacy endpoint (death from any cause, MI, stroke or transient ischaemic attack, ischaemia-driven revascularisation) occurred in 8.9% of the physiology-guided group and 13.7% of the angiography-guided group (RR 0.62, 95% CI 0.47–0.83; p < 0.001). The primary composite safety endpoint (contrast-induced acute kidney injury or major bleeding) occurred in 4.6% versus 7.1%, respectively (RR 0.63, 95% CI 0.43–0.93; p = 0.02).

Many patients with suspected ACS in whom MI was ruled out in the emergency department remain at risk of cardiovascular events. Whether further investigation can reduce this risk is unknown. The TARGET-CTCA trial enrolled patients in whom MI was excluded but the peak high-sensitivity cardiac troponin I or T level exceeded 5 ng/L, indicating intermediate cardiovascular risk. After randomisation, they received outpatient care guided by coronary computed tomography angiography (n = 1587) or standard care (n = 1583). At a median follow-up of 3.0 years, the primary composite endpoint (MI or cardiac death) occurred in 7.1% of the CT-angiography group and 7.3% of the standard-care group (RR 0.95, 95% CI 0.73–1.23; p = 0.71).

Pulmonary hypertension in chronic heart failure (CHF) may be driven by excessive sympathetic nervous system activation, leading to increased pulmonary vascular resistance, right ventricular dysfunction, and adverse outcomes. The PADN-HF-PH trial evaluated the effect of pulmonary artery denervation on pulmonary hypertension and the course of CHF due to left ventricular pathology. Patients were randomised to pulmonary artery denervation plus guideline-directed medical therapy (n = 134) or medical therapy alone (n = 130). At a median follow-up of 338 days,

the primary endpoint – clinical worsening (composite of death, heart/lung transplantation for heart failure, ambulatory worsening of heart failure with or without hospitalisation, decrease in 6-minute walk distance >10% or 30 m) – occurred in 25.7% of the denervation group and 51.5% of the medical-therapy group (RR 0.49, 95% CI 0.30–0.82; p = 0.006). The procedure was associated with very few serious procedural complications.

For patients with left-sided infective endocarditis, a 6-week course of antibiotics is recommended; whether this can be shortened based on clinical response without compromising safety is unclear. In the POET II trial, patients with infective endocarditis caused by *Staphylococcus aureus*, *Enterococcus faecalis*, or streptococci, who were stabilised after 2–4 weeks of treatment, were randomised to discontinue antibiotics (n = 255) or continue standard therapy to a total duration of 4–6 weeks (n = 253). The primary efficacy endpoint – days alive without antibiotics or bacteraemia over 6 months – was 183 versus 169 days (p < 0.001 for superiority); the primary safety endpoint – death from any cause, unplanned cardiac surgery, or symptomatic embolism – occurred in 8.2% versus 10.7% (p < 0.001 for non-inferiority); however, recurrence of bacteraemia or infective endocarditis occurred in 5.1% versus 1.6% (p = 0.04) in the individually tailored and standard antibiotic groups, respectively.

After transcatheter aortic valve replacement (TAVR), subclinical leaflet thrombosis is often observed and visualised on cardiac CT as hypoattenuated leaflet thickening; this may lead to thromboembolic complications. The NOTION-4 trial enrolled patients after successful TAVR without an indication for oral anticoagulation; they were randomised to lifelong antiplatelet monotherapy (n = 176) or to 3 months of DOAC followed by lifelong antiplatelet monotherapy (n = 171). The primary endpoint (leaflet thickening) at 3 months was detected in 31.8% versus 12.1%, and at 1 year in 32.2% versus 28.3% in the antiplatelet monotherapy and combination groups, respectively (p = 0.54). Thus, the difference achieved during DOAC therapy diminished after its discontinuation.

Approximately half of patients undergoing TAVR have concomitant coronary artery disease. PCI is often performed before TAVR, but the optimal sequence of these interventions is not established. The TAVI PCI trial enrolled patients with severe aortic stenosis and coronary artery disease, randomising them to initial valve intervention (n = 498) or initial PCI (n = 498). At 1 year, the primary endpoint (death from any cause, non-fatal MI, ischaemia-driven revascularisation, rehospitalisation related to the valve, procedure, or heart failure, life-threatening, disabling, or major bleeding) occurred in 22.2% of the initial-valve group and 24.2% of the initial-PCI group (p < 0.001 for non-inferiority).

The effect of transcatheter tricuspid valve repair on clinical outcomes, including mortality and hospitalisation for heart failure, in patients with severe tricuspid regurgitation remains uncertain. In the TRIC-I-HF-DZHK24 trial, patients with symptomatic severe tricuspid regurgitation and elevated risk of future heart failure were randomised to tricuspid valve repair plus medical therapy (n = 237) or medical therapy alone (n = 123). At 1 year, the repair group showed a 2.42-fold improvement in the primary hierarchical composite endpoint (death from any cause, hospitalisation for HF, and quality-of-life score; p < 0.001), as well as in the composite of death or hospitalisation for HF over 3 years (p < 0.001).

According to clinical guidelines, catheter ablation is intended to relieve symptoms in patients with AF. The PVI-SHAM-AF trial randomised patients with symptomatic paroxysmal or persistent AF to catheter ablation (n = 173) or sham ablation (n = 89) to determine whether ablation improves AF-related quality of life more than a placebo procedure. The summary AFEQT quality-of-life score increased similarly over 6 months (primary endpoint) from baseline 61.3 to 81.1 in the ablation group and from 59.2 to 74.9 in the sham group (p = 0.36). One death occurred in each

group, unrelated to the study procedure. Catheter ablation did not show superiority over sham ablation in improving AF-related quality of life.

For patients presenting to the emergency department with syncope, diagnosing a cardiac arrhythmic cause remains challenging. The ASPIRED trial randomised patients with syncope of unexplained cause after emergency department evaluation to 14-day ambulatory electrocardiogram monitoring (n = 1004; intervention group) or standard care (n = 966). The mean number of self-reported syncope episodes at 1 year (primary endpoint) was 1.37 ± 5.10 in the intervention group and 1.58 ± 8.56 in the standard-care group (RR 0.89, 95% CI 0.68–1.18; p = 0.42).

Cardiac resynchronisation therapy in patients with symptomatic HF and left bundle branch block can be delivered by biventricular pacing or by His-bundle or left bundle branch pacing. In the His-Alternative II trial, patients with symptomatic HF, LVEF ≤35%, and left bundle branch block were randomised to biventricular pacing (n = 63) or conduction system pacing (n = 85, of which 26 His-bundle and 59 left bundle branch). At 6 months, the mean reduction in left ventricular end-systolic volume (primary endpoint) was 34% in the biventricular group versus 35% in the conduction system pacing group (p < 0.01 for non-inferiority, p = 0.80 for superiority); LVEF increased by a mean of 14% and QRS duration shortened by a mean of 31 ms in both groups. There were no significant differences between groups in improvement in 6-minute walk distance, Minnesota Living with Heart Failure Questionnaire score, NYHA functional class, or NT-proBNP levels.

In the PRAGUE-26 trial, patients with intermediate-high-risk acute pulmonary embolism (haemodynamically stable, ≥1 point on the simplified PESI score, right ventricular dysfunction, elevated cardiac troponin or natriuretic peptide) were randomised to catheter-directed thrombolysis with alteplase plus anticoagulation (n = 280; thrombolysis group) or anticoagulation alone (n = 278; standard-care group). At 7 days, the primary composite endpoint (death from any cause, recurrent pulmonary embolism, cardiopulmonary decompensation, or collapse) occurred in 0.7% of the thrombolysis group and 6.8% of the standard-care group (RR 0.10, 95% CI 0.02–0.44; p < 0.001), with the difference driven mainly by lower rates of cardiopulmonary decompensation or collapse in the thrombolysis group. Clinically significant bleeding by BARC criteria occurred in 4.6% versus 5.0% (p = 0.85) in the thrombolysis and standard-care groups, respectively.

The next Congress of the European Society of Cardiology is planned to be held in Amsterdam (Netherlands) from 29 August to 1 September 2027.

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