INFECTION

Endocarditis: oral versus intravenous antibiotics

As recommended by the current guidelines, patients with infective endocarditis (IE) on the left side of the heart — an infection of the valves most commonly caused by bacteria — are typically treated with antibiotics administered intravenously in the hospital. The results of the POET trial presented at the 2018 ESC Congress and published simultaneously in the *New England Journal of Medicine* show that in stable patients with IE, a switch to oral antibiotics is noninferior to continued intravenous therapy. The implementation of oral antibiotic therapy could reduce long hospital stays and the associated physical and psychological burden on the patients.

The majority of complications associated with IE, including need for surgery and death, occur during the initial phase. After this critical phase, stable patients remain in the hospital to continue receiving intravenous antibiotics for up to 6 weeks. "We had some patients for whom this requirement was totally unacceptable and even considered it like a 'jail-sentence'," comments lead investigator Henning Bundgaard.

Looking into options to reduce the length of hospital stays, the investigators prescribed partial oral regimens to patients with IE and discharged them to outpatient treatment in a small pilot study. "The patients were extremely happy with this arrangement and the treatment was successful; this was the initial spark for the POET trial," explains Bundgaard. Only few observational studies had compared the use of oral versus intravenous antibiotics for IE; therefore, this randomized, noninferiority, multicentre trial was needed to evaluate the safety and efficacy of a switch in therapy.

A total of 400 patients with IE on the left side of the heart who were receiving treatment with intravenous antibiotics were randomly assigned to continue intravenous treatment or to switch to oral antibiotics. The primary outcome — a composite of all-cause mortality, unplanned surgery, embolic events, or relapse of bacteraemia, from randomization until 6 months after completion of the antibiotic treatment — occurred in 24 patients (12.1%) of the intravenously treated group and 18 patients (9%) of the orally treated group. With a between-group difference of 3.1% (95% CI −3.4 to 9.6, $P = 0.40$), partial oral therapy met the noninferiority criteria for the primary outcome. The incidence of adverse effects such as allergy was similar between the groups. These findings encouraged the investigators to implement partial oral antibiotic therapy for IE in several cardiology departments in Denmark.

Nevertheless, the trial has some limitations: only stable patients with IE on the left side of the heart caused by specific bacterial strains were enrolled in the trial, although the selected bacteria account for approximately 75% of all IE cases. "Unfortunately, there is not a strong tradition for conducting randomized trials on endocarditis," concedes Bundgaard, "but we hope this finding will be an important new topic in the next guidelines on clinical management of endocarditis," he concludes.

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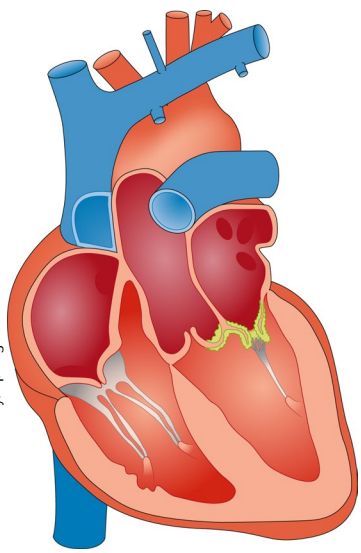

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ORIGINAL ARTICLE Iversen, K. et al. Partial oral versus intravenous antibiotic treatment of endocarditis. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1808312 (2018)

IN BRIEF

ANTICOAGULATION THERAPY

No benefit of rivaroxaban in HF with sinus rhythm

The COMMANDER HF trial, presented at the 2018 ESC Congress, was designed to test the hypothesis that rivaroxaban would be beneficial in patients with heart failure (HF) and coronary artery disease, but without atrial fibrillation, on the basis that thrombin-related pathways are activated in these individuals and predict a poor prognosis. A total of 5,022 patients were randomly assigned to low-dose rivaroxaban (2.5 mg) twice daily or placebo in addition to standard care after treatment for an episode of worsening HF. During follow-up (median 21.1 months), the rate of the primary efficacy end point (a composite of all-cause death, myocardial infarction, or stroke) was not significantly different between rivaroxaban and placebo (25.0% versus 26.2%; HR 0.94, 95% CI 0.84–1.05). Similarly, no significant difference was observed in the rate of the principal safety outcome (21.8% versus 22.1%; HR 0.80, 95% CI 0.43–1.49).

ORIGINAL ARTICLE Zannad, F. et al. Rivaroxaban in patients with heart failure, sinus rhythm, and coronary disease. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1808848 (2018)

THROMBOSIS

Rivaroxaban for prevention of VTE

Rivaroxaban given to medically ill patients after discharge from hospital does not reduce the risk of venous thromboembolism (VTE), according to data from the MARINER trial presented at the 2018 ESC Congress. A total of 12,024 patients who were at increased risk of VTE were randomly assigned at discharge from hospital to 10 mg of rivaroxaban once daily or placebo for 45 days. No significant difference in the rate of the primary efficacy end point (a composite of symptomatic VTE or death from VTE) was observed between rivaroxaban and placebo (0.83% versus 1.10%; HR 0.76, 95% CI 0.52–1.09). The rate of the principal safety outcome (major bleeding) was similar in the two groups (0.28% versus 0.15%; HR 1.88, 95% CI 0.84–4.23).

ORIGINAL ARTICLE Spyropoulos, A. C. et al. Rivaroxaban for thromboprophylaxis after hospitalization for medical illness. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1805090 (2018)

ACUTE CORONARY SYNDROMES

Early invasive assessment of NSTE-ACS

Very early invasive coronary angiography (ICA) does not improve clinical outcomes compared with ICA performed within 2–3 days in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS), according to the results of the VERDICT trial presented at the 2018 ESC Congress. A total of 2,147 patients who were admitted to hospital in Copenhagen, Denmark, with suspected NSTE-ACS were randomly assigned to ICA performed very early or according to standard care (a median of 4.7 h or 61.6 h after randomization, respectively). During follow-up (median 4.3 years), the rate of the primary end point (a composite of all-cause death, nonfatal recurrent myocardial infarction, or hospital admission for refractory myocardial ischaemia or heart failure) was not significantly different between the two groups (27.5% versus 29.5%; HR 0.92, 95% CI 0.78–1.08). However, in patients at the highest risk (GRACE score > 140), very early ICA improved the primary end point (HR 0.81, 95% CI 0.67–1.01, $P = 0.023$).

ORIGINAL ARTICLE Kofoed, K. F. et al. Early versus standard care invasive examination and treatment of patients with non-ST-segment elevation acute coronary syndrome: the VERDICT (Very EaRly vs Deferred Invasive evaluation using Computerized Tomography) – randomized controlled trial. *Circulation* https://doi.org/10.1161/CIRCULATIONAHA.118.037152 (2018)