除細動前の抗凝固薬による新たな治療選択肢 (Abstract 5715)

ENSURE-AF：AF除細動においてエドキサバンはワルファリンと同等に安全かつ有効である

ENSURE-AF: Edoxaban is as safe and effective as warfarin at AF cardioversion

除細動施行前に抗凝固療法が必要な心房細動（AF）患者は、エドキサバン-非ビタミンK拮抗経口抗凝固薬-による治療により恩恵をこうむる可能性がある。このENSURE-AFトライアルは2016年ESC Congressで発表され、同時に*Lancet* に掲載された。エドキサバンは、よく管理された最適なエノキサパリン／ワルファリン療法に比べ、大出血および血栓塞栓発症率が同等であった。この結果は経食道心エコー（TEE）ガイド下、抗凝固薬による前治療、および併存疾患によらず同等であった。実臨床レベルでは、今回のスタディの結果、新たにAFと診断された抗凝固療法非施行患者は、TEE不可または3週間前から治療ができない場合には、除細動のわずか2時間前にエドキサバンを開始すればよいことが示された。

Full Text

Patients with atrial fibrillation (AF) who need anticoagulation before undergoing cardioversion may benefit from treatment with edoxaban - a non-vitamin K antagonist (VKA) oral anticoagulant (NOAC), according to results of the ENSURE-AF trial.

Edoxaban is "an effective and safe alternative" to standard therapy, which uses VKAs, said investigator Andreas Goette, MD, from St. Vincenz-Hospital, Paderborn, Germany, who presented the Hot Line results at ESC Congress 2016, with simultaneous publication in The *Lancet*.

While VKA anticoagulation works well, it has a major limitation in that it requires regular monitoring and dose adjustment to ensure that patients reach anticoagulation targets, explained Prof Goette. This can sometimes delay cardioversion for several weeks.

"At a practical level, our study results show that newly diagnosed non-anticoagulated AF patients can start edoxaban as early as two hours prior to their cardioversion procedure if they have access to transoesophageal echocardiography (TEE) or 3 weeks prior without."

Edoxaban was previously shown to be safe and effective compared to standard VKA therapy (enoxaparin/warfarin) among patients with AF in the ENGAGE AF-TIMI 48 study, but the impact of electrical cardioversion was not systematically assessed in that study.

ENSURE-AF, the largest randomized clinical trial of anticoagulation for cardioversion in patients with AF, "provides the largest prospective trial data for a NOAC in this clinical setting," noted Prof Goette. "Results suggest that edoxaban is an effective and safe alternative to standard enoxaparin/warfarin, a VKA therapy."

The phase 3b study, involving 239 study sites in 19 countries in Europe and the United States, included 2,199 patients with documented non-valvular AF who were scheduled for electrical cardioversion after anticoagulation therapy.

A total of 1,095 patients were randomized to receive edoxaban, while the remaining 1,104 received enoxaparin/warfarin (dosing varied depending on patient characteristics).

Of these 988 (90.2%) and 966 (87.5%) patients, respectively, were cardioverted either electrically or spontaneously, some with the use of transoesophageal echocardiography (TEE).

The primary efficacy objective of this study was to compare the incidences of the composite endpoint of stroke, systemic embolic event (SEE), myocardial infarction (MI) and cardiovascular (CV) death between the two groups at day 28 (ITT analysis).

This endpoint occurred at a comparable rate in both groups: 0.5% patients in the edoxaban arm vs. 1.0% in the enoxaparin/warfarin arm (OR=0.46; 95% CI, 0.12–1.43)
The primary safety outcome was a composite endpoint of major and clinically relevant non-major (CRNM) bleeding events at 30 days.

This also occurred at a comparable rate 1.5%and 1.0% respectively (OR=1.48; 95% CI, 0.64–3.55).

In short, "edoxaban had similar rates of major bleeding and thromboembolism compared to well-managed, optimized enoxaparin/warfarin therapy. The results were similar whether TEE-guidance was used or not, whether patients had received prior anticoagulation or not, and in patients with a broad range of associated comorbidities."

The study was funded by Daiichi Sankyo. Professor Goette has served as a consultant for Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, and Pfizer, and a speaker for Astra Zeneca, Bayer, Berlin Chemie, Bristol-Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, Medtronic, Pfizer, and Sanofi-Aventis.

Conference News