リバーロキサバンを用いた前治療により除細動が早められる可能性がある（Presentation #4945）

X-VERT：電気的除細動を施行される患者において、リバーロキサバンを用いた経口抗凝固療法はビタミンK拮抗薬の安全な代替療法となり得る

X-VERT: Oral anticoagulation with rivaroxabon is safe alternative for patients undergoing elective cardioversion

心房細動（AF）を正常な心調律に服するために電気的除細動を施行される患者において、リバーロキサバンを用いた経口抗凝固療法はビタミンK拮抗薬（VKA）の安全な代替療法となり得る、との研究結果が2014年European Society of Cardiology Congressで発表された。X-VERTは、電気的（97.6%）または薬物的（2.4%）除細動を予定された患者1,504人を対象とした前向きランダム化トライアルである。全体で、1,002人の患者が経口リバーロキサバン20mgを1日1回内服する群に、そして502人がVKA（ワルファリンまたは他のVKAを医師の裁量で投与）を内服する群にランダムに割り付けられた。患者は早期（58%）または後期（42%）除細動を行う群のいずれかに割り付けられた。リバーロキサバンによる治療を受けた患者は、脳卒中または一過性脳虚血発作、末梢動脈塞栓、心筋梗塞、および心血管死から成る複合アウトカムのリスクがVKA治療群と同等であった。リバーロキサバンの実際的な利点はVKAで治療された患者と比較し除細動までの時間が短いことで示された。早期除細動群では、ランダム割り付けと除細動との間隔は両治療群で同等であった（中央値1日）が、後期群ではリバーロキサバンで治療された患者はVKA治療群よりも除細動待機期間が有意に短かった（中央値22日対30日、p<0.001）。

Full Text

Oral anticoagulant therapy with rivaroxaban is a safe alternative to Vitamin K antagonist (VKA) therapy in patients with atrial fibrillation who are undergoing elective cardioversion to restore a normal heart rhythm, according to results presented at ESC Congress 2014.

In addition, rivaroxaban may potentially have one important advantage over VKAs, the study suggests.

Findings from the X-VeRT (eXplore the efficacy and safety of once-daily oral riVaroxaban for the prevention of caRdiovascular events in patients with nonvalvular aTrial fibrillation scheduled for cardioversion) trial were presented in a congress Hot Line session.

"The practical advantage of rivaroxaban was demonstrated by the short time to cardioversion compared to patients treated with VKAs," said the study's co-principal investigator Riccardo Cappato, M.D., from the University of Milan, in Milan, Italy. However, since time to cardioversion was not a prespecified outcome of the study, this finding should be interpreted with caution, he added.

"While the use of VKAs before and after cardioversion to reduce the risk of clotting is the current standard of care, endorsed by guidelines from the ESC as well as the American Heart Association, American College of Cardiology, and Heart Rhythm Society, a major obstacle to this practice is that at least 3 weeks of treatment is required to achieve adequate anticoagulation," noted co-principal investigator Michael Ezekowitz M.D. , Ph.D., from the Sidney Kimmel Medical School at the Thomas Jefferson University in Philadelphia Pennsylvania.

The pharmacological characteristics of rivaroxaban are particularly useful in the setting of elective cardioversion because it has a rapid onset of action, within 2–4 hours, which can expedite cardioversion, he explained.

X-Vert is the first prospective, randomized trial to examine the safety and efficacy of rivaroxaban compared to VKA therapy in patients undergoing elective cardioversion for the treatment of atrial fibrillation.

It included 1 504 patients from 141 centers and 16 countries, who were scheduled to undergo either electrical (97.6%) or pharmacological (2.4%) cardioversion.

Overall, 1 002 patients were randomized to oral rivaroxaban 20 mg once daily and 502 patients to VKA (warfarin or another VKA at the investigator's discretion, based on local standard of care).

Using established guidelines, patients were assigned to either early (58%) or delayed (42%) cardioversion.

Cardioversion in the delayed group was allowed if at least 3 consecutive weeks of adequate anticoagulation was documented prior to cardioversion. VKA anticoagulation was considered adequate if the international normalized ratio (INR) was maintained in the range of 2.0–3.0 for that time period, while anticoagulation with rivaroxaban was considered adequate by drug compliance of at least 80% for that time period.

Cardioversion in the early group was performed within a target range of one to five days after normalized, while patients in the delayed cardioversion group had it performed between 21 and 25 days after normalized.

The study found that compared to patients taking a VKA, patients treated with rivaroxaban had a similar of risk of the primary composite outcome of stroke or transient ischemic attack, peripheral embolism, myocardial infarction, and cardiovascular death. This composite outcome occurred in 0.5% of the rivaroxaban group versus 1.02% of the VKA group, a difference that was not considered statistically significant.

In the early cardioversion group, the primary composite occurred in 0.71% of rivaroxaban-treated patients and 1.08% of VKA-treated patients, whereas in the delayed cardioversion group it occurred in 0.24% and 0.93% patients in the rivaroxaban and VKA groups, respectively.

"Although the study was not powered for statistical significance, the Steering Committee felt that a descriptive comparison of 1500 patients would give clinically meaningful information," explained Professor Cappato.

For the primary safety outcome of major bleeding, there was no difference between the rivaroxaban and VKA groups (0.61% vs. 0.80%, respectively; RR 0.76).

No clinically important differences in the overall cumulative incidence of adverse events and serious adverse events by treatment assignment or by cardioversion strategy were observed.

In the early cardioversion group, the time between normalized and cardioversion was similar in both treatment arms (median 1 day), but in the delayed group, patients treated with rivaroxaban had a significantly shorter wait for cardioversion compared to the VKA-treated patients (median 22 vs. 30 days, P < 0.001) "because of the inability to achieve adequate anticoagulation prior to cardioversion in the VKA group," noted Professor Cappato.

Professor Ezekowitz added that "X-VeRT illustrates the ease of using rivaroxaban in the setting of cardioversion by capitalizing on its rapid onset of action."

In conclusion, Professor Cappato noted "these data are preliminary; however, they offer the first evidence that oral rivaroxaban can be safely used as a possible alternative to VKA therapy for preventing thromboembolic events in patients undergoing elective cardioversion."

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Professor Cappato has received consultancy fees from Boston Scientific, Medtronic, St. Jude, Biosense Webster, ELA Sorin, Boehringer Ingelheim, Bayer HealthCare, and Abbott; Pfizer; speaker's bureau fees from Boston Scientific, Medtronic, St. Jude, Biosense Webster, BARD, sanofi-aventis, Boehringer Ingelheim, Bayer HealthCare, and Abbott; investigator fees from Medtronic, Biosense Webster sanofi-aventis, Cameron Health, BARD, Bayer HealthCare, Abbott, and Pfizer; grants from Boston Scientific, Medtronic, St. Jude, Biosense Webster, BARD, and ELA Sorin; and holds equity and intellectual property rights with Cameron Health.

The co-primary investigator, Dr. Michael Ezekowitz, is a consultant and speaker for Boehringer Ingelheim and a consultant for Pfizer, Sanofi-Aventis, Bristol-Myers Squibb, Portola, Bayer, Daichii Sankyo, Medtronic, Aegerion, Merck, Johnson & Johnson, Gilead, Janssen Scientific Affairs, Pozen Inc., and Coherex.

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