Cardioversione elettrica

Indicazioni, uso dei vecchi e nuovi anticoagulanti

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Disclosure

Speaker fee: Aspen, Astra Zeneca, BMS, Boehringer, Eli Lilly, Daichii Sankio, Bayer, Pfizer, Sanofi

Advisory board member: Eli Lilly, Astra Zeneca, Bayer, Boeheringer, Daiichi Sankyo, BMS, Pfizer, Sanofi

April 2012

Overview

Anticoagulants pericardioversion

Pathophysiological mechanisms

ESC guidelines

New drugs

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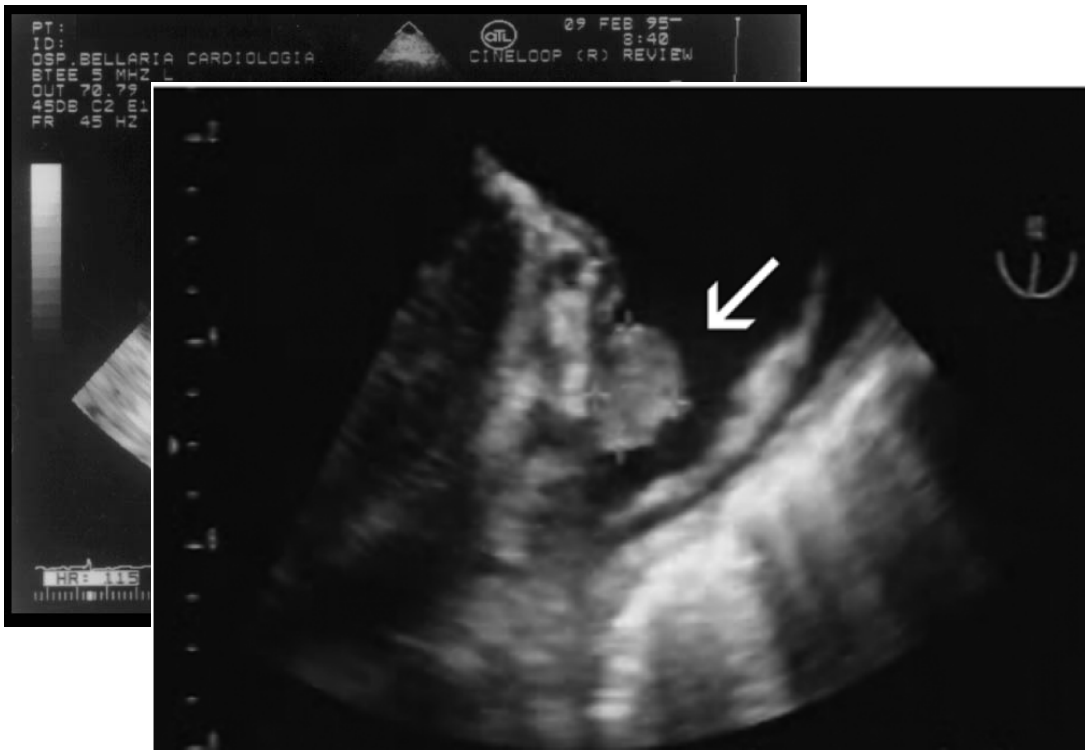

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Anticoagulants pericardioversion

Patients undergoing elective cardioversion recruited in 18 observational studies (n. 3271)

Patients	Stroke/SE
Patients receiving peri CV anticoagulants = 1221	0.3%
Patients not receiving anticoagulants = 2050	2%

RR 0.16 (95% CI, 0.05 – 0.48)

Moreyra E et al. Am Heart J 1995; 129: 71-5

Anticoagulants pericardioversion

The conventional duration of a minimum of 3 weeks therapeutic anticoagulation before cardioversion and a minimum 4 weeks afterward is based on indirect pathophysiologic data and evidence from observational studies and remains arbitrary. Observational

You JJ et al. CHEST 2012; 141(Suppl): e531S

sinus rhythm,[3] this should not be the
determining the duration of anticoagula
cision should involve careful evaluatic
bolic risk in each patient. Considerati
given to the duration of the arrhythmia
age, the presence or absence of structu
ease, and the existence of high-risk cond
a history of embolus, mitral stenosis, or
prosthetic valve. Patients in this latter
require long-term anticoagulation.

It is often stated that anticoagulation

92/4621 pazienti sottoposti a CVE arruolati in 32 studi osservazionali

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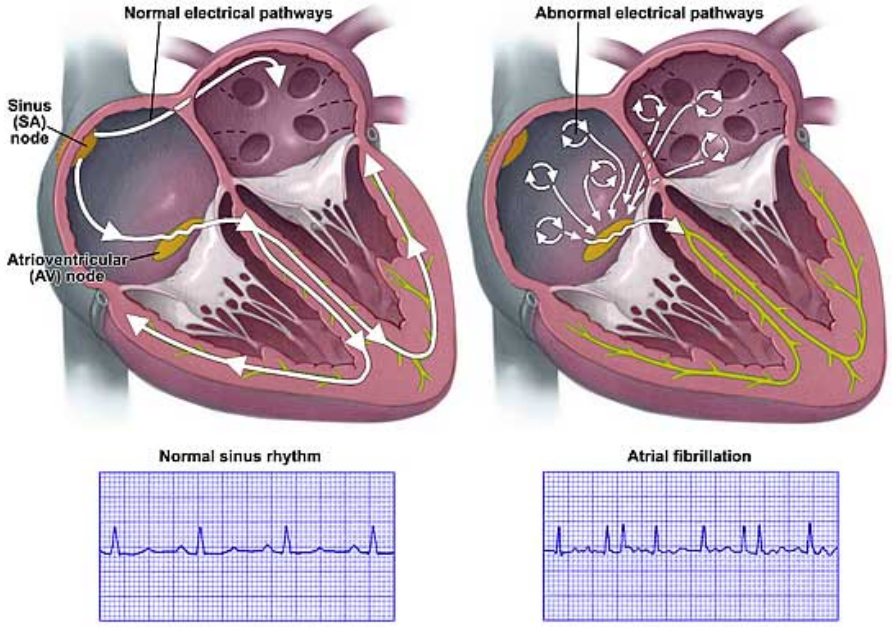
From AF to sinus rhythm.....



Atrial stunning: definition

" a transient depression of atrial and atrial-appendage mechanical function after successful cardioversion of atrial fibrillation, compared with pre-cardioversion state"

-It happens despite restoration of sinus rhythm
-It involves both left atrium and left atrial appendage

Kahn I A. Am Heart J 2003; 145: 787-794

Atrial stunning: characteristics

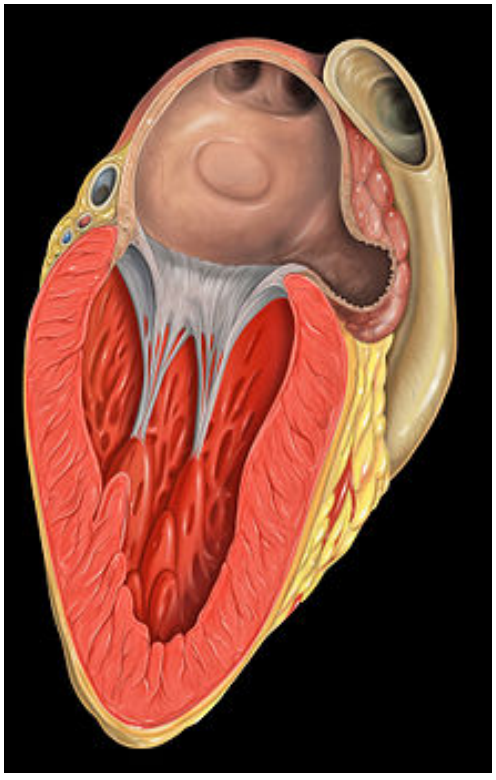
It can **be assessed** with a number of echocardiographic and Doppler scanning studies:

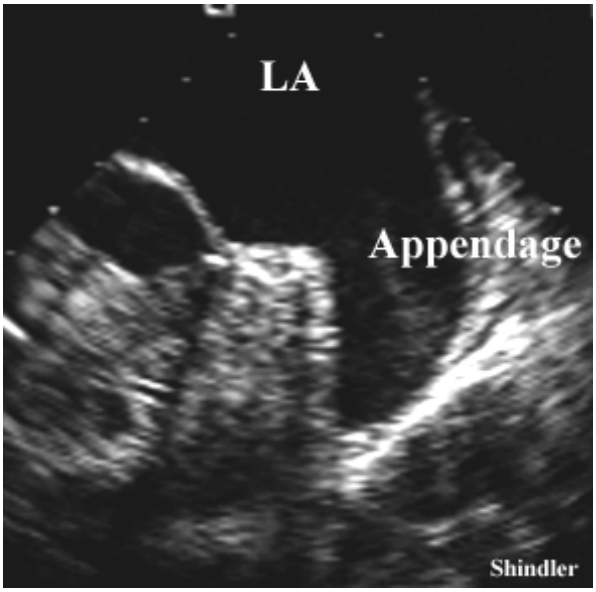
- spontaneous echocardiography contrast
- Transmural inflow velocity and time-velocity integral of A contraction (A-wave)
- Atrial contribution in the total mitral inflow (atrial filling fraction)
- LAA emptying and filling velocities

It can **be associated** with

- TT electrical cardioversion
- Pharmacological cardioversion
- Internal electrical cardioversion
- Spontaneous conversion

Kahn I A. Am Heart J 2003; 145: 787-794





Determinants of atrial stunning

LA and LAA spontaneous echocardiography contrast (new or more evident) → 80% post CV
LAA flow velocity reduction → 53% post CV

- **Duration of preceding AF**
- **Atrial size**
- **Underlying structural heart disease**

…….LA and LAA function improves progressively to the normal levels with time, when the SR is maintained!

Kahn I A. Am Heart J 2003; 145: 787-794

Cellular mechanisms of atrial stunning

AS results from the changes in atrial myocardium that take place during Afib, not at the time of conversion……..

- **Tachicardia-induced atrial cardiomyopathy**
- **Chronic atrial cytosolic calcium overload**
- **Atrial hybernation**
- **Atrial fibrosis**

…….depletion of sarcomere, accumulation of glycogen, changes in mytochondrial shape and size, fragmentation of sarcoplasmic reticulum, dispersion of nuclear cromatin……**fetal de-differentiation**!

Kahn I A. Am Heart J 2003; 145: 787-794

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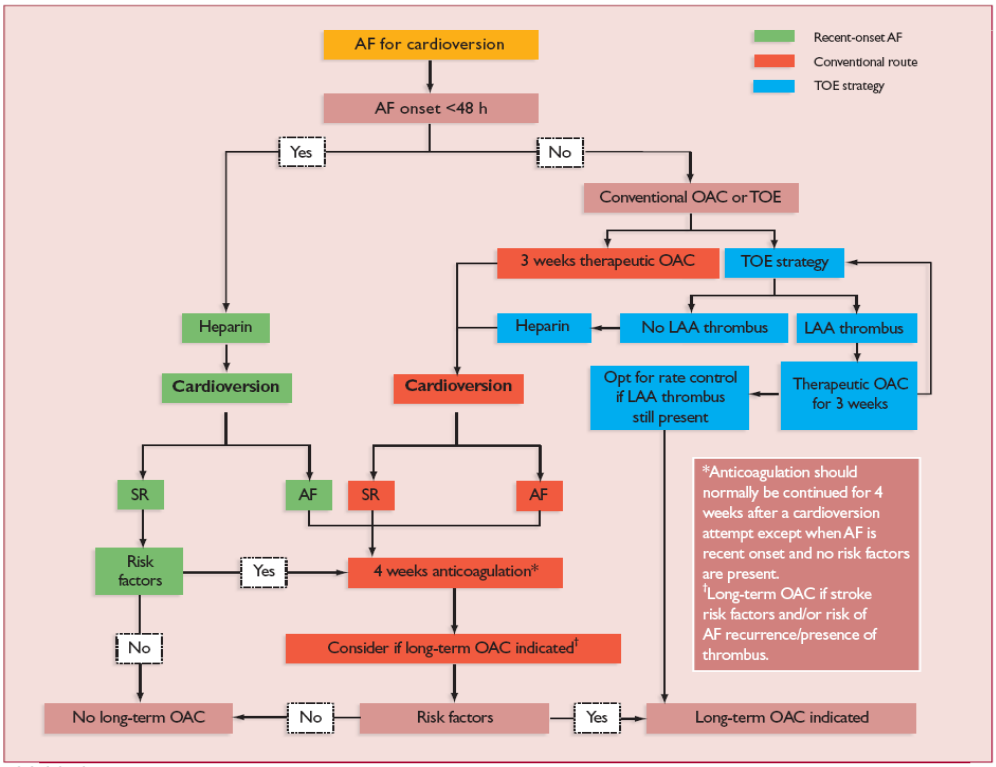
FA: ESC guidelines 2010



ESC 2010

April 2012

Anticoagulation – Peri-cardioversion

Recommendations for prevention of thromboembolism in non-valvular AF – peri-cardioversion

Recommendations	Class	Level
For patients with AF of ≥48 h duration, or when the duration of AF is unknown, OAC therapy (e.g. VKA with INR 2-3 or dabigatran) is recommended for ≥3 weeks prior to and for ≥4 weeks after cardioversion, regardless of the method (electrical or oral/i.v. pharmacological).	I	B
In patients with risk factors for stroke or AF recurrence, OAC therapy, whether with dose-adjusted VKA (INR 2-3) or a NOAC, should be continued lifelong irrespective of the apparent maintenance of sinus rhythm following cardioversion.	I	B

www.escardio.org/guidelines

European Heart Journal 2012;33:2719-2747 - doi:10.1093/eurheartj/ehs253

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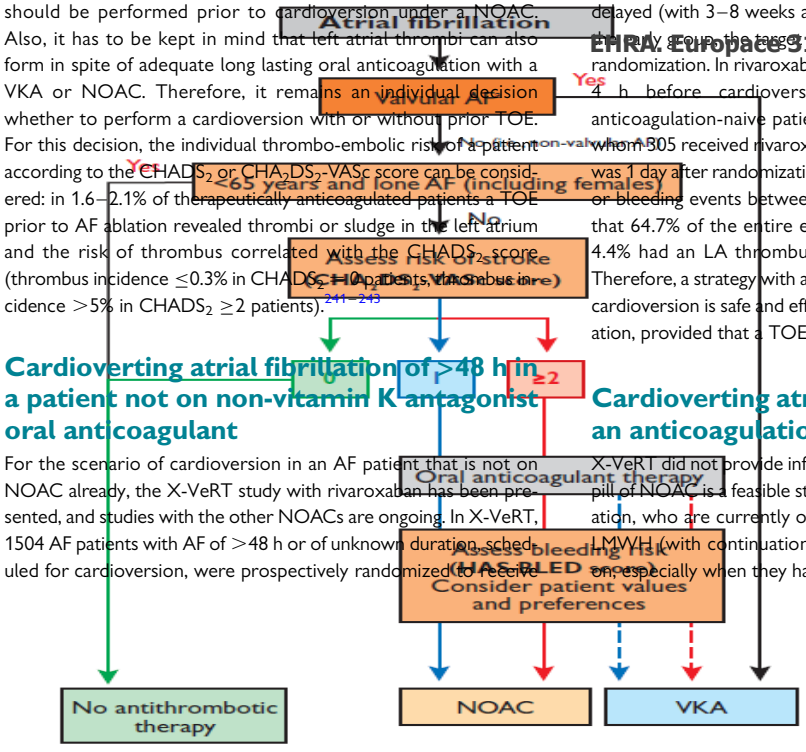
FA: ESC guidelines 2012

should be performed prior to cardioversion under a NOAC. Also, it has to be kept in mind that left atrial thrombi can also form in spite of adequate long lasting oral anticoagulation with a VKA or NOAC. Therefore, it remains an individual decision whether to perform a cardioversion with or without prior TOE. For this decision, the individual thrombo-embolic risk of a patient according to the $CHADS_2$ or CHA_2DS_2-VASc score can be considered: in 1.6–2.1% of therapeutically anticoagulated patients a TOE prior to AF ablation revealed thrombi or sludge in the left atrium and the risk of thrombus correlated with the $CHADS_2$ score (thrombus incidence ≤0.3% in $CHADS_2$ = 0 patients, vs. thrombus incidence >5% in $CHADS_2$ ≥2 patients).[241–243]



Cardioverting atrial fibrillation of >48 h in a patient not on non-vitamin K antagonist oral anticoagulant

For the scenario of cardioversion in an AF patient that is not on NOAC already, the X-VeRT study with rivaroxaban has been presented, and studies with the other NOACs are ongoing. In X-VeRT, 1504 AF patients with AF of >48 h or of unknown duration, scheduled for cardioversion, were prospectively randomized to receive

delayed (with 3–8 weeks anticoagulation before card

EHRA. Europace 31 August, 2015

early group, the target was to cardiovert within 1 randomization. In rivaroxaban patients, the drug was s 4 h before cardioversion. Four hundred an anticoagulation-naive patients entered the early str whom 505 received rivaroxaban. The median time to was 1 day after randomization. There was no differenc or bleeding events between anticoagulant or timing that 64.7% of the entire early group underwent TC 4.4% had an LA thrombus that precluded early c Therefore, a strategy with at least a single NOAC dose cardioversion is safe and effective in patients with AF ation, provided that a TOE is performed prior to car

Cardioverting atrial fibrillation of an anticoagulation-naive patient

X-VeRT did not provide information on whether intak pill of NOAC is a feasible strategy in patients with AF ation, who are currently often cardioverted after a s LMWH (with continuation of anticoagulation for ≥ on, especially when they have an elevated CHA2DS2

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RELY®
Study of stroke prevention in atrial fibrillation

Dabigatran versus warfarin in patients with atrial fibrillation: an analysis of patients undergoing cardioversion

This post hoc analysis aimed to determine the 30-day post-cardioversion stroke rates in patients treated with dabigatran etexilate compared with warfarin

Cardioverted patients during the 3-year study period and 30 day post-cardioversion stroke rates were analysed

Exclusion of left atrial thrombus using transoesophageal echocardiography (TEE) pre-cardioversion was encouraged but not mandatory

Circulation 2011; 123: 131

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Stroke and systemic embolism

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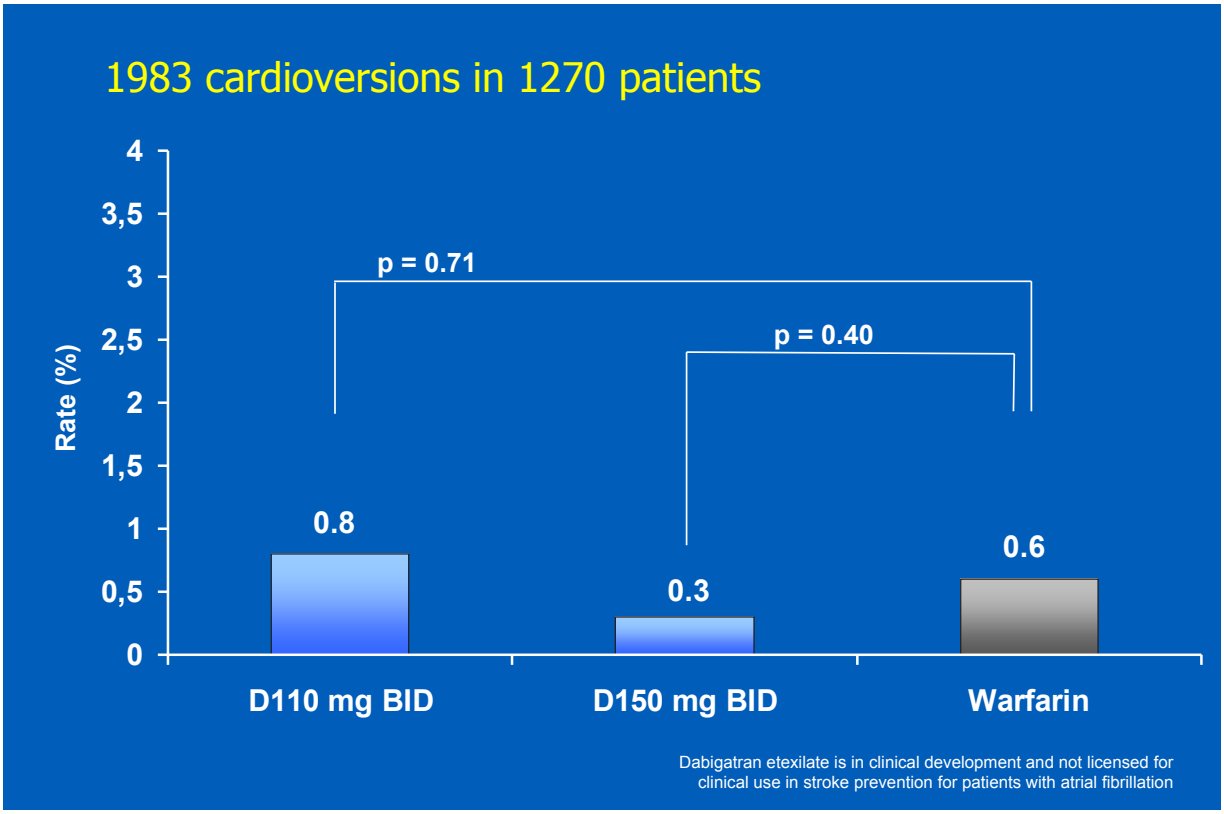
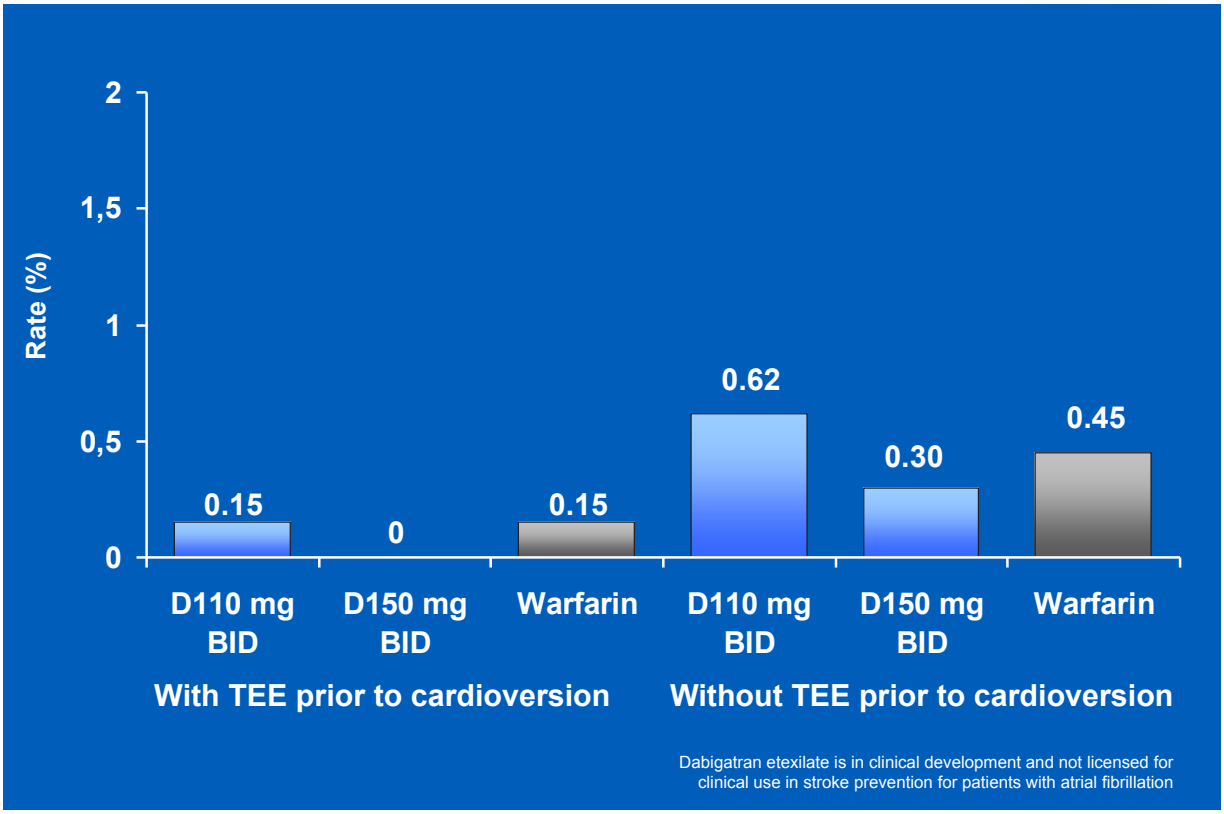
Study of stroke prevention in atrial fibrillation



Stroke and SE with/without TEE

RELY®
Study of stroke prevention in atrial fibrillation



Efficacy and Safety of Apixaban in Patients After Cardioversion for Atrial Fibrillation

Insights From the ARISTOTLE Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation)

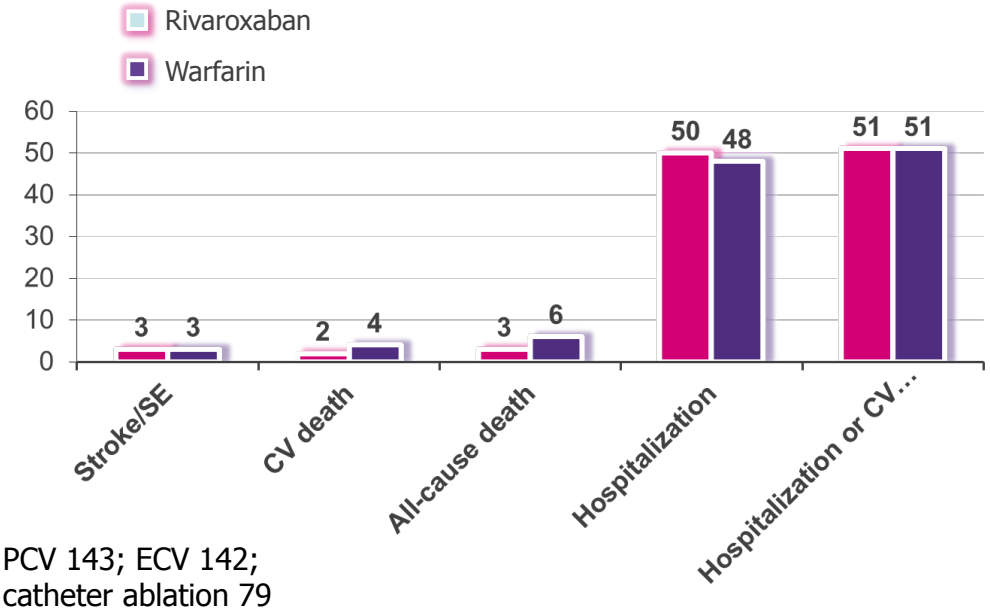
743 cardioversions in 540 patients

Table 2 Clinical Outcomes After Any Cardioversion, Within 30 Days, in Patients Assigned to Either Warfarin or Apixaban

Outcomes	Warfarin (n = 412)	Apixaban (n = 331)	Total (n = 743)
Stroke or systemic embolism	0	0	0
Myocardial infarction	1 (0.2)	1 (0.3)	2 (0.2)
Major bleeding	1 (0.2)	1 (0.3)	2 (0.2)
Death	2 (0.5)	2 (0.6)	4 (0.5)

JAAC 2014; 63: 1082

Patients undergoing PCV/ECV/ablation: the ROCKET AF trial

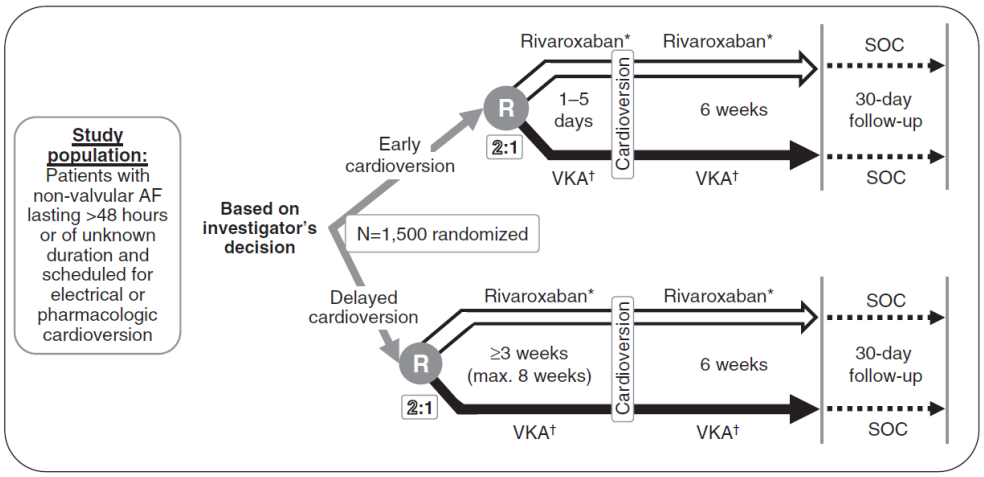


PCV 143; ECV 142; catheter ablation 79

Piccini JP JAAC 2013

X-VERT study design

Figure



X-VERT study design. *20 mg once daily (15 mg once daily if creatinine clearance 30-49 mL/min). †International normalized ratio 2.0 to 3.0. *R*, randomization; *SOC*, standard of care.

Ezekowitz MD et al. *Am Heart J* 2014;167:1998-2006

X-VeRT: primary efficacy endpoints

	Rivaroxaban (N=978)		VKA (N=492)		Risk ratio (95% CI)
	%	n*	%	n*	
Primary efficacy endpoint	**0.51**	**5**	**1.02**	**5**	**0.50 (0.15–1.73)**
Stroke	0.20	2	0.41	2	
Haemorrhagic stroke	0.20	2		0	
Ischaemic stroke		0	0.41	2	
TIA		0		0	
Non-CNS SE		0	0.20	1	
MI	0.10	1	0.20	1	
Cardiovascular death	0.41	4	0.41	2	

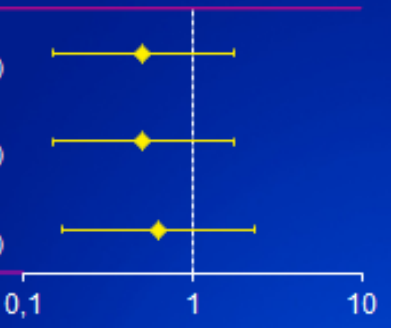
*Number of patients with events; patients may have experienced more than one primary efficacy event
mITT population

Cappato R et al. *Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

X-VeRT

X-VeRT: primary efficacy endpoint by population

	Rivaroxaban % n*/N	VKA % n*/N	Risk ratio (95% CI)
mITT population	0.51 5/978	1.02 5/492	0.50 (0.15–1.73)
ITT population	0.50 5/1002	1.00 5/502	0.50 (0.15–1.72)
Safety population (on-treatment)	0.51 5/988	0.80 4/499	0.63 (0.17–2.34)



- The trend in risk ratio in favour of rivaroxaban was consistent for all populations analysed

*Number of patients with events

Cappato R et al. *Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

X-VeRT

X-VeRT: primary safety endpoints

	Rivaroxaban (N=988)		VKA (N=499)		Risk ratio (95% CI)
	%	n*	%	n*	
Major bleeding	**0.61**	**6**	**0.80**	**4**	**0.76 (0.21–2.67)**
Fatal	0.1	1	0.4	2	
Critical-site bleeding	0.2	2	0.6	3	
Intracranial haemorrhage	0.2	2	0.2	1	
Hb decrease ≥2 g/dl	0.4	4	0.2	1	
Transfusion of ≥2 units of packed RBCs or whole blood	0.3	3	0.2	1	

*Number of patients with events; patients may have experienced more than one primary safety event
Safety population

Cappato R et al. *Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

X-VeRT

X-VeRT results: summary

- First completed prospective, randomized trial of a novel OAC in patients with AF undergoing elective cardioversion
- Low and similar incidence of primary efficacy endpoint events between the treatment arms
- Similar incidence of major bleeding
- Time to cardioversion was similar (early strategy) or significantly shorter (delayed strategy) using rivaroxaban compared with VKA

Cappato R et al. *Eur Heart J* 2014; doi: 10.1093/eurheartj/ehu367;
Cappato R. ESC Congress 2014. Oral presentation 4945

X-VeRT

Conclusions

- Cardioversion is associated with stroke/systemic embolism that usually occurs within the first 10 days
- Thrombus formation is favored by the "atrial stunning phenomenon", that occurs when sinus rhythm is achieved. It is related to many variables like the duration of AF, LA size, an underlying structural heart disease
- Oral anticoagulants are recommended 3 weeks before and 4 weeks after cardioversion (INR target 2.5, range 2-3)
- Dabigatran etexilate as well as apixaban and rivaroxaban may be safe alternatives to warfarin for stroke prevention in patients undergoing cardioversion and have been approved by EMA

April 2012