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Different safety profiles of oral anticoagulants in very elderly non-valvular atrial fibrillation patients. A retrospective propensity score matched cohort study

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Background

- NOACs have shown non-inferiority to warfarin for the prevention of stroke and systemic embolism, with marked reduction in the risk of intracerebral haemorrhage
- Although elderly patients (≥75 years of age) are well represented in phase III clinical trials (30– 40%), less is known of very elderly patients aged ≥80 years
- Aim of the present study was to evaluate the efficacy and safety of NOACs in comparison to well-managed VKAs in very elderly patients with NVAF living in an area well covered by anticoagulation clinics (Veneto Region).

Methods (1)

- Retrospective cohort study
- Two cohorts of patients: one assuming NOACs (rivaroxaban, dabigatran or apixaban), one assuming VKAs
- Demographics, comorbilities, concomitant therapies were recorded
- CHA_2DS_2VASc score and HAS-BLED score were calculated

Methods (2)

- Study endpoints were: ischaemic stroke, major bleeding, myocardial infarction and death from any cause.
- Major bleeding events were further classified as gastrointestinal (GI) bleeding (upper tract, lower tract or unspecified site of bleeding), genito-urinary haemorrhage, intracranial haemorrhage (ICH) or bleeding from other sources

Results (1)

- 15.136 patients (≥80 y) with NVAF (2882 assuming NOACs and 12,254 assuming VKAs). The distribution of patients receiving specific NOAC agents was 30%, 42% and 28% for dabigatran, rivaroxaban and apixaban, respectively.
- Significantly higher CHA_2DS_2-VASc and HASBED score in NOACs group (4.33 ± 1.31 vs. 4.06 ± 1.19 and 2.72 ± 0.90 vs. 2.54 ± 0.85 for NOACs versus VKAs, respectively).
- VKA patients showed higher prevalence of congestive heart failure or left ventricular dysfunction and abnormal renal function.
- Median follow-up was 14.7 months (IQR: 8.1–22.8).

Table 1
Baseline demographics and clinical characteristics of study subjects treated with NOAC or VKA before application of propensity score.

	NOACs ($n = 2882$)	VKAs ($n = 12,254$)	p-Value
Age class			
80–84 years	48,8%	55,1%	p < 0,001
≥ 85 years	51,2%	44,9%	
Gender			
Male	37,4%	40,9%	p < 0,001
Female	62,6%	59,1%	
Comorbidities			
Congestive heart failure	15,0%	17,0%	p = 0,009
Hypertension	81,0%	80,7%	p = 0,721
Ictus/TIA/Thromboembolism	26,7%	13,3%	p < 0,001
Myocardial Infarction	2,7%	2,9%	p = 0,619
Peripheral artery disease	1,8%	2,2%	p = 0,175
Diabetes	17,2%	18,3%	p = 0,170
Cancer	9,8%	9,7%	p = 0,835
Chronic renal disease	4,0%	6,2%	p < 0,001
Chronic liver disease	1,1%	0,9%	p = 0,285
History of bleeding	4,2%	2,7%	p < 0,001
Risk scores at baseline			
CHA_2DS_2VASc, mean ± SD	4,33 ± 1,31	4,06 ± 1,19	p < 0,001
2–3	27,8%	32,9%	p < 0,001
4–5	51,1%	55,1%	
≥6	21,0%	12,0%	
HASBED, mean ± SD	2,72 ± 0,90	2,54 ± 0,85	p < 0,001
Modifiable risk factors			
Hypertension	81,0%	80,7%	p = 0,721
Previous use of aspirin or clopidogrel	49.9%	41,0%	
Concomitant use of NSAID	17.5%	19,4%	p = 0.02

TIA: transient ischemic attack; VKA: vitamin K antagonist; NOAC: non-VKA oral anticoagulants; NSAID: Non-steroidal inflammatory drugs.

Results (2)

- The HR for stroke and major bleeding did not significantly differ among groups (HR 0.98; 95% CI 0.65–1.49 and HR 1.05; 95% CI 0.80–1.37, respectively).
- The risk of ICH was lower with NOACs than VKAs, although not reaching statistical significance (HR 0.66; 95% CI 0.40–1.07).
- The risk of GI bleeding was significantly higher with NOACs as compared with VKAs (HR of 1.73, 95% CI 1.17–2.56). This difference was mainly due to lower tract GI bleeding (HR 2.52, 95% CI 1.28–4.95).
- The risk of death was significantly lower in the NOACs cohort as compared to VKAs (HR of 0.87, 95% CI 0.77–0.99).

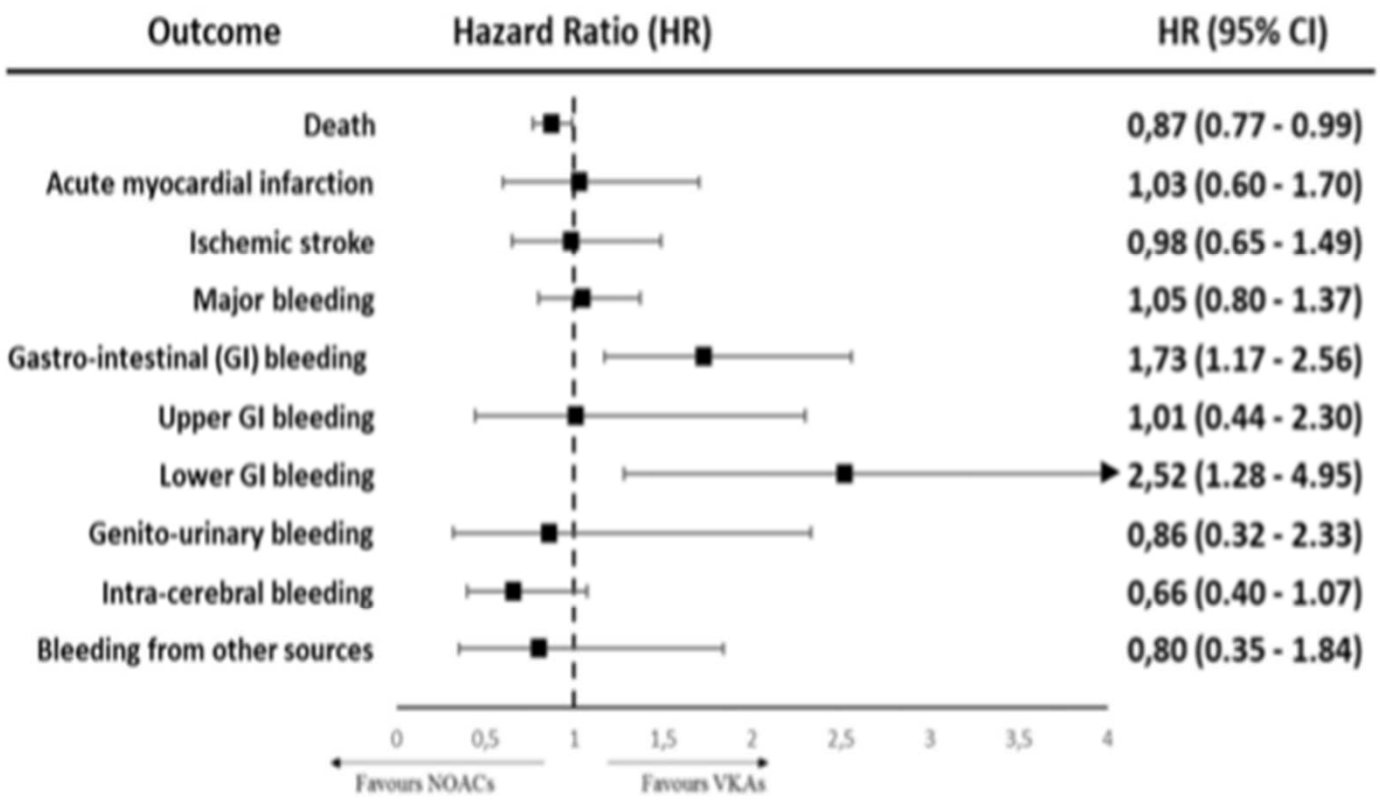

Fig. 2. Study endpoints in the *intention to treat* analysis.

Discussion

- Main result of this study is that NOACs maintained an equivalent effectiveness and safety (with a reduction in mortality rate) and a different pattern of bleeding complications compared to well-managed VKAs
- Compared to VKAs, very elderly patients treated with NOACs displayed a lower risk of intracranial bleeding and a higher risk of GI haemorrhage, especially in the lower tract
- The proposed mechanism to NOACs-related GI bleeding is the increased topical anticoagulant effect due to high concentration of active agent in the GI lumen

Conclusions

- In comparison to well-managed VKA therapy, NOACs in very elderly patients with NVAF reduce intracerebral haemorrhage and increase GI bleeding, mostly from the lower tract.
- Very elderly patients at high risk of GI bleeding (previous GI bleeding, peptic ulcer, diverticulitis, intestinal angiodysplasia, polyps, etc.) should be carefully monitored while on anticoagulation with NOACs.