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Effectiveness and safety of direct oral anticoagulants compared to vitamin-K antagonists: results from a cohort study* in the nationwide French claims and hospitalisation database (SNIIRAM)

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Background

- Direct oral anticoagulants (DOAC): dabigatran, rivaroxaban, apixaban.
- Better benefit-risk than vitamin-K antagonists (VKA) for nonvalvular atrial fibrillation (NVAF) in clinical trials.

Purpose

- To compare the 1-year risk of clinical outcomes for new users of dabigatran or rivaroxaban *versus* VKA in NVAF in real-life setting.

Methods

- **Design:** cohort study of new users of dabigatran, rivaroxaban, or VKA for NVAF in 2013 with 3-year history and 1-year follow-up in the 66 million persons French nationwide claims database (SNIIRAM).
- **Specific NVAF population:** patients with long-term disease or hospitalisation or procedure for atrial fibrillation without valvular disease history, and nor other probable indication.
- **Outcomes: during anticoagulant exposure (on treatment)**
  - Clinical events: hospital admission with main diagnosis of
    - Clinically relevant bleeding (CRB)
    - Arterial thrombotic event (ATE)
    - Acute coronary syndrome (ACS)
  - Death (all-cause)
  - Composite criterion: CRB, ATE, ACS and death.
- **Statistical analysis:**
  - Matched analysis 1:1 on gender, age, high-dimensional propensity score* (hdPS), and date of 1st drug dispensing.
  - 1-year cumulative incidence of outcomes using Kaplan-Meier estimate.
  - Comparison of risk using Cox proportional hazard risk model (death, composite) or Fine and Gray model (other events).

* Probability to be treated by dabigatran *versus* VKA, rivaroxaban *versus* VKA, using a logistic regression model with 500 variables including gender, age, stroke risk factors, bleeding risk factors

Results

- **Population:**
  - Of 371 539 new users of dabigatran, rivaroxaban, or VKA in 2013, **103 101** were included in the specific NVAF population: 27 060 dabigatran, 31 388 rivaroxaban, 44 653 VKA.
  - Patient characteristics showed differences between groups, and were normalized after matching (Tables 1 and 2).
  - For dabigatran *versus* VKA, **20 489 patients** were matched per arm, and **23 053** per arm for rivaroxaban *versus* VKA.

Table 1. Patient characteristics in all and matched specific NVAF populations: dabigatran versus VKA

	All patients		Matched patients		Standardized difference (%) Dabigatran *versus* VKA		
	Dabigatran n = 27 060	VKA n = 44 653	Dabigatran n = 20 489	VKA n = 20 489	Crude	Adjusted	Matched
Gender, %					-10.4	0.1	0.0
Male	56.4	51.2	54.5	54.5			
Age at index date (in years)					-40.8	-1.3	-0.2
Mean (± SD)	73.2 (11.8)	77.9 (11.1)	75.3 (10.7)	75.4 (10.7)			
CHA_2DS_2-VASc score ≥ 2, %	77.3	89.5	83.2	83.5			
HAS-BLED score ≥ 3, %	26.5	45.0	31.5	31.5			

Table 2. Patient characteristics in all and matched specific NVAF populations: rivaroxaban versus VKA

	All patients		Matched patients		Standardized difference (%) Rivaroxaban *versus* VKA		
	Rivaroxaban n = 31 388	VKA n = 44 653	Rivaroxaban n = 23 053	VKA n = 23 053	Crude	Adjusted	Matched
Gender, %					-10.1	0.2	0.0
Male	56.2	51.2	54.5	54.5			
Age at index date (in years)					-40.5	-1.6	0.0
Mean (± SD)	73.2 (11.8)	77.9 (11.1)	75.6 (10.7)	75.6 (10.7)			
CHA_2DS_2-VASc score ≥ 2, %	77.1	89.5	83.7	83.9			
HAS-BLED score ≥ 3, %	26.0	45.0	31.3	32.0			

Table 3. One-year cumulative incidence of outcomes in matched specific populations

	One-year cumulative incidence			
	Dabigatran n=20 489	VKA n=20 489	Rivaroxaban n=23 053	VKA n=23 053
Clinically relevant bleeding (CRB), %	2.5	4.4	3.8	4.5
Intracranial haemorrhage, %	0.1	0.7	0.5	0.7
Gastrointestinal bleeding, %	1.3	1.3	1.4	1.3
Arterial thrombotic event (ATE), %	1.6	2.2	2.0	2.1
Acute coronary syndrome (ACS), %	1.2	1.5	1.3	1.6
Death, %	4.9	6.9	5.6	7.3
Composite criterion (CRB, ATE, ACS, death), %	9.3	13.1	11.8	13.8

- **Cumulative incidence of outcomes:**
  - For dabigatran *versus* VKA, the 1-year cumulative incidence of the composite criterion was 9.3% for dabigatran and 13.1% for VKA. For rivaroxaban *versus* VKA, it was 11.6% and 13.8%, respectively.
  - Death was the most frequent event (Table 3).
- **Effectiveness and safety:**
  - For dabigatran *versus* VKA, the risk of all outcomes (ATE, CRB, ACS, death, composite) was significantly lower with dabigatran (Figure 1).
  - For rivaroxaban *versus* VKA, the risk of CRB, death, and composite was significantly lower with rivaroxaban. The risk of ATE was no different between groups, and the risk of ACS was at the significant threshold (Figure 1).

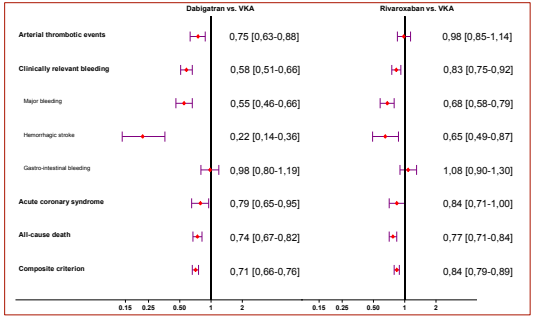

Figure 1. Hazard ratios with 95% CI, dabigatran versus VKA and rivaroxaban versus VKA in matched specific populations

Conclusions

- Different DOAC and VKA prescription patterns, but similar populations after matching.
- Death was the most frequent outcome.
- Better benefit-risk of DOAC *versus* VKA in NVAF:
  - including death and intracranial bleeding
  - without increased risk of gastro-intestinal bleeding.

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