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Risk factors for the primary effectiveness endpoint in secondary prevention of acute coronary syndrome with antiplatelet agents: a cohort* in the nationwide French claims and hospitalisation database

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Background

- The French HTA agency requested a real-life benefit-risk evaluation of ticagrelor compared with clopidogrel and prasugrel in the secondary prevention of acute coronary syndrome (ACS) (EUPAS5987).

Purpose

- **Main objective of the study:** to compare the 1-year incidence of the primary effectiveness endpoint for patients with antiplatelet agent (APA) after an ACS (ticagrelor *vs.* clopidogrel, and ticagrelor *vs.* prasugrel).
- **Objective of this analysis:** to identify risk factors associated with the primary effectiveness endpoint.

Methods

- **Design:** historical cohort of patients hospitalised in 2013 for ACS (STEMI, NSTEMI or unstable angina) with intensive care unit (ICU) stay identified and followed for one year in the French nationwide claims database (*Système National des Données de Santé:* SNDS).
- **Data source:** the SNDS contains individual anonymized information on medical and paramedical care and drugs claims, hospital admissions and death from 66 million persons.
- **APA treatment group:** ticagrelor, clopidogrel or prasugrel ± aspirin
  First APA dispensed within the month after discharge from the first hospitalisation for ACS.
- **Primary effectiveness endpoint:** on APA treatment
  Composite of the first event among hospital admission (primary diagnosis) for ACS with ICU stay, stroke, or death (all-cause).
- **Statistical analysis:**
  - Incidence rate of the composite in person-years (PY)
  - Hazard ratios of risk factors using Cox proportional hazard risk model (multivariate analysis).

Results

- **Population:**
  - Among 76,844 patients hospitalised for ACS with an ICU stay in 2013: 41,954 were included in the study population: 19,796 on clopidogrel, 13,916 on ticagrelor, and 8,242 on prasugrel.
  - Patient characteristics showed differences between groups (Table 1).

Results

Table 1. Baseline characteristics of patients according to first APA treatment

	Clopidogrel n = 19,796	Ticagrelor n = 13,916	Prasugrel n = 8,242
Gender male, %	67.6	76.2	85.6
Mean age, years (± SD)	71.5 (13.1)	63.4 (12.7)	58.1 (10.0)
Primary diagnosis of the index ACS hospitalisation, %			
Unstable angina	41.1	27.1	18.7
STEMI	41.6	54.9	72.4
NSTEMI	17.3	18.0	8.9
Procedures performed (index ACS), %			
Percutaneous coronary intervention	70.3	88.8	93.9
Coronary artery by-pass grafting	0.8	0.1	0.0
Charlson comorbidity index, %			
[0-1]	2.8	3.0	3.7
[2-3]	15.9	40.9	31.3
[4-5]	27.4	35.4	34.3
[6-7]	28.7	15.4	20.7
>7	25.2	5.4	10.7
Risk factors in the previous year,%			
Diabetes mellitus	27.1	20.2	20.7
Hypertension	28.1	14.1	11.5
Coronary artery disease	22.1	12.3	10.9
Acute coronary syndrome	11.0	6.7	5.4
Peripheral arterial disease	8.4	3.7	2.9
Congestive heart failure	8.0	2.6	1.9
Ischemic or undefined stroke	3.5	1.4	0.7
Major bleeding	2.8	1.2	1.0

- The **crude incidence** for the composite of ACS with ICU stay, stroke or death per 100 PY was 14.2 (95% CI [13.6-14.7]) for clopidogrel, 7.1 [6.6-7.6] for ticagrelor, and 5.5 [5.0-6.1] for prasugrel.
- **Risk factors for the primary effectiveness endpoint** associated with a significant increased risk by (Table 2):
  - At least 50%: a Charlson comorbidity index >5;
  - By 20%-50%: age ≥75 years, a poverty index, ICU stay duration >5 days and no PCI during index hospitalisation, and congestive heart failure, peripheral arterial disease, ischemic stroke, abnormal renal function, clopidogrel and prasugrel before index hospitalisation;
  - By 10%-20%: diabetes, hypertension, aspirin before index hospitalisation, and clopidogrel in the month after discharge (vs. ticagrelor).
- **Risk factors for the primary effectiveness endpoint** not associated with a significant increased or decreased risk (data not shown): prasugrel in the month after discharge, female gender, primary diagnosis, duration, and category hospital for index hospitalisation, incident ACS/naïve APA, aspirin, ticagrelor, coronary artery disease, ACS, hospitalised bleeding, cancer, COPD and abnormal liver function before index hospitalisation,

Table 2. Cox proportional hazards for the primary effectiveness endpoint in the total population, n=41,954 (multivariate analysis)

	HR [95% CI]	
Charlson comorbidity index (in categories) (vs. [0-1])		
[2-3]	1.08	[0.80-1.44]
[4-5]	1.15	[0.85-1.56]
[6-7]	1.53	[1.11-2.11]
>7	2.06	[1.47-2.89]
Age (in years) at index hospitalisation (in categories) (vs. [18-60[)		
[60-65[	0.98	[0.84-1.14]
[65-70[	1.15	[0.99-1.34]
[70-75[	1.12	[0.95-1.32]
[75-80[	1.22	[1.04-1.43]
≥ 80	1.41	[1.21-1.66]
Poverty index	1.45	[1.23-1.71
ICU stay duration (in days) during index hospitalisation (in categories) (vs. [1-3])		
[4-5]	1.05	[0.87-1.27]
[6-7]	1.27	[1.03-1.57]
> 7	1.22	[1.01-1.48]
No percutaneous coronary intervention (PCI) during index hospitalisation	1.47	[1.35-1.59]
Cardiac risk factors before index hospitalisation		
Congestive heart failure	1.37	[1.22-1.55]
Peripheral arterial disease	1.23	[1.10-1.38]
Stroke	1.22	[1.04-1.44]
Diabetes	1.17	[1.07-1.28]
Hypertension	1.15	[1.05-1.25]
Abnormal renal function before index hospitalisation	1.30	[1.14-1.48]
Clopidogrel before index hospitalisation	1.28	[1.11-1.47]
Clopidogrel in the month after discharge (vs. ticagrelor)	1.19	[1.08-1.30]
Prasugrel before index hospitalisation	1.47	[1.12-1.92]
Aspirin before index hospitalisation	1.14	[1.05-1.23]

Conclusions

This cohort study in the nationwide French claims database showed:

- Patients treated by clopidogrel, ticagrelor, or prasugrel (± aspirin) after an ACS were very different.
- A Charlson comorbidity index >5 was the risk factor most associated with an increased risk of the primary effectiveness endpoint.

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