Should dual antiplatelet therapy be maintained beyond one year after a myocardial infarction? A cohort study within the French SNDS nationwide claims database

P. Blin[1], N. Danchin[2], J. Bénichou[3], C. Dureau-Pournin[1], E. Guiard[1], D. Sakr[1], J. Jové[1], R. Lassalle[1], C. Droz-Perroteau[1], N. Moore[1,4]

[1]Bordeaux PharmacoEpi, INSERM CIC1401, Univ. Bordeaux, Bordeaux, France – [2]Hôpital Européen Georges Pompidou, Paris, France – [3]CHU Rouen, Rouen, France – [4]Bordeaux University Hospital, Bordeaux, France

This study was funded by the Ministry of Health (PHRCN-18-0745) . It was designed, conducted, and analysed by the Bordeaux PharmacoEpi of the Bordeaux University. It was overseen by independent experts.

Purpose

- Dual antiplatelet therapy (DAPT), aspirin plus a P2Y12-i (clopidogrel, prasugrel or ticagrelor), is recommended for one year after myocardial infarction (MI) for secondary prevention of cardiovascular disease (SP-CVD). Beyond one year maintaining DAPT is controversial.
- The main objective was to compare the 3-year risk of a composite of MI, ischemic stroke (IS)[a], major bleeding (MB) and death between DAPT and single antiplatelet therapy with aspirin (SAPT) beyond one year after MI.

Methods

- **Design:** Cohort study in the French nationwide claims database (SNDS, 99% of the 67 million people).
- **Data source:** The SNDS contains individual pseudonymised information from birth to death and includes outpatient and inpatient information (drug dispensing, hospital discharge summaries, date of death...).
- **Study population:** All adults hospitalized in 2013 or 2014 for acute MI (trigger event) with intensive care unit stay, surviving at least one year without MI or MB, and with a DAPT medication possession ratio (MPR) ≥ 80%, and followed for 3 years after index date (i.e. 365 days after the MI trigger event), except right-censored observations for those who died or discontinued aspirin, with a 60-day grace period.
- **Outcomes (main diagnosis):** primary composite criterion (all-cause death, MI, IS or MB[b]), secondary composite criterion (all-cause death, MI or IS), and individual composite outcomes.
- **Data Analyses:**
  - 3-year cumulative incidence of outcomes using Kaplan-Meier estimate (death, composite) or cumulative incidence function (CIF, other outcomes) to take into account death as competing risk;
  - Association between outcomes and DAPT-SAPT exposure using Cox proportional hazards model (death, composite) and Fine and Gray models (non fatal outcomes) to compare DAPT versus SAPT as time-dependent exposure, adjusted i) for age, gender, exposure to specific treatments (time dependent variables) and ii) for a high-dimensional disease risk score (hdDRS) exposure to specific treatments (time dependent variables). Specific treatments are SP-CVD drugs, oral antidiabetics, insulin, anticoagulants, NSAIDs, corticoids and proton pump inhibitors. Selection of variables for the hdDRS was performed using a combination of Principal Component Analysis and LASSO regression.

[a]Including undefined stroke; [b] Intracranial bleeding, upper gastrointestinal bleeding, other major bleeding or transfusions unrelated to a hospital diagnosis of major bleeding (ICD-10 codes)

Results

- **Main characteristics of population (Table 1):** From the 105,080 adults hospitalised in intensive care units for acute MI in 2013 or 2014, 53,399 were included in the cohort with a mean follow-up of 2,8 years (i.e. 149,301 person-years). The most common reasons for non-inclusion were death (n=12,012) and DAPT MPR < 80% (n=25,000).

Table 1. Main characteristics of the study population

During the 1-year event-free period post trigger MI	Total n = 53,399	
Male, %	74.6	
Median age (years)	64.0	
STEMI (trigger MI), n (%)	42,275	(79.2)
Specific comorbidities, n (%)		
Diabete mellitus	11,632	(21.8)
Congestive heart failure	5,046	(9.4)
Peripheral arterial disease	2,974	(5.6)
Charlson score ≤ 1, n (%)	36,901	(69.1)
≥ 1 PCI during trigger hospitalization, n (%)	43,478	(81.4)
DAPT score <2, n (%)	38,553	(72.2)
P2Y12 inhibitor dispensing, n (%)		
Clopidogrel	22,169	(41.5)
Prasugrel	13,974	(26.2)
Ticagrelor	21,921	(41.1)

- **DAPT and SAPT ASA (Acetyl-salicylic acid, Aspirin) exposure**

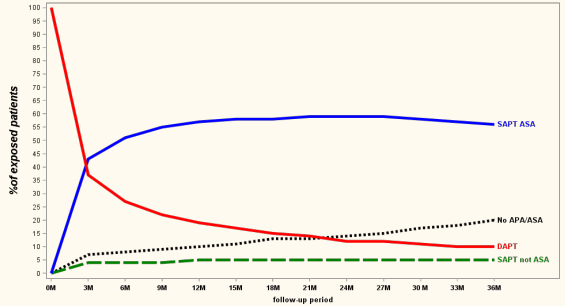
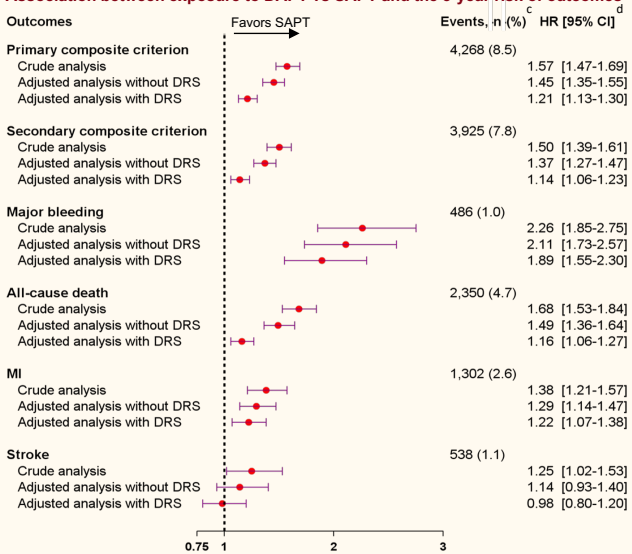


Figure 1. DAPT and SAPT ASA exposure proportion for the 3-year follow-up

- **Association between exposure to DAPT vs SAPT and the 3-year risk of outcomes**



[c](%): 3-year cumulative incidence of outcomes, [d]HR: Hazard Ratio, CI : Confidence Interval

Figure 2. Forest plot of association between DAPT-SAPT exposure and 3-year risk of outcomes

Conclusions

In this nationwide real-life population-based French study, DAPT maintained beyond one year after MI is significantly associated with increased harm compared to SAPT with increased risks of 21% (95% CI [13-30]) for the composite of MI, IS, MB and death (net clinical benefit), 22% [7-38] for MI, 89% [55-130] for MB, 16% [6-27] for death, and no difference for IS.

ESC Congress – 26 – 29 August, 2022, Barcelona
Abstract #82491