Real world risk of major outcomes for type 2 diabetes with stable coronary artery disease without prior MI or stroke and THEMIS-like patients using the SNDS French nationwide claims database

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Aims

The THEMIS randomized trial showed a lower incidence of ischemic cardiovascular events but a higher incidence of major bleeding in ticagrelor plus aspirin group than in placebo plus aspirin group in patients with stable coronary artery disease and type 2 diabetes (CAD-T2DM) without prior myocardial infarction (MI) or stroke (Steg et al, NEJM 2019).

The objective was to estimate the incidence of major outcomes for patients with CAD-T2DM, without history of MI-stroke and, more specifically, for THEMIS-like patients in a real world setting.

Methods

Study design
Cohort study in the French nationwide claims database (SNDS, 86% of the 66 million people).

Data source
The SNDS database contains individual pseudonymised information from 66 million persons on:
- Gender, date of birth, area of residence, date of death;
- Long-term disease registration with associated ICD-10 codes for full insurance coverage (with start and end dates);
- Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs;
- Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the date and duration of hospitalisation, medical procedures.

Study populations
- CAD-T2DM population without prior MI-stroke: all CAD-T2DM prevalent patients without MI-stroke within the 5-year history period identified on 1st January 2014, and followed for 2 years or until death in the database.
- THEMIS-like population: all patients of the previous population with specific criteria (≥ 50 years at index date, without renal failure with dialysis, cirrhosis/liver cancer history, intracranial/gastro-intestinal bleeding for the last 6 months, or anticoagulant/antiplatelet agent 2 months around index date).

Outcomes (primary diagnosis)
- Ischemic or unknown stroke;
- MI;
- Heart failure;
- Major bleeding* (associated diagnosis also considered) including Intracranial bleeding, haemorrhagic stroke, other critical organ or site bleeding, other bleeding, fatal bleeding;
- All-cause death;
- Composite criterion: first event among stroke, MI, or death.

Data analysis
- Estimate of the prevalence proportion on 01/01/2014 with gender and 5-year age classes standardisation according to national INSEE and European (Eurostat) statistics;
- Two-year cumulative incidence/probability of outcomes using Kaplan-Meier estimate (death, composite) or cumulative incidence function (CIF, other outcomes) to take into account death as competing risk.

This study was funded by an unrestricted grant from AstraZeneca. It was designed, conducted, and analysed independently by the Bordeaux PharmacoEpi of the Bordeaux University. It was overseen by independent experts.

Results

Main characteristics of populations: 258 260 patients in the CAD-T2DM population without prior MI-stroke and 64 334 in the THEMIS-like population were included, and presented similar main characteristics (Table 1).

French and European prevalence (Table 2)
- The THEMIS-like prevalence was estimated to be 1.53% French adults, representing about a quarter of CAD-T2DM patients without prior MI-stroke.
- The prevalence was higher for men and increased with age in both populations.
- This results was close to those found in the European population (1.50%).

Two-year cumulative incidence / probability of outcomes (Figures 1 and 2)
For all patients, according to age, the two-year cumulative incidence/probability was:
- Little higher for the CAD-T2DM population without prior MI-stroke than THEMIS-like population for ischemic or unknown stroke (1.7% vs. 5.5%) and MI (1.7% vs. 1.3%).
- Clearly higher for the CAD-T2DM population without prior MI-stroke than THEMIS-like population for heart failure (9.5% vs. 5.3%), major organ specific bleeding (4.9% vs. 3.2%), all-cause death (13.6% vs. 9.7%), and the composite event (16.2% vs. 12.0%).

Conclusions

- In current French practice, the median age of the THEMIS-like population was 6 years older than in the THEMIS trial (i.e. 72 vs 66 years).
- The incidences observed in real world setting for THEMIS-like population after 2 years of follow-up were about double for the composite outcome (i.e. 12.0 vs 6.2%), triple for deaths (i.e. 9.7 vs 3.2%) and quadruple for major bleeding compared to TIMI major bleeding (i.e. 3.2% vs 0.8%) than those of the placebo arm of the THEMIS trial.

Table 1. Main characteristics of the study populations at index date

<table>
<thead>
<tr>
<th>CAD-T2DM population without prior MI-stroke</th>
<th>THEMIS-like population</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 258 260</td>
<td>n = 64 334</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>178 407 (78.3)</td>
</tr>
<tr>
<td>Median age (in years)</td>
<td>73.0</td>
</tr>
<tr>
<td>&gt; 4 years of both CAD and T2DM diagnoses</td>
<td>67 040 (25.0)</td>
</tr>
<tr>
<td>history, n (%)</td>
<td></td>
</tr>
<tr>
<td>History of hypertension, n (%)</td>
<td>204 943 (79.4)</td>
</tr>
<tr>
<td>History of diabetics, n (%)</td>
<td>101 419 (39.3)</td>
</tr>
</tbody>
</table>

Table 2. Estimated 2014 Prevalence of study populations for French and European* adult populations

<table>
<thead>
<tr>
<th>CAD-T2DM population without prior MI-stroke</th>
<th>THEMIS-like population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n (%)</td>
<td>204 943 (79.4)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>53 317 (20.6)</td>
</tr>
<tr>
<td>All, n (%)</td>
<td>258 260 (100.0)</td>
</tr>
</tbody>
</table>

*standardized to 2014 EU population

Figure 1. Cumulative incidence/probability of outcomes during two years of follow-up

Figure 2. Cumulative incidence/probability of outcomes at two years of follow-up (%)