Impact of medication adherence on mortality and cardiovascular morbidity: a population-based cohort study. IMPACT study

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1. Background (1)

The incidence of cardiovascular disease has decreased over the last four decades:

- population-level **lifestyle changes**.
- development of **effective interventions** to treat individuals.

Adherence to prescribed medication is poor for long-term drug treatment.
1. Background (2)

1.3 **Drug therapy**

1.3.1 Offer all people who have had an acute MI treatment with the following drugs:

- ACE (angiotensin-converting enzyme) inhibitor
- dual antiplatelet therapy (aspirin plus a second antiplatelet agent)
- beta-blocker
- statin. [2007, amended 2013]
2. Justification & Hypothesis (1)

Justification

• Due to the **improvement of morbidity and mortality found with the quadruple drug therapy (antiplatelet, beta-blocker, ACEI or ARB and statin)** in patients with established CVD.

• It is necessary **to assess the long-term adherence to these drugs in our population and its relationship with cardiovascular events and mortality.**

2. Justification & Hypothesis (2)

Hypothesis

The patients with established CHD who adhere to drug therapy with the four recommended pharmacological groups have a lower risk of major adverse cardiac events and all-cause mortality compared with patients who do not adhere to drug therapy.
3. Objectives (1)

Main Objective

To assess the relationship between adherences to the four pharmacological groups recommended for secondary prevention and the clinical outcomes of cardiovascular morbidity and mortality in patients with established CHD.

The outcomes which are included as components of the composite endpoint are: all-cause mortality, ACS, and ischaemic stroke.
3. Objectives (2)

Secondary Objectives

1) To assess the incidence of the **composite endpoint** in patients who are adherent to treatment with **all four drugs compared** with patients who are adherent to **any combination of three, two or one drug, or no drug.**

2) To assess the relationship between baseline **socio-demographic and clinical characteristics** and **adherence** to drug therapy.

3) To compare the number of **days on sickness leave** due to any cause according to **adherence** to drug therapy.

4) To estimate **prevalence of use** of the four drug treatments.

5) To describe the **posology prescribed** for the four drugs.
4. Methods (1)
Design, period, population and data sources

**Design:** Population-based cohort study.

**Period:** 2009-2016.

**Population:** Individuals ≥ 18 years with an incident diagnosis of Acute Coronary Syndrome (AMI or unstable angina) admitted in hospital of Catalan Health Institute.

**Data sources:** SIDIAP

**SIDIAP:** contains anonymized clinical information of all 279 PHC centres managed by the ICS, covering about 80% of the population in Catalonia (5.8 million patients) The information is registered by professional heaths in ECAP (electronic health records): comprehensive socio-demographic information, health conditions registered as ICD10 codes, clinical parameters, toxic habits, laboratory test results, GPs prescriptions and their corresponding pharmacy invoice data registered.
4. Methods (2)
Variables

- Exposure definition:
  - Patients exposed: if they are prescribed any of study drug after the episode ACS (up to two months after the event).

- Primary outcome variable:
  - Incidence of major adverse cardiac events

- Adherence definitive:
  - PDC (proportion of days covered) = MPR (medication possession ratio).
4. Methods (3)

MPR (medication possession ratio):

\[
\text{MPR} = \frac{\text{30 Day refills} \times 5 \text{ times}}{\text{January 1 through May 19} \text{ (30 days)} = 187 \text{ Days}} = 80\%
\]

Days supply of the last refill is added to estimate expiration of supply.

**Adherent Patient** > if MPR ≥ 80% or ≥ 75%

[https://rxoutcomesadviser.files.wordpress.com/2011/03/mpr-example.gif](https://rxoutcomesadviser.files.wordpress.com/2011/03/mpr-example.gif)
4. Methods (4)
Statistical analysis

• Demographic and baseline characteristics:

  ß Categorical variables: frequencies and percentages.

  ß Continuous variables: mean (standard deviation) or median (interquartile range).

• Adherence: HRs – using Cox proportional Hazard regression models.
4. Methods (5)
Statistical analysis: algorithm and smooth methods
5. Results (1)

Study Flow chart

16,953 patients diagnosed with ACS during 2009-2016

- 3,456 patients excluded from the study due to loss of follow up in SIDIAP.
- 5,426 patients excluded due to history of ischaemic stroke.

8,071 patients with ACS between 2009-2016 for analysis

- 2,319 women versus 5,753 men
- 6,475 patients included with acute myocardial infarction
- 1,596 patients included with unstable angina and other forms of ACS

ACS, Acute Coronary Syndrome; SIDIAP, System for the Improvement of Research in Primary Care
## 5. Results (2)

Baseline characteristics, laboratory data and comorbidities

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute myocardial infarction (n, %)</strong></td>
<td>6475 (80.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Unstable angina and other forms of ACS (n, %)</strong></td>
<td>1596 (19.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex: Female (n, %)</strong></td>
<td>2318 (28.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years; mean, SD)</strong></td>
<td>65.33 (13.61)</td>
<td></td>
</tr>
<tr>
<td><strong>≥ 65 years (n, %)</strong></td>
<td>4323 (53.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status (n, %): Smokers (n, %)</strong></td>
<td>2320 (31.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol intake (n, %): High risk (n, %)</strong></td>
<td>5 (0.1)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m2; mean, SD)</strong></td>
<td>29.03 (4.71)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI ≥ 30: obesity (%)</strong></td>
<td>2387 (37.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol Total mg/dL (mean, (SD))</strong></td>
<td>208.93 (43.30)</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol LDL mg/dL (mean, (SD))</strong></td>
<td>129.43 (36.57)</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol HDL mg/dL (mean, (SD))</strong></td>
<td>49.03 (13.38)</td>
<td></td>
</tr>
<tr>
<td><strong>Triglycerides mg/dL (mean, (SD))</strong></td>
<td>154.74 (104.22)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes mellitus (n, %)</strong></td>
<td>2170 (26.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Dyslipidaemia (n, %)</strong></td>
<td>3451 (42.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Heart failure (n, %)</strong></td>
<td>297 (3.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension (n, %)</strong></td>
<td>4298 (53.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Peripheral artery disease (n, %)</strong></td>
<td>385 (4.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Renal impairment (%) GFR &lt; 45 ml/min/1.73m2</strong></td>
<td>528 (7.6)</td>
<td></td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome; BMI, body mass index; LDL-C, Low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol. GFR, glomerular filtration rate.
5. Results (3)
Co-medications in use at baseline (% of patients)

- Nitrates (37.2)
- NSAID (20.2)
- Drug used in diabetes mellitus (24.7)
- Calcium channel blockers (16.2)
- Anticoagulant (7.5)
- Digoxin (3.9)

NSAID, non-steroidal anti-inflammatory drugs
5. Results (4)
Population that initiate treatment for secondary prevention (overall and stratified by sex) (%)

- **Antiplatelets**
  - Overall: 91.3
  - Female: 86.4
  - Male: 93.3

- **Statins**
  - Overall: 85.7
  - Female: 80.5
  - Male: 87.8

- **Beta-blockers**
  - Overall: 76.7
  - Female: 72.4
  - Male: 78.4

- **ACEI/ARB**
  - Overall: 66.3
  - Female: 65.1
  - Male: 66.9

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers
5. Results (5)
Study drug combinations for secondary prevention (n)

IECA, angiotensin-converting enzyme inhibitors; ARA, angiotensin-receptor blockers; BBLOC, Beta-blockers; AntiAG, Antiplatelets
5. Results (5)
Study drug combinations for secondary prevention (n)

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets + Statins + Beta-blockers</td>
<td>368 (15.9)</td>
<td>1115 (19.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antiplatelets + Statins + Beta-blockers + ACEI/ARB</td>
<td>968 (41.8)</td>
<td>2879 (50.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antiplatelets + Statins + ACEI/ARB</td>
<td>210 (9.1)</td>
<td>492 (8.6)</td>
<td>0.491</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers

IECA, angiotensin-converting enzyme inhibitors; ARA, angiotensin-receptor blockers; BBLOC, Beta-blockers; AntiAG, Antiplatelets
5. Results (6)

Patients who experience a second event after index date (n)

- ACS, Acute Coronary Syndrome: 46.5%
- ACS: 3752
- Ischaemic stroke: 3041
- Death: 536

*ACS, Acute Coronary Syndrome*
8. Conclusions

- We describe a large set of ACS patients that initiate treatment with the 4 pharmacological groups recommended for secondary prevention.

- Most of the patients are men (71.3%) of ≥ 65 years-old (53.5%) that have had an AMI (80.2%).

- Most of them (91.3%) initiate treatment with antiplatelets. The other pharmacological groups are prescribed with less frequency. There are always more men than women treated.

- Almost half (48%) of patients initiate treatment with a combination of 4 drugs, the difference between men (50%) and women (41.8%) is significative.
9. References


11. ENCePP. ENCePP Resources Database. 2016.http://encepp.eu/encepp/resourcesDatabase.jsp

Moltes gràcies per la seva atenció.

Pharmacist: "and which medication reminder device would you like to use with this prescription?"