# CARDIOTOXICITY OF METALLIC HIP IMPLANTS ANALYSIS OF THE FRENCH NATIONAL HEALTH INSURANCE DATABASES (SNIIRAM)

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## BACKGROUND

Four types of total hip arthroplasty (THA) devices can be distinguished depending on the femoral and acetabular bearing surfaces: Metal-on-Polyethylene (MoP), Ceramic-on-Polyethylene (CoP), Metal-on-Metal (MoM) and Ceramic-on-Ceramic (CoC). Metallic THA (MoP and MoM) are suspected to be associated with an increased risk of cardiotoxicity, due to systemic cobalt intoxication, but the literature provides inconsistent results.

## OBJECTIVE

To study the risk of dilated cardiomyopathy (DCM) or heart failure (HF) associated with metallic THA.

## METHODS: A COHORT STUDY

**Datasource:** this cohort study was based on the French National Health Insurance Information System (SNIIRAM).

**Patients** were aged 55 years or more, with a first THA between 2008 and 2011 and no history of DCM or HF.

**Outcome** was incident DCM or HF diagnosed after the first THA surgery (ICD-10 codes of I42.0, I50.x, I11.0, I13.0, I13.2).

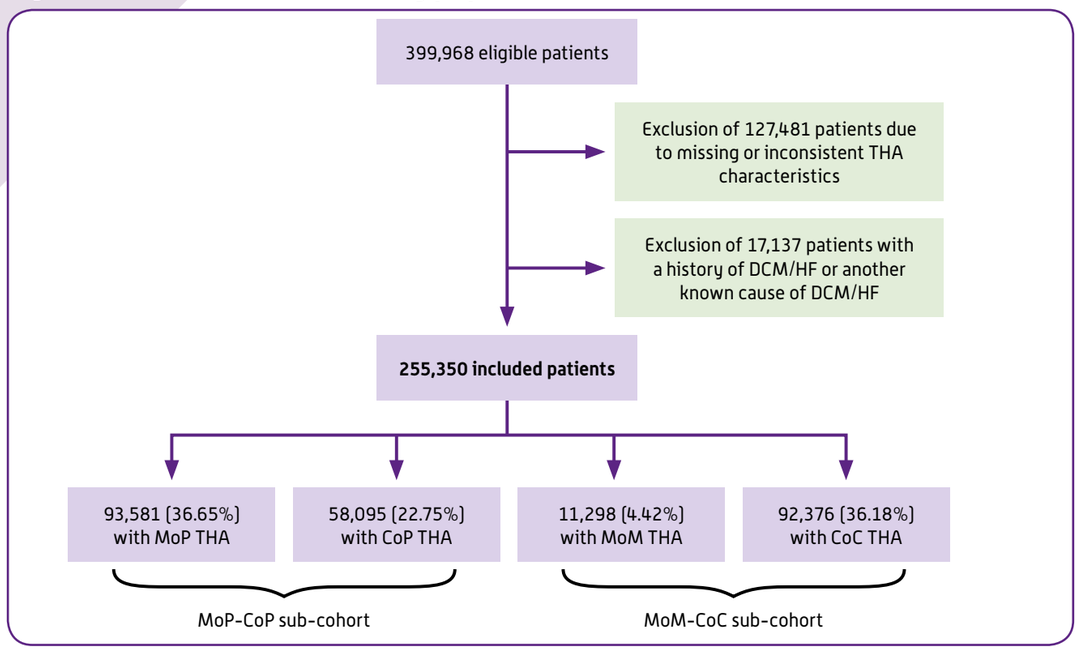
**Exposure** was the bearing couple.

**Follow-up** started from the first THA until DCM or HF, death or 12/31/2015.

**Statistical analyses:** to prevent from indication bias, two sub-cohorts were constituted: a sub-cohort of MoP or CoP patients, and a sub-cohort of MoM or CoC patients. Hazard ratios (HR) of DCM/HF associated with MoP (vs. CoP) and with MoM (vs. CoC) THA were calculated using Cox models adjusted for age, sex, cardiovascular comorbidities at baseline and THA characteristics. Analyses were also stratified by sex and by age.

## RESULTS

***Figure I. Flow-chart of the study population***




In the MoP-CoP sub-cohort, patients were less often males (38.2% vs. 49.4%, $p<0.0001$) and older (74.8±8.2 years *vs.* 67.9±8.0, $p<0.0001$) than in the MoM-CoC sub-cohort.

***Table 1. Baseline characteristics of the study population***

| | MoP-CoP sub-cohort n=151,676 | | | MoM-CoC sub-cohort n=103,674 | | |
|---|---|---|---|---|---|---|
| Baseline characteristics (%) | MoP n=93,581 | CoP n=58,095 | *p-value* | MoM n=11,298 | CoC n=92,376 | *p-value* |
| **Sociodemographic characteristics** | | | | | | |
| Male sex | 36.3 | 41.2 | ** | 54.0 | 48.9 | ** |
| Age (years) [mean (SD)] | 75.9 (8.0) | 73.0 (8.1) | ** | 67.7 (8.1) | 67.9 (8.0) | * |
| ≤ 65 | 12.6 | 20.7 | | 44.0 | 43.6 | |
| 66-75 | 30.6 | 37.5 | | 37.3 | 37.1 | |
| > 75 | 56.8 | 41.8 | | 18.7 | 19.3 | |
| **Cardiovascular comorbidities** | | | | | | |
| Ischaemic cardiovascular disease | 9.5 | 8.3 | ** | 6.9 | 6.3 | * |
| High blood arterial pressure | 63.7 | 60.3 | ** | 52.2 | 50.9 | * |
| **Endocrinal or metabolic comorbidities** | | | | | | |
| Diabetes mellitus | 12.1 | 11.8 | NS | 10.6 | 10.5 | NS |
| Measurable morbid obesity | 11.2 | 12.1 | ** | 12.1 | 11.6 | NS |
| **Lifestyle factors** | | | | | | |
| Measurable chronic alcoholism | 2.0 | 1.9 | NS | 2.3 | 2.1 | NS |
| Measurable tobacco smoking | 7.2 | 7.4 | NS | 8.6 | 8.0 | * |

Mann-Whitney test for age, Chi-square tests for the other variables.
**p<0.01 * p<0.05 NS: not significant

Patients with metallic THA (MoP vs. CoP and MoM vs. CoC) were more often suffering from cardiovascular comorbidities – including Ischaemic cardiovascular disease and High blood arterial pressure – than patients with non-metallic THA (Table 1).

***Table 2. Risk of DCM/HF associated with MoP vs. CoP THA***

| | Incidence of DCM/HF n (Incidence rate per 100 PYs) | | | Multivariate analyses | |
|---|---|---|---|---|---|
| | MoP | CoP | *p-value* | aHR (IC 95%) | *p-value* |
| **Overall** | **11,540 (2.4)** | **5,552 (1.8)** | ** | **1.08 [1.05-1.12]** | ** |
| Stratified by sex | | | | | |
| Men | 4,817 (2.8) | 2,676 (2.1) | ** | 1.07 [1.02-1.12] | ** |
| Women | 6,723 (2.2) | 2,876 (1.5) | ** | 1.09 [1.04-1.14] | ** |
| Stratified by age (years) | | | | | |
| ≤ 65 | 441 (0.7) | 398 (0.6) | * | 1.08 [0.94-1.24] | NS |
| 66-75 | 2,102 (1.3) | 1,428 (1.2) | ** | 1.13 [1.05-1.21] | ** |
| > 75 | 8,997 (3.4) | 3,726 (3.0) | ** | 1.14 [1.10-1.18] | ** |

***Table 3. Risk of DCM/HF associated with MoM vs. CoC THA***

| | Incidence of DCM/HF n (Incidence rate per 100 PYs) | | | Multivariate analyses | |
|---|---|---|---|---|---|
| | MoM | CoC | *p-value* | aHR (IC 95%) | *p-value* |
| **Overall** | **815 (1.2)** | **5,379 (1.1)** | ** | **1.11 [1.03-1.19]** | ** |
| Stratified by sex | | | | | |
| Men | 461 (1.3) | 3,067 (1.2) | NS | 1.04 [0.94-1.15] | NS |
| Women | 354 (1.1) | 2,312 (0.9) | ** | 1.20 [1.07-1.35] | ** |
| Stratifed by age (years) | | | | | |
| ≤ 65 | 156 (0.5) | 960 (0.4) | * | 1.04 [0.88-1.23] | NS |
| 66-75 | 277 (1.1) | 1,939 (1.0) | NS | 1.03 [0.91-1.17] | NS |
| > 75 | 382 (3.3) | 2,480 (2.7) | ** | 1.16 [1.04-1.29] | ** |

In multivariate analyses, Cox models were adjusted for: sex, age at baseline, affiliation with the CMUc (Free complementary healthcare insurance schemes.), THA fixation with cement, use of a modular neck, history of implantation with total knee arthroplasty, coronary stent, ischaemic cardiovascular disease, atrial fibrillation, left ventricular hypertrophy, valvular disease, high blood pressure, depression, sleep disorders, diabetes mellitus, measurable morbid obesity, dyslipidaemia, other endocrinal diseases, hemochromatosis, cancer, chronic respiratory disease, sleep apnoea, serious infection, chronic kidney disease, chronic inflammatory condition, delivery of non-steroidal anti-inflammatory drugs, delivery of specific psychiatric drugs, measurable history of chronic alcoholism or tobacco smoking. **p<0.01 * p<0.05 NS: not significant

- 17,092 cases of incident DCM/HF (875 DCM/16,217 HF) were identified in the MoP-CoP sub-cohort.
- MoP THA were associated with a slight significant increase in DCM/HF risk compared with CoP THA (aHR 1.08 95%CI 1.05-1.12).
- This increased risk was consistent regardless of sex and age (Table 2).

- 6,194 cases of incident DCM/HF (478 DCM/5,716 HF) were identified in the MoM-CoC sub-cohort.
- MoM THA were associated with a slight significant increase in DCM/HF risk compared with CoC THA (aHR 1.11 95%CI 1.03-1.19).
- This risk was more pronounced among women and among patients older than 75 years (interaction tests not significant) (Table 3).

## DISCUSSION

- Metallic THA are associated with a slightly increased risk of DCM or HF, especially MoM THA among women and patients aged over 75 years.
- To our knowledge, this is the first study exploring the association between metallic hip prostheses and cardiotoxicity on a large, unselected and population-based cohort.
- The association between metallic THA and cardiotoxicity should be confirmed in further studies and its nature should be investigated.

**Authors have no conflicts of interest with industries related to studied products.**