

A. MOULIN (anne.moulin@ansm.sante.fr), S. COLAS, A. RUDNICH, B. HEULS, M. ZUREIK, R. DRAY-SPIRA

French National Agency for Medicines and Health Products Safety (ANSM), Division for Science and European Strategy, France

BACKGROUND

Four types of total hip arthroplasty (THA) devices can be distinguished depending on the femoral head and acetabular cup surfaces:

- Metal-on-Polyethylene (MoP), Ceramic-on-Polyethylene (CoP), Metal-on-Metal (MoM) and Ceramic-on-Ceramic (CoC).
- MoM and CoC THA are indicated to younger and more active patients. MoP and CoP to older ones.
- Metallic THA (MoP and MoM) are suspected to be associated with an increased risk of non-Hodgkin's lymphoma (NHL), due to genotoxicity of metallic release on peripheral lymphocytes, but the literature provides inconsistent results.

OBJECTIVE

To estimate the risk of NHL associated with metallic THA

METHODS: A COHORT STUDY

Datasource: the French National Health Insurance Information System (SNIIRAM), the national medico-administrative database.

Patients aged 55 years or more, with a primary THA between 2008 and 2011 for a non-traumatic reason for at least one year, and no history of cancer, organ transplantation or HIV infection were included.

Outcome: incident NHL (ICD-10 codes C82-C86, C884, C915, C963, L412) - **Exposure:** the bearing couple of the THA at baseline

Follow-up started from the primary THA until NHL, death, incident cancer or transplantation, no healthcare consumption for over 18 months or 12/31/2014.

Statistical analyses: two sub-cohorts were constituted: 1- patients with MoP or Cop and 2- patients with MoM or CoC, to prevent from indication biases and to estimate Hazard ratios (HR) of NHL associated with MoP (vs. CoP) and with MoM (vs. CoC) THA with **cause-specific Cox models adjusted** for age, sex, risk factors of NHL, the use of modular neck and the use of bone cement. Analyses were also stratified by sex and by age.

RESULTS

The Cohort comprised **229,378 subjects**: men 42% ; mean age 72 years ; 83 559 MoP; 52,934 CoP; 10,216 MoM; 82,669 CoC.

NHL incidence: 495 incident NHL occurred, resulting in an overall incidence rate of 58.36 NHL/100 000 person-years [53.22 -63.50] (MoP: 65.71 [56.58-74.84]; CoP: 56.77 [46.26-67.28]; MoM: 63.78 [39.72-87.84]; CoC: 51.36 [43.33-59.39]).

Median follow-up was 45 months.

MoP-CoP subcohort (N = 136,493; Table 1)

MoP patients were older (76 vs 73 years)

and more often women (64.9% vs 60.1%).

The risk of NHL did not vary according to THA's bearing neither overall (aHR 1,05 [0,83-1,33]) nor after stratification by age or sex.

MoM-CoC subcohort (N = 92,885; Table 2)

Patients were 68 years old in both groups;

CoC patients were more often women (51.7% vs 47.3%).

The risk of NHL did not vary according to THA's bearing neither overall (aHR 1,14 [0,75-1,73]) nor after stratification by age.

MoM THA were associated with an increased risk of NHL in women (aHR 2,29 [1,35-3,89]) but the risk of NHL did not vary according to THA's bearing among men.

Table 1. Adjusted risks* of NHL associated with MoP vs CoP THA, overall, by sex and age group

Population	N events		HRa* [CI 95%]	p
	MoP	CoP		
Overall	199	112	1.05 (0.83-1.33)	NS
Stratified by sex				
Men	87	49	1.22 (0.85-1.74)	NS
Women	112	63	0.94 (0.68-1.28)	NS
Stratified by age				
Age ≤ 65 years	8	15	0.51 (0.21-1.20)	NS
Age > 65 years	191	97	1.13 (0.88-1.44)	NS

*Cox models adjusted for: sex and age at baseline, use of cement, use of a modular neck, measurable morbid obesity, history of rheumatoid arthritis, and history of a systemic disease among systemic lupus erythematosus, Sjögren syndrome, inflammatory bowel diseases, hepatitis C, or congenital immunodeficiencies.

Table 2. Adjusted risks* of NHL associated with MoM vs CoC THA, overall, by sex and age group

Population	N events		HRa* [CI 95%]	p
	MoM	CoC		
Overall	27	157	1.14 (0.75-1.73)	NS
Stratified by sex				
Men	8	97	0.52 (0.25-1.07)	NS
Women	19	60	2.29 (1.35-3.89)	< 10 ⁻²
Stratified by age				
Age ≤ 65 years	7	48	0.98 (0.44-2.20)	NS
Age > 65 years	20	109	1.18 (0.73-1.92)	NS

DISCUSSION

Overall, we found no increased risk of NHL associated with MoP versus CoP THA, nor with MoM versus CoC THA.

However, in women MoM THA were associated with a two-fold increase in NHL incidence compared to CoC THA.

Strengths of the study include the use of implanted patients (vs general population in previous published studies) as control groups, the large and almost unselected population-based cohort and the ability to account for many known and suspected NHL risk factors.

The absence of association with the MoP bearing is in line with recent literature. To our knowledge, available data to support or contradict the interaction between sex and the MoM couple in their effect on NHL are scarce.

CONCLUSION

Metallic THA are not associated with a short-term increase in NHL incidence overall. The higher rate of NHL found in women implanted with MoM THA warrants further research.

None of the authors have any conflict of interest with industries related to the studied products