Introduction: Metal-on-metal (MoM) total hip arthroplasties (THA) have been reported to result in an increased failure rate (Smith, AJ et al.) compared with other types of bearings, especially in women. Women receiving the MoM bearing are reported to have a higher risk of failure from aseptic loosening and the effects of metal hypersensitivity (Latteir, MJ et al.). Cobalt and nickel are the two most common metals that produce clinically relevant metal sensitization and metal allergy (Schäfer, T et al.). These allergies occur considerably more often in women than in men, possibly contributing to the increased failure rate in women. The prevalence of allergy to nickel was 27.5% in women compared with only 5.1% in men; for cobalt allergies the corresponding prevalences are 4.3% vs. 0.9%, respectively (Dotterud, LK et al.).

An important risk factor for both nickel and cobalt sensitization is ear piercing, a practice that is much more frequent in women than in men (82% vs. 17%). In addition, cigarette smoke contains traces of cobalt and nickel and has also been associated with an elevated risk of nickel sensitization (Thyssen, JP et al.). A prevalence of nickel allergy of 18% among female ever-smokers has been reported compared with 10% among female never-smokers, whereas among males the comparable figures were 2% among male ever-smokers compared with 0% among male never-smokers (Linneberg, A et al.). Whether smoking is a trigger for metal hypersensitivity or adds to the effect of an already present metal allergy is unknown. In either case, one would hypothesize that smoking should be a risk factor for failure of MoM THAs. In this study, we assessed the effect of smoking on revision rates in patients with a small head MoM bearing, contrasting this effect with analogous results for patients with a ceramic-on-polyethylene (CoP) bearing, all with the same cup design.

Methods: Since March 1996 all patients undergoing THA in the Geneva University Hospitals have been enrolled in a prospective hospital-based cohort and followed longitudinally. For this study we restricted entry to all primary THAs (in case of bilateral total hip arthroplasty only the first intervention was included) between January 2001 and December 2011 who had received the same uncemented cup (Morscher press-fit cup), a 28mm head and either a MoM or a CoP bearing. We then compared revision risks through March 31, 2013 among subsets of these patients, classified by smoking status and type of bearing. 1,910 patients corresponded to the inclusion criteria and had information on smoking status, which was abstracted from the anaesthesiology record at the time of the THA surgery. We classified patients as either ever or never smokers. The main outcome of interest was all-cause revision.

We measured the incidence rates of all-cause revision in two sub-cohorts: patients with a MoM bearing, and patients with a CoP bearing. We adjusted the results by sex and by a propensity score (PS), which was used as a summary confounder score. The PS was obtained through multivariate logistic regression, which was used to predict smoking status as a function of sex, type of bearing, age, BMI, ASA score, presence of diabetes, preoperative statin use, Charnley disability grade, diagnosis, stem type, and cup inclination. Then we stratified patients by sex and PS deciles and calculated adjusted incidence rate ratios (IRR) using the Mantel-Haenszel method (Rothman, KJ et al.).

Results: Overall, 1,910 patients were included. Of those, there were 295 women with MoM bearing, 785 women with CoP bearing, 354 men with MoM, and 476 men with CoP bearing. 710 patients (37%) of the whole cohort were ever-smokers, 420 men (51%) and 290 women (27%). Comparison of baseline characteristics revealed that compared with never-smokers, ever-smokers were younger, more often obese, had a higher proportion of ASA 3-4 and Charnley C, and were more likely to have secondary OA. Patients with MoM THAs compared with the CoP groups were younger (63 vs. 73 years), had lower proportions of ASA 3-4, Charnley C and diabetes, more secondary OA and more often uncemented stems.

The mean follow-up period was 6.5 years (range 1.3 - 12.2 years). During that period, 48 THAs (2.5%) were revised. The adjusted incidence rate of revision among ever-smokers was 3.9 times greater than among never-smokers (95% CI 1.3-11) for patients who had a MoM bearing. In contrast, the effect of ever-smoking versus never-smoking on revision rate was only 1.1 among patients with a CoP bearing (95% CI 0.5-2.4). The effect of smoking, measured as a rate ratio, was similar for women and men. For patients with MoM bearings, among women the adjusted IRR for ever-smokers versus never-smokers was 3.4 (95% CI 1.0-12.0), and among men it was 4.0 (95% CI 0.7-23). For patients with CoP bearings, the adjusted IRR for women was 0.9 (95% CI 0.4-2.5) and 1.5 (95% CI 0.4-5.1) for men.

Discussion: We found a strong association between smoking and increased failure of MoM hip arthroplasties, with a similar value for both sexes. In contrast, the association was weak among both sexes with a CoP bearing of the same cup design and head size.

The mechanisms by which smoking influences metal sensitization are not well known. One possible explanation relates to the fact that nickel and cobalt are present in cigarette smoke.

One limitation of our study is that information regarding preexisting metal hypersensitivity was not available for this large cohort. Thus, we were unable to assess the combined and separate influences of smoking and metal allergy on prosthesis.
failure. Second, the number of revisions in each group was relatively small, leading to large confidence intervals and precluding further stratification according to current and former smokers.

**Significance:** Thus far the ability to predict who will develop early prosthesis failure following the insertion of a MoM bearing is very limited. Our findings identify smoking as a possible risk factor for revision, possibly one that interacts with hypersensitization to metals.

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