Bisphenol A and its chlorinated derivatives and myocardial infarction in diabetic patients: case-control studies in two European cohorts

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Background
Bisphenol A (BPA) is an ubiquitous environmental toxicant with endocrine-disrupting properties. During the treatment of drinking water, chlorination leads to the formation of chlorinated derivatives of bisphenol A (ClxBPA) that show a higher level of estrogenic activity than BPA. Studies on the relationship between myocardial infarction (MI) and BPA are controversial, and even absent regarding ClxBPA. Exposure to these endocrine disruptors may promote the mechanisms of atherothrombosis involved in diabetes complications. Our objective was to prospectively evaluate the relationship between exposure to BPA and to ClxBPA and MI in patients with type 2 diabetes.

Methods
Two nested case-control studies in two independent European cohorts (SURDIAGENE-discovery step: 58 case-control pairs and ESTHER replication step: 63 case-control pairs) were considered, focusing on patients with type 2 diabetes. Cases yielded incident primary MI during follow-up and were matched on age, sex and personal cardiovascular history with controls from the same cohort. Exposure was estimated through urinary concentrations of BPA and of ClxBPA at the inclusion date. Unconjugated BPA and ClxBPA concentrations were assessed using a method based on online-SPE-LC-MS/MS. Lower limits of quantification were 500 and 50 pg/mL for BPA and ClxBPA, respectively (Grignon C et al, Anal Bioanal Chem 2016). Measurements of BPA and ClxBPA in spot urine were adjusted to creatinine. Statistical analyses were performed by SAS 9.4. A probability level of 0.05 was chosen for statistical significance.

Results
BPA was more frequently detected in ESTHER than in SURDIAGENE participants (30.2% vs. 16.4%, p=0.0116), while ClxBPA were more frequently detected in SURDIAGENE than in ESTHER participants (17.2% vs. 7.9%, p=0.0282). No association between MI and BPA was found in both case-control studies. ClxBPA detection in urinary samples was significantly associated with first-occurring MI in the SURDIAGENE with OR=3.84 (1.09-13.57) but not in the ESTHER cohort with OR=0.58 (0.03-11.00).

Conclusions
We evidenced an association between MI and exposure to ClxBPA in French diabetic patients, not replicated in German diabetic patients. Participants of both studies were differently exposed to BPA and ClxBPA,
probably due to a different water chlorination process.