

## **Association between metal levels and immune markers in total joint arthroplasty**

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### **INTRODUCTION:**

Total joint arthroplasty (TJA) patients can develop increases serum ion levels of metals including cobalt, chromium, and titanium, but it is unknown whether there is a relationship between metal levels and patient immune profile. We examined the cross-sectional association between serum metal levels and circulating immune cells.

### **METHODS:**

We recruited 115 TJA patients with elevated post-surgery serum metal levels as measured by inductively coupled plasma mass spectroscopy. Cryopreserved peripheral blood mononuclear cells were analyzed with the Maxpar Direct Immune Profiling Assay (Fluidigm), an assay that broadly characterizes major immune cell subsets. Data were acquired on a mass cytometer/CyTOF and were analyzed with the Pathsetter software program. We examined associations of metal levels with the number and distribution of immune cell subtypes (% of total cells) both dichotomously (detectable vs undetectable) and continuously (" $<1$ " ng/mL converted to 0.99 ng/mL).

### **RESULTS:**

Detectable metal levels were found for cobalt (n=53, 47%), chromium (n=45, 40%) and titanium (n=92, 81%). Detectable levels of cobalt and chromium were associated with higher percentage of gamma delta T cells (p=0.004 and p=0.006). On a continuous log scale, both the cobalt (r=0.23, p=0.02) and chromium levels (r=0.24, p=0.01) were associated with higher plasmablasts. Titanium was associated with higher CD4 effector memory T [cells](#) (r=0.18, p=0.05), regulatory T cells count (r=0.25, p=.008) and Th1 CD4 helper cells (r=0.21, p=0.02). Cobalt was also associated with higher gamma delta T cells (r=0.35, p=0.0001).

### **DISCUSSION AND CONCLUSION:**

Increased serum metal ion levels was associated with altered distribution of particular immune cells in the blood. The abundance of gamma delta T cells and plasmablasts in TJA patients with elevated cobalt-chromium levels suggest modulation of both innate and adaptive responses. Further, the abundance of effector memory CD4 cells and T-regulatory cells in patients with elevated titanium levels suggest that this metal may modify T-cell mediated immune responses.