INTRODUCTION
The Cobalt-Chromium alloy for metal on metal (MM) hip prostheses has been in clinical use since the 1960s. MM prostheses have the well-known advantage of superior wear resistance over the conventional polyethylene-on-metal prostheses, hence increasing potential longevity [1]. It is therefore a more suitable alternative for younger patients. Although not yet proven by recent studies the potentially carcinogenic effect of metal ions, mainly cobalt (Co) and chromium (Cr), found in blood and urine of patients, is a serious cause of concern especially in the context of prolonged exposure to the alloy [2]. As suggested by the elastohydrodynamic theory, larger head bearings encourage fluid film lubrication and would consequently decrease wear [3]. We therefore hypothesize that over time, greater serum metal ion concentration may correlate with greater wear rates, and accordingly, to smaller head bearings. This study measures the effects of varying head bearing sizes and patient’s activity level on Co and Cr levels. It also relates metal ions levels with oxidative stress markers (total anti-oxidant status (TAS), total peroxides, and nitrotyrosines), which are thought to be affected by Cr and Co and can ultimately lead to tissue damage [5-6].

METHODS
In this prospective study, we followed 146 patients undergoing total hip arthroplasty (THA) with different head sizes of DePuy Ultamet MM prostheses (75 patients for 36mm group, 52 patients for the 40mm group and 19 patients for the 44mm group). Patient follow-up and clinical data collection occurred at 0.16, 0.33, 1 and 2 years. Patients with bilateral hip involvement, concurrent metal hardware, multiple co-morbidities, inflammatory joint disease or infection were excluded from this study. Informed consent was obtained from all research study participants. The protocol received approval from the SMBD-Jewish General Hospital Research Ethics Committee.

The levels of Co and Cr ions were measured by inductively coupled plasma-mass spectrometry (ICP-MS) from whole blood samples. Oxidative stress markers (TAS, peroxides, and nitrotyrosines) were quantified in the serum of patients using commercial kits (Nitrotyrosine-EIA assay, Oxford Biomedical total anti-oxidant power kit and BiomedicalOxyStat assay). Functional outcome of the patients was measured at each follow-up visit using the Harris Hip Score (HHS) and the University of California Los Angeles (UCLA) Activity Score. The non-parametric Mann-Whitney U test was used to compare head bearing sizes with metal ions concentration. Nonparametric correlations between metal ions concentration and HHS and UCLA scores and oxidative stress markers were investigated using Spearman test performed on Graphpad Prism software (GraphPad Software, La Jolla, CA, USA).

RESULTS
No differences in metal ions concentration were observed between groups at the same follow-up period (Figure 1).

For the HHS correlation, we found a Spearman’s Rho of 0.2008 (P=0.0009) for Co and 0.1899 (P=0.018) for Cr. For the UCLA correlation, a Spearman’s Rho of 0.2742 (P=0.0001) was found for Co and 0.2253 (P<0.001) for Cr. However, these correlations were not statistically significant.

No correlations could be found between plasma markers for oxidative stress and metal ion concentration (Figure 2).

DISCUSSION
In theory, elevated concentrations of metal ions in patients’ blood are a risk factor for carcinogenesis, delayed hypersensitivity reactions and organ toxicity. Even though recent studies show that primary malignancies do not occur at a greater rate than seen in the population, it was previously shown that CoCr particles cause malignant tumors in rats [4]. In vitro studies have demonstrated that Co ions can react with hydrogen peroxide to produce reactive oxygen species (ROS) [5] which can increase DNA, lipid and protein oxidation leading to tissue damage [6]. In this regard, it is increasingly important to have a better understanding of the systemic effects of metal ions released by MM prostheses and also to comprehend the various factors leading to increased metal ions. The results of our study show that there is no relation between MM bearing diameter and level of metal ions released in the blood. It also shows that oxidative stress markers level is not affected by the level of Co or Cr ions. Patient’s level of activity determined by HHS and UCLA scores also didn’t affect ion levels.

SIGNIFICANCE
Our current study is addressed to the rising concern of elevated metal ions following MM THAs. We measured different operative variables to determine their effect on the concentration of metal ions in the blood of patients after THA. We also correlated the level of metal ions to the concentration of plasma oxidative stress markers due to the potential for Co and Cr to induce irreversible oxidative stress damage to several macromolecules.

REFERENCES

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