The Journal of Arthroplasty 31 (2016) S233–S236

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Complications - Other

Is Metal-On-Metal Total Hip Arthroplasty Associated With Neurotoxicity?

Abiram Bala, BA [a, *], Colin T. Penrose, BA, BS [a], Thorsten M. Seyler, MD, PhD [b], Timmothy R. Randell, MD [c], Samuel S. Wellman, MD [b], Michael P. Bolognesi, MD [b]

[a] Duke University School of Medicine, Duke University Medical Center, Durham, NC
[b] Department of Orthopaedic Surgery, Duke University Medical Center, Durham, NC
[c] Mid State Orthopaedic & Sports Medicine Center, Inc., Alexandria, LA

ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form
7 March 2016
Accepted 17 March 2016
Available online 1 April 2016

Keywords:
metal-on-metal
arthroplasty
neurologic side effects
complications
database

ABSTRACT

Background: Isolated case reports in the literature describe systemic neurologic side effects associated with metal-on-metal (MOM) bearing surfaces, yet the incidence of these effects have not been evaluated beyond individual cases. The purpose of this study was to compare new diagnoses of these side effects described in isolated cases in large patient cohorts of MOM vs metal on polyethylene (MOP).
Methods: We queried the entire Medicare database from 2005 to 2012. Total hip arthroplasty (THA) and bearing surface were determined using *International Classification of Diseases, 9th revision* procedure codes. Patients with 5-year follow-up were selected. Using *International Classification of Diseases, 9th revision* codes, we identified new diagnoses of previously reported neurologic side effects: peripheral neuropathy, sensorineural hearing loss, visual impairment, paresthesias, tinnitus, and vertigo. Comorbidities and demographics were collected. Odds ratios, CIs, and *P* values were calculated.
Results: Overall, 29,483 MOM THAs and 23,587 age- and gender-matched MOP THAs were identified. The average Charlson Comorbidity Index was 5 for both groups. MOM and MOP patients had 26 of 30 identical prevalence of Elixhauser-measure comorbidities. There was no statistically significant difference in new diagnoses of any of the side effects at any time point between the 2 groups over 5 years.
Conclusion: This study represents, to our knowledge, the first longitudinal analysis of systemic neurotoxicity after THA in a large cohort of patients. The results of our study suggest that on the large scale, neurologic side effects previously described do not occur as a common attributable complication. Rather, these cases may be due to individual patient hypersensitivity to metal ions.

The second generation of metal-on-metal (MOM) total hip arthroplasties (THAs) gained popularity in the early 2000s because of proposed benefits such as decreased volumetric wear and larger diameter heads [1-4]. This bearing surface, however, rather quickly fell out of favor because of higher complication rates, early revision, and a group of side effects now collectively referred to as adverse reactions to metal debris [5,6]. Many of these adverse reactions, including but not limited to pseudotumor formation and periprosthetic metallosis, are already well described and documented in the literature [7-9].

Although the reports are not exclusive to MOM bearing surfaces, there are isolated cases described in the literature detailing peculiar systemic side effects in patients with, most frequently, a MOM bearing surface, with varying neurologic, cardiac, and endocrine manifestations [10-13]. In specific, the neurologic symptoms described in these reports include cognitive disturbances, visual disturbances, sensorineural hearing loss, paresthesias, and vertigo [14]. Interestingly, in many of these cases, there appears to be a marked improvement in symptoms after revision of the THA [15,16].

Although the link between serum metal ions and systemic toxicity is not well established, there is evidence that suggests a direct impact of the ions on cellular damage. Cobalt and chromium ions have both been implicated in direct DNA damage, immune toxicity, and promotion of inflammation [17-20]. In addition, in certain cases, nerve conduction studies have shown decreased function, and biopsies have shown demyelination of affected nerves [10].

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2016.03.035.

* Reprint requests: Abiram Bala, BA, Duke University Medical Center, Duke University School of Medicine, Box 3269, Durham, NC, 27710.

http://dx.doi.org/10.1016/j.arth.2016.03.035
0883-5403/

Table 1
Patient Demographics.

	MOM	%	MOP	%	OR	95 L	95 U	*P*
Age, y								
Less than 65	3663	12.42	2931	12.43	1.00	0.95	1.05	.99
65-69	7531	25.54	6025	25.54	1.00	0.96	1.04	1.00
70-74	6446	21.86	5157	21.86	1.00	0.96	1.04	1.00
75-79	5933	20.12	4746	20.12	1.00	0.96	1.04	.99
80-84	3832	13.00	3066	13.00	1.00	0.95	1.05	1.00
85 and older	2078	7.05	1662	7.05	1.00	0.94	1.07	.99
Age								
Gender								
Female	16,276	55.20	13,021	55.20	1.00	0.97	1.04	1.00
Male	13,207	44.80	10,566	44.80	1.00	0.97	1.04	1.00
Total	29,483		23,587					

L, lower; MOM, metal on metal; MOP, metal on polyethylene; OR, odds ratio; U, upper.

Given that these neurologic side effects have only been described in very few patients, we wanted to evaluate these symptoms in a large population. As such, the purpose of this study was to evaluate the incidence of new diagnoses of these previously described neurologic side effects in patients with a MOM bearing surface and compare this to patients with a metal-on-polyethylene (MOP) bearing surface in a large Medicare database.

Methods

The Duke Medicine Institutional Review Board approved this study as exempt research. We queried the entire Medicare Standard Analytic Files from 2005 to 2012 using PearlDiver Technologies (West Conshohocken, PA), a database of over 51 million unique patient records. We first identified all patients who had a THA using *International Classification of Diseases, 9th revision* (ICD-9) procedure code 81.51 and Current Procedural Terminology code 27130. Then, using the command language, we isolated all patients who only had one THA performed during the entire study period. Bilateral THAs were excluded to allow for accurate tracking of neurologic side effects from the primary THA, as the database analysis software is limited in its ability to accurately track complications with 2 starting THA procedure time points. Next, we selected only patients who had their index THA performed between 2005 and 2007, to ensure a minimum of 5 years of follow-up for each patient. As the onset of neurologic side effects reported in the literature have occurred on average 2.7 years after primary MOM THA, we believed this would be sufficient follow-up to determine any difference in cumulative incidence between our groups [15]. We did not study hip resurfacing arthroplasty in this study given the differences in tribology, patient population, and complication profile.

To construct our MOM and MOP cohorts, we used the Boolean operator commands from the database to find all patients who had their THA concurrently coded with the bearing surface (ICD-9) procedure code 00.74 for MOP and 00.75 for MOM. In a stepwise fashion, we then matched a group of MOP patients to our MOM cohort by age and gender. The average Charlson Comorbidity Index (CCI), a measure of 10-year predicted mortality, was calculated for each group and compared. The prevalence of 29 comorbidities, based on the standardized Elixhauser measure, was identified for each group [21]. We also included tobacco abuse in the list of comorbidities.

We identified a list of neurologic side effects based on existing reports in the literature. To examine the incidence of new diagnoses of these side effects, we used the "First Instance" command in the PearlDiver language to identify the first time the relevant ICD-9 diagnosis code was found in a patients' record. Then, we examined the incidence of this new diagnosis within 1 year, 2 years, 3 years, 4 years, and 5 years. This method ensured that these

Table 2
Comorbidities.

Elixhauser Comorbidity	MOM	%	MOP	%	OR	95 L	95 U	*P*
Congestive heart failure	2036	6.91	1560	6.61	1.05	0.98	1.12	.18
Valvular disease	1895	6.43	1468	6.22	1.03	0.96	1.11	.34
Pulmonary circulation disorders	577	1.96	405	1.72	1.14	1.01	1.30	.04
Peripheral vascular disease	2159	7.32	1801	7.64	0.96	0.90	1.02	.17
HTN (uncomplicated and complicated)	13,945	47.30	11,279	47.82	0.98	0.95	1.01	.23
Paralysis	254	0.86	169	0.72	1.20	0.99	1.46	.06
Other neurologic disorders	1181	4.01	903	3.83	1.05	0.96	1.15	.30
Chronic pulmonary disease	4058	13.76	3245	13.76	1.00	0.95	1.05	.98
Diabetes without chronic complications	4171	14.15	3461	14.67	0.96	0.91	1.01	.09
Diabetes with chronic complications	686	2.33	610	2.59	0.90	0.80	1.00	.05
Hypothyroidism	3513	11.92	2710	11.49	1.04	0.99	1.10	.13
Renal failure	1077	3.65	929	3.94	0.92	0.85	1.01	.09
Liver disease	413	1.40	349	1.48	0.95	0.82	1.09	.45
Chronic peptic ulcer disease (includes bleeding only if obstruction is present)	30	0.10	25	0.11	0.96	0.56	1.63	.88
HIV/AIDS	82	0.28	74	0.31	0.89	0.65	1.21	.45
Lymphoma	218	0.74	208	0.88	0.84	0.69	1.01	.07
Metastatic cancer	244	0.83	233	0.99	0.84	0.70	1.00	.05
Solid tumor without metastasis	2221	7.53	1865	7.91	0.95	0.89	1.01	.11
Rheumatoid arthritis/collagen vascular diseases	1516	5.14	1329	5.63	0.91	0.84	0.98	.01
Coagulation deficiency	770	2.61	638	2.70	0.96	0.87	1.07	.51
Obesity	1472	4.99	1237	5.24	0.95	0.88	1.03	.19
Weight loss	795	2.70	601	2.55	1.06	0.95	1.18	.29
Fluid and electrolyte disorders	3242	11.00	2528	10.72	1.03	0.97	1.09	.31
Blood loss anemia	454	1.54	309	1.31	1.18	1.02	1.36	.03
Deficiency anemia	3817	12.95	3220	13.65	0.94	0.89	0.99	.02
Alcohol abuse	412	1.40	336	1.42	0.98	0.85	1.13	.79
Drug abuse	287	0.97	206	0.87	1.12	0.93	1.34	.23
Psychoses	748	2.54	614	2.60	0.97	0.87	1.09	.63
Depression	1843	6.25	1454	6.16	1.01	0.95	1.09	.68
Smoking	2693	9.13	2150	9.12	1.00	0.94	1.06	.94
Cohort total	29,483		23,587					

HIV, human immunodeficiency virus; HTN, hypertension; L, lower; MOM, metal on metal; MOP, metal on polyethylene; OR, odds ratio; U, upper.