Review Article Metal ions levels between metal-on-metal total hip arthroplasty and metal-on-metal hip resurfacing arthroplasty: a meta-analysis

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Abstract: Several studies have focused on the difference in cobalt and chromium ions concentration between metal-on-metal total hip arthroplasty (MoMTHA) and metal-on-metal hip resurfacing arthroplasty (MoMHRA), but the results are inconclusive. We aimed to conduct a meta-analysis to comprehensively explore the difference with preoperatively and 0.5, 2 and 5 years postoperatively as endpoints. In this study, we searched multiple databases for literature retrieval. The Standardized Mean Difference (SMD) and corresponding 95% confidence interval (CI) for cobalt and chromium levels at each endpoint were calculated. For cobalt ions levels, the SMDs were 0.047, -1.226, -0.460 and -0.106 for preoperatively and 0.5, 2 and 5 years postoperatively, respectively (preoperatively: P = 0.645; 0.5 year postoperatively: P < 0.001; 2 years postoperatively: P=0.090; 5 years postoperatively: P=0.560), demonstrating that patients following MoMHRA had significantly higher cobalt concentrations than those receiving MoMTHA0.5 year postoperatively. In terms of chromium ions, the SMDs were -0.048, -2.995, -0.958 and -0.621 for preoperatively and 0.5, 2 and 5 years postoperatively, respectively (preoperatively: P=0.635; 0.5 year postoperatively: P <0.001; 2 years postoperatively: P=0.006; 5 years postoperatively: P=0.003), which signified that compared with patients receiving MoMTHA, those following MoMHRA had significantly higher chromium levels 0.5, 2 and 5 years postoperatively. In conclusion, our meta-analysis suggests that patients treated with MoMHRA have more odds to be exposure to high levels of cobalt and chromium ions, compared to those receiving MoMTHA. And considering the release of metal ions, the conventional MoMTHA seems to be more beneficial to patients.

Keywords: MoMTHA, MoMHRA, cobalt ions, chromium ions, meta-analysis

Introduction

Hip arthroplasty is regarded as one of the main procedures in orthopedic surgery, and more than 350,000 individuals receive hip implants annually in the United States with a continuously increasing incidence [1]. The total hip arthroplasty (THA) and hip resurfacing arthroplasty (HRA) are the two main implemented surgical approaches in hip arthroplasty [2-4]. The femoral head is replaced by a stemmed femoral component for patients receiving MoMTHA, while for patients following MoMHRA, their femurs are preserved and capped with metal components [5]. Several factors including the age, general health, compliance and lifestyle of patients can influence the functional outcome of individuals treated with hip implants [4].

Wear, causing inflammatory reactions and osteolysis in hip arthroplasty, is a tribological phenomenon in the clinical view and is thought to be mainly responsible for the hip implant failure [1]. The metal-on-metal (MoM) bearing surfaces possess the properties of minimizing wear, decreasing dislocation rates and enhancing stability, which leads to their popularity in hip arthroplasty including both THA and HRA over a decade ago [6, 7]. It has been reported that there are over a million patients receiving largediameter MoM arthroplasty in the form of conventional THA and HRA worldwide since 1996 [8].The disadvantages of polyethylene wear with consecutive osteolysis and dislocation can be partly improved by the usage of MoM bearings [7]. While most MoM hip implants are successful, the release of metal ions such as cobalt and chromium from the MoM hip implants attributed to surface wear is one of the most critical concerns for MoM hip arthroplasty, and increasing levels of cobalt and chromium ions are observed in the blood and urine of patients treated by MoMTHA and MoMHRA [9]. The rise in the concentrations of metal ions may be correlated with higher revision rates resulting from adverse reactions secondary to the release of metal fragments [10].

For patients following MoM hip arthroplasty, the concentrations of metal ions in body fluids are believed to be surrogate measures of metal exposure [11]. Currently, methods to measure the concentrations of cobalt and chromium in the serum have been well established and applied successfully in clinical [12]. And it is controversial whether there is difference in metal ions levels including cobalt and chromium for patients following MoMTHA and MoMHRA. An original exploratory study, performed by Vendittoli and collaborators, observed that there was no significant difference in the cobalt and chromium ions levels between MoMTHA and MoMHRA 2 and 5 years after treatment [13]. However, a case-control study, published in 2015, reported that compared with MoMTHA, cobalt levels were significantly higher for MoMHRA 2 years after treatment, while the difference was not significant in cobalt levels between MoMTHA and MoMHRA 5 years after treatment; for chromium ion levels, patients in MoMHRA had significantly higher chromium levels than those in MoMTHA 2 and 5 years after treatment. Herein, in order to comprehensively estimate the difference in the metal ions concentrations including cobalt and chromium between MoMTHA and MoMHRA, we conducted the present meta-analysis with 0.5, 2 and 5 years after treatment as endpoints, and the preoperative metal ions levels were also involved.

Materials and methods

Search strategy

Multiple databases including PubMed, EMBASE and Web of science were retrieved from inception to Dec. 23 2015. We used (Hip resurfacing) OR (ASR) OR (BHR) OR (Birmingham Hip Resurfacing) OR (Articular Surface Replacement) AND (total hip arthroplasty) AND (metal ion) OR cobalt OR chromium) as search term. The reference lists of retrieved reviews were also manually examined to prevent any mission of potentially relevant studies.

Inclusion and exclusion criteria

The following inclusion criteria were predefined: (1) all participants received MoMTHA or MoMHRA; (2) all studies were case-control designs regarding to the serum or blood levels of chromium or cobalt ions, or both; (3) two treatment arms were MoMTHA and MoMHRA, respectively; (4) studies in which the raw data could be retrieved. The exclusion criteria were as follows: (1) studies employing a single arm; (2) the THA was not conventional 28 mm MoMTHA; (3) duplicated studies; (4) article types such as letters, meta-analysis, comments and news.

Data extraction

Two reviewers were independently employed to assess the eligibility of literatures according to the above inclusion and exclusion criteria. A third reviewer was consulted to resolve the disagreements. The following data was collected from eligible studies: the first author, year of publication, implant type, the number of patients in each group, gender ratio of male, methods of analysis for the concentration of metal ions and follow-up time.

Statistical analysis

We firstly evaluated the heterogeneity among the incorporated studies, which was identified by χ^2 , using Cochran Q statistic. The heterogeneity degree was quantified by I² index. If there was in the absence of significant heterogeneity (I² <50%), the Inverse-Variance (I-V) fixed-effects model was selected for the calculation of the SMD with 95% CI. Alternately, the Der-Simonian and Laird (D-L) random-effects model was used to calculate the SMD and its corresponding 95% CI. The STATA 12 software (STATA Corp LP, College Station, Texas, United States) was applied to construct the forest plots that were used to illustrate the relatively quantitative effects of each included study addressing the same issue. The Begg's test was adopted to examine the publications bias, and the Egg-



Figure 1. Flow chart of study selection and specific reasons for exclusion from the mete-analysis.

Author	Year	Impla	int Type	No.	Gender (male)	Method of Analysis	Sam- ple	Follow-up Time
Pepijn Bisseling	2015	THA	An uncemented tapered stem and threaded titanium cup with a poly- ethylene insert with a metal liner were placed (Zweymuller Classic) together with a metal 28 mm head (Metasul) (Zimmer Orthopedics, Warsaw, Indiana, USA).	33	63.64%	ICP-MS	whole blood	58 ± 8.1 (month)
		HRA	Both components made of a cast, heat-treated solution-annealed Co-Cr alloy (Conserve plus; Wright Medical Technology, Arlington, Tennessee, USA).	38	55.26%			
José M.H. Smolders	2011	THA	A threaded titanium cup with a polyethylene insert with a metal liner was inserted (Zweymuller Classic; Zimmer Orthopedics, Warsaw, Indiana, USA) together with a metal 28 mm head (Metasul; Zimmer Orthopedics, Warsaw, Indiana, USA).	32	62.50%	ICP-MS	blood and serum	-
		HRA	Both components made of a cast, heat-treated solution-annealed Co-Cr alloy (Conserve plus; Wright Medical Technology, Arlington, Tennessee, USA).	60	60.00%			
José M.H. Smolders	2011	THA	Anuncemented tapered stem and a threaded titanium cup with a polyethylene insert with a metal liner was placed (Zweymuller Classic; Zimmer Orthopedics, Warsaw, IN) together with a metal 28-mm head (Metasul; Zimmer Orthopedics).	33	63.63%	ICP-MS	blood	-
		HRA	Implanted with both components made of a cast, heat-treated solution-annealed Co-Cr alloy (Conserve plus; Wright Medical Technology, Arlington, TN).	38	68.42%			
A. Moroni	2010	THA	Metasul1 MOM-28-mm-THA (Zimmer, Warsaw, IN, USA)	35	54.28%	GFAAS	serum	58
MD		HRA	MOM-BHR (Smith and Nephew, Memphis, TN, USA),	ohis, TN, USA), 60 50.00%		(month)		
P-A. Vendittoli	2013	THA	Received a CLS-Spotorno femoral stem and an Allofit acetabular shell with a 28-mm Metasul chromium-cobalt (CrCo) bearing surface inlaid into polyethylene insert, and a CrCo femoral head (all Zimmer, Warsaw, Indiana)	53	68.00%	ICP-MS	whole blood	8 (6.6, 9.3) (year)
		HRA	A hybrid Durom CoCr resurfacing implant (Zimmer).	64	63.00%			

ICP-MS: inductively-coupled plasma mass spectrometer. GFAAS: graphite furnace atomic absorption spectrometer.

Metal Ion	Follow-up Time	SMD	Lower Limit	Upper Limit	P (SMD)	 ²	P (Hetero- geneity)	P (Begg's Test)	P (Egger's test)
Cobalt	Preoperatively	0.047	-0.152	0.246	0.645	<0.01%	0.972	0.327	0.970
	0.5 year postoperatively	-1.226	-1.851	-0.602	< 0.001	83.70%	0.000	0.089	0.036
	2 years postoperatively	-0.46	-0.991	0.072	0.090	76.00%	0.001	0.707	0.200
Chromium	5 years postoperatively	-0.106	-0.449	0.237	0.560	28.00%	0.249	1.000	0.499
	Preoperatively	-0.048	-0.248	0.151	0.635	<0.01%	0.892	0.327	0.169
	0.5 year postoperatively	-2.995	-4.063	-1.928	<0.001	90.40%	<0.001	0.089	0.005
	2 years postoperatively	-0.958	-1.643	-0.274	0.006	84.20%	<0.001	1.000	0.533
	5 years postoperatively	-0.621	-0.972	-0.27	0.003	30.50%	0.237	0.296	0.077

Table 2. Meta-analysis of the difference in the metal ions levels between MoMTHA and MoMHRA

er's test was also used for further investigation. The significance level was set at 0.05.

In our analysis, the relevant data in MoMHRA was served as reference. The metal ions levels of cobalt and chromium preoperatively and 0.5, 2 and 5 years postoperatively were extracted for the calculation of SMD with 95% CI. A SMD <0 signifies that the metal ions levels in patients following MoMHRA are higher than those in patients treated with MoMTHA.

Results

Study characteristics

A total of 711 literatures were retrieved after first round search, among which 263 from PubMed, 229 from EMBASE, 219 from Web of science. We eliminated duplications, leaving 413 literatures for further evaluation. After screening titles and abstracts, 122 irrelevant literatures were removed. The remaining 291 literatures were assessed based on our strict inclusion and exclusion criteria, and finally 5 eligible articles were included in our meta-analysis. The study inclusion and exclusion process was illustrated in **Figure 1**. The characteristics of the incorporated studies were displayed in **Table 1**.

Evaluation of the difference in the metal ions levels between MoMTHA and MoMHRA preoperatively

There were 5 eligible studies pooled to appraise the difference in cobalt and chromium concentrations between MoMTHA and MoMHRA before treatment, respectively, and the results were shown in **Table 2**. Considering the small heterogeneity, the fixed-effects model was chosen to calculate the SMD and 95% Cl. The SMDs were 0.047 and -0.048 for cobalt and chromium concentrations, respectively (cobalt: 95% Cl: -0.152-0.246; chromium: 95% Cl: -0.248-0.151, **Figure 2**), and the values of *p* were higher than 0.05 (cobalt: P=0.645; chromium: P=0.635), implying that no significant difference was observed in cobalt and chromium levels between the two treatments preoperatively.

Evaluation of the difference in the metal ions levels between MoMTHA and MoMHRA 0.5 year postoperatively

The difference in cobalt and chromium concentrations between the two groups 0.5 year after treatment was assessed by incorporating 4 eligible studies. The results were recorded in
 Table 2. The random-effects model was applied
for the calculation of the SMD and 95% CI due to the large heterogeneity. The SMDs for both cobalt and chromium were less than 0 (cobalt: SMD=-1.226, 95% CI: -1.851-0.602; chromium: SMD=-2.995, 95% CI: -4.063-1.928, Figure 3), and the values of *P* were less than 0.05. which indicated that the cobalt and chromium concentrations between the two treatments were significantly different 0.5 year postoperatively, and cobalt and chromium levels were significantly higher in patients treated with MoMHRA than those in patients following MoMTHA 0.5 year postoperatively.

Evaluation of the difference in the metal ions levels between MoMTHA and MoMHRA 2 years postoperatively

As for the metal ions levels 2 years postoperatively, 6 studies were included for the analysis.

Metal ions levels between MoMTHA and MoMHRA

Study				%
ID			SMD (95% CI)	Weight
Co				
Pepijn Bisseling (2015)		•	0.02 (-0.45, 0.49)	18.25
P-A. Vendittoli (2013)		*	0.19 (-0.25, 0.63)	20.37
José M.H. Smolders(2011)			0.00 (-0.43, 0.43)	21.57
José M.H. Smolders(2011)			0.00 (-0.43, 0.43)	21.57
José M.H. Smolders(2011)		*	0.03 (-0.44, 0.49)	18.25
Overall (I-squared = 0.0%, p = 0.972)	<	\sim	0.05 (-0.15, 0.25)	100.00
Cr				
Pepijn Bisseling (2015)	*		-0.27 (-0.74, 0.20)	18.10
P-A. Vendittoli (2013)	-	*	0.04 (-0.40, 0.48)	20.47
José M.H. Smolders(2011)			0.00 (-0.43, 0.43)	21.58
José M.H. Smolders(2011)			0.00 (-0.43, 0.43)	21.58
José M.H. Smolders(2011)	*		-0.04 (-0.51, 0.42)	18.26
Overall (I-squared = 0.0%, p = 0.892)	\leq	\geq	-0.05 (-0.25, 0.15)	100.00
738		0	.738	

Figure 2. Forest plot of study evaluating the difference in the metal ions levels between MoMTHA and MoMHRA preoperatively.

Study		%
ID	SMD (95% CI)	Weight
Co		
Pepijn Bisseling (2015)	-0.72 (-1.21, -0.24)	25.39
José M.H. Smolders(2011)	-1.37 (-1.87, -0.87)	25.12
José M.H. Smolders(2011)	-2.13 (-2.69, -1.57)	24.11
José M.H. Smolders(2011)	-0.73 (-1.21, -0.25)	25.39
Overall (I-squared = 83.7%, p = 0.000)	-1.23 (-1.85, -0.60)	100.00
NOTE: Weights are from random effects analysis		
Cr		
Pepijn Bisseling (2015)	-1.06 (-1.55, -0.56)	20.33
P-A. Vendittoli (2013)	• 0.00 (-0.44, 0.44)	20.57
José M.H. Smolders(2011)	-2.62 (-3.30, -1.94)	19.48
José M.H. Smolders(2011)	-2.90 (-3.62, -2.18)	19.30
José M.H. Smolders(2011)	-1.04 (-1.55, -0.54)	20.32
Overall (I-squared = 94.1%, p = 0.000)	-1.50 (-2.50, -0.49)	100.00
NOTE: Weights are from random effects analysis		
Overall (I-squared = 90.7%, p = 0.000)	-1.37 (-1.94, -0.79)	
-3.62	0 3.62	

Figure 3. Forest plot of study assessing the difference in the metal ions levels between MoMTHA and MoMHRA 0.5 year postoperatively.

Metal ions levels between MoMTHA and MoMHRA

Study		%
ID	SMD (95% CI)	Weight
Co		
Pepijn Bisseling (2015)	-0.62 (-1.10, -0.13)	19.07
P-A. Vendittoli (2013)	0.35 (-0.14, 0.85)	18.96
José M.H. Smolders(2011)	-0.63 (-1.46, 0.20)	14.58
José M.H. Smolders(2011)	-1.80 (-2.74, -0.85)	13.21
José M.H. Smolders(2011)	-0.57 (-1.20, 0.06)	17.14
A. Moroni MD (2011)	0.10 (-0.54, 0.75)	17.05
Overall (I-squared = 76.0%, p = 0.001)	-0.46 (-0.99, 0.07)	100.00
NOTE: Weights are from random effects analysis		
Cr I		
Pepijn Bisseling (2015)	-1.78 (-2.35, -1.22)	17.71
P-A. Vendittoli (2013)	0.10 (-0.39, 0.59)	18.23
José M.H. Smolders(2011)	-0.60 (-1.43, 0.23)	15.52
José M.H. Smolders(2011)	-0.81 (-1.65, 0.03)	15.41
José M.H. Smolders(2011)	-1.81 (-2.55, -1.07)	16.26
A. Moroni MD (2011)	-0.87 (-1.54, -0.20)	16.86
Overall (I-squared = 84.2%, p = 0.000)	-0.96 (-1.64, -0.27)	100.00
NOTE: Weights are from random effects analysis		
-2.74 0 2	1 .74	

Figure 4. Forest plot of study evaluating the difference in the metal ions levels between MoMTHA and MoMHRA2 years postoperatively.



Figure 5. Forest plot of study estimating the difference in the metal ions levels between MoMTHA and MoMHRA 5 years postoperatively.

There was significant heterogeneity among pooled studies, and the results were documented in **Table 2**. The SMD for cobalt concentrations was -0.46 (95% Cl: -0.991-0.072, **Figure 4**) with P larger than 0.05, demonstrating that the difference in the cobalt levels between MoMTHA and MoMHRA was not significant 2 years postoperatively. With regard to the chromium concentrations, the SMD was -0.958 (95% Cl: -1.643-0.274, **Figure 4**), and the value of *p* was less than 0.05 (P=0.006), which implied that the chromium levels were significantly higher in patients receiving MoMHRA than those in patients following MoMTHA 2 years postoperatively.

Evaluation of the difference in the metal ions levels between MoMTHA and MoMHRA 5 years postoperatively

With respect to the metal ions concentrations 5 years postoperatively, the fixed-effects model was selected to calculate the SMD and 95% CI. since the heterogeneity was small. The results were displayed in Table 2. The SMD for cobalt concentrations was less than 0 (SMD=-0.106, 95% CI: -0.449-0.237, Figure 5), and the value of p was larger than 0.05 (P=0.560), suggested that no significant difference in the cobalt levels was detected between the two treatments 5 years postoperatively. In terms of the chromium concentrations, the SMD was less than 0 (SMD=-0.621, 95% CI: -0.972-0.270, P=0.003, Figure 5), which indicated that compared with patients following MoMTHA, patients receiving MoMHRA had significantly higher chromium levels 5 years postoperatively.

Publication bias

We used both Begg's test and Egger's test to assess the publication bias in our meta-analysis, and the results were exhibited in **Table 2**. The values of *p* for preoperatively, 2 and 5 years postoperatively in Begg's and Egger's tests were larger than 0.05, which demonstrated that no significant publication bias existed in these analyses. As for 0.5 year postoperatively, although the values of *p* for cobalt and chromium concentrations in Egger's test were less than 0.05, the values of *p* in Begg's test were larger than 0.05, and we still believed that there was no significant publication bias in the analyses.

Discussion

In this study, we performed a meta-analysis to evaluate the difference in cobalt and chromium concentrations between MoMTHA and MoMHRA with preoperatively and 0.5, 2 and 5 years postoperatively as endpoints. Our results show that for cobalt ions, compared with patients receiving MoMTHA, those following MoMHRA are more likely to have higher cobalt concentration 0.5 year postoperatively, while the cobalt concentrations are similar in the two treatments 2 and 5 years postoperatively. As for chromium ions, patients treated with MoMHRA have significant higher chromium levels than those following MoMTHA 0.5, 2 and 5 years postoperatively. The different results for cobalt and chromium can be partly ascribed to a run-in phase and the differences in the metal corrosion, wear mechanisms, orientation of acetabular components and geometry of components between the two treatments [14, 15]. Additionally, as expected, the preoperative cobalt and chromium levels are similar in the two treatments.

Although MoM is the most widely used bearing material in the hip arthroplasty due to its best compromise between wear properties and strength, the MoM hip replacements may product metal ions mainly including cobalt and chromium resulting from wear and corrosion [11, 16]. These metal ions can be released into not only the joint itself but also the surrounding tissue and body fluids, which is probably to be related with the emergence of local and systemic adverse reactions including local tissue toxicity, impaired kidney function, Chromosomal injury, inflammation, soft tissue necrosis and bone loss [11, 17]. It has been admitted that MoM hip arthroplasty causes elevated concentrations of chromium and cobalt in the whole blood [17]. A randomized controlled trial (RCT), which was aimed to explore the metal ion levels after either conventional MoMTHA or MoMHRA, found that patients treated with MoMHRA had significantly higher cobalt and chromium levels than those receiving MoMTHA 0.5 year after treatment [14]. And 2 years after treatment, the chromium levels were still significantly higher in patients following MoMHRA than those in patients receiving MoMTHA [14]. Our results were consistent with those in the above RCT. and we further found that 5 years postoperatively, patients receiving MoMHRA still had significantly higher chromium concentrations, compared with those receiving MoMTHA.

Cobalt, chronically accumulated in blood, has been described as a risk factor for hypothyroidism, hypersensitivity, cardiomyopathy, tumorigenesis and polyneuropathy [18]. With the popularity of metal hip implants, cobalt poisoning becomes more frequent [19]. For patients following large head MoMTHA, high cobalt ions levels in blood ($\geq 4 \mu g/L$), together with pain and swelling, are independent predictor for the presence of pseudotumor, respectively [18]. A case report conducted by Rizzetti et al. recorded the relevant information of a 58-year-old woman who had a left hip arthroplasty and a following revision, and found that the endogenous cobalt-chromium intoxication because of metal wear debris was the main pathogenesis of her symptoms of visual loss, severely deaf and lower limb hyposthenia [2].

Chromium, one of the important microminerals. has been documented to have antioxidant activity and to improve glucose metabolism and insulin action [20, 21]. The serum level of chromium for patients with diabetes or obesity is usually lower than that for healthy subjects, and chromium supplements are commonly recommended to individuals with these two diseases [21]. Polycystic ovary syndrome women are also advised to receive chromium supplementation, especially, in the context of low serum chromium levels [22]. Though, chromium is a cofactor for numerous enzymes and impacts on some biological pathways, it becomes poisonous after a minimal increase in concentration, and has been reported to be carcinogenic and mutagenic in both animal models and human [23]. A review deduced from five anecdotal case reports that over intake of chromium might lead to renal dysfunction [24].

MoMHRA, with claimed advantages including femoral bone stock preservation, less dislocation and improved functional outcomes, has been proposed as an alternative to MoMTHA, and is favored by young and active patients [14, 25]. However, with more concerns on the matter of the release of cobalt and chromium ions after receiving MoMTHA and MoMHRA, it remains inconclusive that whether patients receiving MoMHRA have lower cobalt and chro-

mium concentrations when compared to those following MoMHRA. An observational crosssectional study, published in 2010, found that the difference in cobalt and chromium levels was not significant between MoMTHA and MoMHRA at 2 and 5 years follow up [26]. Interestingly, a case-control study, published in 2011, documented that the chromium concentrations were significantly higher in patients following MoMHRA than those treated with MoMTHA2 years postoperatively [14]. Our meta-analysis, with a large sample size by incorporating relevant data together, has more reliable and precise estimations for the difference in the metal levels between the two treatments. And our meta-analysis detected that patients receiving MoMHRA have more odds to be exposure to high levels of cobalt ions 0.5 year postoperatively and high concentrations of chromium ions 0.5, 2 and 5 years postoperatively when compared with those following MoMTHA, which implied that MoMTHA could not be totally replaced with MoMHRA, even if MoMHRA represents several merits over MoMTHA.

A previous meta-analysis [27], published in 2011, was aimed to compare concentrations of cobalt and chromium ions from MoMTHA implants to that of HRA implants. The previous study only incorporated articles published beore 2010 and appraised the overall difference in the metal ions levels between the two groups regardless of the specific follow-up period after implants. And the researchers found no significant difference in concentrations of cobalt and chromium ions between two groups, even if patients following HRA had lower cobalt ion levels. In the current meta-analysis, we made the comparison between MoMTHA and MoMHRA with 0.5, 2 and 5 years follow-up as endpoints. And in order to have a more reliable assessment, we only included patients receiving 28 mm MoMTHA. Moreover, we pooled two eligible papers published in 2011 [14, 28], one published in 2013 [13] and one published in 2015 [29]. All that leads to different estimations between the previous meta-analysis and the current study.

To our knowledge, the present study is the first meta-analysis to investigate the difference in the metal ions levels at different follow-up time between MoMTHA and MoMHRA. However, when interpreting the results, we should be cautious of the following limitations. Firstly, there are two different methods for the detection of metal ions levels in all the included studies, which may cause bias in our analysis. And with more relevant studies becoming available, subgroup analysis stratified by different methods should be performed. Secondly, studies related to both the serum and the whole blood metal ions levels were incorporated in our analysis, and with sufficient data, subgroup analysis of the serum and the whole blood should be conducted. Additionally, we have not considered the unpublished articles in our study.

In conclusion, the current meta-analysis suggests that cobalt concentrations 0.5 year postoperatively and chromium concentrations 0.5, 2 and 5 years postoperatively are significantly higher in patients treated with MoMHRA than those in patients following MoMTHA. Compared with patients receiving MoMTHA, patients treated with MoMHRA are more likely to be exposure to high levels of cobalt and chromium ions. Considering the possible toxicity of high metal ions levels, MoMHRA should be recommended to individuals in need of hip arthroplasty.

Disclosure of conflict of interest

None.

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