2020

Early post-operative rises in serum metal ion levels in Total Hip Arthroplasty: A prospective cohort study

Michael Le

Early post-operative rises in serum metal ion levels in Total Hip Arthroplasty: A prospective cohort study

Dr Michael LE

BMedSci MD

Submitted in fulfilment of the requirements of Master of Medicine/Surgery

(Thesis by publication)

Publishing Journal: Reconstructive Review

School of Medicine

Sydney Campus

November 2020

Declaration

To the best of my knowledge, this thesis contains no material previously published by another person, except where due acknowledgement has been made.

This thesis is my own work and contains no material which has been accepted for the award of any other degree or diploma in any institution.

Human Ethics (For projects involving human participants/tissue, etc) The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007, updated 2018). The proposed research study received human research ethics approval from the University Of Notre Dame Australia Human Research Ethics Committee (EC00418), Approval Number # 017105S

Print Name: Dr Michael Le

Date: 15th of November 2020

Early post-operative rises in serum metal ion levels in Total Hip Arthroplasty: A prospective cohort study

Dr Michael Le

Master of Medicine/Surgery

School of Medicine

University of Notre Dame Australia

November 2020

ABSTRACT

Background:

Serum Cobalt (Co) and Chromium (Cr) forms part of the diagnostic process for metallosis following Total Hip Arthroplasty (THA). While knowledge exists on longer term metal ion levels, expected early post-operative rises in serum Co and Cr in Metal-on-Polyethylene (MoP) THAs are currently unknown. This study aims to describe early rises in serum Co and Cr at 6 months post-operatively.

Methods: A prospective cohort study of 84 consecutive patients with an uncemented titanium stem from a single THA manufacturer was performed. Patients had either a metal (n=43) or ceramic (n=41) head articulating with a highly cross-linked polyethylene. Serum Co and Cr levels were measured six months post-operatively. Analysis compared mean values between groups and to determined baseline levels. Subgroup analysis investigated the effect of femoral head size and offset on metal ion levels.

Results: A mean difference of 0.002259 ppb (95% CI 0.000449-0.004069 ppb; $p=0.015$) was found when comparing 6-month serum Co in the metal head group compared to baseline. No significant differences were found in serum Cr ($p=0.943$) at six months post-surgery compared to baseline. Mean serum Co levels were higher in the MoP group compared to the CoP (Ceramic-on-Polyethylene) and auxiliary control group ($p=0.012$). There were no differences in serum Cr ($p=0.976$) between the MoP and CoP groups at 6 months post-surgery. Variations in femoral head size and offset did not impact metal ion levels.

Conclusion: At six months post-surgery, a higher magnitude of serum Co exists in metal heads when compared to baseline ($p=0.015$) and to ceramic heads ($p=0.012$). Further study is required to determine whether serum concentrations of metal ions will continue to increase over time which might leads to implant failure and revision.

Level of Evidence: II

ACKNOWLEDGEMENTS

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Australian Government Funding was obtained for the purposes of this Masters Degree under the Research Training Program (RTP) scheme.

Contributors:

1. Dr Dante Maestri BAppSci (Physiotherapy) MD for assistance in the collection of data and analysis.
2. Dr Bob Jang BMed Canterbury hospital, Sydney, Australia for assistance in the collection of data and analysis.
3. Dr. Jason Chinnappa MBBS, MS (Ortho), FRACS (Ortho), FAOA as a co-supervisor and expertise in the area of Orthopaedics.
4. Dr. Sol Qurashi BMed, FRACS (Ortho), FAOA
   Primary supervisor and expertise in the area of Orthopaedics.

LIST OF PUBLICATIONS

1. *Le M, Maestri D, Jang B, Chinnappa J, Qurashi S. Early Post-operative Rises in Serum Metal Ion Levels in Total Hip Arthroplasty – A Prospective Cohort Study. Reconstr Rev. 2020 Nov 2020 ; 1(10).*

Disclosure statement

In the publication of this article, ach author certifies that he has no commercial associations nor has received any financial benefit that might pose a conflict of interest in connection with the submitted article. No research funding was received for this project.

<u>TABLE OF CONTENTS</u>

LIST OF TABLES

BACKGROUND AND LITERATURE REVIEW

Total Hip Arthroplasty (total hip replacement, THA) has been the mainstay and most effective technique for treating osteoarthritic hip joint disease in the last few decades. This type of surgery was described by Wiles in 1958 as being to "relieve symptoms" such as pain, stiffness and deformity(1). It has been pivotal in restoring function and overall quality of life.

The hip joint is a ball-and-socket type diarthrodial joint as stability is achieved via a balance of osseous and soft tissue components(2). Total Hip Arthroplasty involves the removal of damaged areas of bone from the hip joint with replacement of the femoral component (ball and stem) and acetabular component (socket).

The success of hip arthroplasty surgery has been reflected in numerous studies using outcome-based measurements such as WOMAC scores, UCLA and Oxford Hip Scores(3). These outcome-based clinical scores evaluate the extent of physical function, independence with activities and impact of pain. They are validated and have reflected the quality of life improvements granted in the success of hip arthroplasty.

Hip replacement surgery has been a reliable treatment option in treating end stages of hip pathology. These include conditions such as avascular necrosis, hip dysplasia and traumatic intracapsular neck of femur fractures(4). Hemiarthroplasty or partial hip replacement (where only the femoral component is replaced) has also considered a foundation option in treating these types of conditions.

As the prevalence of osteoarthritis grows alongside the growth of Australia's aging population; there continues to be an annual increase in overall procedures performed. This is reflected in the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) which has reported a growth rate of 4.8% within the last 10 years(5).

The success of hip arthroplasty is also limited by its complications. Among an array of potential complications, the most prevalent complications of total hip arthroplasty and hemi-arthroplasty include aseptic loosening, dislocation, infection and fracture(4). Studies have evaluated the extent of these complications by determining the rates of revision. Revision in total hip arthroplasty includes the removal of at least one component of the original implant and replacing it with another(6). This involves the exchange of either the stem, liner, femoral head, acetabular or other bearing component.

Over the last decade, there has been an increase in the number of revision hip procedures being performed; and this is projected to increase(7). Revision procedures are reflected in the AOANJRR data in Australia; with aseptic loosening being the main reason with rates of up to 63%. Trunnionosis is less common although it presents itself as an important clinical challenge in revision surgery.

Trunnionosis in Total Hip Arthroplasty (THA) is the mechanical wear or corrosion occurring at femoral modular head-neck interfaces [1]. Trunnionosis has been attributed to elevated serum levels of cobalt and chromium in THAs (8,9). The release of metal ions has the potential to lead to adverse local tissue reaction, persistent pain, increased wear, physiological dysfunction requiring revision surgery (10–12). Its prevalence ranges between 0.023% to 2% accounting for 1.8% to 3.3% of the total THA revision burden (13–15). Australia's data is reflective of other global registry data for revision alongside prevalence stated in previous studies indicating that it could account for up to 3.3% of the overall burden.

Previous increases in serum metal ion levels were common along metal-on-metal bearing surfaces which resulted in metallosis based reactions and pseudotumor development(16). The advent of new modern bearing surfaces such as metal-on-polyethylene (MoP), ceramic-on-polyethylene (CoP) and ceramic-on-ceramic (CoC) saw a brief period of decline in this phenomenon(17). Only in recent years has the trunnionosis seen an increase in prevalence particularly with the use of modularity(17).

The exact predisposing factors for trunnionosis are currently unclear. However, several aetiologies have been postulated. Shorter, narrower taper designs, longer neck, head size and femoral offset are factors suggested to increase edge loading at the bases causing local stress, micro-motion and subsequent damage (17–19).

There is currently no recommended or published single diagnostic tool to detect trunnionosis(20). Serum cobalt (Co) and chromium (Cr) forms part of the diagnostic process; but consensus regarding its value in routine follow-up is lacking. The mean time from surgery to presentation with clinically significant trunnionosis is between 3.7 and 4.3 years(14). In the absence of symptoms, many patients are not identified until revision surgery. It is not known whether metal ion levels alone should precipitate revision, however patients late to be diagnosed experience higher rates of complications(21,22).

Cobalt and chromium levels in ceramic on ceramic, ceramic on polyethylene and dual mobility bearing couples have only be reported in smaller cohorts with shorter follow-up periods(23). The normal metal ion levels in well-functioning MOP THA bearing couples have not yet been generally accepted(24). Martin et al in their investigation of femoral offset conducted a retrospective cohort study in 80 consecutive patients with asymptomatic MOP

THA at 2 and 5-year follow-up(19). They found the baseline serum cobalt and chromium levels after stratifying identified risk factors to be approximately 0.3ug/L. Craig et al defined abnormal results as cobalt levels greater than 0.59ug/L and chromium levels greater than 40ug/L when investigating the effect of femoral head size in metal-on-polyethylene implants but did not describe the basis for these values(25).

The best available evidence for levels of cobalt and chromium in well-functioning MoP bearing surfaces was demonstrated in a 10-year prospective follow-up study(26). The study measured metal ion levels at 12, 36, 60, 84 and 120 months. The study measured cobalt, chromium and titanium levels at 12, 36, 60, 84 and 120 months but used atomic absorption spectrometry with higher detection thresholds in the earlier stages of serum analysis. The study additionally come to the conclusion that metal release at the modular head-neck junctions was likely the dominant source of serum cobalt and chromium rather than passive dissolution.

Expected early post-operative rises in serum cobalt and chromium are currently unknown. To date no studies in our search of the literature has evaluated the metal ion levels at intervals of less than 12 months in modern bearing couples.

INTRODUCTION

Trunnionosis in Total Hip Arthroplasty (THA) is the mechanical wear or corrosion occurring at femoral modular head-neck interfaces [1]. Trunnionosis has been attributed to elevated serum levels of cobalt and chromium in THAs (8,9). The release of metal ions has the potential to lead to adverse local tissue reaction, persistent pain, increased wear, physiological dysfunction requiring revision surgery (10–12). Its prevalence ranges between 0.023% to 2% accounting for 1.8% to 3.3% of the total THA revision burden (13–15).

The exact predisposing factors for trunnionosis are currently unclear. However, several aetiologies have been postulated. Shorter, narrower taper designs, longer neck, head size and femoral offset are factors suggested to increase edge loading at the bases causing local stress, micro-motion and subsequent damage (17–19). Taper material and bearing surfaces have also been considered as factors affecting trunnionosis (23). The impact of larger femoral head sizes is inconclusive although some studies associate it with higher metal ion levels in Metal-on-Polyethylene (MoP) THAs (25,27,28). Ceramic-on Polyethylene (CoP) THAs have been a suggested solution. However, recent studies have suggested that taper corrosion still remains an issue (29,30).

There is currently no recommended single diagnostic tool to detect trunnionosis (20). Serum cobalt (Co) and chromium (Cr) forms part of the diagnostic process; but consensus regarding its value in routine follow-up is lacking. The mean time from surgery to presentation with clinically significant trunnionosis is between 3.7 and 4.3 years (14). In the absence of symptoms, many patients are not identified until revision surgery. It is not known whether metal ion levels alone should precipitate revision, however patients late to be diagnosed experience higher rates of complications (21,22).

Expected early post-operative rises in serum cobalt and chromium are currently unknown (24). To date no studies in our search of the literature have evaluated the metal ion levels at intervals of less than 12 months in modern bearing couples. The best available evidence for levels of cobalt and chromium in well-functioning MoP bearing surfaces was demonstrated in a 10-year prospective follow-up study by Levine et al(26). Their study measured metal ion levels at 12, 36, 60, 84 and 120 months post THA.

This study aims to determine whether there are early rises in serum cobalt and chromium at 6 months post MoP THA using pre-operative baseline and a CoP THA comparator groups. Additionally, we aimed to determine whether there was a difference in metal ion release based on variations in femoral head size and offset in MoP and CoP THAs.

MATERIALS AND METHODS

A prospective study was performed to evaluate serum cobalt and chromium levels in patients undergoing primary elective THA for osteoarthritis in 2016 and 2017. Following institutional approval (HREC Approval Reference Number: 017105S), 100 consecutive patients aged 18 years or older were enrolled. All patients received an uncemented titanium femoral stem and acetabular component (MicroPort Orthopaedics Inc., Arlington, TN, USA; Dynasty Acetabular component, Profemur L Classic Monoblock Femoral component) using the Supracapsular Percutaneously Assisted Total Hip (SuperPATH) technique with in situ reduction of femoral head on trunnion under direct vision without impaction to avoid taper/trunnion damage as per the standard of care of a single surgeon (SQ) (31). The PROFEMUR L Classic stem taper is made of Titanium Alloy (Ti6AI4V) with a 12/14 morse taper at the head-neck junction, Patients either had a metal (CoCr) (n=50) or ceramic (Biolox Delta, CeramTec North America Corp. Laurens, SC 29360, USA) (n=50) femoral head coupled with a High Cross-Linked Polyethylene (HCPE) liner. Choice of bearing surface was sequentially allocated with the first 50 consecutive patients receiving metal heads and the next 50 consecutive patients receiving ceramic heads.

Patients were deemed ineligible if they hand undergone bilateral THAs, previous joint arthroplasty or underwent another arthroplasty procedure prior to follow-up (n=16).

Following exclusion criteria, of the 100 consecutive cases, eighty-four patients remained. These eighty-four cases with either a metal-on-polyethylene (n=43) or ceramic-on-polyethylene (n=41) were deemed eligible for inclusion.

Demographic data for each patient was collected including age, gender, BMI and previous joint arthroplasty. Implant specific information incorporating femoral head type, size, neck length, offset, trunnion taper design; and acetabular cup type and design were recorded.

The primary outcome was the serum level of cobalt and chromium levels at a single time point (6 months post-operatively). Baseline pre-operative serum Cobalt and Chromium values were determined from a separate group of pre-operative patients (n=50) (Auxiliary control group). Additionally, the CoP group served as a second comparator as its prothesis (femoral head) does not contain cobalt or chromium. Patients were consented at their final pre-operative appointment and underwent pre-operative blood assessment of serum Cobalt and Chromium. Bloods samples were collected from patients into EDTA vacutainers test tubes using a stainless steel needle at the pathology collection centre. Blood samples were transported to the laboratory at ambient temperature for analysis. All blood samples were analysed for Serum Cobalt and Serum Chromium levels by Sullivan Nicolaides Pathology (Sullivan Nicolaides Pathology Pty Ltd, Queensland, Australia). At the standard six-month follow-up, enrolled patients were sent to the same centre for blood collection by trained phlebotomists. All specimens were prepared and transported to one laboratory for analyses.

Statistical Analysis

A priori, we hypothesized there would be no difference in serum cobalt or chromium at 6 months post-operatively between MoP and CoP THAs from a single manufacturer. Additionally, we hypothesized that variations in femoral head size and offset would have no significant impact on metal ion levels at 6 months. With an alpha level of significance set to 0.05, a sample size of 32 patients in each group were required to detect a significant difference at a power level of 0.8. Differences in clinical characteristics between the two groups were evaluated using two-tailed sample T tests for statistical significance of continuous variables. All analyses were completed using Epitools Epidemiological Calculators (Ausvet, Australia).

RESULTS

Patient Demographics

There were no significant differences were observed between the metal and ceramic groups with respect to gender, mean age at time of surgery or BMI. Table 1 outlines the demographic data.

Table 1: Population demographic characteristics

	CoP THA group	MoP THA group	P value
Number of patients	41	43	
Males (%)	57%	56%	
Females (%)	43%	44%	
Age (mean)	62.5 ±12.8	66.2 ±9.46	0.13
BMI (mean)	28.3±4.6	30.3 ±5.4	0.07

Serum Ion Comparisons with Baseline

A primary analysis was performed in which patients were grouped based on whether they had metal (MoP) or ceramic (CoP) heads. Significant difference was found in serum Co levels at 6 months post-surgery compared to baseline (auxiliary control group) in the MoP group (mean difference: 0.00226 ppb, SD 0.00438 ppb, 95%CI 0.000449 ppb – 0.00407 ppb ; p=0.015). No significant difference was found in serum Cr levels (p=0.943) compared to baseline (auxiliary control group) . In the CoP group, no significant difference was found in serum Co or serum Cr levels at 6 months compared to baseline (p=0.833 and p=0.932). Tables 2 and 3 outlines this data.

Table 2: Baseline vs 6 months post MoP THA

	Baseline (n=43)	6/12 post MoP THA (n=43)	P value
Mean Cobalt (ppb)	0.00468	0.00694	**0.015**
Mean Chromium (ppb)	0.00981	0.00978	0.943

Table 3: Baseline vs 6 months post CoP THA

	Baseline (n=41)	6/12 post CoP THA (n=41)	P value
Mean Cobalt (ppb)	0.00468	0.00483	0.833
Mean Chromium (ppb)	0.00981	0.00976	0.932

Metal-on-Polyethylene vs Ceramic-On-Polyethylene

A secondary analysis was performed comparing serum Co and Cr levels between MoP and CoP groups. Significant higher serum Co was found in the MoP group compared to CoP group (mean difference: 0.00211 ppb, SD 0.003774 ppb, 95% CI 0.000471-0.003749 ppb; p=0.012). However no significant difference was found in serum Cr levels between the two groups (p=0.98) at 6 months as well as baseline (auxiliary control group). Table 4 outlines this data.

Table 4: MoP vs CoP 6 months post surgery –serum chromium and cobalt comparison

	MoP THA group (n=43)	CoP THA group (n=41)	P value
Mean Cobalt (ppb)	0.00694	0.00483	**0.012**

Mean Chromium (ppb)	0.00978	0.00976	0.976

Femoral Offset Comparison

The MoP cohort was further divided into standard (n = 10)_and extended offset groups (n = 31). There were no significant differences found in serum Co (p=0.473) or serum Cr (p=0.398) levels between these two groups. Table 5 outlines this data.

Table 5: All standard vs all extended offset

	All Standard Offset	All Extended offset	P-Value
Mean serum cobalt (ppb)	0.00726	0.00550	0.473
Mean serum chromium (ppb)	0.00995	0.00916	0.398

Significant difference was found only when comparing serum Co between MoP (n = 9) and CoP (n = 10)in those with extended offset (p=0.016). Table 6 outlines this data.

In further subgroup analyses, no other significant differences were found when comparing serum Co and Cr levels between MoP standard, MoP extended offset, CoP standard and CoP extended offset groups. Tables 6, 7, 8 and 9 outlines this data.

Table 6: Extended Offset CoP vs MoP-serum chromium and cobalt comparison

	CoP group (n=10)	MoP group (n=9)	P value
Mean serum cobalt (ppb)	0.00420	0.00848	0.016

Mean serum chromium (ppb)	0.00940	0.0138	0.399

Table 7: Standard Offset CoP vs MoP-serum chromium and cobalt comparison

	CoP group (n=31)	MoP group (n=34)	P value
Mean serum cobalt (ppb)	0.00547	0.00653	0.360
Mean serum chromium (ppb)	0.00984	0.01040	0.650

Table 8: Extended vs Standard Offset in MoP-serum chromium and cobalt comparison

	MoP group Extended Offset (n=10)	MoP group Standard Offset (n=31)	P value
Mean serum cobalt (ppb)	0.00849	0.00653	0.280
Mean serum chromium (ppb)	0.00940	0.00984	0.774

Femoral Head Size Comparison

Each cohort (MoP and CoP0 were further divided by head size into small (<36mm) and large (≥36mm). There were no significant differences when comparing head sizes between MoP groups nor the CoP groups. Tables 9, 10, 11 and 12 outlines this data.

Table 9: Femoral head size <36mm, MoP vs CoP

	MoP group femoral head <36mm (n=7)	CoP group femoral head <36mm (n=10)	P value
Mean serum cobalt (ppb)	0.0091	0.0058	0.07
Mean serum chromium (ppb)	0.0096	0.009	0.24

Table 10: Femoral head size ≥36mm – MoP vs CoP metal ion levels

	MoP group (n=37)	CoP group (n=32)	P value
Mean serum cobalt (ppb)	0.008	0.005	0.11
Mean serum chromium (ppb)	0.0105	0.001	0.63

Table 11: CoP – femoral head size of <36mm vs ≥36mm metal ion levels

	CoP femoral head <36mm (n=10)	CoP femoral head 36mm (n=32)	P value
Mean serum cobalt (ppb)	0.0058	0.005	0.47
Mean serum chromium (ppb)	0.009	0.010	0.53

Table 12: MoP – femoral head size of <36mm vs ≥36mm metal ion levels

	MoP femoral head <36mm (n=7)	MoP femoral head ≥36mm (n=37)	P value
Mean serum cobalt (ppb)	0.0091	0.0079	0.75
Mean serum chromium (ppb)	0.0096	0.0105	0.63

DISCUSSION

In recent times there has been a growing clinic concern for metal ion release from trunnionosis in THAs (17). Whilst not routinely measured, serum ion levels are important in the work-up of poorly performing THAs (20,32,33). Currently, there exists minimal information on expected metal ion levels in patients with modern bearing coupled THAs (34,35).

Results from this study showed a significant elevations in mean serum cobalt six months post-operatively in the MoP group but not in the CoP comparator group. Despite this, the mean short-term serum Co levels were within normal laboratory limits. No significant differences were found in serum Cr in either the MoP or CoP group compared to baseline levels. A differential elevation in cobalt has been attributed to greater solubility properties and localised head-neck modular precipitation of chromium orthophosphate (13,36). This is consistent with literature suggesting that cobalt rises in a ratio of 1-5:1 in modular neck THAs (36–38). Despite a lack of demographic difference between MoP and CoP groups, it is also important to consider ceramic heads more often being used in younger patients due to reports of improved wear rates (36,39).

The current evidence on femoral head size and offset variation in relation to serum metal ion levels remains inconclusive(21). It has been speculated that increasing femoral head size would lead to increased tribocorrosion secondary to increased torque at the trunnion (19,40). However, results from this study failed to identify any significant association with increased ion levels when stratifying based on head size regardless of bearing type. This might be a type 2 error as the subgroups used for head size analysis were relatively small (<10). Hence the result is inconsistent with prior studies (25,30). White et al in their analysis of metal heads found a significant difference between serum cobalt levels in the 36mm group compared to the

32mm group. Similarly, Craig et al found a significant increase in serum cobalt levels in the 36mm group compared to the 28mm group. Interestingly there no significant differences between the 40mm group compared to 28mm group; although this lack of difference may be attributed to increased offset in the 28mm group. Bolland et al conducted a longer term study (mean follow up of 62 mths), they showed high rate of failure and high wear at the trunnion-head interface and passive corrosion of the stem, rising concern with using larger head on a conventional 12 taper (41). The FEA simulation study by Laverniaet al. highlighted the potential influence of head size on trunnionosis. They showed that regardless of head material used, stress levels (underneath the junction between head and trunnion) had a direct correlation to head diameter. Therefore a larger head size could lead to high rate of trunnionsis (40).
There was a significant difference in serum Co levels only when comparing the MoP to CoP groups with extended femoral offset. There were no other significant differences in serum Co or Cr levels between MoP or CoP groups regardless of offset type. This result is in contrast to recent findings and laboratory-based studies demonstrating increased movement at the head-neck junction for higher offsets (19,21). Martin et al found a significant increase in serum cobalt in those with increased offset. Significant differences in increased serum chromium were found only when comparing very high femoral offset (+7 to 9mm) to low offset (-2 to 1mm). However, it should also be noted that the average time to follow-up in this study was 28.7 (24.4-58.9) months. The differences in our study may not yet be apparent at six months.

There are a number of limitations to this study. Firstly, the baseline serum metal levels were taken from 50 pre-operative patients unrelated to our study cohort. Ideally pre-operative serum levels in our study cohort should have been used. Hence, a second comparator was found in the CoP group as the prosthesis was without any sources of Cobalt or Chromium. Secondly, this study did not account for potential confounders such as medical comorbidly such as renal insufficiency and level of daily activity level. Renal insufficiency is known to affect metal ion levels (42) although there were no patients with major renal disease in our cohort. Differences in occupational exposure, diet and nutritional supplementation are also known to affect ion levels (13,43).

To our knowledge, this is the largest prospective study of metal ion levels concerning trunnionosis in a consecutive cohort based on sample size calculations and power analysis. However, subgroup comparisons concerning variations in implant components only included small numbers in each. The subgroup analyses were likely underpowered, leading to a type 2 error. A study with a larger sample size with adequate power would better reflect the impact of implant specific variations. It is unclear whether a "running-in" period exists as with older metal-on-metal implants where Co and Cr levels gradually stabilise(44). Long term prospective cohort studies suggest that metal ion levels continue to increase with time and did not plateau (26,45). Jacobs et al in a prospective longitudinal study found that at 36 months they were 5-8 times pre-operative levels (45). Therefore, continued surveillance is necessary to determine if serum concentrations of metal ions will increase overtime in our cohort. Future research could focus on identifying those at risk of trunnionosis through detection of early post-operative serum metal ion rises.

CONCLUSIONS

This study allows a number of conclusions to be made. Rises in serum cobalt exist in the early stages post THA. At six months, increases were apparent in Metal-on-Polyethylene THAs when compared to baseline ($p=0.015$) and Ceramic-on-Polyethylene THAs ($p=0.012$). Serum metal ion levels were not affected by implant specific variations.

IMPLICATIONS AND FUTURE DIRECTIONS

To our knowledge, this is the largest prospective study of metal ion levels concerning trunnionosis in a consecutive cohort based on sample size calculations and power analysis. However, subgroup comparisons concerning variations in implant components only included small numbers in each. The subgroup analyses were likely underpowered, leading to a type 2 error. A study with a larger sample size with adequate power would better reflect the impact of implant specific variations.

The baseline levels of serum Cr and Co were taken from an unrelated population sample of 50 health patients who had not yet received THAs at the time of testing. Ideally, baseline pre-operative levels should have been taken from the same population group. This would reduce the effect of confounders. Pre-operatively patients may have had pre-existing elevated levels of metal ions. This may have affected post-operative results, analysis and interpretation.

As alluded to previously this study did not account for potential confounders such as medical comorbidities. Differences in a person's occupational exposure, diet and nutritional supplementation are also known to affect ion levels (13,43). Future studies should account for these confounders.

It is intended for this study to be the first evaluation of a longer term, longitudinal follow-up of serum chromium and cobalt levels. This will provide perspective on how these levels change with time and whether early rises are reflective of exponential deterioration of an implant. It this can be identified then both local and systemic adverse events can be prevented through early intervention such as revision surgery.

Continued surveillance is necessary to determine if serum concentrations of metal ions will increase overtime. Future research could focus on identifying those at risk of trunnionosis through detection of early post-operative serum metal ion rises. It is unclear whether a "running-in" period exists where serum metal ion levels gradually stabilise(44). However, Longer term prospective cohort studies suggest that metal ion levels continue to increase with time and did not plateau (26,45). A previous study found that at 36 months they were 5-8 times pre-operative levels (45).

For now, this study suggests that early rises in serum cobalt do exist in the early stages post THAs in Metal-on-Polyethylene THAs. Further studies should also investigate the impact of various implant components on serum metal ions. Additionally, since clinically significant manifestations of trunnionosis is uncommon; it is of high likelihood that patients in our study will not go on to develop significant symptoms to warrant revision. Hence, future studies should incorporate a larger sample size. Ultimately, if results from further studies become clinically significant then it may help guide management of complications arising from THAs.

REFERENCES

1. Wiles P. The surgery of the osteo-arthritic hip. Br J Surg. 1958 Mar;45(193):488–97.

2. Baker-LePain JC, Lane NE. Relationship between joint shape and the development of osteoarthritis: Curr Opin Rheumatol. 2010 Sep;22(5):538–43.

3. Gandhi R, Perruccio AV, Mahomed NN. Surgical management of hip osteoarthritis. Can Med Assoc J. 2014 Mar 18;186(5):347–55.

4. Karachalios T, Komnos G, Koutalos A. Total hip arthroplasty: Survival and modes of failure. EFORT Open Rev. 2018 May;3(5):232–9.

5. Australian Orthopaedic Association National Joint Replacement Registry. Annual Report. Adelaide: AOA; 2000-2015.

6. Holt G, Hook S, Hubble M. Revision total hip arthroplasty: the femoral side using cemented implants. Int Orthop. 2011 Feb;35(2):267–73.

7. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030: J Bone Jt Surg. 2007 Apr;89(4):780–5.

8. Goldberg JR, Gilbert JL, Jacobs JJ, Bauer TW, Paprosky W, Leurgans S. A multicenter retrieval study of the taper interfaces of modular hip prostheses. Clin Orthop. 2002 Aug;(401):149–61.

9. Porter DA, Urban RM, Jacobs JJ, Gilbert JL, Rodriguez JA, Cooper HJ. Modern Trunnions Are More Flexible: A Mechanical Analysis of THA Taper Designs. Clin Orthop Relat Res. 2014 Dec;472(12):3963–70.

10. Bosker BH, Ettema HB, van Rossum M, Boomsma MF, Kollen BJ, Maas M, et al. Pseudotumor formation and serum ions after large head metal-on-metal stemmed total hip replacement. Risk factors, time course and revisions in 706 hips. Arch Orthop Trauma Surg. 2015 Mar;135(3):417–25.

11. Cooper HJ, Della Valle CJ, Berger RA, Tetreault M, Paprosky WG, Sporer SM, et al. Corrosion at the head-neck taper as a cause for adverse local tissue reactions after total hip arthroplasty. J Bone Joint Surg Am. 2012 Sep 19;94(18):1655–61.

12. Chana R, Esposito C, Campbell PA, Walter WK, Walter WL. Mixing and matching causing taper wear: corrosion associated with pseudotumour formation. J Bone Joint Surg Br. 2012 Feb;94(2):281–6.

13. Cooper HJ, Urban RM, Wixson RL, Meneghini RM, Jacobs JJ. Adverse Local Tissue Reaction Arising from Corrosion at the Femoral Neck-Body Junction in a Dual-Taper Stem with a Cobalt-Chromium Modular Neck: J Bone Jt Surg-Am Vol. 2013 May;95(10):865–72.

14. Weiser MC, Lavernia CJ. Trunnionosis in Total Hip Arthroplasty: J Bone Jt Surg. 2017 Sep;99(17):1489–501.

15. Whitehouse MR, Endo M, Zachara S, Nielsen TO, Greidanus NV, Masri BA, et al. Adverse local tissue reactions in metal-on-polyethylene total hip arthroplasty due to trunnion corrosion: the risk of misdiagnosis. Bone Jt J. 2015 Aug;97-B(8):1024–30.

16. Davis DL, Morrison JJ. Hip Arthroplasty Pseudotumors: Pathogenesis, Imaging, and Clinical Decision Making. J Clin Imaging Sci. 2016 Apr 29;6:17.

17. Mistry JB, Chughtai M, Elmallah RK, Diedrich A, Le S, Thomas M, et al. Trunnionosis in total hip arthroplasty: a review. J Orthop Traumatol Off J Ital Soc Orthop Traumatol. 2016 Mar;17(1):1–6.

18. Hussenbocus S, Kosuge D, Solomon LB, Howie DW, Oskouei RH. Head-Neck Taper Corrosion in Hip Arthroplasty. BioMed Res Int. 2015;2015:1–9.

19. Martin JR, Camp CL, Wyles CC, Taunton MJ, Trousdale RT, Lewallen DG. Increased Femoral Head Offset is Associated With Elevated Metal Ions in Asymptomatic Patients With Metal-on-Polyethylene Total Hip Arthroplasty. J Arthroplasty. 2016;31(12):2814–8.

20. Kwon Y-M. Evaluation of the Painful Dual Taper Modular Neck Stem Total Hip Arthroplasty: Do They All Require Revision? J Arthroplasty. 2016 Jul;31(7):1385–9.

21. Berstock JR, Whitehouse MR, Duncan CP. Trunnion corrosion: what surgeons need to know in 2018. Bone Jt J. 2018 Jan;100-B(1_Supple_A):44–9.

22. Lash NJ, Whitehouse MR, Greidanus NV, Garbuz DS, Masri BA, Duncan CP. Delayed dislocation following metal-on-polyethylene arthroplasty of the hip due to 'silent' trunnion corrosion. Bone Jt J. 2016 Feb;98-B(2):187–93.

23. Barlow BT, Ortiz PA, Boles JW, Lee Y-Y, Padgett DE, Westrich GH. What Are Normal Metal Ion Levels After Total Hip Arthroplasty? A Serologic Analysis of Four Bearing Surfaces. J Arthroplasty. 2017;32(5):1535–42.

24. Malek IA, King A, Sharma H, Malek S, Lyons K, Jones S, et al. The sensitivity, specificity and predictive values of raised plasma metal ion levels in the diagnosis of

adverse reaction to metal debris in symptomatic patients with a metal-on-metal arthroplasty of the hip. J Bone Joint Surg Br. 2012 Aug;94(8):1045–50.

25. Craig P, Bancroft G, Burton A, Collier S, Shaylor P, Sinha A. Raised levels of metal ions in the blood in patients who have undergone uncemented metal-on-polyethylene Trident-Accolade total hip replacement. Bone Jt J. 2014 Jan;96-B(1):43–7.

26. Levine BR, Hsu AR, Skipor AK, Hallab NJ, Paprosky WG, Galante JO, et al. Ten-year outcome of serum metal ion levels after primary total hip arthroplasty: a concise follow-up of a previous report*. J Bone Joint Surg Am. 2013 Mar 20;95(6):512–8.

27. Dyrkacz RMR, Brandt J-M, Ojo OA, Turgeon TR, Wyss UP. The influence of head size on corrosion and fretting behaviour at the head-neck interface of artificial hip joints. J Arthroplasty. 2013 Jun;28(6):1036–40.

28. Pereira X, Moga I, Harrington M, Patel P, Ismaily S, Noble P. Variables Influencing Tribo-Corrosion Of Modular Junctions In Metal-on-Polyethylene THR. In 2014.

29. Kurtz SM, Kocagöz SB, Hanzlik JA, Underwood RJ, Gilbert JL, MacDonald DW, et al. Do ceramic femoral heads reduce taper fretting corrosion in hip arthroplasty? A retrieval study. Clin Orthop. 2013 Oct;471(10):3270–82.

30. White PB, Meftah M, Ranawat AS, Ranawat CS. A Comparison of Blood Metal Ions in Total Hip Arthroplasty Using Metal and Ceramic Heads. J Arthroplasty. 2016;31(10):2215–20.

31. Qurashi S, Chinnappa J, Rositano P, Asha S. SuperPATH® Minimally Invasive Total Hip Arthroplasty - An Australian Experience. Reconstr Rev. 2016 Jul 15;6(2):43–8.

32. Weiser MC, Chen DD. Revision for taper corrosion at the neck-body junction following total hip arthroplasty: pearls and pitfalls. Curr Rev Musculoskelet Med. 2016 Mar;9(1):75–83.

33. Devlin JJ, Pomerleau AC, Brent J, Morgan BW, Deitchman S, Schwartz M. Clinical features, testing, and management of patients with suspected prosthetic hip-associated cobalt toxicity: a systematic review of cases. J Med Toxicol Off J Am Coll Med Toxicol. 2013 Dec;9(4):405–15.

34. Tan SC, Teeter MG, Del Balso C, Howard JL, Lanting BA. Effect of Taper Design on Trunnionosis in Metal on Polyethylene Total Hip Arthroplasty. J Arthroplasty. 2015 Jul;30(7):1269–72.

35. Campbell PA, Kung MS, Hsu AR, Jacobs JJ. Do retrieval analysis and blood metal measurements contribute to our understanding of adverse local tissue reactions? Clin Orthop. 2014 Dec;472(12):3718–27.

36. Meftah M, Haleem AM, Burn MB, Smith KM, Incavo SJ. Early corrosion-related failure of the rejuvenate modular total hip replacement. J Bone Joint Surg Am. 2014 Mar 19;96(6):481–7.

37. Vundelinckx BJ, Verhelst LA, De Schepper J. Taper Corrosion in Modular Hip Prostheses. J Arthroplasty. 2013 Aug;28(7):1218–23.

38. Walsh CP, Hubbard JC, Nessler JP, Markel DC. Revision of Recalled Modular Neck Rejuvenate and ABG Femoral Implants. J Arthroplasty. 2015 May;30(5):822–6.

39. Wang S, Zhang S, Zhao Y. A comparison of polyethylene wear between cobalt-chrome ball heads and alumina ball heads after total hip arthroplasty: a 10-year follow-up. J Orthop Surg. 2013 Jul 8;8:20.

40. Lavernia CJ, Iacobelli DA, Villa JM, Jones K, Gonzalez JL, Jones WK. Trunnion-Head Stresses in THA: Are Big Heads Trouble? J Arthroplasty. 2015 Jun;30(6):1085–8.

41. Bolland BJRF, Culliford DJ, Langton DJ, Millington JPS, Arden NK, Latham JM. High failure rates with a large-diameter hybrid metal-on-metal total hip replacement. J Bone Joint Surg Br. 2011 May 1;93-B(5):608–15.

42. Estey MP, Diamandis EP, Van Der Straeten C, Tower SS, Hart AJ, Moyer TP. Cobalt and Chromium Measurement in Patients with Metal Hip Prostheses. Clin Chem. 2013 Jun 1;59(6):880–6.

43. US Food and Drug Administration. Information about soft tissue imaging and Metal Ion Testing [Internet]. US Food and Drug Administration; 2019 [cited 2019 Mar 23]. Available from: https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/MetalonMetalHipImplants/ucm331971.htm

44. Sampson B, Hart A. Clinical usefulness of blood metal measurements to assess the failure of metal-on-metal hip implants. Ann Clin Biochem Int J Biochem Lab Med. 2012 Mar 1;49(2):118–31.

45. Jacobs JJ, Skipor AK, Patterson LM, Hallab NJ, Paprosky WG, Black J, et al. Metal release in patients who have had a primary total hip arthroplasty. A prospective, controlled, longitudinal study. J Bone Joint Surg Am. 1998 Oct;80(10):1447–58.