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Original Article

601 metal-on-metal total hip replacements with 36 mm heads a 5 minimum year follow up: Levels of ARMD remain low despite a comprehensive screening program

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ABSTRACT

Background: We conducted a retrospective study to assess the clinical outcome, failure rate, and reason for failure of a large consecutive series of 36 mm MoM Corail/Pinnacle total hip replacements (THRs).
Methods: Between 2006 and 2011, 601 consecutive 36 mm MoM THRs were performed (585 patients). Patients were followed according to the UK Medicines and Healthcare Products Regulatory Agency (MHRA) guidelines. All patients were accounted for and 469 patients (78%) were clinically and radiographically assessed. 328 females and 141 males with a median age of 73 (range 36–94 years) and a median follow up of 7.2 years (range 5.2–9.7 years) were followed. Clinical data included blood cobalt and chromium, Oxford Hip Score (OHS), plain radiograph, ultrasound of hip and intra-operative findings in those patients who had revision surgery.
Results: 56 patients died of causes unrelated to their hip replacement. The mean survivorship of the implant was 92.8% (range 91.6–94%, 95% CI) at a median time to follow up of 84 months (62–113 months).

The functional outcome was good with a median OHS of 38 out of 48 (23–44). The dislocation rate was 0.99%, with all these 6 cases requiring revision.

476 patients had blood tests. 100 patients (21%) had elevated levels of either cobalt above MHRA guidelines of 7 parts per billion (120 and 135 nmol/L respectively for cobalt and chromium). Cobalt was elevated independently of chromium in 75% of the cases (but never vice versa).

The mean cup inclination angle was 42°. Each incremental stem size increase resulted in a decrease in cobalt by 11 nmol/L.

The most common reason for revision was adverse reaction to metal debris (ARMD) (12 cases).
Conclusion: This paper is the largest and longest follow up of 36 mm MoM THRs. Using the MHRA guidelines for follow up, the revision rates of this cohort has remained low compared to other studies, but unacceptably higher than that of other bearing surfaces.
Level of evidence: III.

1. Introduction

The revision rate of the most popular MoM total hip replacement in the world, the Pinnacle MoM hip, varies widely according to the clinical unit. The joint registry with the largest collection of data is the UK NJR which at 10 years has shown revision rates of 15.69 (13.70–17.95 with a 95% confidence

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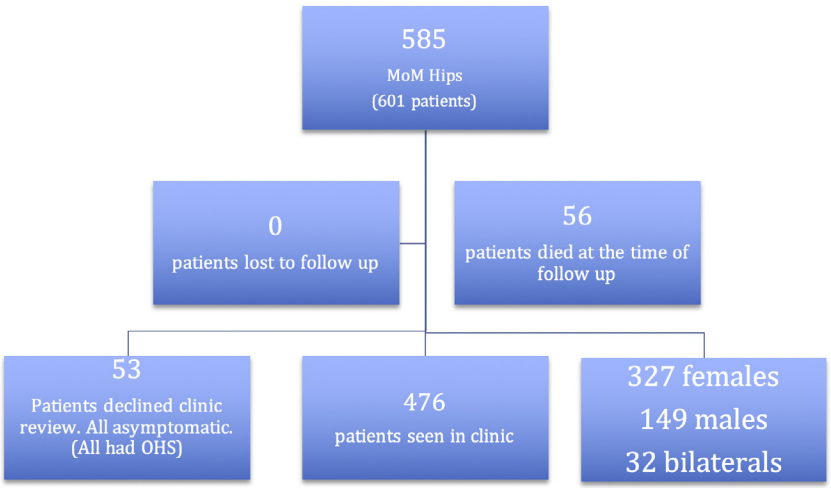

Fig. 1. Patient demographics.

interval) and a cluster of high revision rates in the NE of England.[27] This raw figure includes all head sizes and the XL head.

Reports in the literature have raised concerns about the adverse effects of metal on metal bearings in hip arthroplasty.[2,9,10]

Adverse soft tissue reactions causing local tissue damage,[1] pain,[2,9,11–16] metallosis and metal ions potentially being carcinogenic were the main concerns (ARMD).[17–24] Implants such as the ASR system (DePuy Orthopaedics, Johnson & Johnson, Warsaw, IN, USA) experienced high failure rates and were recalled from the market.[25–28]

The same concerns were extended to all metal on metal bearing hip replacements/resurfacings and in 2012 The Medicines and Healthcare Products Regulatory Agency (MHRA) (UK) issued guidelines to assess the performance and safety of these implants.

The Corail/Pinnacle is the most popularly used THR in the UK with 80,842 implanted according to the National Joint Registry (NJR) of England and Wales. The aim of this study was to assess the clinical performance of the 36 mm head Pinnacle MoM hip replacement. Our objectives were to quantify the clinical outcome, failure rate and cause of revion/failure.

2. Patients and methods

Between 2006 and 2011 a total of 601 (566 patients) MoM THRs were performed at a single center using a 36 mm head. After concerns for MoM THRs were raised and the MHRA had set guidelines, a screening program was set up. Patients with a MoM hip replacement performed at this center were identified using the England and Wales NJR, the electronic hospital patient theatre list system and individual surgeons' logbooks. To ensure inclusion of all patients, every theatre logbook since 2006 was checked for metal on metal hip replacements. This was crosschecked with the number of metal liners provided by the manufacturer (DePuy, Warsaw, IN, USA) to this Hospital Trust.

To ensure that 100% of patients were accounted for, we used the database from our own research department, the NJR of England and Wales, HES (Hospital Episodes Statistics for England and Wales) and the Office for National Statistics (Fig. 1).

2.1. MoM follow-up clinic

All identified patients were sent a letter inviting them to attend a follow up clinic (led by the head surgeon). A standardized follow-up protocol, including the Oxford Hip Score (OHS),[29,30] was used for each patient. Blood was taken for cobalt and chromium levels and a plain radiograph taken. Inclination angle was assessed by the method described by Reito et al.[34]

Patients were allocated into either "asymptomatic hip" or "symptomatic hip" by the reviewing clinician. Symptomatic hips were defined as those with pain around the hip joint and/or mechanical hip symptoms (clicking/clunking or giving way). If the clinician was unsure as to the source of the symptoms during the one-on-one consultation, the patient was allocated to the symptomatic group (Fig. 2).

2.2. Whole blood metal ion levels

Blood for metal ion analysis was sampled with a 21-gauge needle and collected in trace element tubes containing sodium ethylenediaminetetracetic acid (EDTA). Samples were measured by inductively coupled plasma mass spectrometry for whole blood cobalt (Co) and chromium (Cr) levels.[3] Normal ranges were given as 0–120 nmol/L for Co, and 0–135 nmol/L for Cr (equivalent to 0–7 ppb) as set by the MHRA. The cost of a combined cobalt and

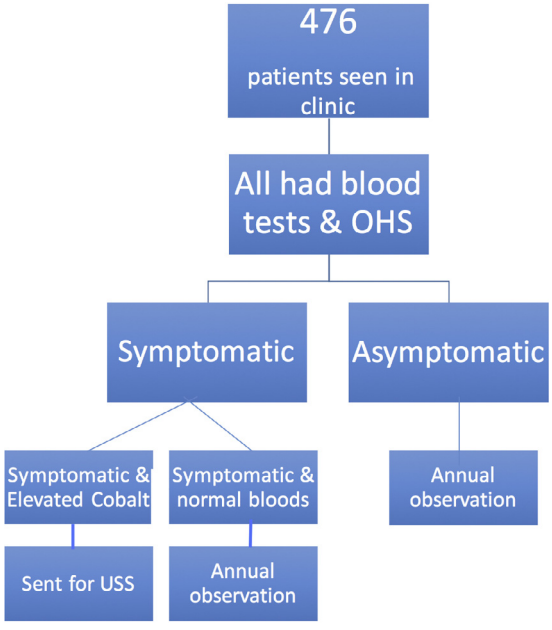

Fig. 2. Clinic treatment flow diagram

chromium assay is $62 and the cost of individual cobalt or chromium is $47.

We highlighted those patients with cobalt and chromium levels greater than 4 ppb (>69 nmol/L and >78 nmol/L respectively). These cut off levels are those postulated by Hart et al.[39] above which there is an increased risk of revision due to ARMD.

2.3. Imaging

Patients are followed up on an annual basis with plain pelvic radiographs and the above blood tests. Symptomatic patients and those with elevated blood metal ions were referred for an ultrasound on the anterior and lateral aspects of the painful hip with a high frequency probe of 9–13 MHz (Sonoline Antares – Siemens). A single radiologist with an interest and experience in ARMD performed this. Ultrasound has been shown to be a reliable diagnostic tool in the assessment of ARMD.[49–51]

2.4. Sources of funding

All MoM hip follow up clinics were paid for by DePuy-Johnson & Johnson.

2.5. Definition of ARMD

Joints were defined as having ARMD in the presence of

1. Macroscopic evidence of metal debris in the synovium/surrounding tissue at the time of revision.
2. The presence of a pseudo-tumor or pseudocapsule at the time of revision.
3. Histological evidence of ALVAL as described by Amstutz.[16]

If dislocation occurred in the absence of the above 3 it was counted as a true independent dislocation. Infection was ruled out with clear samples from at least 5 individual samples taken from the time of revision.

2.6. Revisions

All decisions to revise were made by and performed by the senior authors (SY, AJS). Clear indications were those patients that were symptomatic and had elevated metal ions and/or abnormal ultrasound findings (pseudotumour/pseudocapsule or soft tissue destruction). Stems were retained when well fixed with no signs of infection and with no macroscopic evidence of neck taper damage. Infection was eliminated by low C-reactive protein (CRP)/erythrocyte sedimentation rate (ESR) and white cell count (WCC). All cups were removed and sent to the London Retrieval Unit at Imperial College, London, for analysis (this does not form part of this study).

All soft tissue histological analysis was graded for ALVAL as set by Amstutz and co-workers.[12]

3. Results

Between January 2006 and August 2011, 601 sequential MoM hip replacement operations were performed in 585 patients (32 bilateral MoM THRs). The sizes of bearings were 36 mm in all cases. The femoral implant was the Corail in four forms: 351 standard offset collared [KA], 135 standard offset collarless [KS], 77 varus neck implants [KLA] and 38 high offset [HO] (DePuy-Johnson & Johnson) stems.

There were 328 female and 141 male patients in this group (32 bilateral hips) [312 hips in females and 121 in men]. The average age (median) at follow up was 80 years and the average age of primary surgery was 73 years (36–94 years).

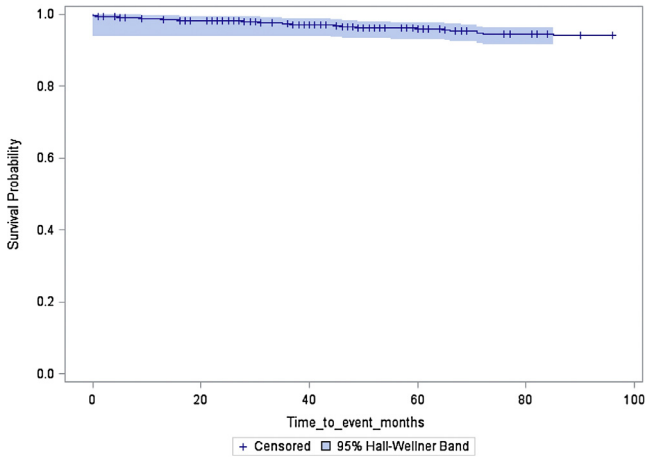

Fig. 3. Kaplan–Meier survivorship curve.

53 patients (53 hips) were contacted by telephone, as they were unable or unwilling to attend the clinic. Oxford Hip Scores and a symptomatic history were taken but no bloods were obtained. All of these reported themselves as being asymptomatic.

56 out of the 585 patients died more than 30 days after hip replacement and of causes unrelated to their hip replacement (Fig. 1) and no patients were lost to follow up. The mean survivorship of the implant was 92.8% (range 91.6–94%, 95% CI) at a median time to follow up of 7.2 years (range 5.2–9.7 years) (Fig. 3 and Table 1).

In those patients still alive and unrevised at the time of follow up, the functional outcome was very good with a median OHS of 38 out of 48 (23–44). The dislocation rate was 0.99%, with all of these requiring a minimum of open reduction.

Of the 469 patients that had blood tests, 100 patients (21%) had elevated levels of either cobalt and/or chromium above the level described in the MHRA medical device alert on MoM[52] hips of 7 parts per billion (120 and 135 nmol/L respectively for cobalt and chromium). Cobalt was elevated independent of chromium levels in 75% of cases. Chromium was never independently elevated.

The mean cup inclination angle was 42°. Increasing stem size inversely correlated with blood cobalt levels (increase in 1 stem size results in a decrease of 11 nmol/L).

The most common reason for revision was for ARMD (Table 2).

Table 1
Kaplan–Meier survivorship with 95% CI.

Means and medians for survival time			
Mean[a]	Median	95% confidence interval	
Estimate	Std. error	Lower bound	Upper bound
92.780	.607	91.591	93.969

[a] Estimation is limited to the largest survival time if it is censored.

Table 2
All reasons of revisions.

Reason for revision	Number revised
Dislocation	6
Infection	4
Patient request	1
Leg length discrepancy	2
ARMD	12
Aseptic loosening – normal bloods/US	4

Table 3
All patients revised for ARMD.

Age	Gender	Symptoms	US findings	Co (mmol/L)	Cr (mmol/L)	Synovial thickening	Osteolysis	Trochanteric pseudotumour	Iliopsoas pseudotumour	ALVAL score
76	F	Groin pain	Cystic mass	5	5	Yes	No	No	No	6
68	F	"Lateral" hip pain	Cystic mass	283	138	Yes	Yes	No	No	5
69	M	Groin pain/clunking	Cystic mass	206	197	Yes	Yes	No	Yes	5
84	F	Groin pain	Muscle loss	133	39	Yes	No	Yes	Yes	9
66	F	Clunking	Nil	356	255	Yes	No	No	Yes	1
87	F	General pain	Muscle loss	130	119	Yes	Yes	No	Yes	8
75	M	No pain	Cystic mass	12	4	Yes	No	No	No	5
80	M	No pain	Cystic mass	14	5	Yes	No	No	No	5
82	F	Groin pain	Nil	22	6	Yes	No	No	No	1
72	F	General pain	Nil	86	7	Yes	Yes	No	No	5
71	F	Groin pain	Nil	152	32	Yes	Yes	No	No	5
81	F	"Clicking"	Nil	131	46	Yes	No	No	No	1

Table 4
US findings of those patients with AMRD.

Grade	US
No pseudotumour	11
Thin walled fluid filled pseudocyst (class 1)	7
Fluid filled pseudocyst with thick walls (class 2a)	3
Pseudotumour with thick/irregular walls and atypical contents (2a)	1
Solid pseudotumour (class 3)	1
Total number of cases	12

3.1. Revision rates

20 patients had already been revised before the start of the MHRA follow up program (17 due to reasons other than adverse reaction to metal debris [ARMD] and 3 to direct ARMD). A further 9 patients with ARMD were picked up in the follow up program (Table 2).

56 patients had died for other reasons not associated with the hip replacement; these patients are included in the survivorship analysis only (Fig. 1).

The mean survivorship was 92.8% (range 91.6–94%, 95% CI) at maximum follow of 10 years (Table 1 and Fig. 3).

29 hips (25 patients) have been revised (Table 2). Of these 29 hips, 12 had been revised for adverse reaction to metal debris (ARMD) (Tables 3 and 4).

3.2. Blood metal ions

Of the 469 patients seen in clinic, 100 had cobalt ions above MHRA guidelines (21%).

In total, 39 patients were symptomatic (8%). 6 patients were both symptomatic and had elevated ions. All of these were revised (see Fig. 4). The remaining 33 symptomatic patients had cobalt and chromium levels within recommended limits.

Of the 469 patients seen in clinic, 430 patients were asymptomatic (92%). 94 of those had cobalt levels above the MHRA guidelines. All of these were offered further ultrasound imaging (which was unremarkable) (Fig. 5). The remaining 336 patients had normal cobalt and chromium levels.

5 (1%) patients had an increased chromium level above MHRA suggested limit (>135 nmol/L). The serum chromium level was never independently elevated without an associated cobalt elevation.

Regressional analysis showed no correlation between cup inclination and blood metal ion levels.

3.3. Radiological findings

All 100 patients with elevated metal ions had an ultrasound scan performed by a musculoskeletal radiologist. 5 had signs of pseudocyst/pseudocapsule and 2 with evidence of soft tissue destruction. These 7 were revised. See Table 4.

The mean cup inclination angle was 42°.[41]

3.4. Oxford Hip Scores

501 OHSs were available (including patients who declined a clinical appointment but were happy for telephone consultation). 462/501 hips (92%) were asymptomatic. 39 (7.8%) were symptomatic.

Sequential OHS were taken at 12 months and then annually after the start of the follow up program. The average OHS for the entire study group at 12 months was 42/48. The average OHS for the entire study group at 60 months was 38/48.

The average OHS of the symptomatic (29) and asymptomatic (42) groups was significantly different ($p < 0.001$).

The OHS did not correlate with the serum cobalt (coefficient 0.05) or the serum chromium (coefficient 0.05). There was no significant difference in the OHS for asymptomatic patients with or

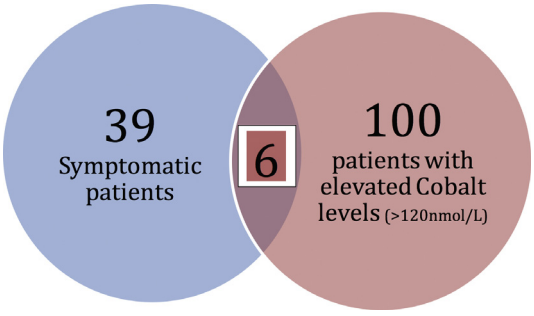

Fig. 4. Symptomatic patients with elevated cobalt levels.

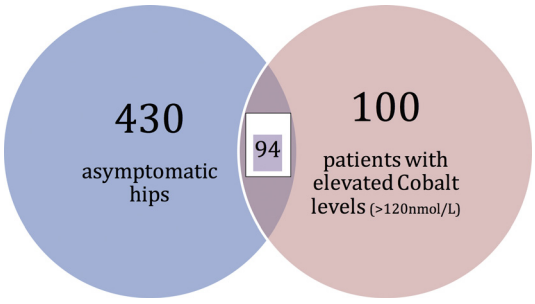

Fig. 5. Asymptomatic patients with elevated cobalt levels.

Table 5
Regressional analysis of stem type, size and cobalt levels.

Model type	Unstandardized coefficients		Tsd coefficient	*t*	Sig.	95% CI for *B*	
	B	Std. error				Lower bound	Upper bound
(Constant)	175.047	33.776		5.183	0.000	108.669	241.424
KLA	−11.074	2.773	−.213	−3.993	.000	−16.524	−5.624
KA	−9.173	14.395	−.031	−.637	.524	−37.463	19.118
KS	6.613	12.562	.026	.526	.599	−18.074	31.3000
KAR	12.323	22.962	.026	.537	.592	−32.803	57.449
KHO	6.064	19.327	.015	.314	.754	−31.918	44.046
Dependent variable: cobalt (mmol/L)							

Model type	Unstandardized coefficients		Standardized coefficients, beta	*t*	Sig.	95% CI for *B*	
	B	Std. error				Lower bound	Upper bound
(Constant)	165.874	33.452		4.959	0.000	100.133	231.616
KLA	−11.074	2.773	−.213	−3.993	.000	−16.524	−5.624
KA	−9.173	14.395	−0.44	−.637	.524	−19.118	37.463
KS	15.786	16.468	0.061	.961	.337	16.498	48.070
KAR	21.496	25.826	0.045	.832	.406	−29.259	72.251
KHO	15.237	22.338	.037	.682	.496	−28.662	59.136
Dependent variable: cobalt (mmol/L)							

without raised metal ions (41 vs. 40, $p = 0.62$). There was no significant difference in the OHS for symptomatic patients with or without raised metal ions (32 vs. 27, $p = 0.19$).

3.5. Stem size/shape and metal ion levels

Regressional analysis showed that the larger (and by inference the stiffer) the implant the less the cobalt released (every increase in stem size was associated with an decrease in serum cobalt by 11 nmol/L). This is a significant difference ($p = 0.001$) (Table 5).

Regressional analysis showed no correlation between the revision rates and the type of stem used (either high off-set [HO], varus [KLA], KA [standard collared], KS [standard collarless]).

Similarly, no one stem type is associated with increased cobalt levels.

4. Conclusion

The aim of this follow up study was to assess the rates of ARMD, revision for any reason and the factors correlating to failure in a cohort of patients that had undergone a THR with the withdrawn MoM liner and head in an otherwise popular and successful hip replacement. The United Kingdom MHRA guidelines were used as a framework for follow up. We contrast the results by Lainiala et al.[42] (Finland) who also used the MHRA guidelines for their study group of 378 hips and also Hug et al.[43] (Duke University, USA) who reviewed arthroplasties or resurfacing with the withdrawn ASR implant (Table 6).

4.1. Survivorship and ARMD

The Kaplan–Meier survivorship shows that the 'mean survivorship' at 10 years is 92.8% (range 91.6–94%, 95% CI) (Fig. 2). This figure is higher than other studies and it should be noted that the majority of revisions were due to issues not related to metallosis. At 7 and 10 years the NJR data[27] shows a 9.05% and 15.69% failure rate respectively. In the long term we expect the number of revision attributable to ARMD to increase as shown by other studies and the NJR.

Even at this relatively early stage of follow up, the levels of revision for ARMD remain lower than other studies (12 cases out of 469 seen in clinic).[42,43] Other studies of this implant indicate that serum cobalt levels are stabilized after 2 years. The results in this study reflect the literature on the Pinnacle-Corail MoM hip (including pooled data) which shows good survivorship at 5 years (99.4%) to 9-year survivorship at 99.4%.[44] This conflicts with a study of the 36 mm MoM by Lainiala et al.[42] in which the 9-year survivorship was 86% (95% CI 82–90%) once the MHRA program had been started. Hug et al. had a 13% revision rate at a mean follow up of their ASR (THRs) at a mean of 45 months (Table 6).

4.2. Metal ion analysis

The serum metal ion levels were unhelpful in predicting who will have an undesired metal reaction and those that may need a revision. The serum cobalt levels showed no correlation in symptoms, OHS or pathology. Of the 12 patients that had a proven ARMD following revision in our study group, just three had raised cobalt levels (range 206–356 nmol/L) and the others did not. The highest cobalt level (1396 nmol/L) was found in an asymptomatic patient with a normal ultrasound and OHS of 48/48.

The chromium level showed no correlation in symptoms or pathology.[39,40] Serum chromium levels were raised above MHRA guidelines in 5 of 469 (1%) patients. Only 1 of these hips was symptomatic hence did not correlate with the OHS. Chromium levels were never independently raised of cobalt. At our test center, not performing the additional chromium assay will save £14.6 per patient and has no bearing on the treatment algorithm. Our patients have had repeat serum metal ions levels and this would be an annual saving of £12,802 for the total cohort follow-up.

Table 6
Comparison of MoM cohort follow-ups.

Study group	Number of implants	Type of implant	Mean time of follow up (years)	Number of revisions	Revisions directly due to ARMD	Mean Co levels (nmol/L)	Mean Cr levels (mmol/L)
This study group	585	36 mm Corail-Pinnacle	7.5	29 (4.9%)	12 (2.0%)	49 (5–1396)	39 (5–680)
Lainiala et al.	203	36 mm Corail-Pinnacle	6.3	34 (17%)	29 (14%)	27.8 (13–32)	20.13 (17–47)
Hug et al.	190	ASR resurfacing and THR	3.3	24 (13%)	14 (%)	250 (34–569)	115 (23–635)

Hart et al.[31] reported that cobalt (rather than chromium) is the more active ion that initiates an inflammatory reaction further adding to the argument that chromium assessment is not necessary.[33]

It is postulated that hard on hard bearing surfaces (MoM and CoC) allow less wettability and therefore greater friction. This in turn transfers increased torque on both the cup/acetabulum and also the neck-taper junctions.[46]

After comparing MoM THRs and resurfacings there is evidence that a singularly elevated cobalt level (without chromium) could be more attributable to corrosion at the head-neck trunnion.[45]

Whether the newly decreased taper size has any influence on the amount of cobalt released is not yet known.[47]

It has also been shown that the levels of cobalt ion release due to corrosion at the head-neck taper also decreases the stiffer and femoral implant.[48] Our study confirmed that the larger and hence stiffer implants had lower cobalt release (each increasing stem size decreased serum cobalt by around 11 nmol/L [$p > 0.01$]).

4.3. OHS and symptomatology

The OHS was useful for finding which patients have a problem with their hip but it cannot predict which ones will have raised metal ions. Neither can it predict which patients will go on to develop an undesired metal reaction (such as ARMD).

4.4. The MHRA guideline

A comprehensive treatment algorithm for MoM hip replacements has already been suggested by the American Hip Society and published in the *Journal of Bone and Joint Surgery (Br)*.[38]

All patients with elevated metal ion levels who expressed concern have been offered a revision operation. To date, only one asymptomatic patient (with normal USS) has requested this option [1/585 (0.17%)].

Despite these results, MoM bearing surfaces are no longer used in our center following the concerns of patients, industry and clinicians. We shall continue to closely follow this cohort of 36 mm bearing MoM hip and report any further changes.

5. Discussion

The Corail-Pinnacle uncemented THR remains a popular and successful hip arthroplasty.[37] MoM THRs have been withdrawn from the market. The MHRA program for monitoring MoM THRs was adopted and the results at a median follow up of 6.4 years show an overall revision rate of 5.4% (of which 2.2% were directly attributable to ARMD). While lower than other similar studies, this failure rate is still unacceptably high and we expect further failures as time progresses.

Conflicts of interest

The authors have none to declare.

References

1. Mahendra G, Pandit H, Klinskey K, Murray D, Gill HS, Athanasou N. Necrotic and inflammatory changes in metal on metal resurfacing hip arthroplasties. *Acta Orthop.* 2009;80:653–659.
2. Catelas I, Wimmer M. New insights into wear and biological effects of metal-on-metal bearings. *J Bone Joint Surg Am.* 2011;93(Suppl2):76–83.
3. http://www.njrcentre.org.uk/njrcentre/AbouttheNJR/Publicationsandreports/Annualreports/tabid/86/Default.aspx.
9. Browne JA, Bechtold CD, Berry D, Hansenn A, Lewallen D. Failed metal-on-metal hip arthroplasties. *Clin Orthop Relat Res.* 2010;468:2313–2320.
10. Natu S, Sidaginamale RP, Gandhi J, Langton DJ, Nargol AV. Histopathological features of periprosthetic soft tissue reactions seen in association with failed metal on metal hip arthroplasties. *J Clin Pathol.* 2012;65(May (5)):409–418.
11. Haddad FS, Thakrar RR, Hart AJ, et al. Metal-on-metal bearings, the evidence so far. *J Bone Joint Surg Br.* 2011;93(May (5)):572–579.
12. Campbell P, Ebramzadeh E, Nelson S, Takamura K, de Smet K, Amstutz H. Histological features of pseudotumour-like tissue from metal-on-metal hips. *Clin Orthop Relat Res.* 2010;468:2321–2327.
13. Clayton RA, Beggs I, Salter DM, et al. Inflammatory pseudotumour associated with femoral nerve palsy following metal-on-metal resurfacing of the hip. A case report. *J Bone Joint Surg Am.* 2008;90:1988–1993.
14. Campbell P, Shimmin A, Waltter L, Solooan M. Metal sensitivity as a case of groin pain in metal-on-metal hip resurfacing. *J Arthroplasty.* 2008;23:2080–2150.
15. Gruber FW, Böck A, Tratting S, Litner F, Ritsch P. Cystic lesion of the groin due to metallosis: a rare long-term complication of metal-on-metal arthroplasties. *J Arthroplasty.* 2007;22(September (6)):923–927.
16. Doorn PF, Mirra JM, Campbell PA, Amstutz HC. Tissue reaction to metal-on-metal hip prostheses. *Clin Orthop Relat Res.* 1996;329(suppl):5187–5205.
17. Keegan GM, Learmouth ID, Case CP. A systematic review comparison of the actual, potential and theoretical effects of cobalt and chromium exposures from industry and surgical implants. *Clin Rev Toxicol.* 2008;38:645–674.
18. Case CP, Lankamer VG, James C, et al. Widespread dissemination of metal debris from implants. *J Bone Joint Surg Br.* 1994;76:701–712.
19. Doherty AT, Howell RT, Ellis LA, et al. Increased chromosome translocation and aneuploidy in peripheral blood lymphocytes of patients having revision arthroplasty of the hip. *J Bone Joint Surg Br.* 2001;83:1075–1081.
20. Parry MC, Bhabra G, Sood A, et al. Thresholds for indirect DNA damage across cellular barriers for orthopaedic biomaterials. *Biomaterials.* 2010;31:4477–4483.
21. Keegan GM, Learmouth ID, Case CP. Orthopaedic metals and their potential toxicity in the arthroplasty patient. A review of current knowledge and future strategies. *J Bone Joint Surg Br.* 2007;89:567–573.
22. Onega T, Baron J, Mackenzie T. Cancer after total hip arthroplasty: a meta-analysis. *Cancer Epidemiol Biomarkers Prev.* 2006;15:1532–1537.
23. Wagner P, Olsson H, Lindgren L, Robertsson O, Ranstam J. Increased cancer risks among arthroplasty patients: 30 year follow-up of the Swedish arthroplasty register. *Eur J Cancer.* 2011;47:1061–1071.
24. Smith J, Dieppe P, Porter M, Blom A. Risk of cancer in first seven years after metal-on-metal hip replacement compared with other bearings and general population: linkage study between the National Joint Registry of England and Wales and hospital episode statistics. *BMJ.* 2012;344:e2383.
25. Seppännen M, Mäkelä K, Virolainen R, Remes V, Pulkinnen P, Eskelinen A. Hip resurfacing arthroplasty: a short term survivorship of 40 hips from the Finnish arthroplasty register. *Acta Orthop.* 2012;83(June (3)):207–213.
26. De Steiger. Hang JR, Miller IN, Graves SG, Davidson DC. Five-year results of the ASR XL acetabular system and the ASR hip resurfacing system: an analysis from the Australian Orthopaedic Association National Joint Registry. *J Bone Joint Surg Am.* 2011;93(December (24)):2287–2293.
27. Link to the NJR UK for 2010 – http://www.njrcentre.org.uk/njrcentre/AbouttheNJR/Publicationsandreports/Annualreports/tabid/86/Default.aspx.
28. Link to the 2010 MHRA alert for metal-on-metal prostheses – http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con079162.pdf.
29. Murray DW, Fitzpatrick R, Rogers K, et al. The use of the Oxford hip and knee scores. *J Bone Joint Surg Br.* 2007;89(8):1010–1014.
30. Dawson J, Fitzpatrick R, Murray D, Carr A. Comparison of measures to assess outcomes in total hip replacement surgery. *Qual Health Care.* 1996;5:81–88.
31. Hart AJ, Quinn PD, Lali F, et al. Cobalt from metal-on-metal hip replacements may be the clinically relevant active agent responsible for periprosthetic tissue reactions. *Acta Biomater.* 2012;8(October (10)):3865–3873.
33. Malek IA, King A, Sharma H, 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;94(August (8)):1045–1050.
34. Reito A, Puolakka T, Paakkala A, Pajamaki J. Assessment of the inter- and intraobserver reliability in the determination of radiographic version and inclination of the cup in metal-on-metal hip resurfacing. *Int Orthop.* 2012;36:519–525.
37. Gioe TJ, Sharma A, Tatman P, Mehle S. Do "premium" joint implants add value?: analysis of high cost joint implants in a community registry. *Clin Orthop Relat Res.* 2011;469(January (1)):48–54.
38. Lombardi AV, Barrack RL, Berned KR, et al. The Hip Society. Algorithmic approach to the diagnosis and management of metal-on-metal arthroplasty. *J Bone Joint Surg Br.* 2012;94-B(suppl A):14–18.
39. Hart A, Sabah SA, Bandi AS, et al. Sensitivity and specificity of blood cobalt and chromium metal ions for predicting failure of metal-on-metal hip replacement. *J Bone Joint Surg Br.* 2011;93(October (10)):1308–1313.
40. Hart AJ, Sabah S, Henckel J, et al. The painful metal-on-metal hip resurfacing. *J Bone Joint Surg Br.* 2009;91(June (6)):738–744.
41. Hart AJ, Buddhdev P, Winship P, Faria N, Powell JJ, Skinner JA. Cup inclination angle of greater than 50 degrees increases whole blood concentrations of cobalt and chromium ions after metal-on-metal hip resurfacing. *Hip Int.* 2008;18(3):212–219.
42. Lainiala O, Eskelinen A, Elo P, et al. Adverse reaction to metal debris is more common in patients following MoM total hip replacement with a 36 mm femoral head than previously thought. *Bone Joint J.* 2014;96-B:1610–1617.
43. Hug K, Watters T, Vail TP. The withdrawn ASR™ THA and hip resurfacing systems: how have our patients fared over 1 to 6 years? *Clin Orthop Relat Res.* 2013;471:430–438.
44. Liudahl AA, Liu SS, Goetz DD, Mahoney CR, Callaghan JJ. Metal on metal total hip arthroplasty using modular acetabular shells. *J Arthroplasty.* 2013;28:867–871.

45. Garbuz DS, Tanzer M, Greidanus NV, et al. The John Charnley Award: Metal-on-metal hip resurfacing versus large-diameter head metal-on-metal total hip arthroplasty: a randomized clinical trial. *Clin Orthop Relat Res.* 2010;468:318.
46. Bishop NE, Hothan A, Morlock MM. High friction moments in large hard-on-hard hip replacement bearings in conditions of poor lubrication. *J Orthop Res.* 2013;31(May (5)):807–813.
47. Langton DJ, Sidaginamale R, Lord JK. Taper junction failure in large-diameter metal-on-metal bearings. *Bone Joint Res.* 2012;1:56–63.
48. Kurtz SM, Kocagöz SB, Hanzlik JA, et al. Do ceramic femoral heads reduce taper fretting corrosion in hip arthroplasty? A retrieval study. *Clin Orthop Relat Res.* 2013;471(October (10)):3270–3282.
49. Singisetti K, Raju P, Langton D, Nargol A. Ultrasound is reliable in the diagnosis of adverse reaction to metal debris following metal on metal arthroplasty. http://www.bjjprocs.boneandjoint.org.uk/content/94-B/SUPP_XXXVII/550?related-urls=yes&legid=jbjsbrproc;94-B/SUPP_XXXVII/550&cited-by=yes&legid=jbjsbrproc;94-B/SUPP_XXXVII/550.
50. Nishii T, Sakai T, Takao M, Yoshikawa H, Sugano N. Is ultrasound screening reliable for adverse local tissue reaction after hip arthroplasty? *J Arthroplasty.* 2014;29(December (12)):2239–2244.
51. Lainiala O, Elo P, Reito A, Pajamäki J, Puolakka T, Eskelinen A. Good sensitivity and specificity of ultrasound for detecting pseudotumors in 83 failed metal-on-metal hip replacements. *Acta Orthop.* 2015;86(June (3)):339–344.
52. MHRA on-line guidelines; https://www.gov.uk/drug-device-alerts/metal-on-metal-mom-hip-replacements-guidance-on-implantation-and-patient-management.

Further reading

53. Macnair RD, Wynn-Jones H, Wimhurst JA, Toms A, Cahir J. Metal ion levels not sufficient as a screening measure for adverse reactions in metal-on-metal hip arthroplasties. *Arthroplasty.* 2013;28(January (1)):78–83.
54. Lombardi Jr AV, Skeels MD, Berend KR, Adams JB, Franchi OJ. Do large heads enhance stability and restore native anatomy in primary total hip arthroplasty? *Clin Orthop Relat Res.* 2011;469(June (6)):1547–1553.
55. Howie DW, Holubowycz OT, Middleton R. Large Articulation Study Group.Large femoral heads decrease the incidence of dislocation after total hip arthroplasty: a randomized controlled trial. *J Bone Joint Surg Am.* 2012;94(June (12)):1095–1102.