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Metal-on-metal hip implants: do they impair renal function in the long-term? A 10-year follow-up study

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Abstract
Introduction The aim of our study was to investigate a potential influence of elevated serumcobalt and serum-chromiumlevels on renal function at minimum 10 years after implantation of a metal-on-metal hip.
Materials and methods Between November 1992 and June 1994 98 patients (44 m, 54 f) with an average age of 56 (22–79) years received a metal-on-metal bearing Metasul™. At the time of the 10-year follow-up, 15 patients had died and 8 were lost to follow-up. The remaining 75 patients had laboratory analysis including serumcreatinine and full blood cell count as well as chromium and cobalt serumlevels.
Results Ten years postoperatively the median serumcreatinine level was 0.86 (0.55–1.51) mg/dl, the serumcreatinine clearance Ccr was in the normal range. The hemogram did not differ from that measured at the time of surgery. The median serumcobalt concentration was 0.75 (0.3–50.10) µg/l and the serumchromium concentration was 0.95 (0.3–58.6) µg/l, 10 years postoperatively.
Conclusion Our long-term data do not show any influence of serum cobalt or chromium concentrations on renal function following total hip arthroplasty.

Keywords Hip arthroplasty · Metal-on-metal · Serummetal-levels · Cobalt · Chrom

Introduction

The linear polyethylene wear rate is thought to be the major cause of osteolysis and long-term failure of total hip arthroplasty [19, 22]. In joint simulator tests metal-on-metal bearings produced 100-fold less wear debris than metal-on-polyethylene couplings. Therefore second generation metal-on-metal bearings were reintroduced to reduce polyethylene particle-induced osteolysis in total hip replacement [3].

The long-term biological and potential toxic effects of cobalt and chromium wear-particles of metal-on-metal articulations are not well known. Unlike the majority of organic chemicals, metals are indestructible and cannot be eliminated from tissues by metabolic degradation; therefore they can only be cleared out by renal or gastrointestinal excretion. Since the capacity for elimination is limited, metals have the tendency to accumulate in the body. Because they may act at the molecular, cellular, tissue or organ level, they often lead to chronic effects like autoimmune and connective tissue diseases, delayed-type hypersensitivity, mutagenicity or carcinogenicity [10, 13].

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Furthermore, cobalt is said to induce hypoxaemia, which is illustrated by the increase in erythropoietine and erythrocyte production [12]. There is evidence that hypoxaemia plays an important role in the pathogenesis of progressive renal disease [17, 18].

Physiologic serumchromium and serumcobalt levels are under the detection limit of 0,3 µg/l of atomic absorption spectroscopy. Investigating the serummetal-levels of patients with metal-on-metal arthroplasties, increased chromium and cobalt serum levels have been identified [9]. Chronic renal failure leads to high metal serum levels and has been shown to be a contraindication to metal-on-metal articulations [8]. Our study was undertaken to investigate the potential negative long-term effects on kidney function resulting from cobalt and chromium wear in total hip arthroplasties with metal-on-metal bearing.

Materials and methods

Between November 1992 and June 1994 98 patients got hip arthroplasties at our institution using a tapered rectangular titanium stem (Zweymüller™-Alloclassic™; Zimmer GmbH, Winterthur, Switzerland) and a metal-on-metal bearing, made from CoCrMo alloy (Metasul™; Zimmer, Winterthur, Switzerland). The head diameter was 28 mm in all cases. During the study period seven of these patients had bilateral hip replacement using the same type of prosthesis.

Among the examined patients 54 were females and 44 males, with an average age of 56 (22–79) years at the time of operation. At the time of the most recent follow-up, 15 patients had already died. In these cases we noted the date of death, the preoperative diagnosis, the date of the last follow-up and if possible the cause of death. Eight patients were "lost to follow-up", and two patients were bedridden and therefore information was gathered over the phone. Three patients had chronic renal failure prior to implantation of the artificial hip joint and therefore were excluded from the analysis. One of them was dependent on haemodialysis since a chronic pyelonephritis and immunological rejection, and two others had kidney transplantation because of systemic lupus erythematosus and cystic kidney.

The most common preoperative diagnoses were primary osteoarthritis, secondary arthritis due to dysplasia of the hip, avascular necrosis of the femoral head and rheumatoid arthritis.

Preoperatively and at the 10-year follow-up visit blood samples were taken with disposable needles (Becton, Dickinson and Company, Franklin Lakes, NJ) for serum creatinine and full blood analysis. The serum creatinine reference value was given as 0.5–1.1 mg/dl in our laboratory. Using the simplified modification of diet in renal disease (MDRD) formula [15], we estimated the creatinine clearance Ccr to indicate early renal cell destruction. The Ccr-reference value is based on ≥110 ml/min for males and ≥95 ml/min for females at the age of 30; after of year 30 a 10-year step reduction of 10 ml/min was considered.

For serum cobalt and serum chromium analysis, cobalt-free Vacutainer™ needles and Vacutainer™ glass tubes without additives were used for blood collection. The serum levels were determined using a 5100-ZL™ atomic absorption spectrometer (PerkinElmer, Shelton, Conneticut, USA) at a wavelength of 242.5 nm for cobalt and 357.9 nm for chromium. The detection limit is 0.3 µg/l in our laboratory; concentrations below the detection limit were defined as 0.15 µg/l to allow statistical calculation. To avoid any bias of the serum concentrations we excluded patients who had had contralateral total hip replacement, implantation of any additional cobalt- or chromium-containing orthopaedic or dental devices or patients taking vitamins.

All patients were asked to fill in a questionnaire to gather information on possible kidney-disease that might have developed after implantation of the total hip endoprosthesis.

Measurements of continuous variables taken preoperatively and 10 years postoperatively are described by median and range and are compared using the paired *t*-test for variables exhibiting approximately normally distributed changes and the sign test for all other variables. Two-sided *P*-values lower than 0.05 are considered as statistically significant. The SAS system V9.1 (2003 SAS Institute Inc., Cary, NC, USA) was used for statistical analysis.

Results

At the follow-up the median serum cobalt level was 0.75 (0.3–50.10) µg/l and the median serum chromium level 0.95 (0.3–58.6) µg/l, respectively. The median serum creatinine value at 10 years was 0.86 (0.55–1.51) mg/dl, compared to a median serum-creatinine of 0.88 (0.63–1.21) mg/dl ($P = 0.609$) preoperatively (see Table 1). Sixty of our patients had serum creatinine levels within the normal range, while seven patients showed increased levels. Five of them had values below 1.5 mg/dl, but two patients clearly exceeded the reference limit with a serum creatinine of 1.51 and 1.74 mg/dl, respectively. One of these patients had had elevated serum creatinine levels prior to surgery. The median preoperative serum creatinine level of the other six patients was 1.02 mg/dl and thereby within the upper reference limit. The glomerular filtration-rate Ccr increased from 77.50 (53.46–106.51) ml/min for females and 86.22 (62.47–114.60) ml/min for males to 76.89 (52.03–110.01) ml/min and 87.90 (62.08–154.02) ml/min, respectively ($P < 0.0001$). With a median age of 68 years (female) and

Table 1 Proportion of patients according of their renal function

	Creatinine preoperatively	Creatinine 10 year postoperatively
≤1.10 mg/dl	66	60
1.11–1.50 mg/dl	5	5
>1.50 mg/dl	0	2

66 years (male), the median Ccr-rate was within the age-dependent reference limit 10 years postoperatively.

The preoperative hemograms do not differ from those taken at the 10-year follow-up visit (see Table 2). The median preoperative erythrocyte value was 4.25 (3.15–5.63) × 10²/l compared with 4.50 (3.30–5.60) × 10²/l 10 years postoperatively ($P = 0.011$). The hematocrit and hemoglobin value increased from 38.8 (29.6–51.0 mg/dl) and 125 (105–171) g/l, respectively, to 40.8 (34.9–51.4) mg/dl ($P = 0.003$) and 139 (111–169) g/l ($P < 0.0001$). The preoperative median platelets were 243.000 (160.000–430.000)/l, compared to 252.000 (138.000–499.000)/l ($P = 0.367$) at 10 years.

In the statistical analysis, the red blood count and the Ccr showed a significant increase. Regarding the values, they are all in the normal range, and therefore, though being statistically significant, the changes have no clinical relevance.

Discussion

Baseline information about the in vivo behaviuor of second-generation metal-on-metal articulations has already been given [9, 11], but until now there has been only limited knowledge about the possible adverse effects on renal function due to corrosion products [4, 7, 16]. With respect to the fact that the main elimination mechanism of serum cobalt and serum chromium is renal [12, 14], the aim of our study was to investigate potential negative long-term effects on kidney function resulting from cobalt and chromium wear in total hip arthroplasties with metal-on-metal bearing.

Generally, diet is the main source of exposure to cobalt and chromium [5, 6]. Histological evaluation of rats fed with 100 mg/kg chromium per day showed an increased chromium concentration in the kidney [2]. Also, cases of acute tubular necrosis associated with the use of a chromium picolinate-containing dietary supplement were reported [20, 21]. Considering the in vivo corrosion, a typical surface mass loss with an alloy release rate of 15 µg/cm² per day and a total passive release rate of 30 µg per day could be calculated [7]. Comparing to the total body concentration and dietary food intake it is obvious that the metal released from CoCr implants is not significant for total body concentration in the short term. In an in vitro cytotoxisity test particulate chromium and cobalt–chromium alloy were well tolerated up to 1 mg/ml. Only a 100,000-fold higher cobalt concentration than in patients with metal-on-metal total hip replacements, leads to the development of cytoplasmic vacuolation and extensive cell death [1].

The present study was performed in a series of 98 patients, all getting a uniform implant. The median serum cobalt level was 0.75 (0.3–50.10) µg/l and the median serum chromium level was 0.95 (0.3–58.6) µg/l 10 years postoperatively. A decade after operation time the median serum creatinine [0.86 (0.55–1.51) mg/dl] as well as the creatinine clearance (Ccr) [females: 76.89 (52.03–110.01) ml/min; males: 87.90 (62.08–154,02) ml/min], a more sensitive value for renal function, was within the normal ranges.

To indicate cobalt-induced renal hypoxaemia, the red blood cell accumulation model was chosen in this study. All of our patients had a normal hemogram, and there was no elevated erythrocyte production or any other change in the full blood count. Statistically, the red blood count increased significantly (see Table 2), but it must be considered that the measured values are all in the normal range;

Table 2 Hemogram and renal function preoperative—10 year postoperatively

	Preoperative	10 years postoperatively	*P*-value
Serum creatinine[a] (0.5–1.1 mg/dl)	0.88 (0.55–1.51) mg/d	0.86 (0.63–1.21) mg/dl	$P = 0.609$
Creatinine clearance[a,b] (Ccr)	Females: 77.50 (53.46–106.5) ml/min Males: 86.22 (62.47–114.6) ml/min	Females: 76.89 (52.03–110.0) ml/min Males: 87.90 (62.08–154.02) ml/min	$P < 0.001$
Erythrocytes[a] (4.00–5.00 10²/l)	4.26 (3.18–5.63) 10²/l	4.50 (3.30–5.60) 10²/l	$P = 0.011$
Hematocrit[a] (38.0–44.0 mg/dl)	38.8 (29.6–51.0) mg/dl	40.8 (34.9–51.4) mg/dl	$P = 0.003$
Haemoglobin[a] (125–160 g/l)	125 (105–171) g/l	139 (111–169) g/l	$P = 0.002$
Platelets[a] (150.000–360.000/l)	243.000 (160.000–430.000)/l	252.000 (138.000–499.000)/l	$P = 0.368$

[a] Reference values from the medical laboratory of the University of Vienna, AKH Wien

[b] The Ccr reference value is based on ≥110 ml/min for male and ≥95 ml/min for female at the age of 30; after year 30 a 10-year step reduction of 10 ml/min was considered

therefore these changes have no clinical relevance. Furthermore, renal hypoxaemia is a main trigger for tubulointerstitial fibrosis [17, 18]. Seven of our patients showed elevated creatinine levels 10 years after surgery. The median preoperative serum-creatinine level of these patients was 1.02 (0.81–1.21) mg/dl and thereby within upper reference limit at the time of hip replacement. The median cobalt level of these seven patients was 0.90 (0.15–8.40) μg/l, and the median chromium concentration was 1.4 (0.50–4.10) μg/l. In addition, increased age may be associated with elevated creatinine levels. The average age in this subgroup was 81 (73–89) years.

The study cohort includes seven patients getting bilateral metal-on-metal articulation during the follow-up period. Their median serum creatinine [0.88 (0.62–1.20) mg/dl] and creatinine clearance (Ccr) [females: 75.69 (52.5–103.0) ml/min; males: 79.32 (62.08–96.56) ml/min] as well as their hemograms did not differ from the values of patients with unilateral hip arthroplasty.

Three patients were suffering from chronic renal failure at the time of follow-up. In all three cases the diagnosis of renal insufficiency had been established prior to surgery. All patients had undergone kidney transplantation before the time of hip surgery. One patient suffered from a rejection and is now subject to hemodialysis. The cobalt and chromium levels of one of these patients highly exceeded the reference values, with cobalt at 60.6 μg/l and chromium at 20.5 μg/l. The two others had values within the normal range. An established diagnosis of renal failure or any preliminary stage of chronic renal failure should be deemed to be contraindications for the use of metal-on-metal articulations [8].

One patient had markedly elevated serum levels (cobalt, 50.10 μg/l; chromium, 58.6 μg/l) probably due to impingement. In this case, we could not detect a decreased renal function; the serum creatinine was 0.91 mg/dl and the creatinine clearance (CCr) was 71.71 ml/min, both within the normal range.

A limitation of our investigation is the evaluation of renal function by laboratory analysis only. There are no histological sections to illustrate changes in the renal parenchym caused by cobalt-induced hypoxaemia of our very patients. However, there is a report on histology of two kidney transplants, which had failed in patients with increased serum metal levels (cobalt, 134.4 μg/l, chromium, 48.7 μg/l) [8]. These two cases were not related to a toxic effect but due to an immunological rejection.

The small number of patients is a further limitation of the study. Its strengths, on the other hand, were the use of a uniform implant and the incorporation of 10-year post-surgical data.

This is, to our knowledge, the first minimum 10-year follow-up publication with regards to possible negative effects on renal function after second-generation metal-on-metal hip replacement. In this study group, no diagnosis of acute or chronic renal failure was established in any of the analysed patients in the 10-year period since the arthroplasty. Although the number of patients is rather small, we do not have evidence of an increased rate of renal failure in the long run.

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