

Supplementary article data

Worse health-related quality of life and hip function in female patients with elevated chromium levels

A prospective study of 659 patients with a recalled THR metal-on-metal implant

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Supplementary data

The effect of blood metal ions on PROMS in patients with the ASR XL THR

^a Beta coefficient is the expected change in outcome that accompanies one unit change in exposure.

^b 95% confidence intervals of the beta coefficient.

^c Significant p-values.

Table 3. The effect of Co and Cr concentrations ≥ 7 ppb on VAS Pain score

	Beta coefficient ^a	95% CI ^b	p-value
Age	0.01	-0.01 to 0.02	0.4
Gender	0.07	-0.30 to 0.44	0.7
Contralateral articulation	0.35	-0.17 to 0.87	0.2
Chromium	-0.36	-1.9 to 1.1	0.6
Cobalt	-0.14	-0.56 to 0.28	0.5
Chromium: Gender	0.94	-0.85 to 2.7	0.3

Table 4. The effect of Co and Cr concentrations ≥ 10 ppb on VAS Pain score

	Beta coefficient ^a	95% CI ^b	p-value
Age	0.01	-0.01 to 0.02	0.4
Gender	0.06	-0.30 to 0.41	0.8
Contralateral articulation	0.45	-0.07 to 0.97	0.09
Chromium	0.10	-1.6 to 1.8	0.9
Cobalt	-0.48	-1.0 to 0.04	0.07
Chromium: Gender	2.0	-0.30 to 4.3	0.09

Table 5. The effect of Co and Cr concentrations ≥ 7 ppb on the UCLA activity score

	Beta coefficient ^a	95% CI ^b	p-value
Age ^c	-0.05	-0.07 to -0.03	< 0.001
Gender ^c	-0.56	-0.98 to -0.14	0.01
Contralateral articulation	-0.60	-1.2 to < 0.001	0.05
Chromium	1.5	-0.20 to 3.25	0.08
Cobalt	0.06	-0.43 to 0.54	0.8
Chromium: Gender ^c	-3.1	-5.1 to -1.0	0.003

Table 6. The effect of Co and Cr concentrations ≥ 10 ppb on the UCLA activity score

	Beta coefficient ^a	95% CI ^b	p-value
Age ^c	-0.05	-0.07 to -0.03	< 0.001
Gender ^c	-0.60	-1.0 to -0.19	0.004
Contralateral articulation ^c	-0.66	-1.3 to -0.07	0.03
Chromium	1.9	-0.003 to 3.8	0.05
Cobalt	0.04	-0.55 to 0.64	0.9
Chromium: Gender ^c	-4.6	-7.3 to -2.0	< 0.001

The effect of blood metal ions on PROMS in patients with the ASR HR**Table 7. The effect of Co and Cr concentrations ≥ 7 ppb on the EQ-5D index**

	Beta coefficient ^a	95% CI ^b	p-value
Age	< 0.001	-0.00 to 0.00	0.6
Gender	-0.03	-0.08 to 0.02	0.3
Contralateral articulation	-0.04	-0.11 to 0.03	0.2
Chromium	-0.07	-0.31 to 0.16	0.6
Cobalt	0.08	-0.08 to 0.24	0.3
Chromium: Gender	-0.15	-0.37 to 0.06	0.2

Table 8. The effect of Co and Cr concentrations ≥ 10 ppb on the EQ-5D index

	Beta coefficient ^a	95% CI ^b	p-value
Age	<0.001	-0.00 to 0.00	0.7
Gender	-0.04	-0.09 to 0.01	0.1
Contralateral articulation	-0.05	-0.11 to 0.02	0.2
Chromium	-0.05	-0.30 to 0.21	0.7
Cobalt	-0.03	-0.15 to 0.10	0.7
Chromium: Gender	-0.01	-0.30 to 0.28	1

Table 9. The effect of Co and Cr concentrations ≥ 7 ppb on the Harris hip score

	Beta coefficient ^a	95% CI ^b	p-value
Age	0.07	-0.09 to 0.23	0.4
Gender ^c	-3.6	-7.1 to -0.09	0.04
Contralateral articulation	-2.6	-7.2 to 2.0	0.3
Chromium	-4.1	-20.4 to 12.2	0.6
Cobalt	6.3	-4.8 to 17.4	0.3
Chromium: Gender	-11.8	-27.0 to 3.3	0.1

Table 10. The effect of Co and Cr concentrations ≥ 10 ppb on the Harris hip score

	Beta coefficient ^a	95% CI ^b	p-value
Age	0.07	-0.09 to 0.22	0.4
Gender ^c	-3.9	-7.3 to -0.52	0.02
Contralateral articulation	-2.5	-7.0 to 2.0	0.3
Chromium	-5.6	-23.2 to 12.1	0.5
Cobalt	4.3	-4.3 to 13.0	0.3
Chromium: Gender	-17.0	-36.9 to 2.9	0.09

Table 11. The effect of Co and Cr concentrations ≥ 7 ppb on VAS Pain score

	Beta coefficient ^a	95% CI ^b	p-value
Age	-0.01	-0.03 to 0.01	0.2
Gender	-0.03	-0.43 to 0.38	0.9
Contralateral articulation	0.21	-0.33 to 0.74	0.5
Chromium	0.55	-1.3 to 2.5	0.6
Cobalt	-0.92	-2.2 to 0.37	0.2
Chromium: Gender	1.3	-0.49 to 3.0	0.2

Table 12. The effect of Co and Cr concentrations ≥ 10 ppb on VAS Pain score

	Beta coefficient ^a	95% CI ^b	p-value
Age	-0.01	-0.03 to 0.01	0.2
Gender	0.05	-0.35 to 0.46	0.8
Contralateral articulation	0.24	-0.30 to 0.77	0.4
Chromium	-0.22	-2.3 to 1.9	0.8
Cobalt	-0.03	-1.1 to 1.0	1
Chromium: Gender	0.95	-1.4 to 3.3	0.4

Table 13. The effect of Co and Cr concentrations ≥ 7 ppb on the UCLA activity score

	Beta coefficient ^a	95% CI ^b	p-value
Age ^c	-0.04	-0.06 to -0.02	< 0.001
Gender ^c	-0.70	-1.2 to -0.24	0.001
Contralateral articulation	-0.26	-0.87 to 0.34	0.4
Chromium	0.69	-1.5 to 2.9	0.3
Cobalt	-0.45	-1.9 to 1.0	0.6
Chromium: Gender	-0.76	-2.8 to 1.3	0.6

Table 14. The effect of Co and Cr concentrations ≥ 10 ppb on the UCLA activity score

	Beta coefficient ^a	95% CI ^b	p-value
Age ^c	-0.04	-0.06 to -0.02	< 0.001
Gender ^c	-0.76	-1.2 to -0.31	0.001
Contralateral articulation	-0.29	-0.89 to 0.32	0.4
Chromium	-1.3	-3.6 to 1.1	0.3
Cobalt	0.31	-0.85 to 1.5	0.6
Chromium: Gender	0.72	-1.9 to 3.4	0.6

Appendix

Threshold for the blood metal ion levels

The thresholds for the blood metal ion levels, 7 and 10 ppb, were set according to previously published results (Kwon, 2014; MHRA, 2012). We made 2 attempts to confirm the feasibility of these thresholds.

First, we attempted to estimate the threshold using piecewise linear regression splines (Muggeo, 2013). We did observe significant associations between the PROMs used and the blood metal ion levels, but the ion levels explained only fractions

of the observed PROM values. The low signal-to-noise ratio probably made a major contribution to the failure of this model to converge and produce threshold estimates.

The depiction of the relationship between the blood metal ion levels and PROMs is demonstrated for the readers using restricted cubic splines. The thresholds used are justified to a certain extent by the depicted splines, but this should be interpreted with caution.

Muggeo V M R. Estimating regression models with unknown break-points. *Statistics in Medicine* 2003; 22: 3055–71.

The EQ-5D index

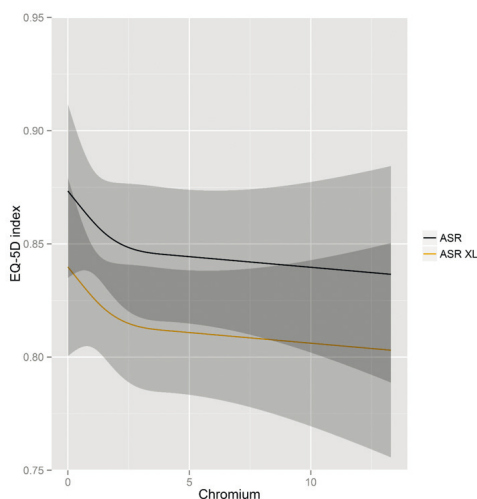


Figure 5. The relationship between the chromium ion levels (in ppb) and EQ-5D index in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

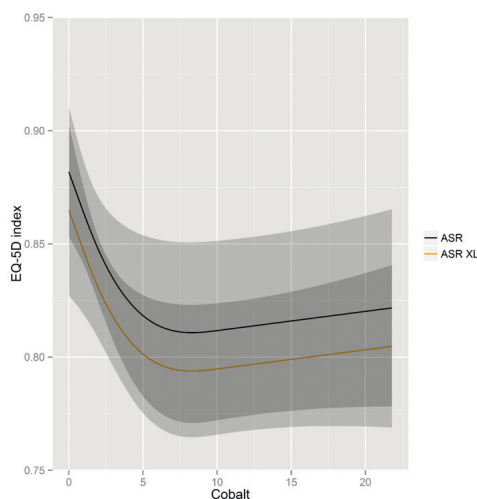


Figure 6. The relationship between cobalt ion levels (in ppb) and EQ-5D index in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

The Harris hip score

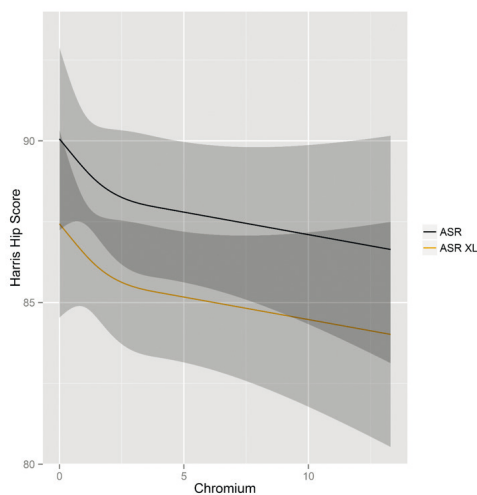


Figure 7. The relationship between the chromium ion levels (in ppb) and Harris hip score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

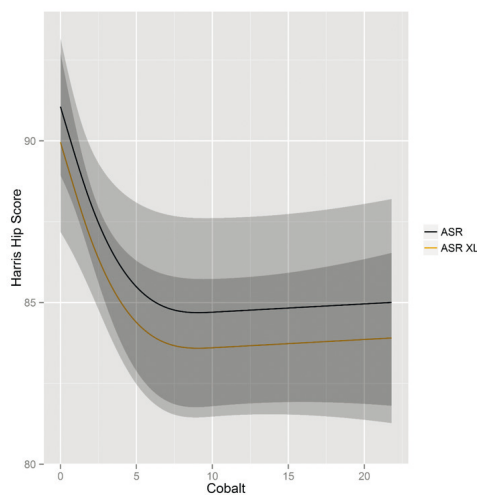


Figure 8. The relationship between cobalt ion levels (in ppb) and Harris hip score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

The VAS Pain score

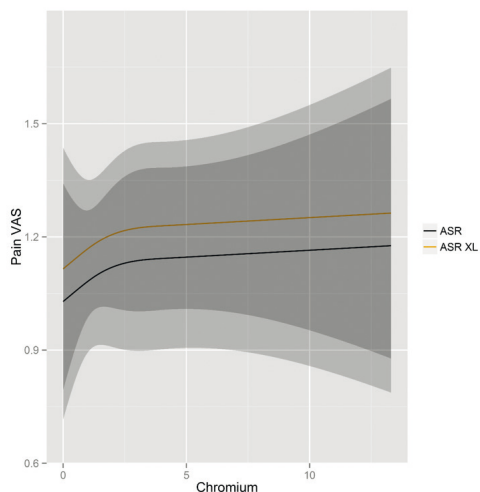


Figure 9. The relationship between chromium ion levels (in ppb) and VAS Pain score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

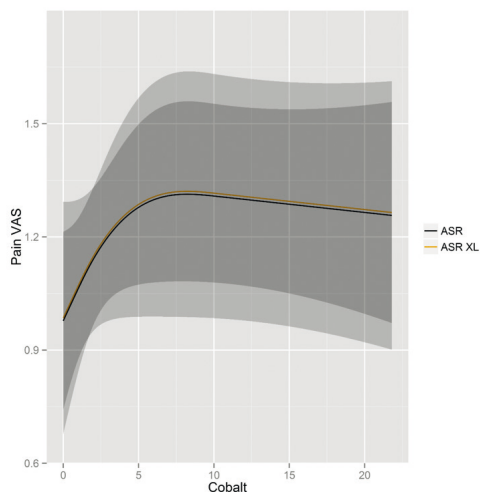


Figure 10. The relationship between cobalt ion levels (in ppb) and VAS Pain score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

The UCLA activity score

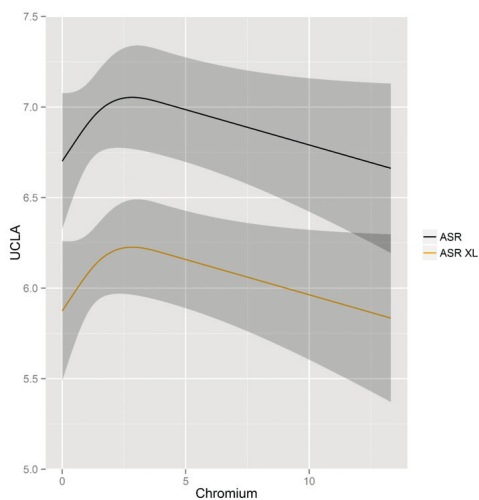


Figure 11. The relationship between chromium ion levels (in ppb) and UCLA score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.

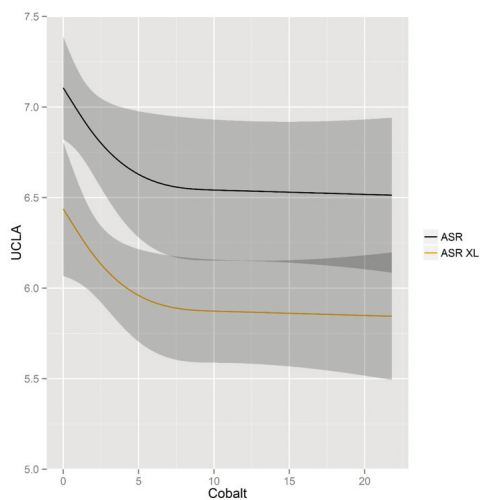


Figure 12. The relationship between cobalt ion levels (in ppb) and UCLA score in patients with the ASR HR prosthesis and in patients with the ASR XL THR prosthesis.