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Metal-on-Metal Hip Replacement: MRI Signal Intensities of Different Body Tissues and Their Relations to Blood Metal Ion Levels

Einat Slonimsky MD[1,5]*, Tammar Kushnir PhD[1,5]*, Assaf Kadar MD[2,5], Aharon Menahem MD[2,5], Alon Grundshtein MD[2,5], Steven Velekes MD[3], Merav Lidar MD[4], Shmuel Dekel MD[4] and Iris Eshed MD[1,5]

[1]Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer, Israel
[2]Department of Orthopedic Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[3]Department of Orthopedic Surgery, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[4]Department of Orthopedic Surgery, Assuta Medical Center, Tel Aviv, Israel
[5]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv Israel

ABSTRACT: **Background:** Metal-on-metal total hip prostheses (MoM-THR) have been shown to produce hypersensitivity reactions and fluid collection (pseudotumor) by the hip as well as high blood metal ions levels (BMILs).

Objectives: To evaluate the magnetic resonance imaging (MRI) signal-to-noise ratio (S/N) in selected body tissues around the hip of patients who underwent MoM hip replacement and to correlate to BMILs.

Methods: Sixty-one MRI hip examinations in 54 post-MoM-THR patients (18 males, 36 females, mean age 65 years) were retrospectively evaluated independently by two readers. The mean S/N ratio in a region of interest was calculated for periprosthetic pseudotumor collection (PPC), the bladder, fat, and muscle on axial T1w, FSE-T2w, and short tau inversion recovery (STIR) sequences on the same location. BMILs were retrieved from patient files.

Results: PPC was detected in 32 patients (52%) with an average volume of 82.48 mm^3. BMIL did not correlate with the presence of PPCs but positively correlated with the PPC's volume. A trend for positive correlation was found between BMILs and S/N levels of STIR images for muscle and bladder as well as for PPC and cobalt levels. A trend for correlation was also seen between BMIL with PPC's T1 w S/N.

Conclusions: Alteration of MRI S/N for different hip tissues showed a tendency for correlation with BMILs, possibly suggesting that metal deposition occurs in the PPC as well as in the surrounding tissues and bladder.

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KEY WORDS: signal intensity, signal-to-noise ratio (S/N), metal-on-metal total hip replacement (MoM-THR), blood metal ions, pseudotumor

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*The first and second authors contributed equally to this study

Contemporary metal-on-metal (MoM) total hip replacement (THR) implants have become increasingly popular among younger populations that require hip replacement surgery. One of the benefits of MoM-THR is the reported long-term low wear rate [1]. However, release of metal debris from this type of implant, in which the metal is usually an alloy of cobalt and chromium, was reported to cause a soft tissue disease with the formation of periprosthetic fluid collection. This phenomenon was termed periprosthetic pseudotumor collection (PPC) or inflammatory pseudotumor [2]. Other accepted terms for this phenomenon include aseptic, lymphocyte-dominated vasculitis-associated lesions (ALVAL) [3] and adverse reactions to metal debris (ARMD) [4].

The pathogenesis of a PPC formation is not fully understood [5]. The common theory is that a corrosive process leads to shedding of metal ions around the implant, which induces an immunological response that results in its formation. Sheared metal particles also diffuse into the blood. Elevated metal ion levels have been detected in the urine [5] and organs [6] of patients with MoM prostheses.

Disseminated concentrations of cobalt and chromium have raised concerns about cellular toxicity, chromosomal damage, and adverse local soft tissue reactions [7]. Thus, the formation of periprosthetic complications as well as elevated blood metal ion levels have raised concern regarding the long-term safety of MoM prostheses [8].

Specific imaging modalities used to detect abnormal soft tissue reaction include magnetic resonance imaging (MRI) and ultrasound. MRI is excellent for assessing soft tissues, but susceptibility artifacts from the metal components of the MoM hip prosthesis reduce image quality [9]. This difficulty led to the development of dedicated MRI sequences for reducing metallic artifacts, thus allowing for visualization of periprosthetic tissues [10].

PPC is the principal MRI finding in MoM disease. The typical fluid signal intensity (SI) is isointense on T1-weighted

(T1w) and hyperintense on T2-weighted (T2w) images compared to muscle [11]. The SI of the PPC is expected to vary with its content [11]. Paramagnetic metal ions and deposited particles induce paramagnetic/susceptibility relaxation mechanisms on the neighboring water protons. Therefore, if metal ions and metal precipitates are present in the PPC and in the surrounding tissues, the measured MRI SI of these tissues is expected to change [11].

In the current study, we aimed to evaluate the correlation between the SI and size of the PPC and other periprosthetic tissues with blood metal ion levels. We hypothesized that metal ions, which had shed from the prostheses and accumulated in the PPC and in the surrounding tissues of patients after MoM-THR, will modulate SI and will correlate with the patient's blood metal ion levels.

PATIENTS AND METHODS

All sequential MRI examinations that were performed for the evaluation of the hip of patients after MoM-THR in our institution between 2010 and 2012 were retrospectively evaluated for the presence of a PPC and for the SI of the PPC and its surrounding tissues. Blood levels of chromium and cobalt ions recorded within 3 months of the MRI examination were retrieved from patient files.

The retrospective analysis of MRI examinations and data extraction from patient files was approved by the local ethics committee. Informed consent was waived.

MRI EXAMINATIONS

All of the study patients underwent MRI of the pelvis and hip on a 1.5 T MRI unit (Optima, GE Healthcare, Milwaukee, WI, USA) using a body volume coil in a supine position. Imaging protocol consisted of a metal reduction dedicated protocol with sequences with increased pixel bandwidth (620 MHz) and matrix size up to 448 × 336; axial and coronal T1w spin-echo, short tau inversion recovery (STIR) and T2w sequences; T1w: TR/TE =533 /7.7ms, field of view (FOV) = 24 cm, number of excitations (NEX) = 2, slice thickness = 4 mm, Gap = 0 mm, echo train length (ETL) = 4. STIR: TR/TE = 6100/50 ms, TI = 129 ms, FOV = 42 cm, NEX = 2, slice thickness = 4 mm, Gap =1 mm, ETL = 9; T2w: TR /TE= 5789/ 102 ms, FOV = 44 cm, NEX = 2, slice thickness = 4 mm, Gap = 0 mm, ETL = 16.

Minor protocol adjustments were made when required by extrinsic parameters, such as a patient's body habitus.

MRI examinations were evaluated separately by an experienced musculoskeletal radiologist and a 3rd year intern for the presence of a PPC and for tissue SI measurements. Prior to this reading, a learning session on 10 cases that were not part of the MRIs under investigation was conducted to recognize findings indicative of PPC on an MRI and to establish guidelines in the reporting of MRI findings between the readers.

MRI EVALUATION

A PPC was defined as any cystic mass in continuity with the hip joint. Isolated distension or thickening of a non-communicating trochanteric bursa was not considered. Both the size and the SI of the PPC were recorded. The SI was measured by marking a circular region of interest (ROI) with an average size of 160 mm2 on the PPC, bladder, fat, and muscle on axial T1w, STIR, and T2w images. All measurements were performed on the same slice, which was carefully selected to present minimal metal artifacts. For consistency purposes, ROI was placed in all patients in the middle of the collection, bladder, the ipsilateral gluteus maximus muscle, and the fat superficial to this muscle.

Volume of the PPC was estimated using the largest parameters of width, height, and anterior-posterior axis of the PPC.

The results of the two readers were averaged.

For calculation of signal-to-noise ratio (S/N), the average SI of the PPC, bladder, muscle, and fat ROIs was divided by standard deviation of air (noise) on the same slice.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software version 11 (SPSS Inc., Chicago, IL, USA). Significance was assumed at *P* values smaller than 0.05. Pearson's correlation coefficient was computed to assess the relationship between blood metal ion levels and the evaluated parameters, such as PPC volume and tissue S/Ns. Bonferroni correction was used to counteract for multiple comparisons. Two-way mixed analysis (for scoring and raters) intraclass correlation coefficient (ICC) was calculated to assess consistency and to evaluate agreement between the readings of the two readers of SI in the different sequences and tissues. ICC values were interpreted as follows: 0–0.2 = poor agreement, 0.3–0.4 = fair agreement, 0.5–0.6 = moderate agreement, 0.7–0.8 = strong agreement, and > 0.8 = almost perfect agreement.

RESULTS

A total of 61 MRI examinations of the hip from 54 patients (18 males, 36 females; mean age 65 years, range 32–86) were retrospectively evaluated. Forty-seven of them underwent unilateral MoM-THR and seven underwent bilateral MoM-THR (in which the contralateral non-MoM-THR operation was performed before the MoM-THR). Implants were all large-head MoM hip prostheses (ASR; DePuy, Leeds, UK; 49 modular stemmed prostheses, 12 hip resurfacing). The average time from surgery to MRI was 4.1 years (range: 1.9–6.1).

Of the 61 MRI examinations available for evaluation, 32 PPCs were detected on 32 (52%) hips of 30 patients (mean age 65.3 years, 10 males, 20 females). In two subjects with bilateral MoM-THR, bilateral collections were recorded.

Patient characteristics regarding the presence of a PPC and their blood metal levels are summarized in Table 1.

Table 1. Patient characteristics according to the presence of periprosthetic pseudotumor collection

	No PPC (n ± SD)	PPC (n ± SD)
n	29	32
Age (years)*	63.8 ± 10	65.3 ± 10
Volume (mm3)	NA	82.5 ± 95
Co (μg/L)*	33.8 ± 55	49.5 ± 66
Cr (μg/L)*	14.3 ± 25	19.1 ± 26

SD = standard deviation, PPC = periprosthetic pseudotumor collection, Co = cobalt blood ion levels, Cr = chromium blood ion levels, NA = not applicable

*Differences between patients with and without PPC regarding age and Co and Cr were not statistically significant ($P > 0.05$).

BLOOD METAL ION LEVELS AND PERIPROSTHETIC PSEUDOTUMOR COLLECTION

Almost perfect agreement was seen between the two readers in the SI registration with intraclass correlation of 0.89–0.99.

There was a trend toward higher BMIL in patients with a PPC compared with those without, but without statistical significance [Table 1]. There was no correlation between blood metal ion levels and the presence of a PPC (cobalt: $r = 0.74$, $P = 0.50$; chromium: $r = 0.7$, $P = 0.59$).

In patients with PPC, there was a significant correlation between blood metal ion levels and the PPC volume (cobalt/chromium: $r = 0.4/0.6$, $P = 0.05/0.001$). This was also true when applying the Bonferroni correction. No significant correlation was seen between the PPC volume and its S/N.

The average S/N of the evaluated tissues in the patient group is presented in Table 2 and the Pearson correlations between blood metal ions and the tissue S/Ns are summarized in Table 3. Overall, blood cobalt levels significantly correlated with the S/Ns on STIR for the PPC, muscle, and bladder, which was also the case for chromium and the S/Ns of the muscle and bladder. There was a positive significant correlation between the PPC S/N and the metal ion levels on the T1w sequence. These results lost their significance after performing the Bonferroni correction.

DISCUSSION

The high failure rate of MoM-THR is now a well-recognized complication [2,12] with the formation of PPCs [12,13]. A PPC was detected in 52% of our cohort. This percentage is in accordance with its reported incidence of 35–60% on MRI [14-17]. In our cohort, patients with a detected PPC on MRI had higher cobalt and chromium levels compared to those without a PPC, although the difference was not significant, possibly due to the relatively small cohort size. Indeed, Malek and co-authors [17] described a significant difference in the median plasma cobalt and chromium levels between 209 symptomatic MoM-THR patients with and without a PPC. The same was also described by Chang et al. [18] in 156 MoM-THR patients. Conversely, Newton and colleagues

Table 2. Mean signal-to-noise ratios of the patients' selected tissues

	STIR (n ± SD)	T1w (n ± SD)	T2w (n ± SD)
PPC	124.9 ± 75.4	46.7 ± 30	393.2 ± 32
Muscle	33.0 ± 18.2*	49.6 ± 30*	106.8 ± 64
Bladder	170.5 ± 91*	32.5 ± 20*	266.5 ± 101
Fat		23.6 ± 76*	250.0 ± 221

SD = standard deviation, PPC = periprosthetic pseudotumor collection, STIR = short tau inversion recovery

*$P \le 0.05$

Table 3. Pearson's correlation coefficients between blood metal ion levels and signal-to-noise ratios of the selected tissues in the different sequences

		STIR		T1w		T2w	
		r	P	r	P	r	P
PPC	Co	0.50	0.05*	0.36	0.05*	0.22	0.26
	Cr	0.40	0.07	0.45	0.02*	0.14	0.48
Muscle	Co	0.40	0.05*	0.19	0.32	0.38	0.05*
	Cr	0.40	0.04*	0.31	0.12	0.25	0.21
Bladder	Co	0.47	0.01*	0.16	0.4	-0.086	0.66
	Cr	0.39	0.04*	0.25	0.21	-0.10	0.62
Fat	Co			0.13	0.5	0.39	0.04*
	Cr			0.21	0.28	0.28	0.16

PPC = periprosthetic pseudotumor collection, STIR = short tau inversion recovery, Co = cobalt blood ion levels, Cr = chromium blood ion levels

*$P \le 0.05$

[19] showed that PPCs were not associated with blood metal ion levels, and suggested that a patient's susceptibility to metal ions is more influential than blood ion levels.

In the current study, metal ion levels in the blood correlated significantly with the PPC volume. Chang et al. [18] found the same association between blood metal ion levels and the size of the PPC. It is reasonable to assume that increased surface areas in larger PPCs enable a higher diffusion rate of the metal ions into the blood. However, this assumption needs further validation.

In general, correlation was found in the current study between blood metal ion levels and the S/N of PPC, muscle, and bladder on STIR and T1w sequences. However, after using the Bonferroni correction, no significant correlation was seen, potentially indeed correcting for oversampling. However, the fact that correlation between the S/N and metal ion levels in the blood was repeatedly found in many of the parameters evaluated implies that such correlation does exist and its disappearance in the Bonferroni correction might be influenced by the small cohort size. This assumption should be tested in a larger cohort

Biopsies performed on periprosthetic tissue in patients who underwent revision of MoM-THR verified the accumulation of plasma cells in association with macrophages containing metallic wear-debris particles [20]. Metal particles were also found on such periprosthetic tissues by atomic absorption spectrometry [21]. These findings suggest that the tendency for correlation found in our study between tissue S/N and blood metal ion levels might be caused by metal ion deposition within the tissues evaluated. The effect on SI and S/N of the disseminated metal ions or their precipitates is composed of a paramagnetic effect of the dissolved ions and a susceptibility effect of the metal atoms (especially cobalt) aggregates. This could contribute to the reduced SI and S/N found in the PPCs in both STIR and T1-w sequences in our study and to the tendency for correlation between the S/N of the PPC and the levels of metal ions in the blood.

It is difficult to quantitatively predict the expected SI of various tissues examined by MRI sequences since it is affected by many factors in addition to the susceptibility effects of metal aggregates. These factors include the metallic hip itself and the increased protein and water content induced by inflammation. Therefore, the tendency for correlation between blood metal ion level and tissue SI seen in the current study could be also indirectly affected by metal deposition causing tissue inflammation. Still, similar to plasma concentration of metal ions [22], S/N of the periprosthetic tissues may indicate wear occurring in patients with MoM-THR.

In the current study, a tendency for positive correlation was suggested between the S/N of the bladder on STIR and blood metal ions levels. Newton and colleagues [19] used inductively coupled plasma mass spectrometry analysis and demonstrated high urinary metal concentrations of both cobalt and chromium relative to blood concentrations, with threefold levels of cobalt compared to chromium. The authors suggested that chromium had far less renal excretion than cobalt. Although both metals are excreted in the urine, cobalt is transported from local tissues to the blood and eliminated rapidly in the urine by active secretion, whereas chromium is protein-bounded in the plasma and undergoes slow urinary excretion [19]. Another explanation for the high levels of cobalt compared to chromium may be the different percentage of these metals in the prosthesis alloy (63% for cobalt and 30% for chromium).

MRI was shown to have a strong predictive value for the detection of adverse tissue response in the form of PPC around a failed MoM hip arthroplasty and was also predictive of severe tissue damage [23]. The biologic pathway leading to the formation of PPCs is complex. Ion particles released from the implants are cytotoxic once ingested by phagocytosis, accounting for the necrosis seen within the lesions [24]. There are also histological features compatible with a type IV hypersensitivity allergic reaction [3] that eventually lead to the formation of an aseptic PPC collection [20]. Patients with maximal PPC synovial thickness and fluid volume on MRI as well as low signal intensity deposits and soft tissue edema had more tissue damage and higher periprosthetic scores [25]; that is, a more advanced histological reaction on revision operations [23]. The low signal intensity particles, the result of metal shedding, and the aggregates potentially caused the PPC SI reduction seen in our study.

The retrospective nature of the current study and the relatively small cohort are limitations of the current study. Due to the retrospective nature of the study, rigorous standardization of all MRI parameters was precluded.

Histological correlations, which would have strengthened our results, were not carried out.

CONCLUSIONS

In conclusion, although the interpretation of the correlation between S/Ns of the evaluated tissues and blood metal ion levels is complex, our measurements imply a correlation between the levels of metal ions and MRI S/N values for the STIR and T1w sequences. Our results suggest that metal deposition occurs in the periprosthetic fluid collection as well as in the surrounding tissues and the bladder in patients post-MoM-THR.

Correspondence
Dr. I. Eshed
Dept. of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer 5265601, Israel, Tel Hashomer 52621, Israel
Phone: (972-3) 530-2498
Fax: (972-3) 530-2220
email: iriseshed@gmail.com

References

1. Sieber HP, Rieker CB, Kottig P. Analysis of 118 second-generation metal-on-metal retrieved hip implants. *J Bone Joint Surg Br* 1999; 81 (1): 46-50.
2. Boardman DR, Middleton FR, Kavanagh TG. A benign psoas mass following metal-on-metal resurfacing of the hip. *J Bone Joint Surg Br* 2006; 88 (3): 402-4.
3. Willert HG, Buchhorn GH, Fayyazi A, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. *J Bone Joint Surg Am* 2005; 87 (1): 28-36.
4. Langton DJ, Jameson SS, Joyce TJ, Hallab NJ, Natu S, Nargol AV. Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement: a consequence of excess wear. *J Bone Joint Surg Br* 2010; 92 (1): 38-46.
5. Iavicoli I, Falcone G, Alessandrelli M, et al. The release of metals from metal-on-metal surface arthroplasty of the hip. *J Trace Elem Med Biol* 2006; 20 (1): 25-31.
6. Urban RM, Jacobs JJ, Tomlinson MJ, Gavrilovic J, Black J, Peoc'h M. Dissemination of wear particles to the liver, spleen, and abdominal lymph nodes of patients with hip or knee replacement. *J Bone Joint Surg Am* 2000; 82 (4): 457-76.
7. Davies AP, Sood A, Lewis AC, Newson R, Learmonth ID, Case CP. Metal-specific differences in levels of DNA damage caused by synovial fluid recovered at revision arthroplasty. *J Bone Joint Surg Br* 2005; 87 (10): 1439-44.
8. Medicines & Healthcare products Regulatory Agency (MHRA). Medical device alert: all metal-on-metal (MoM) hip replacements. http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con079162.pdf 2010. [Accessed 2015]
9. Laakman RW, Kaufman B, Han JS, et al. MR imaging in patients with metallic implants. *Radiology* 1985; 157 (3): 711-4.
10. Eustace S, Goldberg R, Williamson D, et al. MR imaging of soft tissues adjacent to orthopaedic hardware: techniques to minimize susceptibility artefact. *Clin Radiol* 1997; 52 (8): 589-94.
11. Yanny S, Cahir JG, Barker T, et al. MRI of aseptic lymphocytic vasculitis-associated lesions in metal-on-metal hip replacements. *AJR Am J Roentgenol* 2012; 198 (6): 1394-402.

12. Pandit H, Glyn-Jones S, McLardy-Smith P, et al., Pseudotumours associated with metal-on-metal hip resurfacings. *J Bone Joint Surg Br* 2008; 90 (7): 847-51.
13. Glyn-Jones S, Pandit H, Kwon YM, Doll H, Gill HS, Murray DW. Risk factors for inflammatory pseudotumour formation following hip resurfacing. *J Bone Joint Surg Br* 2009; 91 (12): 1566-74.
14. Wynn-Jones H, Macnair R, Wimhurst J, et al., Silent soft tissue pathology is common with a modern metal-on-metal hip arthroplasty. *Acta Orthop* 2011; 82 (3): 301-7.
15. Mistry A, Cahir J, Donell ST, Nolan J, Toms AP. MRI of asymptomatic patients with metal-on-metal and polyethylene-on-metal total hip arthroplasties. *Clin Radiol* 2011; 66 (6): 540-5.
16. Hart AJ, Satchithananda K, Liddle AD, et al. Pseudotumors in association with well-functioning metal-on-metal hip prostheses: a case-control study using three-dimensional computed tomography and magnetic resonance imaging. *J Bone Joint Surg Am* 2012; 94 (4): 317-25.
17. 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 (8): 1045-50.
18. Chang EY, McAnally JL, Van Horne JR, et al. Relationship of plasma metal ions and clinical and imaging findings in patients with ASR XL metal-on-metal total hip replacements. *J Bone Joint Surg Am* 95 (22): 2015-20.
19. Newton AW, Ranganath L, Armstrong C, Peter V, Roberts NB. Differential distribution of cobalt, chromium, and nickel between whole blood, plasma and urine in patients after metal-on-metal (MoM) hip arthroplasty. *J Orthop Res* 2012; 30 (10): 1640-6.
20. Davies AP, Willert HG, Campbell PA, Learmonth ID, Case CP. An unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. *J Bone Joint Surg Am* 2005; 87 (1): 18-27.
21. Natu S, Sidaginamale RP, Gandhi J, Langton DJ, Nargol AV. Adverse reactions to metal debris: histopathological features of periprosthetic soft tissue reactions seen in association with failed metal on metal hip arthroplasties. *J Clin Pathol* 2012; 65 (5): 409-18.
22. De Smet K, De Haan R, Calistri A, et al., Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing. *J Bone Joint Surg Am* 2008; 90 (Suppl 4): 202-8.
23. Nawabi, D.H., et al., MRI predicts ALVAL and tissue damage in metal-on-metal hip arthroplasty. *Clin Orthop Relat Res* 2014; 472 (2): 471-81.
24. Mabilleau G, Pandit H, Jinnah RH, Sabokbar A. Biological response to common surface bearings used in orthopaedics. *J Surg Orthop Adv* 2008; 17 (1): 34-9.
25. Campbell P, Ebramzadeh E, Nelson S, Takamura K, De Smet K, Amstutz HC. Histological features of pseudotumor-like tissues from metal-on-metal hips. *Clin Orthop Relat Res* 2010; 468 (9): 2321-7.

Capsule

Gut microbiome and serum metabolome alterations in obesity and after weight-loss intervention

Emerging evidence has linked the gut microbiome to human obesity. Liu et al. performed a metagenome-wide association study and serum metabolomics profiling in a cohort of lean and obese young, Chinese individuals. The authors identified obesity-associated gut microbial species linked to changes in circulating metabolites. The abundance of *Bacteroides thetaiotaomicron*, a glutamate-fermenting commensal microbe, was markedly decreased in obese individuals and was inversely correlated with serum glutamate concentration. Consistently, gavage feeding with *B. thetaiotaomicron* reduced plasma glutamate concentration and alleviated diet-induced body-weight gain and adiposity in mice. Furthermore, weight-loss intervention by bariatric surgery partially reversed obesity-associated microbial and metabolic alterations in obese individuals, including the decreased abundance of *B. thetaiotaomicron* and the elevated serum glutamate concentration. These findings identify previously unknown links between intestinal microbiota alterations, circulating amino acids and obesity, suggesting that it may be possible to intervene in obesity by targeting the gut microbiota.

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Eitan Israeli

Capsule

Varus thrust and incident and progressive knee osteoarthritis

To determine if varus thrust, a bowing out of the knee during gait (i.e., the first appearance or worsening of varus alignment during stance), is associated with incident and progressive knee osteoarthritis, Sharma and colleauges undertook an osteoarthritis initiative ancillary study. The incident osteoarthritis sample included 4187 knees (2610 persons); the progression sample included 3421 knees (2284 persons). In knees with osteoarthritis, thrust was associated with progression as assessed by each outcome measure, with adjustment for age, gender, body mass index, and pain on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale. In knees without osteoarthritis, varus thrust was not associated with incident osteoarthritis or other outcomes. After adjustment for alignment, the thrust–progression association was attenuated, but an independent association persisted for partial-grade JSN and JSW loss outcome models. WOMAC pain and alignment were consistently associated with all outcome measures. Within the stratum of varus knees, thrust was associated with an increased risk of progression.

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Eitan Israeli

"No one can terrorize a whole nation, unless we are all his accomplices"

Edward R. Murrow, (1908–1965), American broadcast journalist