



Letters to the Editor

Letter to the Editor on ‘The Prevalence of Positive Findings on Metal Artifact Reduction Sequence Magnetic Resonance Imaging in Metal-on-Metal Total Hip Arthroplasty’: Part 1
**To the Editor:**

We read with great interest the article by Lindgren et al [1]. The authors use ordinal logistic regression (OLR) to correlate predictor variables against primary outcome variables. OLR is used to report proportional odds ratios which authors do not report. The interpretation of the proportional odds ratios relies on the proportional odds (PO) assumption, which is the most important underlying assumption when performing OLR. The PO assumption relies on the equal relationships between each pair of outcome groups. This means that predictor coefficients that describe the relationship between absent pseudotumor (PT) and type I/II/III PT are the same as those that describe the relationship between absent PT/type I and type II/III.

As is the case with assumptions of proportional hazards with Cox regression analysis, the assumption of PO should be investigated in some way. The authors do not take into account the PO, or at least fail to report it. Authors state that predictor variables were assessed while controlling for age and sex. With fixed-sized metal-on-metal bearings, as in the present study, the effect has been reported or there has been a strong trend toward it [2–4]. It is very likely that the effect of gender is not constant across different outcome variable partitions (PT absent vs type I/II/III, absent/type I vs type II/III, and so forth) resulting in the violation of the PO assumption. Hence, gender should be included as a predictor variable on its own, or alternatively, the partially proportional model should be reported.

Another worrisome issue in the present study is the implementation of multivariate linear regression to assess the association between the serum metal ion levels and the predictor variables. As numerous studies have clearly shown and which is also readily seen in Figures 3 and 4, the distribution of untransformed metal ion levels is highly skewed and clearly not normally distributed. The very same issue is seen with Harris Hip Scores. The normality of the error terms is an underlying assumption when performing linear regression analysis. Owing to the nature of the investigated variables, it is inevitable that regression diagnostics will be performed, that is, to investigate the distribution of error terms and residuals to see whether it is appropriate to use linear regression. The authors even report the line of fitted values in the scatter plots (Figs. 3 and 4), but the aforementioned diagnostics are not performed or at least not shown. Moreover, as can be clearly seen in Figures 3 and 4,

there are few extreme outliers, and, due to the estimation method in the linear regression, the results are most likely rendered severely toward significant β coefficients by these outliers.

Finally, we fully agree with the authors and their conclusions. It should be noted, however, that in addition to the aforementioned important issues with statistical methods, the authors' conclusions are based on a patient cohort with loss to follow-up of 87% (379 of 434 hips). The risk of selection bias is, therefore, enormous.

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Letter to the Editor on ‘The Prevalence of Positive Findings on Metal Artifact Reduction Sequence Magnetic Resonance Imaging in Metal-on-Metal Total Hip Arthroplasty’: Part 2
**To the Editor:**

We read with great interest the article by Lindgren et al [1]. Unfortunately, we have concerns regarding the statistical methods used in their study.

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In the study, the authors use ordinal logistic regression (OLR) to correlate predictor variables against primary outcome variables. OLR serves as an extension and alternative to binary logistic regression analysis, should the primary outcome be an ordinal variable (ie, Likert scaled poor/fair/good/excellent) rather than a dichotomous type (yes/no). This is an important distinction, and with it, arises many assumptions that must be met by the data.

The authors use the following: “ordinal nature of the primary outcome” [1]. An important aspect in any research is the correct choice of the outcome or dependent variable related to the study hypothesis. Consequently, we feel that the definition of the main outcome variable has not been chosen in the most optimal manner.

Pseudotumors (PTs) are classified in the study according to Hauptfleisch et al [2]. PTs are, therefore, classified as absent or type I, II, or III. The authors make a bold assumption with the ordinal nature of this PT classification. Although the natural history of PTs has been under investigation for many years now, the evidence of how these periprosthetic masses, referred to as pseudotumors, progress and evolve is still ambiguous [3–7]. Most importantly, there is absolutely no evidence, for or against, as to whether PTs are thick walled or even solid at the beginning of their natural history. Thus, the assumption of ordinal nature is violated. Owing to the nature of the outcome variable, we feel multinomial logistic regression would have been a more appropriate method to use in the present study.

The authors report the correlation of the “presence and severity” of PTs with different predictor variables [1]. However, it remains unclear whether presence and severity are meant to be equal terms since only 1 odds ratio (OR) is reported each time. The use of the terms could also be interpreted to mean that severity indicates the results of OLR, whereas presence indicates the OR when comparing patients without PT with those with any type of PT. Moreover, the authors should have stated that the ORs reported are actually proportional ORs since OLR is used.

Finally, in the present study, serum chromium (Cr) levels were associated with the severity of PT. Therefore, the authors could have stated that the proportional OR for serum Cr levels was 1.10 when treating Cr as a continuous variable. We assume this since no cutoff values or categories were reported. Proportional OR of 1.10 for serum Cr indicates that for a 1-unit increase (1 ppb) in serum Cr, the log odds of type II PT vs absent PT or type I combined are $\log(1.10)$ greater assuming that all other variables in the model are held constant. It is also a matter of discussion whether this 1 ppb increment truly has equally greater proportional OR across all levels of serum Cr when considering the high skewness of metal ion levels. Contradicting this, both serum Cr and cobalt were lower in patients with type I PT compared with those without.

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Response to Letter to the Editor on ‘The Prevalence of Positive Findings on Metal Artifact Reduction Sequence Magnetic Resonance Imaging in Metal-on-Metal Total Hip Arthroplasty’



In Reply:

We appreciate the opportunity to discuss the recent queries from Dr Reito and his associates and feel their concerns and knowledge in the natural history of pseudotumors (PT) can only improve the research in this arena. Despite the concerns brought up by the group, the message of the article is unchanged, and unfortunately, we feel that they may be missing the forest for the trees. Ultimately, we report that positive findings of PT on metal artifact reduction sequence (MARS) magnetic resonance imaging (MRI) are present in both symptomatic and asymptomatic patients who underwent prior metal-on-metal (MoM) total hip arthroplasty (THA). We conclude that all factors must be considered when evaluating the patient with MoM THA. We hope that this message is not lost by the questions raised. Regardless, in response to the concerns of Dr Reito and his associates, we provide the following.

Ordinal Logistic Regression

Reito and his associates express concerns over the use of ordinal logistic regression in our study “The Prevalence of Positive Findings on Metal Artifact Reduction Sequence Magnetic Resonance Imaging in Metal-on-Metal Total Hip Arthroplasty” [1]. They suggest that a multinomial regression model would be more appropriate and remark that the assumption of ordinal nature was violated. They support this argument by stating, “there is absolutely no evidence, for or against, as to whether PT are thick-walled or even solid at the beginning of their natural history.” Given the uncertainty of the

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