

## Normalization of mechanical power to anthropometric indices: impact on its association with mortality in critically ill patients

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# **NORMALIZATION OF MECHANICAL POWER TO ANTHROPOMETRIC INDICES – IMPACT ON ITS ASSOCIATION WITH MORTALITY IN CRITICALLY ILL PATIENTS**

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Dear Editor,

Recently, we showed how mechanical power (MP) was associated with patient-centered outcomes in two large prospective cohorts of critically ill patients under invasive ventilation [1]. Normalization of MP, e.g., to the predicted body weight (PBW), has been put forward [2]. One recent paper showed MP normalized to PBW to be a better predictor of mortality than the absolute MP, at least in ARDS patients [3]. We here report the results of a posthoc analysis of the datasets used in our abovementioned publication [1]. We tested the hypothesis that MP normalized to three common anthropometric indexes, i.e., PBW, body mass index (BMI), and body surface area (BSA) are better predictors of in-hospital mortality than absolute MP in critically ill patients under invasive ventilation.

A detailed description of the methods and models used for the analyses is found in the **eMethods** in the **Supplement**. The two cohorts were merged, and patients were stratified for presence or absence of ARDS at start of ventilation. Multiple imputation was used to impute missing data. Mixed-effect multivariable regression with center as random effect was used for all outcome measures; models were calculated after standardization of continuous variables, and estimates were calculated in relation of one standard deviation increase of predictor to facilitate the comparison.

The two cohorts included a total of 8,191 analyzable patients under invasive ventilation (**eTable 3**). The **Figure** shows the adjusted odds ratios (OR) for in-hospital mortality. Absolute MP,  $MP_{PBW}$ ,  $MP_{BMI}$  and  $MP_{BSA}$  were all three associated with in-hospital mortality; the strongest association was found with  $MP_{BMI}$  and  $MP_{BSA}$ . Similar patterns were found for other outcomes, as shown in the **eFigures 6 to 10** in the **Supplement**. There was no significant interaction

between the effect of MP, absolute or normalized, on primary and secondary outcomes and the presence of ARDS, meaning that presence of ARDS did not affect the associations found for the whole cohort. Sensitivity analyses, as described in **eMethods** yielded similar findings.

The findings of this posthoc analyses add to the first report on normalization of MP [3]. The finding  $MP_{BMI}$  had a stronger association with in-hospital mortality may be surprising [4], since *absolute* lung size will not increase with an increase in body fat. However, higher BMI may increase the risk of atelectasis during ventilation, and such decreasing *functional* lung size [5]. Thus, normalizing MP to BMI may better reflect MP delivered per unit of ventilated lung tissue, i.e., the ‘intensity of ventilation’ [2] – for the same amount of MP, risk of ventilation-induced lung injury increases if the amount of *aerated* lung is lower, or when there is more ventilation heterogeneity. Since there was no significant interaction, the results are consistent across the subgroups, and the overall effect estimate could be seen as the most appropriate estimate of treatment effects within the subgroups. Lack of statistical significance in ARDS patients was probably a result of the lack of power in this subgroup.

This analysis has some limitations. First, it's *posthoc* nature should be considered when interpreting the findings. Residual confounding may also mar the findings, although we attempted to account for this by using several adjustments and models. Since the datasets used in this study are for clinical purposes and the present analysis is a secondary analysis of these data, we cannot guarantee that plateau pressure was collected under standard conditions, i.e., in the absence of spontaneous breathing efforts, at an adequate level of sedation, and with a sufficiently long end-inspiratory pause. Finally,

while several anthropometric indices could be associated with outcomes in patients under invasive ventilation, the idea of the present analysis was to look for the effects of normalizing MP, and not adjusting, for commonly used indices.

If the current findings are confirmed by other investigations, we advise investigators not only to report the absolute MP, but also MP normalized to anthropometric indices like PBW, BMI or BSA.

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**LEGEND TO FIGURE**

**Figure** – Associations between non-normalized mechanical power (MP), MP normalized to PBW, and MP normalized to BMI, and in-hospital mortality in critically ill patients under invasive ventilation, and in patients stratified for the presence or absence of ARDS at start of invasive ventilation.













Abbreviations: MP, mechanical power; PBW, predicted body weight; BMI, body mass index; CI, confidence interval.

Odds ratios were adjusted by relevant covariates known to predict outcome, including age, scaled prognostic score (SAPS II or APACHE IV score), Oxford acute severity illness score (OASIS), Sequential Organ Failure Assessment (SOFA) score on day 1, arterial pH,  $\text{PaO}_2/\text{FiO}_2$ , mean arterial pressure,  $\text{SpO}_2$ , temperature, and arterial  $\text{PaCO}_2$ . \*,  $p$  for interaction between MP and presence of ARDS at start of invasive ventilation (absence of interaction infers that the effect is consistent with the overall effect independent of presence of ARDS).

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Measurements	Survivors	Non-Survivors		Odds Ratio (95% CI)	p value	p for Interaction*
<b>All Patients (n = 8191)</b>						
Absolute MP (J/min)	20.0 ± 8.6	20.7 ± 9.1		1.10 (1.03 - 1.16)	0.002	0.765
MP PBW (J/min/kg PBW)	0.31 ± 0.13	0.33 ± 0.14		1.07 (1.01 - 1.14)	0.022	0.820
MP BMI (J/min/kg/m2)	0.69 ± 0.33	0.73 ± 0.36		1.13 (1.06 - 1.21)	< 0.001	0.849
MP BSA (J/min/m2)	10.1 ± 4.1	10.7 ± 4.4		1.12 (1.06 - 1.20)	< 0.001	0.897
<b>Patients without ARDS (n = 7323)</b>						
Absolute MP (J/min)	19.7 ± 8.5	20.3 ± 9.0		1.09 (1.02 - 1.16)	0.009	
MP PBW (J/min/kg PBW)	0.31 ± 0.13	0.32 ± 0.14		1.06 (0.99 - 1.13)	0.050	
MP BMI (J/min/kg/m2)	0.68 ± 0.32	0.72 ± 0.35		1.13 (1.05 - 1.20)	< 0.001	
MP BSA (J/min/m2)	10.0 ± 4.0	10.5 ± 4.3		1.11 (1.04 - 1.19)	0.001	
<b>Patients with ARDS (n = 868)</b>						
Absolute MP (J/min)	22.6 ± 9.0	23.4 ± 9.5		1.08 (0.91 - 1.29)	0.360	
MP PBW (J/min/kg PBW)	0.36 ± 0.15	0.37 ± 0.15		1.03 (0.86 - 1.24)	0.743	
MP BMI (J/min/kg/m2)	0.78 ± 0.35	0.82 ± 0.38		1.08 (0.91 - 1.28)	0.347	
MP BSA (J/min/m2)	11.6 ± 4.4	12.1 ± 4.8		1.07 (0.90 - 1.28)	0.403	

0.75 1.0 1.25 1.5  
Odds Ratio (95% CI)  
Decrease Mortality      Increase Mortality