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The Authors reply: Comment on: "Handgrip weakness, low fat-free mass, and overall survival in non-small cell lung cancer treated with curative-intent radiotherapy" by Burtin et al.

We want to thank Dr Shafieesabet and Dr Doehner for the critical appraisal[1] of our findings.[2]

The normative values for handgrip strength based on UK Biobank data include the 5th, 10th, and 25th percentile. While the authors propose the 5th percentile as cut-off to define handgrip strength as abnormally low, they also emphasize that the clinical relevance and prognostic value of this cut-point needs to be established. We a priori defined weakness using the 10th percentile based on our previous research in COPD, showing that the 10th percentile was the best prognostic factor in these patients.[3]

Further, we fully agree that cancer cachexia is an established prognostic marker in patients with non-small cell lung cancer. Not surprisingly, we find a strong association between body mass index (BMI) and fat-free mass index (FFMI) in our dataset (r = 0.76, $p < 0.001$). Therefore, we preferred not to combine them in one model due to multicollinearity. When we replace FFMI by BMI (as a continuous variable or a dichotomous variable identifying underweight patients defined as BMI < 18.5 kg/m^2) in our multivariate model in patients with good functional status (WHO performance status 0 or 1), handgrip weakness remains a significant prognostic factor while BMI does not. This might be due to the observation that only 39 of 794 patients were underweighted, of which 13 also presented with handgrip weakness. Therefore, our data lack power to firmly investigate the prognostic role of BMI. Unfortunately, we did not record weight loss in our database.

Interestingly, when excluding all underweighted patients, our findings remain unchanged, which suggests that FFMI and handgrip weakness can provide additional prognostic information in patients with a BMI within normal ranges. A more heterogeneous sample including a higher proportion of patients with features of cachexia is needed to explore to what extent body weight, fat-free mass, and handgrip strength can provide complementary prognostic information.

The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.[4]

Chris Burtin
REVAL Rehabilitation Research, Faculty of Rehabilitation Sciences, Hasselt University, Agoralaan Gebouw A, Diepenbeek, Limburg, Belgium
chris.burtin@uhasselt.be

Jacques Bezuidenhout
Department of Radiation Oncology (Maastro Clinic), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

Karin J.C. Sanders
Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands

Anne-Marie C. Dingemans
Department of Respiratory Medicine, GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

Annemie M.W.J. Schols
Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands

Stephanie T.H. Peeters
Department of Radiation Oncology (Maastro Clinic), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

Martijn A. Spruit
Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands
Department of Research & Development, CIRO, Horn, The Netherlands

Dirk K.M. De Ruysscher
Department of Radiation Oncology (Maastro Clinic), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

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