

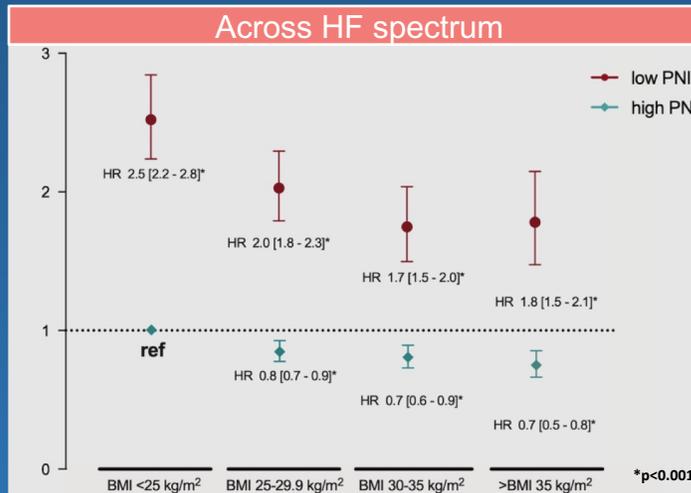
# The impact of malnutrition on the obesity paradox – Fat is not enough

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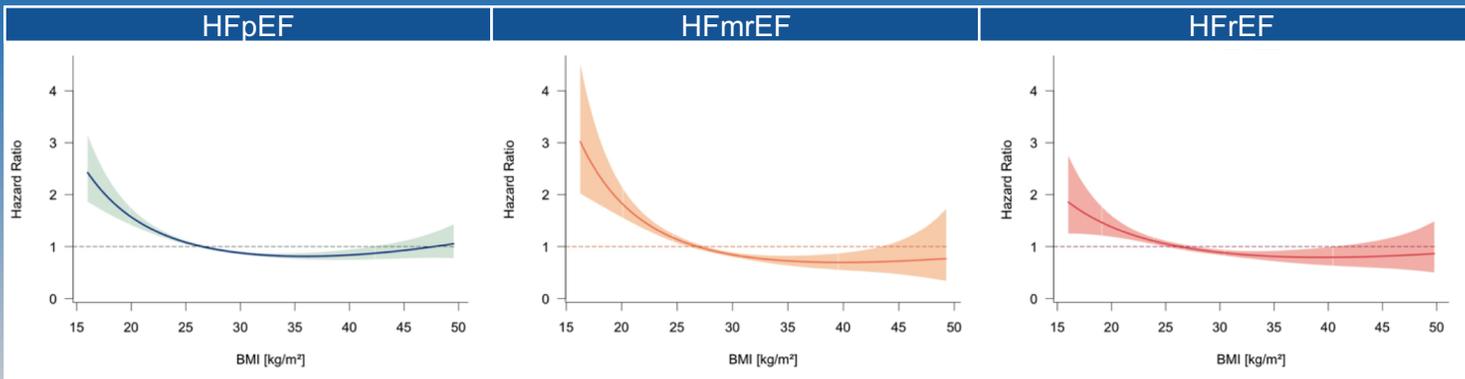
**Background.** High body mass index (BMI) is paradoxically associated with better outcome in patients with heart failure. The impact of malnutrition on the association between BMI and outcome has not been investigated yet.

**Methods.** In this observational study patients with heart failure classified as HFpEF, HFmrEF or HFrfEF according to the current guideline diagnostic criteria were included. Data was retrieved from the Viennese-community healthcare provider network between 2010 and 2020. The relationship between BMI and survival accounting for nutritional status was investigated. Nutritional status was assessed by the prognostic nutritional index (PNI) and was available in 10,005 patients. Patients were classified by the presence (PNI<45) or absence (PNI≥45) of malnutrition.



**Figure 2.** Hazard ratios (HRs) for all-cause mortality with 95% confidence intervals are shown for BMI in relation to low and high PNI.

**Results.** Of the 11,995 patients enrolled, 6,916 (58%) had HFpEF, 2,809 (23%) HFmrEF and 2,270 HFrfEF (19%). Median age was 70 years (IQR: 61 to 77) and the majority of patients were men (67%). During a median follow-up time of 44 months (IQR 19-76) a total of 3,718 (31%) deaths were observed. Across the spectrum of heart failure an inverse relationship between BMI and survival was observed (Figure 1). Good nutritional status as indicated by high PNI was associated with improved survival (HFpEF: HR 0.93 [0.92-0.93], HFmrEF: HR 0.92 [0.91 to 0.93], HFrfEF: HR 0.93 [0.92 to 0.94], p<0.001). Compared to patients with low BMI (<25 kg/m<sup>2</sup>) and high PNI, the hazard for patients with low PNI of the same BMI category was 2.5-fold higher; similarly, in patients stratified to higher BMI categories (>25kg/m<sup>2</sup>) with low PNI, risk was up to 2.0-fold higher (p<0.001 for all) (Figure 2).



**Figure 1.** Restricted spline curves examining the association of body-mass-index and all-cause mortality in HFpEF, HFmrEF and HFrfEF.

**Conclusion.** The obesity paradox seems to be an inherent characteristic of chronic diseases as HF regardless of phenotype. Albeit malnutrition significantly changes trajectory of outcome with regards to BMI alone: obese patients with malnutrition have a considerably worse outcome compared to their well-nourished counterparts, outweighing protective effects of high BMI alone. In this context, routine recommendation towards weight loss in patients with obesity and HF should generally be made with caution and focus should be shifted on nutritional status.