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letter to the editor

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'Pre-cachexia': a non-existing phenomenon in cancer?

We read with great interest the article by Blum et al. [1] who reported an important validation study on the diagnostic framework of cancer cachexia. For patients with cancer, cachexia is a major problem associated with reduced physical functioning [2], tolerance to anti-cancer therapy [3] and survival [2]. Despite the growing knowledge on the pathophysiology of cachexia, assessment in clinical practice is limited due to lack of adequate diagnostic criteria. The past years, experts developed a diagnostic framework [4] but validation studies were still awaited. Blum et al. reported that differentiation of cachexia from no cachexia using the proposed framework worked out successfully with significant and clinically relevant differences in laboratory values, food intake, performance status and survival [1].

With limited treatment options for cancer cachexia, focus has been shifting to pre-cachexia, a potential early stage of cachexia, in which (multi-modal) interventions may slow down the process of cachexia [4]. Blum et al. defined pre-cachexia as weight loss >1 kg but <5% of usual body weight/6 months [1] and found that, by using these criteria, survival rates were not different from those of patients without cachexia. The authors state that 'the pre-cachexia stage might be better defined by additional factors representing the cachexia domain, for instance CRP and appetite loss' [1].

In our cancer centre, we assessed these additional factors and weight loss in 200 patients before start of treatment with (combination) chemotherapy in a prospective study. Pre-cachexia was defined as:

(1) Weight loss of >1.0 kg, but <5%;
(2) C-Reactive protein ≥8.0 mmol/l, the upper limit of normality in our hospital;
(3) Appetite loss: the section AC/S-12 of the FAACT questionnaire ≤24 points [5].

We recruited 85 females and 115 males with a mean age of 64 years (±10 years). The patients were diagnosed with lung cancer (stages II–IV, $n = 83$, 41.5%), stage IV colorectal cancer ($n = 54$, 27.0%), prostate cancer ($n = 40$, 20.0%) or breast cancer ($n = 23$, 11.5%).

Weight loss was present in 40 patients (20%); inflammation in 107 patients (64%) and anorexia in 16 patients (8.5%), but the combination of the three was only found in one patient, resulting in a pre-cachexia prevalence of 0.5%.

Extending the cut-off value for anorexia measured by FAACT to ≤30, as has been suggested by the Special Interest Group 'Cachexia-Anorexia in Chronic Wasting Diseases' from ESPEN, increased the prevalence of pre-cachexia from one to four patients (2%).

Based on these preliminary data, we conclude that the clinical relevance of pre-cachexia in patients with cancer seems to be limited, as the present framework identifies only very few patients, no matter what anorexia cut-off is used. We question whether further studies or refinement of the diagnostic framework will lead to a more adequate clinical tool for pre-cachexia. Still, we have the opinion that optimal early nutritional support for patients with cancer can prevent the development of cancer cachexia. Therefore, clinical trials confirming the relevance of optimal nutritional support for patients with cancer to improve their quality of life and treatment outcome are warranted. In addition, we look forward to further improve the diagnostic framework of cancer cachexia.

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disclosure

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