both studies, there is a data contamination by inappropriate HPV16 classification, enrichment of HPV-negative patients in the OPX population and unknown smoking status of HPV16-positive patients, which all lead to inaccurate conclusions. Although there are not enough data to recommend any HPV16 testing algorithm, the combination of p16 with a 70% cutoff and HPV DNA testing by polymerase chain reaction (PCR) is a well-accepted standard that offers high sensitivity and specificity. Since the combination of p16 and HPV PCR provides significantly higher sensitivity and specificity for HPV16 positivity, current clinical trials should not rely on a single surrogate biomarker. Appropriate HPV classification is absolutely necessary and warrants accurate testing. A low rate of enrollment of R/M SCCCHN HPV16-positive patients into clinical trials may pose as an accrual challenge, but premature conclusions may lead to an elimination of potentially efficacious drugs from clinical practice.

K. Misiukiewicz1*, M. Bonomi2, E. Demicco3 & M. Posner1
1Department of Medicine, Division of Hematology and Medical Oncology, The Tisch Cancer Institute at Mount Sinai Hospital, New York
2Department of Medicine, Division of Hematology and Medical Oncology, Wake Forest Baptist Medical Center, Winston-Salem
3Department of Pathology, Mount Sinai Hospital, New York, USA  (*E-mail: krzysztof.misiukiewicz@mssm.edu)

disclosure
The authors have declared no conflicts of interest.

references
doi: 10.1093/annonc/mdu194
Published online 29 May 2014

‘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.

S. Blauwhoff-Buskermolen1,2*, M. A. E. de van der Schueren1,3, H. M. W. Verheul2 & J. A. E. Langius1,4

Departments of 1Nutrition and Dietetics, Internal Medicine and 2Medical Oncology, VU University Medical Center, Amsterdam 3Faculty of Health and Social Studies, Department of Nutrition, Sports and Health, HAN University of Applied Sciences, Nijmegen 4Academy of Health, The Hague University of Applied Sciences, The Hague, The Netherlands

(*E-mail: s.buskermolen@vumc.nl)

disclosure

MAE dvdS: Nutricia Advanced Medical Nutrition Oncology Advisory Board. All remaining authors have declared no conflicts of interest.

references


doi: 10.1093/annonc/mdu178 Published online 14 May 2014

Should we use the angiotensin-converting enzyme inhibitors for the treatment of anti-VEGF-induced hypertension?

Arterial hypertension is a class effect of anti-vascular endothelial growth factor (VEGF) therapies, including the monoclonal antibody bevacizumab which is used in advanced ovarian, colon, renal and lung cancers [1]. There is no clear recommendation for the management of anti-VEGF-induced hypertension. Data are conflicting regarding the role of the renin-angiotensin system (RAS) on angiogenesis [2] and a recent review suggested that an angiotensin-converting enzyme inhibitor (ACEi) could favor a protumoral microenvironment [3].

In our institution, a calcium-channel blocker is used in first intention to treat anti-VEGF-induced hypertension, while an ACEi is used only in second intention in case of uncontrolled hypertension or when the hypertension is associated with proteinuria.

From 2006 to 2011, we used single-agent bevacizumab to treat 37 patients with relapsing ovarian cancer (ROC).