letters to the editor

Significance of the prognostic stratification of extranodal extension in colorectal cancer

We have to thank Huang and Yang for their very interesting letter [1], in which they comment a recent meta-analysis of our group of research [2], as well as a subsequent letter on the same topic [3]. We recognize as important points those highlighted by Huang et al., particularly when they pointed out that colon and rectal cancer are different in anatomic site, embryological origin, function and also in metastatic patterns. At the same time, we still consider of value the results of our manuscript, in which we present the analysis on the prognostic value of extranodal extension (ENE) of nodal metastasis considering colon and rectal cancer as one entity only. Notably, we have also presented the hazard ratios of a significant number of studies and, in the subsequent letter, we have indicated that the location has not been recognized as a probable moderator of our findings ($P = 0.229$). The approach to consider colon and rectal cancer together was further justified by the fact that the staging systems do not consider separately such neoplasms. Notably, the prognostic role of ENE has been shown in diverse other cancer types [4, 5] and its importance independently from specific anatomic subdistinctions is further suggested by the case of carcinoma of pancreas versus that of papilla of Vater [5].

In our meta-analysis and in our letter, we address the prognostic impact of ENE in both colon and rectal cancers, but without suggesting a unique staging system for these two neoplasms. Indeed, we recognize that the current TNM staging system needs improvements, and the inclusion of ENE might be one of these.

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disclosure

The authors have declared no conflicts of interest.

references

1. Huang Q, Yang H. Prognostic impact of extra-nodal extension on colon and rectal cancer should be investigated separately. Ann Oncol 2016; 27: 956–957.
2. Veronese N, Nottegar A, Pea A et al. Prognostic impact and implications of extracapsular lymph node involvement in colorectal cancer: a systematic review with meta-analysis. Ann Oncol 2016; 27: 42–48.
3. Luchini C, Nottegar A, Pea A et al. Extranodal extension is an important prognostic parameter for both colonic and rectal cancer. Ann Oncol 2016; 27: 955–956.
4. Luchini C, Nottegar A, Solmi M et al. Prognostic implications of extranodal extension in node-positive squamous cell carcinoma of the vulva: a systematic review and meta-analysis. Surg Oncol 2016; 25: 60–65.
5. Luchini C, Veronese N, Pea A et al. Extranodal extension in N1-adenocarcinoma of the pancreas and papilla of Vater: a systematic review and meta-analysis of its prognostic significance. Eur J Gastroenterol Hepatol 2016; 28: 205–209.

Positron emission tomography (PET) as a predictive measure in patients with metastatic pancreatic cancer and normal CA19-9 levels at baseline

Two recent MPACT subanalyses (Chiorean et al. and Ramanathan et al. *Ann Oncol.* 2016) demonstrated evidence that decreases from baseline in carbohydrate antigen 19-9 (CA19-9) and tumor uptake of radioactively labeled glucose (^{18}F-FDG) as measured by positron emission tomography (PET) imaging were each significantly associated with longer overall survival (OS) in patients who received first-line treatment with *nab*-paclitaxel plus gemcitabine or gemcitabine for metastatic pancreatic cancer [1, 2]. These modalities are complementary approaches to monitor treatment efficacy in most patients. However, we raised the question of whether tumor response measured by PET could predict outcome for a subset of patients (15%–20%) with pancreatic cancer who do not secrete elevated levels of CA19-9 [3, 4]. In the MPACT trial, more patients experienced a metabolic response (MR) measured by PET imaging than a tumor response measured by computed tomography. PET imaging may be particularly valuable to predict outcomes in patients without elevated baseline CA19-9 levels.