Preoperative Carcinoembryonic Antigen Level as an Independent Prognostic Factor in Colorectal Cancer. Further Comments

To the Editor:

In the January issue of *Jpn J Clin Oncol*, Wang et al. (1) found that preoperative carcinoembryonic antigen (CEA) levels are an independent prognostic factor in non-metastatic colorectal cancer patients after curative surgery. As the authors correctly pointed out, the prognostic significance of CEA is controversial in these patients. In order to explain the contradictory results that can be found in the biomedical literature, Wang et al. proposed various hypotheses. Among these, they indicated that the numerous studies that have been published so far may have used different analytical methods to measure CEA or, in other words, different CEA kits. Indeed, many published studies were performed over a very long period of time which coincided with important improvements in analytical methods. Immunoenzymatic methods and monoclonal antibodies have thus progressively replaced radioimmunoassays based on polyclonal antibodies, resulting in different specificities and sensitivities (2).

However, another hypothesis was not clearly proposed by Wang et al. In fact, not only the analytical methods, but also the preanalytical methods can be heterogeneous in the various studies. Preanalytical methods can be even more heterogeneous than analytical methods, because preanalytical methods include the patients’ preparation before the blood is sampled (diet duration, smoking, physical exercise, etc), time of blood sampling [in relation to well-known CEA circadian variations (3)], materials and methods used for blood sampling and duration and conditions of sample transport and storage before the measurements (freezing and thawing of serum, etc.) (3,4). Thus, randomly distributed CEA variations of more than 50% cannot be excluded from one study to another (3,4).

The problem is that when one carefully scrutinizes the numerous published studies and clinical trials that evaluated the prognostic significance of CEA levels in these patients, one can easily note that not only did very few papers indicate the analytical methods used, but also the preanalytical methods were even more rarely indicated. It would therefore be impossible for an independent team to reproduce precisely both the analytical and preanalytical methodologies used in these numerous studies—a basic principle of good science.

Indeed, it remains to be demonstrated that it is possible to compare the prognostic values of any laboratory variable measured using different, partly known or unknown analytical and/or preanalytical methodologies, even if this is common practice in most primary studies published in this biomedical field (5). In another type of cancer, it has even been clearly demonstrated that the prognostic significance of a laboratory variable may change depending on the analytical and preanalytical methods (6).

Therefore, it seems clear that: (i) CEA results can only be used for prognostic purposes by authors who have demonstrated its independent prognostic significance in their own hospitals and CEA results obtained using other analytical or preanalytical methods cannot be used by these authors; (ii) in future studies published in this field, both the analytical and the preanalytical methods used should be clearly indicated by the authors; (iii) individual laboratory reports should always mention the analytical and preanalytical methods used.

References


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