Survival in Microsatellite-Unstable Colorectal Cancer

To the Editors: We read with interest Malesci et al’s article in the recent issue of Clinical Cancer Research (1). They showed that microsatellite instability (MSI) was a significant stage-dependent predictor of survival in patients with colorectal cancer. Malesci et al. introduced our previous results and also showed that patients with transforming growth factor-β RII–mutated MSI cancer had better survival rates than those patients with stable cancer (MSS; ref. 2). It is controversial with regard to the efficacy of 5-fluorouracil adjuvant therapy for MSI cancer. They stated that the administration of adjuvant chemotherapy should not be withheld by assuming a more favorable outcome in patients with MSI cancer, with which we completely agree based on our previous results (2). They also compared survival rates between stage-matched MSI and MSS cancers and failed to show improved survival in patients with MSI. To conclude, however, that MSI cancers do not show better prognosis compared with stage-matched MSS cancers, there is a significant issue to be discussed in their study.

In a survival analysis of Malesci et al’s study, the prognostic significance of tumor location was not taken into account. Previous studies have shown that distal colon cancers exhibit significantly better survival than proximal cancers (3–5). Wolmark et al. examined patients from the National Surgical Adjuvant Project for Breast and Bowel Cancer trials to determine the prognostic significance of tumor location and showed that tumor location was a strong prognostic discriminator, and that lesions located in the distal colon showed better survival than those in the proximal colon (3). Kawazuma et al. also showed that patients with distal colon cancer exhibited significantly better survival rates than patients with proximal colon cancer (4). We have also shown that proximal MSI cancers present different characteristics from distal cancers (5). In Malesci et al’s article, however, the vast majority of cancers were located in the proximal colon in the MSI group (81%), whereas only 28% were in the MSS group. Considering that the proximal colon cancers showed poorer survival rates than the distal cancers, this may have lowered the survival rate of the MSI group. To show that the MSI cancers do not present a better prognosis than MSS cancers, they need to analyze not only the stage but also the location of matched MSI and MSS cancers. In Malesci et al’s study, there seems to be a significant selection bias, especially in the MSI group, which contained a high proportion of proximal cancers showing poorer survival rates than the distal cancers.

Toshiaki Watanabe
Yoko Yamamoto
Hideki Yamada
Tamuro Hayama
Yoshiko Aoyagi
Keisuke Nakamura
Hajime Shibuya
Department of Surgery,
Teikyo University School of Medicine,
Tokyo, Japan

References

Takashi Kobunai
Personalized Medicine Research Laboratory,
Tokushima Research Center,
Taiho Pharmaceutical Co., Ltd.,
Tokushima, Japan
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Toshiaki Watanabe, Yoko Yamamoto, Hideki Yamada, et al.


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