Is it possible that advanced-stage gastric cancer patients can be cured by surgery alone?

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DEAR EDITOR,

We have read the article entitled "The clinicopathological and genetic differences among gastric cancer patients with no recurrence, early recurrence, and late recurrence after curative surgery" published in the January issue of the *Journal of the Chinese Medical Association* with much interest.[1] Dr. Chen's group tried to integrate the molecular (genetic) difference into the conventional clinicopathological parameter to evaluate the impact on the recurrence pattern in the gastric cancer (GC) patients after curative surgery. Based on their results, the authors concluded that *PIK3CA* amplifications were frequently detected in diffuse-type GC with early recurrence and *ARID1A* mutations were more common in patients with single-site recurrence, suggesting targeted therapy and immunotherapy might be helpful for the aforementioned patients.[1] We congratulated their successful publication. However, we have found some uncertainties of their article.

We are wondering to know why GC patients with positive lymph node metastases could be classified as those who can be successfully by curative surgery (completely or totally resected tumors). Although we are not familiar with the staging system of GC, in our limited knowledge in the management of patients with gynecologic cancers, the presence of lymph node metastases is always considered the "systemic diseases."[2–4] Additionally, a bigger tumor size classified by tumor node metastasis staging system above pT3-4 may have a higher risk of therapeutic failure when only curative surgery is applied, similar to the cervical cancer,[5] suggesting that it is not a better idea to use surgery alone in the management of patients with pT3-4 and/or N+ GC. In fact, the current NCCN guidelines recommend adjuvant treatment rather than surgery alone in patients with pT3-4 and/or N+ GC,[6] suggesting that only application of surgery alone for GC patients with pT3-4 and/or the presence of lymphadenopathy was at a higher risk of under treatment. In Dr. Chen's article, we found the percentage of the adjuvant therapy was very similar without a statistically significant difference among three groups (13.6%, 13.4%, and 13.4%, respectively).[1] However, based on the recommendation of NCCN guidelines, many patients who are recommended to have an adjuvant therapy did not receive postoperative adjuvant therapy.

Additionally, as shown by authors, *ARID1A* mutations were more common in patients with single-site recurrence, suggesting that this molecular biomarker may be an indicator for the better prognosis.[1] By contrast, *PIK3CA* amplifications were more common in diffuse-type GC with early recurrence, suggesting the worse prognosis. However, the authors did not distinguish the difference between both, and the authors commented that all should be treated with targeted therapy and/or immunotherapy.[1] In fact, we believed that targeted therapy for *PIK3CA* pathway may take advantages in diffuse-type GC patients, but the role of adjuvant targeted therapy and immunotherapy may add little impact on the DFS or OS of GC patients. It is important that any additional or postoperative adjuvant therapy should be balanced between the therapeutic efficacy and the therapy-related toxicity to patients, particularly for those patients with *ARID1A* mutations. The optimal therapeutic goal of adjuvant therapy had better include the more confidence to the curative surgery, a better chance to minimize the damage to the surrounding tissue or systemic toxicity to human bodies, and subsequently, a higher quality of life after initial curative therapy.[7,8]

Despite aforementioned questions, the authors' attempt to integrate the molecular pathology into the conventional clinicopathological parameters in the prediction of GC patients is worthy of encouragement.[1] The spread of molecular pathology has paved the way for patient-tailored strategies, with the aim of improving short- and long-term outcomes.[6,7,9] Overall, we appreciate the authors' great work exploring the limitation of conventional clinicopathological parameters in the prediction of outcomes in GC patients who were treated with curative surgery. Surgery still represents the mainstay of treatment of all stages of GC,[6] similar to our experience in the management of uterine cancers.[3,10] We did not argue the value of the current article, and by contrast, we hope to learn more from the authors with positive response.

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2023) 86: 348-349.

Received December 24, 2022; accepted December 30, 2022.

doi: 10.1097/JCMA.0000000000000873.

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