



Comment on De Felice et al, “Intensified Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer in Elderly Patients: Toxicity, Disease Control, and Survival Outcomes”

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To the Editor:

We read the interesting article by De Felice et al.¹ The authors retrospectively reviewed the treatment compliance, toxicity rates, and long-term clinical outcomes of 26 elderly patients aged ≥ 70 years who received intensified neoadjuvant chemo-radiotherapy (CRT) for locally advanced rectal cancer. Intensified CRT consisted of 50.4 to 54 Gy radiotherapy with concomitant oxaliplatin (50 mg/m²/wk) and 5-fluorouracil (200 mg/m² in 5 daily continuous infusions). Six (23%) patients had a clinical complete response after the end of CRT. Of the 26 patients, 24 (92.3%) underwent surgery. All the patients had acute CRT-associated toxicity; however, severe acute toxicity was recorded in 5 (19.2%) patients. The 2- and 5-year overall survival rates were 86.9% (95% confidence interval [CI], 64.3%-95.6%) and 70.6% (95% CI, 45.4%-85.8%), respectively. The 2- and 5-year disease-free survival was estimated at 70.6% (95% CI, 46.6%-84.9%) and 65.5% (95% CI, 42.3%-81.3%), respectively. We believe that the current study is an important study, because there is limited data with respect to the optimal treatment modality of elderly patients with rectal cancer. Most of the data were obtained from the subgroup analyses of large multi-centric studies conducted on patients with rectal cancer or subgroup analyses of population-based studies. Moreover, in most of the large multi-centric studies, elderly patients were excluded from the analyses. Therefore, the definitive clinical data to guide treatment decisions among those patients aged ≥ 70 years are scarce, although it is more prevalent in the elderly.²

We have couple of concerns regarding this article. Population-based studies revealed that many elderly patients who initiate combined modality therapy for colorectal cancer do not complete treatment.³ In the current study, all the patients completed the

scheduled CRT. In this population of elderly patients, who were initially deemed fit to receive combined modality therapy for rectal adenocarcinoma, approximately 83% required treatment deviations, including early termination, treatment interruptions, or dose reductions.⁴ Besides comorbid diseases, treatment-related toxicity, and being unfit to curative surgery, the high rates of treatment deviations might have been a reason for lack of treatment benefit. Therefore, we wonder if there is an association between the treatment deviations and treatment success/survival in the current study.

In most of the studies conducted on elderly patients, dose reductions are preferred instead of dose intensification. In the current study, the authors intensified the neoadjuvant CRT protocol. We believe that this is a logical approach because most of the patients over 70 years of age could not undergo surgery, which is an important part of curative treatment in locally advanced rectal cancer. The authors revealed that this dose-intensified regimen is well-tolerated in this population of elderly patients. In the current study, 24 (92.3%) patients underwent surgery (16 patients had conservative surgery, and Miles surgery was performed in 7 patients). Of the remaining 2 patients, 1 patient died before surgery, and 1 patient with a clinical complete response after CRT was treated to a wait-and-see approach because of comorbidities. The authors reported a late surgical treatment complication in 1 patient, which clinically consisted of an anastomotic fistula. We wonder if there were any acute post-surgical complications. Because the authors intensified the neoadjuvant CRT regimen, we wonder whether this dose intensification exacerbated the acute surgical complications or not.

In conclusion, this is an important study, considering that dose intensification is a logical treatment strategy for this patient population. Despite increased comorbid conditions, the authors did not observe poor treatment compliance or a negative effect on survival with dose-intensified CRT. We consider that the authors' response to the above comments would clarify their interesting and valuable work.

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