Editorial Commentary



# The role of adjuvant therapy in the treatment of pT3N0 rectal cancer

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*Comment on:* Quinn TJ, Rajagopalan MS, Gill B, *et al*. Patterns of care and outcomes for adjuvant treatment of pT3N0 rectal cancer using the National Cancer Database. J Gastrointest Oncol 2020:11;1-12.

Received: 06 April 2020; Accepted: 27 April 2020; Published: 30 December 2020.

doi: 10.21037/dmr-2020-11

**View this article at:** http://dx.doi.org/10.21037/dmr-2020-11

In this well written paper, Quinn *et al.* (1) on the pattern and outcome of adjuvant strategy in United States for patients with pT3N0 rectal cancer.

Patients with pT3N0 stage are a sub-group of patients with rectal cancer within the wider category of so-called locally advanced rectal cancers (LARC) which include cancers ranging from early pT3N0 up to the advanced pT4N2 with infiltration of mesorectal fascia.

The paper of Quinn *et al.* investigates on a still unresolved question: is adjuvant therapy useful for patients with pT3N0 rectal cancer and which is the best adjuvant combination? Management of this stage ranges from the neoadjuvant chemoradiotherapy (nCRT) followed by adjuvant chemotherapy to the surgery alone without any further treatment. As stated by Quinn *et al.*, there are no randomized controlled trials that address this cohort of patients, therefore the best treatment regimen is still matter of debate. Using the National Cancer Database, the authors conducted a retrospective observational study to evaluate the impact of adjuvant treatment on the overall survival of patients with pT3N0 stage.

The main findings of the study were that patients who received adjuvant chemotherapy had a significantly better 3-year overall survival (83.3%, chemotherapy alone; and 86.0%, chemoradiation) than patients who did not receive chemotherapy (66.7% surgery alone, and 67.4% surgery followed by radiotherapy). Moreover, the addition of radiotherapy to chemotherapy improved overall survival only in the small group of patients with positive surgical margins, while in those with negative surgical margins the addition of radiotherapy to chemotherapy did not add any improvement on survival.

The strength of the study relies on the large sample size and on the accurate statistical analysis.

Conversely, limitations are principally related to the retrospective design of the study, the use of a single outcome (overall survival), and the lack of data which are used in clinical practice to recommend adjuvant hemotherapy. For example, the number of lymph node harvested on the surgical specimen is used to consider the surgery as adequate (>12 lymph-node, not requiring further chemotherapy), or inadequate (<12 lymph nodes, requiring adjuvant chemotherapy) (2). Unfortunately, this data is not available.

A further potential drawback of the study relies on the lack of T3 subclassification which could increase the risk stratification within this stage. According to the Mercury trial, the treatment of T3 rectal tumors is better defined using the magnetic resonance imaging (MRI) subclassification which subdivides T3 cancer in T3 a-b-c-d- depending on the depth of mesorectum infiltration (3). ESMO guidelines suggest to manage T3a-b MRI-defined rectal cancer as stage I rectal cancer, i.e., total mesorectal excision alone without any neoadjuvant or adjuvant treatment (4). On the opposite, T3b-c should receive neoadjuvant therapy. Unfortunately, the study of Quinn *et al.* does not report on the T3 subclassification and cannot help to answer this question.

In conclusion, this study shows that an encouraging overall survival, more than 80%, may be reached with surgery followed by adjuvant chemotherapy. Radiotherapy

seems to play a marginal role as adjuvant treatment and its role seems to be appropriated only in patients with pT3N0 rectal cancer with circumferential margin infiltrated.

## Acknowledgments

*Funding:* None.

## Footnote

*Provenance and Peer Review:* This article was commissioned by the Editorial Office, *Digestive Medicine Research*. The article did not undergo external peer review.

*Conflicts of Interest:* Both authors have completed the ICMJE uniform disclosure form (available at: http://dx.doi.org/10.21037/dmr-2020-11). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



doi: 10.21037/dmr-2020-11

**Cite this article as:** Pucciarelli S, Barina A. The role of adjuvant therapy in the treatment of pT3N0 rectal cancer. Dig Med Res 2020;3:109.

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