



Ascension St. John Hospital

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Dear Ms. Gregory:

On behalf of the Rectal Cancer Group at the Van Elslander Cancer Center, we respectfully request the NCCN Guidelines for the treatment of moderately advanced rectal cancer to be modified to also include transanal full thickness local excision in selected patients whose tumors exhibit complete clinical response after neoadjuvant therapy.

Rationale

At the present time, the NCCN Guidelines for T3 N0/N1 rectal cancer allow a watch and wait policy for selected tumors exhibiting complete response established by careful clinical and imaging assessment in centers with experienced multidisciplinary teams. This pathway is allowed, despite the absence of any randomized trials that insure the safety of this approach, and moreover, a potential concern of an increased distant metastatic rate in patients who later develop tumor regrowth.¹

Full thickness local excision after complete clinical response to neoadjuvant therapy has the advantage of confirming the CR pathologically. This is obviously an important prognostic factor because of the expected very low recurrence rate in this situation, which helps put patients' (and doctors') minds at ease.²⁻⁸ The presence of level I evidence confirming the long-term safety of transanal full thickness local excision (LE) when compared to total mesorectal excision (TME) adds to the sense of security in pursuing this approach.⁹

There are few reports and even wider perception that LE in this setting is associated with frequent and severe toxicity.¹⁰⁻¹² We disagree with this notion. LE is reported to cause severe complications when: the radiation dose is modestly escalated; oxaliplatin is added to capecitabine during the concurrent chemo-radiotherapy phase; resection of the gross residual abnormality is performed with an unnecessary normal tissue margin; or the surgical dissection is carried out to the mesorectal fascia.

Limited data from our center¹³ indicate that LE can be done with a very favorable toxicity profile if: the radiation dose is limited to 50.4 Gy; the residual gross disease is excised without any mucosal margin (LE in this setting is a biopsy and has no therapeutic value); and dissection through the dentate line is avoided.

Similar results are cited by Guerri et al.,¹⁴ who reported the complications rate in a series of 425 patients who were treated by either LE alone (120 patients) or after neoadjuvant radiation therapy (350 patients). Only 10% of the patients experienced minor complications with major complications affecting

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only 1.4% of the cohort under study. Stipa et al.,² in a study of 43 patients treated by neoadjuvant therapy followed by LE, reported grade III complications in only 1 patient, while 5 other patients experienced grade I or grade II adverse effects. Please also notice that the GRECCAR12 trial, launched by one of the largest and most reputable group in the rectal cancer research, is currently recruiting patients and offering LE to patients with CR in both arms of the study.

Currently only very few US patients diagnosed with moderately advanced rectal cancer are offered a rectal preservation approach. We believe that the recognition of LE as a possible NCCN pathway will increase the confidence of many surgeons to offer this conservative approach to their patients because of the certainty of the pathological response which would alleviate, to some extent, the burden and anxiety associated with the possibility of tumor regrowth, and the very complex follow-up schedule which is required following a watchful waiting approach.

Sincerely,



Amr Aref, MD

Chief, Radiation Oncology

Signing on behalf of Amer Alame, MD Colorectal Surgeon and Ahmed Abdalla MD Fellow

Members of the Rectal Cancer Group

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