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Importance of Tumor Regression Grade in ypStage III Rectal Cancer Patients Treated with Neoadjuvant Chemoradiotherapy



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Purpose/Objective(s): Complete and partial tumor regressions are associated with improved long-term outcome in patients with rectal cancer after neoadjuvant chemoradiotherapy (NCRT). ypStage III rectal cancer consists of lymph node positive patients with heterogeneous prognosis. Introducing tumor regression grade (TRG) into heterogeneous ypStage III rectal cancer may provide clue on selecting out patients who might acquire maximal benefit from intensified adjuvant treatment. This study was performed to evaluate the prognostic impact of the tumor regression grade in ypStage III rectal cancer patients treated with NCRT.

Materials/Methods: In this retrospective study, 287 patients with locally advanced rectal cancer received NCRT at our institution from 2003 to 2015. ypStage III patients were classified into two subgroups based on the combination of ypStage and TRG: ypStage III patients with good TRG (TRG 3-4) and ypStage III patients with poor TRG (TRG 1-2).

Results: Median follow-up time was 51.3 months. 5-year overall survival (OS) and 5-year distant metastasis-free survival (DMFS) were 86.0% and 78.5%, respectively. When ypStage III patients were divided into ypStage III & TRG 3-4 subgroup and ypStage III & TRG 1-2 subgroup, ypStage III & TRG 1-2 patients had worse 5-year OS (95.8% vs. 62.0%, $p = 0.023$) and 5-year DMFS (78.8% vs. 56.1%, $p = 0.073$) compared to the ypStage III & TRG 3-4 patients. And there were no differences between the ypStage II subgroup and the ypStage III & TRG 3-4 subgroup in terms of the 5-year OS (86.9% vs. 95.8%, $p = 0.405$) and 5-year DMFS (79.3% vs. 78.8%, $p = 0.683$). Multivariate analyses showed that grouping patients into 3 modified subgroups – ypStage 0-I, ypStage II/ypStage III & TRG 3-4, and ypStage III & TRG 1-2 – clearly divides patients and this grouping itself becomes the most important prognostic factor for predicting OS ($p < 0.001$) and DMFS ($p < 0.001$).

Conclusion: Degree of tumor regression after NCRT significantly divided heterogeneous ypStage III rectal cancer patients into two groups: ypStage III patients with good TRG (TRG 3-4) and ypStage III patients with poor TRG (TRG 1-2). Therefore, TRG may be used to discern a high-risk group

in ypStage III patients who might benefit from more intensified adjuvant treatment.

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Clinical Outcomes of Rectal Squamous Cell Carcinomas Treated with Chemoradiotherapy with or Without Surgery: A Rare Cancer Network Study.



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Purpose/Objective(s): Rectal Squamous Cell Carcinoma (R-SCC) is a rare disease. The therapeutic approach is not well established. We report the clinical results of a large, multicentric study promoted by the Rare Cancer Network.

Materials/Methods: This study included 77 adult non-metastatic R-SCC patients treated in 13 American and European Institutions (M/F = 54/23). Median age was 59 years (range: 25 - 87). Curative Radiotherapy (RT) was delivered in 72 patients, usually with concomitant CT ($n = 62$) as radical ($n = 47$), neoadjuvant ($n = 17$) or postoperative treatment ($n = 8$). Pelvic RT volume always encompassed internal iliac and presacral nodes, + external nodes ($n = 17$) or + external and inguinal nodes ($n = 39$), up to a median total dose of 45 Gy (range: 30 – 65 Gy, 1.8 – 3 Gy/fraction). A boost was delivered in 40 patients, with external beam radiotherapy ($n = 36$), up to a median total dose of 18 Gy (range: 5.4 – 30.6 Gy), or with brachytherapy ($n = 4$) up to a total dose of 25-33.4 Gy. Surgery was delivered in 30 patients, as LAR ($n = 9$), APR ($n = 14$) or Trans-Anal Resection ($n = 5$).

Results: Median follow-up was 59.6 months (Range, 3.1 – 268). Five-year overall survival, cancer specific survival, local control (at the anal level), loco-regional control (at the anal and/or the pelvic nodes level), metastases-free survival, and disease-free survival were 83% + 7% (95% Confidence Interval), 85% + 7%, 85% + 7%, 83% + 7%, 82% + 7% and 76% + 10%, respectively. Better 5-year LRR rates were reported in patients receiving exclusive chemoradiotherapy compared to those who received combined surgery and chemoradiotherapy (88% vs 71%, Log-rank p -value 0.03). Noteworthy, no differences were seen in terms of distribution of stages amongst these two therapeutic approaches. At univariate analysis, T stage (T1-2 vs T3-4), N status (N0 vs N+), and Stage (I-II vs IIIA-B) did not statistically influence the 5-year loco-regional control rate. Patients with a IIIB stage presented a statistically lower 5-year loco-regional control rate (66% vs 85%, log-rank p -value = 0.003). Salvage APR was realized in only 2/47 patients who received exclusive chemoradiotherapy. Toxicity data were available for all the patients: 51/77 patients presented a G1-4 acute toxicity (66%), while late G1-4 toxicity was reported in 32/77 patients (41%). Acute and late toxicity scores were available for 57 (74%)

and 64 (83%) patients, respectively. The rates of grade >3 acute and late toxicity were 14% and 12%, respectively.

Conclusion: Chemoradiotherapy seems to be the treatment of choice for R-SCC, as it allows good clinical outcomes and sphincter saving procedures, with acceptable severe toxicity rates. Stage IIIB patients present lower loco-regional control rates and are probably the best candidates to multi-disciplinary approaches.

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Prognostic Implications of Altering the Nodal Staging for Anal Cancer in the American Joint Committee on Cancer 8th (AJCC8) Edition Staging Manual



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Purpose/Objective(s): The AJCC8 has altered nodal staging for squamous cell carcinoma of the anus (SCCA). Nodal stage is now binary (N0 or N+) in contrast to AJCC7's three-tiered grouping based on nodal site (N1-N3). AJCC8 has also split AJCC7 overall stage II disease into IIA/IIB and stage III into IIIA/IIIB/IIIC. In this study, we use the National Cancer Database (NCDB) data to evaluate the effect of AJCC8 nodal stage by T stage on 5-year overall survival (OS). We hypothesize that 5-year OS for each T stage will be similar for patients with former AJCC7 N1-3 groups. The survival differences for the new AJCC8 overall stage grouping and subsets of the new AJCC8 IIIA and IIIC stage groups is also evaluated.

Materials/Methods: The NCDB was used to identify patients with SCCA from 2004–2013. Inclusion criteria were: age \geq 18; SCCA; Stage (AJCC7) I-III; no surgery; Patients treated with radiation (RT) and chemotherapy; all patients treated definitively without palliation; all RT performed at same institution; total RT dose 36–59.4 Gy; RT to pelvis, nodes, and soft tissue only; RT fractions 25–40; RT time from 25–180 days; and IMRT or 3D only. RT total dose included target volume plus any boost. Each T stage within the AJCC7 was compared with increasing nodal stage. The new AJCC8 stage groups and subsets were compared using log rank tests.

Results: There were 6,751 patients who met the inclusion criteria. The 5-year OS by AJCC8 stage was I=81%, IIA=78%, IIB=64%, IIIA=69%, IIIB=59%, IIIC= 57%. For node negative patients, the 5-year OS was T1N0=81%, T2N0=78%, T3N0=65%, and T4N0=59%. In the new AJCC8 IIIA group, there was no difference in 5-year OS for T1N+ or T2N+ patients (70.3% vs 68.6%, p=0.09). However, a difference in 5-year OS was observed for AJCC7 T1 N1-3 (p = 0.0047) and AJCC7 T2 N1-3 patients (p = 0.0389). Table 1

Abstract SU_1_2007; Table 1

AJCC 8th Stage	5-year OS (%)	AJCC 7th Stage	5-year OS (%)	p-value
T1N+	68.6	T1N1	82.9	0.0047
		T1N2	69.4	
		T1N3	46.1	
T2N+	69.0	T2N1	76.0	0.0389
		T2N2	65.6	
		T2N3	63.6	

demonstrates the 5-year OS differences between AJCC7 and AJCC8 for early T stages with increasing N stage. In the AJCC8 IIIC group, there was no difference in 5-year OS for T3N+ or T4N+ patients (58% vs 55%, p=0.81). With increasing AJCC7 nodal stage, there was no OS difference for T3 (AJCC7 T3N1=54%, T3N2=64%, T3N3=55% p=0.19) or T4 (AJCC7 T4N1=61%, T4N2=41%, T4N3=59% p=0.35) disease.

Conclusion: This analysis demonstrates that the AJCC7 nodal staging retains prognostic significance for early T stages. For AJCC8 T1/T2 tumors with lymph node involvement, OS is inferior among patients with more advanced nodal stage (AJCC7 N1-3). This difference is not apparent with AJCC8 T3/T4 tumors. The survival in the stage IIIA AJCC8 group is heterogeneous and is largely driven by the burden of nodal disease in patients with T1/T2 cancers.

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The Utility of Positron Emission Tomography (PET) To Guide Radiation Therapy Target Volume Determination as Compared with Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) for Rectal Cancer



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Purpose/Objective(s): The role of positron emission tomography (PET) in the management of locally advanced and oligometastatic rectal cancer to guide radiation therapy (RT) treatment volumes is unclear. We investigated the pre-treatment use of PET scans obtained during initial workup to determine its effect on the RT treatment volumes in patients with locally advanced and oligometastatic rectal cancer.

Materials/Methods: A list of locally advanced and oligometastatic rectal cancer patients treated in the department of radiation oncology from 01/2004 through 11/2017 was compiled. Those that received palliative RT were excluded from analysis. A review of each patient's medical record identified those that had undergone a PET scan prior to initiation of any oncologic interventions. Oncology provider notes were reviewed, and the reports and images of PET scans were compared to those of computed tomography (CT) and magnetic resonance imaging (MRI) staging studies. In addition, PET scans were individually reviewed to determine if RT treatment volumes, including fields and contour volumes, were altered by the PET results.

Results: One hundred ninety-six patients were identified. Of those, 50 patients (26%) had undergone PET scans prior to treatment. The majority of PET scans were acquired as part of routine initial work up (n=40), some were specifically obtained to evaluate an equivocal finding seen on CT imaging (n=7) or secondary to a patient's inability to have IV contrast (n=3). The median age of patients undergoing PET was 56 and the median distance of the primary tumor from the anal verge was 7.5 cm. The majority of patients (66%) had clinical stage III disease followed by 18% and 16% of patients being classified as Stage IV and Stage II, respectively. The results of the PET scan changed the clinical stage in 2 (4%) patients and the RT plan in 3 (6%) patients. Of the 3 patients with a change in RT plan, 1 patient had additional metastatic disease identified and as a result, definitive RT was not offered. The additional 2 patients had alterations in radiation fields and contour volumes to cover additional nodal disease seen on PET, which was not appreciated on the original CT and MRI imaging. Additionally, MRI identified a greater number of suspicious lymph nodes compared to PET. The mean number of lymph nodes identified by MRI was 3.1 (range: 0–23) compared to 1.7 by PET (range: 0–12).

Conclusion: Pre-treatment PET scans in patients with rectal cancer did not influence the RT plan or management in the vast majority of cases reviewed. These results demonstrate that PET appears to provide little