



Adjuvant therapy in patients with rectal adenocarcinoma treated with neoadjuvant chemoradiotherapy and radical resection in pathological stages I–III

Leonardo S. Lino-Silva^{1^}, César Zepeda-Najar^{2^}, Rosa A. Salcedo-Hernández^{3^}

¹Surgical Pathology, Instituto Nacional de Cancerología, Tlalpan, Mexico City, Mexico; ²Surgical Oncology, Hospital Angeles Tijuana, Tijuana, Baja California Norte, Mexico; ³Surgical Oncology, Instituto Nacional de Cancerología, Tlalpan, Mexico City, Mexico

Correspondence to: Leonardo S. Lino-Silva, MD, MSc, MEd. Anatomic pathology professor, Gastrointestinal Pathology Division and Melanoma Division, Instituto Nacional de Cancerología de México (Mexico's National Cancer Institute), Av. San Fernando # 22, Sección XVI, Tlalpan, Mexico City, CP 14080, Mexico. Email: saul.lino.sil@gmail.com.

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Surgery is the cornerstone to the cure of colorectal cancers. Resection techniques for rectal tumors have been substantially improved thanks to the knowledge of dissemination mechanisms, thereby increasing cure rates; however, the best oncological results for patients with locally advanced stages have been obtained by combining the use of chemotherapy and radiotherapy with the surgery. Once the primary treatment is completed, there is an open debate on whether to continue the adjuvant therapy, especially with patients who have downstaging. We read with great interest the work of Zhang *et al.* (1), where they evaluated the effect of adjuvant chemotherapy on the survival of patients with adenocarcinoma of the middle and lower rectum treated with preoperative chemoradiotherapy (NCRT) + radical resection of the rectum with negative margins in the pathological stage pT0- T2 N0. Based on their results, we can conclude that patients with NCRT stages 0-II (excluding T3 and T4 tumor stages) cancers with complete resection who received adjuvant chemotherapy had a survival similar to those who did not receive it (79.1% *vs.* 82.9%, $P=0.442$), however, it must be considered that patients in the “non-adjuvant” group had a higher proportion of anastomosis leaks (19.3%

vs. 6.6%, $P=0.042$) and were older (61.2 *vs.* 55.6 years, $P=0.012$), factors that they seem to have a poor prognosis. The factor that was definitely associated with better disease-free survival at 5 years was the administration of NCRT + chemotherapy (total NCRT), a fact that has been consistently shown to be associated with better oncological results (2), so it would provide clarity to Zhang's report to stratify for the use of total NCRT; however, given the low proportion of cases in the adjuvant group ($n=30$) this may not be possible. Also, although it is established that a total mesorectal excision (TME) was performed in the patients, the quality of TME is not established, and this is a very important information since its correlation with oncological outcomes is well known (3). We are interested in this issue, so we present an analysis of the use of adjuvant chemotherapy in our patients with stages II and III adenocarcinoma of the lower and middle rectum in the period from 2010 to 2017, with tumor stages pT3 and pT4 and who received NCRT 3–6 cycles of capecitabine or CapeOX + 50.4 Gy of radiotherapy (none patient received total NCRT). We find a total of 161 patients, with a median age of 58 years (range, 23–85 years) and, as can be seen in *Table 1*, the clinicopathologic characteristics known as

[^] ORCID IDs: Leonardo S. Lino-Silva: 0000-0002-7394-5123; César Zepeda-Najar: 0000-0002-4913-7695; Rosa A. Salcedo-Hernández: 0000-0003-4537-8034.

Table 1 Analysis of 161 patients with rectal adenocarcinoma treated with preoperative chemoradiotherapy + radical surgery divided according to adjuvant therapy use

Variable	Non-adjuvant therapy (n=33)	Adjuvant therapy (n=128)	P
Age—median (interquartile range), year	59 [53–64]	58 [49–65]	0.453
ypT stage, n (%)			
ypT0	1 (3.0)	4 (3.1)	0.442
ypT2	7 (21.2)	46 (35.9)	
ypT3	21 (63.6)	67 (52.3)	
ypT4	4 (12.1)	11 (8.6)	
ypN, n (%)			
ypN0	19 (57.6)	65 (50.8)	0.104
ypN1	11 (33.3)	60 (46.9)	
ypN2	3 (9.1)	3 (2.3)	
Pathological stage, n (%)			
Stage 0-I	0	0	0.486
Stage II	19 (57.6)	65 (50.8)	
Stage III	14 (42.4)	63 (49.2)	
Tumor deposits, n (%)			
No	26 (81.3)	108 (84.4)	0.668
Yes	6 (18.8)	20 (15.6)	
Histologic grade, n (%)			
Low grade	20 (60.6)	86 (67.3)	0.667
High grade	12 (36.4)	38 (29.7)	
No primary tumor	1 (3.0)	4 (3.0)	
Lymphovascular invasion, n (%)			
No	27 (81.8)	98 (76.6)	0.518
Yes	6 (18.2)	30 (23.4)	
Venous invasion, n (%)			
No	29 (87.9)	113 (88.3)	0.949
Yes	4 (12.1)	15 (11.7)	
Perineural invasion, n (%)			
No	28 (75.8)	97 (75.8)	0.998
Yes	8 (24.2)	31 (24.2)	
Resection, n (%)			
R0	25 (75.8)	111 (86.7)	0.121
R1	8 (24.2)	17 (13.3)	
Mesorectal quality, n (%)			
Adequate	31 (93.9)	119 (93.0)	0.929
Inadequate	2 (6.1)	9 (7.0)	

Table 1 (continued)

Table 1 (continued)

Variable	Non-adjuvant therapy (n=33)	Adjuvant therapy (n=128)	P
Number of resected lymph nodes, median (interquartile range)	13 [10–17]	13 [10–16]	0.764
Outcome, n (%)			
Alive without disease	15 (45.5)	66 (51.6)	0.283*
Dead	7 (21.2)	23 (18.0)	
Alive with disease	7 (21.2)	34 (26.6)	
Dead without disease	4 (12.1)	5 (3.9)	
Follow-up, median (interquartile range), months	39 [16–70]	44 [29–64]	0.427

*, P values are based on Mann-Whitney U test for numerical variables and chi-square or Fisher exact test as appropriate; *, comparison between alive vs. dead results in a P value of 0.170.

factors associated with prognosis in this type of patients are completely balanced between the groups. Survival analysis with the Kaplan-Meier method shows that patients who did not receive adjuvant therapy had a disease-specific survival of 72.4 months compared to 75.3 months for those who received it ($P=0.523$, log-rank test) and an overall survival of 63.1 vs. 71.9 months ($P=0.127$, log-rank test).

Our results confirm the findings found by Zhang (1), in another type of population and in a sample that predominantly received adjuvant treatment and that did not receive total NCRT. Furthermore, we found that there was no difference when considering early stages with pT3-4 tumors, neither lymph node disease nor tumor deposits. These findings establish the basis for developing a clinical trial in which this type of patient is randomized to receive or not adjuvant treatment in a standardized prospective cohort to settle this question at once.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/atm-20-5088>). 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.

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