

**ROLE OF ADJUVANT CHEMOTHERAPY FOR STAGE II COLON CANCER:
EXPERIENCE OF THE MOHAMMED VI UNIVERSITY HOSPITAL CENTER AT
ONCOLOGY CENTER IN MARRAKESH**

***M. Saadoune, M. Elkhadir, M. Darfaoui, A. Elomrani, M. Khouchani**

Department of Radiotherapy, Mohamed VI University Hospital, Marrakech, Morocco.

***Corresponding Author: M. Saadoune**

Department of Radiotherapy, Mohamed VI University Hospital, Marrakech, Morocco.

Article Received on 03/01/2023

Article Revised on 24/01/2023

Article Accepted on 14/02/2023

ABSTRACT

Stage II colon cancer (CC) is probably one of the best prognosis gastrointestinal tumors seen in our consultations, but often takes a lot of time for physicians to determine appropriate treatment because of the limited benefit of adjuvant chemotherapy (CT) in these patients, together with the limited evidence in this situation. How to choose the best treatment for each individual patient is thus dependent on molecular (microsatellite instability/microsatellite stability status) and clinico-pathological features relevant enough to classify these tumors into low-, intermediate- and high-risk stage II disease and to choose an appropriate attitude for each of these subgroups. The goal of this study was to report the experience of patients with stage II colon cancer in our center as well as the use of adjuvant systemic chemotherapy following curative surgery.

KEYWORDS:

MATERIALS AND METHODS

This is a retrospective study that included 60 patients diagnosed with stage II colon cancer from January 1st, 2012, to December 31st, 2019 in the oncology department of Mohammed VI University Hospital in Marrakesh.

RESULTS

The median age was 58,6 years (between 36 and 80 years). The sex ratio was 1.22 (33 women / 27 men). Cancer was revealed by occlusion in thirty-five percent of cases.

The most common tumor site was left colon in 43 cases (71.6%) and right colon in 17 cases (28.3%).

All patients underwent surgical treatment. The surgery was complete.

The histological factors of poor prognosis were: poorly differentiated tumor in 2 cases (3.4%), stage T4 in 16 cases (26.6%), presence of vascular emboli in 32 cases (53.4%), and insufficient lymph node dissection 15 cases (25%).

Microsatellite instability was observed in 20.8% of patients.

35 patients received adjuvant chemotherapy type 8 cycles of Xelox (25 cases) or 12 cycles of Folfox (10 cases).

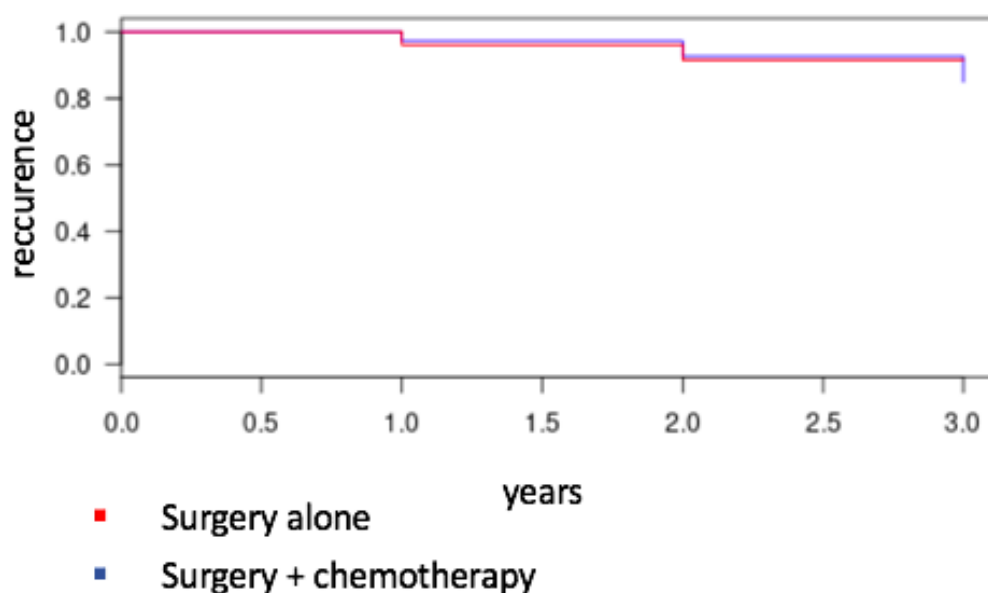
After a follow-up of three years, there was recurrence in three cases (8.5%) in the group who received chemotherapy and in two cases (8%) in the group of patients who did not receive adjuvant chemotherapy.

Table 1: Clinicopathologic characteristics of patients.

Variables		Surgery alone	Surgery + chemotherapy	n	p
		(n = 25)	(n = 35)		
Age, median		61.8 (±12.2)	56.9 (±13.6)	60	0.47
Symptoms, n	undefined	7 (28%)	7 (20%)	14	<0.001
	Obstruction	1 (4%)	20 (57%)	21	-
	pain	17 (68%)	8 (23%)	25	-
Degree of differentiation, n	well	3 (12%)	3 (8.6%)	6	0.7
	moderate	22 (88%)	30 (86%)	52	-
	poor	0 (0%)	2 (5.7%)	2	-
Vascular	Positive	4 (16%)	28 (80%)	32	<0.001

emboli/perineural invasion, n	negative	21 (84%)	7 (20%)	28	-
Laterality, n	Right	7 (28%)	10 (29%)	17	0.96
	left	18 (72%)	25 (71%)	43	-
Microsatellite instability, n	undefined	8 (32%)	13 (37%)	21	0.027
	MSI	9 (36%)	3 (8.6%)	12	-
	MSS	8 (32%)	19 (54%)	27	-
Lymph nodes dissection, n	≥12	22 (88%)	23 (66%)	45	0.0494
	<12	3 (12%)	12 (34%)	15	-
Gender, n	Male	9 (36%)	18 (51%)	27	0.24
	Female	16 (64%)	17 (49%)	33	-
Stage, n	T3	24 (96%)	20 (57%)	44	<0.001
	T4	1 (4%)	15 (43%)	16	-
Progression after 3 years, n	stability	23 (92%)	32 (91%)	55	1
	reccurence	2 (8%)	3 (8.6%)	5	-

Progression after 3 years



DISCUSSION

Adjuvant chemotherapy (AC) is commonly considered for patients with stage II colon cancer who are classified as high risk. AC was associated with a survival benefit in high-risk patients. The benefits were mainly observed in patients with T4 disease.^[4]

Many studies are controversial about the indication of AC in stage II colon cancer; one study showed that adjuvant chemotherapy was associated with better overall survival in low-risk stage II disease. These results from a large-scale sample challenge current guideline and the need for better risk stratification. Further study with more robust variables is warranted to determine best practices for AC.^[5]

Concerning location, AC improved 5-year OS independent of tumor location and appeared to compensate for the difference in survival observed

between right-sided and left-sided tumors in the group without chemotherapy.^[6]

other high-risk factors, including less than 12 lymph nodes in the surgical specimen, perineural or lymphovascular invasion, poorly differentiated or undifferentiated tumor grade, intestinal obstruction, and tumor perforation, may be considered for AC.^[7]

MSI status must be determined before treatment because it is a prognostic and predictive factor for the response to chemotherapy.^[8]

More recent studies have evaluated a shorter chemotherapy regimen of three months compared to the standard six-month regimen in high-risk stage II and stage III patients. These studies have also shown that for this group, three months of Xelox chemotherapy is not inferior to 6 months of Xelox, which allows for greater

compliance with chemotherapy and significantly less toxicity.^[9]

Screening for CDX2 in tumors of patients with stage II colon cancer could be incorporated into the decision algorithm and administering adjuvant therapy to the CDX2-negative subgroup is a valuable management strategy under a wide range of plausible hypotheses.^[10,11]

The results of a study suggest that the combination of tumor budding and tumor-infiltrating lymphocytes (TILs) as tumor-host antagonists might be helpful tool in adjuvant treatment decisions in stage II and III colon cancer.^[12]

CONCLUSION

In spite of the relatively small size of our study, it showed results similar to those described in the literature. Many studies evaluating biomarkers are underway to make the decision more clarified.

REFERENCES

1. Recio-Boiles A, Cagir B. Colon Cancer. 2022 Jan 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. PMID: 29262132.
2. Akiyoshi T, Kobunai T, Watanabe T. Recent approaches to identifying biomarkers for high-risk stage II colon cancer. *Surg Today*, 2012 Nov; 42(11): 1037-45. doi: 10.1007/s00595-012-0324-4. Epub 2012 Sep 9. PMID: 22961195.
3. Fujita S, Yamamoto S, Akasu T, Moriya Y. Outcome of patients with clinical stage II or III rectal cancer treated without adjuvant radiotherapy. *Int J Colorectal Dis.*, 2008 Nov; 23(11): 1073-9. doi: 10.1007/s00384-008-0513-1. Epub 2008 Jul 2. PMID: 18594841.
4. Kumar A, Kennecke HF, Renouf DJ, Lim HJ, Gill S, Woods R, Speers C, Cheung WY. Adjuvant chemotherapy use and outcomes of patients with high-risk versus low-risk stage II colon cancer. *Cancer*, 2015 Feb 15; 121(4): 527-34. doi: 10.1002/cncr.29072. Epub 2014 Oct 20. PMID: 25332117.
5. Reif de Paula T, Gorroochurn P, Simon HL, Haas EM, Keller DS. A national evaluation of the use and survival impact of adjuvant chemotherapy in Stage II colon cancer from the national cancer database. *Colorectal Dis.*, 2022 Jan; 24(1): 40-49. doi: 10.1111/codi.15937. Epub 2021 Oct 18. PMID: 34605166.
6. Mukkamalla SKR, Huynh DV, Somasundar PS, Rathore R. Adjuvant Chemotherapy and Tumor Sidedness in Stage II Colon Cancer: Analysis of the National Cancer Data Base. *Front Oncol*, 2020 Sep 15; 10: 568417. doi: 10.3389/fonc.2020.568417. PMID: 33042845; PMCID: PMC7523086.
7. Baxter NN, Kennedy EB, Bergsland E, Berlin J, George TJ, Gill S, Gold PJ, Hantel A, Jones L, Lieu C, Mahmoud N, Morris AM, Ruiz-Garcia E, You YN, Meyerhardt JA. Adjuvant Therapy for Stage II Colon Cancer: ASCO Guideline Update. *J Clin Oncol*, 2022 Mar 10; 40(8): 892-910. doi: 10.1200/JCO.21.02538. Epub 2021 Dec 22. PMID: 34936379.
8. Ribic CM, Sargent DJ, Moore MJ, et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. *N Engl J Med.*, 2003; 349: 247-257.
9. J. Souglakos*, I. Boukovinas, S. Kakolyris, S. Xynogalos, et al. Three- versus six-month adjuvant FOLFOX or CAPOX for high-risk stage II and stage III colon cancer patients: the efficacy results of Hellenic Oncology Research Group (HORG) participation to the International Duration Evaluation of Adjuvant Chemotherapy (IDEA) project. *Annals of Oncology*, 2019; 0: 1–7.
10. Piero Dalerba, M.D., Debashis Sahoo, Ph.D., Soonmyung Paik, M.D., Xiangqian Guo, et al. CDX2 as a Prognostic Biomarker in Stage II and Stage III Colon Cancer. *N Engl J Med*, 2016; 374: 211-222.
11. Abdelrahman AE, Ibrahim DA, El-Azony A, Alnagar AA, Ibrahim A. ERCC1, PARP-1, and AQP1 as predictive biomarkers in colon cancer patients receiving adjuvant chemotherapy. *Cancer Biomark*, 2020; 27(2): 251-264. doi:10.3233/CBM-190994
12. Lang-Schwarz C, Melcher B, Dregelies T, Norouzzadeh Z, Rund-Küffner S, Lang-Schwarz K, Vieth M, Sterlacci W. Adjuvant chemotherapy in stage II and III colon cancer: the role of the "budding and TILs-(tumor-infiltrating lymphocytes) combination" as tumor-host antagonists. *Int J Colorectal Dis.*, 2021 Aug; 36(8): 1765-1779. doi: 10.1007/s00384-021-03896-9. Epub 2021 Mar 20. PMID: 33745027; PMCID: PMC8279987.