

Impact of Adjuvant Chemotherapy on Outcomes in Appendiceal cancer

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INTRODUCTION

The impact of using adjuvant chemotherapy following cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with appendiceal adenocarcinoma is not known. Guidelines per National Comprehensive Cancer Network (NCCN) state that data are quite limited for appendiceal adenocarcinoma and advises practitioners to consider chemotherapy per NCCN guidelines for colon cancer. A review of current clinical practice at NCCN member institutions showed practitioners commonly use colorectal cancer data. However, there are recent studies that showed molecular differences between appendiceal and colorectal cancer indicating a different biology and potentially different response to similar treatments. The extrapolation of data from colorectal cancer studies to guide chemotherapeutic choices in appendiceal cancer may be misleading.

OBJECTIVES

The aim of this study was to assess the impact of adjuvant chemotherapy following complete cytoreduction in appendiceal cancer based on histopathological grade and differentiation.

METHODS

Retrospective medical record review of all patients with appendiceal adenocarcinoma treated at our institution between 2006 and 2015. Kaplan-Meier plots were used to summarize overall survival (OS) and relapse-free survival over time, and log-rank tests and Cox proportional hazards models were used to test for differences in survival between groups.

RESULTS

A total of 103 patients with appendiceal adenocarcinoma received care at our institution during the study period. Complete cytoreduction (cytoreductive score 0-1) was achieved in 68 patients (66%). Of these 68 patients, 26 received adjuvant chemotherapy. The most common regimens were capecitabine (n = 11), capecitabine plus oxaliplatin (n = 7), and 5-FU plus oxaliplatin (n = 6). Tumor histopathology and grade, and the ability to achieve complete cytoreduction were significant predictors of overall survival. The median OS for non-low-grade and well-differentiated tumor patients who received adjuvant chemotherapy following complete cytoreduction was 9.03 years, compared to 2.88 years for patients who did not receive adjuvant chemotherapy (P = .02). Among low-grade and well-differentiated tumor patients who underwent complete cytoreduction, there was no statistically significant difference in OS between those who received adjuvant chemotherapy and those who did not.

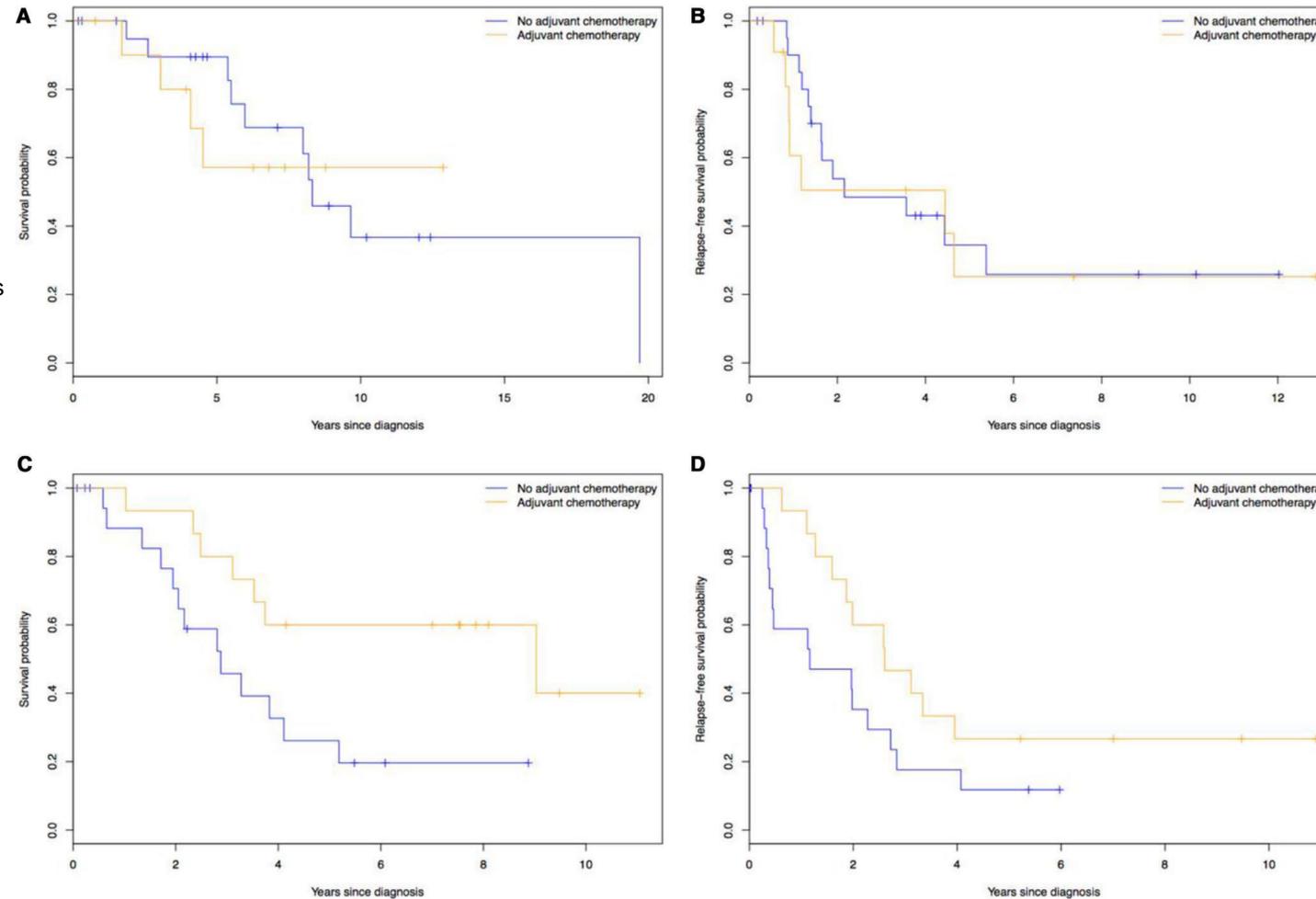


Figure 1. Kaplan Meier curves for overall survival and relapse free survival showing differential impact of adjuvant chemotherapy following complete cytoreduction in low-grade or well differentiated tumors (A&B) and non-low grade or well-differentiated tumors (C&D).

	n	Median OS in years (95% CI) ^{a,b}	Median RFS in years (95% CI) ^{a,b}
Effect of adjuvant chemotherapy after complete cytoreduction in low-grade or well-differentiated adenocarcinoma			
No adjuvant chemotherapy	22	8.32 (5.98, -)	2.16 (1.63, -)
Adjuvant chemotherapy	11	- (4.08, -)	4.45 (0.90, -)
Effect of adjuvant chemotherapy after complete cytoreduction in non-low-grade or well-differentiated adenocarcinoma			
No adjuvant chemotherapy	20	2.88 (2.05, -)	1.16 (0.45, 2.84)
Adjuvant chemotherapy	15	9.03 (3.53, -)	2.60 (1.87, -)

Table 1. Varied impact of adjuvant chemotherapy following complete cytoreduction depending on histopathological grade and differentiation.

a-The P-values given are from a log-rank test.

b-Omitted values were not estimable due to censoring.

DISCUSSION

Given that appendiceal cancer is a very heterogenous entity, we analyzed the impact of adjuvant chemotherapy based on low-grade/well-differentiated tumors vs non-low grade/ well-differentiated tumors. Prior studies suggested a differential benefit for systemic chemotherapy in patients with moderate and high-grade mucinous tumors but not for low-grade mucinous tumors. We found similar differential benefit with adjuvant chemotherapy in this study. Among patients who underwent complete cytoreduction, adjuvant chemotherapy was associated with longer median OS only in the moderate-to-poorly differentiated and signet-ring adenocarcinoma patients but not in patients with low-grade mucinous neoplasm or well-differentiated adenocarcinoma.

CONCLUSIONS

Adjuvant chemotherapy following complete cytoreductive surgery seems to have significant benefit in overall survival in patients with moderate- to high-grade and signet-ring cell appendiceal tumors. Complete cytoreduction significantly influences oncologic outcomes in patients with appendiceal neoplasms. A large multi-institutional study is necessary to further analyze outcomes by each individual category.