Less is More: Risk Factors and Survival Outcomes of Overtreatment for Early-Stage Colorectal Cancer

Daniel R. S. Habib BA[1], Matthew Shou BA[1], James L. Rogers BS[1], Kevin Sun BS[1], Chen Chia Wang BS[1], Aimal Khan MD[2]

[1] Vanderbilt University School of Medicine, [2] Vanderbilt University Medical Center

SCHOOL OF MEDICINE VANDERBILT UNIVERSITY

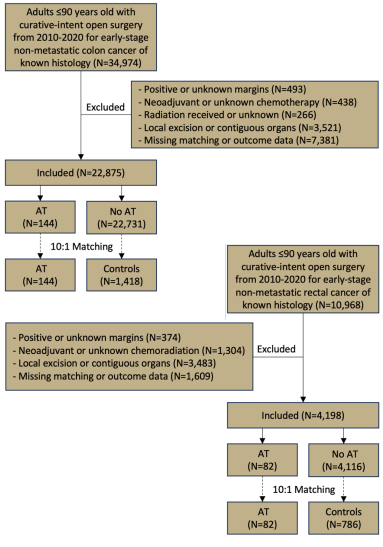
VANDERBILT UNIVERSITY MEDICAL CENTER

Introduction

- After cT1-2N0M0 colorectal cancer (CRC) surgery without upstaging, observation is recommended while adjuvant therapy (AT) constitutes overtreatment.
- Guideline-discordant treatment exhibits worse outcomes,[1] but no study has assessed CRC overtreatment in the past decade.[2,3]
- **Aim**: Determine risk factors and overall survival (OS) impact of AT in early-stage CRC

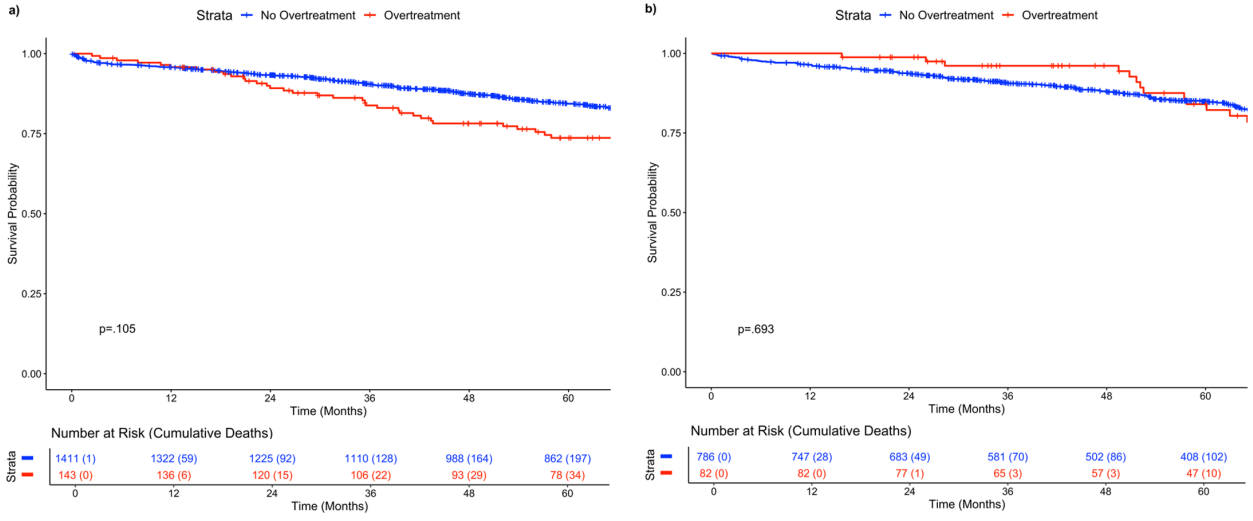
Methods

- **Population**: National Cancer Database (NCDB) CRC patients
- **Statistical Analysis**: Multivariable logistic regression of risk factors; 10:1 propensity score matching, Kaplan-Meier analysis, and Cox regressions of patients with and without AT
- **Covariates**: Age, sex, race, insurance, income, Charlson-Deyo Comorbidity Index, facility type, facility case volume, grade, histology, pathologic T stage



Results

Figure 1. Kaplan Meier Survival Analyses by Overtreatment for (a) Colon and (b) Rectal Cancer



Overtreatment was not associated with worse OS for rectal cancer but exhibited a non-significant trend to worse OS for colon cancer.

Table 1. Multivariable Logistic Regressions by Overtreatment

	Colon		Rectum	
Variable	**aOR (95% CI)**	**P Value**	**aOR (95% CI)**	**P Value**
Age (1 Year Increase)	**0.96 (0.95-0.98)**	**<.001**	1.00 (0.97-1.02)	.770
Female Sex (vs Male)	0.73 (0.52-1.02)	.063	0.88 (0.56-1.38)	.565
Race (vs White)				
Black	**1.94 (1.26-2.99)**	**.002**	1.35 (0.60-3.01)	.471
Other	**2.04 (1.06-3.95)**	**.034**	0.75 (0.23-2.42)	.630
Private Insurance	0.87 (0.58-1.30)	.488	1.10 (0.62-1.95)	.743
Above Median Income	0.71 (0.51-1.00)	.050	0.83 (0.53-1.33)	.443
Any Comorbidity (vs No Comorbidity)	0.83 (0.57-1.20)	.311	0.71 (0.41-1.23)	.225
Research/Academic Facility	0.78 (0.51-1.19)	.246	0.69 (0.40-1.20)	.194
Top Quartile Facility Case Volume	0.80 (0.51-1.25)	.325	0.95 (0.54-1.68)	.857
Poor/Undifferentiated (vs Well/Moderately Differentiated)	1.58 (0.95-2.64)	.080	**2.61 (1.44-4.76)**	**.002**
High-Risk Histology (vs Nonmucinous Adenocarcinoma)	1.76 (0.98-3.15)	.057	**3.20 (1.22-8.40)**	**.018**
pT2 (vs pT1)	**1.66 (1.19-2.33)**	**.003**	**2.58 (1.59-4.19)**	**<.001**

Colon cancer overtreatment was associated with younger age non-white race, and pathologic stage T2 vs T1.

- Non-significant trends for male sex, low income, poor/undifferentiated grade, and high-risk histology

Rectal cancer overtreatment was associated with pathologic stage T2 vs T1, poor/undifferentiated grade, and high-risk histology.

Table 2. Multivariable Cox Regressions for Overall Survival

	Colon		Rectum	
Variable	**HR (95% CI)**	**P Value**	**HR (95% CI)**	**P Value**
Age (1 Year Increase)	**1.06 (1.05-1.07)**	**<.001**	**1.07 (1.05-1.09)**	**<.001**
Female Sex (vs Male)	**0.76 (0.61-0.95)**	**.014**	0.85 (0.62-1.18)	.336
Race (vs White)				
Black	**1.35 (1.02-1.79)**	**.034**	**1.86 (1.14-3.05)**	**.014**
Other	0.70 (0.39-1.25)	.230	0.60 (0.22-1.64)	.318
Private Insurance	0.75 (0.57-1.00)	.052	0.91 (0.61-1.37)	.664
Above Median Income	0.91 (0.73-1.14)	.423	0.76 (0.56-1.03)	.073
Any Comorbidity (vs No Comorbidity)	**1.71 (1.38-2.12)**	**<.001**	**1.47 (1.06-2.02)**	**.019**
Research/Academic Facility	**1.33 (1.02-1.74)**	**.037**	0.73 (0.47-1.16)	.182
Top Quartile Facility Case Volume	0.76 (0.56-1.02)	.071	0.87 (0.54-1.40)	.556
Poor/Undifferentiated (vs Well/Moderately Differentiated)	0.91 (0.65-1.27)	.587	1.02 (0.66-1.57)	.934
High-Risk Histology (vs Nonmucinous Adenocarcinoma)	1.21 (0.82-1.78)	.338	**2.20 (1.10-4.40)**	**.025**
pT2 (vs pT1)	1.01 (0.81-1.25)	.954	1.14 (0.79-1.66)	.480
Overtreatment	**1.40 (1.01-1.93)**	**.042**	1.05 (0.66-1.68)	.844

Colon cancer overtreatment was independently associated with worse OS.

Rectal cancer overtreatment was not independently associated with worse OS.

Discussion

- Our study algins with previous work[2] yet is unique in assessing current colon cancer data and is the first to assess rectal cancer overtreatment.
- Younger and non-white patients exhibit worse CRC outcomes,[4,5] which might explain why they are more likely to be overtreated.
- The results highlight the importance of guideline adherence since systemic toxicity risk outweighs potential survival benefit.
- **Limitations**:
  - Small overtreatment sample
  - Limited NCDB surgical outcomes
  - Might not capture all factors that influence treatment decisions

Conclusion

- Overtreatment of early-stage colon (0.6%) and rectal cancer (2.0%) is rare.
- Patient and tumor characteristics were associated with increased odds of overtreatment depending on cancer type.
- Overtreatment was significantly associated with worse OS in colon cancer but not rectal cancer

References

1. Boland GM, Chang GJ, Haynes AB, et al. Association between adherence to National Comprehensive Cancer Network treatment guidelines and improved survival in patients with colon cancer. Cancer. 2013;119:1593-1601.
2. Kneuertz PJ, Chang GJ, Hu C-Y, *et al.* Overtreatment of Young Adults With Colon Cancer. *JAMA Surg.* 2015;150:402.
3. Chagpar R, Xing Y, Chiang Y-J, et al. Adherence to Stage-Specific Treatment Guidelines for Patients With Colon Cancer. J Clin Oncol. 2012;30:972-979.
4. You YN. Young-Onset Colorectal Cancer: Is It Time to Pay Attention? Arch Intern Med. 2012;172:287.
5. Alexander DD, Waterbor J, Hughes T, et al. African-American and Caucasian disparities in colorectal cancer mortality and survival by data source: An epidemiologic review. Cancer Biomarkers. 2007;3:301-313.

Daniel R. S. Habib
Website: danielrshabib.github.io
Daniel.r.habib@vanderbilt.edu
@danielrshabib

SCAN ME