Cigarette smoking and its impact on the survival outcomes and molecular features of metastatic colorectal cancer patients

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INTRODUCTION

Tobacco use is the most preventable cause of cancer.[1] Smoking itself accounts for approximately 30% of all cancer-related deaths in the United States.[2] Furthermore, colorectal cancer (CRC) is the second most common cause of cancer death in the United States. In 2020, approximately 147,950 individuals were diagnosed with CRC and 53,200 died from the disease.[3] 11%-22% of these new CRC cases were attributable to tobacco use.[4] Although past studies have demonstrated a significant association of cigarette smoking with CRC incidence and mortality, there is very little existing literature that has shown the impact of cigarette smoking on the outcomes of metastatic colorectal cancer (CRC).[5] The impact of smoking on the survival and features of metastatic CRC patients remains unclear.

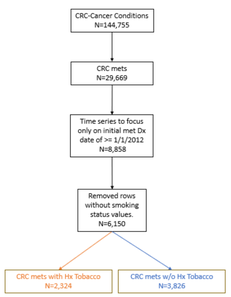
AIMS

Aim 1: Identify the clinical, laboratory, and pathology features of colorectal cancer patients who smoke and compare them with those who do not smoke. This will focus on a dozen specific characteristics previously identified as critical to overall survival. These correlations will be helpful in interpreting survival outcomes in Aim 2.

Aim 2: Explore the association of smoking with overall survival of metastatic colorectal cancer patients. I will use an institutional database to explore the impact of smoking with survival after diagnosis. I will use a multivariate model to incorporate known existing prognostic factors explored in Aim 1.

Aim 3: Explore the molecular pathology of how cigarette smoking is associated with colorectal cancer. Genetic and environmental factors cause accumulation of genetic and epigenetic mutations, altering the stem cells or stem cell-like cells in the base of colon crypts, which may progress to more aberrant versions. Cancerous mutations involve several different genes that may be exacerbated by smoking. I will use an existing database to explore association of smoking with key mutations of interest for CRC.

METHODS



FIGURES

Overall Survival of Metastatic CRC with Smoking Status

Smoker	Mean[a] Estimate	Mean[a] Std. Error	Mean[a] 95% CI Lower Bound	Mean[a] 95% CI Upper Bound	Median Estimate
No	212.661	3.455	205.889	219.434	279.167
Yes	201.421	4.204	193.181	209.661	233.000
Overall	209.492	2.697	204.207	214.777	274.583

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.118	1	.077

Test of equality of survival distributions for the different levels of Smoker.

Overall Survivial of Metastatic CRC Smokers/Non-Smokers Between Males and Females

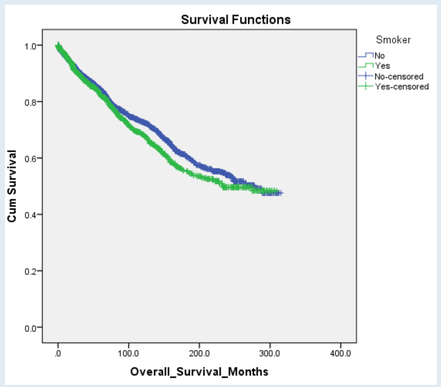
Means and Medians for Survival Time

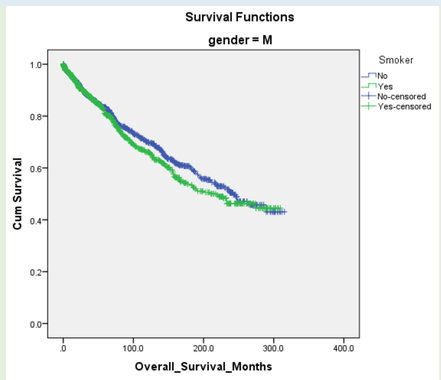
gender,	Smoker	Mean[a] Estimate	Mean[a] Std. Error	Mean[a] 95% CI Lower Bound	Mean[a] 95% CI Upper Bound	Median Estimate	Median Std. Error	Median 95% CI Lower Bound	Median 95% CI Upper Bound
F	No	218.262	4.677	209.095	227.429	.	.	.	.
	Yes	206.941	6.357	194.481	219.402	.	.	.	.
	Overall	216.982	3.848	209.440	224.524	.	.	.	.
M	No	205.355	4.990	195.574	215.136	242.833	19.078	205.440	280.226
	Yes	194.751	5.372	184.221	205.281	219.583	27.504	165.676	273.490
	Overall	201.771	3.704	194.510	209.031	232.667	16.872	199.598	265.736
Overall	Overall	209.492	2.697	204.207	214.777	274.583	.	.	.

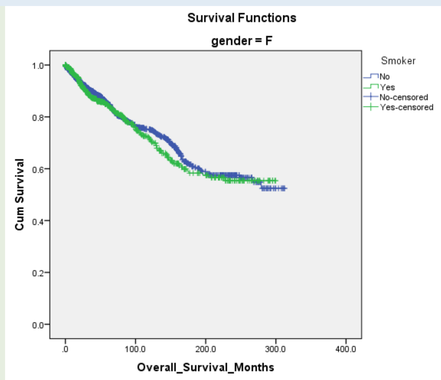
a. Estimation is limited to the largest survival time if it is censored.

Pairwise Comparisons

	gender,	Smoker	No Chi-Square	No Sig.	Yes Chi-Square	Yes Sig.
Log Rank (Mantel-Cox)	F	No			.634	.426
		Yes	.634	.426		
	M	No			1.202	.273
		Yes	1.202	.273		







Chi Square Test KRAS x Smoker Status

Smoker * KRAS_status, Crosstabulation

Smoker			KRAS_status, Mutated	Wildtype	Total
Smoker	No	Count	2323	586	284	3193
		Expected Count	2319.4	608.8	264.7	3193.0
	Yes	Count	1418	396	143	1957
		Expected Count	1421.6	373.2	162.3	1957.0
Total		Count	3741	982	427	5150
		Expected Count	3741.0	982.0	427.0	5150.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	5.957[a]	2	.051
Likelihood Ratio	6.003	2	.050
N of Valid Cases	5150		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 162.26.

Symmetric Measures

		Value	Approximate Significance
Nominal by Nominal	Phi	.034	.051
	Cramer's V	.034	.051
N of Valid Cases		5150	

Chi Square Test BRAF x Smoker Status

Smoker * BRAF_Status, Crosstabulation

Smoker			BRAF_Status, Mutated	Wildtype	Total
Smoker	No	Count	2835	110	248	3193
		Expected Count	2855.7	107.9	229.4	3193.0
	Yes	Count	1771	64	122	1957
		Expected Count	1750.3	66.1	140.6	1957.0
Total		Count	4606	174	370	5150
		Expected Count	4606.0	174.0	370.0	5150.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	4.474[a]	2	.107
Likelihood Ratio	4.551	2	.103
N of Valid Cases	5150		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 66.12.

Symmetric Measures

		Value	Approximate Significance
Nominal by Nominal	Phi	.029	.107
	Cramer's V	.029	.107
N of Valid Cases		5150	

RESULTS

The aims of this research study were to associate cigarette smoking with survival outcomes and molecular features of metastatic colorectal cancer patients by analyzing an institutional database. Preliminary data suggests that smoking history has a modest effect on overall survival in metastatic patients compared to a non-smoker. It also suggests that there may be a correlation between smoking and KRAS/BRAF mutations in metastatic CRC patients.

CONCLUSION

Smoking is linked to survival outcomes and molecular features of metastatic colorectal cancer. The association of smoking with colorectal cancer and its clinical, pathological, epidemiological, and molecular features still needs to be better understood. Future research findings will help point to risk factors involved with smoking in colorectal cancer patients and at-risk patients. Further findings may help to identify markers and patterns that will lead to a faster metastatic CRC diagnosis and an overall better prognosis (improved survival rate and increased survival time). Ultimately, the findings should aim to push forward the agenda of smoking cessation in metastatic CRC patients, at-risk patients, and the general population.

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