

Can we Predict Rectal Cancer Outcomes using Clinical Data? A Comparative Analysis of Different Techniques.

By

**Karina Krishnan
Beachwood High School (Grade 11)
Beachwood, OH, 44122**

The Research Question

The objective of this study is to determine which pre-surgery and Magnetic Resonance Imaging (MRI) variable(s) are significantly associated with rectal cancer outcomes -measured by the **pathologic T-Stage, pathologic N-Stage, pathologic M-Stage**, under the TNM (Tumor, Node, Metastasis) system that describes the extent of the primary tumor based on its size and invasion into surrounding tissues, for patients diagnosed with locally advanced rectal cancer, or **recurrence**. This is important for prognostic assessment, surgical planning, and the evaluation of treatment response, in the context of multidisciplinary rectal cancer care. Different methodologies are utilized to determine whether there are any consistent predictors of rectal cancer outcomes.

Introduction

Rectal cancer is a kind of cancer that forms in the tissues of the rectum. Cancer inside the rectum and cancer inside the colon are often referred to together as colorectal cancer (CRC). CRC is the third most common cancer and the second leading cause of cancer-related deaths in the world with an estimated number of 1.8 million new cases and about 881,000 deaths worldwide in 2018. Multiple factors are involved in this variation, including risk factor exposure, demographic variations, in addition to genetic susceptibility, and genetic mutations and their effect on the prognosis and treatment response (see Baidoun et al., 2021). As described by Borgheresi et al (2022) in the Journal of Clinical Medicine, among people diagnosed with metastatic CRC, approximately 70% to 75% of patients survive beyond 1 year, 30% to 35% beyond 3 years, and fewer than 20% beyond 5 years from diagnosis. The American Cancer Society (ACS) estimates 152,810 new cases of colorectal cancer in 2024. According to estimates, men will account for 81,540 cases, and women will account for 71,270. Of these, 106,590 cases will be colon cancer, and 46,220 cases will be rectal cancer (American Cancer Society, Cancer Facts and Figures 2024) Out of new CRC cancer diagnoses, 20% of patients have metastatic disease at presentation and another 25% present with localized disease will later develop metastases. (Biller et al., 2021)

While rectal and colon cancers are similar in many ways, their treatments are quite different. This is mainly because the rectum is barely separated from other organs and structures. The primary treatments for metastatic rectal cancer include chemotherapy, biologic therapy, immunotherapy, or their combinations. Rectal cancer management has evolved significantly in recent years, with imaging playing an increasingly central role in treatment planning and outcome prediction. The use of high-resolution imaging, particularly MRI, has become indispensable in managing rectal cancer. Its ability to provide detailed prognostic information, guide treatment decisions, and assess treatment response makes it a cornerstone of modern rectal cancer care. As imaging technologies continue to advance, their role in predicting and improving patient outcomes is likely to become even more significant.

Rectal cancer staging usually uses the TNM (Tumor, Node, Metastasis) staging system. The stage of cancer (whether it affects the inner lining of the rectum only, involves the whole rectum, or has spread to lymph nodes, nearby organs, or other places in the body). In the TNM system, a stage I, II, III, or IV (also written as 1, 2, 3, or 4) is assigned, defined as follows:

- o Stage 0 (carcinoma in situ)
 - o Stage I (also called stage 1) rectal cancer: stage I rectal cancer, cancer has formed in the mucosa (innermost layer) of the rectum wall and has spread to the submucosa (layer of tissue next to the mucosa) or to the muscle layer of the rectum wall.
 - o Stage II (also called stage 2) rectal cancer
 - o Stage III (also called stage 3) rectal cancer
 - o Stage IV (also called stage 4) rectal cancer
- Thus, as a rule, a higher number, such as stage IV, means cancer has spread more
- o Rectal cancer can recur (come back) after it has been treated. This is recurrence.

Clinical TNM is also determined via imaging before any treatment (including surgery). Chemoradiation is a primary treatment.

This research aims to analyze the associations of pre-surgery variables (or the control variables) and MRI variables on cancer outcomes above by determining which variables are significantly associated with rectal cancer outcomes – pathologic T-Stage, pathologic N-Stage, pathologic M-Stage, and recurrence (defined above) – using Logit and Tobit regression, Lasso regression, Ridge regression, and ElasticNet regression. The small sample but high-dimensional data used in my analysis is collected from Case Western Reserve University's Department of Biomedical Engineering, from 55 patients treated at *University Hospitals Cleveland Medical Center*.

Variables

The TNM stage system describes the extent of the primary tumor based on its size and invasion into surrounding tissues. Most patients undergo total mesorectal excision surgery (TME), during which a large portion if not the entire rectum is removed. Tissue from the surgically excised specimen is then extracted and analyzed under a microscope to determine pathologic TNM. Pathologic TNM is determined after surgery.

Outcome variables

There are 4 outcome variables (see American Joint Committee on Cancer (AJCC) TNM staging rules:

<https://www.cancer.gov/types/colorectal/patient/rectal-treatment-pdq>):

- **pathologic T-Stage (path_t_stage):** Takes the value of 0 through 4: where 0 indicates no evidence of primary tumor is found; 1 indicates when a small tumor is confined to the rectal wall without invading surrounding structures; 2 indicates a tumor that has invaded through the rectal wall but is confined to nearby structures without involving lymph nodes or distant metastasis; 3 indicates a tumor that has penetrated through the rectal wall and may involve nearby organs or structures, possibly with lymph node involvement; 4 indicates a tumor that has spread to adjacent organs or tissues and may involve nearby lymph nodes.
- **pathologic N-Stage (path_n_stage):** Indicates whether cancer has spread to nearby lymph nodes and, if so, to what extent, taking the values of 0 through 2, where 0 indicates that no regional lymph node metastasis is present (that is, cancer cells have not spread to nearby lymph nodes); 1 indicates the presence of regional lymph node metastasis, but it is limited in extent or confined to a certain number of nearby lymph nodes; 2 indicates a more extensive spread of cancer cells to nearby lymph nodes or a greater number of lymph nodes affected compared to stage 1.
- **pathologic M-Stage (path_m_stage):** Indicates whether cancer has spread to distant sites beyond the primary tumor and nearby lymph nodes, and taking the values of 0 through 1, where 0 indicates that cancer cells have not spread to distant organs or tissues beyond the primary tumor site and nearby lymph nodes; 1 indicates the presence of distant metastasis, where cancer cells have spread to distant organs or tissues; 2 indicates a more extensive spread of cancer cells to distant sites compared to stage 1.
- **Recurrence:** An indicator variable that takes the value of 0 if the patient did not experience cancer recurrence within a specified follow-up period after completing initial treatment for rectal cancer, and 1 if the patient experienced cancer recurrence within the specified follow-up period after completing initial treatment for rectal cancer.

The explanatory variables are in 2 categories – pre-surgery or control variables and imaging variables – as defined below:

Pre-surgery variables or control variables

- **Sex** (0 = female; 1 = male)
- **BMI** (the patient's Body Mass Index)
- **Race** (2= African American; 1 = Hispanic/ Asian; 0 = White)
- **days_from_diagnosis_to_surgery**
- **initial_cea**: The initial level of Carcinoembryonic Antigen (CEA) in the blood that may be produced by some types of cancer cells, including colorectal cancer, often used as a tumor marker, particularly for monitoring colorectal cancer, although elevated CEA levels can also be associated with other conditions. CEA concentration is measured in nanograms per milliliter (ng/mL). The typical reference range for CEA is usually considered to be less than 3 to 5 ng/mL for people without cancer.
- **days_from_neo_xrt_to_surgery**: Neoadjuvant therapy often administered before surgery aims to shrink the tumor, reduce the risk of cancer spread, and improve surgical outcomes. After completing neoadjuvant therapy, there is typically a period of time before the surgical intervention takes place. It provides time for the effects of neoadjuvant therapy to take full effect, potentially reducing the size of the tumor and facilitating a less extensive surgical procedure. It provides a window for patient recovery and optimization of surgical conditions. It may influence treatment outcomes and postoperative complications.

Initial staging, also called Clinical TNM, is determined via imaging before any treatment (including surgery).

- **init_clinical_staging_t**: Initially, the patient is at the T stage in cancer staging systems, in the TNM (Tumor, Node, Metastasis) system, which indicates the extent of the primary tumor based on its size and invasion into surrounding tissues. The higher the number the higher the size and invasion.
- **init_clinical_staging_n**: Initially, the patient is at the N stage indicating whether cancer has spread to nearby lymph nodes and, if so, to what extent. The higher the number, the higher the spread.
- **init_clinical_staging_m**: Initially, the patient is at the M stage indicating whether the cancer has spread to distant sites beyond the primary tumor and nearby lymph nodes. M0 typically indicates that there is no evidence of distant metastasis; the cancer has not spread to distant sites. M1 indicates the presence of distant metastasis; the cancer has spread to distant organs or tissues.

Imagining variables:

- **signet_ring_features:** An indicator for the presence or absence of signet ring cell features within the tumor tissue. Signet ring cells are characterized by their appearance under the microscope, where the nucleus of the cell is displaced to the periphery by mucin droplets, giving the cell a signet ring appearance. The presence or absence of signet ring cell features can have implications for tumor behavior, treatment response, and prognosis.
- **mucin_present:** An indicator for the presence or absence of mucin within the tumor tissue. Mucin is a jelly-like substance produced by certain types of cancer cells, including those found in mucinous adenocarcinomas. The tumor is classified as a mucinous adenocarcinoma, where the cancer cells produce mucin, or the tumor is classified as a non-mucinous adenocarcinoma, where mucin production by cancer cells is not observed. Mucinous rectal cancer has a poorer prognosis.
- **distance_to_proximal_margin:** The distance between the tumor margin and the proximal (nearest) surgical margin. Indicates how close the tumor is to the edge of the resected tissue closest to its origin within the colon or rectum, in mm. A smaller value suggests that the tumor is closer to the proximal surgical margin, indicating that the surgical resection may have been more challenging or that there may have been a higher risk of incomplete resection. A larger value indicates that the tumor is further away from the proximal surgical margin, suggesting a greater margin of safety and potentially a more favorable outcome regarding the completeness of tumor resection.
- **distance_to_distal_margin:** The distance between the tumor margin and the distal (farthest) surgical margin. This distance indicates how close the tumor is to the edge of the resected tissue farthest from its origin within the colon or rectum, in mm. A smaller value suggests that the tumor is very close to the distal surgical margin, indicating a potential risk of incomplete resection or involvement of the surgical margin by tumor cells. A larger value indicates that the tumor is further away from the distal surgical margin, suggesting a greater margin of safety and potentially a more favorable outcome regarding the completeness of tumor resection. Surgeons aim to achieve an adequate margin of normal tissue around the tumor to ensure complete removal of the cancer while minimizing the risk of leaving residual tumor cells behind.
- **number_of_lymph_nodes_exam:** This is the total number of lymph nodes examined during pathological evaluation after surgical resection for rectal cancer. This measurement is crucial for accurately staging the cancer and assessing the extent of lymph node involvement. A larger number of lymph nodes examined typically indicates a more thorough evaluation and provides a better assessment of lymph node status.
- **number_of_positive_lymph_n:** This is the count of lymph nodes that tested positive for cancer metastasis during pathological evaluation after surgical resection for rectal cancer. This measurement is significant for determining the extent of lymph node involvement by cancer cells. A value of 0 indicates that none of the examined lymph nodes showed evidence of cancer metastasis. Increasing values (e.g., 1, 2, 3, etc.) represent the

number of lymph nodes that tested positive for cancer metastasis, with each increment indicating additional lymph nodes involved by cancer cells.

- **lymphovascular_invasion:** This is the presence or absence of lymphovascular invasion (LVI) within the tumor tissue. Lymphovascular invasion is a pathological finding indicating the invasion of cancer cells into lymphatic or blood vessels surrounding the tumor. The values taken could be 1 indicating the absence of lymphovascular invasion; 2 representing the presence of lymphovascular invasion; or 3, which introduces a potential refinement or grading of lymphovascular invasion. It may indicate a more extensive or severe invasion of lymphatic or blood vessels by cancer cells compared to the presence of invasion indicated by a value of 2 that may influence treatment decisions, including the intensity of adjuvant therapy and the frequency of surveillance for disease recurrence.
- **perineural_invasion:** Indicates the presence or absence of perineural invasion (PNI) within the tumor tissue. Perineural invasion is a pathological finding indicating the invasion of cancer cells into the nerve fibers surrounding the tumor. Perineural invasion is associated with an increased risk of cancer recurrence and metastasis. Its presence suggests a more aggressive tumor behavior and may influence treatment decisions and prognosis estimation. A value of 1 indicates the absence of perineural invasion. In other words, there is no evidence of cancer cells invading the nerve fibers within the tumor tissue. A value of 2 indicates the presence of perineural invasion. In this case, cancer cells have been identified invading the nerve fibers within the tumor tissue. The presence of perineural invasion is typically associated with a poorer prognosis, as it indicates a higher likelihood of cancer spreading beyond the primary tumor site along nerve pathways.
- **peritumor_lymphocytic_resp:** This captures the degree or extent of peritumoral lymphocytic response observed in the tumor microenvironment. Peritumoral lymphocytic response refers to the presence of lymphocytes (a type of white blood cell) around the tumor tissue, which can indicate the immune system's response to the presence of cancer cells. A value of 1 indicates a minimal or absent peritumoral lymphocytic response. In other words, there are few lymphocytes present around the tumor tissue. A value of 2 indicates a moderate peritumoral lymphocytic response. In this case, there is a noticeable presence of lymphocytes around the tumor tissue, suggesting an immune response to the tumor. A value of 3 indicates a marked or intense peritumoral lymphocytic response. In this scenario, there is a significant infiltration of lymphocytes around the tumor tissue, indicating a robust immune reaction against the tumor. A more pronounced peritumoral lymphocytic response is often associated with a better prognosis in some types of cancer. It suggests an active immune response against the tumor, which may inhibit tumor growth and metastasis. Patients with tumors showing a marked peritumoral lymphocytic response may potentially benefit from immunotherapy, which aims to enhance the body's immune response against cancer cells.
- **large_vessel_invasion:** Indicates the presence or absence of large vessel invasion (LVI) within the tumor tissue. Large vessel invasion is a pathological finding indicating the invasion of cancer cells into larger blood vessels or veins near the tumor. A value of 2 indicates the absence of large vessel invasion. In other words, there is no evidence of cancer cells invading larger blood vessels or veins within the tumor tissue. A value of 3 indicates

the presence of a large vessel invasion. In this case, cancer cells have been identified as invading larger blood vessels or veins within the tumor tissue. Large vessel invasion, particularly when present (value of 3), is associated with a poorer prognosis and increased risk of cancer spreading to distant sites via the bloodstream. Its presence is associated with a higher risk of cancer recurrence, metastasis, and poorer survival outcomes. Patients with evidence of large vessel invasion may require more aggressive treatment approaches, such as additional adjuvant therapy (e.g., chemotherapy) or targeted therapy, to reduce the risk of disease recurrence and improve outcomes.

- **ulceration_present:** Indicates the presence or absence of ulceration in the tumor tissue. Ulceration in cancer typically refers to the formation of an ulcer or an open sore on the surface of the tumor. A value of 1 indicates the absence of ulceration. In other words, there is no evidence of an ulcer or open sore on the surface of the tumor. A value of 2 indicates the presence of ulceration. In this case, an ulcer or open sore is present on the surface of the tumor. A value of 3 introduces a potential refinement or grading of ulceration. It may indicate a more extensive or severe ulceration compared to the presence of ulceration indicated by a value of 2. The presence of ulceration may be associated with a more aggressive tumor behavior and poorer prognosis in some cases. Ulcerated tumors may be more prone to bleeding, local invasion, and metastasis. Ulceration may influence treatment decisions, as ulcerated tumors may require additional interventions to control symptoms such as bleeding or pain.

Hypothesis

Among the various pre-surgery and MRI variables available for colorectal cancer patients, Initial staging, or Clinical TNM among the pre-surgery variables, and the extent of lymph node involvement by cancer cells, in imaging variables are significantly associated with pathologic TNM and recurrence, consistently across all the different regression methods used.

Methods

All the continuous explanatory variables are first standardized into the *z scores* by subtracting the sample mean and dividing by sample standard deviation, to remove the dimensionality for the data but preserve the variability. Then three different regression techniques are utilized to determine whether any variable of the variables is consistently and significantly associated with outcomes. For analyzing the first 3 outcome variables Tobit regression (ordered outcomes) is used, and for the last outcome variable, Logit regression (binary outcomes) is utilized. LASSO and Ridge regression methods, as well as a combination of the two, called ElasticNet regression, are also used.

- Tobit and Logit Regressions: Since the dependent variables are not continuous variables, we use the Tobit regression method for `path_t_stage`, `path_n_stage`, and `path_m_stage` which can take ordered values, and the Logit regression method for `recurrence` that is 0 or 1 indicator variable.
- LASSO Regression: LASSO (Least Absolute Shrinkage and Selection Operator) performs variable selection and regularization by imposing penalties on the regression coefficients. LASSO regression reduces some regression coefficients to zero, effectively selecting the variables that are most important to the response variable. I changed the penalty function and only reported the non-zero coefficient variables in different penalty function scenarios for comparative analysis with LASSO. The use of concave penalties, such as the smoothly clipped absolute deviation (SCAD) and minimax concave penalty (MCP) has increased, demonstrating their effectiveness in improving model performance over traditional LASSO methods. Recent advancements also include the integration of non-convex penalties in LASSO regression, which aims to reduce bias and improve variable selection consistency. Therefore, I used adaptive LASSO, SCAD, and MCP.
- Ridge Regression: In Ridge regression, overfitting deals with multicollinearity problems by imposing penalties on the regression coefficients. Unlike LASSO, Ridge regression does not reduce the coefficients to zero, but it stabilizes the model by making all the coefficients smaller. To identify which variable is the primary determinant, look at the absolute value of the coefficient: a larger absolute value of the coefficient usually indicates that the variable has a greater influence on the response variable. Generally, coefficients with absolute values greater than 0.1 (when predictors are standardized) can be considered large enough to be practically significant. ElasticNet is also chosen for its ability to combine the advantages of LASSO and Ridge regression, providing a robust approach to handling high-dimensional data and multicollinearity. It offers a balanced solution by performing variable selection and ensuring model stability, leading to improved predictive performance. The integration of both L1 and L2 penalties allows ElasticNet to address the limitations of each method individually, making it a preferred choice in various predictive modeling scenarios.

Using Stata and Python programming, the regression results are examined with (a) only the imaging variables and (b) with both imaging variables and pre-surgery variables (or control variables).

Results

Table 1 shows the Tobit and Logit regression results. Only the significant (at 1% level) variables are shown in bold coefficients. Panel A shows the results with only the imaging explanatory variables, while Panel B shows the results with the pre-surgery variables also added in.

Table 1: Tobit and Logit Regression Results:

The table shows only the significant coefficients, in such a way that we do not show a method when no variable was significant in that method.

Panel A: Imaging Variables only

Significant Coefficients for Path T Stage	Tobit
mucin_present	2.879

Significant Coefficients for Path M Stage	Tobit
number_of_positive_lymph_n	0.274
lymphovascular_invasion	3.314

Panel B: Imaging Variables and Pre-surgery variables

Significant Coefficients for Path M Stage	Tobit
number_of_positive_lymph_n	0.572
lymphovascular_invasion	0.393
sex	-4.353

The results show that **number_of_positive_lymph_n** and **lymphovascular_invasion** imaging variables are significantly associated with **path M Stage** outcome in both Panels A and B.

Table 2 depicts the Adaptive LASSO regression, SCAD, and MCP results. Panel A shows the results with only the imaging explanatory variables, while Panel B shows the results with the pre-surgery variables also added in.

Table 2: LASSO Regression:

The table shows only the significant coefficients, in such a way that we do not show a method, when no variable was significant in that method.

Only the significant variables across at least 2 of these methods are shown in bold coefficients.

Panel A: Imaging Variables only

Non-Zero Coefficients for Path T Stage	Adaptive Lasso	SCAD	MCP
number_of_positive_lymph_n	0.073	0.036	
distance_to_proximal_margin		-0.031	
number_of_lymph_nodes_exam		0.044	

Non-Zero Coefficients for Path N Stage	<i>Adaptive Lasso</i>	SCAD	MCP
number_of_positive_lymph_n	0.214	0.156	0.090

Non-Zero Coefficients for Path M Stage	<i>Adaptive Lasso</i>	SCAD	MCP
number_of_positive_lymph_n	0.044		
distance_to_proximal_margin		-0.034	
distance_to_distal_margin		-0.022	
number_of_lymph_nodes_exam		-0.045	

Panel B: Imaging Variables and Pre-surgery variables

Non-Zero Coefficients for Path T Stage	<i>Adaptive Lasso</i>	SCAD	MCP
number_of_positive_lymph_n	0.073	0.054	
Sex		-0.367	-0.340
init_clinical_staging_m		-0.174	-0.217
Bmi		0.158	0.058
days_from_diagnosis_to_surgery		-0.190	-0.132
distance_to_distal_margin		0.079	0.026
number_of_lymph_nodes_exam		0.024	

Non-Zero Coefficients for Path N Stage	<i>Adaptive Lasso</i>	SCAD	MCP
number_of_positive_lymph_n	0.214	0.144	0.060
Race		0.177	0.297
init_clinical_staging_m		0.217	0.346

Non-Zero Coefficients for Path M Stage	<i>Adaptive Lasso</i>	SCAD	MCP
number_of_positive_lymph_n	0.044		
Race		0.209	0.200
init_clinical_staging_m		0.148	0.206
Bmi		-0.046	
days_from_neo_xrt_to_surgery		0.047	

distance_to_proximal_margin		-0.018	
distance_to_distal_margin		-0.044	
number_of_lymph_nodes_exam		-0.035	-0.030

Non-Zero Coefficients for Recurrence	<i>Adaptive Lasso</i>	SCAD	MCP
init_clinical_staging_m		-0.024	

Results show that **number_of_positive_lymph_n** imaging variable is significantly associated with **path T Stage** and **path N Stage** outcomes in both Panels A and B. Among the pre-surgery or control variables, **init_clinical_staging_m** appears to be a significant predictor of **path T Stage**, **path N Stage** and **path M Stage** outcomes, and **race** appears to be a significant predictor of **path N Stage** and **path M Stage** outcomes in Panel B.

Table 3 shows the Ridge regression and ElasticNet regression results. Only the significant variables in both methods are shown in bold coefficients. Panel A shows the results with only the imaging explanatory variables, while Panel B shows the results with the pre-surgery variables also added in.

Table 3: Ridge and ElasticNet Regression:

The table shows only the significant coefficients, in such a way that we do not show a method when no variable was significant in that method.

Panel A: Imaging Variables only

Significant Coefficients for Path N Stage	Ridge	ElasticNet
number_of_positive_lymph_n	0.691	0.656
lymphovascular_invasion	0.147	

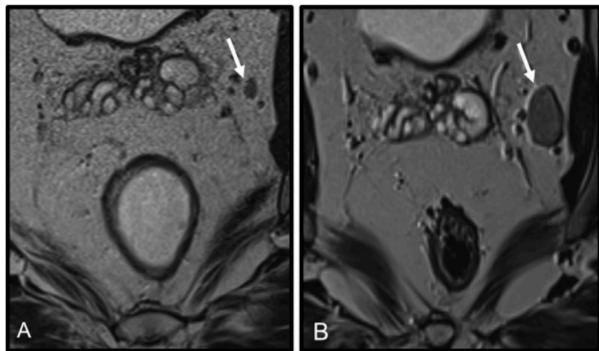
Panel B: Imaging Variables and Pre-surgery variables

Significant Coefficients for Path N Stage	Ridge	ElasticNet
init_clinical_staging_m	0.177	
number_of_positive_lymph_n	0.514	0.562
large_vessel_invasion	-0.139	

Results show that **number_of_positive_lymph_n** imaging variable is significantly associated with **path N**

Stage both Panels A and B.

The figure below shows no significant positive lymph nodes (A) compared to the presence of a positive lymph node (B) as shown by the arrow (see Wetzel et al., 2022).



Discussion

In general, across almost all methods I used, the “**number_of_positive_lymph_n**” imaging variable is significant and positively associated with **path_t_stage**, **path_m_stage**, and **path_n_stage** outcomes. The **number_of_positive_lymph_n** refers to the number of lymph nodes to which cancer has spread, also known as the n-stage. It makes sense clinically that lymph nodes are associated with poorer outcomes. More severe cancer spreads to lymph nodes and can spread to other parts of the body via the lymphatic system, leading to poorer outcomes. Kroon et al (2022) in the *European Journal of Surgical Oncology* explains the importance of understanding lymph node metastasis. Between 15% and 20% of patients with locally advanced rectal cancer have metastases to the lateral lymph nodes (LLNs) in the pelvic side wall at diagnosis. Sluckin et al (2022) in *Clinical Colorectal Cancer*, argue that LLNs in low, locally advanced, rectal cancer have proven implications for local recurrence rates, which increase drastically in the presence of persistently enlarged LLN and require awareness and knowledge from radiology, radiation oncology, and surgery to ensure proper treatment.

Among control or pre-surgery variables, **init_clinical_staging_m** and **race** are generally significantly associated with **path_t_stage**, **path_m_stage**, and **path_n_stage** outcomes. **init_clinical_staging_m** refers to clinical M, or metastatic, stage, determined at diagnosis prior to any treatment. Doctors will try to figure out whether it has spread, and to what extent. Despite receiving comparable first-line treatment and achieving comparable response rates, black patients demonstrated inferior survival compared to white patients. That is to say, factors such as pathologic and genetic mediators are important contributors to racial disparity in rectal cancer survival.

Conclusion

Results support the *hypothesis* that among the various pre-surgery and MRI variables available for colorectal cancer patients, `number_of_positive_lymph_n` (imaging variable), and `init_clinical_staging_m` and `race` (pre-surgery variable) appear to be significantly associated with pathologic TNM and recurrence. There are only 55 cases in this analysis, so this is a small sample, yet offers multidimensional data. As the number of cases grows, further testing can be done. For instance, the results can be more reliable with the inclusion of an initial fit period and a subsequent test period. With advancing imaging technologies, the role of imaging in predicting and improving patient outcomes is likely to grow even more significant in the future.

Acknowledgments and References:

I thank Professor Dr. Satish Viswanath <satish.viswanath@case.edu>, Mr. Thomas DeSilvio <tgd15@case.edu> and Dr. Charlems Alvarez Jimenez <cxa220@case.edu> of the Department of Biomedical Engineering, Case Western Reserve University for the data, and regular guidance in this project.

Adam Wetzel, Satish Viswanath, Emre Gorgun, Ilker Ozgur, Daniela Allende, David Liska, Andrei S Purysko, Staging and Restaging of Rectal Cancer with MRI: A Pictorial Review, Seminars in Ultrasound, CT and MRI, Volume 43, Issue 6, 2022, Pages 441-454, ISSN 0887-2171, <https://doi.org/10.1053/j.sult.2022.06.003>

Alessandra Borgheresi, Federica De Muzio, Andrea Agostini, Letizia Ottaviani, Alessandra Bruno, Vincenza Granata, Roberta Fusco, Ginevra Danti, Federica Flammia, Roberta Grassi, Francesca Grassi, Federico Bruno, Pierpaolo Palumbo, Antonio Barile, Vittorio Miele, and Andrea Giovagnoni "Lymph Nodes Evaluation in Rectal Cancer: Where Do We Stand and Future Perspective." Journal of Clinical Medicine. 2022 May; 11(9), 2599,

American Cancer Society (ACS), *Cancer Facts and Figures* 2024

Emma Veach¹ Ismael Xique¹ Jada Johnson¹ Jessica Lyle Israel Almodovar, Kimberly F. Sellers² Calandra T. Moore³ Monica C. Jackson, "Race matters: analyzing the relationship between colorectal cancer mortality rates and various factors within respective racial groups." Public Health, 10 November 2014.

Firas Baidoun, Kholoud Elshiwly, Yasmine Elkeraie, Zahi Merjaneh, George Khoudari, Muhammad Talal Sarmini, Mohamed Gad, Muneer Al-Husseini, Anas Saad, Colorectal Cancer Epidemiology: Recent Trends and Impact on Outcomes, Curr Drug Targets, 2021;22(9), ages: 998-1009.

Hidde M. Kroon, Lotje A. Hoogervorst, Nicole Hanna-Rivero, Luke Traeger, Nagendra N. Dudi-Venkata, Sergei Bedrikovetski, Mir anda Kusters, George J. Chang, Michelle L. Thomas, Tarik Sammour, "Systematic review and meta-analysis of long-term oncological outcomes of lateral lymph node dissection for metastatic nodes after neoadjuvant chemoradiotherapy in rectal cancer.", European Journal of Surgical Oncology, Volume 48, Issue 7, July 2022, Pages 1475-1482.

Leah H. Biller, Deborah Schrag, "Diagnosis and Treatment of Metastatic Colorectal Cancer: A Review." *JAMA*. 2021;325(7): 669-685.

National Cancer Institute Website: <https://www.cancer.gov/types/colorectal/patient/rectal-treatment-pdq>

Tania C. Sluckin, Alice M. Couwenberg, Doenja M.J. Lambregts, Sanne-Marije J.A. Hazen, Karin Horsthuis, Philip Meijnen, Regina G.H. Beets-Tan, Pieter J. Tanis, Corrie A.M. Marijnen, Miranda Kusters, "Lateral Lymph Nodes in Rectal Cancer: Do we all Think the Same? A Review of Multidisciplinary Obstacles and Treatment Recommendations", *Clinical Colorectal Cancer*, Volume 21, Issue 2, June 2022, Pages 80-88.

Umit Tapan, ShinYin Lee, Janice Weinberg, VijayaB. Kolachalama, Jean Francis, Marjory Charlot, Kevan Hartshorn, Vipul Chitalia. "Racial differences in colorectal cancer survival at a safety net hospital" *Cancer Epidemiology*, Volume 49, August 2017, Pages 30-37.