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Mackenzie Malone

Date

Influence of Surgeon Volume on the Survival from Stage III Colon Cancer

By

Mackenzie Malone Master of Public Health

Epidemiology

Kevin C. Ward, PhD MPH CTR Committee Chair Influence of Surgeon Volume on the Survival from Stage III Colon Cancer

By

Mackenzie Malone

B.S. University of Georgia 2013

Thesis Committee Chair: Kevin C. Ward, PhD MPH CTR

An abstract of A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Science in Public Health in Epidemiology 2015

Abstract

Influence of Surgeon Volume on the Survival from Stage III Colon Cancer By Mackenzie Malone

Background: Surgeon volume has been found to be associated with improved survival for colon cancer patients undergoing curative colon resection as part of treatment. The aim of this study is to further explore this relationship among patients with late stage colon cancer.

Methods: We conducted a retrospective population-based cohort study utilizing linked Surveillance, Epidemiology, and End Results (SEER)- Medicare database. We identified 15,009 patients aged 65 years and older diagnosed with a primary diagnosis of stage III colon cancer in a SEER area and treated with colon resection between 2000 and 2009. Surgeons were identified using individual surgeon identification numbers. Average surgeon volume was based on the number of colon resection claims submitted over the 10-year study period and the years where at least one colon resection was performed. Outcome measures were 30 day overall mortality and 5-year cause specific mortality. Kaplan-Meier survival curves were used to estimate survival probabilities. Coxproportional hazard models were used to estimate adjusted hazard ratios.

Results: A total of 3,999 individual surgeons were identified as primary surgeons of cohort members. A statistically significant improvement in survival was observed as the volume of operating surgeon increased (P < .0001). In the adjusted analysis there was an observed statistically significant decrease in risk of either mortality outcome associated with increased surgeon volume (P < .0001 for both 30-day and 5-year mortality). The observed inverse association was stronger in the short-term survival analysis when compared to the long-term survival analysis.

Conclusions: The annual average surgeon volume of the primary treating surgeon may predict mortality outcomes following a colon resection for patients with stage III colon cancer. Therefore, improvement in colon cancer care should focus on quality of operating surgeon. Further research is needed to explore the optimal surgeon volume required to observe the most benefit in survival outcomes.

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Acknowledgements

I would like to thank Dr. Kevin Ward for the guidance and feedback he has provided through the completion of this project, both his insight and time was much appreciated. I would also like to thank my friends and family for their support throughout the duration of this project and my education.

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Background

Colon Cancer: Burden and Mortality

In the United States, colorectal cancer is the third most common incident cancer and the third most common cause of cancer death among both men and women. The American Cancer Society, with use of data attained from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results Program (SEER) and the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR), estimated 96,830 new cases of colon cancer to occur in 2014 and 50,310 deaths from colon and rectum cancers combined (1, 2). According to most recent SEER statistics, the 5-year survival rate from colon cancer is 64.0% for all stages combined, with survival decreasing by severity of disease. The 5-year survival rates for localized, regional and distant colon cancer are 90.8%, 70.9%, and 12.7% respectively (3). It has been estimated that up to two-thirds of all colorectal cancers are preventable by colonoscopy (4, 5), and decreases in trends of incidence have been observed since 1998 predominantly due to the increase in screening (6, 7).

Colon Cancer Staging

The American Joint Committee on Cancer (AJCC) works to formulate systems of classification for cancer staging. The staging of cancer is designed to enable physicians to classify patients in terms of predicted survival, to aid in the selection of the most effective treatments, to determine patient prognosis and to evaluate cancer control measures (8). The tumor (T), node (N), metastasis (M) system for colon is based on the depth of tumor invasion into the colonic wall, the number and location of lymph nodes involved, and the presence or absence of distant metastasis (9). Stage III colon cancer is characterized by positive lymph node involvement and is divided into three subcategories based on depth of invasion and number of lymph nodes involved. Stage IV colon cancer is identified by presence of metastasis (8).

Standard of Care

Treatment for patients with cancer of the colon varies by tumor location and stage of disease at diagnosis. Surgical extraction of the primary tumor and surrounding lymph nodes, or colectomy, is the most effective option for potentially curable colon cancer cases. The safety and efficiency of colectomy has been improved through advances surgical technique, anesthesia, and other supportive measures (10). Curative colon resection followed by adjuvant chemotherapy has been the standard of care for stage III colon cancer patients for prolonged disease free survival and overall survival since the early 1990s (11, 12). Generally, those who do not receive adjuvant chemotherapy have inferior outcomes, with reported recurrence rates of 30.8% among patients with stage III colon cancer (13). In addition, curative surgery accompanied by adjuvant chemotherapy reduces the risk of death by one third as compared to surgery alone (11, 14). This reduction in mortality and recurrence due to use of chemotherapy agents has been observed across all age groups, indicating the benefit of adjuvant chemotherapy is similar in patients across age groups (15). However, in practice older patients with stage III colon cancer are less likely to receive adjuvant chemotherapy (15-17).

Other Predictors of Survival

Outside of disease stage (lymph node involvement and metastasis) and completion of treatment, there are a number of other factors associated with improved survival of colon cancer. Several studies have reported higher survival rates among females compared to males (18-21). Two recent studies, examined the possible variation in association between gender and colorectal cancer survival by age, where women below the age of 50 appeared to have improved survival compared to men of the same age, an opposite association was found for those over the age of 50 (22, 23). A recent retrospective review of nine phase III chemotherapy trials in patients with advanced stage colorectal cancer evaluated outcomes in younger patients versus older patients, defined as patients less than 40 years of age and greater than 50 years of age, respectively (24). Younger age was associated with shorter progression free survival, however there was no observed difference in overall survival. In a recent analysis of 24-first line clinical trials and 20,023 patients with metastatic colorectal cancer conducted by Lieu et al. (25), a Ushaped association was found between age and risk of death. Both older patients and younger patients had increased risk of death when compared to middle aged adult patients, an increased risk of 19% was observed for patients closer to 19 years of age whereas an increased risk of 42% was observed among patients closer to 90 years of age, with a reference age of 57(25).

Among the general US population, whites have consistently shown a superior survival rate from colorectal cancer when compared to blacks (26-28). This difference is suspected to be due in part to disease presentation, as blacks are more likely to be diagnosed at a later stage (29, 30), however even after adjustment for stage, colorectal cancer survival among blacks remains inferior to whites (27, 31). Marital status has shown to have an influence on survival from a number of cancer sites (32-34), including colon cancer (35, 36). In a recent study conducted by Wang, et al., statistically significant survival benefit from colon cancer was observed among married patients compared to single patients, with roughly a 12% reduction in mortality observed for both men and women (35).

Surgeon Volume

The association between increased hospital volume and surgical procedures is well established (37-40). A study by Birkmeyer et al. aimed to assess the association between surgeon volume and operative mortality for eight cardiovascular procedures and cancer resections among 474,108 Medicare recipients. An observed decrease in postoperative mortality among patients treated by high volume surgeons compared to low volume surgeons was found for all eight procedures (41). Similar inverse associations have been seen in a number of studies investigating decreased mortality and operating surgeon volume for high-risk cancer treatment surgeries (42-46).

Surgeon Volume and Colon Cancer

Previous studies have explored various associations between increased procedure volume of the surgeon who performed the primary colon resection and overall improved outcomes following colon resection, including outcomes such as in-hospital death, length of stay, cost (47), ostomy rates (48), and the need for reoperation (49). Mortality outcomes and procedure volume of the surgeon performing the resection, controlling for other covariates, has been well studied among colorectal cancer, as well as among solely colon cancer patients.

In a retrospective study investigating the associations between hospital and surgeon volume with decreased morbidity and mortality following an elective colon resection, where surgeon volume was ranked into three groups by mean annual cases, increased surgeon volume was associated with a statistically significant decrease in mortality (OR: 0.75, 95% CI: 0.65, 0.86) (50). This study also found that when analyzed separately, while controlling for the other, only surgeon volume was significantly associated with improved outcomes (50). A study by Schrag et al., which utilized linked SEER-Medicare data, categorized surgeon volume into quartiles based on the total number of claims for colon resections during the study period, 1991-1996. This study saw roughly a 6% increase in 2-mortality in the volume-adjusted analysis when comparing the lowest quartile of surgeon volume to the highest (RR: 1.06) (48).

In an Australian study restricted to patients with stage II colon cancer (according to AJCC staging guidelines), researchers saw roughly a 20% increase in overall survival in patients treated by a high-volume surgeon, more than 25 resections over the ten year period, compared to the low volume group, ten or less resections (51).

This described association of increased operating surgeon volume and improved colon cancer survival is consistent (52-58). These studies, although all controlling for stage of disease, do not provide much insight on the association of surgeon volume and the short and long term survival of late stage (stage III) colon cancer patients. Further research is needed to determine the possible improved survival outcomes associated with surgeon volume among patients with a poor prognosis at the time of diagnosis.

Introduction

In the United States, colorectal cancer is the third most common incident cancer and the third most common cause of cancer death among both men and women (1, 3). Staging for colon cancer is based on three elements: penetration of the tumor through the intestine wall, number of positive lymph nodes present, and presence of metastasis (9). Surgical resection provides the only curative option for patients with early stage disease without presence of metastasis (10). Curative colon resection followed by adjuvant chemotherapy is the standard of care for stage III colon cancer patients for prolonged disease free survival and overall survival (11, 12).

Depending on the exact tumor staging, the 5-year survival rates for patients with non-metastatic colon cancer, stages I through III, range from 50 to 95 percent (59). Several studies have investigated the discrepancies in colon cancer survival rates. Factors related to individual characteristics, geographic location, and other environmental factors, were found to be associated with colon cancer outcomes (18, 25, 32, 60).

High surgeon and hospital volume have repeatedly been associated with greater survival in relation to various surgical procedures (37-41). A direct volume-outcome association was observed in relation to several high-risk cancer treatment procedures (44, 46, 50). An association between surgeon and hospital volume and colon cancer related outcomes has been reported previously (48-51). However, when analyzed individually, adjusting for each other, only surgeon volume was associated with lower mortality (50). Previous studies have focused on all stages of disease or primarily early stage disease, which has a better prognosis at time of diagnosis (49, 51). Further research is needed to determine whether surgeon volume affects the survival of patients with only late stage colon cancer. Therefore, the aim of this study is to investigate an association between high surgeon volume and the short term overall survival and long term cause-specific survival for patients undergoing colon resection for treatment of stage III, operable colon cancer.

Methods

Study Data and Cohort

We conducted a retrospective cohort study using data obtained from the linkage of Surveillance, Epidemiology, and End Results (SEER) registries and Medicare claims. The SEER program registries routinely collect data on patient demographics, primary cancer site, tumor stage at diagnosis, and follow-up for vital status and is a representative sample of all cancer cases among the US population. We searched the linked Medicare records for patients with colon cancer as a first primary diagnosis (N = 183, 126). Medicare beneficiaries aged 65-years and older diagnosed in SEER regions with a microscopically confirmed first primary stage III colon cancer from 2000 through 2009 and treated with a colon resection were eligible for inclusion. Patients who had not been continuously enrolled in Medicare Parts A and B or enrolled in an HMO for the year prior to diagnosis and 3 months after diagnosis were excluded. This ensured that sufficient claims were available to determine preexisting comorbidities to be controlled for in the analysis and to properly document the resection. Only patients with definitive colon resection claims found in the Medicare inpatient records (MEDPAR) were included in the analysis. Patients diagnosed based on an autopsy report or death certificate were not included in the study cohort. Each MEDPAR resection was then linked to corresponding physician claims (NCH) in order to identify the surgeon performing the resection. Patients with discordant MEDPAR and NCH colon resection dates or missing surgeon provider identification numbers were further excluded. Patients with discordant dates of death in the SEER and Medicare data were excluded to ensure more accurate

survival time from resection to reported death. For the purpose of this analysis patients who received chemotherapy prior to the colon resection date or with unknown tumor grade, site, or extent of disease were also excluded, leaving a final cohort of 15,009 men and women. The detailed inclusion and exclusion criteria for the study population can be seen in Table 1. The SEER-Medicare database is a de-identified secondary database and is released for research purposes following local institutional IRB approval and a signed data use agreement. This study was reviewed and approved by the Institutional Review Board at Emory University.

Surgeon Volume

Surgeon identity was obtained using a number unique to each physician (UPIN) that has been mandatory on Medicare claims for reimbursements since 1991. Physician reimbursement claims are recorded separately from hospital claims and are available in Medicare files. Only surgeons who performed the primary colon resection in cases where patients had more than one procedure were used in creating the surgeon volume variable. Each colon resection in the dataset was associated with a single surgeon. Surgeons were then ranked based on the yearly average number of colon resections performed, for cases of any stage, determined by the total number of claims submitted over the study period in years where at least one colon resection was performed. Surgeon case volume was classified as high, medium or low based on the observed distribution of average annual surgeon volume. High volume was defined as greater than the 90th percentile (>9 resections per year), medium volume was defined as less than the 50th percentile (<4 resections per year). The cutoffs were chosen based off author discretion and a recent

analysis using surgeon volume conducted by Damle, et al (61). A summary of the average annual surgeon volume levels over the study period can be seen in Table 2. *Dependent Variable*

Outcome measures included 30-day overall survival and 5-year cause specific survival. Cause specific mortality and all cause mortality were obtained from the SEER data. Survival time was determined using the Medicare date of death and the date of colon resection (Survival days = (Date of Death – Colon Resection Date)). Survival was assessed both at 30 days and again 5 years post treatment where survival time was converted to months for 60 months follow up (Survival months= (Survival days/ 30.242)). For the short-term survival analysis patients who died of any cause during the 30-day follow up period were considered an event. For the 5-year analysis patients who were presumed alive or died of other causes were censored at the study end point. Follow-up data for cohort members were available up until December 31, 2011. *Covariates*

Potential confounding variables available in SEER data were age at diagnosis (categorized for analysis), sex, race, marital status, geographic region, and census track income level. Select tumor characteristics, including tumor grade, colon subsite, and the extent of disease (confined to the colon versus outside the colon), were also considered and included in the analysis. Co-morbid conditions and adjuvant chemotherapy were created from the claims data. Co-morbid conditions were calculated using a macro provided on the SEER-Medicare website which calculates a modified version of the Charlson comorbidity index (62). Patients who initiated chemotherapy treatment within four months of the colon resection date, as determined using ICD-9 codes (9925 and

9928) and HCPCS codes (964XX, 965XX, Q0083-Q0085, J9000-J9999) were identified as receiving adjuvant chemotherapy.

Statistical Analysis

Chi-square tests were used to assess differences in the distribution of patient characteristics across surgeon volume levels. Cancer-specific 5–year survival was estimated using the Kaplan-Meier survival curve method from the time follow-up began until patients died or were censored. Cox proportional hazard models were used to adjust for covariates while assessing the association of surgeon volume on short-term and long-term survival. All covariates thought to be confounders *a priori* were tested for satisfaction of the proportional hazard assumption and were included in the final model. All suspected interaction terms were found insignificant. Receipt of chemotherapy was not included in the model for 30-day survival, due to the previously stated definition of this variable and having too few events among the chemotherapy group within the follow up period. All statistical tests were performed using a significance level of 0.05 and all procedures were performed using SAS 9.4 software.

Results

A total of 15,009 adult men and women diagnosed with stage III colon cancer between 2000 and 2009 and underwent colon resection for treatment comprised our study sample. There were 3,999 unique surgeons who performed the primary colon resections on the cohort members during the ten-year study period. The distribution of physicians and patients by surgeon volume is given in Table 2. The average annual surgeon volumes among surgeons in the low, medium and high volume groups were 2.5 procedures per year, 5.9 procedures per year, and 12.4 procedures per year respectively.

Patient characteristics according to surgeon volume level can be seen in Table 3. The majority of the patients were female (58.4%) and white (84.8%). Patients were similar across strata of surgeon volume for gender and number of comorbid conditions. Patients who were married, white, or diagnosed in the Northeast were more likely to be treated by a high volume surgeon. Furthermore patients who were in the highest income quartile, were treated with chemotherapy, were classified as having a high-grade tumor, or had a tumor confined to the colon were also more likely to be treated by a high volume surgeon. In contrast, patients who were unmarried, of black or other race, in the lowest income quartile, or had a tumor that extended outside the colon were slightly more likely to be treated by a low-volume surgeon.

The overall 5–year survival probabilities by surgeon volume can be seen in Figure 1. There is a statistically significant improvement in survival as surgeon volume increases (P < .0001). Two proportional hazards models were carried out to adjust for potential confounding of the covariates (Table 4). The first model assessed the influence of

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surgeon volume on the 5 – year cause-specific survival from stage III colon cancer.

There was a statistically significant decrease in risk of mortality associated with increased surgeon volume. An 18% decrease in risk of 5–year mortality was observed among those treated by a medium volume surgeon compared to those treated by a low volume surgeon (HR: 0.82, 95% CI: (0.77, 0.86)). Additionally, there was a 31% decrease in 5–year mortality observed among those treated by a high volume surgeon compared to those treated by a low volume surgeon (HR: 0.69, 95% CI: (0.62, 0.76)). A statistically significant decrease in 5–year mortality was also observed among patients who were female, married, or younger than 80 years of age. In contrast, there was an observed increase in risk of 5-year mortality among patients with multiple comorbid conditions, patients living in the South, patients who did not receive chemotherapy, and patients with undesirable tumor characteristics, such as a high-grade tumor or extension of the tumor outside of the colon wall (Table 4).

The second analysis assessed the influence of surgeon volume on the short-term 30-day survival of stage III colon cancer. A similar inverse association was observed between increased surgeon volume levels and 30-day mortality. Among patients treated by medium volume surgeons, there was an observed 15% decrease in mortality when compared to patients treated by low volume surgeons (HR: 0.85, 95% CI: (0.74, 0.98)). The greatest survival was again observed among patients of high volume surgeons. When compared to patients of low volume surgeons, patients of high volume surgeons had an observed hazard ratio of 0.56 (95% CI: (0.41, 0.76)). In this analysis race, geographic location, and comorbid conditions were no longer associated with the mortality outcome (Table 4).

Discussion

Among the large population based cohort of U.S. Medicare patients diagnosed with a primary stage III colon cancer between 2000 and 2009, we found a strong association between surgeon volume and both short-term and long-term survival. Increased surgeon volume showed to yield more favorable outcomes among patients with late stage colon cancer, with patients operated on by medium- or high-volume surgeons having a reduced risk of mortality. These findings are consistent with previous research observing the benefits of increased surgeon volume on the outcomes of patients undergoing surgery as part of cancer treatment (42, 48-50).

The observed inverse association between increased surgeon volume and risk of death in our study confirms the results of other authors who have explored the influence of surgeon volume on colon cancer outcomes in other stages of disease presentation. A study conducted by Drolet et al. observed a 25% decrease in risk of death among patients treated by surgeons performing at minimum of ten resections a year compared to those treated by surgeons who perform four or less resections (50). Schrag et al. conducted a similar analysis using the linked SEER-Medicare dataset limited to patients with colon cancer. There was an observed 2% reduction in crude mortality among patients operated on by surgeons with high volume when compared to low volume (48). An Australian study by Morris et al. restricted to only colon cancer patients with stage II disease, as defined by the AJCC staging guidelines, observed a similar association. Roughly a 20% increase in survival was observed in patients treated by surgeons with the highest frequency of colon resections, more than 25 resections over the ten year study period,

compared to patients treated by surgeons with the lowest frequency of colon resection, 10 or less resections (51). Although our study is the first to observe this association among a cohort of late stage colon cancer patients, it confirms the influence of surgeon experience on the outcome of the treated patient.

A potential explanation in the discrepancy among the strength of observed associations between surgeon volume and colon cancer mortality outcomes may relate to the definition of surgeon volume. Definitions of the surgeon volume variable vary from one study to the next, often having to do with the chosen denominator. When defining surgeon volume, a number of studies have used the frequency of colon resections performed on study cohort members over the study period. The frequency of procedure is often categorized into volume levels using terciles or quartiles (48, 49, 51). For the present analysis volume was defined using average annual colon resections, for cases of any stage, for years where the surgeon performed at least one colon resection. Average annual caseload has previously been used in defining surgeon volume into even terciles (58). We used a similar approach as Damle et al. to define surgeon volume categories according to the distribution of annual volume (61). The average annual number of colon resections performed by operating surgeon needed to yield optimal postoperative outcomes is unknown, however it is clear that increased surgical volume significantly improves mortality for colon cancer patients, with even more benefit observed among late stage patients.

Both of the strengths and limitations of our study are due to the nature of the dataset used. The use of SEER-Medicare for evaluating surgeon volume is limiting because the data only allow for the inclusion of Medicare patients residing in SEER

regions. This limitation could lead to the underestimation of the true number of colon resections performed annually by operating surgeons and misclassification of surgeon volume. The use of this data for this survival analysis is also a limitation as the lack in access to dates of last contact makes censoring patients according to loss to follow-up difficult. This limitation is not likely to influence the observed results, however, as we know from SEER data that a very small percentage of patients are lost to follow-up. Furthermore, surgeon UPIN numbers submitted by Medicare were missing for 396 patients with stage III colon cancer, who thus had to be excluded from the study sample potentially adding to possible misclassification of the surgeon volume variable. Our analysis also did not include hospital volume, which has been previously observed as an important predictor of mortality outcomes following colon resection for treatment of colon cancer (48). Possible underlying confounding of this unmeasured variable could influence the observed association.

In contrast to these limitations our study has a number of strengths. All patients in the dataset are Medicare beneficiaries, controlling for potential issues related to access to medical care. In addition, because the average age at diagnosis for colon cancer patients is after the age of 65 (63) and the Medicare patients included in our analysis are all 65 years and older our study should provide a fair representation of colon cancer patients and treatment experiences in the United States.

Further research is needed to evaluate the mechanisms through which surgeon volume improves colon cancer outcomes. Our study suggests that for patients with stage III colon cancer, surgeon volume is an important indicator for both short and long term mortality. Though this finding is consistent with previous research, there is still

Conclusion and Public Health Significance

With colorectal cancer being the third most common malignancy in the United States and the third most common cause of cancer death (1), improvement in care and long term survival for these patients is of great importance. According to most recent SEER statistics, the 5-year survival rate from colon cancer is 64.0% for all stages, with survival decreasing by severity of disease. The 5-survival rates for localized, regional and distant colon cancer are 90.8%, 70.9%, and 12.7% respectively (3). Our study confirms the previously observed significant improvement in survival among colon cancer patients treated with colon resection by high volume surgeons compared to those treated by low volume surgeons (48-50). This is an important finding in improving the cancer treatment and survival. Surgeon experience has been shown to improve the outcomes for high risk cancer treatment surgeries (42), this benefit can also be seen among patients with more advanced disease requiring a more extensive operation, as in our study. Treatment by a specialized surgeon may improve cancer outcomes and reduce mortality among late stage cancer patients. However, the number of procedures performed annually by the operating surgeon needed to generate the most improved result is unsure. Future research is also needed to explore the possible mechanisms of care, in order to explain this observed association.

It is also important to note the financial burden of colon cancer due to the cost of treatments and cancer related care. Being the third most common incident cancer and third most common cause of cancer mortality, colon cancer has a tremendous impact on health care costs. In 2010, the cost of treating colorectal cancer was estimated as more

than \$14 billion, with almost half of this spending being within the first year after diagnosis (64). It is also important to note that increased procedure volume of the primary operating surgeon is associated with reduced adverse outcomes following colon resection, including outcomes such as in-hospital death, length of stay (47), ostomy rates (48), and the need for reoperation (49). Thus, with the high prevalence of colon cancer and the high-cost of disease, improvement in care should be a target in reducing complications and thus reducing treatment costs. The increased surgeon volume of the primary treating surgeon for patients with stage III colon cancer may improve health care costs by reducing postoperative complications in addition to improving survival.

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Tables and Figures

Reason for Exclusion	Number Excluded	Number Included
Colon cancer not only cancer or first primary	45,847	183,126
Primary site on rectosigmoid junction	592	182,534
Colon cancer diagnosed before 2000	1,331	181,203
Colon cancer reported from death certificate or autopsy only	2,265	178,938
Diagnostic confirmation	5,054	173,884
Colon cancer not Stage III	133,476	40,408
Definitive colon resection not recorded in PEDSF file	366	40,042
Histology not included in AJCC definition	279	39,763
Not enrolled in Medicare at the time of diagnosis	9,860	29,903
Did not have a corresponding inpatient claim for colon resection	6,714	23,189
Did not receive colon resection in the first three months of diagnosis	745	22,444
Not continuously enrolled 1 year prior to colon cancer diagnosis	3,734	18,710
Not continuously enrolled 4 month after colon resection	175	18,535
Did not have a corresponding NCH claim recording the colon resection	599	17,936
NCH claim recording the definitive colon resection were denied	216	17,720
No colon resection claim filed by the primary surgeon	81	17,639
MEDPAR and NCH claim not matched	95	17,544
Surgeon PIN missing	771	16,773
HCPCS MF indicating assistant surgeon or postoperative management	317	16,456
HCFA Specialty code other than general surgery or colorectal surgery	5	16.451
Not able to decide the unique PIN for the primary surgeon	17	16.434
1		-, -
Additional Exclusion for Analysis:		
Enrollees less than 65 years	709	15,715
Received neoadjuvant Chemotherapy	10	15,705
Unknown tumor characteristics	672	15,033
Medicare date of death discordant with SEER	24	15,009
FINAL COHORT TOTAL		15,009

Table 1. Exclusion Criteria for the Creation of Final Cohort, SEER-Medicare 2000-2009 (N = 15,009)

Study I eriou, 2000-2007			
Surgeons	Low	Medium	High
Definition of group ^a	<4	4-9	>9
Surgeons, n	3,026	888	85
Cases ^b , n	7,616	6,045	1,348
Average annual volume ^c	2.5	5.9	12.4

Table 2. Summary of Average Annual Surgeon Volume Levels over the Study Period, 2000-2009

^a Average number of colon resections for cancer per active year during study period ^b Total number of eligible cases during the study period included in the cohort ^c The average annual volume of the operating surgeons within each surgeon volume level

		Percent (%) patients per surgical volume level ^a			
Patient Characteristics	Total (%)	Low (<4)	Medium (4-9)	High (>9)	P-value ^b
	N = 15,009	N = 7,616	N = 6,045	N = 1,348	
Male	41.6	41.5	41.9	41.0	0.796
Marital status					<.001
Married	47.8	46.0	49.5	50.7	
Unmarried	48.2	49.8	47.0	45.3	
Unknown	3.9	4.2	3.5	4.1	
Age at diagnosis (years)					0.023
65-69	14.9	15.8	13.8	14.4	
70-74	21.3	21.4	21.5	20.4	
75-79	23.6	23.2	23.5	25.5	
≥ 80	40.3	39.6	41.2	39.7	
Race					<.001
White	84.8	82.6	87.0	87.7	
Black	8.7	10.0	7.3	7.2	
Other	6.5	7.4	5.7	5.1	
Geographic region					<.001
West	36.0	43.0	30.2	22.9	
Midwest	15.2	11.1	18.4	24.5	
South	26.3	28.3	25.5	18.2	
Northeast	22.5	17.6	26.0	34.4	
Census tract income c					<.001
Lowest Quartile	17.9	20.1	15.8	15.3	
Second Quartile	27.4	29.4	26.2	20.7	
Third Quartile	27.7	26.9	28.8	27.7	
Highest Quartile	27.0	23.6	29.3	36.3	
Comorbid conditions					0.374
None	57.5	57.4	57.2	59.5	
One	25.0	24.9	25.6	23.1	
Multiple	17.4	17.6	17.2	17.4	
Adjuvant chemotherapy					0.010
Yes	50.9	49.8	51.8	53.5	
No	49.1	50.2	48.2	46.5	
Grade					<.001
Low $(1 - 2)$	68.4	69.9	67.5	63.9	
High (3 − 4)	31.6	30.1	32.5	36.1	
Colon Subsite					<.001
Right	53.3	52.1	53.9	57.6	
Тор	19.5	19.1	20.3	18.6	
Left	27.2	28.8	25.8	23.9	
Extent of Disease					<.001
Confined	10.7	9.7	11.2	14.0	
Outside	89.3	90.3	88.8	86.1	

 Table 3. Characteristics of 15,009 stage III colon cancer patients treated with colon resection, by procedure volume of surgeon who performed primary resection, SEER-Medicare 2000-2009

^a Surgeon volume defined as the average number of colon cancer resections performed per year by the operating surgeon in years were at least one colon resection was performed during the study period, 2000-2009

^bPearson-Chi square tests were used for all variables across surgeon volume levels

^c Unknown census tract income level not shown due to sparse data

	E voor	nortality	20 day mantality	
Independent Veriable	<u> </u>	05% CT a	<u>JU – UAY I</u> Hazard ratio	05% CT a
	11azal u 1 auv	75 /0 CI	114241 U 14110	75 /0 CI
Surgeon Volume	1.00		1.00	
Low(<4)	1.00		1.00	
Medium (4 - 9)	0.82	(0.77, 0.86)	0.85	(0.74, 0.98)
Hign (>9)	0.69	(0.62, 0.76)	0.56	(0.41, 0.76)
Sex	1.00		1.00	
Male	1.00		1.00	
Female	0.91	(0.86, 0.96)	0.71	(0.61, 0.82)
Marital status	0.00		0.67	(0.57.0.70)
Married	0.90	(0.84, 0.95)	0.67	(0.57, 0.78)
Unmarried	1.00		1.00	
Unknown	1.05	(0.92, 1.20)	1.22	(0.91, 1.63)
Age at diagnosis (years)	0.50		0.42	(0.00.0.57)
65-69	0.78	(0.71, 0.85)	0.43	(0.33, 0.57)
70-74	0.82	(0.76, 0.89)	0.53	(0.43, 0.65)
75-79	0.85	(0.79, 0.91)	0.59	(0.49, 0.70)
≥ 80	1.00		1.00	
Race				
White	1.00		1.00	
Black	1.02	(0.92, 1.12)	0.92	(0.72, 1.18)
Other	0.84	(0.75, 0.95)	0.74	(0.54, 1.02)
Geographic region				
West	1.00		1.00	
Midwest	1.08	(0.99, 1.17)	0.92	(0.74, 1.15)
South	1.15	(1.07, 1.23)	1.05	(0.88, 1.25)
Northeast	1.11	(1.03, 1.20)	1.00	(0.82, 1.21)
Census tract income				
Highest quartile	1.00		1.00	
Third quartile	0.99	(0.92, 1.06)	1.14	(0.94, 1.40)
Second quartile	1.01	(0.94, 1.09)	1.27	(1.04, 1.55)
Lowest quartile	0.99	(0.91, 1.08)	1.38	(1.10, 1.73)
Area not tracked	0.70	(0.45, 1.09)	0.32	(0.04, 2.28)
Comorbid conditions		(0.10, 0.00)		(0.0.1,0)
None	1.00		1.00	
One	1.05	(0.99, 1.12)	1.00	(1 03 1 41)
Multiple	1 23	(1 14 1 32)	1.30	(1.00, 1.11) (1.10, 1.53)
Adjuvant Chemotherany	1.25	(1.1.1, 1.52)	1.50	(1.10, 1.55)
Received	1.00			
Not received	1.00	(1 82 2 05)		
Grade	1.75	(1.82, 2.05)		
$L_{ow}(1, 2)$	1.00		1.00	
Low (1-2)	1.00	$(1 \ 27 \ 1 \ 52)$	1.00	(1.09, 1.42)
$ \begin{array}{c} \text{High} (3-4) \\ \text{Calar Subsite} \end{array} $	1.45	(1.57, 1.55)	1.24	(1.06, 1.45)
	1.00		1.00	
Kight	1.00	(0, 02, 1, 05)	1.00	
	0.98	(0.92, 1.05)	1.1/	(0.99, 1.39)
Leit	0.93	(0.87, 0.99)	1.1/	(0.99, 1.37)
Extent of Disease	1.00		1.00	
Contined	1.00		1.00	
Outside	2.93	(2.58, 3.32)	1.73	(1.27, 2.36)

Table 4. Cox proportional hazard analysis for the association of surgeon case volume and 5 – year survival, SEER-Medicare 2000-2009 (N= 15,009)

^a CI: confidence interval

^b Surgeon volume defined as the total number of colon cancer resections performed by the operating surgeon during the study period, 2000-2009

Figure 1. Kaplan-Meier Curve of Survival Probabilities by Survival Months, According to Surgeon Volume (N = 15,009)



Appendix A: Exploratory Analysis Tables

Male 41.6 40.3 42.4 0.008 Marital status	Patient Characteristics	Total (%) N = 15.009	<u>Event (%)</u> ^a N = 5.697	$\frac{\text{Censored (\%)}^{\text{b}}}{\text{N} = 9.312}$	P-Value
Marital status <th<< td=""><td>Male</td><td>41.6</td><td>40.3</td><td>42.4</td><td>0.008</td></th<<>	Male	41.6	40.3	42.4	0.008
Married 47.8 44.0 50.2 Unmarried 48.2 51.8 46.1 Unknown 3.9 4.3 3.7 Age at diagnosis (years) <.001	Marital status		1010		<.001
Unmarried 48.2 51.8 46.1 Unknown 3.9 4.3 3.7 Age at diagnosis (years) $65-69$ 14.9 12.1 16.6 $70-74$ 21.3 18.7 22.9 $75-79$ 23.6 21.9 24.6 ≥ 80 40.3 47.3 35.9 Race 0.005 White 84.8 85.3 84.5 Black 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 0.802 Lowest Quartile 17.8 18.1 17.7 Second Quartile 27.5 56.5 58.1 One 25.0 24.9 25.1 Multiple 17.4 18.6 <td>Married</td> <td>47.8</td> <td>44.0</td> <td>50.2</td> <td></td>	Married	47.8	44.0	50.2	
Unknown 3.9 4.3 3.7 Age at diagnosis (years) <.001	Unmarried	48.2	51.8	46.1	
Age at diagnosis (years) <.001	Unknown	3.9	4.3	3.7	
65-69 14.9 12.1 16.6 70-74 21.3 18.7 22.9 75-79 23.6 21.9 24.6 ≥80 40.3 47.3 35.9 Race 0.005 White 84.8 85.3 84.5 Black 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 0.802 Lowest Quartile 27.2 27.6 27.1 Third Quartile 27.6 27.1 47.4 Area not tracked 0.4 0.4 0.4 Comorbid conditions 0.014 0.014 0.014 None 57.5 56.5 58.1 0.01 Ves 50.9 41.1 57.0 50.9 41.0	Age at diagnosis (years)				<.001
70-74 21.3 18.7 22.9 75-79 23.6 21.9 24.6 ≥80 40.3 47.3 35.9 Race 0.005 White 84.8 85.3 84.5 Black 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 0.802 Lowest Quartile 27.2 27.6 27.1 Third Quartile 27.6 27.1 7.1 Highest Quartile 26.9 26.6 27.1 Area not tracked 0.4 0.4 0.4 One 25.0 24.9 25.1 Multiple 17.4 18.6 16.7 Again on tracked 0.4 0.4 0.4 None 57.5 5	65-69	14.9	12.1	16.6	
75-79 23.6 21.9 24.6 ≥80 40.3 47.3 35.9 Race 0.005 White 84.8 85.3 84.5 Black 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 0.802 Lowest Quartile 17.8 18.1 17.7 Second Quartile 27.2 27.6 27.1 Third Quartile 26.9 26.6 27.1 Area not tracked 0.4 0.4 0.4 Comorbid conditions 0.014 0.4 0.4 None 57.5 56.5 58.1 0 Multiple 17.4 18.6 16.7 .001 Yes 50.9 41.1 57.0 .001	70-74	21.3	18.7	22.9	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	75-79	23.6	21.9	24.6	
Race 0.005 White 84.8 85.3 84.5 Black 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 0.802 Lowest Quartile 17.8 18.1 17.7 Second Quartile 27.2 27.6 27.1 Third Quartile 27.6 27.1 11 Area not tracked 0.4 0.4 0.4 Comorbid conditions 0.014 0.014 None 57.5 56.5 58.1 One 25.0 24.9 25.1 Multiple 17.4 18.6 16.7 Adjuvant chemotherapy <001	>80	40.3	47.3	35.9	
White84.885.384.5Black8.79.08.5Other6.55.77.0Geographic region0.005West36.034.337.1Midwest15.215.315.2South26.327.425.6Northeast22.523.022.2Census tract income0.802Lowest Quartile17.818.117.7Second Quartile27.227.627.1Third Quartile26.926.627.1Area not tracked0.40.40.4Comorbid conditions0.014None57.556.558.1One25.024.925.1Multiple17.418.616.7Adjuvant chemotherapy $<$ 001Yes50.941.157.0No49.158.943.0Grade $<$ 001Low (1 - 2)68.462.5Right53.355.452.0Top19.519.919.3Left27.224.828.7Extent of Disease $<$ 001Confined10.74.4	Race				0.005
Black Other 8.7 9.0 8.5 Other 6.5 5.7 7.0 Geographic region 0.005 West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 Lowest Quartile 27.2 27.6 27.1 Third Quartile 27.6 27.1 7.1 Highest Quartile 26.9 26.6 27.1 Area not tracked 0.4 0.4 0.4 Comorbid conditions 0.014 0.014 None 57.5 56.5 58.1 One 25.0 24.9 25.1 Multiple 17.4 18.6 16.7 Adjuvant chemotherapy <001	White	84.8	85.3	84.5	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Black	8.7	9.0	8.5	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Other	6.5	5.7	7.0	
West 36.0 34.3 37.1 Midwest 15.2 15.3 15.2 South 26.3 27.4 25.6 Northeast 22.5 23.0 22.2 Census tract income 0.802 Lowest Quartile 17.8 18.1 17.7 Second Quartile 27.2 27.6 27.1 Third Quartile 27.6 27.4 27.7 Highest Quartile 26.9 26.6 27.1 Area not tracked 0.4 0.4 0.4 Comorbid conditions 0.014 None 57.5 56.5 58.1 One 25.0 24.9 25.1 Multiple 17.4 18.6 16.7 Adjuvant chemotherapy <001 <001 Yes 50.9 41.1 57.0 No 49.1 58.9 43.0 Grade <001 <001 Low $(1-2)$ 68.4 62.5 72.0 High $(3-4)$ 31.6 37.5 28.0 Colon Subsite <001 <001 Right 53.3 55.4 52.0 Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease <001	Geographic region				0.005
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	West	36.0	34.3	37.1	
South Northeast26.327.425.6Northeast22.523.022.2Census tract income0.802Lowest Quartile17.818.117.7Second Quartile27.227.627.1Third Quartile26.926.627.1Area not tracked0.40.40.4Comorbid conditions0.0140.4None57.556.558.1One25.024.925.1Multiple17.418.616.7Adjuvant chemotherapy<.001	Midwest	15.2	15.3	15.2	
Northeast22.523.022.2Census tract income0.802Lowest Quartile17.818.117.7Second Quartile27.227.627.1Third Quartile27.627.427.7Highest Quartile26.926.627.1Area not tracked0.40.40.4Comorbid conditions0.014None57.556.558.1One25.024.925.1Multiple17.418.616.7Adjuvant chemotherapy<.001	South	26.3	27.4	25.6	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Northeast	22.5	23.0	22.2	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Census tract income				0.802
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Lowest Quartile	17.8	18.1	17.7	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Second Quartile	27.2	27.6	27.1	
Highest Quartile Area not tracked 26.9 0.4 26.6 0.4 27.1 0.4 Comorbid conditions0.014None 57.5 56.5 One 25.0 24.9 25.1 Multiple 17.4 17.4 18.6 	Third Quartile	27.6	27.4	27.7	
Area not tracked 0.4 0.4 0.4 0.4 Comorbid conditions0.014None 57.5 56.5 58.1 One 25.0 24.9 25.1 Multiple 17.4 18.6 16.7 Adjuvant chemotherapy $<.001$ Yes 50.9 41.1 57.0 No 49.1 58.9 43.0 Grade $<.001$ Low $(1 - 2)$ 68.4 62.5 72.0 High $(3 - 4)$ 31.6 37.5 28.0 Colon Subsite $<.001$ Right 53.3 55.4 52.0 Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease<<.001	Highest Quartile	26.9	26.6	27.1	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Area not tracked	0.4	0.4	0.4	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Comorbid conditions				0.014
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	None	57.5	56.5	58.1	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	One	25.0	24.9	25.1	
Adjuvant chemotherapy<.001Yes 50.9 41.1 57.0 No 49.1 58.9 43.0 Grade<.001	Multiple	17.4	18.6	16.7	
Yes 50.9 41.1 57.0 No 49.1 58.9 43.0 GradeLow $(1-2)$ 68.4 62.5 72.0 High $(3-4)$ 31.6 37.5 28.0 Colon SubsiteRight 53.3 55.4 52.0 Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease<	Adjuvant chemotherapy				<.001
No49.158.943.0Grade<.001	Yes	50.9	41.1	57.0	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	No	49.1	58.9	43.0	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Grade				<.001
High (3 - 4) 31.6 37.5 28.0 Colon Subsite <.001	Low $(1 - 2)$	68.4	62.5	72.0	
Colon Subsite <.001 Right 53.3 55.4 52.0 Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease <.001	High $(3-4)$	31.6	37.5	28.0	
Right 53.3 55.4 52.0 Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease <	Colon Subsite				<.001
Top 19.5 19.9 19.3 Left 27.2 24.8 28.7 Extent of Disease <.001	Right	53.3	55.4	52.0	
Left 27.2 24.8 28.7 Extent of Disease <.001	Тор	19.5	19.9	19.3	
Extent of Disease <.001	Left	27.2	24.8	28.7	
Confined 10.7 4.4 14.5	Extent of Disease				<.001
Commea 10.7 4.4 14.5	Confined	10.7	4.4	14.5	
Outside 89.3 95.6 85.5	Outside	89.3	95.6	85.5	

Table 5. Associations between patient and tumor characteristics and 5-year mortality,SEER-Medicare 2000-2009 (N=15,009)

^a Defined as cause specific death within the 5 year follow up period

^b Survival past the 5 year follow up or non-cancer related death ^c Time between diagnosis and colon resection, lowest quartile chosen as reference

Patient Characteristics	Total (%) N = 15.009	$\frac{\text{Event (\%)}^{a}}{N = 872}$	$\frac{\text{Censored (\%)}^{\text{b}}}{N = 14.137}$	P-Value
Male	41.6	44.4	41.4	0.087
Marital status	11.0		11.1	< 001
Married	47.8	33.8	48.7	
Unmarried	48.2	60.3	47.5	
Unknown	3.9	59	3.8	
Age at diagnosis (years)	5.9	5.7	5.0	<.001
65-69	14.9	6.7	15.4	
70-74	21.3	13.1	21.8	
75-79	23.6	17.7	23.9	
≥ 80	40.3	62.6	38.9	
Race				0.114
White	84.8	86.2	84.7	
Black	8.7	8.9	8.7	
Other	6.5	4.8	6.6	
Geographic region				0.178
West	36.0	35.8	36.0	
Midwest	15.2	13.5	15.3	
South	26.3	29.1	26.1	
Northeast	22.5	21.6	22.5	
Census tract income				0.001
Lowest Quartile	17.8	21.4	17.6	
Second Quartile	27.2	29.9	27.1	
Third Quartile	27.6	26.4	27.7	
Highest Quartile	26.9	22.1	27.2	
Area not tracked	0.4	0.1	0.4	
Comorbid conditions				<.001
None	57.5	47.7	58.1	
One	25.0	27.6	24.9	
Multiple	17.4	24.7	17.0	
Adjuvant chemotherapy				<.001
Yes	50.9	0.1	54.1	
No	49.1	99.9	45.9	
Grade				<.001
Low $(1 - 2)$	68.4	62.4	68.8	
High $(3 - 4)$	31.6	37.6	31.2	
Colon subsite				0.169
Right	53.3	50.8	53.5	
Top	19.5	21.8	19.4	
Left	27.2	27.4	27.2	
Extent of Disease				<.001
Confined	10.7	4.8	11.0	
Outside	89.3	95.2	89.0	

 Table 6. Associations between patient and tumor characteristics and 30-day mortality,

 SEER-Medicare 2000-2009 (N=15,009)

^a Defined as cause specific death within the 5 year follow up period ^b Survival past the 1 month follow up ^c Time between diagnosis and colon resection, lowest quartile chosen as reference