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Diagnosis Setting and Colorectal Cancer Outcomes: The Impact of Cancer Diagnosis in the Emergency Department

D Weithorn¹, V Arientyl¹, I Solsky¹, G Umadat², R Levine¹, B Rapkin², J Leider², H In^{1,2}

¹Montefiore Medical Center/Albert Einstein College of Medicine, Department of Surgery, Bronx, NY, USA

²Albert Einstein College of Medicine, Department of Epidemiology and Population Health, Bronx, NY, USA

Abstract

BACKGROUND—The rate of diagnosis of colorectal cancer (CRC) in the Emergency Department (ED), its characteristics, and its effect on outcomes have been poorly described.

MATERIALS AND METHODS: Chart review was conducted to identify presenting clinical setting leading to diagnosis, symptoms, and history of colonoscopy for CRC patients diagnosed at a single institution from 2012–2014. Patients diagnosed with CRC as a result of an ED visit (EDDx) were compared with those diagnosed following presentation to other settings (non-EDDx).

RESULTS: Of 638 patients meeting inclusion criteria, 271 (42.4%) were diagnosed through the ED (EDDx). These patients were more likely to be older than 80 years (29.89% vs 19.35%), have Medicare (59.78% vs 42.78%) or Medicaid (23.62% vs 12.81%) insurance, have stage IV cancer (45.02% vs 18.26%), and be symptomatic at time of presentation (94.83% vs 64.03%). EDDx patients were less likely to ever have had a colonoscopy (21.77% vs 41.69%). In a model adjusted for patient demographics, cancer stage, presence of symptoms and history of prior colonoscopy, EDDx was associated increased mortality (HR: 1.89, 95% CI: 1.3–2.8). On stratifying survival by stage, it was found that for all stages, EDDx was associated with decreased survival.

Corresponding author: Haejin In, MD, MPH, MBA, Department of Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, 1300 Morris Park Ave. #112, New York, NY 10461, hin@montefiore.org, (718) 379-6865.

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CONCLUSION: Over 40% of CRC patients received their diagnosis through the ED. EDDx was associated with a nearly two-fold mortality risk increase. EDDx should be considered a marker of poor outcomes for CRC and may be related to unaccounted patient-level or systems-level factors. Efforts should be made to identify modifiable risks of cancer diagnosis in the ED to improve cancer outcomes.

Keywords

“Colorectal Neoplasms”; “Emergency Service, Hospital”; “Neoplasms/diagnosis”

INTRODUCTION

Colorectal cancer (CRC) is a disease that should generally be diagnosed in the outpatient setting due to clinical suspicion or through routine screening.¹ Early detection of CRC through screening is available and is associated with improved survival.² CRC screening is covered by all insurance plans, endorsed by various organizations and adherence is tracked for most institutions.² CRC is also a highly prevalent disease and primary care clinicians routinely refer patients for colonoscopy for suspicious symptoms.³ Given these efforts for screening and early detection as well as familiarity of clinicians with CRC, ideally, most CRC should be detected in outpatient setting or as a result of screening.⁴ However, patients continue to be diagnosed with CRC in the Emergency Department (ED).

Studies have demonstrated worse outcomes and more advanced disease in patients with CRC who required emergent surgery.^{5–7} Few domestic studies have examined the clinical setting of CRC diagnosis and its implications. Studies looking at which types of patients present to ED show that these patients were older, more likely to be female, have lower income, and present with more advanced disease.^{5,8} Foreign studies of CRC diagnosis in the ED largely concurred with domestic data, demonstrating more advanced disease at presentation with worse disease free survival.⁷ These patients were more likely to be older and have lower socioeconomic status and have less primary care follow up.⁹ They also had longer lengths of stay and higher in-hospital mortality.¹⁰

The aim of the current study was to conduct a retrospective cohort analysis of all CRC cases at a single urban academic medical institution over a 3-year period to (1) determine the rate of ED diagnosis for CRC (EDDx), (2) compare factors related to increased EDDx with cases diagnosed in other settings, and (3) examine outcomes of patients with EDDx.

METHODS

Patient selection

Patients included for analysis were patients age 18 and older, diagnosed with colorectal adenocarcinoma between 2012–2014 at Montefiore Medical Center (MMC). MMC is a large urban medical center in New York City serving a socioeconomically challenged patient population.¹¹ Patients with missing data, non-adenocarcinoma malignancies (neuroendocrine, liposarcoma, goblet cell, etc.), and Stage 0 disease were excluded. Those

with unknown setting of diagnosis, unknown reason for presentation, and those who never received treatment at MMC were also excluded.

Patient-specific variables and cancer-specific variables

Cancer specific data was collected from MMC's Cancer Registry and combined with other pertinent demographic and clinic data obtained from the Montefiore clinical data repository, which is maintained by the Albert Einstein College of Medicine Department of Epidemiology's Study Management Unit. Patient-specific variables included gender, age (18–49, 50–64, 65–79, 80+), number of comorbidities, race (Black, White, Other), and insurance (private, Medicare, Medicaid, other). Cancer registry-specific covariates included AJCC Stage, grade (I-II: well or moderately differentiated, III: poorly differentiated, cell type not determined), death and censoring information. Comorbidities were captured using Elixhauser comorbidity measures applied to ICD9 codes recorded in the medical records at the time of cancer diagnosis. Elixhauser comorbidity measures uses ICD-9-CM (International Classification of Diseases, Ninth Edition, Clinical Modifications) diagnosis codes to create 29 Elixhauser comorbidity measures. Comorbidities were examined in the models as a count of present comorbidities. Patient data was collected with approval of Albert Einstein College of Medicine's Institutional Review Board (IRB). A waiver of informed consent was granted by the IRB.

Chart Review:

Chart review was performed by the lead author to determine whether patients received their CRC diagnosis following presentation to an ED or in a non-ED setting. Patients were considered to have EDDx if they presented to an ED with a complaint not previously investigated elsewhere that led to the CRC diagnosis. Manual chart review allowed us to capture the documentation of an ED visit as the setting of the first evaluation in any medical facility, not just MMC. Patients who presented to settings other than the ED for evaluation of their initial symptoms, as well as those referred to the ED for management of complaints discovered in the outpatient setting were considered to not have received an ED diagnosis (non-EDDx). During the chart review, data was also collected on the patients' presenting symptom and most recent screening colonoscopy, which was considered to be the last colonoscopy done without evidence of symptoms. If a tumor was diagnosed on routine screening colonoscopy, that was considered the most recent colonoscopy. If colonoscopy reports were not available, descriptions of results in provider's notes were assumed to be accurate. Non-colonoscopy modalities of CRC screening were not examined. Receipt of definitive treatment was coded as surgery with or without other therapy, chemotherapy without surgery or radiation therapy, radiation with or without chemotherapy, palliative surgery or no treatment. Loop ileostomies and other palliative surgeries not for curative intent were not considered "definitive treatment". Dates of diagnosis, definitive treatment initiation and surgery were also collected.

Statistical analysis

Patients with EDDx were compared to non-EDDx patients. Patient and cancer-specific variables and symptoms were compared between the two groups. A logistic regression model was also used to determine predictors for EDDx. The Kaplan-Meier method was used

to estimate overall survival between both groups. Cox proportional hazards regression was used to estimate the Hazard Ratio (HR) for mortality given a CRC diagnosis in the ED after adjusting for relevant confounding variables. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Demographics

839 patients were identified of which 638 met inclusion criteria (Figure 1). Of these patients, 271 (42.4%) had EDDx. Patients with EDDx were more likely to be older than 80 years of age (29.89% vs 19.35%, $p=0.0023$) and more likely to have Medicare (59.78% vs 42.78%, $p<0.0001$) or Medicaid (23.62% vs 12.81%, $p<0.0001$) insurance. They were more likely to be stage IV (45.02% vs 18.26%, $p<0.0001$), and have 3 or more comorbidities (70.5% vs. 63.5%, $p=0.0178$). 94.8% of EDDx patients reported symptoms while only 64.0% of non-EDDx patients had symptoms at time of presentation ($p<0.0001$). The presenting symptoms were also notably different: for EDDx patients pain was the predominant presenting symptom (44.4% vs 17.9%, $p<0.0001$) while in non-EDDx patients, bleeding or anemia was more common (61.7% vs 39.9%, $p<0.0001$). EDDx patients had markedly lower rates of ever having had a colonoscopy (21.77% vs 41.69%, $p<0.0001$). Among patients with history of prior colonoscopy, 13.6% of EDDx patients had a colonoscopy >10 years since the time of presentation vs. 1.3% in the non-EDDx group ($p<0.0001$). EDDx patients were more likely to have had surgery on the same admission as diagnosis (31.7% vs 4.6%, $p<0.0001$) (Table 1).

Logistic regression model to determine predictors for EDDx

After adjusting for other variables in the model, we found that EDDx was associated with having symptoms (OR 6.9, 95% CI 3.6–13.3), having stage 4 compared to stage 1 disease (OR 3.8, 95% CI 2.0–7.1), and having Medicare (OR 4.8, 95% CI 2.6–8.8) or Medicaid (OR 4.4 95% CI 2.4–8.1) over private insurance. Patients that had had prior colonoscopy were less likely to have EDDx (OR 0.52, 95% CI 0.3–0.9) (Table 2).

Survival

Figure 2 shows that EDDx patients did markedly worse in unadjusted overall survival, with 2-year survival of 63% vs 86% ($p<0.0001$). The adjusted Cox regression model shows that EDDx had markedly worse outcomes compared to non-EDDx (HR 1.89, 95% CI 1.3–2.8) after controlling for other variables in the model, including age, number of comorbidities, stage and insurance status. As expected, worse survival was also seen with age over 80 years (HR 2.37, 95% CI 1.2–4.7), Medicare (HR 2.0, 95% CI 1.1–3.5) or Medicaid (HR 2.2, 95% CI 1.1–4.2) insurance, stage IV disease (HR 7.9, 95% CI 3.9–15.9), and higher grade tumors (Grade III vs I/II: HR 2.1, 95% CI 1.4–3.2) (Table 3).

Survival was also examined stratified by stage. For all stage groups, EDDx patients did worse compared to non-EDDx patients (log-rank test: stage 1: $p=0.0004$, stage 2: $p=0.0032$, stage 3: $p=0.0921$ and stage 4: $p=0.0833$) (Figure 3a–d).

DISCUSSION

We found that over 40% of patients received a CRC diagnosis in the emergency department and that this was associated with an almost two-fold increase in mortality. This mortality difference between EDDx and non-EDDx patients persisted despite stratifying by other confounders, including cancer stage and comorbidities; and EDDx was found to be an independent prognosticator of poor patient outcomes. Patients presenting to the ED mostly presented with symptoms, with pain, bleeding and anemia being the most common presenting symptoms in the ED. Nearly half of the patients presenting in the ED had never had a colonoscopy suggesting that this remains a critical area that can be targeted for improvement.

Cancer patients can be diagnosed via multiple different pathways including screening, outpatient evaluation or ED presentation. There is a lack of U.S. based studies that seek to capture the magnitude of colorectal cancer diagnosis resulting from an emergency room visit. This is largely due to lack of a universal tracking system for patients which makes it difficult to track patients beyond a single hospital system, particularly if they did not obtain the diagnosis or have surgery during the index admission (first admission that eventually led to the cancer diagnosis). In the United Kingdom (UK), the single payer system National Health Service (NHS), allows for all patients to be tracked across different locations. Barrett et al. reported 26%, while Raine et al. reported that 32.5% of cancers were diagnosed due to an emergency admission in the UK.^{14,17} Our study sought to overcome our inability to obtain information across systems by conducting a detailed review of medical records to find all records (including hand written notes) describing presenting symptoms and the setting where they first sought care for this problem. Our finding of 42% is higher but imaginable with our study being a single institution study from a large academic urban hospital serves as a safety net hospital for the region. Patients in this demographic may be more prone to utilizing the ED as their primary source of care. The high rates of EDDx for CRC patients is in line with our other investigation of gastric cancer patients at the same medical center where we found that approximately 50% of them were diagnosed through the ED, and that EDDx was also associated with worse outcomes.¹⁶

Studies have found that certain patient factors such as older age and low socio-economic status are associated with emergent presentation of their cancer and these patients tend to have more advanced disease and lower survival.^{8,12,13,15,17} As such, it is not surprising that in our study the EDDx cohort tended to be older, have Medicaid insurance and were more commonly diagnosed to be stage IV. While some of the higher overall mortality associated with EDDx is related to the higher percentage of stage IV cancers in the EDDx group, we found also found that EDDx patients had higher mortality even when examined by stage. This is unsurprising as patients presenting with cancer emergencies are known to have worst outcomes.^{5,21} However, our finding that EDDx patients were less likely to have private insurance or prior colonoscopy suggests that healthcare access issues, disparities in health literacy, and socioeconomic factors may be a contributing factor to the poor outcomes observed for EDDx patients. We also found EDDx patients to be older and with more comorbidities compared to their non-EDDx peers. In our study, this was pronounced in the stage I cohort, resulting in markedly poor outcomes observed for the stage 1 EDDx group. In

a more detailed investigation of these patients, we found that this was the result of the Stage 1 EDDx patients having lower rates of initial definitive treatment (70.8%) compared to over 90% for all other Stage 2–4 EDDx and non-EDDx patients. The lack of definitive treatment suggests that the poor survival observed for the Stage 1 EDDx group is more likely from their comorbid conditions and less likely from their cancer. However our examination of overall survival and not cancer-specific survival limits our ability to untangle this finding.

While socioeconomic determinates of health may explain higher ED diagnosis for all cancer types, it is also important to acknowledge that unlike other cancers, screening is available for CRC and colonoscopy plays a critical role in CRC prevention. A benefit of screening is that it can identify CRC prior to the development of symptoms. We found lower rates of colonoscopy, higher rates of symptoms and later stages of cancer for EDDx. The American Cancer Society recently updated its guidelines for colorectal cancer screening, recommending that average risk individuals start screening with either a stool-based test or a visual exam (e.g., colonoscopy) starting at age 45, though other societies recommend starting screening at age 50.¹ It is believed that more than fifty percent of the decline in CRC mortality can be attributed to the increased acceptance and uptake of CRC screening.¹⁸ It is therefore concerning that the EDDx patients in our study were less likely to ever have had a colonoscopy (21.77% vs 41.69%, $p<0.05$). Furthermore, for those patients who did have a prior colonoscopy, 13.6% of EDDx patients had a colonoscopy >10 years since the time of presentation vs. 1.3% in the non-EDDx group, suggesting that EDDx patients are potentially less adherent with guidelines for ongoing screening. Clearly, increased screening is critical to reducing EDDx. However, potential reasons why some patients do not undergo screening is complex including issues related to fear, misinformation, and access to care.¹⁹ Strategies to increase colorectal cancer screening have been reported; however, they likely have to be tailored to different settings to be successful.²⁰

This study contributes to the growing literature that EDDx is an episode of care that can be targeted to improve outcomes for CRC patients. Worst outcomes for EDDx do not appear to be driven by tumor biology alone, and is likely related to issues in healthcare access and disparities. Therefore, a future area of research may be to target areas with high rates of EDDx for focused community outreach and engagement to reduce barriers to health care. A strength of this study is that patient information was manually collected through clinical chart review rather than relying on administrative data. This allowed us to obtain details on presence of an ED visit and colonoscopy history beyond our hospital system alone, as well as more specific information on presenting symptoms at time of diagnosis and clinically relevant data such as cancer stage. However, the study is limited in that as a single center investigation, the results are not generalizable. Furthermore, the retrospective data collection prevented assessment of barriers for colonoscopy such as health beliefs, attitudes and knowledge about CRC screening. We were also unable to assess reasons for enhanced use of ED services, including social and economic barriers in accessing non-ED sources of care. Additionally, this study is limited that stage may be inaccurate for patient who did not undergo surgery thus influencing stage specific analysis. The oncologic quality of the surgery (such as negative margin, number of lymph nodes examined) was also not taken into account and may account for some of the difference in survival. We were also unable to obtain information on insurance at time of presentation and instead used insurance at time of

discharge which may mask differences. Lastly, only overall survival was examined and consideration of competing risks may weaken our finding of worst survival in EDDx patients.

CONCLUSION

Over 40% of CRC patients received their diagnosis through the ED. EDDx was associated with a nearly two-fold mortality risk increase. EDDx should be considered a marker of poor outcomes for CRC and may be related to unaccounted patient-level or systems-level factors such as reduced access to screening and less access to treatment after diagnosis. Efforts should be made to identify and intervene on modifiable risk factors for EDDx to improve CRC outcomes.

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Figure 1.
Selection Criteria

Figure 2.
Overall survival for all stages. ($p < 0.0001$)

Figure 3(A-D):
Overall Survival by Stage. A ($p=0.0004$), B ($p=0.0032$), C ($p=0.0921$), D ($p=0.0833$)

Table 1.

Characteristics of Colorectal Cancer Patients With and Without ED Diagnosis

Characteristic		ED (%) N=271	Non-ED (%) N=367	P-value
Age (years)	18 to <50	11.4	7.9	0.0023
	50 to <65	26.2	35.2	
	65 to <80	32.5	37.6	
	80	29.9	19.4	
Gender	F	51.7	51.0	0.8599
	M	48.3	49.1	
Number of comorbidities	0	3.0	1.09	0.0178
	1	10.3	10.6	
	2	14.0	18.3	
	3+	70.5	63.5	
Race	unknown	2.2	6.5	0.1043
	Black	38.0	30.8	
	White	34.7	42.0	
	Other	27.3	27.3	
Insurance	Private	15.1	41.4	<0.0001
	Medicare	59.8	42.8	
	Medicaid	23.6	12.8	
	Other	1.5	3	
Stage	1	10.7	28.3	<0.0001
	2	17.3	26.4	
	3	26.9	27.0	
	4	45.0	18.3	
Grade	I and II	56.5	70.6	0.0011
	III	22.9	16.1	
	Unknown	20.7	13.4	
Any Symptom	Yes	94.8	64.0	<0.0001
	No	5.2	36.0	
Common Symptoms	Pain	44.4	17.9	<0.0001
	Bleeding or Anemia	39.7	61.7	
	Nausea, Vomiting,	13.6	19.2	
	Obstruction			
Prior Colonoscopy	Other	2.3	1.3	<0.0001
	Yes	21.8	41.7	
	Never	47.6	24.0	
	Unknown	30.6	34.3	
Timing of last colonoscopy	Same year (includes screening colonoscopy)	3.4	68.6	<0.0001
	1 to 5 years	50.9	20.9	
	5< to 10 years	32.2	9.2	
	>10 years	13.6	1.3	

Characteristic	ED (%) N=271	Non-ED (%) N=367	P-value
Surgery on same admission as diagnosis	31.7	4.6	<0.0001

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Table 2.

Logistic regression model predicting diagnosis of cancer in the Emergency Department

Characteristic		OR (95% CI)	P-value
Age (years)	18 to <50	1.69 (0.81–3.52)	0.1631
	50 to <65	Ref	
	65 to <80	0.67 (0.34–1.31)	0.2409
	80	1.09 (0.53–2.26)	0.8212
Gender	F	ref	
	M	1.13 (0.77–1.65)	0.5461
Number of comorbidities	0	Ref	
	1	1.04 (0.22–4.90)	0.9586
	2	0.71 (0.16–3.16)	0.6502
	3+	0.93 (0.22–3.96)	0.9192
Race	Unknown	0.53 (0.09–3.12)	0.4862
	White	Ref	
	Black	1.43 (0.89–2.32)	0.141
	Other	0.92 (0.57–1.51)	0.7529
Insurance	Private	Ref	
	Medicare	4.79 (2.59–8.85)	<0.0001
	Medicaid	4.39 (2.37–8.11)	<0.0001
	Other	1.27 (0.32–5.05)	0.7307
Stage	1	ref	
	2	1.19 (0.64–2.22)	0.5793
	3	1.62 (0.89–2.97)	0.118
	4	3.83 (2.05–7.15)	<0.0001
Grade	I and II	Ref	
	III	1.23 (0.75–2.02)	0.4067
	Unknown	1.18 (0.65–2.15)	0.5782
Prior Colonoscopy	Yes	0.52 (0.31–0.88)	0.0138
	Never	ref	
	Unknown	0.42 (0.27–0.66)	<0.0001
Any Symptom	Yes	6.93 (3.59–13.36)	<0.0001
	No	ref	

Table 3.

Cox Regression Predicting Overall Survival

Parameter		HR (95% CI)	P-value
Diagnosis Location	ED	1.89 (1.26–2.85)	0.0023
	Non-ED	Ref	
Age (years)	18 to <50	0.63 (0.27–1.43)	0.2659
	50 to <65	ref	Ref
	65 to <80	1.80 (0.93–3.47)	0.0804
	80	2.37 (1.20–4.68)	0.013
Number of comorbidities	0	ref	Ref
	1	0.23 (0.07–0.81)	0.0221
	2	0.30 (0.10–0.88)	0.0284
	3+	0.57 (0.21–1.52)	0.2575
	Unknown	0.55 (0.14–2.22)	0.4018
Insurance	Private	ref	Ref
	Medicare	1.99 (1.13–3.51)	0.0176
	Medicaid	2.17 (1.12–4.23)	0.0222
	Other	1.48 (0.33–6.70)	0.6132
Stage	1	Ref	Ref
	2	1.51 (0.70–3.24)	0.2938
	3	1.61 (0.75–3.43)	0.2189
	4	7.90 (3.92–15.93)	<0.0001
Gender	Male	0.81 (0.57–1.13)	0.2093
	Female	Ref	Ref
Race	White	Ref	Ref
	Black	0.78 (0.53–1.15)	0.2037
	Other	0.53 (0.33–0.83)	0.0055
Grade	I and II	Ref	Ref
	III	2.10 (1.38–3.19)	0.0006
	Unknown	1.79 (1.15–2.77)	0.0099
Symptom	yes	0.91 (0.54–1.56)	0.74
	no	ref	Ref
Prior Colonoscopy	Yes	1.14 (0.73–1.78)	0.5726
	No	Ref	Ref
	Unknown	1.31 (0.86–2.00)	0.2092