Published in final edited form as:

Clin Gastroenterol Hepatol. 2014 October ; 12(10): 1702–1707.e3. doi:10.1016/j.cgh.2014.02.036.

Risk Stratification of Emergency Room Patients with Crohn's Disease Could Reduce Computed Tomography Use by Nearly Half

Shail M. Govani, M.D., M.Sc.^{*}, Amanda S. Guentner, M.D.^{*}, Akbar K. Waljee, M.D., M.Sc.^{*,+}, and Peter D.R. Higgins, M.D., Ph.D., M.Sc.^{*}

^{*}Division of Gastroenterology, Department of Internal Medicine, University of Michigan

^{*}Department of Internal Medicine, University of Michigan

⁺Veterans Affairs Center for Clinical Management Research, Ann Arbor, MI

Abstract

Background/Aims—Computed Tomography (CT) is a useful tool in Crohn's disease (CD) to assess disease activity and exclude complications. Excessive radiation has been associated with increased risk of malignancy. We aimed to identify automatable algorithms with a high negative predictive value (NPV) of a significant CT finding in patients with CD presenting to the emergency department.

Methods—We conducted a retrospective review of a tertiary center's medical records to identify adults with a diagnosis of CD who presented from 2000–2011. Logistic regression was used to model (1) complications [perforation, abscess or other serious finding] and (2) inflammation.

Results—There were 1095 visits for 613 individuals with a CT scan within 24 hours of arrival. The average number of CTs was 1.8 with a range of 1–31. Complications occurred in 16.8% of CTs. Inflammation was found in 54.5% of CTs while any new/worse finding was found in 67.2%. Using 10-fold cross validation to evaluate our models, the area under the receiver operating characteristic curve for the complications model is 0.80 (95% CI: 0.74–0.86) and the inflammation model is 0.71 (95% CI: 0.68–0.74). Scanning only patients with model-predicted complications would reduce scans by 43.0%, with a miss rate of 0.8% (4/491).

Conclusions—Patients presenting to the emergency department with CD undergo CT scanning frequently but have no significant findings in 32.8% and complications in only 17%. Models with high NPVs were identified and could aid physicians in the decision to avoid CT scans in patients

Corresponding Author Contact Information: Peter D.R. Higgins, 6520 MSRB I, Box 0682, 1150 West Medical Center Drive, Division of Gastroenterology, University of Michigan, Ann Arbor, MI 48109, United States of America, Phone 734-763-7278, Fax 734-763-2535, phiggins@umich.edu.

Conflict of Interest: the authors have no conflict of interest to declare.

Author contributions:

SMG: Study concept and design, acquisition of data, analysis and interpretation of data; drafting of manuscript, statistical analysis

ASG: acquisition of data

AKW: analysis and interpretation of data, statistical analysis, critical revision of manuscript

PDRH: study concept and design, analysis and interpretation of data, statistical analysis, critical revision of manuscript and study supervision

with low likelihood of a positive scan. Studies are needed to validate these models beyond a single center.

Keywords

Inflammatory Bowel Disease; Computed Tomography; Crohn's Disease

Introduction

CT scan use has dramatically increased over the course of the last 20 years as access has increased¹. Imaging modalities, including CT, play a critical role in the care of patients with Crohn's disease (CD), allowing clinicians to assess the extent of disease and the presence of penetrating complications. As CT scans have become easier to obtain, younger patients with CD may become exposed to very large cumulative doses of radiation, with 11% exposed to more than 50mSv, a level associated with increased risk of malignancy^{2,3}. Approximately 30% of this radiation exposure occurs in the emergency department setting and 75% of it is due to CT scans⁴. Young age at diagnosis, history of penetrating disease (fistulas and abscesses), history of multiple abdominal surgeries, and use of intravenous steroids and infliximab have been associated with higher cumulative radiation doses among patients with CD⁵.

We aimed to use logistic regression to develop two algorithms that would predict the probability of complications or inflammation detected by CT scan in patients with CD presenting to the emergency department with abdominal symptoms. Ideal algorithms would have a high negative predictive value, giving physicians the confidence to forgo CT scanning in patients with low risk for complications and inflammatory disease activity.

Methods

After receiving IRB approval, the electronic records database at the University of Michigan was queried for patients over the age of 18 with a diagnosis of CD by ICD-9 code 555.x who visited the emergency department between 2000 and 2011. Demographics, gender, age at emergency department visit and labs (obtained within 24 hours of the emergency department visit) were also electronically abstracted. The charts were then manually reviewed (SMG and ASG) to determine medications, chief complaint, whether a CT scan occurred within 24 hours of arrival and if so, the CT findings. Review of CT findings was performed by reviewers blinded to the lab results. Patients who did not actually have Crohn's disease upon review of records, did not undergo CT scan of the abdomen and pelvis with IV and PO contrast, or presented for a trauma complaint were excluded (see Figure 1 for details).

Obstruction was defined by the presence of a transition point requiring nasogastric tube decompression or surgical intervention. Patients were only classified as having appendicitis if they underwent surgery. Inflammation was defined by the presence of mucosal enhancement and/or increased vascular markings. Isolated wall thickening was not considered to be evidence of inflammation. Malignancies were only classified as a finding if they were new/unexpected findings. Urolithiasis was defined if there was no other explained cause of pain and/or findings of complications related to stones.

The two outcomes modeled were the presence of 1) new or worsening complications [perforation, abscess, appendicitis, new malignancy, pyelonephritis, urolithiasis, diverticulitis, pancreatitis, or another serious finding (PA+)] that would change clinical decision making, and 2) active intestinal inflammation. Statistical analysis was performed using SAS 9.3 (Cary, NC). Descriptive comparisons were performed using either the student's t-test for continuous values or the chi square test for categorical values.

Logistic regression was used to model the outcomes. Candidate models were developed with the best subset selection method in SAS using all predictors with a p value <0.05. All laboratory predictors were considered candidate variables in the process. Models were built with complete case analysis. Each visit was treated as a separate encounter so that repeat visits with the same patient were included in the model building process. The final model for each outcome was chosen for its superior negative predictive value and sensitivity. As CRP and ESR are missing in approximately 50% of the visits, we developed separate models for the 2 outcomes both with and without these predictors. The best model for each outcome is presented in this text while the other models can be found in the supplementary data.

In modeling outcomes when an external validation cohort is not available, a 10-fold cross validation is preferred. In this approach, the data are divided into 10 subsets of size N/10, and models are trained on a pooled group of 9 subsets, and tested on the 10th subset. This is repeated 9 additional times (using a different subset for testing accuracy each time), and the internally validated mean accuracy is reported in the results section⁶. By performing 10-fold cross validation, the effect of repeated measures in model building and test accuracy are minimized. The AuROC and associated confidence interval displayed are a result of the cross-validation process.

Results

The initial data query resulted in 2875 emergency department visits for 1281 individuals (Supplementary Figure 1: Subject Flow Diagram). After excluding patients without CD and those presenting with a traumatic complaint, there were 2472 emergency department visits for 1011 individuals. The average number of visits was 2.4 with a maximum of 56. Of these individuals, 613 had at least 1 CT scan (maximum: 31 in one individual). There were a total of 1095 CT scans. The average number of CT scans per individual was 1.8. At the beginning of the decade, CT was obtained on 25.8% of the emergency department visits. By 2011, CT use had increased to 41.9% of emergency department visits. The average age of the population at their first emergency department visit was 39.6 years. The population was 55% female and 87.3% Caucasian. Details of the population demographics comparing those who underwent CT scans and those who did not are located in Table 1. The admission rate was higher among those undergoing CT scan (89.0% versus 74.8%, $p<0.0001$). Patients who underwent CT scanning were more likely to be younger, male and be taking ciprofloxacin. Approximately half of the population did not have inflammatory markers drawn within 24 hours of the ER visit (49% missing ESR, 51% missing CRP). The remaining lab values were missing in less than 10% of the patients.

In our population with CD, 54 patients were discharged from the emergency department and returned within 30 days. Of this group, 42 did not obtain a CT scan on the initial visit. Among those 42 patients, the return visit included a CT scan 28.6% of the time. No cases of PA+ were identified on these CT scans while 41.7% of them did have inflammation.

Details on the CT findings are presented in Table 2. Overall, 67.2% had a new/worse finding on CT while 10.7% had an abnormal finding which was previously known or improving, and only 16.8% had a complication that would change clinical management.

Individual predictors of complications (PA+) and inflammation in univariate analyses can be found in Table 3. Notably, current use of medications including biologics did not predict the finding of inflammation. Similarly, use of biologics did not predict the finding of PA+ in univariate analysis. Mean lab values for each outcome are presented in supplementary data.

The best multivariable model predicting complications (PA+) included only the variables CRP and ESR. The estimates for this model are found in Table 4. Using 10-fold cross validation, this model has an AuROC of 0.80 (95%CI: 0.74–0.86). By evaluating the sensitivity, specificity and predictive values at each predicted probability, we chose a predicted probability cutoff of 6%, at which point the model has a sensitivity of 93.8% and negative predictive value of 98.1% for perforation, abscess, or other clinically significant finding (Figure 1a). An alternate model for PA+ that does not include ESR and CRP is presented in the supplementary materials.

An easily calculated equation of complications using only ESR and CRP was also constructed. Combining ESR with $5 \times \text{CRP}$ and not scanning patients with a value of 10 or lower has a sensitivity of 96.9% and negative predictive value of 97.8%. While this calculation is easy to use, the percentage of patients who would avoid a CT scan based on this cutoff was only 18.5%. Using this simple formula in our cohort would have avoided 91 CT scans, and missed complications in 2 out of the 491 patients (1 case of diverticulitis and 1 case of pyelonephritis).

The model that best predicted inflammation included absolute monocyte count (AMC), absolute lymphocyte count (ALC), absolute eosinophil count (AEC), hemoglobin, aspartate aminotransferase (AST), mean platelet volume (MPV) and mean corpuscular hemoglobin (MCH). The estimates for this model are found in Table 4. The AuROC for this model is 0.71 (95%CI: 0.68–0.74). A predicted probability cutoff of 8% has a sensitivity of 99.8% and a negative predictive value of 93.3%. The ROC curve for 10-fold validation and a table showing the test characteristics at the defined cutoff are shown in Figure 1b. While ESR and CRP are both significant univariate predictors of inflammation, we could not construct optimal multivariate models where all elements were significant that retained either of these important labs. We present an alternate model with ESR forced into a multivariate model in the supplementary material.

Discussion

The annual number of emergency department visits for patients with CD has increased by more than 2 fold over the decade studied. There was also an increase in the rate of CT

imaging as part of their evaluation, and patients were more likely to be admitted to the hospital as the decade progressed. As a tertiary care institution, CT use would likely be higher than the national average, as patients likely have more complicated disease. A recent study from a similar large tertiary care center also revealed frequent use of CT among patients with CD⁷. In contrast to that study, the percentage of patients admitted at our institution did significantly increase from the beginning of the decade to the end (63% to 87%). Among those undergoing CT scans, the prevalence of certain findings differed somewhat from the literature⁷. These percentages differ due to different definitions used for abscess (we included perianal abscess) and obstruction (defined rigidly as requiring NG tube placement or surgery). When only perforation and non-perianal abscess are considered, our percentages are very similar to those reported by Kerner, et al. (10.9% versus 10.3%).

It is difficult to determine how much radiation our patients were exposed to in this time period. The amount of radiation administered during CT scanning can vary dramatically from one institution to another. Even within one institution, the dose can vary depending on the size of the patient and whether the scan was protocolled as a low dose CT enterography. While CT technology is improving and the amount of radiation per CT appears to be decreasing, data from as recently as 2009⁸ indicates a range of 4–90 milliSieverts (mSv) depending on the protocol. While our patients underwent 1.8 CTs on average over the course of the decade, this underestimates the actual radiation exposure as this did not include any of their outpatient radiologic studies, CTs obtained more than 24 hours after arrival, or those obtained at outside facilities. Our understanding of the risk associated with radiation is based on epidemiological studies of atomic bomb survivor cohorts and nuclear industry workers. Using this information and biological studies, a government taskforce has developed risk estimates for cancer based on radiation dose⁹. Based on the number of emergency department CTs performed at our institution, it is expected that at least 1 additional attributable radiation-associated cancer will occur in these 1011 individuals⁸.

To help reduce this risk, we have developed the models reported here. By separating the outcomes of complications (PA+) and inflammation (I), we feel that we have given practitioners the ability to triage these patients more effectively. Additionally, the model to predict complications is an excellent model with a negative predictive value of 98.1%, which should give physicians more confidence that they will rarely miss an emergency by forgoing CT evaluation. For ease of use, we also presented an easy to use equation to predict complications (no scan for $ESR+5*CRP > 10$). While this guideline is powerful and easy to use, we were able to save more patients from radiation by using the logistic regression model with better performance characteristics and a similar miss rate.

In patients with an elevated probability of PA+, a standard CT of the abdomen and pelvis should be performed with non-barium contrast, to avoid the risk of barium peritonitis. If the predicted probabilities of both inflammation and PA+ were low, then we would expect that physicians could consider forgoing CT evaluation (Figure 2). If the predicted probability of complications was low and the probability of inflammation exceeded our thresholds, then the physician could choose between treating the patient for intestinal inflammation if their symptoms are consistent with a CD flare, or consulting with a gastroenterologist as to whether further imaging (CT enterography or MR enterography) is needed. In our study, CT

enterography made up only a small percentage of the studies performed (16.1%). Those patients with a low risk of perforation (PA+) and a significant risk of inflammation would likely have benefited from the reduced radiation exposure of the CT enterography protocol if a modality with radiation exposure was chosen.

One of the limitations of this study was the exclusion of obstruction as an outcome. Despite multiple attempts, we were unable to successfully create models with good performance characteristics to identify intestinal obstruction. We would suggest that if there are clinical signs or symptoms suggesting obstruction, that patients undergo abdominal X-rays. If concern for obstruction remains based on clinical grounds, an appropriate CT could then be obtained.

The implementation of these models would have a significant effect on both cost and radiation-associated cancers. If only patients with a PA+ score above the threshold of 6% underwent CT in the emergency department, 211 (43.0%) of the 491 patients in the model would not have been exposed to further radiation. If every Crohn's patient in the U.S. were to undergo 1 CT per decade in the emergency department setting, that would total approximately 540,000 CT scans in the next 10 years¹⁰. Using this algorithm could reduce that number to 308,340. Applying these assumptions to the radiation induced cancer data, this could prevent up to 256 cancers in the USA (assuming an even gender ratio and average age of 40). Using the most recent CMS fee schedule data, this would also save 349 dollars per CT for a total savings of \$80.8 million¹¹ per decade. Data from HCUPnet regarding emergency department visits in 2010 indicate that there were 81,000 visits where Crohn's disease was the primary diagnosis so these estimates for CT use in the emergency department are likely conservative¹².

These models are limited in that they are retrospective and represent data from one center. While our internal validation with 10-fold cross validation shows that these models have good performance characteristics, further external validation studies are needed to determine whether these models are generalizable to CD patients elsewhere. We are in the process of implementing the use of these models in our EPIC-based EMR and prospectively testing these models. We hope to validate these models and study the effects on CT use in emergency department patients with Crohn's disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support:

Dr. Govani's research is supported by the IBDWG GI Fellows Research Awards, funded by an unrestricted educational grant from UCB, Inc.

Dr. Waljee's research is funded by a VA HSR&D CDA-2 Career Development Award 1IK2HX000775.

Abbreviations

AEC	Absolute Eosinophil Count
ALC	Absolute Lymphocyte Count
AMC	Absolute Monocyte Count
AST	Aspartate aminotransferase
AuROC	Area under the Receiver Operating Characteristic Curve
CBC	Complete Blood Count
CD	Crohn's disease
CRP	C-Reactive Protein
CT	Computed Tomography
ED	Emergency Department
ESR	Erythrocyte Sedimentation Rate
I	Inflammation
IBD	Inflammatory Bowel Disease
MCH	Mean Corpuscular Hemoglobin
MPV	Mean Platelet Volume
PA+	Perforation, abscess or other serious outcome

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ROC Curve for Complications Model

AuROC (10-Fold Cross Validation): 0.80 (95%CI: 0.74-0.86)

ROC Curve for Inflammation Model

AuROC (10-Fold Cross Validation): 0.71 (95%CI: 0.68-0.74)

Figure 1.

ROC Curve for Individual Models. This figure depicts sensitivity versus 1-specificity for the model depicting PA+ (a) and inflammation (b). The bottom right corner of each figure shows a classification table for each outcome compared to the prediction by the model at the defined cutoffs (6% for PA+ and 8% for inflammation).

Figure 2.

CT Algorithm for Patients with CD presenting to the emergency department. If obstruction is suspected, we suggest abdominal films to exclude this. The models shown here help to ensure the correct imaging modality and protocol is selected.

Table 1

Comparison of Crohn's Disease patients who underwent CT to those who did not.

	No CT	Underwent CT	p value
Male (%)	600 (43.6)	522 (47.7)	0.04
Average Age (StdDev)	40.6 (16.8)	38.2 (14.6)	<0.01
Ethnicity (%)			0.99
Caucasian	1181 (85.8)	940 (85.8)	
African American	162 (11.8)	129 (11.8)	
Other	34 (2.5)	26 (2.4)	
Narcotic use	435 (31.6)	328 (30.0)	0.38
ASA use	475 (34.5)	413 (37.7)	0.10
Steroid use	369 (26.8)	306 (28.0)	0.52
Immunomodulator use	497 (36.1)	402 (36.7)	0.75
Biologic use	266 (19.4)	232 (21.2)	0.26
Ciprofloxacin Use	69 (5.0)	77 (7.0)	0.03
Metronidazole Use	101 (7.3)	85 (7.8)	0.69
Admitted	1030 (74.8)	974 (89.0)	<0.01

Table 2**CT Findings**

CT Findings	n (1095)	%
Normal	272	24.8
Obstruction	108	10.0
Abscess (not peri-anal)	104	9.5
Fistula (not peri-anal)	86	7.9
Stricture without Obstruction	46	4.2
Peri-anal abscess	25	2.3
Peri-anal fistula	17	1.6
Perforation	15	1.4
Diverticulitis	12	1.1
Pancreatitis	9	0.8
Appendicitis	8	0.7
Urolithiasis (complication)	3	0.3
Cholecystitis	2	0.2
Pulmonary Embolus	2	0.2
Pyelonephritis	2	0.2
Cholangitis	2	0.2
Non-GI cancer (new)	1	0.1
SMA syndrome	1	0.1
Peritonitis	1	0.1
Internal hernia	1	0.1
Hepatic abscesses	1	0.1
Hepatic Infarction	1	0.1
PA+	184	16.8
Inflammation	597	54.5

Table 3

Univariate analysis of PA+ and Inflammation

Characteristic	PA+ Univariate Statistics			Inflammation Univariate Statistics		
	OR	95%CI	p value	OR	95%CI	p value
White Blood Count (K/mm ³)	1.08	1.04–1.11	<0.0001	1.04	1.01–1.07	0.003
Hemoglobin (g/dL)	0.83	0.77–0.90	<0.0001	0.95	0.90–1.01	0.53
Platelet Count (K/mm ³)	1.002	1.001–1.003	<0.0001	1.002	1.001–1.003	<0.0001
Mean Corpuscular Volume (fL)	0.99	0.97–1.01	0.50	0.95	0.93–0.96	<0.0001
Absolute Neutrophil Count (K/mm ³)	1.09	1.06–1.13	<0.0001	1.05	1.02–1.08	0.0003
Albumin (g/dL)	0.54	0.42–0.69	<0.0001	0.80	0.66–0.96	0.02
CRP (mg/dL)	1.13	1.09–1.17	<0.0001	1.07	1.04–1.11	<0.0001
ESR (mm/hr)	1.03	1.02–1.04	<0.0001	1.01	1.00–1.02	0.003
Age (per year)	1.00	0.99–1.01	0.80	0.98	0.97–0.99	<0.0001
Gender (F versus M)	1.10	0.80–1.52	0.55	0.66	0.52–0.83	0.0006
Steroid Use	1.31	0.93–1.84	0.12	1.25	0.96–1.63	0.10
Ciprofloxacin Use	2.60	1.57–4.31	0.0002	1.06	0.66–1.69	0.81
Metronidazole Use	2.23	1.36–3.66	0.002	1.03	0.66–1.61	0.88
Immunomodulator Use	0.90	0.64–1.26	0.55	1.15	0.90–1.47	0.27
Biologic Use	1.04	0.71–1.53	0.84	0.83	0.62–1.11	0.21

Table 4

Multivariable Model for PA+ and Inflammation

PA+ Model			
Variable	OR	95% CI	P value
C-Reactive Protein (CRP) (mg/dL)	1.10	1.05–1.15	<0.0001
Erythrocyte Sedimentation Rate (ESR) (mm/hr)	1.02	1.01–1.03	0.001
Inflammation Model			
Variable	OR	95% CI	P value
Absolute Monocyte Count (AMC) (K/MM ³)	2.74	1.83–4.09	<0.0001
Hemoglobin (g/dL)	1.09	1.02–1.18	0.02
Aspartate Aminotransferase (AST) (IU/L)	0.98	0.97–0.99	<0.0001
Mean Corpuscular Hemoglobin (MCH) (pg)	0.85	0.81–0.90	<0.0001
Mean Platelet Volume (fL)	0.79	0.70–0.90	0.0002
Absolute Lymphocyte Count (ALC) (K/MM ³)	0.77	0.66–0.91	0.002
Absolute Eosinophil Count (AEC) (K/MM ³)	0.31	0.11–0.89	0.03