Predicting Pathologically Complicated Appendicitis Using Ubiquitous Clinical and Laboratory Data

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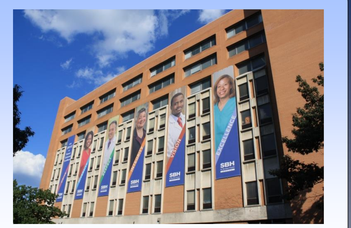

Introduction

Appendectomy is the most frequently performed emergency surgical procedure worldwide and in the US [16]. Acute appendicitis presents in two forms; complicated and uncomplicated. To date the management of uncomplicated acute appendicitis has been surgical with emergent appendectomy. Antibiotic treatment alone of uncomplicated acute appendicitis has been proven to be effective [7, 9, 11, 16, 17], however has not gained wide acceptance in US medical practice. Complicated appendicitis has been successfully treated with antibiotics and when needed percutaneous drain placement [5].

With viable nonoperative options for treatment of uncomplicated appendicitis, accurate prediction of pathologically complicated appendicitis is necessary. With varying success, some authors have attempted to predict this pathological outcome using combinations of clinical, laboratory and/or radiographic values. [2,6,12]

Some of these predictive mechanisms rely on laboratory values that may not be part of initial workup of abdominal pain; for example, c-reactive protein (CRP) [12], fibrinogen [2], or calprotectin level [6] may play a predictive role but are not ubiquitously available.

While abscess or purulent peritonitis on CT are evidence of complicated appendicitis, other CT evidence of appendicitis such as diameter of appendix may be predictive [19]. Adding another layer of complexity, CT evidence of appendicolith may limit nonoperative treatment success of uncomplicated appendicitis. [14] Finally, effective scoring systems and/or physician clinical gestault may obviate the need for radiographic diagnosis of appendicitis. [10]

Our goal was to develop a scoring system based on ubiquitous or simplified clinical and laboratory values to distinguish pathologically uncomplicated appendicitis from complicated appendicitis. An effective predictive scoring system could guide use of nonoperative management of appendicitis. We also examined the association of appendiceal diameter and presence of appendicolith to uncomplicated and complicated appendicitis.

Methods

A retrospective analysis of patients who had been admitted for appendicitis between December 29, 2009 and December 31, 2014 at St. Barnabas Hospital, Bronx, NY was performed. St. Barnabas Hospital is a not-for-profit acute-care community teaching hospital 450 bed hospital and level I trauma center located in the south central Bronx.

The electronic medical record (EMR) was then queried using International Classifications of Disease, Ninth Revision (ICD 9) codes to select for cases relating to appendicitis.

The diagnosis of acute appendicitis was established with physical examination, laboratory tests, ultrasound examination and/or abdominal computed tomography. This was further corroborated with operative reports and pathologic findings when applicable.

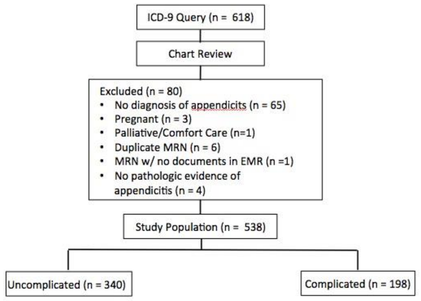

Table 1: Exclusion criteria

Study Variables

We abstracted demographic data, including gender, age, body mass index (BMI), and number of self-reported comorbid conditions. We recorded time of onset of abdominal or gastrointestinal symptoms to clinical presentation (in days), using physician and nursing documentation.

Vital sign data were collected from the first set of recorded vitals. Laboratory data was abstracted from first blood draw in the emergency department and included white blood cell count (WBC) and total bilirubin. We tabulated the number of systemic inflammatory response syndrome (SIRS) criteria met and defined the presence SIRS as two SIRS criteria (WBC >12,000/mm3 or <4000/mm3, RR > 20, HR > 90, Temperature >100.4F or <96.8F being present.

We also abstracted outcome data, including postoperative length of stay, days of intravenous antibiotics, days until resumption of regular diet and postoperative complications. Postoperative complications included early readmission (i.e. within 30 days of diagnosis), mortality (i.e. within 90 days of diagnosis of appendicitis) and revisit rates; defined as clinic or emergency room visits after the first post-operative visit within 30 days of diagnosis.

Simplified radiographic data were abstracted, including width of the appendix and presence of appendicolith.

Complicated appendicitis was defined as phlegmon, peri-appendiceal abscess or suppuration of the appendix, intra-abdominal abscess, gangrene/necrosis, perforation, diffuse purulent peritonitis, carcinoid or mucinous neoplasm. This was determined by review of pathologic specimens, operative findings, or computed tomography findings if no procedure was performed.

Statistical Analysis

We performed a two-tailed two-sample unequal variance t test on our study variables comparing them in complicated and uncomplicated appendicitis. All analyses were done using Excel for Mac 2011 version 14 (Microsoft Corporation). Based on convention, the significance level was set as P < .05.

Results

Data for patients showing the type of appendicitis are demonstrated in table 2.

Uncomplicated	338
Complicated	198
Phlegmon	4
Local Abscess/ Suppurative appendicitis	48
Remote Abscess	3
Gangrenous	126
Perforation	11
Purulent Peritonitis	2
Carcinoid	3
Mucocele	1

Table 2: Type of appendicitis with number of subjects

The significant findings are summarized in Table 3. Complicated appendicitis was associated with more elevated laboratory and clinical markers; temperature, heart rate, WBC, and total bilirubin. Patients with complicated appendicitis were more likely to have SIRS present. Both the presence and number of appendicoliths was more likely, and width of the appendix was likely to be larger for complicated appendicitis. Number of comorbid conditions present was found to be higher in complicated appendicitis. There was no significant difference in BMI of subjects with complicated appendicitis (p=0.40), gender of the patient in complicated appendicitis (p=0.21), or respiratory rate (p=0.23). Presence of Human Immunodeficiency Virus (HIV) positivity seemed to be associated with complicated appendicitis but did not achieve statistical significance (p=0 .066).

Variable (p value)	Uncomplicated	Complicated
Temperature (5.5e-3)	98.4 +/- .04	98.6 +/- .08
Heart Rate (1.65e-4)	84.2 +/- .9	90.9 +/- 1.5
WBC (1.38e-3)	13.0 +/- .23	14.3 +/- .34
SIRS (5.57e-3)	.39 +/- .03	.51 +/- .04
Number of SIRS Criteria (4.66e-4)	1.3 +/- .05	1.6 +/- .07
Total Bilirubin (5.45e-6)	.95 +/- .03	1.21 +/- .05
Appendicolith (0.018)	.36 +/-.03	.5 +/- .05
Width (1.36e-3)	10.05 +/- .15	10.91 +/- .22
Number of Co-morbidities (.02)	.6 +/- .06	.8 +/- .11
Age (3.35e-3)	30.4 +/- .8	34.7 +/- 1.3

Table 3: Mean +/- standard error of the mean for uncomplicated vs complicated appendicitis.

Using variables determined to have statistical significance from the above analysis attention was then turned to generating a predictive clinical scoring tool for complicated appendicitis. Each variable was assigned a point value and the scores tabulated for patients in both complicated and uncomplicated groups.

WBC >12 or < 4	1
Temperature > 100.4F or < 96.8F	1
HR > 90	1
Respiratory Rate > 20	1
Total Bilirubin > or = to 1.2	1
Presence of an appendicolith	If yes = 1
Width >10mm	1

Table 4: Scoring tool for complicated appendicits

A Score of 0-3 was determined to be low risk for complicated appendicitis, a score of 4-5 was indeterminate for complicated appendicitis, and a score of 6 or more was high risk for complicated appendicitis.

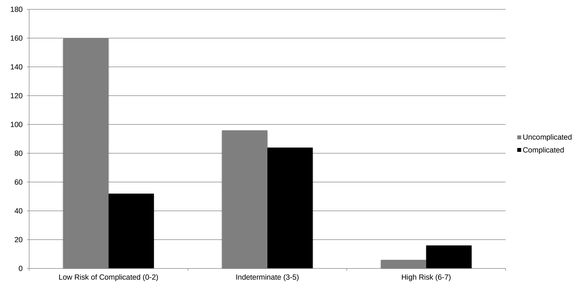

Table 5: Stratification of subjects using predictive model

Internal validation of this model was then performed using our previously collected data (including pathologic determination of complicated appendicitis). Patients considered low risk using the scoring tool for complicated appendicitis were proven pathologically to have uncomplicated appendicitis in 75.5%. Patients who scored high risk using the scoring tool for complicated appendicitis were proven pathologically to have complicated appendicitis in 72.7%. The Sensitivity for low scores in determining uncomplicated appendicitis is 61.1%. And the Specificity for a high score correlating to complicated appendicitis was 97.7%.

Discussion

Pathologically complicated appendicitis is associated with an increased probability of morbidity, especially when a surgical intervention is performed. A study performed in 2003 demonstrated that in patients with abscess related to acute appendicitis, immediate operation was associated with much higher morbidity and unique complications such as fistula, wound dehiscence, and ileus. Morbidity was 67% in the immediate operation group compared to 24% in the expectant management arm. [4] Bat et al demonstrated a higher complication rate in complicated appendicitis when compared to uncomplicated appendicitis. Intrabdominal abscess rate was 19.5 +/- 3.1 for complicated and 14.35 +/- 3.3 in uncomplicated. Similar results showed increased wound infection and incisional hernia in complicated appendicitis patients. [4]

The current accepted pathophysiologic model suggests that uncomplicated appendicitis will progress to complicated appendicitis with time and that delay to operative intervention unnecessarily puts the patient at risk of increased operative morbidity. This accounts for part of the reason why appendectomy is the most commonly performed emergent surgical procedure both in the US and worldwide. However complicated appendicitis (such as necrosis or gangrene, or localized perforation without abscess) are not always readily apparent based on now ubiquitous tomography imaging findings prior to operative intervention.

Given the association of complicated appendicitis with operative complication a predictive model for complicated appendicitis could be useful clinically to help determine which patients warrant operative intervention, especially in clinical scenarios in which surgical intervention could pose great risk of harm to the patient (severe cardiac compromise or bleeding diathesis). Surgery could be offered to expedite recovery with a minimal assumption of risk in uncomplicated appendicitis for those deemed to be appropriate operative candidates.

Our scoring tool for complicated appendicitis requires external validation. In order for it to become widely used it must be proven to predict complicated appendicitis in clinical settings outside of our institution and patient populations with characteristics different from ours.

Of note HIV positivity did not correlate with presentation as complicated appendicitis. According to the Center for Disease Control Bronx, New York has a high rate of HIV with 49.5 cases per 100,000 people [12]. Our study did not find any association with complicated appendicitis suggesting that immunocompromised status may not have an association with complicated appendicitis. However this requires further study as many factors that were not investigated could contribute to this finding such as whether patients are on highly affective antiretroviral therapy (HAART) have undetectable viral load, or adequate CD4 counts

Inherent limitations to our model include that we derive our predictive model based off of historical data. This assumes that the factors determined to be predictive will remain somewhat constant in the increasingly complex system of medical care we practice in. Additionally we defined and then collected the data. Significant data was used to determine the predictive model. It is possible that there are still undetermined clinically measurable variables, which we did not consider during the data collection phase, which have yet to be defined that are critical to prediction of complicated appendicitis.

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