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Increased anatomic severity in appendicitis is associated with outcomes in a South African population

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Abstract

Background—Severity of emergency general surgery diseases (EGS) has not been standardized until recently. The American Association for the Surgery of Trauma (AAST) proposed an anatomic severity grading system for EGS diseases to facilitate communication and quality comparisons between providers and hospitals. Previous work has demonstrated validity of the system for appendicitis in the United States. In order to demonstrate generalizability, we aim to externally validate this grading system in South African patients with appendicitis.

Methods—Patients with acute appendicitis during 2010–2016 were identified at multi institutional sites within South Africa. Baseline demographics and procedure types were recorded and AAST grades were assigned based on intraoperative findings. Outcomes included duration of stay, mortality, and Clavien-Dindo complications. Summary statistical univariate and nominal logistic regression analyses were performed to compare AAST grade and outcomes.

Results—A total of 1415 patients with a median [IQR] age of 19 years [14–28] were included (55% male). 100% underwent appendectomy: 63.5% completed via midline laparotomy, 36.5% via limited incision (31.8% via McBurney incision and 4.7% via laparoscopy). Overall 30-day mortality rate was 1.4% with an overall complication rate of 44%. Most common complications included: surgical site infection (n=147, 10.4%), pneumonia (n=105, 7.4%), and renal failure (n=64, 4.5%). Distribution of AAST grade is as follows: Grade 0 (10, 0.7%), Grade I (247, 17.4%), Grade II (280, 19.8%), Grade III (158, 11.3%), Grade IV (179, 12.6%), and Grade V

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Author Contributions:

M.C.H., J.M.A., and D.L.C. designed this study, for which D.L.C. provided vision. V.Y.K., J.L.B., G.L., and D.L.C. contributed to data collection. M.C.H. and V.Y.K. conducted data analysis. M.C.H. and J.M.A. wrote the manuscript, for which M.C.H. generated figures. M.C.H., V.Y.K., J.M.A., J.L.B., S.F.P., M.D.Z., and D.L.C. performed critical editing.

(541, 38.2%). Increased median [IQR] AAST grades were recorded in patients with complications, 5 [3–5], compared to those without, 2 [1–3], $p=0.001$. Duration of stay was increased for patients with higher AAST grades: IV and V (10.6 ± 5.9 days) versus I and II (3.6 ± 4.3 days), $p=0.001$. AUROC analysis to predict presence of any complication based on AAST grade was 0.90.

Conclusion—The AAST EGS grading system is valid to predict important clinical outcomes in a South African population with an increased degree of severity on presentation. These results support generalizability of the AAST EGS grading system for appendicitis in a developing nation.

Level of evidence—Level 4 – Multi institutional retrospective study

Study type—Retrospective multi institutional study

Keywords

Emergency General Surgery; Quality of care; Grading; Global Surgery

Background

It has been estimated by the Lancet Commission for Global surgery that there is an large unmet demand for surgical care in low middle income countries (LMIC) (1,2). The provision of safe surgical care in LMIC remains a challenge for global health (2–4). Urgent and emergent interventions are often needed to avoid significant morbidity and mortality as sequelae from common surgical diseases (5). One such common surgical disease, acute appendicitis, has been documented to have disproportionate disease burden in South Africa, with demonstrably poorer outcomes attributed to delays in presentation, and lack of access to healthcare (3–8).

Currently, there is no internationally accepted simple and reproducible method to classify the severity of acute appendicitis. Surgical care for acute appendicitis in LMICs may be improved by the utilization of a standardized classification of disease severity. This may 1) enhance communication between surgeons, 2) improve reporting and stratification of disease severity to allow for meaningful comparison of outcomes between centers and countries. To address the lack of standard disease classification in the United States, the American Association for the Surgery of Trauma (AAST) recently created a system utilizing various clinical, pathologic, imaging and operative findings to generate a disease specific severity grade for all common general surgical emergencies (9–11). This grading system is based upon the Organ Injury Scale (OIS), which has been externally validated in trauma. Just as with grading of injury in trauma, the AAST emergency general surgery grading system provides an anatomic based, time independent methodology for assessing a patient's disease (11). This system as it pertains to acute appendicitis is tabulated in Table 1. Previous work demonstrated the validity of the grading system in a western tertiary referral center in the United States which services a predominantly Caucasian rural and urban population (12). This grading system, however, has not been validated in an international population with variable stages of appendicitis and access to care. In this study we aim to demonstrate the international generalizability of the AAST emergency general surgery (EGS) grading system in patients for appendicitis by applying it to a large cohort of South African patients with

acute appendicitis. We hypothesize that the grading system will be sufficiently valid and robust to stratify patients' disease severity at operation in this population and that increasing AAST EGS grade will directly correlate with increasing levels of morbidity.

Methods

This is a retrospective multi-institution cohort study undertaken by the authors. Institutional Review Board approvals were obtained prior to conducting the study from both the Mayo Clinic and from the Biomedical Research Committee of the University (BREC) of Kwa Zulu Natal. The database in Pietermaritzburg has class approval form BREC (BCA 221/13). A prospectively maintained database for patients was queried for patients with a diagnosis of appendicitis and subsequent appendectomy from 2010 to 2016. Baseline demographic information, symptoms, vital signs, laboratory data, operation types, complication types and rates according to National Surgical Quality Improvement Program (NSQIP) definitions (13), subsequent interventions as graded by the Clavien-Dindo system (14), subsequent laparotomy rate, patient referral location (urban/rural), intensive care unit days, duration of stay and 30 day mortality rates were recorded. Patients included have operative management. Non-operative management or utilization of drains is not performed in this setting.

Description of Pietermaritzburg South Africa and Hospital System

The city of Pietermaritzburg is the capital of KwaZulu-Natal (KZN) province and is the largest city in the western half of KZN. There are nearly one million people in the city and it is served by a variety of hospitals: Grey's Hospital (tertiary), Edendale Hospital (regional), Northdale Hospital (district). Western KwaZulu-Natal is a predominantly rural province with a population of two million people. Referrals from the rural population to the south and west in the Sisonke District of KwaZulu-Natal come directly to Edendale. The Pietermaritzburg Metropolitan Surgical Service (PMSS) maintains a prospective digital registry, which captures data at our institutions (15,16). Ethics approval to maintain the registry has been obtained from the Biomedical Research Ethics Committee (BCA221/13 BREC) of the University of Kwa Zulu-Natal and from the Research Unit of the Department of Health. This digital registry is unique and has been discussed in the literature (16). The clerking medical staff enters the data onto an electronic pre-prepared clerking sheet. This process is the clerking process for all new admissions so the clinical data is entered in real time. As the data is entered it is then directly incorporated into the registry. The completed pre-prepared clerking sheet is then printed and becomes the patient's clinical record. At operation and at discharge a similar process is followed. This system combines the functions of a medical registry and a medical record system. It also combines an electronic system with a paper-based system and has been called the Hybrid Electronic Medical Registry (16).

Definition of patient referral location

In this patient population (Figure 1), those presenting from Sisonke district were considered rural. Patients who present from the uMgungundlovu district were considered urban. Patients who also were transferred from rural hospitals within the Sisonke district were also considered rural. Patients who otherwise presented from surrounding areas within

Pietermaritzburg were considered urban. The geographical relationship of each hospital with regard to the referral population within KwaZulu-Natal defined rural versus urban. Patients presenting or referred from hospitals outside of Pietermaritzburg were considered rural.

AAST Grade Assignment for Appendicitis

The AAST grade (Table 1) was assigned for acute appendicitis from retrospective operative report findings. Grades were independently assigned from patients' operative report findings by two authors (VYK, JLB) with a third reviewer for any discrepancies and final score arbitration (MCH). Inter-rater reliability was determined utilizing kappa coefficient, with 95% confidence intervals (CIs) (17).

Statistical Analyses

Univariate analyses to assess the relationship of AAST grade and clinical outcomes were performed using two tailed t-tests. All continuous variables were described using means with standard deviations (SD) if normally distributed and medians with inter-quartile ranges if gross skewness was present. Categorical variables were summarized as proportions. Variables on univariate analyses with $p < 0.05$ were included in a multivariable nominal regression analysis in order to determine risk factors predictive for the development of post-operative complication. All data analyses were performed using JMP (SAS Institute, Inc. Cary NC). GraphPad Prism (GraphPad Software, Inc. La Jolla CA) was utilized for all visual graphics.

Results

Patient demographics and overall outcomes

During the study period 1,415 patients met criteria and were included. The median [IQR] age in this population was 19 [14–28] years; 55% male. 663 patients (47%) presented from a rural setting. All patients underwent surgical exploration and appendectomy through a variety of approaches; 63.5% via midline laparotomy, 31.8% via McBurney incision, and 4.7% via laparoscopy. The overall complication rate was 44% (n=621). The 30-day mortality rate was (n=20, 1.4%). Complication types and rates included surgical site infection (n=147, 10.4%), pneumonia (n=105, 7.4%), and renal failure (n=64, 4.5%). The re-exploration rate was 53.7% (n=761). Median [IQR] duration of stay was 5 days [2–9].

Patient presentation

The median [IQR] duration of preoperative symptoms to their first contact with a healthcare system for the entire cohort was 3 [2–5] days. Migratory pain was reported by 35% of patients whereas 65% had non-migratory or non-specific abdominal pain. Patients presented with localized peritonitis at presentation more frequently than generalized peritonitis (58% vs 32%, $p = 0.001$). Further details regarding presentation symptoms, physiology, operative methods, and post-outcomes are presented in Table 2. Physiologic parameters at presentation included a median temperature of 37.3 °C [36.7–38 °C], median heart rate of 110 beats per minute [88–112], and median white blood cell count of $14 \times 10^9/\text{liter}$ [11–18 $\times 10^9$].

AAST Grade and Clinical Outcomes

Distribution of AAST grade is as follows: Normal (10, 0.7%), Grade I (247, 17.4%), Grade II (280, 19.8%), Grade III (158, 11.3%), Grade IV (179, 12.6%), and Grade V (541, 38.2%). On multivariable nominal regression analysis, risk factors that were independently associated with the development of a post-operative complication included the following included the following ($p < 0.05$): increasing AAST grade (Grade II OR 2.36; 95% CI 1.05–6.39, Grade III OR 8.18; 95% CI 3.7–20.7, Grade IV OR 30.1; 95% CI 14–74.8, Grade V OR 109.1; 95% CI 52.1–267.5), the presence of peritonitis at admission (OR 3.77; 95% CI 2.63–5.42), and greater than three days of preoperative symptoms (OR 1.86; 95% CI 1.32–2.60). Figure 4 demonstrates the increasing odds for developing a post-operative complication for increasing AAST grade using grade I as a reference. The overall kappa coefficient for inter-rater reliability of grade assignment, 0.71 (95% CI, 0.63 – 0.77) with 1203 of 1415 scores (85%) concordant between the two initial reviewers.

Discussion

In HICs, early recognition and timely surgical therapy have dramatically reduced the morbidity and mortality related to acute appendicitis (18). Unfortunately, appendicitis continues to have disparate outcomes in different populations around the world and remains associated with increased severity and worse outcomes in South Africa when compared to appendicitis in other LMIC (19–21). Patients with appendicitis in South Africa have increased rates of perforation and poorer outcomes (22). Reduced access to advanced imaging techniques, and inability of power prognostic clinical decision making tools (Alvarado score) to aid clinicians at primary care facilities, in addition to the patient behavior patterns and environment are all factors contributing to this increased anatomic severity (23).

Meaningful comparison and benchmarking of outcomes for acute appendicitis between centers and countries, while critical for the improvement of care and outcomes, is hampered by the lack of a standardized system for classifying the severity of disease (24). In light of this, there is increased emphasis on developing a standardized system to classify the severity of emergency general surgical diseases and quantify surgical outcomes in both HIC's and LMIC's (25). Until now, the AAST grade for appendicitis had only been applied to a homogenous population within the United States (12). Our study has shown the generalizability of the AAST grade to a patient cohort from a LMIC with a very different spectrum of disease severity. This is important as the lack of a uniform system of classifying severity has made it difficult to provide universal evidence based recommendations for acute appendicitis. Previous scoring systems, such as the Alvarado score, are only utilized for diagnosis and not the measurement of severity, which is a distinct advantage that the AAST grading system offers (23,26). An operative severity classification like the AAST grading system is a more accurate and meaningful method to direct disease specific research and interventions rather than simple binary approach of simple versus complicated disease.

Future study for the optimal management of advanced emergency general surgery diseases is needed. In this cohort, the presence of advanced disease (AAST grade III or greater) was more prevalent than AAST I or II. Determination what type of operative or non-operative

management is best for progressive disease states (AAST III, IV, V) with advanced anatomic and physiologic severity, may permit providers options for more rationale approaches toward appendicitis therapy. Currently, it is difficult to assess anatomic severity without advanced imaging and this may not always be available in LMICs. Furthermore, the presence of peritonitis and variable associated differential diagnoses may encourage surgeons in LMICs to forgo imaging and proceed to an operative management.

In this population, a significant majority of patients underwent laparotomy for what was determined to be phlegmon or abscess related appendicitis. Patients present with advanced disease severity, as is reflected in our cohort, and this demonstrates the underutilization of non-operative or minimally invasive techniques for appendicitis. As disease severity increases, the utilization of laparotomy increased. Research focused on strategies, such as anatomic grading in the preoperative setting using ultrasound or CT scanning, to avoid or reduce the need for emergency laparotomy for advanced appendicitis with concomitant morbidity in LMICs is necessary. The long term focus of appendicitis research in this population would be to increase the availability of non-operative management strategies for patients whose disease severity is potentially compatible.

Increasing anatomic severity as assigned by the AAST grade was associated with an increasing rate of laparotomy due to the broad spectra of etiologic causes of peritonitis in South Africa. Laparoscopy in a resource-constrained environment is associated with major logistical issues. The majority of patients from SA presented late (partly due to difficulty in access surgical facilities) and commonly with generalized peritonitis and severe sepsis likely the reason for more common use of midline laparotomy and fewer laparoscopic approaches. Moreover, the use of laparoscopy for complicated appendicitis remains unclear for increasing appendicitis severity using the AAST grading system. In South Africa, it is not known whether the adoption of a skillset common to trainees and staff in the USA will be broadly extrapolated throughout the country. The reduction in wound complications and pain would benefit the patient and deserves further study. It is evident that optimal management strategies for complex abdominal surgical emergencies differ and that laparoscopic feasibility is highly dependent upon the operator's experience and operating environment as well as the patient's status. The relaparotomy rate of 53% is elevated. In the South African cohort, delayed presentation with late pathology and advanced physiologic insult are much more common compared with data from the developed world (6,18). Relook laparotomy is usually broadly divided into two approaches either planned or on demand. The merit of each approach remains controversial. Due to late presentation and increased severity of intra-abdominal contamination, the threshold for relook is often much lower for this cohort. The need for repeat laparotomy in the South African setting is previously reported extensively (6–7, 18–20). Currently, the South African authors follow an on demand approach and have a low threshold for repeat surgery. Difficult and complex intraabdominal interloop collections rather than discrete, dependent abscess type collections are often encountered in South Africa (19,20). This makes it hard to see how percutaneous drainage alone will suffice to manage these patients. As access to interventional radiology improves it could be possible to reduce the reliance on repeat surgery for severe appendicitis.

The AAST grading system allows for standardized international reporting of the severity of acute appendicitis. Nevertheless there are a number of limitations to this study. Significantly, the AAST grades were assigned retrospectively. While our agreement statistic demonstrated substantial reliability between observers, the data used was based on the review of operative reports which may contain varied degrees of detail. Any preoperative association for surgical management using AAST grade is limited as the association of imaging findings is only validated retrospectively using CT (12). As data reporting from institutions in LMIC improves with the development of national emergency surgery registries, similar in structure to the National Surgical Quality Improvement Program (NSQIP), more accurate assessment and benchmarking of global outcomes of acute appendicitis using the AAST grading system will be feasible. This may allow for the meaningful comparison of outcomes and allow for ongoing monitoring to identify improvements.

The AAST grading of acute appendicitis is generalizable to an international LMIC population and, grade for grade, patients in South Africa have worse outcomes. The AAST grading system provides a robust framework for global reporting on appendicitis. This is a significant advance towards accurately determining burden of disease within LMIC's and provides a tool for policy makers to quantify and address disparities in outcomes stratified by disease severity. Likely, international validation of the AAST grading systems for other emergency surgical diseases will be possible.

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Figure 1.
Relationship of population density within KZN, South Africa

Figure 2.

Increasing complication severity (Clavien-Dindo classification) is associated with increased anatomic severity as defined by AAST grade

Figure 3.
Increased AAST Grade and the duration of preoperative appendicitis symptoms is associated with increasingly invasive procedures

Figure 4.

The odds ratio (95% CI) of a post-operative complication increases with anatomic severity as defined by AAST Grade (*Any Complication as compared to Grade I)

Table 1

AAST grading system for appendicitis as described by Shafi (9).

Grade	Operative AAST Description of Appendicitis	N (%)
Normal	Normal appendix	10 (0.07%)
Grade I	Acutely Inflamed Appendix, Intact	247 (17.4%)
Grade II	Gangrenous Appendix, Intact	280 (19.8%)
Grade III	Perforated Appendix with Local Contamination	158 (11.3%)
Grade IV	Perforated Appendix with Periappendiceal Phlegmon or Abscess	179 (12.6%)
Grade V	Perforated Appendix with Generalized Peritonitis	541(38.2%)

Patient Characteristics

Table 2

<i>Characteristics</i>	Normal	AAST Grade					V	P value
		I	II	III	IV	V		
N (%)	10 (0.07%)	247 (17.4%)	280 (19.8%)	158 (11.3%)	179 (12.6%)	541 (38.2%)		
Male %	30	56.7	66	63.3	63.1	44.9		0.001
Female %	70	43.3	44	36.7	36.9	55.1		0.001
Median age[IQR] (years)	28 [18–32]	20 [15–26]	18 [12–26]	19 [13–31]	18 [14–31]	19 [14–31]		0.001
<i>Clinical Presentation</i>								
Median[IQR] duration of illness (days)	1 [1–2]	2 [1–3]	2 [1–3]	3 [2–5]	4 [2–5]	5 [3–7]		<0.0001
Localized peritonitis %	100	82.2	95	61.4	75.4	21.6		<0.0001
Generalized peritonitis %	0	17.8	5	38.6	24.6	78.4		<0.0001
Median temperature (°C)	36 [36–36]	37 [36–37]	37 [37–37]	37 [36–38]	37 [36–38]	37 [36–38]		<0.0001
Median heart rate (bpm)	78 [65–93]	90 [80–101]	95 [84–105]	100 [88–110]	100 [88–112]	110 [99–137]		<0.0001
Median white blood cell count ($\times 10^9/L$)	9 [4–13]	12 [10–15]	13 [11–15]	14 [11–20]	15 [12–18]	16 [12–20]		<0.0001
<i>Surgical Method</i>								
Local incision (%)	0	74.2	79.3	16.5	8	1		<0.0001
Laparoscopy (%)	0	12.9	8.2	3.8	1	0.5		<0.0001
Midline Laparotomy (%)	100	12.9	12.5	79.7	91	98.5		<0.0001
Relaparotomy (%)	0 (0%)	2.2	1.4	14.4	33.1	86.1		<0.0001
<i>Post Operative Outcomes</i>								
Open Abdomen (n, %)	0	0	0	5 (4.8%)	5 (3.8%)	236 (46.9%)		<0.0001
ICU admission (n, %)	0	0	0	1 (1.2%)	0	120 (26.8%)		<0.0001
Median[IQR] ICU days	0	0	0	0	0	1 [0–7]		<0.0001
Median[IQR] Duration of Stay	3 [2–5]	2 [2–3]	2 [2–3]	5 [4–7]	6 [4–7]	10 [7–14]		<0.0001
Wound Sepsis (n, %)	0	0	7 (2.5%)	13 (8.2%)	29 (16.2%)	98 (18.1%)		<0.0001
Pneumonia (n, %)	0	1 (0.4%)	5 (1.8%)	6 (3.8%)	12 (6.7%)	81 (14.9%)		<0.0001
Renal Failure (n, %)	0	1 (0.4%)	1 (1.6%)	5 (3.2%)	3 (1.7%)	54 (10%)		<0.0001
Death (n, %)	0	1 (0.4%)	0	0	2 (1.1%)	17 (3.1%)		<0.0001