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Increased risk of malignancy for patients older than 40 years with appendicitis and an appendix wider than 10 mm on computed tomography scan: A post hoc analysis of an EAST multicenter study

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ABSTRACT

Background: The incidence of underlying malignancy in appendicitis ranges between 0.5% and 1.7%. We sought to identify the subset of patients with appendicitis who are at increased risk of appendiceal malignancy.

Methods: Using the Eastern Association for the Surgery of Trauma Multicenter Study of the Treatment of Appendicitis in America: Acute, Perforated, and Gangrenous database, we included all patients from 28 centers undergoing immediate, delayed, or interval appendectomy between 2017 and 2018. Univariate then multivariable analyses were performed to compare patients with and without malignancy and to identify independent demographic, clinical, laboratory, and/or radiological predictors of malignancy. Akaike information criteria for regression models were used to evaluate goodness of fit.

Results: A total of 3,293 patients were included. The median age was 38 (27–53) years, and 46.5% were female patients. On pathology, 48 (1.5%) had an underlying malignancy (adenocarcinoma [60.4%], neuroendocrine [37.5%], and lymphoma [2.1%]). Patients with malignancy were older (56 [34.5–67] vs 37 [27–52] years, $P < .001$), had longer duration of symptoms before presentation (36–41 vs 18–23 hours, $P = .03$), and were more likely to have a phlegmon on imaging (6.3% vs 1.3%, $P = .03$). Multivariable analyses showed that an enlarged appendiceal diameter was independently associated with malignancy (odds ratio = 1.06, 95% confidence interval = 1.01–1.12; $P = .01$). The incidence of malignancy in patients >40 years with an appendiceal diameter >10 mm on computed tomography was 2.95% compared with 0.97% in patients ≤40 years old with appendiceal diameter ≤10 mm. The corresponding risk ratio for that population was 3.03 (95% confidence interval: 1.24–7.42; $P = .02$).

Conclusion: The combination of age >40 and an appendiceal diameter >10 mm is associated with a greater than 3-fold increased risk of malignancy in patients presenting with appendicitis.

Introduction

Appendectomy for acute appendicitis is one of the most common emergency general surgery procedures in the United States, with an estimated 300,000 procedures performed per year.[1] A shift in the treatment practices of patients presenting with complicated appendicitis has been noted in recent years, with many suggesting that an initial nonoperative management is superior to appendectomy in this patient population.[2–6] Evidence from randomized-controlled trials show that patients presenting with uncomplicated acute appendicitis may also be managed safely nonoperatively with antibiotics.[2,4,7,8] After successful resolution of the index episode, the routine performance of an interval appendectomy in patients successfully managed nonoperatively still remains a subject of much controversy.[4–6]

The most common causes of acute appendicitis are thought to be lymphoid hyperplasia and fecalith impaction.[9] Appendiceal

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cancer is responsible for 0.5% of all gastrointestinal neoplasms and for about 1% of all colon cancers.[10,11] The rate of appendiceal cancer in appendicectomy specimens varies between 0.5% and 1.7% in the literature.[10,12] Appendiceal tumors are classified into 2 main groups: neuroendocrine tumors (most common primary type—formerly known as carcinoids) and adenocarcinomas.[13] Adenocarcinomas are very aggressive tumors that may require a right hemicolectomy for an oncologic safe resection.[10] Due to the low incidence and lack of sensitive diagnostic tools, the presence of appendiceal malignancy is rarely suspected preoperatively and appendiceal malignancies are usually discovered incidentally on postoperative pathology reports.[2,14–16] Even when symptomatic, appendiceal malignancies most commonly present with symptoms indistinguishable from acute appendicitis.[14]

The risk factors for the presence of an underlying malignancy in a patient presenting with acute appendicitis are not well established.[14] Complicated appendicitis by itself has been associated with an increased risk of underlying malignancy. The risk is even higher in patients presenting with a periappendiceal abscess compared with patients with uncomplicated appendicitis.[2] Contradictory data exist regarding the risk of appendiceal tumors in patients presenting with an inflammatory mass. Although some studies report similar rates of malignancy in patients presenting with uncomplicated acute appendicitis compared with patients presenting with an inflammatory mass, others report increased tumor rates in the latter.[11,17] Older patients with acute appendicitis have also been found to be at a higher risk for an underlying tumor.[12,18]

In this study, we sought to use prospectively collected multicenter data to identify the subset of appendicitis patients who are at a particularly increased risk of appendiceal malignancy. We hypothesized that patient characteristics (eg, demographics and comorbidities) and clinical presentation, in addition to laboratory and radiological findings, in cancer patients differ from those of patients presenting with benign appendicitis.

Methods

Data source

This is a post hoc analysis using data obtained from the Eastern Association for the Surgery of Trauma Multicenter Study of the Treatment of Appendicitis in America: Acute, Perforated, and Gangrenous (MUSTANG) database. The MUSTANG database is a prospectively collected database for all patients presenting with appendicitis between January 2017 and June 2018 in 28 hospitals across the United States. It includes emergency department, imaging, laboratory, intraoperative, and longitudinal outcomes data (up to 1 year after index hospitalization discharge). Patient demographics, clinical presentation of acute appendicitis, Charlson comorbidity index, smoking history, immune status, laboratory inflammatory markers, and radiologic imaging findings were captured and included in our analysis.

Patient selection

We included all patients who received a diagnosis of appendicitis, had a computed tomography (CT) scan in the preoperative work-up, and did not have missing information for the results of the pathology report. Our population was divided into 2 cohorts based on the results of the pathology report (benign versus malignant). For the purposes of this study, we defined malignancy as a postoperative pathological diagnosis of adenocarcinoma, neuroendocrine tumor, or lymphoma of the appendix. Mucoceles were not included in the analysis. Patients included in our study did not have to undergo surgical management during index hospitalization. Patients who received an interval appendectomy and were diagnosed with a malignant disease at that point were also included. Multivariable regression models were constructed for the identification of independent predictors of underlying malignancy.

Statistical analysis

Continuous data were analyzed using the Mann-Whitney *U* test. Results are presented as median and interquartile range. Categorical variables were analyzed using Fisher exact test. Results are reported as number of patients and percentages. After univariate analyses, multivariable regression models were constructed, including all available demographic, initial presentation, laboratory, and CT-finding variables, and the best model was selected using the Akaike information criterion. The variance inflation factor was used and no multicollinearity was detected among the variables included in our multivariable regression models. Finally, using clinically and historically relevant cutoffs, we calculated the relative risk for presence of an underlying malignancy in patients from the MUSTANG database. A P value of <.05 was considered statistically significant. All statistical analyses were performed using Stata v15.1 (StataCorp, College Station, TX) and RStudio version 1.2.1335.

Ethical oversight

All hospitals participating in this multicenter database were required to get institutional review board approval and data use agreements were signed. Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted at the University of Miami.[19] All information included in the database were deidentified.

Results

A total of 3,293 patients were included; 48 (1.5%) had confirmed appendiceal malignancy, specifically adenocarcinoma ($n = 29$), neuroendocrine tumors ($n = 18$), and B-cell lymphoma ($n = 1$) of the appendix. In both the benign and malignant cohorts, the majority of the patients, 3,207 (98.8%) and 47 (97.9%), respectively, underwent appendectomy during their index hospitalization. Most patients underwent a laparoscopic appendectomy (92.7%). Table I summarizes the demographics, clinical presentation, and laboratory data of the patient population. In summary, patients with an underlying malignancy were older (median age 56 [34.5–67] vs 37 [27–52] years old, $P < .001$), had longer duration of symptoms (median duration 36–41 vs 18–23 hours, $P = .03$), and were less likely to present with nausea (58.3% vs 73.8%, $P = .02$), vomiting (22.9% vs 49.3%, $P = .01$), anorexia (34.8% vs 51.8%, $P = .01$), and migration of the pain to the right lower quadrant (59.6% vs 74.9%, $P = .03$). Charlson's comorbidity index was also significantly higher in patients with malignant appendicitis (1.5 [0–3] vs 0 [0–1], $P < .001$). On physical examination, patients with malignancy were less likely to present with a Rovsing's sign (17.6% vs 36.7%, $P = .02$). Owing to the aforementioned differences regarding clinical presentation, the interquartile range of Alvarado scores of patients with an underlying malignancy was lower, even though the median score was the same compared to benign appendicitis (median score 6 [4.5–6] vs 6 [5–7], $P = .001$).

Table II shows the differences in the CT findings between patients with malignant versus benign appendicitis. The presence of a phlegmon was significantly associated with the presence of underlying malignancy (6.3% vs 1.3%, $P = .03$). Intraoperative findings and patients' mortality are summarized in Table III. Briefly, patients

Table I
Demographics, clinical presentation, and laboratory between patients presenting with a benign versus malignant appendicitis

Variables	Benign ($n = 3,245$)	Malignancy ($n = 48$)	*P* value
Age (y), median [IQR]	37 [27–52]	56 [34.5–67]	< .001*
Male sex, (%)	1,724 (53.1)	21 (43.8)	.24†
BMI (kg/m^2), median [IQR]	28 [24.2–31.9]	25.9 [23.85–31.25]	.51*
Duration of symptoms (h), median [IQR]	18–23 [12–17, 48–53]	36–41 [12–17, >96]	.03*
Nausea, (%)	2,395 (73.8)	28 (58.3)	.02†
Vomiting, (%)	1,401 (49.3)	11 (22.9)	.01†
Anorexia, (%)	1,638 (51.8)	16 (34.8)	.01†
Diarrhea, (%)	561 (17.4)	9 (18.8)	.85†
Migration to RLQ, (%)	2,400 (74.9)	28 (59.6)	.03†
Prior episodes, (%)	273 (8.6)	3 (6.5)	.79†
Charlson comorbidity index, median [IQR]	0 [0–1]	1.5 [0–3]	< .001*
Prior abdominal surgery, (%)	719 (22.2)	17 (35.4)	.04†
Steroids, (%)	57 (1.8)	2 (4.2)	.21†
Chemotherapy, (%)	17 (0.5)	1 (2.1)	.23†
Other immunosuppression, (%)	52 (1.6)	1 (2.1)	.54†
Tobacco, (%)			.11†
Current	594 (18.3)	7 (14.6)	
Former	462 (14.3)	13 (27.1)	
Never	2183 (67.4)	28 (58.3)	
Temperature (Celsius), median [IQR]	36.9 [36.6–37.2]	36.7 [36.5–37.3]	.12*
Heart rate (bpm), median [IQR]	86 [74–97]	97 [81–103]	.01*
Systolic blood pressure (mmHg), median [IQR]	131 [118–142]	134 [124–151]	.03*
RLQ tenderness, (%)	3,177 (97.9)	45 (93.8)	.08†
Diffuse tenderness, (%)	467 (14.7)	10 (21.3)	.21†
RLQ rebound tenderness, (%)	919 (28.7)	10 (21.3)	.33†
Diffuse rebound tenderness, (%)	63 (2.0)	0 (0)	1.00†
Rovsing's sign, (%)	925 (36.7)	6 (17.6)	.02†
Obturator sign, (%)	329 (14.4)	4 (12.9)	1.00†
Psoas sign, (%)	340 (14.8)	5 (15.6)	.80†
Alvarado score, median [IQR]	6 [5–7]	6 [4.5–6]	.001*
Clinical AAST appendicitis severity, (%)			1.00†
Grades 1,2, and 3	3,157 (98.0)	48 (100)	
Grade 4	15 (0.5)	0 (0)	
Grade 5	51 (1.6)	0 (0)	
White blood cell (K/uL), median [IQR]	13.4 [10.6–16.1]	12.9 [11.0–15.1]	.33*
Polymorphonuclear cells, (%)	80.7 [73.2–85.8]	80.4 [71.3–86.5]	1.00*

AAST, American Association for the Surgery of Trauma; *BMI,* body mass index; *IQR,* interquartile range; *RLQ,* right lower quadrant.
* Mann-Whitney *U* test.
† Fisher exact test.

Table II
CT findings between patients presenting with a benign versus malignant appendicitis

Variables	Benign ($n = 3,245$)	Malignancy ($n = 48$)	*P* value
Local inflammatory changes, (%)	2,762 (85.1)	36 (75.0)	.07*
Contrast non-filling of appendix, (%)	107 (3.3)	4 (8.3)	0.08*
Appendiceal wall necrosis, (%)	193 (5.9)	4 (8.3)	0.53*
Air in appendiceal wall, (%)	45 (1.4)	0 (0)	1.00*
Periappendiceal fluid, (%)	543 (16.7)	6 (12.5)	0.56*
Contrast extravasation, (%)	2 (0.1)	0 (0)	1.00*
Regional soft tissue swelling, (%)	206 (6.3)	6 (12.5)	.13*
Diffuse abdominal/pelvic inflammation, (%)	14 (0.4)	0 (0)	1.00*
Free intraperitoneal fluid or air, (%)	324 (10.0)	5 (10.4)	.81*
Perforated appendicitis, (%)	164 (5.1)	5 (10.4)	.10*
Phlegmon, (%)	41 (1.3)	3 (6.3)	.03*
Cecal inflammation, (%)	255 (7.7)	6 (12.5)	.27*
Appendicolith, (%)	1,040 (32.0)	12 (25.0)	.35*
CT diameter (mm), median [IQR]	12 [10–14]	12.5 [11–16]	.06†
Image AAST appendicitis severity, (%)			.59*
Grade 1	2212 (72.1)	32 (71.1)	
Grade 2	92 (3.0)	1 (2.2)	
Grade 3	482 (15.7)	5 (11.1)	
Grade 4	220 (7.2)	6 (13.3)	
Grade 5	61 (2.0)	1 (2.2)	

AAST, American Association for the Surgery of Trauma; *IQR,* interquartile range.
* Fisher exact test.
† Mann-Whitney *U* test.

Table III
Operative data between patients presenting with a benign versus malignant appendicitis

Variables	Benign (n = 3,245)	Malignancy (n = 48)	P value
Initial operative approach, (%)			.10*
Laparoscopic single incision	8 (0.2)	0 (0)	
Laparoscopic 3 incision	3,143 (98.0)	44 (93.6)	
Open approach	49 (1.5)	3 (6.4)	
Other	6 (0.2)	0 (0)	
Final operative approach, (%)			.28*
Laparoscopic single incision	8 (0.2)	0 (0)	
Laparoscopic 3 incision	3,003 (93.7)	42 (89.4)	
Open, midline incision	93 (2.9)	2 (4.3)	
Open, RLQ incision	78 (2.4)	2 (4.3)	
Open, other incision	7 (0.2)	0 (0)	
Other	17 (0.5)	1 (2.1)	
Conversion to open from laparoscopic, (%)	129 (4.0)	1 (2.1)	.51*
Intraoperative findings, (%)			
Normal appearing appendix	53 (1.6)	0 (0)	1.00*
Acutely inflamed, intact	2,318 (71.4)	29 (60.4)	.11*
Perforated with local contamination	290 (8.9)	5 (10.4)	.62*
Perforated with phlegmon or abscess	153 (4.7)	7 (14.6)	.01*
Perforated with generalized purulence	128 (3.9)	2 (4.2)	.71*
Gangrenous appendix, intact	142 (4.4)	1 (2.1)	.72*
Gangrenous appendix, local contamination	105 (3.2)	1 (2.1)	1.00*
Gangrenous with phlegmon or abscess	59 (1.8)	3 (6.3)	.06*
Gangrenous with generalized purulence	53 (1.6)	1 (2.1)	.55*
Abscess	87 (2.7)	6 (12.5)	.002*
Serous abdominal/pelvic fluid	188 (5.8)	1 (2.1)	.52*
Purulent abdominal/pelvic fluid	321 (9.9)	4 (83.3)	1.00*
Other	159 (4.9)	3 (6.3)	.51*
Intraoperative adverse event, (%)	39 (1.2)	2 (4.17)	.12*
Operative duration (min), median [IQR]	57 [41–76]	56 [36–76]	.41†
Mortality (in-hospital), (%)	5 (0.2)	0 (0)	1.00*
Mortality (30 d), (%)	3 (0.1)	1 (2.1)	.06*

IQR, interquartile range; *RLQ,* right lower quadrant.
* Fisher exact test.
† Mann-Whitney *U* test.

with an underlying malignancy were more likely to have a perforated appendicitis with phlegmon or abscess (14.6% vs 4.7%, $P = .01$) and were more likely to have an abdominal abscess (12.5% vs 2.7%, $P = .002$). No differences were noted regarding the duration of the surgical procedure and in-hospital mortality.

The results of the multivariable regression analysis are shown in Table IV. In summary, only appendiceal diameter on CT imaging was identified as an independent predictor for the presence of underlying malignancy (odds ratio = 1.06, 95% confidence intervals: 1.01–1.12, $P = .01$). For every millimeter increase in the appendiceal diameter on CT imaging, the odd of underlying malignancy increased by 6%. Based on previously published work on the topic of malignancy in patients presenting with acute appendicitis, we dichotomized the age variable using the cutoff of 40 years old.[12,17,18] The incidence of appendiceal cancer in patients ≤40 years old with an appendiceal diameter ≤10 mm was 0.97%. On the other hand, the incidence of appendiceal cancer in patients >40 years old with an appendiceal diameter >10 mm was 2.95%. The corresponding risk ratio for the presence of cancer in a patient >40 years old with >10 mm appendiceal diameter compared to a patient ≤40 years old with ≤10 mm appendiceal diameter presenting with acute appendicitis was 3.03 with 95% confidence intervals (1.24–7.42) (Fig 1).

Discussion

In this multi-institutional study of appendicitis, we show that patients older than 40 years with an appendiceal diameter greater than 10 mm are 3 times more likely to have an underlying malignancy compared with patients younger than 40 with a diameter less than 10 mm. To our knowledge, this is the first time in the literature that appendiceal diameter on imaging has been identified

Table IV
Independent predictors for the presence of underlying malignancy in patients presenting with acute appendicitis

Multivariable	Odds ratio	95% CI	P value
Age	1.02	0.99–1.06	.15
Charlson comorbidity index	1.12	0.87–1.41	.35
Duration of symptoms (every 5 h increase)	1.06	0.99–1.13	.06
CT presence of appendicolith	0.49	0.19–1.08	.10
CT contrast nonfilling of appendix	2.82	0.80–7.66	.06
CT perforated appendix	0.35	0.02–1.80	.32
CT phlegmon	3.48	0.51–13.91	.12
CT diameter, mm	1.06	1.01–1.12	.01

AIC = 343.9
AIC, Akaike information criterion; *CI,* confidence interval.

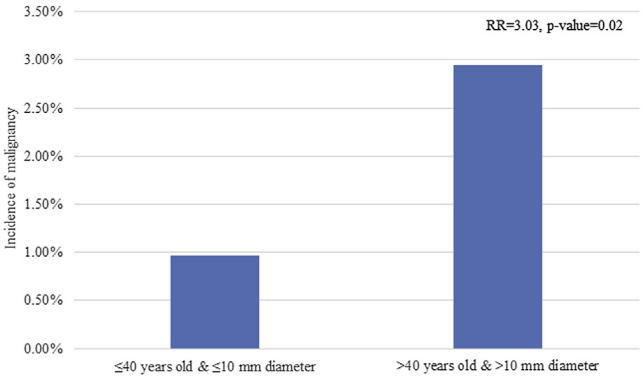

Fig 1. Incidence of malignancy and risk ratio for patients >40 years old with an appendiceal diameter >10 mm. *RR*, relative risk.

as an independent predictor of appendiceal cancer in patients presenting with appendicitis. We believe that the diameter is larger in patients with underlying malignancy due to the chronic and gradual obstruction of the appendiceal lumen from the tumor mass, although further research is necessary to prove this hypothesis.

Appendiceal cancer is rare; however, its true incidence may be underestimated owing to the limited preoperative diagnostic abilities. As a result, some patients may have a missed diagnosis when treated nonoperatively. The rate of appendiceal cancer is reported to be increasing within the past decade.[20] Previous studies have failed to identify radiologic factors that can predict the presence of an underlying malignancy in patients presenting with acute appendicitis.[21,22] Over the past years, there has been growing interest in managing both complicated and uncomplicated appendicitis nonoperatively.[16] Nonoperative management of acute appendicitis without an interval appendectomy would lead to worse outcomes in patients with underlying malignancy.[23,24] The literature that identifies interval appendectomy as a risk factor for an appendiceal tumor may be simply reflecting the shift in the management of acute appendicitis with higher rates of nonoperative management.[12,17,18,22] Although several authors have argued against the routine performance of interval appendectomies in patients with complicated appendicitis that experience complete resolution of symptoms, due to the high rates of complications and low risk of recurrence, our data suggests that we would be overlooking the risk of an underlying malignancy when opting out of interval appendectomies, especially in patients older than 40 years with an appendiceal lumen wider than 10 mm on CT.[5,12,25–29]

Previous studies have identified various factors associated with malignancy, including age.[12,17,18] Some suggested that underlying malignancies should also be suspected in all patients who present with an inflammatory mass or an abscess.[11,30] In other reports, female sex, appendiceal perforation, underlying Crohn's disease, longer duration of symptoms, and lower admission hemoglobin have been suggested as risk factors.[31–33] Similar to our study, Pickhardt et al investigated 65 patients presenting with appendicitis who had an underlying neoplasm.[34] The authors described that patients with appendiceal malignancy tend to have a diameter larger than 15 mm. Using that cutoff, they found that the sensitivity of CT scan for the diagnosis of underlying malignancy was 86%.[34] Our study is different, because we compared patients with underlying malignancy to a control group of patients with acute appendicitis but without underlying malignancy, and we identified CT diameter larger than 10 mm as the an independent predictor for malignancy.

Another area of debate among surgeons is colonoscopy after nonoperative management of acute appendicitis. Since most malignancies present in patients older than 40, patients managed nonoperatively should be offered a screening postoperative colonoscopy.[5,35,36] Furthermore, synchronous colonic cancer is reported to occur in up to 3% of patients with appendiceal tumor.[37,38] Considering all the above, some authors also suggest the use of colonoscopy in all patients older than 40 presenting with acute appendicitis irrespective of surgical or nonoperative management.[39,40] Based on the results of our study, we have identified a specific subgroup of patients older than 40 years with an appendiceal diameter larger than 10 mm who would particularly benefit from colonoscopy and an interval appendectomy, when managed nonoperatively.

Our study has a few limitations. First, our patient population size is small, especially those with malignancy. However, the reported incidence of appendiceal malignancy in our patient population was in accordance with the literature.[10,12] Second, we did not find age as a continuous variable to be associated independently with underlying malignancy. Failure to achieve significance in the multivariable regression and due to our small population size, we decided not to use specific age cutoffs in our multivariable regression models and to use historic data for the age from the literature. Third, mucoceles were not included in the analysis; although not malignant per se, failure to remove can have devastating consequences to the patient. However, this study also has the strength of being a prospectively collected database including patients from 28 rural and urban centers across the United States with geographic representation of all areas that can help in the generalizability of our results. The most important addition to the existing literature includes the identification of a specific subset of older patients with enlarged appendiceal diameter as one at a particularly high risk for malignancy and thus warranting a more aggressive follow-up and surgical approach.

In conclusion, the combination of age >40 years and an appendiceal diameter >10 mm is associated with a greater than 3-fold increased risk of malignancy in patients presenting with appendicitis. Such findings are important for patient counseling and perhaps suggest that those patients, when managed nonoperatively, should undergo screening colonoscopy and an interval appendectomy.

Conflict of interest/Disclosure

The authors declare that they have no conflicts of interest or disclosures.

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References

1. Mason RJ. Surgery for appendicitis: is it necessary? *Surg Infect (Larchmt)*. 2008;9:481–488.
2. Lietzen E, Gronroos JM, Mecklin JP, et al. Appendiceal neoplasm risk associated with complicated acute appendicitis-a population based study. *Int J Colorectal Dis*. 2019;34:39–46.
3. Keckler SJ, Tsao K, Sharp SW, Ostlie DJ, Holcomb 3rd GW, St Peter SD. Resource utilization and outcomes from percutaneous drainage and interval appendectomy for perforated appendicitis with abscess. *J Pediatr Surg*. 2008;43:977–980.
4. Sippola S, Gronroos J, Tuominen R, et al. Economic evaluation of antibiotic therapy versus appendicectomy for the treatment of uncomplicated acute appendicitis from the APPAC randomized clinical trial. *Br J Surg*. 2017;104:1355–1361.
5. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg*. 2007;246:741–748.
6. Simillis C, Symeonides P, Shorthouse AJ, Tekkis PP. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). *Surgery*. 2010;147:818–829.
7. Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: The APPAC randomized clinical trial. *JAMA*. 2015;313:2340–2348.
8. Vons C, Barry C, Maitre S, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet*. 2011;377:1573–1579.
9. Limaiem F, Arfa N, Marsaoui L, Bouraoui S, Lahmar A, Mzabi S. Unexpected histopathological findings in appendectomy specimens: A retrospective study of 1627 cases. *Indian J Surg*. 2015;77(Suppl 3):1285–1290.
10. Guraya SY. Do we still need to perform routine histological examination of appendectomy specimens? *J Clin Diagn Res*. 2015;9:PL01.
11. Teixeira Jr FJR, Couto Netto SDD, Akaishi EH, Utiyama EM, Menegozzo CAM, Rocha MC. Acute appendicitis, inflammatory appendiceal mass and the risk of a hidden malignant tumor: a systematic review of the literature. *World J Emerg Surg*. 2017;12:12.
12. Furman MJ, Cahan M, Cohen P, Lambert LA. Increased risk of mucinous neoplasm of the appendix in adults undergoing interval appendectomy. *JAMA Surg*. 2013;148:703–706.
13. Hatch QM, Gilbert EW. Appendiceal neoplasms. *Clin Colon Rectal Surg*. 2018;31:278–287.
14. Kelly KJ. Management of appendix cancer. *Clin Colon Rectal Surg*. 2015;28:247–255.
15. Kalpande S, Pandya J, Sharma T. Adenocarcinoma mimicking appendicular lump: a diagnostic dilemma-a case report. *World J Surg Oncol*. 2016;14:283.
16. Khan K, Patil S, Roomi S, Shiwani MH. Appendicular Neuroendocrine Neoplasm is Associated with Acute Appendicitis - Don't Miss the Boat. *Chirurgia (Bucur)*. 2019;114:461–466.
17. Carpenter SG, Chapital AB, Merritt MV, Johnson DJ. Increased risk of neoplasm in appendicitis treated with interval appendectomy: single-institution experience and literature review. *Am Surg*. 2012;78:339–343.
18. Wright GP, Mater ME, Carroll JT, Choy JS, Chung MH. Is there truly an oncologic indication for interval appendectomy? *Am J Surg*. 2015;209:442–446.
19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377–381.
20. Siddharthan RV, Byrne RM, Dewey E, Martindale RG, Gilbert EW, Tsikitis VL. Appendiceal cancer masked as inflammatory appendicitis in the elderly, not an uncommon presentation (Surveillance Epidemiology and End Results (SEER)-Medicare Analysis). *J Surg Oncol*. 2019;120:736–739.
21. Kunduz E, Bektasoglu HK, Unver N, Aydogan C, Timocin G, Destek S. Analysis of appendiceal neoplasms on 3544 appendectomy specimens for acute appendicitis: Retrospective cohort study of a single institution. *Med Sci Monit*. 2018;24:4421–4426.
22. Schwartz JA, Forleiter C, Lee D, Kim GJ. Occult appendiceal neoplasms in acute and chronic appendicitis: A single-institution experience of 1793 appendectomies. *Am Surg*. 2017;83:1381–1385.
23. Loftus TJ, Raymond SL, Sarosi Jr GA, et al. Predicting appendiceal tumors among patients with appendicitis. *J Trauma Acute Care Surg*. 2017;82:771–775.
24. Seawell J, Sciarretta JD, Pahlkotter M, Muertos K, Onayemi A, Davis JM. The understated malignancy potential of nonoperative acute appendicitis. *Am Surg*. 2019;85:712–716.
25. Bagi P, Dueholm S. Nonoperative management of the ultrasonically evaluated appendiceal mass. *Surgery*. 1987;101:602–605.
26. Hoffmann J, Lindhard A, Jensen HE. Appendix mass: conservative management without interval appendectomy. *Am J Surg*. 1984;148:379–382.
27. Nitecki S, Assalia A, Schein M. Contemporary management of the appendiceal mass. *Br J Surg*. 1993;80:18–20.
28. Tekin A, Kurtoglu HC, Can I, Oztan S. Routine interval appendectomy is unnecessary after conservative treatment of appendiceal mass. *Colorectal Dis*. 2008;10:465–468.
29. Talan DA. Cancer of the appendix and nonoperative treatment of appendicitis shared decision making. *J Surg Oncol*. 2019;120:1060–1061.
30. Mallinen J, Rautio T, Gronroos J, et al. Risk of appendiceal neoplasm in periappendicular abscess in patients treated with interval appendectomy vs follow-up with magnetic resonance imaging: 1-year outcomes of the Peri-Appendicitis Acuta randomized clinical trial. *JAMA Surg*. 2019;154:200–207.
31. Sadot E, Keidar A, Shapiro R, Wasserberg N. Laparoscopic accuracy in prediction of appendiceal pathology: oncologic and inflammatory aspects. *Am J Surg*. 2013;206:805–809.
32. West NE, Wise PE, Herline AJ, Muldoon RL, Chopp WV, Schwartz DA. Carcinoid tumors are 15 times more common in patients with Crohn's disease. *Inflamm Bowel Dis*. 2007;13:1129–1234.
33. Todd RD, Sarosi GA, Nwariaku F, Anthony T. Incidence and predictors of appendiceal tumors in elderly males presenting with signs and symptoms of acute appendicitis. *Am J Surg*. 2004;188:500–504.
34. Pickhardt PJ, Levy AD, Rohrmann Jr CA, Kende AI. Primary neoplasms of the appendix manifesting as acute appendicitis: CT findings with pathologic comparison. *Radiology*. 2002;224:775–781.
35. Teixeira PG, Demetriades D. Appendicitis: changing perspectives. *Adv Surg*. 2013;47:119–140.
36. Sylthe Pedersen E, Stornes T, Rekstad LC, Martinsen TC. Is there a role for routine colonoscopy in the follow-up after acute appendicitis? *Scand J Gastroenterol*. 2018;53:1008–1012.
37. Cerame MA. A 25-year review of adenocarcinoma of the appendix. A frequently perforating carcinoma. *Dis Colon Rectum*. 1988;31:145–150.
38. Whitfield CG, Amin SN, Garner JP. Surgical management of primary appendiceal malignancy. *Colorectal Dis*. 2012;14:1507–1511.
39. Lai HW, Loong CC, Tai LC, Wu CW, Lui WY. Incidence and odds ratio of appendicitis as first manifestation of colon cancer: a retrospective analysis of 1873 patients. *J Gastroenterol Hepatol*. 2006;21:1693–1696.
40. Narayanswami J, Smith DA, Enzerra M, Rahnemai-Azar AA, Kikano E, Ramaiya NH. "-Omas" presenting as "-itis": acute inflammatory presentations of common gastrointestinal neoplasms. *Emerg Radiol*. 2019;26:433–448.