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Incidence of appendiceal neoplasms in appendectomy patients

Ricardo E. Núñez-Rocha^{1,2}, Felipe Girón^{1,2*}, Lina Rodríguez², Daniela Camargo-Gómez², Carolina Restrepo-Bonilla³, Rocío Del Pilar López Panqueva^{1,2}, Manuel Cadena^{1,2}, Ricardo Nassar^{1,2}, Gabriel E. Herrera-Almarío^{1,2} and Juan David Hernández-Restrepo^{1,2}

Abstract

Background Non-operative management has been suggested as a therapy for uncomplicated appendicitis. Notwithstanding, the risk of missing an appendiceal tumor must be considered, being the surgical piece crucial to rule out neoplasms. Therefore, we aim to determine the incidence of appendiceal neoplasms in patients with acute appendicitis, tumor types and the importance of the anatomopathological study of the surgical piece.

Study design Retrospective study in which we described patients who underwent emergent appendectomy with histopathological findings of appendiceal neoplasms from January 2012 to September 2018. Descriptive analysis included demographic variables, diagnostic methods, and surgical techniques.

Results 2993 patients diagnosed with acute appendicitis who underwent an emergency appendectomy. 64 neoplasms of the appendix were found with an incidence of 2,14%. 67.2% were women, the mean age was 46,4 years (± 19.5). The most frequent appendiceal neoplasms were neuroendocrine tumors (42,2%), followed by appendiceal mucinous neoplasms (35,9%), sessile serrated adenomas (18,8%), and adenocarcinomas (3,1%). In 89,1% of the cases, acute appendicitis was determined by imaging, and 14% of cases were suspected intraoperatively. Appendectomy was performed in 78,1% without additional procedures.

Conclusions Appendiceal tumors are rare and must be ruled out in patients with suspected acute appendicitis. The incidence of incidental neoplasms is higher in this study than in the previously reported series. This information must be included in decision-making when considering treatment options for acute appendicitis.

Keywords Appendiceal neoplasms, Appendectomy, Appendicitis, Neuroendocrine tumor, Appendiceal mucinous neoplasms, Sessile serrated adenomas

*Correspondence:

Felipe Girón

felipegiron15@gmail.com

¹Hospital Universitario Fundación Santa Fe de Bogotá, Calle 119 No. 7-14, Bogotá, DC, Colombia

²School of Medicine, Universidad de los Andes, Cundinamarca, Colombia

³Hospital Universitario San Ignacio, Bogotá, Colombia



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Introduction

Appendectomy has been widely accepted as first-line management for acute appendicitis in the absence of abscess formation or peritonitis [1–4]. However, recent studies randomized clinical trials have shown that in the short term, medical management with antibiotics is a safe alternative treatment option for cases of uncomplicated acute appendicitis [1, 5–7]. Nevertheless, the possibility of appendiceal neoplasms incidental diagnosis must be taken into account [4, 5, 8–10].

Tumors of the appendix are unusual entities, mainly diagnosed incidentally in the anatomopathological study of appendectomy pieces, and rarely suspected before or during a surgical procedure [5, 6, 8, 11–15]. Therefore, the study of the appendiceal sample is crucial both to diagnose the presence of neoplasms, as well as to determine their histological subtype [4, 10, 12, 15]. This information is useful for both establishing prognosis and outcomes, as well as for determining requirements for additional treatment [4, 10, 12, 15], accounting for tumor size, location, level of infiltration, and the resection margin status [12, 15]. The histological characteristics of appendiceal neoplasms are strong predictors of patients' survival and must be included in the staging [5, 10, 16, 17]. Failure to detect appendiceal cancer delays diagnosis [6] which could lead to either an increase in the incidence of colon cancer [3, 18, 19] (mainly in patients over 40 years [5, 19, 20]) or to neoplastic disease due to perforation or rupture of a mucinous tumor (*Pseudomyxoma peritoneum*) [4, 21]. Despite tumors of the appendix being an infrequent diagnosis, the finding of these cases indicates the importance and need for the anatomopathological study of all the segments extracted during surgery [22].

These neoplasms correspond to less than 0,5% of all tumors of the gastrointestinal tract [23, 24], and are found in approximately 1% of the specimens from appendectomies [23–25]. Its incidence is low but has increased as reported by different international series [9–11]. Worldwide, it varies between 0,2% and 2,5% [5, 11, 25] (between 0,07% and 0,8% in Chile [11], 0,78% in Turkey [15], 0,9% in Spain [18], between 0,9% and 1,7% in the United States [6], 1,24% in Finland [5], 2,3% in Japan [9], and <3% in Tunisia [16]). In Colombia, the incidence of tumors of the appendix is unknown. Therefore, we aimed to determine the incidence of appendiceal neoplasms in a cohort of patients with acute appendicitis, the histopathological types, the demographic factors of the patients, and to evaluate the importance of the routine anatomopathological study of the extracted surgical specimen.

Methodology

After Institutional Review Board's approval, a retrospective study composed of patients with diagnosed acute appendicitis who underwent emergency appendectomies at a tertiary referral hospital was conducted. Over 7,5 years between January 2012 and September 2018, 2993 clinical records were reviewed. Patients over 18 years old, and those who underwent appendectomy for acute appendicitis, were included. Patients with previously known diagnoses of an appendiceal tumor, those undergoing right hemicolectomy (RHC), and patients who underwent appendectomy for a different indication than acute appendicitis, were excluded. To clarify, individuals with an Alvarado rating ranging from 1 to 4 were discharged. Alvarado scoring ranging from 5 to 6, were sent to ultrasound examination and abdominal CT scans if needed. Individuals with an Alvarado rating of 7 to 10 were directly diagnosed with acute appendicitis and underwent appendectomy. Demographic variables (such as the age of presentation and gender), as well as diagnostic methods, surgical techniques (including the extension of the resection), and the histological type described in the pathology report, were analyzed using descriptive statistics. The follow-up on these patients was continued until the first postoperative control.

Results

Of the 2993 samples of appendectomies analyzed, 64 neoplasms of the appendix were found (as shown in Table 1), representing an incidence of 2,14%. The demographic characteristics of the subjects are summarized in Table 2. 67,2% were women, and the mean age for men was 46,4 years (± 19.5). In 89,1% of the cases, the diagnosis of acute appendicitis was determined through imaging, with a suspicion of an appendiceal tumor in 12,5% of them. In 78,1% of the cases, appendectomy was performed without requiring additional interventions. 98,4%

Table 1 Distribution of appendiceal neoplasms and degrees of differentiation (n = 64)

Variable	n(%)
Benign	23(35.9)
Mucinous neoplasm of appendix	23 (35.9)
Low grade of differentiation	20 (86.9)
High grade of differentiation	1 (4.3)
No degree of differentiation	2 (8.7)
Premalignant lesions	12 (18.8)
Sessile serrated adenoma	
High-grade dysplasia	1 (8.3)
No high-grade dysplasia	11 (91.6)
Malignant	29 (45.3)
Neuroendocrine tumor	27 (42.2)
Well-differentiated (G1)	25 (92.6)
Moderately differentiated (G2)	2 (7.4)
Adenocarcinoma	2 (3.1)
Well-differentiated	1 (0.5)
Poorly differentiated	1 (0.5)

Table 2 Demographic and clinical characteristics of the patients (n = 64)

Variable	n(%)
Female	43 (67.2)
Male	21 (32.8)
Age (average, SD)	46.4 (19.4)
Diagnosis of acute appendicitis	
Clinical (not imaging)	7 (10.9)
Imaging	57 (89.1)
Abdomen Ultrasound	9 (15.78)
Computed tomography of the abdomen	45 (78.9)
Magnetic resonance imaging of the abdomen	1(1.7)
Computed Tomography Urography	1 (1.7)
Positron emission tomography	1 (1.7)
Suspicion of appendiceal neoplasm	
Clinical	0 (0)
Imaging	8 (12.5)
Intraoperative	9 (14.1)
No suspicion of neoplasia	47 (73.4)
Type of surgical procedure	
Open appendectomy	1 (1.6)
Laparoscopic appendectomy	63(98.4)
Extension of the resection	
Appendectomy without other procedure	50 (78.1)
Appendectomy associated with another procedure	14 (21.9)

of the procedures performed were through a laparoscopic approach and there was no need for conversion. The re-intervention and complications rates were 0%. Of the cases

that were diagnosed with appendiceal neoplasms, 14% were suspected intraoperatively.

The most frequent appendiceal neoplasm found was the neuroendocrine tumor (NET) reported in 27 patients (42,2%), of which 62,9% of the cases were women (Fig. 1), with an average age of presentation of 32.7 (±12.3) years. In none of these patients, a tumor was suspected before the surgical procedure, and only in 2 cases (7,4%), there was an intraoperative suspicion of a tumor. According to the classification of the American Joint Committee of Cancer (AJCC) [27], well-differentiated tumors (G1) were found in 92,6% of the cases, while the remaining 7,4% were moderately differentiated (G2). 58.6% were tumors smaller than 1 cm, and only 2 specimens (6.9%) exceeded 2 cm in size (as shown in Table 3). In 89,7% of the cases, tumor-free resection margins were reported regarding malignant tumors.

The second most frequent tumor was mucinous neoplasm of the appendix (AMN) reported in 23 samples (35,9%), of which 69,6% were women (Fig. 1). The average overall age of presentation was 62.1 (±17) years. Suspicion of neoplasm in the computed abdominal tomography was made in 7 cases (30,4%), mucocele of the appendix was suspected in 6 patients, and the presence of a mass in the cecum was suspected in 1 case. An appendiceal tumor was suspected during the surgical procedure in 7 patients (30,4%). 86,9% were AMNs with a low degree of differentiation. In 7 of the samples, mucin

Distribution of appendiceal neoplasms by sex

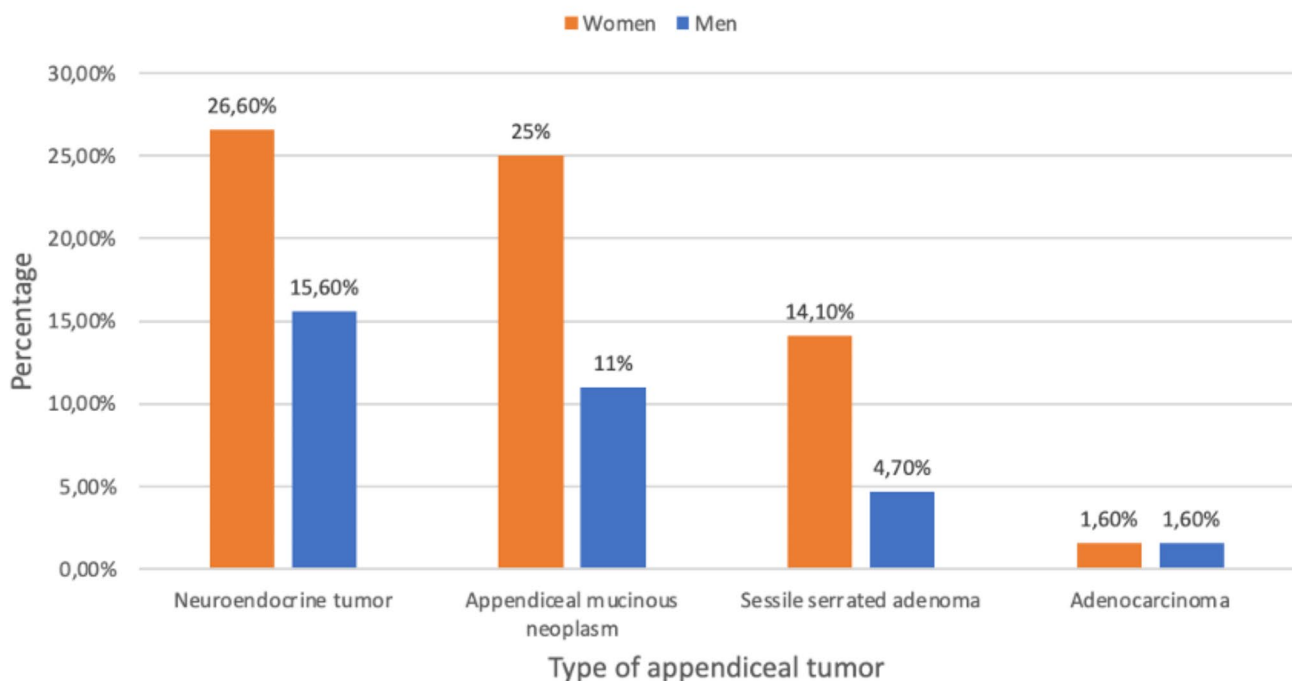


Fig. 1 Distribution of appendiceal neoplasms by sex

Table 3 Histopathological characteristics of the malignant tumors of the appendix (n = 29)

Variable	Characteristic	n(%)
Size (centimeters)	< 1	17 (58.6)
	1–2	8 (27.6)
	> 2	2 (6.9)
	No data	2 (6.9)
Parietal commitment	Mucous membrane	0 (0)
	Submucosa	3 (10.3)
	Muscular	6 (20.7)
	Subserosa	9 (31.0)
	Serosa	3 (10.3)
	NA	8 (27.6)
Commitment of the mesoappendix	Yes	7 (24.1)
	No	2 (6.9)
	NA	20 (69)
Lymphovascular invasion	Yes	1 (3.4)
	No	23 (79.3)
	NA	5 (17.2)
Resection margins	Committed	1 (3.4)
	Free	26 (89.7)
	NA	2 (6.9)

Table 4 Histopathological characteristics of mucinous neoplasms of the appendix (AMN) (n = 23)

Variable	Characteristic	n(%)
Mucin content	Yes	7 (30.4)
	No	4 (17.4)
	No data	12 (52.2)
Perforated appendicitis	Yes	7 (30.4)
	No	4 (17.4)
	No data	12 (52.2)
Section edges	Committed	2 (8.7)
	Free	19 (82.6)
	No data	2 (8.7)

content was found, and also 7 presented perforations (as shown in Table 4). In 82,6% of the cases, tumor-free resection margins were reported.

The sessile serrated adenoma (SSA), considered a pre-malignant lesion, was the third most frequent appendiceal tumor in this series, reported in 12 cases (18,8%). The mean age was 46 (± 15.6) years. Of the 12 SSAs, 9 cases (75%) were women (Fig. 1), and the average age

Table 5 Conduct suggested by the surgery group after the histopathological report (n = 64)

Variable	n(%)
Discharge after surgery	11 (17.2)
SSA without high grade dysplasia	6 (54.5)
Well-differentiated NET	4 (36.4)
AMN low grade	1 (9.1)
Follow-up by surgery	16 (25)
AMN low grade	7 (43.7)
NET well-differentiated	6 (37.5)
SSA without high grade dysplasia	1 (6.3)
SSA dysplasia with high grade	1 (6.3)
AMN high grade	1 (6.3)
HCD indication	10 (15.6)
NET well-differentiated	5 (50)
AMN of low grade	2 (20)
Adenocarcinoma well and poorly differentiated	2 (20)
Moderately differentiated NET	1 (10)
HIPEC indication	3 (4.7)
AMN of low grade	3 (100)
Monitoring by endocrinology	5 (7.8)
Well-differentiated NET	5 (100)
Follow-up by oncology	2 (3.1)
NET well-differentiated	1 (50)
AMN of low grade	1 (50)
Patients who did not return to control	17 (26.5)
AMN of low grade	8 (47.1)
NET well-differentiated	5 (29.4)
SSA dysplasia with high grade	4 (23.5)

SSA=sessile serrated adenoma, NET=neuroendocrine tumor, AMN=appendiceal mucinous neoplasm, RHC=right hemicolectomy, HIPEC=hyperthermic intraperitoneal chemotherapy

of presentation was 44.8 years (± 15.8). In none of the patients, a tumor was suspected before or during the surgical procedure. 91,6% were SSAs without high-grade dysplasia. In 58,3% of the cases, tumor-free resection margins were reported.

The lowest frequency neoplasm found in the series was adenocarcinoma present in only 2 specimens (3,1%). The ratio of women to men was 1:1, with an average age of presentation of 54 years. One of the cases was reported as a well-differentiated neoplasm, and the other was poorly differentiated. Neither of the tumors was suspected before the surgical procedure. In one case, non-tumor-free resection margins were reported. Table 5 summarizes the surgical approach, according to the histopathological report of the appendectomy specimen.

Discussion

Our population shows that appendiceal tumors incidentally found in emergent appendectomies are significant, with an incidence of 2,14%, similar to those reported

worldwide, between 0,2% and 2,5% [5, 11, 25]. From 2012 to 2018, an increase in the number of new cases of appendiceal neoplasms was evidenced (Fig. 2). It is a fact that appendiceal neoplasms are rare and non-frequent entities found incidentally in surgical specimens of appendectomies [5, 18], and the importance of studying these surgical specimens for detecting appendiceal tumors, and establishing histologic subtypes, prognosis, and further treatment becomes a priority [4, 10, 12, 15].

Currently, the treatment of acute appendicitis is controversial since most recent literature has shown that the conservative management of these patients with the use of antibiotics in selected cases, is a viable and promising non-invasive option [1, 5, 6]. Notwithstanding, the increasing incidence of appendiceal tumors has shown the importance and need to carry out an anatomopathological study of the resected sample from surgery [22].

Different studies evaluating the non-operative management of uncomplicated acute appendicitis, such as the APPAC [1] and the CODA trial [26] have proven safety and non-inferiority of such treatment and have confirmed the possibility of a non-surgical management option for acute appendicitis. Nevertheless, the percentage of appendiceal neoplasms in the group of patients who did not undergo appendectomy is unclear. Moreover, advanced stages of a possible appendiceal neoplasm could be more frequently presented due to not intervening surgically in these patients leading to increased morbidity and mortality in this specific group of patients [3, 8, 18, 19]. Nevertheless, it is still unclear if this difference is statistically significant.

M. Enblad et al. [3] showed that patients who underwent non-surgical management of acute appendicitis had an increase in the incidence of neoplasms of both the appendix and the right-sided colon in all age groups compared to the general population. In the case of right colon

cancer, the increased incidence is lasting 5 years after appendicitis, except for the population under 20 years [3]. Furthermore, in cases in which signs and symptoms of appendicitis are still present even though a patient has been conservatively treated, the surgeon must raise an alert to rule out an underlying neoplasm that may be causing the symptoms, not detected previously by imaging because of diagnostic methods limitations [3, 27].

Appendicular inflammatory masses can be presented in 2 to 6% of cases, with a higher risk of appendiceal neoplasms that may vary between 5,2 and 12% [28, 29]. Moreover, these cases can be considered controversial since there is the possibility of non-surgical management [4]. Therefore, the surgical team must highly consider performing interval appendectomy [20]. Meanwhile, in this study, malignant tumors were the most common, followed by benign and premalignant lesions respectively. Most surgical procedures were performed by laparoscopy (98,4%). In the APPAC study [1], open appendectomies were more frequent, which could eventually have increased morbidity in the group of patients who underwent surgery.

Among the limitations of this study are the relatively small number of patients, its retrospective nature, and the lack of longer follow-up. Further prospective studies are needed to evaluate the impact of non-surgical management of appendiceal inflammatory processes in terms of morbidity and mortality of appendicular neoplasms.

Conclusion

Tumors of the cecal appendix must be considered as differential diagnoses to be ruled out in patients with suspected acute appendicitis. Unfortunately, they do not present specific signs or symptoms and are not suspected or evidenced before, or during surgical intervention, so their diagnosis remains incidental after the

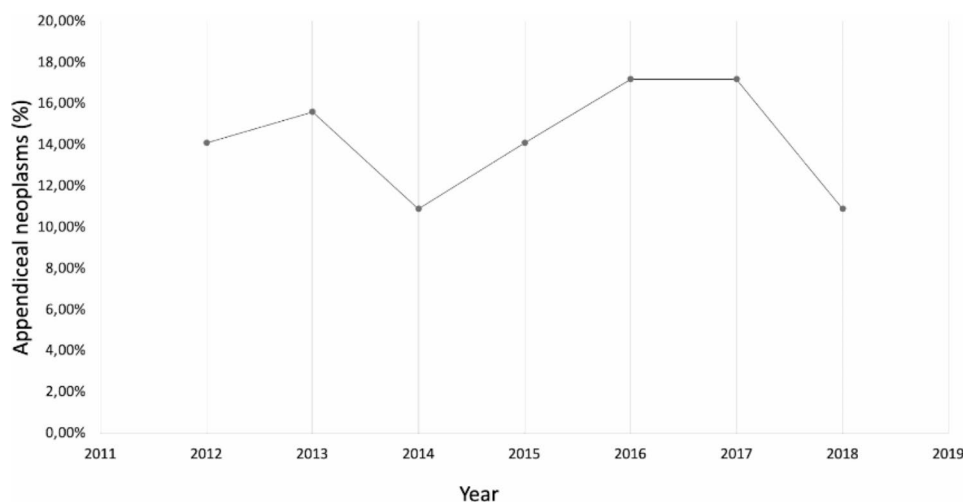


Fig. 2 Distribution of appendiceal neoplasms per year

anatomopathological analysis of the surgical samples obtained from appendectomies. Appendiceal tumors are infrequent. However, the increasing incidence reported in recent international series, including the current one, enhances the need for the surgeon to discard this pathology as a cause of acute appendicitis. The possibility of incidentally diagnosing appendiceal neoplasms should be considered when making decisions about the appropriate management for acute appendicitis, whether surgical or not, considering that the histopathological analysis of the surgical specimen should be used for diagnostic purposes and to determine the requirement for additional treatment.

Abbreviations

RHC	Right hemicolectomy
NET	Neuroendocrine tumor
AJCC	American Joint Committee of Cancer
AMN	Mucinous neoplasm of the appendix
SSA	Sessile serrated adenoma
APPAC	The Appendicitis Acuta project
HIPEC	Hyperthermic intraperitoneal chemotherapy

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12893-023-02183-4>.

Supplementary Material 1

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To our patients.

Author's contributions

Felipe Girón: verified the data and substantially contributed to the conception and design of the study; acquisition, analysis, and interpretation of the data, drafting of the manuscript and revising the final version for publication. Ricardo Núñez: verified the data and substantially contributed to the conception and design of the study; acquisition, analysis, and interpretation of the data, drafting of the manuscript and revising the final version for publication. Lina Rodríguez: substantially contributed to the acquisition, analysis, and interpretation of the data, and revision of the manuscript. Daniela Camargo Gómez: verified the data and substantially contributed to the conception and design of the study; acquisition, analysis, and interpretation of the data, drafting of the manuscript and revising the final version for publication. Carolina Restrepo-Bonilla: substantially contributed to the acquisition, analysis, and interpretation of the data, and revision of the manuscript. Rocío López: substantially contributed to the acquisition, analysis, and interpretation of the data, and revision of the manuscript. Manuel Cadena: substantially contributed to the acquisition, analysis, and interpretation of the data, and revision of the manuscript. Ricardo Nassar: substantially contributed to the acquisition, analysis, and interpretation of the data, and revision of the manuscript. Gabriel E. Herrera-Almarino: verified the data and substantially contributed to the conception and design of the study; acquisition, analysis, and interpretation of the data, and drafting of the manuscript. Juan David Hernández-Restrepo: substantially contributed to the acquisition, analysis, and interpretation of the data, revision of the manuscript and giving the final approval for the final version ahead of publication as Chief and principal researcher.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Institutional Review Board's approval from University Hospital Santa Fe Foundation from Bogota was obtained for this study. Informed consent was obtained from all subjects and/or their legal guardian(s) for this study. All procedures performed in this study complied with the specified in the Helsinki Declaration of 1964 and succeeding amendments.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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