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Appendiceal diverticulitis and acute appendicitis: Differences and similarities

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ABSTRACT

Introduction: Acute appendiceal diverticulitis is an unusual cause of acute abdomen, considered clinically indistinguishable from acute appendicitis.

Material and methods: In a historic cohort study with 27 cases of appendiceal diverticulitis and 54 cases of acute appendicitis, we compared clinical characteristics, diagnostic tests and pathology findings of the two processes.

Results: Mean age at presentation was lower in acute appendicitis (37.24 ± 19.98 *vs.* 54.81 ± 17.55 years, p < 0.001), with significant differences between men (33.33 ± 15.89 *vs.* 57 ± 18.02 years, p < 0.001) but not between women (41.76 ± 24.87 *vs.* 50.44 ± 16.69 years, p = 0.34). In the diverticulitis group, 48.15 % had leukocytosis *vs.* 81.48 % in the appendicitis group (p = 0.02); there was no difference in leukocyte count (13770.37 ± 4382.55 *vs.* 14279.63 ± 4268.59, p = 0.61). Patients with appendiceal diverticulitis had a higher incidence of appendiceal mucocele (p = 0.01) and a lower proportion of appendiceal gangrene (p = 0.03). There were no differences in appendiceal perforation or ulceration. Symptom duration before emergency department attendance (71.61 ± 85.25 hours *vs.* 36.84 ± 33.59 hours; Z = -3.1 p = 0.002), duration of surgery (85 ± 40 minutes *vs.* 60 ± 21 minutes, Z = -3.2, p = 0.001) and the presence of appendicular plastron was higher in patients with diverticulitis *vs.* appendicitis (8 *vs.* 5 patients [p = 0.01, Odds ratio 2.2]).

Conclusions: Appendiceal diverticulitis presents a series of clinical, epidemiological and pathological differences with respect to acute appendicitis. The former shows a more indolent course with delayed diagnosis.

Key words: Acute appendiceal diverticulitis. Acute appendicitis. Acute abdomen. Mucinous cystadenoma. Appendiceal mucocele. Colorectal cancer.

INTRODUCTION

Acute appendiceal diverticulitis (AAD) is a rare cause of acute abdomen, with an incidence of 0.004 % to 2.1 % in patients undergoing surgery for acute appendicitis, which is why it has been considered a variant of the latter (1,2).

The two entities have traditionally been considered clinically indistinguishable, with an exclusively pathological differential diagnosis upon examination of the surgical specimen. However, some recent studies suggest that AAD, with presentation at a greater age, a more insidious course, late diagnosis and a higher rate of complications such as appendiceal perforation, has clinical characteristics which differ from those of acute appendicitis (3,4). Owing to its higher rate of complications, some authors have attempted to establish certain measurable characteristics using imaging techniques to facilitate the early diagnosis of AAD (5-7).

Recently, a possible association has been described between AAD and various intestinal neoformative processes such as mucinous cystadenoma, intestinal carcinoid tumors and colon adenocarcinoma (8-10).

The objective of this study was to compare AAD with acute appendicitis, understanding acute appendicitis as the gold standard for acute abdominal pain in right ileac fossa. We analyzed specific clinical, radiological and pathological variables of AAD and acute appendicitis that could help make a correct preoperative diagnosis in the emergency department (ED), thus reducing the risk of complications in clinical course.

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MATERIAL AND METHODS

We performed a historical cohort study of patients with suspected acute appendicitis undergoing surgery at our hospital between January 2000 and January 2012. Twenty seven cases of acute abdomen secondary to AAD were selected. These patients were considered as cases. During this period, 4,736 patients with initially suspected acute appendicitis were treated. To carry out a comparative study, 54 of these patients were randomly selected as controls using randomization software (two controls per case). Since the objective of the study was to assess possible differences between groups in variables such as age, sex, etc. these variables were not matched between cases and controls and unconditioned randomization was used. All patients included in this study gave informed consent. The correct assignment of patients to the group of cases was confirmed by pathologic examination of the surgical specimen resected.

The medical records of the patients included in the study were reviewed and we recorded the following data: Age and age group, sex, smoking status, symptoms, diagnostic procedure, peripheral blood leukocytosis, site of the diverticula, type of diverticula, presence of appendicular plastron, presence of perforation, gangrene, ulceration or mucocele, duration of symptoms before the indication for surgery, duration of surgery and postoperative hospital stay in both groups. We also analyzed the possible relationship of AAD with mucinous cystadenomas, carcinoid tumors and colon cancer.

Statistical analysis

Analysis of the distribution of quantitative variables (whether they followed a normal distribution or not) was assessed using Kolmogoroz-Smirnov test. Student's t test or Mann Whitney U test were used, as appropriate.

In the analysis of qualitative variables, the statistical significance of these variables was assessed using Chi square test (χ^2) or Fisher's exact test for small samples, as appropriate. Odds ratios (OR) were calculated to assess the magnitude of the non- association between these variables.

Differences with a p value < 0.05 were considered significant. All statistical calculations were performed using SPSS version 15.0.

RESULTS

The study included 27 cases of AAD and 54 controls with acute appendicitis. AAD was present in 0.57 % of all patients undergoing surgery for acute abdomen, with initially suspected acute appendicitis.

Table I shows the demographic characteristics and smoking status of patients with AAD *versus* acute appendicitis. The results showed significantly earlier presentation of acute appendicitis than AAD (37.24 ± 19.98 years *vs.* 54.81 ± 17.55 years; p < 0.001). This difference was particularly evident in patients younger than 40 years, with only 5 cases of AAD compared to 40 cases of appendicitis. For the age groups above 40 years, no differences were observed between cases and controls.

No gender differences in presentation were observed; however, on analysis of age of presentation according to gender, statistically significant differences were found between men (33.33 ± 15.89 years *vs.* 57 ± 18.02 years, p < 0.001) but not between women (41.76 ± 24.87 *vs.* 50.44 ± 16.69 years, p = 0.34) diagnosed with acute appendicitis *versus* AAD

Table I. Demographic characteristics and smoking status of patients with appendiceal diverticulitis *vs.* acute appendicitis

	Appendiceal diverticulitis (n = 27)	*Acute appendicitis (n = 54)*	*p / Odds ratio*
Age (years)	54.81 ± 17.55	37.24 ± 19.98	< 0.001
Age groups (years)			
< 30	1	23	< 0.001
30-39	4	17	
40-49	7	2	
50-59	4	3	
60-69	5	1	
> 70	6	8	
Gender			
Male	18	33	0.62
Female	9	21	
Age and gender			
Male	57 ± 18.02	33.33 ± 15.89	< 0.001
Female	50.44 ± 16.69	41.76 ± 24.87	0.34
Smoking			
Yes	10	13	0.70
No	15	28	

respectively. Nor did we find significant gender differences on analysis of smoking status (data collected for 66 patients).

No differences in clinical symptoms were found for the two processes (Table II). Abdominal pain alone or associated with other clinical manifestations was the most common symptom in both. In most patients, the preoperative diagnosis made in the ED was of acute appendicitis; none were diagnosed with AAD. A diagnosis other than appendicitis was suspected in only three patients who were subsequently diagnosed with AAD. Specifically, two had concomitant sigmoid diverticulitis and the third patient had septic shock of abdominal origin secondary to perforated appendiceal diverticulitis and secondary peritonitis. The study of symptom duration before ED attendance showed that patients with AAD reported having symptoms for longer periods than those who had acute appendicitis (71.61 ± 85.25 hours *vs.* 36.84 ± 33.59 hours, Z = -3.1, p = 0.002). Similarly, the duration of surgery was significantly higher in patients with AAD compared to those with acute appendicitis (85 ± 40 minutes fronts to 60 ± 21 minutes, Z = -3.2, p = 0.001). The presence of appendicular plastron was noted in 8 cases with AAD *versus* 5 controls with acute appendicitis (p = 0.01, OR 2.2).

Analysis of preoperative laboratory test results showed no significant differences between groups. Leukocytosis in peripheral blood was analyzed using an upper limit of 12,000, above which systemic inflammatory response syndrome (SIRS) was deemed to be present. By this criterion, 48.15 % of cases with AAD had leukocytosis compared with 81.48% of controls (P = 0.02, OR 2.5), but no significant difference was observed in mean leukocyte count between cases and controls (13770.37 ± 4382.55 / mm^3 *vs.* 14279.63 ± 4268.59/mm^3, respectively; p = 0.61). Pathological analysis of cecal appendix samples showed no significant differences in perforation or ulceration (p = 0.14 and 1 respectively) but a significantly greater presence of appendiceal mucocele was observed in the AAD group (3 *vs.* 0, p = 0.01, OR 3.2) and a greater presence of gangrene in the acute appendicitis group (8 *vs.* 0; p = 0.03; OR 1.58).

The mean number of diverticula found at pathologic examination was 1.35, with 22 of 27 surgical specimens (81.5 %) presenting a single diverticulum.

Follow-up of the occurrence of intestinal tumors possibly related with AAD showed no differences in mucinous cystadenomas and appendiceal carcinoids; however, 3 patients with AAD developed colon cancer during follow-up *versus* none in the acute appendicitis group (p = 0.01).

Finally, analysis of postoperative hospital stay showed significant differences between groups, with significantly longer stay for the AAD group (9.19 ± 17.13 *vs.* 2.74 ± 1.5 days, p = 0.007).

DISCUSSION

Appendiceal diverticulosis was first described in 1893 by Kelynack (1,11-13). Its incidence varies in different series between 0.004 % and 2.1 % (1,2). In our series, the incidence of AAD was 0.57 % of patients undergoing surgery for acute abdomen with right ileac fossa pain suggestive of acute appendicitis.

Appendiceal diverticula are classified as congenital or acquired (14). Congenital diverticula involve all the layers –mucosa, submucosa, muscular and serous, and are therefore rarely perforated. The congenital form is exceedingly rare, having been observed in only 0.0014 % of 50,000 appendices in one study. The acquired form is characterized by absence of the muscular layer, which explains its higher tendency to perforation (15,16).

AAD is known to present at an older age than acute appendicitis, with a cutoff around 30 years of age. In our patients, acute appendicitis presented earlier than diverticulitis (37.24 ± 19.98 years *vs.* 54.81 ± 17.55 years, p < 0.001); however, the cut-off in our series was 40 years of age. There were few cases of diverticulitis before this age: Only 5 (18 %) *vs.* 40 patients (74 %) in the appendicitis group. Above this age, we found no significant difference in the distribution of patients.

Although male gender has been described as a risk factor for AAD (11-13,17,18), in our series the distribution and the mean age at presentation by sexes were not different for women (41.76 ± 24.87 years *vs.* 50.44 ± 16.69 years, p = 0.34), but among men appendicitis appeared earlier than AAD (33.33 ± 15.89 years *vs.* 57 ± 18.02 years age; p < 0.001).

AAD is habitually underdiagnosed by clinicians, radiologists and surgeons, because of its clinical features. Classically, AAD primarily presents with pain not associated with nausea, vomiting or anorexia (1,2,11-13). In our study, pain was consistently the most common symptom in both groups. Detailed analysis of presenting symptoms revealed no differences in any symptoms, except that diarrhea was significantly more common in the group with acute appendicitis (p = 0.017) and not present in the AAD group. As reported previously (4), AAD in our series was not diagnosed preoperatively in any case.

A recent publication has highlighted the importance of early diagnosis of diverticulosis/AAD leading to early appendectomy, even in the absence of major clinical symptoms, given the high rate of clinical complications associated with AAD (7). Thus, certain ultrasound or CT data have been described that could help establish the preoperative diagnosis of AAD (5-7). Regarding ultrasonography, useful findings for the diagnosis of this entity have been found. According to these and other studies (19), an inflamed diverticulum presents with a hypoechoic signal surrounded by echogenic fat. Other authors (5) referring to acute suppurative appendicitis have reported that edematous mucosa and submucosa is typically seen as a hyperechoic ring within which there is a ring filled with liquid, while in AAD all inflamed appendix layers are thicker and echogenic, as is their interior, indicating the presence of air. The retrospective analysis performed

Table II. Clinical and diagnostic characteristics of patients with appendiceal diverticulitis *vs.* acute appendicitis

	Appendiceal diverticulitis (n = 27)	*Acute appendicitis (n = 54)*	*p / Odds ratio*
Clinical symptoms			
Abdominal pain	15	29	0.19
Fever	1	0	
Change in bowel habit	1	0	
Pain + fever	4	3	
Pain + vomiting	5	8	
Pain + vomiting + fever	1	5	
Pain + diarrhea	0	7	
Pain + vomiting + diarrhea	0	1	
Pain + diarrhea + fever	0	1	
Appendicular plastron	8	5	0,01 / OR = 2.2
Duration of symptoms (hours)	71.61 ± 85.25	36.84 ± 33.59	Z = -3.1 p = 0.002
Duration of surgery (minutes)	85 ± 40	60 ± 21	Z = -3.2 p = 0.001
Emergency dept. diagnosis			
Acute appendicitis	24	54	0.01 / OR = 0.7
Other	3	0	
Diagnosis			
Clinical symptoms	11	15	0.1
Ultrasound	12	36	
Computed tomography	4	3	
Leukocytosis			
Yes	13	44	0.02 / OR =2.5
No	14	10	
Leukocytosis (mean)	13770.37 ± 4382.55	14279.63 ± 4268.59	0.61
Complications: anatomic pathology			
Perforation			
Yes	7	7	0,14
No	20	47	
Gangrene			
Yes	0	8	0.03 / OR = 1.58
No	27	46	
Ulcerated			
Yes	8	16	1
No	19	38	
Mucocele			
Yes	3	0	0.01 / OR= 3.2
No	24	54	
Cystadenoma			
Yes	2	1	0.21
No	25	53	
Hospitalization (days)	9.19 ± 17.13	2.74 ± 1.5	0.007

in our study revealed no useful radiological criteria for the preoperative diagnosis of appendiceal diverticulitis. On the one hand, this may be because ultrasound imaging is a technician-dependent technique and radiologist unfamiliarity with this disease makes it difficult to diagnose, and because of technological differences of ultrasound equipment used over a relatively long period of time. On the other hand, although CT is considered the most useful tool for detecting AAD (20), the low number of CT scans performed in our patients meant we lacked sufficient data for statistical analysis. A prospective study would be required to assess the usefulness of these radiological findings.

The average number of leukocytes found on preoperative laboratory analysis was lower in the AAD group (13770.37 ± 4382.55 *vs.* 14279.63 ± 4268.59, p = 0.61), but not significantly so, in agreement with the findings of other authors (17,18). However, the presence of leukocytosis (defined as leukocyte count greater than 12,000) was significantly lower in the AAD compared to the group with acute appendicitis (48.15 % *vs.* 81.48 %, p = 0.02).

Traditionally, the diagnosis of AAD is delayed due to its more indolent course compared to appendicitis, leading to a greater number of perforations, with consequently increased recuperation time and a 30-fold increase in early mortality (1,14,21,22). Usually, perforation occurs towards the mesoappendix, inducing localized peritonitis, unlike in acute appendicitis where perforation usually spreads to the free peritoneal cavity and leads to diffuse peritonitis (1). In our series, the mean duration of symptoms before the patient visited the ED was significantly higher in the AAD group (71.61 ± 85.25 hours *vs.* 36.84 ± 33.59 hours, Z = -3.1 p = 0.002), which suggests a more insidious process that did not alarm the patient and delayed seeking medical help. This delay in patient care may help explain the longer surgery duration of intervention in patients with AAD compared with acute appendicitis (85 ± 40 minutes *vs.* 60 ± 21 minutes, Z = -3.2, p = 0.001), along with a greater number of appendicular plastrons in the AAD group (8 *vs.* 5 patients, p = 0.01, odds ratio 2.2). These findings also seem to support the notion of a more indolent course in AAD than in acute appendicitis. However, there were no significant differences in pathologically determined complications (perforation and ulceration) between groups. Gangrene was more frequent in the group with acute appendicitis (p = 0.03, OR 1.58), while mucocele was more frequent in the AAD group (p = 0.01, OR 3.2). More advanced age, the presence of appendiceal plastrons and longer surgery times explain the longer hospital stay times of patients with AAD (9.19 ± 17.13 days *vs.* 2.74 ± 1.5; p = 0.007).

Recently, some researchers have observed an association between AAD and appendiceal neoplasms. Lamps et al. (8) reported 32 cases of mucinous neoplasms, of which 8 (25 %) were associated with diverticula, with a 42 % probability of mucinous neoplasm being associated with diverticulosis. A possible explanation for this relationship is that the appendiceal mucosa herniates through penetrating vessels or an area of previous perforation. Thus, the obstruction may play an important role in the pathogenesis of AAD because the dysplastic epithelium produces mucin, increasing intraluminal pressure and leading to herniation of the mucosa (8). In our study, the presence of appendiceal mucocele was exclusively limited to patients with AAD (p = 0.01). On the other hand, although cystadenomas were more frequent in the AAD group, the difference with respect to the appendicitis group was not significant (7.4 % *vs.* 1.8 %).

Regarding the relationship of AAD with other digestive neoformative processes, Dupre et al. (9) observed that 48 % of appendix specimens from patients with diverticulosis contained 5 cases of well-differentiated neuroendocrine tumors (carcinoid), 3 cases of mucinous adenomas, 1 case of tubular adenoma and 2 cases of mucinous adenocarcinoma. Habitually, neuroendocrine tumors are located at the tip of the appendix. However, the authors noted that neuroendocrine tumors associated with diverticular disease were located in the medial or proximal portion of the appendix.

In our study, no difference in the occurrence of these tumors was observed, but there was a significant difference in the appearance of colorectal cancer during follow-up of the patients studied (3 cases in the AAD group *versus* 0 in the appendicitis group). The relationship of colorectal cancer with colonic diverticulitis has been analyzed, since these diseases are very common in Western countries and both show increased incidence with advanced age (23). However, results regarding this relationship are contradictory (24-27). In our study, three patients with AAD developed colorectal cancer *versus* none in those with acute appendicitis; this is probably related with their age (since all three patients were older than 50 years, a recognized risk factor for the development of colorectal cancer), rather than a possible causal relationship. Logistic regression analysis controlling for gender and age would be required to clarify this. Given the sample size of our study, such analysis was not feasible.

In conclusion, in our experience AAD presents a number of interesting differences with respect to acute appendicitis, namely in epidemiological characteristics, age at presentation, gender, clinical and pathological complications as well as duration of symptoms before visiting the ED. The presence of appendiceal plastrons in AAD suggest a more indolent course that leads to delayed diagnosis and increased surgery times. These factors induce longer hospital stay for patients with AAD. Given these results, we believe that AAD could be classified as a distinct clinical entity from acute appendicitis, so it is important to consider this when faced with a case of "atypical" appendicitis. The possible relationship of AAD with certain digestive tumors remains to be determined in future studies.

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