Acute appendicitis may no longer be a predominant disease of the young population

Bruno Monteiro Pereira[1,2,3,4], Cecília A. Mendes[2], Rafael M. Ruano[2], Ingrid Neves[2], Rafael L. Curado[2], Rafael de Oliveira[2], Giovanni Beraldo[2], Juliana Matsuguma[2], Juliana Horiuchi[2], Alcir E. Dorigatti[2]

[1]Post Graduation and Research Division, Masters Program in Health Applied Sciences, Vassouras University, Vassouras, RJ, Brazil
[2]Grupo Surgical, Acute and Critical Care Surgery Group, Campinas, SP, Brazil
[3]Program Director, Terzius Institute of Education, Campinas, SP, Brazil
[4]Director, General Surgery Residency Program, Campinas Holy House, Campinas, SP, Brazil

Abstract

Background: Some authors consider acute appendicitis as the main cause of acute surgical abdomen. Incident in all ages, contemporary literature suggests that is more frequent in children and young adults, male predominantly. This study aims to test the hypothesis that the disease in question is no longer prevalent in young adults (excluding children) in the surveyed region.

Methods: 1150 cases of emergency surgery were performed and prospectively analyzed. 300 cases of appendicitis in adults were selected and variables studied. Patients under 13 years old were excluded.

Results: 190 patients older than 60 years had a diagnosis of acute appendicitis confirmed by biopsy. There is a predominance of males. The elderly population takes less time to seek medical assistance and has fewer complications, despite being more often admitted to the ICU due to other comorbidities.

Conclusions: A trend regarding acute appendicitis epidemiology may exist. In the specific studied region acute appendicitis is no longer a disease prevalent in young adults. Surgeons and emergency physicians must be aware that acute appendicitis may no longer be predominantly common in young adults in their own specific region. Multicenter studies are needed to determine whether these data are reproduced in a geographical area of greater extent.

Key words: appendicitis, acute, prevalence.

Anestezjologia Intensywna Terapia
2019; 51, 4: 289–294

Otrzymano: 16.04.2019,
zaakceptowano: 25.06.2019

ADRES DO KORESPONDENCJI:
Bruno M. Pereira, MD, MSc, PhD, University of Vassouras, Brazil, e-mail: dr.bruno@gruposurgical.com.br

Appendicitis is defined as inflammation of the inner lining of the vermiform appendix that spreads to its other parts. Despite diagnostic and therapeutic advances in medicine, appendicitis remains a clinical emergency and according to some authors is the main cause of acute surgical abdomen [1, 2]. Incident in all ages, the contemporary literature reports it to be more frequent in young adults, predominantly males [2–4]. However, the alternative perception evaluated by a private care group working with acute care surgery and trauma in a city of three million people approximately of a specific region has led to the development of the hypothesis that a possible paradigm shift regarding the prevalence of acute appendicitis in this studied region could exist. The aim of this study is to test the hypothesis that the diagnosis of acute appendicitis is no longer prevalent in young adult patients in this selected geographic region. As a secondary objective, this research correlates acute appendicitis with some important variables as well as related complications.

Appendicitis may occur for several reasons, such as an infection of the appendix, but the most important factor is the obstruction of the appendicular lumen. Left untreated, appendicitis has the potential for severe complications, including perforation or sepsis, and may even cause death.

The clinical presentation of acute appendicitis is notoriously inconsistent. The classic history of anorexia and periumbilical pain followed by nausea, right lower quadrant (RLQ) pain, and vomiting occurs in 50% of cases. The most common symptom is abdominal pain followed by other features including nausea (61–92%), anorexia (74–78%), vomiting (75%) and diarrhea or constipation (18%).

Należy cytować anglojęzyczną wersję: Pereira BM, Mendes CA, Ruano RM, et al. Acute appendicitis may no longer be a predominant disease of the young population. Anaesthesiol Intensive Ther 2019; 51, 4: 283–288. doi: https://doi.org/10.5114/ait.2019.87332

Abdominal pain typically begins as periumbilical or epigastric pain, which then migrates to the RLQ. Patients usually lie down, flex their hips, and draw their knees up to reduce movements and to avoid worsening their pain. The duration of symptoms is less than 48 hours in approximately 80% of adults but tends to be longer in elderly persons and in those with perforation [5, 6].

Physical examination includes primarily specific findings: rebound tenderness, pain on percussion, rigidity, and guarding. RLQ tenderness is present in 96% of patients, but is also nonspecific. Left lower quadrant (LLQ) tenderness may be the major manifestation in patients with *situs inversus* or in patients with a lengthy appendix that extends into the LLQ, but this is an uncommon scenario. Male infants and children occasionally present with an inflamed hemiscrotum. In pregnant women, RLQ pain and tenderness dominate in the first trimester, but in the latter half of pregnancy, right upper quadrant (RUQ) or right flank pain may occur.

The following accessory signs may be present in a variety of patients:

- Rovsing sign (RLQ pain with palpation of the LLQ): suggests peritoneal irritation,
- obturator sign (RLQ pain with internal and external rotation of the flexed right hip): suggests the inflamed appendix is located deep in the right hemipelvis,
- Lapinski sign (RLQ pain with compression and upwards mobilization of the limb): suggests an inflamed appendix,
- psoas sign (RLQ pain with extension of the right hip or with flexion of the right hip against resistance): suggests that an inflamed appendix is located along the course of the right psoas muscle,
- Dunphy sign (sharp pain in the RLQ elicited by a voluntary cough): suggests localized peritonitis,
- RLQ pain in response to percussion of a remote quadrant of the abdomen or to firm percussion of the patient's heel: suggests peritoneal inflammation,
- Markle sign (pain elicited in a certain area of the abdomen when the standing patient drops from standing on toes to the heels with a jarring landing): has a sensitivity of 74%.

Some laboratory tests are not specific for appendicitis, but they may be helpful to confirm diagnosis in patients with an atypical presentation or are useful to complement diagnostic propaedeutics, such as:

- White blood cells (WBC) > 10.5 G L^{-1}: 80–85% of adults with appendicitis, neutrophilia > 75–78% of patients. Less than 4% of patients with appendicitis have a WBC count less than 10.5 G L^{-1} and neutrophilia less than 75%. In infants and elderly patients, WBC count is especially unreliable because these patients may not mount a normal response to infection. In pregnant women, the physiologic leukocytosis renders the complete blood count useless for the diagnosis of appendicitis.
- C-reactive protein (CRP): CRP levels > 1 mg dL^{-1} are common in patients with appendicitis. Very high levels of CRP in patients with appendicitis indicate gangrenous evolution of the disease, especially if it is associated with leukocytosis and neutrophilia. In adults who have had symptoms for longer than 24 hours, a normal CRP level has a negative predictive value of 97–100% for appendicitis.
- Liver and pancreatic function tests.
- Urinalysis (for differentiating appendicitis from urinary tract conditions).
- Urinary β-hCG (for differentiating appendicitis from early ectopic pregnancy in women of childbearing age).
- Urinary 5-hydroxyindoleacetic acid (5-HIAA): HIAA levels increase significantly in acute appendicitis and decrease when the inflammation shifts to necrosis of the appendix. Therefore, such a decrease could be an early warning sign of perforation of the appendix.

Imaging studies are the state-of-the-art diagnostic methods for acute appendicitis. Ultrasonography may offer a safer alternative as a primary diagnostic tool for appendicitis, with CT scanning used in those cases in which ultrasonograms are negative or inconclusive. A healthy appendix usually cannot be viewed with ultrasonography; when appendicitis occurs, the ultrasonogram typically demonstrates a noncompressible tubular structure 7–9 mm in diameter. Vaginal ultrasonography alone or in combination with a transabdominal scan may be useful to determine the diagnosis in women of childbearing age. Computed tomography (CT) scanning with oral contrast medium or rectal Gastrografin enema has become the most important imaging study in the evaluation of patients with atypical presentations of appendicitis.

Appendectomy remains the only curative treatment of appendicitis. The surgeon's goals are to evaluate a relatively small population of patients referred for suspected appendicitis and to minimize the negative appendectomy rate without increasing the incidence of perforation [6].

METHODS

The Surgical Acute Care Surgery Group (SACSG) comprises seven acute care surgeons who are responsible for the coverage of six private hospitals from a total of nine private hospitals in a region of approximately three million habitants.

A prospective observational study of all surgical cases admitted by SACSG from March 2013 to March 2015 was performed. All case-related information was stored in a database, using Microsoft

Excel software for MAC 2011. Statistical analysis was performed using the SPSS Statistics 17 software (Windows freehold MAC). For the association of variables, the χ^2 test was used, and for population comparative assessment, the non-parametric Mann-Whitney test was used.

According to the World Health Organization (WHO), the elderly are all individuals aged 60 years and over. The same age cut-off was applied for these analyses. Patients under 13 years old were excluded. Following this definition, the studied population was divided into older and younger than 60 years as shown in Figure 1.

Initially the number of emergency procedures performed in the research period was analyzed together with the following variables: sex, smoking habit, hypertension, diabetes, time of evolution until seeking medical assistance, appendicitis grade, ICU admission, length of hospital stay, general complications related to surgery, mild complications (seroma, infection of wound, suture skin dehiscence) and severe complications (appendicular stump dehiscence, fistulas, abdominal wall dehiscence), and deaths during the same hospitalization.

The present study does not include any personal information such as name, personal documents or hospital registry. This is only an observational analysis of clinical evaluation from when the diagnosis was performed. Consequently, a waiver of informed consent was obtained from the research ethics committee of the institutions involved.

RESULTS

The total number of urgency/emergency procedures performed by the group was of 1150 in a period of two consecutive years (March 2013 to March 2015). The general population analysis showed 550 patients older than 60 years, a little under the majority of 600 patients under 60 years old ($P < 0.05$). From this initial number ($n = 1150$), 300 cases were of acute appendicitis diagnosed and confirmed by pathological examination, representing an average of 3.12 appendectomies performed in a week. 850 patients were excluded with other etiologic diagnosis and therefore did not belong to the study group. From the sub-selection of patients undergoing appendectomy, 190 of them were older than 60 years. 110 patients were younger than the age set by the WHO (World Health Organization) as a cut-off between the elderly and non-elderly population ($P < 0.05$). From these patients with acute appendicitis diagnosis, 186 were males and 107 were older than 60 years ($P < 0.05$).

Almost half of the studied population, 41.66% ($n = 125$), claimed to be smokers, 69.8% ($n = 87$) of them being classified as elderly. As well as in the elderly group, the number of non-smokers in the youth population exceeded the number of smokers ($n = 72$ and $n = 38$ respectively). 103 patients were older than 60 years and were non-smokers. However, the statistical analyses revealed a non-significant P value ($P = 0.056$).

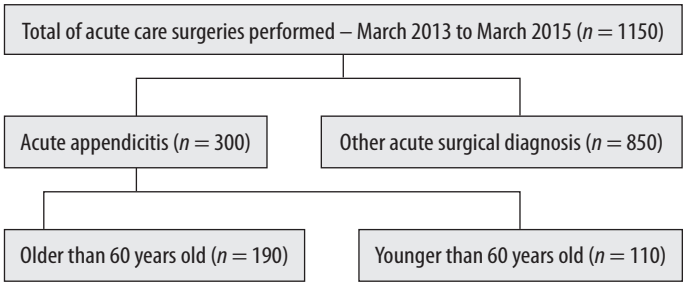

FIGURE 1. Studied population flowchart

From the population of 300 individuals, 60 were diabetic type I or type II (33% of the population), 12% old-aged ($P < 0.05$). This group of authors also evaluated the hypertensive patients who were diagnosed with appendicitis and underwent surgery. Most of the patients were not hypertensive ($n = 163$). The population on hypertension treatment ($n = 137$) was predominantly older than 60 years ($n = 101$).

In this studied set of patients, two-thirds of the total sought medical help with evolution time estimated in less than 4 days ($n = 200$). 44% of them were less than sixty years old and sought medical assistance with more than 4 days, compared with 26% of the elderly population ($P < 0.05$).

The incidence of appendicitis grade I and II in elderly patients was greater ($n = 134/70\%$) than that of grade III and IV ($n = 56/30\%$), $P < 0.05$. In the youth population the distribution of the disease behaved more evenly (grades I–II = 57/51% and graded III–IV = 53/49%) but in both groups initial grades (I and II) were prevalent.

When comparing the degree of appendicitis with the time of evolution of the disease in both populations, it was observed that grades III and IV are highly prevalent on more than 4 days of symptoms. In the young population the incidence of grades III and IV in patients with over 4 days of evolution was 95% ($n = 42$ of 49). In the elderly population the incidence of grades III and IV was lower, 76% ($n = 39$ of 51), with a non-significant P value ($P = 0.23$). The ICU and hospital length of stay were also evaluated. 8.4% ($n = 16$) of the senior population required hospitalization in the ICU, while 5.45% ($n = 6$) of young people remained in intensive care for some period of time. The majority of patients over 60 years old ($n = 190$) remained in hospital for less than 3 days ($n = 162/85\%$) as well as the

TABLE 1. Patients submitted to appendectomy and studied variables

Factor	Older than 60 years old (n =190)	Younger than 60 years old (n = 110)	$P < 0.05$
Gender			
Male	107	79	Significant
Female	83	31	Significant
Smokers			
Yes	87	38	Not significant
No	203	72	Not significant
Diabetes mellitus			
Yes	23	37	Significant
No	167	73	Significant
Hypertension			
Yes	101	36	Significant
No	89	74	Significant
Days of evolution			
> 4	51	49	Significant
< 4	139	61	Significant
Classification			
Grade I–II	134	56	Significant
Grade III–IV	57	53	Significant
Hospital length of stay			
> 3 days	28	41	Significant
< 3 days	162	69	Significant
ICU admission			
Yes	16	6	Not significant
No	174	104	Not significant
Complications			
Yes	46	44	Significant
No	144	66	Significant
Deaths			
Yes	0	1	Not significant
No	190	109	Not significant

younger population (n = 69/63%). Hospitalization greater than 3 days corresponded to 14.7% (n = 28) in the group above 60 years old and 37% (n = 41) in the group aged less than 60.

24% (n = 46) of the senior population evolved with some kind of complication (larger or smaller). The young population evolved with 40% (n = 44) of complications ($P < 0.05$). 93.9% of these complications were either seroma or wound infection.

There was no death in the group older than 60 years and only 1 death in the group less than 60 years old.

Only two patients, in the young group, had a pathological diagnosis of cancer (adenocarcinoma and carcinoid tumor), implying a 0.66% incidence in this series.

The Mann-Whitney test proved that the two groups are independent ($P < 0.05$).

Table 1 summarizes the variables studied in the population of patients undergoing appendectomy.

DISCUSSION

Acute appendicitis affects around 10% of the population and is, therefore, one of the most prevalent surgical emergencies [4–8]. Many authors characterize appendicitis as a predominant disease of young people; however, the cases operated by our group over the last two years have led us to advance the hypothesis that a shift of this paradigm could be occurring. On the rationale that the diagnosis of acute appendicitis is trending to higher prevalence in the elderly when compared to a younger population in the specific studied geographic area, this group of authors resorted to a prospective registration database, with analysis of all acute appendicitis cases treated with surgery and with confirmed biopsy.

This study represents the analysis of 300 patients operated on in six private hospitals of an urban/metropolitan area, composed of 20 municipalities having around 3 million inhabitants. All these private hospitals are emergency referred facilities and serve either the population of the metropolitan area, or adjacent municipalities. In common, the six institutions have adopted a new duty system with expert acute care surgeons who facilitate the registration of urgent and emergency surgical cases, improving as well the quality of care and prognosis of these patients as demonstrated in the studies conducted around the world [6, 9, 10].

From March 2013 to March 2015, 1150 acute care surgery cases were registered in these institutions. These two consecutive years were therefore analyzed. The same group composed of seven acute care surgeons operated on an average 47.9 emergency cases per month. Most of these cases were classified as acute abdomen including inflammatory, perforations and obstructions. There were only 5 cases of trauma, including 3 penetrating and 2 blunt trauma mechanisms that were admitted in the private setting. This low incidence rate of trauma cases occurred because most trauma cases were transferred by emergency medical service from the trauma scene to public or university trauma hospitals outside the city limits. Four emergency cases in the gynecology/obstetric field, including 2 cases of abortion and 1 case of hemorrhagic ovarian cyst, were registered. After exclusion of all cases, other than acute appendicitis with histopathological confirmation, a total of 300 patients submitted to appendectomy were found. The very first analysis has

already revealed divergent results of contemporary literature, favoring the authors' hypothesis [11].

The total number of patients over 60 years old with appendicitis reveals in itself a paradigm shift in this region (n = 190 elderly compared with 110 young patients).

The male population remains the most prevalent population with an acute appendicitis diagnosis, corroborating current literature data. The present research has demonstrated no relationship of acute appendicitis in the young or elderly group with smoking and/or diabetes mellitus (DM). However, the authors were surprised when they found that the incidence of DM is higher in the younger population when compared to seniors. Maybe the contemporary diet has an influence on this result. On the other hand, the number of seniors who eventually are diabetics but unaware of the disease seems to be fairly high worldwide [12–15].

In this studied geographic area, patients undergoing surgery for acute appendicitis had the highest rate of hypertension. However, with the even distribution between groups, the authors were led to understand that there is no obvious relationship between appendicitis and hypertension.

A third part of the studied population sought medical assistance with over 4 days of evolution. In this scenario two comments are important: 1. Part of this group did postpone medical help due to intellectual deficit, not understanding the illness severity and its natural worsening evolution; 2. Another part of this group eventually sought medical assistance at the Emergency Room and were released home with painkillers and no robust diagnosis, raising thereby the morbidity of the disease. After statistical analysis, a uniform distribution was found in the group less than sixty years old seeking medical assistance in more or less than four days from the onset of appendicitis symptoms. Nevertheless, it was observed that the senior population searched for medical help and obtained a high number of positive diagnoses in less than four days from the symptoms onset. In general the incidence of complicated appendicitis was not prevalent, about 1/3 cases in our database. But when looking at the youth population only, almost 50% of those were classified as grades III or IV, representing 44% of the young population with a diagnosis above 4 days of disease evolution. Thus, we conclude that the youth population more often has later diagnosis and consequently clinical severe presentations of acute appendicitis when compared with the senior population (26.8%). More than two-thirds of the elderly patients presented with appendicitis grades I or II.

Although this group of authors understand that the laparoscopic approach for appendicitis treatment is the standard of care [15], many difficulties are found in our experience to perform all appendectomies by laparoscopy, such as laparoscopic materials and device availability, insurance approvals, surgeons' surgical skills, etc. Thus, 80% of appendectomies registered here were performed through laparotomies.

It is important to mention that the only case of death in this study refers to a 34 year-old morbidly obese patient with 7 days of evolution (appendicitis grade IV) on the date of diagnosis, admitted with septic shock due to acute peritonitis. The severity of the case, added to long ICU hospitalization with subsequent complications, led to the patient's death. In general hospital length of stay did not exceed 3 days, with the vast majority not requiring hospitalization in the ICU (Table 1). This is also consistent with current literature demonstrating low hospitalization length of stay mainly for low-grade appendicitis [5–10].

Complications were observed in this research with an increased rate. The senior group presented a rate of 23.1% of complications while the young group presented a rate of 40%. Although this research did not emphasize complications, the high incidence of complications, especially in the young group, has intrigued the authors. Seroma was the most common complication in both groups. No further investigation to find out the reason for high seroma incidence was performed, although aseptic and technical aspects were all reviewed. Major complications occurred including one case of abdominal wall dehiscence, due to subcutaneous abscess, and one case of incisional hernia, both in the young group.

Finally, we conclude that in the studied population there is an important trend regarding age prevalence of appendicitis, maybe due to global aging of the population or perhaps for some other reason not determined in this study. Surgeons and emergency physicians must be aware that acute appendicitis may be no longer predominantly common in young adults in their own specific region. Multicenter studies are needed to determine whether this hypothesis is reproducible in other locations.

ACKNOWLEDGEMENTS

1. Financial support and sponsorship: none.
2. Conflict of interest: none.

REFERENCES

1. Brook I. Bacterial studies of peritoneal cavity and postoperative surgical wound drainage following perforated appendix in children. Ann Surg 1980; 192: 208-212.
2. Walker A, Hatch Q, Drake T, et al. Predictors of appendiceal perforation in an equal access system. J Surg Res 2014; 190: 87-92. doi: 10.1016/j.jss.2014.02.028.
3. Dzabic M, Boström L, Rahbar A. High prevalence of an active cytomegalovirus infection in the appendix of immunocompetent patients with acute appendicitis. Inflamm Bowel Dis 2008; 14: 236-241. doi: 10.1002/ibd.20299.

4. Zaitsev VT, Gurevich ZA, Brusnitsyna MP, Osadchaia EN, Chernenko MM. Prevalence of acute appendicitis among the population of a large city. Sovetskoe zdravookhranenie/Ministerstvo Zdravookhraneniia SSSR 1977; 40-44.
5. Yeh B. Evidence-based emergency medicine/rational clinical examination abstract. Does this adult patient have appendicitis? Ann Emerg Med 2008; 52: 301-303. doi: 10.1016/j.annemergmed.2007.10.023.
6. National Guideline Clearinghouse (NGC). Guideline summary: Clinical policy: critical issues in the evaluation and management of emergency department patients with suspected appendicitis. National Guideline Clearinghouse (NGC), Rockville (MD). Available at: http://guideline.gov/content.aspx?id=15598. Accessed: 18.11.2013.
7. Lin KB, Chan CL, Yang NP, et al. Epidemiology of appendicitis and appendectomy for the low-income population in Taiwan, 2003-2011. BMC Gastroenterol 2015; 15: 18. doi: 10.1186/s12876-015-0242-1.
8. Yang E, Cook C, Kahn D. Acute appendicitis in the public and private sectors in Cape Town, South Africa. World J Surg 2015; 39: 1700-1707. doi: 10.1007/s00268-015-3002-z.
9. Page DE, Dooreemeah D, Thiruchelvam D. Acute surgical unit: the Australasian experience. ANZ J Surg 2014; 84: 25-30.
10. Poh BR, Cashin P, Dubrava Z, Blamey S, Yong WW, Croagh DG. Impact of an acute care surgery model on appendicectomy outcomes. ANZ J Surg 2013; 83: 735-738. doi: 10.1111/ans.12351.
11. Omari AH, Khammash MR, Qasaimeh GR, Shammari AK, Yaseen MK, Hammori SK. Acute appendicitis in the elderly: risk factors for perforation. World J Emerg Surg 2014; 9: 6. doi: 10.1186/1749-7922-9-6.
12. Mota M, Popa SG, Mota E, et al. Prevalence of diabetes mellitus and prediabetes in the adult Romanian population: PREDATORR study. J Diabetes 2016; 8: 336-344. doi: 10.1111/1753-0407.12297.
13. Mutowo M, Gowda U, Mangwiro JC, Lorgelly P, Owen A, Renzaho A. Prevalence of diabetes in Zimbabwe: a systematic review with meta-analysis. Int J Public Health 2015; 60: 1-11. doi: 10.1007/s00038-014-0626-y.
14. Taheri Tanjani P, Moradinazar M, Esmail Mottlagh M, Najafi F. The prevalence of diabetes mellitus (DM) type II among Iranian elderly population and its association with other age-related diseases, 2012. Arch Gerontol Geriatr 2015; 60: 373-379. doi: 10.1016/j.archger.2014.11.012.
15. Agresta F, Ansaloni L, Catena F, Verza LA, Prando D. Acute appendicitis: position paper, WSES, 2013. World J Emerg Surg 2014; 9: 26. doi: 10.1186/1749-7922-9-26.