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Influence of sarcopenia and frailty in the management of elderly patients with acute appendicitis

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Abstract

In developed countries, the average life expectancy has been increasing and is now well over 80 years. Increased life expectancy is associated with an increased number of emergency surgical procedures performed in later age groups. Acute appendicitis is one of the most common surgical diseases, with a lifetime risk of 8%. A growing incidence of acute appendicitis has been registered in the elderly population and in the oldest groups (> 80 years). Among patients > 50-year-old who present to the emergency department for acute abdominal pain, 15% have acute appendicitis. In these patients, emergency surgery for acute appendicitis is challenging, and some important aspects must be considered. In the elderly, surgical treatment outcomes are influenced by sarcopenia. Sarcopenia must be considered a precursor of frailty, a risk factor for physical function decline. Sarcopenia has a negative impact on both elective and emergency surgery regarding mortality and morbidity. Aside from morbidity and mortality, the most crucial outcomes for older patients requiring emergency surgery are reduction in function decline and preoperative physical function maintenance. Therefore, prediction of function decline is critical. In emergency surgery, preoperative interventions are difficult to implement because of the narrow time window before surgery. In this editorial, we highlight the unique aspects of acute appendicitis in elderly patients and the influence of sarcopenia and frailty on the results of surgical treatment.

Key Words: Acute appendicitis; Appendectomy; Elderly; Frailty; Sarcopenia

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Core Tip: The global proportion of older subjects is steadily increasing. This is associated with an increased number of emergency surgical procedures performed in this age group. Acute appendicitis is one of the most common surgical diseases, with a lifetime risk of 8%. A growing incidence of acute appendicitis has been registered in the elderly population and in the oldest age group (> 80 years). In this editorial, we highlight the characteristics of acute appendicitis in elderly patient and the influence of sarcopenia and frailty on the results of surgical treatment.

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INTRODUCTION

The global proportion of older subjects is steadily increasing[1]. By convention, a chronological age equal to or greater than 65 years is considered elderly. A cut-off of 75 years or older has recently been suggested based on improvements in physical function over the past 20 years[2]. In fact, in many countries, especially in developed ones, the average life expectancy has increased and far exceeds 80 years[1]. This is associated with an increased number of emergency surgical procedures performed in this age group[3-5].

Acute appendicitis is one of the most common surgical diseases, with a lifetime risk of 8%[6-8]. A growing incidence of acute appendicitis has been registered in the elderly population and in the oldest age group (> 80 years)[8-10]. Among patients > 50-year-old who present to the emergency department for acute abdominal pain, 15% have acute appendicitis [11].

In this editorial, we highlight the unique aspects of acute appendicitis in elderly patients and the influence of sarcopenia and frailty on the results of surgical treatment.

CHARACTERISTICS OF ACUTE APPENDICITIS

Emergency surgery for acute appendicitis in the elderly is challenging[4]. Some important aspects must be considered. The first aspect is the difficulty of diagnosis because elderly patients may not present the characteristic clinical signs of acute appendicitis[12]. There is still controversy on whether the presentation of acute appendicitis in the elderly patients significantly differs from those in the younger age groups[13]. Signs of peritonitis may become evident with reduced peristalsis and severe tenderness[14,15]. Furthermore, as age increases, the ability to perceive pain decreases, and due to reduced thermoregulatory response and abnormalities in the response to endogenous pyrogens, approximately 30% of patients aged 65 years or older with acute infection show a lower febrile response[15].

Second, the incidence of complicated acute appendicitis is higher in elderly patients[11,16]. The prevalence of complicated appendicitis increases with age. If the prevalence is approximately 20% in patients under 40 years of age, this increases up to 37% in patients between 40 years and 64 years of age to reach higher than 55% in patients over seventy and higher than 70% in patients over 80[11,17]. However, acute appendicitis is not a progressive disease[12]. Complicated and uncomplicated forms of appendicitis are two distinct entities with different pathophysiology[14]. Gangrene with transmural necrosis, perforation, the presence of appendicoliths, abdominal abscess and/or diffuse peritonitis characterize complicated acute appendicitis, while suppurative or phlegmonous changes prevail in uncomplicated forms.

Third, the use of abdominal computed tomography (CT)-scan to make the diagnosis is frequent in elderly[18]. This is the most accurate method for distinguishing uncomplicated from complicated appendicitis[19,20]. The increased use of CT in elderly patients leads to a decrease in negative appendectomy rates by 10%. The frequency of negative appendectomy is up to 16% in younger patients[21]. The complication rate in elderly patients with negative appendectomy was higher than in younger patients (25% *vs* 3%, $P < 0.05$)[22]. Considering that the complication rate in elderly patients with negative appendectomy is higher than in younger patients, the preoperative diagnosis in these patients should be as accurate as possible.

A fourth aspect to consider is the time elapsed from hospitalization until surgery. Typically, up to approximately 72% of elderly patients are operated on more than 12 h after admission compared to approximately 35% of younger patients[9, 23]. Furthermore, 37% of elderly patients are operated on more than 24 h after admission, although this interval does not appear to cause any increase in postoperative complications[24]. However, it is important to remember that acute appendicitis is a time-dependent disease[25]. Source control within 6 h of abdominal sepsis onset was associated with a reduced risk-adjusted odds of 90-day mortality. In elderly patients with acute appendicitis, once operation is indicated,

we suggest performing appendectomy as soon as possible. Prioritizing the rapid identification of septic foci and initiation of source control interventions can reduce the number of avoidable deaths among patients with sepsis.

In the elderly patient, the best treatment for acute appendicitis is surgery[17,26,27]. Recent meta-analyses have shown that appendectomy seems even more effective than non-operative treatments. The finding of a 20% recurrence rate in patients > 80 years of age undergoing non-surgical treatment suggests that antibiotics may be a treatment option only in selected patients with uncomplicated appendicitis[28]. Anyway, a frail patient cannot tolerate repeated septic episodes.

Laparoscopic appendectomy is the standard of care in acute appendicitis. Several clinical studies have demonstrated the advantages of laparoscopic appendectomy over open surgery. In meta-analysis on the elderly population, mortality, postoperative complications, and length of hospital stay were significantly lower when using the laparoscopic approach *vs* an open surgery[29,30]. Despite the advantages of the minimally invasive technique, there is an increased risk of conversion from laparoscopy to open appendectomy in elderly patients[31]. The rate of laparoscopies performed on older adults varies significantly, ranging from 19.3% to 67%[29,32]. The most common cause of conversion is peri-appendiceal infiltration/an inflammatory mass, which makes sectioning of the appendix difficult and requires less or more extensive ileocolic resection.

Furthermore, older patients have an increased risk of appendiceal neoplasm. A recent study on 989 patients undergoing emergency appendectomy showed an overall incidence of appendiceal neoplasm of 9.3% (92 patients). The rate of appendiceal neoplasm increased with age (3.8% in younger patients and 13.0% in patients between 40 years and 89 years). In the study, appendectomy was performed in all cases. The conversion rate was significantly higher in patients with appendiceal neoplasm (21.6% *vs* 6.7% in acute appendicitis, $P < 0.001$)[33].

Predicting outcomes in emergency surgery is challenging due to the heterogeneous mix of patients, pathologies, indications and urgency of surgery. Increasingly, emergency laparotomies are performed on older patients with complex medical conditions who subsequently encounter increased postoperative morbidity and mortality[34]. In appendectomy, mortality varies from 0.74% to 8% in the elderly and increases with age, while it is 0.04%-1% in the general population[21, 26]. Advanced age adversely affects clinical diagnosis, the stage of the disease and outcomes. Late presentation, delayed diagnosis, presence of perforation and co-morbidities are associated with poor outcome from surgery in elderly patients.

Postoperative complications can affect up to 46.2% of elderly patients compared to 9.3% of younger patients[31]. Surgical site infection occurs in 9.0%-15.4% of elderly patients, compared to 2.6%-3.7% of younger patients[35]. In elderly, independent factors for postoperative complications include anemia, a history of heart disease, chronic renal failure, and open appendectomy surgery[16]. A recent meta-analysis showed that elderly patients have an increased risk of complicated appendicitis (RR, 2.38; 95%CI: 2.13, 2.66), peritonitis (RR, 1.88; 95%CI: 1.36, 2.59), and conversion from laparoscopic to open appendectomy (RR, 3.02; 95%CI: 2.31, 3.95). In addition, the risk of overall postoperative complications (RR, 2.59; 95%CI: 2.19, 3.06), intra-abdominal abscess (RR, 1.84; 95%CI: 1.15, 2.96) and wound infection (RR, 3.80; 95%CI: 2.57, 5.61) was higher among the elderly[31].

SARCOPENIA AND FRAILTY

In the elderly, postoperative complications are also influenced by sarcopenia[10,36]. Sarcopenia must be considered a precursor of frailty, a risk factor for physical function decline[37]. Sarcopenia has shown a negative impact on both elective and emergency surgery regarding mortality and morbidity[38-41]. Aside from morbidity and mortality, the most crucial outcomes for older patients requiring emergency surgery are reduction in function decline and preoperative physical function maintenance[42]. Therefore, predicting the decline in functionality is crucial. It should be noted, however, that preoperative interventions are difficult to implement in emergency/urgent conditions due to the narrow time window before surgery[41].

A recent observational study of 610 patients undergoing emergency laparotomy showed that sarcopenia and myosteatosis were both associated with increased risk of morbidity, 30-day and 1-year mortality[40].

Sarcopenia is a morbid condition that directly involves the skeletal muscles with repercussions at a multisystem level [43]. Although with wide individual variability, approximately 1%-2% of muscle mass is lost every year after the fifth decade of life for a total reduction of 30%-50% by the age of 80. It is a preventable but chronic and reversible process.

Sarcopenia has been used as a prognostic tool to identify patients at risk for complications and adverse events in the postoperative period[24,44]. In this scenario, it has been documented that geriatric patients with lower body mass index, reduced muscle area, and marked sarcopenia detected by CT-scan tend to have an increased risk of complicated acute appendicitis[45].

Clinically, sarcopenia induces a reduction in muscular strength, both dynamic and static, with an increased risk of functional decline, disability and frailty, a reduction in the ability to maintain balance with an increased risk of falls and fractures, consequences on bone trophism, thermoregulation, basal energy production, regulation of body composition, and glucose homeostasis[46]. Muscle trophism is the consequence of a balance between anabolic and catabolic stimuli. In the elderly, a prevalence of the catabolic state is documented, which becomes predominant if comorbidities occur. In these cases, the muscle mass also suffers the effects of the general catabolic state in which the organism finds itself.

The European Working Group on Sarcopenia in Older People recommends the simultaneous presence of loss of muscle mass associated with reduced muscle strength or performance for the diagnosis of sarcopenia[46,47]. To evaluate these criteria, there are several investigations that differ in terms of sensitivity[48,49]. This variability accounts for the different prevalence percentages of sarcopenia found across various studies. Several biochemical markers have shown a strong association with sarcopenia, including low levels of vitamin D, IGF-1 and high levels of parathyroid hormone, C-reactive protein, TNF- α , and IL-6[50]. In addition to these, other indices significantly correlate with reduced muscle mass and

performance. However, a specific and sensitive marker of sarcopenia that allows for rapid and early diagnosis has not yet been identified.

Frailty is the most problematic expression of aging characterized by a state of vulnerability to any stressful event. It is due to the reduced homeostatic reserve of the organism which follows the functional decline of various physiological systems. The repercussions on the socio-health level are notable. In fact, it has been demonstrated that frailty is associated with an increased risk of negative outcomes, such as disability, hospitalization and death[51,52]. Frailty in the emergency surgical patient has been recently characterized in both older and younger populations[53]. Frailty can be difficult to identify in emergency settings[54]. Fusario *et al*[55] showed that the Emergency Surgery Frailty Index score is a useful and simple prognostic marker for frailty status in surgical elderly patients. The score may support the surgeon in decision for an adequate healthcare plan and preoperative preparation.

An increased risk of postoperative complications in elderly patients undergoing emergency laparotomy is usually associated with an increased frailty score[56]. These patients have more frequent admission to the intensive care unit and an increased length of stay. Furthermore, the mortality rate in frail patients was higher (17%) compared to less than 1% in non-frail patients ($P = 0.01$)[56]. In a study of 5728 older adults undergoing appendectomy, frail patients were documented to have higher mortality (frail 1.0% *vs* non-frail 0.3%, $P = 0.001$) and severe complications (14.2% *vs* 8.0%, $P < 0.0001$). In multivariable logistic regression, frailty was associated with increased mortality (OR 3.34; 95%CI: 1.28-8.66), severe complications (OR 1.51; 95%CI: 1.17-1.93) and discharge to facility (OR 2.80; 95%CI: 2.00-3.93)[57].

On the other hand, it has been noted that a modified Frailty Index and a Brief Geriatric Assessment do not correlate with prolonged hospitalization or higher risk for postoperative complications after appendectomy in elderly patients[52]. In this scenario, the evaluation of sarcopenia status can add further information regarding the general condition of the patient that could make the therapeutic choice personalized.

Based on the current knowledge, most studies are performed on samples of patients enrolled for elective, scheduled surgery, which allows optimizing the patient in the preoperative period[58,59].

In an emergency setting, the situation appears more complex, with patients in whom it has not been possible to carry out an in-depth preoperative evaluation, often with the inflammatory/septic process causing greater general fragility[36, 38]. As highlighted in recent studies, sarcopenic patients undergoing surgery are expected to be at higher risk of complications than patients with normal muscle mass. Therefore, in this setting, sarcopenia evaluation is a potential parameter that could support the surgeon during the decision-making process[36,60]: an older and sarcopenic patient cannot tolerate a prolonged septic status, so in these cases a surgical approach should be preferred over a conservative treatment in all type of acute appendicitis. In this context, the use of artificial intelligence could be useful[61].

CONCLUSION

The diagnosis of acute appendicitis in the elderly remains a clinical challenge. The elderly patient presents a diagnostic challenge. The presentation of the disease may be atypical in relation to the physiological changes due to age and a wider variety of conditions for differential diagnosis. Comorbidities and their associated polypharmacy affect the appropriate choice of imaging modality. In these patients, CT-scan is often performed for diagnosis, even in emergency settings. In such conditions, the total psoas muscle index and total psoas muscle area can be easily calculated on CT-scan. The gold standard approach is surgical treatment, although not all elderly patients may be suitable for surgery. It is therefore essential that the treatment plan be organized for each individual case, also in relation to the skills of the individual institution or surgeon.

FOOTNOTES

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