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Association between the Alvarado score and surgical and histopathological findings in acute appendicitis.

Associação entre o escore de Alvarado, achados cirúrgicos e aspecto histopatológico da apendicite aguda.

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A B S T R A C T

Objective: to compare the results of the Alvarado score with the surgical findings and the results of the histopathological examination of the appendix of patients operated on for acute appendicitis. **Methods:** we conducted an observational study with a cross-sectional design of 101 patients aged 14 years and over undergoing emergency appendectomy. The evaluation comprised the Alvarado score, gender, age, ethnicity and time of evolution. We obtained data regarding the surgical aspect of the appendix, postoperative complications and the result of the histopathological examination. The pre-established confidence interval was 95%. We calculated sensitivity, specificity, positive and negative predictive values of the score, and performed an analysis through the ROC curve. **Results:** we found a statistically significant (p=0.002) association between the Alvarado score and the diagnostic confirmation using a cutoff score of six or greater, with a sensitivity of 72% and a specificity of 87.5%. A score greater than or equal to six showed a greater tendency to present more advanced stages of acute appendicitis in both surgical and histopathological findings when compared with a score lower than six. Males presented greater chances of complications when compared with females (p=0.003). **Conclusion:** the Alvarado score proved to be a good method for diagnostic screening in acute appendicitis, since scores greater than or equal to six are associated with a higher probability of diagnostic confirmation and more advanced stages of the acute disease.

Keywords: Appendectomy. Diagnosis. Emergencies. Appendicitis.

INTRODUCTION

Abdominal pain is the most prevalent presentation in emergency care[1], acute appendicitis (AA) being the most common cause of abdominal urgency[2], and appendectomy, the gold standard for AA treatment, is the most frequently performed emergency surgery in the world[3]. Approximately 90 to 100 patients per 100,000 inhabitants will have this disease per year[4] and it is estimated that the risk of developing AA throughout life is between 7% and 8%[3], 8.6% in men and 6.7% in women[5]. This incidence is higher in adolescents and young adults, the population most affected between 25 and 35 years of age[6].

The classic form of AA can be readily diagnosed and treated. However, the presence of atypical features may make diagnosis difficult, since typical symptoms and compatible laboratory abnormalities may be absent in 20% to 33% of patients, especially during the initial stages[1]. In such cases, imaging research may be useful in establishing a correct diagnosis[7]. Among the exams, there is a limited role in radiological examination, which is useful to rule out other diseases that cause acute abdomen. Ultrasonography has a high rate of false positive and false negative results[8]. Computed tomography is the exam of choice due to its high sensitivity and specificity[9], but it is expensive and not available in all centers. In addition, in cases of typical AA, its use may delay appendectomy and increase the risk of perforation[10]. The definitive method for confirming the diagnosis of AA is the histopathological examination of the appendix[11].

Clinical diagnosis may lead to a non-therapeutic appendectomy rate of 15% to 30%[12], and the rate of undiagnosed perforated AA may reach 3.4%, since AA symptoms may overlap with urologic, abdominal, and gynecological ones[13]. Thus, late or incorrect diagnosis can result in multiple

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complications, such as surgical site infections, perforation, abscesses, sepsis and death[14]. Correct diagnosis and early surgical intervention are the best methods to reduce morbidity and mortality, hospitalization time and treatment costs[15].

It is relevant to incorporate in clinical practice tests such as scores that aid in the diagnosis of AA[16]. There are numerous risk classifications whose objective is to identify low, medium and high-risk patients for AA, allowing later investigations to be stratified according to the same[17]. Among these tests, the Alvarado score was designed with the intention of reducing the number of requested imaging tests[18]. Alvarado described a scoring system based on eight predictive clinical factors to improve the assessment in the diagnosis of AA, which produces a maximum score of ten points and includes symptoms and clinical signs, and laboratory findings[19].

The present study aims to compare the results of the Alvarado score with the surgical findings and the results of the histopathological examination of patients operated on for acute appendicitis.

METHODS

The study followed the guidelines and regulatory norms for research involving human subjects proposed by Resolution nº 466/2012 of the National Health Council. We collected the data after approval of the Unisul Ethics in Research Committee - CEP - under the opinion 2,362,539, and by having the consent form signed by the participants or by their guardians in cases of minors under 18 years of age. This is an observational study with a cross-sectional design. The sample consisted of 101 patients aged 14 years and older with suspected acute appendicitis who underwent appendectomy in the period from April 1st to September 30, 2017, attended at a hospital in southern Santa Catarina. We excluded patients that had missing data and those unable to provide the information necessary for the study.

The applied interview contained the patients' gender, age and ethnicity, time of evolution and the Alvarado score. The latter included migration of pain, anorexia, nausea and/or vomiting, pain at decompression of the right iliac fossa (FID), increase in temperature and leukogram left shift. One point was added to each filled criterion, but leukocytosis and defense in the lower right quadrant, which adding two points each[19]. After the end of the interview collection period, we consulted the electronic medical records to obtain the surgical aspect of the appendix and the data regarding possible postoperative complications. Subsequently, we accessed the data system of the region reference laboratory for the results of the histopathological examination, which provided the report with classification in normal appendix, incipient AA, AA, purulent AA and gangrenous AA[20]. We calculated the Alvarado score at the time of the database construction.

We archived and tabulated the data in a spreadsheet, using the EpiInfo 3.5.4 program and analyzing it with the statistical software SPSS (Statistical Package for the Social Sciences) version 20.0. We present the quantitative data in measures of central tendency and dispersion and the qualitative ones in percentages and in absolute numbers. To verify the association between the variables of interest, we used the Chi-square test for the comparison of proportions and the Student's T-test or Man-Whitney test for comparison of means. The pre-established confidence interval was 95%, p=0.05. We calculated the sensitivity and specificity of the score in the studied population, as well as its positive and negative predictive values, and then performed an analysis through the ROC curve.

RESULTS

Of the 101 patients evaluated, 49 patients were female (48.5%) and 52 male (51.5%). The median age was 29 years, with an interquartile range of 19. As for ethnicity, the majority of the patients were Caucasians, 92.1%.

Regarding the Alvarado score, the most frequent presentation was sudden decompression pain in the right iliac fossa, in 92%, followed by leukocytosis in 84.2%, anorexia in 77.2%, nausea and/or vomiting in 75.2%. Migration of the pain, right lower quadrant defense of the abdomen, elevation of temperature and leukogram left shift were present at a lower frequency, 56.4%, 47.5%, 38.6% and 15.8%, respectively.

For the evaluation of the Alvarado score, computing the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), as well as for the association of the score with the other study variables, we adopted cutoff points of the score greater than or equal to five, six and seven, according to the ROC curve. This indicated a cutoff greater than 5.5 as being statistically significant (Figure 1). Thus, 86.1% obtained a score greater than or equal to five, 67.3% obtained a score greater than or equal to six, and 36.6%, greater than or equal to seven.

Considering the analysis of the Alvarado score data of the 101 participants, we observed that 2% scored two points, 1% scored three points, 10.9% scored four points, 18.8% scored five points, 30.7% scored six points, 17.8% scored seven points, 5.9% scored eight points, 10.9% scored nine points, and 2.0% scored ten points. The score equal or higher than six presented sensitivity and specificity of 72% and 87.5%, respectively, with PPV of 98.53% and NPV of 21.21%, with accuracy of 73.27%. For the score greater than or equal to five, sensitivity was 88.17%, specificity 37.5%, PPV and NPV, 94.25% and 21.43%, respectively. For values greater than or equal to seven, the sensitivity, specificity, PPV and NPV were 38.71%, 87.5%, 97.3% and 10.94%, respectively.

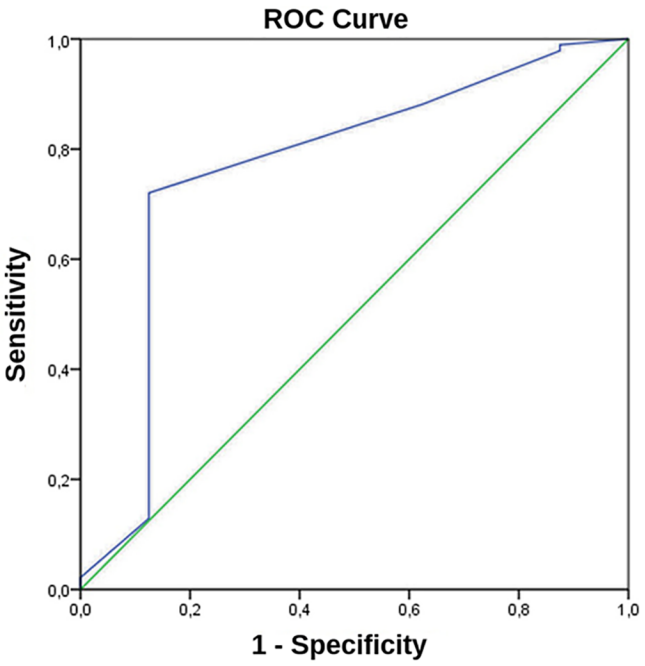

Figure 1. *ROC Curve.*

The time between onset of pain and appendectomy was mostly (77.2%) between one and three days, being shorter than one day in 13.9% and greater than three days in 8.9%. The surgical aspect found was mostly phases I and II, with distribution of 4% phase 0, 36.6% phase I, 35.6% phase II, 20.8% phase III and 3% phase IV.

Diagnostic confirmation with histopathology occurred in 92.1%, with a non-therapeutic appendectomy rate of 7.9%, totaling eight patients, of whom 75% were female. The results of the histopathological findings were incipient AA in 7.9%, AA in 53.5%, suppurative AA in 29.7% and gangrenous AA in 1%.

The postoperative complication rate was 17.9%, wound infection being the main, followed by metabolic ileus and fever, with respectively 6.9%, 5% and 4%. Dehiscence and hematoma of operative wound occurred in 1% each.

We found statistical significance (p=0.002) between the Alvarado score and the diagnostic confirmation using a cutoff score greater than or equal to six, showing a greater chance of AA diagnosis for such results. For the other cutoff points adopted, we observed no statistically significant differences (Table 1).

Associating the Alvarado score with age and gender and using the cutoff point greater than or equal to six rendered no statistical significance association (Table 2).

We found no statistical significance association between the Alvarado score and the AA surgical and histopathological findings (Table 3). However, we observed that the score greater than or equal to six showed a greater tendency to present more advanced phases of AA in both the surgical and histopathological aspects when compared with scores lower thansix.

We observed a disagreement between the surgical findings, mainly phases 0, I and II, with the

Table 1. *Association between the Alvarado score and diagnostic confirmation by histopathology.*

Score	Diagnostic confirmation	Absence of confirmation	p
<5	11 (11.8%)	3 (37.5%)	
≥5	82 (88.2%)	5 (62.5%)	0.079
<6	26 (9.28%)	7 (87.5%)	
≥6	67 (72%)	1 (12.5%)	0.002
<7	57 (61.3%)	7 (87.5%)	
≥7	36 (38.7%)	1 (12.5%)	0.252

Table 2. *Association between the Alvarado score and sociodemographic data.*

Variable	Score <6	Score ≥6	p
Gender			
Male	20 (40.8%)	29 (59.2%)	0.090
Female	33 (25%)	23 (88.5%)	
Age	26±20	29±18	0.789

Table 3. *Association between the Alvarado score and the surgical and histopathological findings.*

Variable	Score <6	Score ≥6
Surgical findings		
Phase 0	3 (75%)	1 (25%)
Phase I	11 (29.7%)	26 (70.3%)
Phase II	13 (36.1%)	23 (63.9%)
Phase III	6 (28.6%)	15 (71.4%)
Phase IV	0 (0%)	3 (100%)
Histopathology findings		
Incipient AA	2 (25%)	6 (75%)
AA	15 (27.8%)	39 (72.2%)
Suppurative AA	9 (30%)	21 (70%)
Gangrenous AA	0 (0%)	1 (100%)

histopathological results. Table 4 shows the surgical aspects related to the diagnostic confirmation by histopathology.

We did not observe a relationship between the Alvarado score and the presence of complications with any of the cutoff points adopted. However, even in a non-statically significant way, we observed that the complications were present when the scores were higher, with cutoff points greater than or equal to five and six (Table 5).

Of the patients presenting with complications, the majority had suppurative AA at histopathology, 55.5%, followed by AA with 16.6%, incipient AA and normal appendix with 11.1% each, and gangrenous AA, with 5.5%. In these same patients, the most common surgical finding was phase III, in 38.8%, followed by phase I, in 33.3%, phase II, in 22.2%, and phases 0 and IV, with 5.5% each.

There was no statistical significance between the time of evolution and any of the variables, not even the presence of complications. Of the patients presenting with complications, 5.5% had an evolution of less than one day, 16.6% had a prolonged evolution, greater than three days, and 77.7% had a one to three-day evolution. Of those who had four or more days of evolution, 37.5% had complications.

There was no association of postoperative complications with any other variable besides gender, males presenting a greater chance of complications when compared with females (p=0.003), representing 83.3% of the complications.

DISCUSSION

In the present study, cases of AA were more prevalent in males, in agreement with similar studies[21-24], as well as the median age found, which was 29 years, similar to studies in which the higher prevalence of AA occurs in the second and third decades[7,21,23,24].

The frequency of each of the criteria of the Alvarado score was similar to the findings of Memon *et al*.[25] and Rodrigues and Sindhu[26], but differed from Swami *et al*.[24], who observed a predominance of defense in lower right quadrant and the migration of pain, and a lower presence of leukocytosis. The same happened with the Brazilian study by Sousa-Rodrigues *et al*.[21] in which the elevation of temperature occurred in a greater proportion,

Table 4. *Surgical findings and diagnostic confirmation.*

Surgical finding	Diagnostic confirmation	Absence of confirmation
Stage 0	0 (0%)	4 (100%)
Phase I	33 (89.2%)	4 (10.8%)
Phase II	36 (100%)	0 (0%)
Phase III	21 (100%)	0 (0%)
Phase IV	3 (100%)	0 (0%)

Table 5. *Association between the Alvarado score and postoperative complications.*

Score	Presence of complications	Absence of complications	p
<5	1 (5.6%)	6 (33.3%)	
≥5	17 (94.4%)	13 (15.7%)	0.454
<6	6 (33.3%)	27 (32.5%)	
≥6	12 (66.7%)	56 (67.5%)	1
<7	12 (66.7%)	52 (62.7%)	
≥7	6 (33.3%)	31 (37.3%)	0.795

85.1% against 38.6%, also differing in pain at decompression, and in the presence of defense in the lower right quadrant. As for leukocytosis, we found similar results. The divergences observed may be related to the difference between the populations studied and the way of evaluating the criteria.

The most prevalent Alvarado scores were six, five and seven points, and the majority of the studied population presented a score greater than or equal to five, lower than those found by Sousa-Rodrigues *et al*.[21], in which the most prevalent were seven, eight and six points, respectively. Abdelrahim *et al*.[27] presented more prevalent scores greater than or equal to seven, and the same happened with a study in the South African population[28], which added higher points to the score. On the other hand, Memon *et al*.[25] found data similar to ours, the majority of patients displaying a score of five or six.

Jalil *et al*.[7] and Cedillo-Alemán *et al*.[18] had findings that coincided with the present study regarding sensitivity, specificity, PPV and NPV. Memon *et al*.[25] found higher VPP and NPV. The study by Genzo Ríos *et al*.[22] compared sensitivity and PPV for values of the score greater than or equal to five and seven, those being higher when the cutoff point was lower. In the present study, we observed that when the cutoff point increased, sensitivity and NPV fell, but specificity and PPV increased. We observed the inverse when the cutoff point was lower.

There was an association between the Alvarado score and the diagnostic confirmation by histopathology when using a cutoff point greater than or equal to six, and the rate of non-therapeutic appendectomy was 7.9%, predominantly in the female gender. Similarly, Swami *et al*.[24] found that a score greater than seven resulted in diagnostic confirmation in 90.9%, and Lima *et al*.[23] observed that 98.75% of the patients submitted to appendectomy had AA confirmed and of those who did not, 75% were female, which can be explained due to the overlap of gynecological symptoms in females[13]. Genzo Ríos *et al*.[22] obtained a similar rate of non-therapeutic appendectomy, 5.68%, but without distinction between genders. In contrast, Jalil *et al*.[7] observed a higher rate of non-therapeutic appendectomy in men.

In a study by Quesada Suárez *et al*.[29], the diagnosis was confirmed in 86%, and of those submitted to non-therapeutic appendectomy, the majority presented scores between five and seven. In a study by Abdelrahim *et al*.[27], all patients submitted to non-therapeutic appendectomy had a score below seven. In the present study, all unconfirmed patients had a score less than or equal to five, with the exception of one patient, who scored nine points.

The studies with greater disagreements were the ones form Rodrigues and Sindhu[26], in which the majority of patients with a confirmed diagnosis had a score of lower than 7.8, contrary to the other studies that associate higher scores with diagnostic confirmation, and Memon *et al*.[25], whose rate of non-therapeutic appendectomy was 28.7%, numbers relatively higher than those of the present study. Such divergence can be attributed to the difference between the populations studied and the pre-selected sample contained in this study, where the included patients were those submitted to appendectomy.

The study by Jalil *et al*.[7] showed that patients with a score greater than or equal to seven were more likely to have more advanced stages of AA at histopathology. In the present study, even without statistical association, the score greater than or equal to six showed a greater tendency to more advanced stages of AA at histopathology

compared with a score lower than six. Such observations were also made by Ospina *et al*.[30]. The histopathological findings of this study were mainly AA and suppurative AA, in agreement with Sudhir *et al*.[31].

The surgical aspect found was mostly phases I and II. For Swami *et al*.[24], most of the appendages presented only inflammatory characteristics, representing the initial stages of AA, in agreement with the present study, as well as with those of Silva *et al*.[32] and Nutels *et al*.[33], Brazilian studies on AA complications that found predominantly early stages. In the national case-control study of Iamarino *et al*.[34], there was a greater predominance of the suppurative and gangrenous phases, and in Sousa-Rodrigues *et al*.[21], the most prevalent phases were III and II, respectively, considered slightly more advanced than those we found. Sousa-Rodrigues *et al*.[21] showed a statistically significant correlation between the Alvarado score and the surgical findings, different from us, who found no statistical relevance in such association. We observed, however, that using the cutoff point greater than or equal to six showed a greater tendency to more advanced AA phases in the surgical findings when compared with a score lower than six. Significantly disagreeing, studying the South African population, Kong *et al*.[28] observed predominantly advanced, already perforated phases. Such discrepancy may due to the differences in the populations of the studies, as well as the availability of access to health services.

Sousa-Rodrigues *et al*.[21] found a time between onset of symptoms and appendectomy of approximately 32.4±5.4 hours, data similar to those found in this study. Ospinal *et al*.[30] showed a relationship between the evolution time greater than 36 hours and the presence of necrosis, different from the present study, in which there was no association of evolution time with diagnosis or with the presence of necrosis. In Genzo Ríos *et al*.[22], the time of evolution also did not show relation with diagnosis. Findings in Nutels *et al*.[33] showed that a longer evolution resulted in greater complications, and patients with more than four days of evolution had a complication rate of 57.2%. In the present study, 77.7% of the patients presented complications between one and three days, which can be attributed to the observed predominance of this time of evolution. Among those who had four or more days of evolution, 37.5% had complications.

When comparing the findings of the complications with the literature, we observed that they suffer alterations according to the studied population and the variables that surround them, as found by the South African study[28]. In that study, the population had lower socioeconomic conditions and longer disease progression; 59.5% had perforated AA, and of those, 29.7% had perforated AA associated with intra-abdominal sepsis and 70.2% had an association with generalized sepsis. Conversely, in our study the rate of postoperative complications was 17.9%, the main complication being surgical wound infection, results similar to the ones from Nutels *et al*.[33], with complications rates of 17.2%, wound infection also being the most common. However, they observed death outcome in 0.9%, differing from the present study, with mortality rate zero. In a study by Lima *et al*.[23], only 5.96% of the patients presented complications, and wound infection was the most frequent. In the case-control study of Iamarino *et al*.[34], the most frequent complication was intra-abdominal abscess, followed by surgical wound infection, differing from the present study, but with wound infection still displaying a significant frequency.

In our study, the majority of patients sustaining complications presented suppurative AA at histopathology, and in these same patients the most common surgical finding was phase III, consistent with the work of Silva *et al*.[32], in which patients with appendix necrosis without perforation (phase III) were 3.32 times more likely to have postoperative complications. Nutels *et al*.[33] demonstrated a higher percentage of postoperative complications also in phases III and IV, and Iamarino *et al*.[34] observed that complications occurred more frequently in the perforated and gangrenous phases, evolutionary phases slightly more advanced than those found in the our study.

We found no relationship between the Alvarado scores and the presence of complications, but there were higher scores in complicated cases, an association also seen by Jalil *et al*.[7]. In the present study, male patients presented higher complications rates, as observed by Nutels *et al*.[33] and Iamarino *et al*.[34]; Lima *et al*.[23] observed that evolution to death was more frequent in males. For Silva *et al*.[32], on the other hand, female patients were 1.94 times more likely to have postoperative complications.

Despite any differing result, the Alvarado score represents a good method for AA diagnostic screening, since scores greater than or equal to six are associated with a greater probability of histopathological diagnostic confirmation. We should also emphasize that the Alvarado score is a simple, accessible and easy-to-use method that can accelerate the diagnosis and, thus, reduce disease evolution time and postoperative complications. As seen in the present study, higher scores may be associated with more advanced phases of AA, including correlations with more advanced findings in the histopathological examination, and with greater postoperative complications, demonstrating their importance.

R E S U M O

Objetivo: *comparar o resultado do escore de Alvarado com os achados cirúrgicos e com os resultados do exame histopatológico do apêndice de pacientes operados por apendicite aguda.* **Métodos:** *estudo observacional com delineamento transversal de 101 pacientes com 14 anos de idade ou mais, submetidos à apendicectomia de urgência. A avaliação continha o escore de Alvarado, pontuação no escore, sexo, idade, etnia dos pacientes e tempo de evolução. Foi obtido o aspecto cirúrgico do apêndice, dados a respeito das complicações pós-operatórias e o resultado do exame histopatológico. O intervalo de confiança pré-estabelecido foi de 95%. Foram calculadas sensibilidade, especificidade, valor preditivo positivo e negativo do escore, e realizada uma análise através da curva ROC.* **Resultados:** *a associação entre o escore de Alvarado e a confirmação diagnóstica utilizando como ponto de corte uma pontuação maior ou igual a seis encontrou-se significância estatística (P=0,002), com sensibilidade de 72% e especificidade de 87,5%. A pontuação maior ou igual a seis mostrou maior tendência a apresentar fases mais avançadas da apendicite aguda tanto no aspecto cirúrgico quanto histopatológico, quando comparado a uma pontuação menor que seis. O sexo masculino apresentou maiores chances de complicações quando comparado ao sexo feminino (P=0,003).* **Conclusão:** *o escore de Alvarado se mostrou um bom método para triagem diagnóstica na apendicite aguda, já que pontuações maiores ou iguais a seis estão associadas a uma probabilidade maior de confirmação diagnóstica e de quadros mais avançados da doença aguda.*

Descritores: *Apendicite. Apendicectomia. Diagnóstico. Emergências.*

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