MMP

Origiale article

CORRELATION OF SCORING SYSTEMS WITH HISTOPATHOLOGICAL FINDINGS AND THEIR IMPORTANCE IN REDUCING THE PERCENTAGE OF UNNECESSARY APPENDECTOMIES

КОРЕЛАЦИЈА НА СКОРИНГ СИСТЕМИТЕ СО ХИСТОПАТОЛОШКИОТ НАОД И НИВНОТО ЗНАЧЕНИЕ ВО НАМАЛУВАЊЕ НА ПРОЦЕНТОТ НА НЕПОТРЕБНИ АПЕНДЕКТОМИИ

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Abstract

Introduction. Acute appendicitis (AA) is one of the most common emergency surgical conditions, where emergency laparotomy is necessary. However, perforation rates and negative laparotomies during this procedure have not been reduced. The purpose of this paper was to evaluate the importance of the scoring systems in the differenttial diagnosis for setting an indication for appendectomy.
Method. Prospective comparisons of the values of 4 scoring systems were performed among 60 patients: Alvarado, Appendicitis Inflammatory Response (AIR), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) and Tzanakis. Values for the scores were determined in all patients treated with lower right quadrant (LRQ) abdominal pain, under a differential diagnosis of AA. After the appendectomy (open surgery or laparoscopic), a correlation was obtained between the histopathologic findings (HP) and the corresponding latent values.
Results. In the study 63.33% of the patients were male. Distribution of patients according to the values of the three different systems (Alvarado, RIPASA and Tzanakis) showed that the largest number of patients had values higher than 8 and AIR values of 7- 8. In the study, 95% of the operated patients were positive for appendicitis compared to the histopathological finding. 80% of the surgeries included on-time appendectomy, 15% delayed diagnosis, and 5% were found to be with an unnecessary appendectomy. According to the HP findings of those with positive findings, 77.2% of the cases had appropriate preoperative ultrasonographic (US) diagnosis. A statistically significant association of the scores with HP findings (promptly phlegmonous, promptly gangrenous, late perforated and unnecessary) was found only for the Alvarado, AIR, Tzanakis, and no statistically significant associationwas found for the RIPASA score.
Conclusion. Scoring systems are useful diagnostic tools for appendectomy indication. Using one or a combination of two or more scoring systems reduces the percentage of unnecessary appendectomies.

Keywords: acute appendicitis, scoring systems, diagnosis, appendectomy

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Абстракт

Вовед. Акутен апендицитис (АА) е една од најчестите итни хируршки состојби, каде е индицирана лапаротомија. Сепак, при оваа состојба,стапките на перфорации и негативни лапаротомии не се намалени. Целта на трудот е да се процени значењето на скоринг системите во диференцијалната дијагноза за поставување на индикација за апендектомија.
Метод. Кај 60 пациенти, направено е проспективно компарирање на вредностите на 4 скоринг системи: Алварадо, Appendicitis inflammatory response (Апендицитис инфламаторен одговор-АИО), Raja Isteri Pengiran Anak Saleha Appendicitis-РИПАСА и Тзанакис. Вредноста за скоровите се одредени кај сите пациенти примени со болка во долен десен квадрант (ДДК) на абдоменот, под диференцијална дијагноза за АА. По апендектомија, (класична или лапароскопска), направена е корелација помеѓу добиениот хистопатолошки наод (ХП) и соодветните вредности на скоровите.
Резултати. Во студијата 63.33% од испитаници беа од машки пол. Дистрибуцијата на пациентите согласно висината на вредностите на трите различни (Алварадо, РИПАСА и Тзанакис) скора, покажа дека најголем број на пациенти се со вредности на скорот поголемо од 8, а кај АИОС за вредности на скорот 7-8. Во студијата, 95% од оперираните пациенти имаа позитивен патохистолошки наод во однос на АА. Кај 80% од оперираните се работеше за нав-

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ремена апендектомија, кај 15% за закаснета дијагноза, а кај 5% најдено е непотребна апендектомија. Согласно добиениот ХП наод од тие со позитивен наод кај 77,2% од случаевите се работеше за соодветна предоперативна ултрасонографска (УС) дијагноза. Статистички сигнификантна асоцираност на скоровите со ХП наод (навремен флегмонозен, навремен гангренозен, закаснето перфориран и непотребна) се покажа само за скоровите Алварадо, АИО, Тзанакис, додека кај РИПАСА скорот асоцираноста остана несигнификантна.

Заклучок. Скоринг системите се корисни дијагностики алатки при индикација за апендектомија. Со користење на комбинација на два или повеќе скоринг системи може да се намали процентот на непотребни апендектомии.

Клучни зборови: акутен апендицитис, скоринг системи, дијагноза, апендектомија

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Introduction

Acute appendicitis (AA) is the most common cause of acute abdominal pain and emergency abdominal surgery. AA can occur during any period of life of the general population, with the highest incidence in children and adolescents. Delayed treatment of AA is associated with prolonged hospitalization, increased percentage of perforations (34%-75%), operative wound infections (1%-11%), pelvic abscesses (2%-7%), and late intraabdominal adhesions [1-5].

The most commonly used methods for diagnosing AA are disease history, physical examination and laboratory blood analysis. Diagnosis of AA based only on clinical and laboratory data results in high negative rates of appendectomy and missed diagnoses with increased morbidity [6-8]. Atypical presentation is more difficult to diagnose, with additional diagnostic methods being used, such as US, computed tomography, and magnetic resonance imaging. However, early diagnosis is highly dependent on the experience of the surgeon [9-15].

AA therapy can be conservative and surgical. Early surgical intervention is the gold standard for preventing blind perforations. However, the high rate of unnecessary negative appendectomies leads to unnecessary morbidity and even mortality. Clinical scoring systems are inexpensive, repeatable, and easily applicable tools in the preoperative period of AA diagnosis developed to reduce the rate of adverse appendectomies. Today, more scoring systems are used for diagnosing AA, mostly Alvarado, Tzanakis, Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA), Appendicitis Inflammatory

Response score (AIR), but new ones are emerging. Scoring systems incorporate different variables: demographic data (sex, age), clinical symptoms and signs, laboratory values (complete blood count, leukocytes, urine, C-reactive protein, etc.) and radiological examinations [16-19]. The Alvarado score is widely used in the diagnosis of AA because of its availability and low cost; it also avoids exposing the patient to radiation when using computed tomography. RIPASA score is a newer score that has more sensitivity and specificity than the Alvarado score. On the other hand, AIR and Tzanakis have recently used several clinical criteria and two simple laboratory tests (CRP and complete blood tests), but also US, which can lead to better and faster diagnosis of AA [16-19]. The gold standard in the diagnosis of AA is histopathological (HP) evaluation of the specimen after surgery. The purpose of this study was to correlate the values of different scoring systems with the histopathological finding and to evaluate their impact on reducing the percentage of unnecessary appendectomies.

Materials and methods

This prospective cohort study was conducted at the University Clinic of Surgical Diseases "St. Naum Ohridski"-Skopje, Macedonia. The ethical and legal requirement in accordance with the International Helsinki Protocol was received before the start of this study. Consent was obtained from all patients. The study included 60 patients over the age of 14, admitted in the hospital during the trial duration due to pain in the LRQ and suspected of AA. The preoperative diagnosis was established by disease history, clinical examination, and laboratory analysis that included total leukocyte count, neutrophil percentage, and CRP in the blood. All patients underwent preoperative US examination with appropriate criteria for AA: lumen diameter >6 mm, periappendiceal collection, appendicolith. Standardized demographic, symptom and symptom questionnaires, laboratory values, US findings and scoring data for Alvarado, AIR, Tzanakis, and RIPASA scoring system were completed for all patients. All patients underwent a classic or laparoscopic appendectomy. Each sample was sent for HP analysis. Patients without informed consent, with a previous history of urolithiasis, pelvic inflammatory disease, pregnant women and children under 14 years of age were excluded from the study. Table 1 shows all 4 examined scoring systems: Alvarado (8 parameters), AIR (7), Tzanakis (4) and RIPASA (18).

Table 1. Tracked scores

Parameters			Alvarado	AIR	RIPASA	Tzanakis
Parameters	Female				0.5	
	Male				1.0	
	Age/under 39,9				1,0	
	Age/ over 40				0.5	
Symptoms - signs	Pain in the low right quadrant or right iliac fossa				0.5	
	Migration pain in LRQ		1		0.5	
	Palpatory pain sensitivity in LRQ		2	1	1.0	4
	Rebound palpatory sensitivity in LRQ		1		2.0	3
	Rigid RLQ				1.0	
	Rowing / positive sign				2.0	
	Muscular defense/guarding	*Light*		1		
		Medium		2		
		Strong		3		
	Nausea / vomiting		1	1	1.0	
	Anorexia		1		1.0	
	Body temperature	*Raised*	1			
		>38.5 C°		1		
		37 - 39,5 C°			1.0	
	Time duration of	*< 48 hours*			1.0	
	the symptoms	*> 48 hours*			0.5	
Laboratory values		*74- 84*		1		
	Polymorphonuclear leukocytes %	*≥ 85*		2		
		left shift of the neutrophils> 75%	1			
	Raised white blood cells	*> 10000*	2		1.0	
		10000 – 14999		1		
		> 12000				2
		≥ 15000 sv/sic		2		
	C - reactive	*10- 49 gr/l*		1		
	Protein	*≥ 50 gr/l*		2		
	Urinalysis	*Negative*			1.0	
Radiological m.	Ultrasonography	*Positive*				6
		Total value:	10	12	16.5	15

Guide for Scores Interpretation, Alvarado: <4-unlikely AAA; 4-7-suspected AA; > 7-AA definitive, AIR: 0-4-low probability of AA; 5-8 probability of AA; 9-12 high probability of AA, RIPASA: <5- most likely AA malabsorption; 5-7 low probability of AA; 7.5-11.5-probable AA; > 12-AA definitive, Tzanakis: <5 unlikely for AA; 6-10 probable AA; > 10 highly probable AA

Patients were monitored from the time of admission to the time of discharge. Patients were monitored twice daily for vital parameters. The HP findings were analyzed at the Institute of Pathology, Faculty of Medicine-Skopje. Statistical analysis was performed using the statistical software package Statistica for Windows 7.0 and standard statistical package (SPSS v 20). Results are presented with descriptive statistics, mean±SD. Student's t-test was used for comparison of the two groups. For comparison of 2 groups with categorical normal (nominal) variables X2 test was used. And for comparison of more than 2 groups ANOVA analysis was performed.

Results

In our study group of 60 operated patients, 63.33% were men and 36.67% women, with a mean age of 35.86± 15.15 years. Palpatory pain in the lower right quadrant was present in all 60 patients, anorexia in 54(90%), nausea and vomiting in 59(98.33%), and low right quad-

Table 2. Demographic, clinical and laboratory characteristics of the study population

Characteristics of the analyzed patients(N = 60)	
Age (years)	35.86±15.15(15 - 77)
Males	36.11±17.10 (63.33%)
Females	35.44±11.40 (36.67%)
Time of onset of symptoms (in hours)	42.616667(3-180)
Migration pain in RLQ	30(50%.)
Anorexia	54(90%)
Nausea / vomiting	59(98.33%)
Palpatory sensitivity in RLQ	60(100%)
Rebound palpatory sensitivity	34(56.67%)
Diffuse abdominal pain	16(26.6%)
Raised temperature (≥37.3°C)	24(40%)
Leukocytosis(10^9/ l)	14.01±3.7 (5.1-22.9)
Differential neutrophils (75% neutrophils)	76.41±15.98 (11.1-94%)
CRP (mg / l)	82.45±81.98 (0.2-320)
Ultrasonography	
Acute	78.33%
Normal	21.66%

rant pain in 14(23.33%) patients. Migration pain as the first symptom was present in 30 patients. Rebound palpatory pain was present in 34(56.67%) patients. Elevated body temperature (≥37.3°C) was present in 24(40%) patients (Table 2). Of the total number of respondents, 26(43.3%) underwent classical surgery, while the remaining 34(56.6%) underwent laparoscopic surgery.

Table 3 shows that 95% of operated patients were positive for AA in relation to HP finding. Eighty percentages of patients were operated on for timely appendectomy, 15% for delayed diagnosis, and 5% for unnecessary appendectomy.

Regarding leukocyte values, the highest mean was in timely gangrenous appendectomies (15.08±3.76), and the lowest in unnecessary appendectomies (7.90±2.43), while in the neutrophils, no statistically significant difference was observed. The highest mean value for CRP was in timely gangrene appendectomies (107.21±83.10) and the lowest in unnecessary appendectomies (14.40±9.58) (Table 4).

Table 3. Histopathological findings

Histopathological findings	Number	Percentage %
Normal AA	3	5
Phlegmonous AA	32	53.3
Gangrenous AA	16	26.6
Phlegmonous perforated AA	2	3.33
Gangrenous perforated AA	7	11.6

Table 4. Association of inflammatory markers with histopathological finding

	Histopathological findings				
	On-time Phlegmonous N=32	On-time Gangrenous N=16	Delayed Perforated N=9	Unnecessary N=3	p
Leukocytes	13.97 ± 3.67	15.08 ± 3.76	14.29± 2.62	7.90 ± 2,43	0.020
Neutrophils	75.07± 19.35	82.10 ± 9.00	77.17 ± 6.66	58.10± 12.41	n.s.
CRP	72.05 ± 89.19	107.21 ± 83.10	98.16 ± 46.03	14.40 ± 9.58	0.011

Table 5. Ultrasonographic finding and scoring systems

	Ultrasonography		
	Negative N=13	Positive N=47	p
Alvarado	8.38 ±1.04	8.29 ±1.24	n.s.
AIR	8.07±1.75	7.94 ± 1.69	n.s.
RIPASA	10.42±1.45	10.67 ±1.89	n.s.
Tzanakis	7.85±1.52	12.91 ±1.84	0.000

Of the preoperatively performed US examinations, 77.2% of those with positive HP findings were diagnosed with appropriate and 22.8% had an inappropriate US diagnosis. Only at the Tzanakis score there was a statistically significant difference concerning positive and negative US findings (Table 5).

The distribution of patients according to the values of the four scoring systems (Table 6) showed that the largest

Table 6. Distribution of patients concerning recent histopathological finding

	Scores				Histopathological findings		
	Alvarado	AIR	Tzanakis	RIPASA	AA	late	unnecessary
< 7	4 (6.67%)	12 (20%)	5 (8.33%)	0	2 (3.33%)	0	2 (3.33%)
7– 8	27 (45%)	28 (46.67%)	0	5 (8.33%)	20 (33.33%)	6 (10%)	1 (1.66%)
> 8	29 (48.33%)	20 (33.33%)	55 (91.66%)	55 (91.66%)	26 (43.33)	3 (5%)	0

number of patients (28) was in group of 7 to 8 in AIR, while in relation to the other three scoring systems, at the value of almost >8, 29 patients in Alvarado, 55 in RIPASA and Tzanakis.Of all four scoring systems, patients with scores <7 did not receive HP for delayed appendectomies, whereas only two (3.33%) had unnecessary appendectomy according to HP findings. Most patients with delayed appendectomies were in the group with 7-8 scoring values. According to the HP findings, the majority of patients were in the group of promptly appendectomies, and that was in the group with scores of >8 present in all three systems (Alvarado, RIPASA, and Tzanakis). Only in the AIR score the highest percentage of promptly appendectomy occurred at the value of score 7-8.

Table 7 shows that according to the obtained HP findings, there was a statistically significant difference in all three systems (Alvarado, AIR, Tzanakis) relative to the histopathological finding, with the highest values obtained in gangrene HP finding (for Alvarado 8.75±1.18, p=0.011; for AIR 8.56±1.67, n=0.007, and for Tzanakis 13.37±2.42, n=0.004), whereas in RIPASA there was no statistically significant difference in baseline values with HP findings.

Table 7. Association of scoring systems (Alvardo, AIR, RIPASA, and Tzanakis) with histopathological finding

| | Histopathological findings | | | | |
	On-time Phlegmonous N=32	On-time Gangrenous N=16	Delayed Perforated N=9	Unnecessary N=3	p
Alvarado	8.34 ± 1.06	8.75± 1.18	8.11± 1.27	6.33 ± 0.58	0.011
AIR	7.93± 1.64	8.56± 1.67	8.00 ± 1.00	5.00± 1.00	0,007
RIPASA	10.64 ± 1.81	11.22 ± 1.89	10.00 ± 1.44	9.00 ± 1.00	n.s.
Tzanakis	11.34 ± 2.77	13.37 ± 2.42	10.67 ± 2.65	12.00 ± 1.73	0.004

Discussion

Appendectomy is one of the most common procedures in general surgery. The overall incidence of AA ranges around 8.6% for men and 6.7% for women. The lifetime risk of possible appendectomy is about 12% in men and 23% in women [1-3]. In our study, a higher percentage of the total number of patients was male (63.33%). Men do not differ significantly from women in the outcome of appendicitis as a definitive diagnosis based on a HP finding.

In our study, the average age of the patients was 35.86 ±15.15 years and correlated with the results found in the literature. Forty percentages of the patients were >39 years of age, which did not correspond to the distribution in other studies [20]. We consider that as a tertiary institution we take care of patients from both primary and secondary health care centers from where this adult population is most often referred to our facilities. Concerning clinical manifestation, palpatory pain sensitivity in LRQ was present among all 60 patients, followed by nausea-vomiting in 59, and anorexia in 54. These data coincide with the data from the literature [2,3], confirming the fact that this triad of symptoms and signs (LRQ pain, anorexia, nausea and vomiting) should give rise to a suspicion of a AA diagnosis.

Acute appendicitis as a surgical problem is also associated with an acute-phase inflammatory response. Blood tests are often unclear. In our study higher values of the leukocyte >10,000 mm3 were present in 50(83.34%) patients. In relation to the histopathologic findings statistically significant highest leukocyte count of 15.08± 3.76 was found among the gangrenous appendectomies, while the lowest among the unnecessary appendectomies (7.90±2.43). A similar result was shown in the study of Zuhoor K. *et al.* [21].

The high value of CRP is associated with the highest percentage of inflamed appendixes. In our study, the high CRP value supported the surgical diagnosis. Significantly higher CRP was characteristic of promptly gangrene appendectomies, while the lowest for unnecessary appendectomies (107.21±83.10 g/l; 14.40±9.58 g/l, p=0.011). These results correlate with results in the literature regarding inflammatory appendectomies [11,22]. There are several studies in the literature about the importance of CRP value, which has undoubtedly high specificity and sensitivity. Yokohama *et al.* clearly confirm that CRP levels can predict the severity of AA and consequently the mode of treatment [23].

Preoperative US examination showed that 78.3% of patients had a positive AA, while 21.7% had a normal appendix. According to the obtained HP findings, in 77.2% of the cases it was appropriate and in 22.8% it was inappropriate US diagnosis. In terms of scores, however, only Tzanakis showed a statistically significant difference in negative versus positive US findings. The data in the study by Chafri S. *et al.* differ in the percentage of unnecessary appendectomies (15%) [24]. However, diagnostic modalities such as US or CT in developing countries can significantly increase healthcare costs [10-15].

The length of hospitalization in our study was 4.42±2.93 days with a shorter mean compared to literature data. In the Cochrane Database the mean length of hospital stay for unnecessary appendectomies is 21.4 and for delayed appendectomies 14.7 [25]. Thus, the overall hospital stay of patients with unnecessary appendectomies is longer than those with delayed appendectomies, which differs in our study where the median value of unnecessary was 3 days and that of delayed 4.11.

According to the HP findings, the majority of cases were with phlegmonous AA 48(80%), followed by a finding of perforated AA 9(15%), and the least with normal AA 3(5%). In the study of Arif E. *et al.*,of 1255 patients, 70.1% were phlegmonous, 11.8% were perforated, 6.06% were negative, and 12.03% with other pathology [26]. The study by Shafri S. *et al*, however, finds that it is not necessary to send all samples for HP analysis to avoid unnecessary expense, thereby reinforcing the need for a more accurate diagnosis. In our Institution per-protocol, each sample obtained as a result of appendectomy is sent for HP analysis. Our practice supports the study of Anel B. *et al.*, according to which sending all samples for HP analysis enables the diagnosis of malignancy present in 1% of a patient who often presents as a neuroendocrine tumor of the appendix, adenocarcinoma or mucinous [27].

The scoring system should contain simple parameters to assist in the treatment decision-making process. The purpose of scoring systems is to make a difference between AA and non-specific abdominal pain.

Difficulties in the differential diagnosis of AA, especially in atypical presentations, lead to the risk of appendicular perforation and more severe infections (abscess,

sepsis), which increases morbidity and mortality [5-12]. On the other hand, due to inadequate diagnosis, negative or unnecessary appendectomies are on the rise, ranging from 20% to 40 % [5-7]. Good clinical assessment of the surgeon is considered an important prerequisite for the diagnosis of AA [13]. In our study regarding HP findings, the largest number of unnecessary appendectomies occurred in the group with values <7 (only in 2(3.33%) patients). Regarding the number of delayed appendectomies, the majority of patients were in the 7-8 group (6 patients), as well as three in the scoring group >8. The largest number of promptly appendectomies was in patients with a score of >8. Distribution of patients according to the height of the scoring values showed that in all 3 scales (Alvarado, RIPASA, and Tzanakis) the highest values were in the group of >8, except in the AIR score where the distribution was highest in the group of values of 7-8. Regarding the values of the scores according to the obtained HP findings, there was a statistically significant difference in all three scores (Alvarado, AIR, Tzanakis), with the highest values obtained in gangrene HP finding (for Alvarado 8.75±1.18, p=0.011; 8.56±1.67, n=0.007, and for Tzanakis 13.37±2.42, n=0.004) where as in RIPASA there was no statistically significant difference in the baseline values with the histopathological finding.

Most of the studies show dominance of Alvarado score and the same corresponds to our study, however when only using this scoring system, it shows some disadvantages. According to the study of Klan and Rehman [28], the Alvodaro score is a simple test that depends on the presence and absence of variables involved in the test. A more recent systematic review of S.A. Kabir *et al.* points to the fact that this test is difficult to apply to women of childbearing age and to children [7]. In many studies, as well as in the study of Karami *et al.*, the RIPASA scoring system is more sensitive and specific than the Alvarado score, AIR and Tzanakis score where CRP and US are used in addition to clinical and laboratory parameters, providing better statistical data in the diagnosis of AA. However, the combined use of two or more scoring systems provides better statistics in reducing the percentage of unnecessary appendectomies. The importance of scoring systems is also seen in the fact that they are already incorporated into recommendations for the diagnosis of AA [29].

One of the limiting factors of our study is the analysis of a smaller number of patients, thus limiting the possibility for significant conclusions. Regarding the results of the US findings, the second limiting factor is that in our institution, patients are examined by different radiologists, with subjectivity present in their diagnosis, but a factor which, given the emergency of the condition, could not be limited to a single radiologist.

Conclusion

Scoring systems are useful in the early diagnosis of AA in the indication for appendectomy. The proper single or combined use of multiple scoring systems in the diagnosis of AA contributes to a decrease in the percentage of unnecessary and delayed appendectomies. The use of scoring systems, their simple design, and simple applicability, allows to reduce the rate of unnecessary appendectomies, as well as to enable faster diagnosis and reduction of delayed appendectomies.

Conflict of interest statement. None declared.

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