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Differentiation of inflammatory from non-inflammatory causes of acute scrotum using relatively simple laboratory tests: Prospective study

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Children

Abstract *Objective:* The differential diagnosis of an acute scrotum is of great importance in clinical practice and may be difficult in some cases. The aim of this study was to differentiate inflammatory from non-inflammatory causes of acute scrotum using relatively simple laboratory tests which can be performed quickly and easily outside a hospital setting.
Patients and methods: From 2007 to 2010, 85 boys with acute scrotum were included in this prospective study. There were 28 boys with inflammatory and 57 with non-inflammatory causes. We investigated the role of erythrocyte sedimentation rate, C—reactive protein, leukocyte, white blood cell differential count, alkaline phosphatase, creatine kinase and child's age in differential diagnosis of the acute scrotum, differentiating inflammatory from non-inflammatory causes of the disease. We used receiver operating characteristics (ROC) analysis and logistic regression analysis.
Results: Statistically significant parameters in accurate differentiation between inflammatory and non-inflammatory causes of the acute scrotum were C-reactive protein ($p = 0.001$) and child's age ($p < 0.001$). These two parameters yielded the probability of an inflammatory outcome in the etiology of acute scrotum with sensitivity of 75% and specificity of 69.1%.
Conclusion: C—reactive protein and child's age are helpful in differentiating inflammatory from non-inflammatory causes of the acute scrotum.

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Introduction

Acute scrotal pain is a common pediatric surgical emergency. Acute scrotum is defined as an acute painful swelling of the scrotum or its contents accompanied by local signs and general symptoms [1]. The differential diagnosis of an acute scrotum includes spermatic cord torsion, torsion of testicular appendage, acute epididymitis, trauma, incarcerated hernia, hydrocele, testicular tumors, idiopathic scrotal edema and testicular infarction [1–3]. The acute scrotum is a diagnostic dilemma because of its diverse etiologies and the extreme tenderness over the area that makes clinical examination difficult. Torsion of the spermatic cord is of major concern because it requires immediate surgical intervention. The incidence of spermatic cord torsion among patients with acute scrotum varies from 18% to 45% depending on the age of the patient [4]. The diagnosis of spermatic cord torsion has to be made within the first 4–6 h, as otherwise the condition can lead to irreversible ischemic injury to the testis, especially if complete spermatic cord torsion is presented [5]. Current diagnostic methods are non-specific, time consuming, and not always available, resulting in loss of diagnostic time [5,6]. Additionally, blood samples are routinely obtained in patients with an acute scrotum. During infection or tissue injury, the elevated white blood cell (WBC) count and erythrocyte sedimentation rate (ESR) are accompanied by alteration in the concentrations of several serum proteins [6].

The aim of this study was to differentiate inflammatory from non-inflammatory causes of acute scrotum using relatively simple laboratory tests: C-reactive protein (CRP), WBC count, WBC differential count, alkaline phosphatase (ALP), creatine kinase (CK) and ESR, which can be performed quickly and easily outside a hospital setting.

Patients and methods

Patients

From 2007 to 2010, 85 children operated on for acute scrotum, in the Department of Pediatric Surgery, University Hospital Split, were enrolled in this prospective study. Patients with a known condition of the immune system as well as those on immunosuppressive or non-steroidal anti-inflammatory medications were excluded ($n = 4$). Mean age at the time of diagnosis was 11.2 years (range 6 months–18 years). The diagnosis was based on history, physical examination, routine blood and urine tests, and operative exploration. There were 28 boys (33%) with epididymitis, 13 (15%) with testicular torsion and 44 (52%) with torsion of testicular appendage. The patients were divided into two groups: inflammatory causes (28) and non-inflammatory (testicular torsion and torsion of testicular appendage) causes (57).

Laboratory parameters

ESR was determined in all patients before therapeutic interventions using the modified Westergren method. White blood cell count and white blood cell differential count were analyzed using an auto blood analyzer (Advia 2120, Bayer, Germany). ALP, CK and CRP were analyzed using the Abbott Architect (Abbott, USA). CRP was measured using turbidimetric analysis. The blood samples were centrifuged for 10 min at 4000 rpm. The turbidity, resulting from the reaction between serum and the specific antibody, was measured by the photometric method.

Statistical analysis

The data were analyzed using the Mann–Whitney and Chi-square tests (Statistica for Windows Release 10.0, Statsoft, Tulsa, OK, USA). Differential diagnosis between inflammatory and non-inflammatory causes of the acute scrotum was considered to determine a cut-off point for each investigated parameter using receiver operating characteristics (ROC) curves. Diagnostic parameters were calculated using routine equations. All p values less than 0.05 were considered to indicate statistical significance.

Results

A total of 85 patients with acute scrotum were operated on because of suspicion of testicular torsion, and divided into two groups based on final diagnoses (Table 1).

Table 1 Comparison between two groups of patients with acute scrotum.

Patient parameter	Median (range)		
	Inflammatory cause ($n = 28$)	Non-inflammatory cause ($n = 57$)	p[a]
CRP (mg/L)	3.25 (0.2–57.7)	1.25 (0.1–55)	0.001
ESR (mm/h)	7.5 (1–34)	8 (1–35)	0.69
ALP (U/L)	189 (74–245)	184 (52–278)	0.779
CK (U/L)	116 (63–316)	130.5 (48–755)	0.05
Age (years)	12.5 (5–18)	10 (0.1–16)	<0.001
Duration of symptoms (h)	24 (6–150)	24 (3–240)	0.509
WBC ($\times 10^9$)	8 (5.1–19.1)	9.4 (5.3–23)	0.038
Neutrophils (%)	67.25 (48–85)	59 (27–88)	0.015
Lymphocytes (%)	22.5 (8–39)	29 (8–60)	0.008
Monocytes (%)	7 (0–11)	7 (2.5–12.3)	0.811
Basophils (%)	0.8 (0–9)	0.5 (0–11)	0.599
Eosinophils (%)	2 (0–5)	1.5 (0–10)	0.914

[a] Mann–Whitney test.

Of the group with inflammatory causes of acute scrotum, an increase in serum CRP level was seen in 18 patients (64%). In contrast, only 15 children (26%) with non-inflammatory causes of acute scrotum showed a significant increase in serum CRP level. Of the children with inflammatory causes an increase in serum neutrophil level was seen in 10 (35%), while 11 children (19%) with non-inflammatory causes showed a significant increase in this parameter.

Mean age at time of diagnosis was 2.5 years older in children with inflammatory causes of acute scrotum ($p < 0.001$). An at least 2.6-fold increase in the serum CRP level was seen in children with inflammatory causes ($p = 0.001$). The parameters of ESR, WBC, differential WBC count, ALP and CK were less sensitive and specific (Table 1).

There were no difference in duration of symptoms between the compared groups ($p = 0.509$). Mean duration of symptoms was 24 h, with range 6—150 h for children with inflammatory causes and 3—240 h for those with non-inflammatory causes.

According to ROC curves, the best cut-off points for differentiation between epididymitis and non-inflammatory causes of the acute scrotum were 2.35 mg/L for CRP, 61.5% for neutrophils and 11.5 years for age (Fig. 1). The sensitivity for CRP, neutrophils and age was 75%, 75% and 67.9%, respectively. Specificity for CRP, neutrophils and age was 69%, 59.6% and 61.4%, respectively (Table 2).

The inflammatory etiology of acute scrotum is 3.2-fold more common in children older than 11.5 years of age, 2.1-fold more common in children with neutrophils over 61.5%, and 6.7-fold more common in children with a CRP value greater than 2.35 mg/L. Using multiple logistic regression, we found that CRP ($p < 0.001$) and age of the child ($p = 0.031$) were associated with inflammatory outcome (Tables 3 and 4).

Discussion

Testicular pain or swelling, often referred to as the acute scrotum, has a number of causes. The history and physical examination can significantly narrow the differential diagnosis of an acute scrotum, if not establish the exact cause [2,4]. None of the conditions responsible for acute scrotal pain or swelling has a single pathognomonic finding, but the combined background information and physical findings frequently suggest the correct diagnosis. The exact diagnosis is of great importance since therapeutic consequences vary with respect to the cause of the condition [2,4—7].

Imaging studies have been devised for correct diagnosis and in order to overcome the problem of misdiagnosing testicular torsion as epididymitis and vice versa. Real-time ultrasound, Doppler ultrasound, testicular scintigraphy and magnetic resonance imaging are important modalities in confirming the clinical assessment, but are often not available in an emergency, especially at night [6,8—16].

In the present study, we evaluated the diagnostic accuracy of CRP, WBC count, WBC differential count, ALP, CK and ESR in patients operated for acute scrotum. These parameters are quickly and easily accessible for analysis, which is extremely important, because unnecessary loss of time in determining the correct diagnosis can be devastating in the case of a child's testis.

The values of ESR and CRP increase in the case of an inflammatory cause of acute scrotum [5,6]. Asgari et al. investigated the diagnostic accuracy of CRP and ESR in 120 patients with an acute scrotum, age range 1—86 years. They found a statistically significant difference in CRP and ESR values between patients with inflammatory and non-inflammatory causes of acute scrotum ($p < 0.001$). The patients with epididymitis had higher CRP and ESR values than others. According to ROC curves, the best cut-off points for differentiation between epididymitis and non-inflammatory causes of acute scrotum were 24 mg/L for CRP and 15.5 mm/h for ESR, with specificity of 100% and sensitivity of 93.4% for ESR and specificity of 85% and sensitivity of 95.6% for CRP [5]. Doehn at al. investigated the value of acute phase proteins in serum and plasma of 104 patients with an acute scrotum, age range 13—85 years. They found that patients with epididymitis showed an at least 4-fold elevation of CRP. In these patients, the sensitivity for CRP was 96.2% and specificity was 94.2%. The

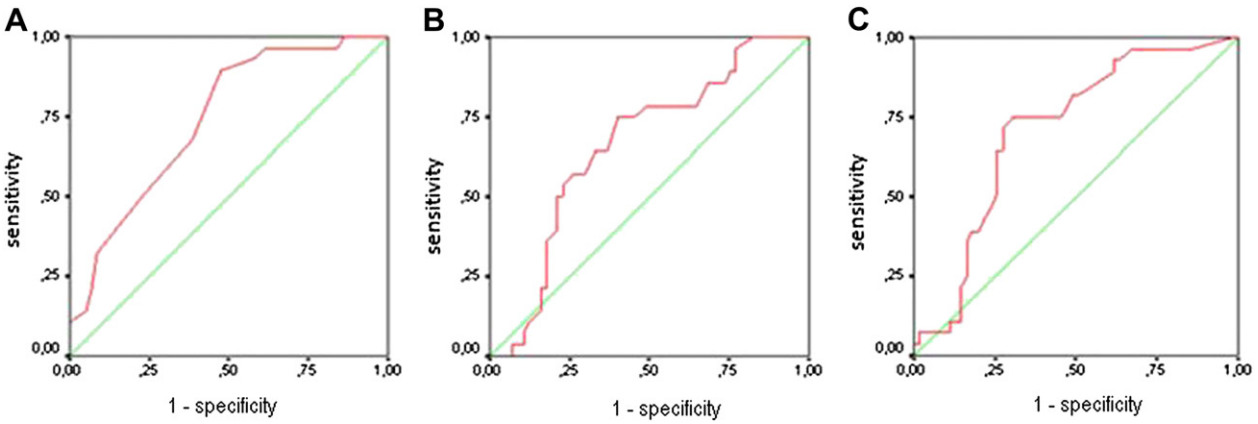

Figure 1 ROC curves. (A) Age = 0.741, 95% CI (0.634—0.847), $p < 0.002$. (B) Neutrophils = 0.663, 95% CI (0.544—0.783), $p < 0.015$. (C) CRP = 0.708, 95% CI (0.594—0.822), $p < 0.001$. CI = confidence interval.

Table 2 ROC results for diagnostic parameters of CRP, neutrophils and age.

Parameter	Cut-off	Sensitivity (%)	Specificity (%)	*p*
CRP (g/L)	2.35	75	69	<0.001
Neutrophils (%)	61.5	75	59.6	<0.015
Age (years)	11.5	67.9	61.4	<0.002

difference between patients with epididymitis and those with non-inflammatory conditions was statistically significant ($p < 0.001$).The best cut-off point for CRP was 24 mg/L. The remaining investigated parameters (haptoglobin, fibrinogen, alpha1-acid glycoprotein, transferrin, WBC, body temperature) were less sensitive and specific [6]. Chiang et al. investigated etiology and the clinical features of testicular torsion and epididymo-orchitis in infants younger than 3 months. They concluded a high suspicion for epididymo-orchitis in patients with abnormal physical signs and laboratory findings [17].

In our study, there were 85 boys, in two groups, with age range 6 months—18 years. Using ROC analysis and logistic regression, we found that the age of the child and CRP are statistically significant parameters in the differentiation of epididymitis and non-inflammatory causes of an acute scrotum. The parameters of ESR, WBC, differential white blood cell count, ALP and CK were less sensitive and specific. To the best of our knowledge, this is the first such study to use logistic regression for statistical analysis and the first to be limited only to the pediatric population.

The differential diagnosis of the acute scrotum in children is challenging. Physical examination and history are sometimes of little help. While most diagnostic tests are not precise or are not always available in the limited golden time for diagnosis of this condition, child age and serum level of CRP can provide helpful information easily and rapidly. Our findings confirm that these tests can be helpful in the differentiation of acute epididymitis from other non-inflammatory causes of acute scrotum. We suggest CRP measurement in all children before making the decision to perform surgery. However, in the case of any doubt, all patients should undergo an operative exploration to exclude testicular torsion.

Table 3 Results of logistic regression.

	Cut-off	Odds ratio[a]	*p*
Age (years)	<11.5 >11.5	2.8 (1.29—8.3)	0.048
Neutrophils (%)	<61.5 >61.5	2.07 (0.66—6.45)	0.212
CRP (g/L)	<2.35 >2.35	5.56 (1.84—16.8)	0.002

[a] Odds ratio with 95% CI for inflammatory outcome.

Table 4 Results of multiple logistic regression.

	Cut-off	Odds ratio[a]	*p*
Age (years)	<11.5 >11.5	3.2 (1.11—9.1)	0.031
CRP (g/L)	<2.35 >2.35	6.7 (2.3—19.5)	<0.001

[a] Odds ratio with 95% CI for inflammatory outcome.

Conflict of interest statement

Jakov Meštrović and other co-authors have no conflict of interest.

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