

Role of Doppler Ultrasonography and C-Reactive Protein in Patients with Acute Scrotum

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Abstract

This research was designate with an intention to find the role of Doppler ultrasonography (DUS) and C-reactive protein (CRP) in patients with acute scrotum. A sum of 80 (mean age 23±2.1 years) consequential patients were recruited for a period of six months between July 2015 and January 2016 in this prospective study. Collected data confined age, medical history, and clinical symptoms. DUS was performed with a linear array transducer (10-15 MHz) connected to HI vision Avius ultrasound unit; Hitachi. CRP was measured using turbidimetric analysis through the Cobas Integra analyzer system (Test CRPL2, 0-293); Roche Diagnostics. Statistical analysis was accomplished using the standard Statistical Package for the Social Sciences version 20 for Windows; Microsoft. Fitted achievement values for DUS in the diagnosis of testicular torsion, epididymo-orchitis, and varicocele were respectively 100%, 91% and 88% for sensitivity, 92%, 71%, and 90% for specificity, and 94%, 83%, and 89% for accuracy. An increased in the serum CRP level (63.2±40.2 mg/L) was seen in an inflammatory cause of the acute scrotum. In contrast, there was no increase in CRP level (8±3.1 mg/L) in the non-inflammatory cases ($P < 0.0001$). Scrotal DUS is a highly precise preoperative diagnostic instrument, thereby confirm its course application in the incipient triage of patients with acute scrotum. Serum level of CRP can afford useful advice for differentiation between inflammatory and other reasons of the acute scrotum.

Keywords: acute scrotum, c-reactive protein, Doppler ultrasonography

1. Introduction

Acute scrotum assigns to the abrupt attack of scrotal erythema, swelling, or ache. Its a frequent onset in the casualty department (Aso et al., 2005; Günther & Rübben, 2012; Remer et al., 2012). A watchful historiology, a perfect physical exploration, and suitable diagnostic judgment can essentially pinch the discriminating diagnosis. The variety of etiologies narrated to this clinical appearance companion the diagnosis a perplexed one, and an unbiased and trustworthy imaging process is required (Yagil et al., 2010). The most ordinary discriminating diagnoses of the acute scrotum contain torsion of the spermatic cord and acute epididymitis or epididymo-orchitis. Less frequent diagnoses comprehend: Strangulated hernia, segmental testicular infarction, testicular tumor, and idiopathic scrotal edema (Esposito et al., 2012; Rebonato, D'Andrea, & Scialpi, 2013).

Prompt diagnosis is needed to discriminate surgically correctable lesions from abnormalities that can be

adequately satisfied with medical therapeutics alone. Clinical symptoms and physical investigation are often not enough for determinate diagnosis due to ache and swelling that hindrance a correct palpation of the scrotal contents. For patients coincided with a scrotal mass, it is important to determine whether the mass is inside or outside the testicle. This is necessary since most of lesions found in the testicle are malignant, while other lesions found outside the testicle are commonly benign (D'Andrea et al., 2013). In practice, early differentiation of spermatic cord torsion from acute epididymitis is of utmost importance. Differentiation of these two conditions is sometimes challenging; detection of spermatic cord torsion must be made within the first 4 to 6 hours, otherwise it can induce an irrevocable ischemic damage to the testis and destruction of gonads, particularly in case a whole spermatic cord torsion, i.e., a 720-degree rotation, is present. Physical examination and history can make the diagnosis in two-thirds, but in one third of patients with acute scrotum, further assessments such as laboratory studies and imaging would be required (Kogan, Hadziselimovic, Howards, Huff, & Snyder, 2002; Schneck & Bellinger, 2002).

Ultrasound affords valuable anatomical detail; when color and power Doppler appearance are added, testicular perfusion can be evaluated (D'Andrea et al., 2013). Doppler ultrasonography (DUS) is a safe examination that deficiency ionizing radiation and is highly accurate in the exploration of intra-scrotal abnormalities; therefore, it is proposed currently the first exploration modality for the examination of the acute scrotum. A DUS study include gray scale appearance, color, and spectral Doppler flow of the scrotal lining, primarily the testis and epididymis. By empowering the discrimination between surgical emergencies, such as testicular torsion and traumatic testicular rupture, which bidding direct scrotal examination to preclude testicular detriment, and surgical non-emergencies and nonsurgical entities, scrotal DUS has befit the authoritative diagnostic proof on which the curative access in patients with acute scrotum is supported (Schalamon et al., 2006; Vijayaraghavan, 2006; Hamm, 1997).

An infectious or inflammatory process can alter the serum levels of acute-phase proteins and erythrocyte sedimentation rate (ESR), and so do the irritating sources of the acute scrotum. This may help early diagnosis; however, the value of these nonspecific inflammatory parameters has not been elucidated yet. In a retrospective study on 104 patients with acute scrotum, it was shown that serum level of C-reactive protein (CRP) is an assistant in discriminating epididymitis from noninflammatory circumstances resembling spermatic cord torsion or neoplasm (Asgari et al., 2006; Doehn et al., 2001).

However, the literature lacks ample prospective evaluation. This research was designated with an intention to find the role of DUS and CRP in patients with acute scrotum.

2. Method

2.1 Study Population

After receiving approval from the local ethics committee, a sum of 80 consequential patients presenting with acute scrotum in the area of the study, were recruited sonographically for a period of six months between July 2015 and January 2016 in this prospective cohort study. Informed consent was given for this research in accordance with institutional guidelines. Laboratory investigation of C-reactive protein level in patients with acute scrotum was conducted.

Patients with an acute scrotum visited within the first 24 hours of pain initiation were enrolled. The exclusion criteria were the existence of one of the subsequent circumstances: Patients with an understood state of the immune system as well as those on immune-suppressive or non-steroidal anti-inflammatory medications, acute myocardial infarction, burns, anemia, congestive cardiac failure, multiple myeloma, and scrotal mass.

Collected data confined age, medical history, and clinical symptoms. The patients were treated correspondingly to history, physical investigation, laboratory exams, scrotal ultrasonography, and respond to manual detorsion maneuver if required. Serum level of CRP was measured at the time of admission.

2.2 Doppler Ultrasonographic Examination

Scrotal ultrasound using brightness mode (B-mode) with high frequency and color Doppler were performed in patients using a linear array transducer (10-15 MHz) connected to HI vision Avius ultrasound unit; Hitachi (Figure 1). Lower resolution linear array (4-8 MHz) and convex (3.5 MHz) probes were employed for examinations of swollen scrotums. Initial examination was executed under high gain (80 dB to 90 dB) and low gain (60 dB to 70 dB) sensitivity for more detailed inspection during ultrasonography.

B-mode begin in the inguinal canal on the symptomatic side and expand along the spermatic cord to terminate in the scrotum. Scanning in the long axis and short axis view was done. Examinations were accomplished with the patient supine on transverse and longitudinal scrotal axes. On B-mode, the testis and epididymis size, texture,

and focal findings were rated and compared with the contralateral testicle. Doppler ultrasound was applied to confirm and describe the arterial and venous blood stream in the testes and epididymis (Yagil et al., 2010; Vijayaraghavan, 2006).

Ultrasound scanning was conducted on a 24 hour basis by the same Sonologist in the area of the study, to avoid any bias or faulty results. For the intend of this research, the results of all scrotal DUS examinations executed during the duration of the study were collected and reconsidered, with specific concentration on the features of testicular torsion, orchitis, epididymitis, detorsion, testicular trauma, scrotal edema, hydrocele, and varicocele (Vijayaraghavan, 2006).

The subsequent characteristic features were searched for: Tortuosity of the cord, an acute alter in the direction of the cord, and appearance of the whirlpool sign. Whirlpool sign was considered in the following aspect: When tortuosity of the spermatic cord was present and a transverse scan of the cord above the area of tortuosity was gained. Then the probe was moved down along the cord, and a rotation of the cord constructions was checked. Positive whirlpool sign considered when an acute rotation is detected. If the location and the axis of rotation of whirlpool sign was not detected, the same maneuver was repeated in all likely angles of the tortuous cord (Yagil et al., 2010; Vijayaraghavan, 2006). Ultrasonographic signs for testicular torsion were testicular swelling, reduced echogenicity, and lack or decreased testicular blood supply. On the other hand, testicular lesions with increased or decreased echogenicity beside the absence of internal blood supply and intact tunica albuginea were the characteristic features of testicular hematoma (Vijayaraghavan, 2006). Also sonographic features of both the testicle and epididymis were observed (Yagil et al., 2010; Vijayaraghavan, 2006).



Figure 1. Hitachi (HI vision) Avius ultrasound unit

In case a hydrocele was detected, its character was noted. Then the same protocol was iterated using color flow imaging. Spectral Doppler was done in appropriate pathological conditions. The same process was conducted on the other side and extra-testicular scrotal findings were also searched for.

2.3 C-Reactive Protein

After DUS, CRP was deliberated using turbidimetric analysis using Cobas Integra analyzer system (Test CRPL2, 0-293); Roche Diagnostics for the quantitative immunological determination of human CRP (Figure 2).



Figure 2. Cobas Integra analyzer system (Test CRPL2, 0-293; Roche Diagnostics, Switzerland)

The blood specimen were centrifuged for 10 minutes at a rate of 4000 rev/min. The turbidity resulted from the interaction between the serum and the particular antibody for CRP, was measured using the photometric manner (Meštrović et al., 2013; Pakzad, 2001). The reference ranges were less than 8 mg/L for adults and less than 10 mg/L for children (Pakzad, 2001).

2.4 Clinical Evaluation

Conservative or surgical direction after the clinical appraisalment and DUS examination was assessed. Surgical recite, lesion findings, and conclusive diagnoses were recorded. The DUS finding was compared to the terminal diagnosis to decide whether the preoperative diagnosis was accurate or had been confined in the discriminating diagnosis.

2.5 Data Analysis

The results were summarized as mean \pm SD in a form of comparison tables. Analysis was accomplished by applying the standard Statistical Package for the Social Sciences (SPSS) version 20 for Windows; Microsoft. A *P*-value < 0.0001 was considered significant.

3. Results

In this prospective cohort study a sum of 80 patients presented with acute scrotum were investigated using scrotal DUS. In addition, serum CRP level was measured individually in each case. The mean age of the patient's \pm SD was 23 \pm 2.1 years (age ranges from 18 up to 65 years). Results concerning medical history and clinical presentations of the patients were presented in Table 1.

Table 1. Medical history and clinical presentations in patient with acute scrotum

Medical history and clinical presentation	Frequency	Percentage
Medical history		
None	31	39%
Inguinal hernia repair	9	11%
Trauma	23	29%
Hydrocelectomy	17	21%
Clinical presentation		
Nausea/vomiting	17	21%
Fever/rigors	29	36%
Dysuria	11	14%

Scrotal pain	78	98%
Scrotal swelling	37	46%
Scrotal erythema/edema	16	20%
Absent cremasteric reflex	7	9%

An overview of the results of the radiological imaging studies was given in Table 2. The sonographic diagnosis was testicular torsion in 6 (8%) patients. A small amount of hydrocele was detected in 2 (33%) these patients. On color flow imaging, there was an absence of intratesticular blood flow. These patients underwent surgical exploration, which revealed the presence of testicular torsion.

Ten patients had features of testicular hematoma, which disclose a non affected testis and hematoma of the scrotum. Two cases were represented scrotal hematoma weren't accompanied by testicular hematoma was documented sonographically. There were distinctive signs of epididymo-orchitis in 13 (16%) patients with a rapid blood flow on color flow imaging for the epididymis and testis. The malady affected the left testis in 4 (31%) and the right testis in 9 (69%) patients. Five of the 13 patients underwent surgical procedure and were assured to have epididymo-orchitis. Conservative management was applied appropriately to treat the rest of the patients.

Table 2. DUS findings in patients with acute scrotum

DUS findings	Frequency	Percentage
Testicular torsion	6	8%
Testicular abscess	2	3%
Testicular hematoma	10	13%
Testicular rupture	3	4%
Orchitis	21	26%
Epididymitis	11	14%
Epididymo-orchitis	13	16%
Hydrocele	43	54%
Varicocele	9	11%
Scrotal abscess	1	1%
Scrotal hematoma	12	15%
Inguinal hernia	1	1%

Note. DUS=Doppler ultrasonography.

Minimal degree of hydrocele was presented in 43 (54%) patients. In 2 patients affected with a hydrocele, there were features of testicular torsion as was listed previously in the results. Hydrocele was suggested to be developed in the rest 41 (51%) due to other testicular pathologies as the diagnosed 21 (26%) cases of orchitis, 11 (14%) epididymitis and 13 (16%) epididymo-orchitis. Varicolectomy was used to treat 7 (78%) cases of infertile patients. The remaining 2 (22%) patients were treated conservatively and followed clinically.

Eighteen (23%) of the patients acknowledged underwent surgical exploration as shown in Table 3. DUS performance values in the diagnosis of testicular torsion, epididymo-orchitis, and varicocele were respectively 100%, 91% and 88% for sensitivity, 92%, 71%, and 90% for specificity, and 94%, 83%, and 89% for accuracy. Positive predictive value (PPV) was 83% for both testicular torsion and epididymo-orchitis and 88% for varicocele. Negative predictive value (NPV) was 100%, 83%, and 90% for each.

Table 3. DUS findings in patients with acute scrotum

DUS findings	True	True	False	False	Sensitivity	Specificity	Accuracy	PPV	NPV
	+, n	-, n	+, n	-, n					
Testicular torsion	5	12	1	0	100%	92%	94%	83%	100%
Epididymo-orchitis	10	5	2	1	91%	71%	83%	83%	83%
Varicocele	7	9	1	1	88%	90%	89%	88%	90%

Note. DUS=Doppler ultrasonography, PPV=positive predictive value, NPV=negative predictive value.

After DUS, serum CRP level was measured in the inflammatory and non-inflammatory inducers of the acute scrotum, an increased in the serum CRP levels (63.2 ± 40.2 mg/L) was seen in all patients affected with an inflammatory cause of the acute scrotum. In contrast, there was no increase in CRP level (8 ± 3.1 mg/L) in the non-inflammatory causes of acute scrotum as presented in Table 4. The two tailed *P*-value was < 0.0001 and by agreed criteria, this variance was estimated to be exceedingly statistically significant.

Table 4. CRP level in the inflammatory and non-inflammatory causes of acute scrotum

Parameters	Inflammatory causes of the acute scrotum	Non-inflammatory causes of the acute scrotum	<i>P</i> -value
No. of patients	48	84	<i>P</i> <
Mean \pm SD CRP (mg/L)	63.2 ± 40.2	8 ± 3.1	0.0001

Note. CPR= C-reactive protein.

4. Discussion

Acute scrotum is a diagnostic predicament because of the multiform etiologies and excessive regional pain, which constitute a clinical investigation very laborious (Cavusoglu et al., 2005). Differential diagnosis of acute scrotum by history and physical examination is difficult in one-third of patients, mandating a rapid and accurate diagnostic tool (Pakzad, 2001). The history and clinical examination can significantly straitened the discriminating diagnosis of an acute scrotum, if not found the correct cause (Mäkelä, Lahdes-Vasama, Rajakorpi, & Wikström, 2007; Yang et al., 2011). The precise diagnosis is of great importance since curative consequences varied regard to the reason of the state (Asgari et al., 2006; Molokwu, Somani, & Goodman, 2011).

Ultrasound has been related for accurate diagnosis and in a direction to solve the problem of misdiagnosing testicular torsion as epididymitis and vice versa. Different diagnostic radiology modalities are important in confirming the clinical assessment (Rizvi, Ahmad, Siddiqui, Zaheer, & Ahmad, 2011; Cokkinos et al., 2011). Doppler investigation is considered the fundamental diagnostic modality for such evaluations (Buckley & McAninch, 2006). However, there are conditions that may show indecisive outcomes on color Doppler imaging. The torsion-detorsion occurrence may show testicular hyperemia, mocking an inflammatory situation (Ralls, Larsen, Johnson, & Lee, 1991; Middleton, Siegel, Melson, Yates, & Andriole, 1990). Baud et al. (1998) and Arce et al. (2002), found that all these pitfalls happen due to fault assessment of a condition that is induced elsewhere, and they intended to investigate the spermatic cord instantly since positive torsion appears there.

In this study DUS presented a unique ability in detection a wide variety of abnormalities that lead to the development of signs and symptoms that characterized acute scrotum as presented in Table 2. Also the results obtained by DUS in Table 3, helps in identifying pathological cases need instant surgical intervention when the clinical search is indecisive. Where the fitted accomplishment values for Doppler in the examination of testicular torsion, epididymo-orchitis, and varicocele were respectively 100%, 91% and 88% for sensitivity, 92%, 71%, and 90% for specificity, and 94%, 83%, and 89% for accuracy. The PPV was 83% for both testicular torsion and epididymo-orchitis and 88% for varicocele. NPV was 100%, 83%, and 90% for each. Calculated performance values for DUS in this study could be compared to the findings of Guichard et al. (2008) and Buckley et al. (1998). Where DUS had been shown to have 71% to 100% sensitivity and 77% to 80% specificity for testicular injury. In addition, the findings in this study were supported by Baud et al. (1998) and Kalfa et al. (2004), where they examined the spermatic cord in its whole extent, containing the inguinal region, and explained a helical twist of the cord at the outer inguinal ring diagnostic of torsion, independent of the color flow imaging results.

They delineated high specificity and sensitivity of this sign and the degree of inessential surgical intervention was 0%.

There is a high value of CRP in the condition of an inflammatory disorders lead of acute scrotum (Asgari et al., 2006; Doehn et al., 2001). CRP finding is speedily and readily approachable for analysis, which is very essential, as an inessential waste of time in finding the right cause can be withering in the condition of a child's testis (Meštrović et al., 2013). Asgari et al. (2006) and Doehn et al. (2011), described a statistical significant difference ($P < 0.001$) in CRP value among subjects with inflammatory and non-inflammatory inducers of the acute scrotum. They also determine that subjects affected with epididymitis presented an increase of CRP values of 4-fold. The best cutoff values for CPR for discriminating between epididymitis and non-inflammatory inducers of acute scrotum were 24 mg/L, with a specificity and sensitivity of 85% and 95.6% respectively (Doehn et al., 2011). Based on our findings in 80 patients affected with acute scrotum (Table 4), CRP showed a statistically significant difference between inflammatory and non-inflammatory inducers of the acute scrotum. CPR values were 63.2 ± 40.2 mg/L and 8 ± 3.1 mg/L in inflammatory and non-inflammatory inducers of acute scrotum respectively ($P < 0.0001$). Also a CRP elevation of 4-fold was detected in the patients present with inflammatory inducers of acute scrotum as orchitis, epididymitis, and epididymo-orchitis.

This research was limited by a difference factors, firstly its choice bias; thus, the complicity and condition diversity may have been marginally skewed and not generalized. Secondly, clinical follow-up was unavailable for patients; thus, there were no results concerning the achievement of Doppler in this group of cases in need for follow-up. Moreover, and also in view of the size of the sample (80 patients present with features of acute scrotum) that have been studied; the authors find that the obtained results cannot be generalized to the whole of society.

In conclusion, acute scrotum is a complicated situation with a various clinical and ultrasound characters. The usage of fast scrotal DUS at the point of care is very beneficial in acute scrotum. Excellent diagnostic achievement, particularly the high sensitivity, specificity, and accuracy for testicular torsion, epididymo-orchitis, and varicocele confirms the course application of Doppler ultrasound as a preoperative diagnostic instrument in the commencing triage of cases present with acute scrotum. However, most diagnostic trial are not accurate enough or otherwise not practicable in the restricted golden time for the proof of inflammatory and non-inflammatory inducers of acute scrotum, serum level of CRP can afford useful advice readily and quickly.

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Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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