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Research Article

Shear wave elastography in the diagnosis of rhabdomyolysis

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Rhabdomyolysis is a life-threatening skeletal muscle disease, the time of diagnosis and initiation of treatment which directly affects the likelihood of developing acute kidney injury and the quality of recovery of muscle function. The ultrasound method of diagnostics is accessible and can be used at the stage of primary diagnosis, but it has low a sensitivity of 68% and specificity of 57% when using such ultrasound symptoms as a diffuse expressed increase of echogenicity (homogeneous or heterogeneous), a disorder of transverse striation of the muscle structure and high volume of the muscular tissue damage (over 30%).

The possibility of ultrasonic elastography in the diagnosis of rhabdomyolysis in 95 patients admitted with suspected damage to muscle tissue is discussed. Comparison of the parameters of shear wave elastography in patients with rhabdomyolysis and patients with other diseases manifested by muscle edema (muscle contusion, inflammatory myopathies, post-exercise muscle edema), as well as with the control group, significant differences were noted ($p < 0.01$) allows to determine the quantitative ultrasound characteristics of muscle tissue, pathognomonic for rhabdomyolysis. The use of shear wave elastography with obtaining lateral wave velocity of less than 1.64 m/s increased the sensitivity and specificity of the method in the diagnosis of rhabdomyolysis to 75 and 62%, respectively.

A logit model with integrated use of elastography indices was developed, with a diagnostic accuracy of 77%. During muscle recovery, there was an increase in lateral wave velocity to the level of control group values, which can be used as one of the markers of patient recovery.

Keywords: inflammatory myopathies; muscle edema; myalgia; rhabdomyolysis; shear wave elastography; skeletal muscles; ultrasound diagnostics of muscle.

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Научная статья

Эластография сдвиговой волны в диагностике рабдомиолиза

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Рабдомиолиз является жизнеугрожающим заболеванием скелетных мышц, скорость постановки диагноза и начала лечения которого напрямую влияют на вероятность развития острого почечного повреждения и качество восстановления мышечной функции. Ультразвуковой метод диагностики является доступным и может быть применен на этапе первичной диагностики, но имеет невысокие характеристики чувствительности — 68 % и специфичности — 57 % при использовании таких ультразвуковых симптомов, как диффузное выраженное повышение эхогенности (однородное или неоднородное), нарушение поперечной исчерченности структуры мышцы и большой объем поражения мышечной ткани (более 30 %).

Рассматриваются возможности ультразвуковой эластографии в диагностике рабдомиолиза у 95 пациентов, поступающих с подозрением на повреждение мышечной ткани. При сравнении параметров эластографии сдвиговой волны пациентов с рабдомиолизом и пациентов с другими заболеваниями, проявляющимися мышечным отеком (ушибы мышц, воспалительные миопатии, постнагрузочный мышечный отек), а также контрольной группы отмечаются значимые различия ($p < 0{,}01$), что позволяет определить количественные ультразвуковые характеристики мышечной ткани, патогномоничные для рабдомиолиза. Использование эластографии сдвиговой волны с получением значений скорости боковой волны менее 1,64 м/с повысило чувствительность и специфичность метода в диагностике рабдомиолиза до 75 и 62 % соответственно.

Разработана логит-модель с комплексным использованием показателей эластографии, диагностическая точность которой составила 77 %. В процессе восстановления мышечной ткани отмечалось увеличение скорости боковой волны до уровня значений контрольной группы, что может быть использовано как один из маркеров выздоровления пациента.

Ключевые слова: воспалительные миопатии; миалгия; мышечный отек; рабдомиолиз; скелетные мышцы; ультразвуковая диагностика мышц; эластография сдвиговой волны.

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BACKGROUND

Rhabdomyolysis is characterized by the destruction of skeletal muscles, causing the release of intracellular contents into the blood, which can induce life-threatening complications. Although most patients with rhabdomyolysis have a favorable prognosis, acute kidney injury occurs in 7%–10% of them [1]. Studies have confirmed that early diagnostics and timely adequate treatment cannot only prevent complications of rhabdomyolysis but also significantly improve patient prognosis [2, 3].

The diagnosis is made quickly and accurately in the presence of the classic triad of symptoms of rhabdomyolysis, such as myalgia, muscle weakness, and brown urine. However, a similar clinical presentation is noted in <10% of patients at the initial visit. In most cases, the main complaints are local or widespread muscle pain and paresthesia [4]. Thus, the absence of a specific clinical presentation in some situations can underestimate the severity of the patient's condition and late referral to laboratory tests for specific markers of acute muscle damage, namely, creatine phosphokinase (CPK) and blood myoglobin [5].

Studies have reported various signs of rhabdomyolysis during ultrasonography (US), such as muscle thickening, changes in echogenicity, and ground-glass opacity [6, 7]. In this case, US is usually used only to confirm the diagnosis after obtaining laboratory data [8]. However, certain authors present cases where US enabled suspecting acute damage to skeletal muscles with an obliterated clinical presentation, and a blood test of patients was conducted for CPK [9, 10].

US presentation in rhabdomyolysis can vary or not be different from other diseases manifested by edema of muscle tissues, namely, traumatic injuries, inflammatory myopathies, and injuries associated with excessive physical load. Some articles indicate the low specificity of US in detecting muscle edema [7, 11, 12].

The diagnostic characteristics may be increased with the quantitative US technique of shear wave elastography (SWE). It was effective in examining many organs, such as the liver, mammary glands, blood vessels, and prostate gland [13, 14]. SWE is used to diagnose diseases of the musculoskeletal system, such as tendons [15], and some hereditary myopathies [16, 17]. Only a few studies focused on the use of SWE in skeletal muscle lesions [15, 18, 19].

The study aimed to improve the diagnostic efficiency of US in detecting rhabdomyolysis using quantitative SWE.

MATERIALS AND METHODS

All patients provided voluntary informed consent. In total, 95 people were examined. US was performed at primary diagnostics with a clinical presentation of skeletal muscle diseases (complaints of myalgia, limb swelling, and decreased muscle strength).

The patients were divided into two groups. The main group (n = 54) included patients with confirmed acute damage to muscle tissues (increased blood levels of CPK and myoglobin and changes in radiation diagnostic methods). The remaining patients were included in the control group. In the main group, two subgroups were distinguished, namely, patients with confirmed rhabdomyolysis (n = 18) and those with other diseases accompanied by muscle edema (muscle bruises, inflammatory myopathies, delayed-onset muscle soreness, and post-exercise edema). Rhabdomyolysis was verified based on the detection of myoglobinemia of >72 ng/mL.

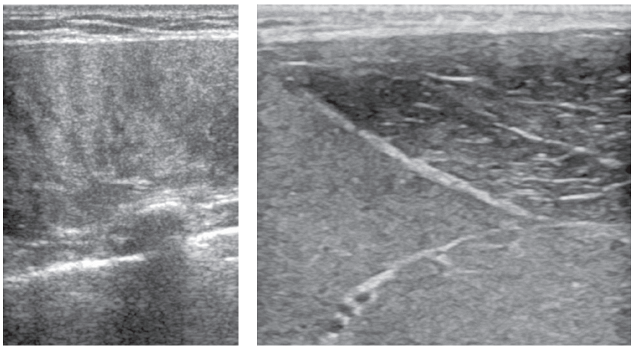
Patients were examined on a diagnostic expert class US scanner Logiq E9 (General Electric, USA). A linear high-frequency transducer for superficial tissues was used. Patient preparation was not required. Scanning was performed in the two-dimensional mode in the area of damage, adjacent area, and opposite areas.

A gel pad was used to eliminate the effect of transducer compression on muscle tissues. SWE was performed with the patient in the supine position and in a state of skeletal muscle relaxation. For visual assessment, a color scale was used, where dark blue and red indicated the minimum and maximum elasticity, respectively. Areas of interest were identified in the middle sections of the muscles without the involvement of tendons and muscle sheaths. To obtain more accurate results, the measurement was performed at several levels with the calculation of the average value. SWE parameters were expressed as lateral wave velocity (V) in m/s and stiffness values (Young's modulus, E) in kPa.

The MedCalc software (version 18.2.1) performed all statistical processing of experimental data. The normality of distribution was determined using the D'Agostino–Pearson test. The quantitative results of the morphometric analysis were expressed as *Me* [1st and 3rd quartiles]. The Mann–Whitney U-test was used to compare groups of SWE values. To determine the cutoff thresholds for lateral wave velocity and stiffness, the receiver operating characteristic (ROC) analysis and comparison of area under the curve (AUC) using the DeLong method were performed. Quantitative characteristics were used by constructing a binary logistic regression equation.

RESULTS

US signs of rhabdomyolysis included a diffuse pronounced increase in echogenicity (homogeneous or heterogeneous), impaired muscle structure cross striation, and large amounts of muscle tissue damage (>30%) (Fig. 1). Rhabdomyolysis was concluded in cases of the detection of all the US symptoms listed.



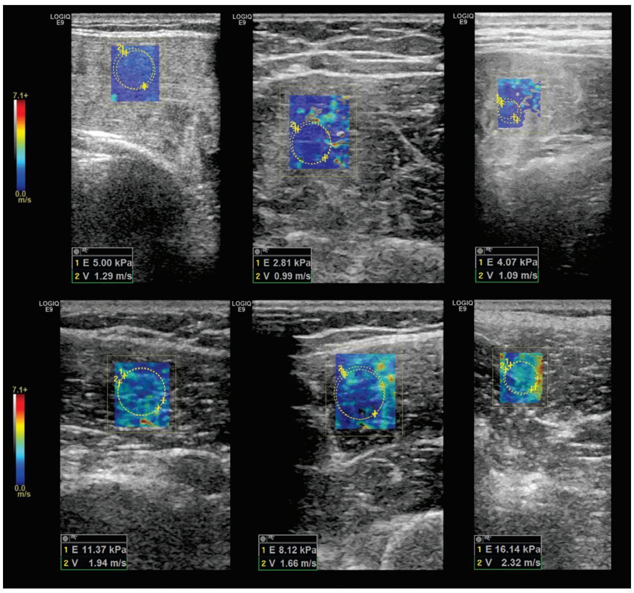
a *b*

Fig. 1. Echograms of rhabdomyolysis of skeletal muscles of various anatomical regions: *a*, back extensor muscle; *b*, medial and lateral heads of the triceps brachii muscle

Twenty-seven cases met the US criteria for rhabdomyolysis. After laboratory verification of rhabdomyolysis, the diagnostic efficiency of US was indicated by a sensitivity of 68%, specificity of 57, and accuracy of 62%. Despite the low sensitivity of the method in diagnosing rhabdomyolysis, the sensitivity of US in the detection of nonspecific edematous changes in muscle tissue (main group) was 74%.

Thus, US enables the detection of muscle edema; however, the absence of characteristic semiotic signs and subjective assessment of the muscle structure echogenicity lead to a large number of type I and II errors. To increase the efficiency of US in diagnosing rhabdomyolysis, a quantitative assessment of the muscle tissue elasticity was performed.

When comparing the muscle tissue stiffness coefficients in m/s and kPa, values in rhabdomyolysis were statistically significantly different both from other diseases manifested by muscle edema (Mann–Whitney *U*-test with Bonferroni correction, $p < 0.001$) and from the control group (Mann–Whitney *U*-test with Bonferroni correction, $p < 0.001$) downward (Fig. 2). Moreover, lateral wave velocity and stiffness in muscle edema did not statistically significantly differ from the control group, with $p = 0.583$ and $p = 0.117$, respectively (Mann–Whitney *U*-test with Bonferroni correction).



a *b* *c*

Fig. 2. Echograms with measurement of SWE parameters; upper row, rhabdomyolysis; lower row, control group: *a*, back extensor muscles; *b*, external vastus muscles; *c*, pectoralis major muscles

Thus, SWE can be used for diagnosing rhabdomyolysis; however, it does not allow the differentiation of other forms of muscle edema from normal muscles.

Cutoff thresholds for SWE for rhabdomyolysis were determined using ROC analysis based on the Youden criterion (Fig. 3). No significant differences were found in the AUC of the obtained curves (DeLong method, $p = 0.9761$).

For the lateral wave velocity, V of 1.64 m/s was optimal, with a sensitivity of 75%, specificity of 62%, and accuracy of 68%. For stiffness, an E value of 6.38 kPa was obtained with a sensitivity of 51%, specificity of 92%, and accuracy of 70%. Separate evaluation of SWE indicators helped improve the efficiency of US diagnostics of rhabdomyolysis compared with the native study but not significantly.

A binary logistic regression model was constructed for the complex use of SWE indicators. Sequential introduction of variables into the model was employed, with the coefficients tested for significance ($p > 0.05$) at each stage.

In the resulting SWE model, a satisfactory coefficient of determination was noted (Nagelkerke $R^2 = 0.38$). The final model equation is presented below:

$$P_+ = \frac{1}{1+e^{-(-0.22391 \cdot E - 1.45259 \cdot V + 0.87874)}},$$

where P_+ is the probability of rhabdomyolysis ($P_+ > 0.5$ is a positive probability); *e*, the base of the natural logarithm; *E*, elastographic stiffness; and kPa, *V* is the lateral wave velocity (m/s).

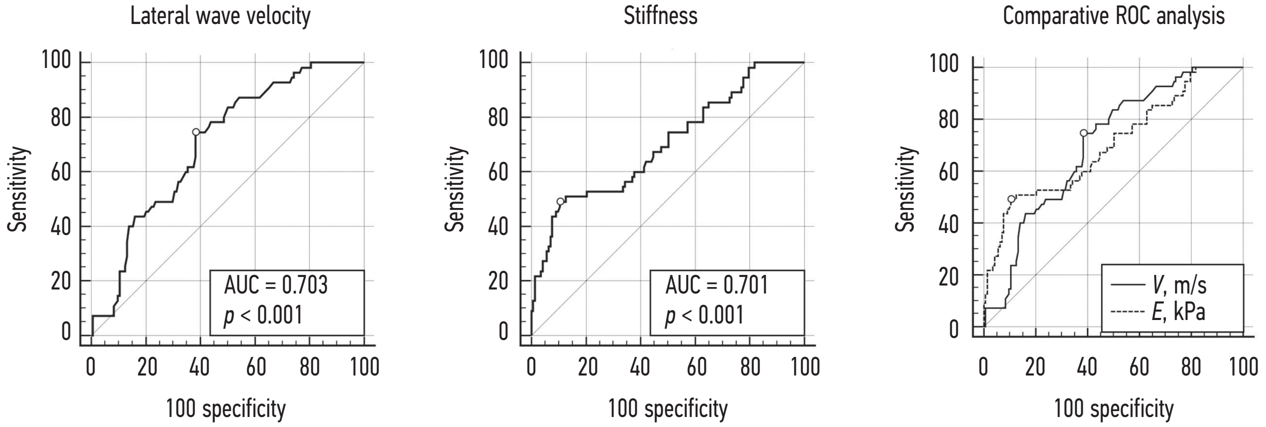


Fig. 3. Diagrams of the ROC analysis of SWE data separately and comparative analysis of ROC curves. The dots indicate the optimal values of the cutoff thresholds by the Youden index

The SWE model enabled classifying cases of rhabdomyolysis with a diagnostic accuracy of 77%. In the ROC analysis of the predicted values at the optimal point, the sensitivity and specificity were 84% and 65%, respectively.

The evaluation of data in the control group revealed an abnormal distribution of SWE indicators. The median values and interquartile range for the lateral wave velocity *V* were 2.03 [1.72; 2.64] m/s, and those for stiffness *E* were 13.22 [10.09; 22.41] kPa.

In five cases, the muscle tissue of patients with rhabdomyolysis was assessed before discharge. Moreover, after recovery, the indicators of the lateral wave velocity of damaged muscles in all patients were included in the interquartile range of the values in the control group.

DISCUSSION

US has a high availability in diagnosing muscle tissue diseases both during the initial examination and disease course. As regards rhabdomyolysis, the speed and accuracy of diagnostics are critical to the prognosis and recovery [3]. Despite the relatively low diagnostic capabilities, even native US provides information about the muscle tissue state, and knowledge of the semiotics of rhabdomyolysis enables suspecting acute damage to skeletal muscles and prescribing specific laboratory tests to confirm or rule it out [8].

The capabilities of native US in detecting rhabdomyolysis are insufficient; however, the method can be used to detect undifferentiated muscle edema, with a sensitivity of 74%. In addition, the method has the following advantages: short examination time, can be performed on patients in serious condition without transportation to other rooms, and absence of exposure to ionizing radiation. In addition to primary diagnostics, US enabled monitoring the state of muscle tissues in patients for the entire stay in the intensive care unit.

The SWE, expressed as the lateral wave velocity, enabled improving the main diagnostic characteristics of US, primarily sensitivity, in the detection of rhabdomyolysis. A decrease in the lateral wave velocity in muscle edema was noted in the diagnostics of inflammatory myopathies [20] and the description of a clinical case of rhabdomyolysis [18]. Elastographic stiffness was decreased by an increase in the extracellular and intracellular water volume during tissue edema, which lead to a decrease in the velocity of lateral wave propagation from the central US beam.

SWE, expressed in stiffness in diagnosing rhabdomyolysis, demonstrated an extremely low sensitivity of 51%, which does not allow its use. With an empirical selection of the cutoff threshold with a balance between sensitivity and specificity, the results did not differ from the qualitative method capabilities because Young's modulus index is calculated from the lateral wave velocity and, therefore, is less accurate than the initially measured value [13]. However, the specificity and accuracy of stiffness were higher than those of the lateral wave velocity.

The comprehensive use of the lateral wave velocity and stiffness using a logistic regression model enabled us to compensate for the heterogeneity of distribution of the sensitivity and specificity of SWE indicators separately and create an equation for determining the probability of rhabdomyolysis with a high accuracy of 77%.

SWE, expressed as lateral wave velocity, allowed the assessment of muscle tissue recovery during convalescence, which is consistent with the scientific studies of Botar-Jid et al. [21] and Alfuraih et al. [20], which demonstrate an increase in SWE indices up to standard values in some edematous and inflammatory lesions with the improvement of the disease course.

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CONCLUSION

Therefore, the developed logit model with the complex use of elastography values helped increase the diagnostic accuracy of US in determining rhabdomyolysis from 62% to 77%. Increasing the lateral wave velocity to the standard values V of 2.03 [1.72; 2.64] m/s indicates the restoration of muscle tissue.

ADDITIONAL INFORMATION

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Conflict of interest. The authors declare no conflict of interest.

Ethical considerations. The study was approved by the local ethics committee of the S.M. Kirov Military Medical Academy (Protocol No. 217 dated December 25, 2018).

Author contributions. All authors made a significant contribution to the study and preparation of the article, read and approved the final version before its publication.

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