Applied Medical Informatics
Original Research Vol. 27, No. 4 /2010, pp: 81-89

Assessment of Sonoelastography as Diagnosis Tool of Inflammatory Myopathies

Carolina BOTAR-JID[1,*], Sorana D. BOLBOACĂ[2], Laura DAMIAN[3], Sorin M. DUDEA[1], Cosmin PANTILIE[4], Sergiu NEDEVSCHI[4], Radu BADEA[5]

[1] "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Department of Radiology, 13 Emil Isac Str., 400023 Cluj-Napoca, Romania.
[2] "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Department of Medical Informatics and Biostatistics, 13 Emil Isac Str., 400023 Cluj-Napoca, Romania.
[3] Cluj District University Hospital, Department of Rheumatology, Cluj-Napoca, Cluj, Romania.
[4] Technical University of Cluj-Napoca, Faculty of Automation and Computer Science, 26-28 G. Baritiu Str., 400027 Cluj-Napoca, Romania
[5] "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Department of Medical Imaging, 13 Emil Isac Str., 400023 Cluj-Napoca, Romania.
E-mails: inabotar@yahoo.com, sbolboaca@umfcluj.ro, lauradamiancj@yahoo.com, dudea@clicknet.ro, Cosmin.Pantilie@cs.utcluj.ro, rbadea2003@yahoo.com

* Author to whom correspondence should be addressed; Tel.: +4-0264-595934; Fax: +4-0264-593847.

Received: 27 September 2010 /Accepted: 25 November 2010 / Published online: 15 December 2010

Abstract
Background: Inflammatory myopathies represent a special group of pathology. Establishing the correct diagnosis in the early phase and a better follow-up are the main objective for improving the life quality of these patients. *Objective*: The aim of this research was to assess the usefulness of sonoelastography in diagnosis of inflammatory myopathies. *Material and Method*: A prospective longitudinal study with a control group was carried out in the Radio-Imaging Department, Cluj-Napoca District University Hospital, Romania, from May 2007 to July 2010. *Measurements*: Image Processing 2.8 software was used to analyze the elastographic images in correlation with clinical and biochemical data was used. *Results*: Analysis of Receiver Operating Characteristic curves statistics for elastography parameters showed significant values for the following parameters: average green color, average blue color, average intensity of color, dispersion of red, dispersion of green, and dispersion of hue. *Conclusions*: Our study highlighted the utility of some elastography parameters in the diagnosis of inflammatory myopathies; the parameter proved to be statistically different in case group compared to control. Anyway, standardization of sonoelastography and larger studies are required to ensure accurate diagnosis, reproductibility and reliability.

Keywords: Receiver Operating Characteristic (ROC) curve; Cutoff value; Dedicated software; Sonoelastography; Inflammatory Myopathies.

Introduction

Inflammatory myopathies represent a group of acquired muscle diseases characterized by primary symmetric proximal muscle weakness that develops along weeks to months, elevated levels of serum muscle enzymes, myopathic changes on electromyography and endomysial inflammation at muscle biopsy [1]. The most frequently seen diseases of the inflammatory myopathies are polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM) [1,2]. The annual incidence is 2-10 cases/1 million persons, with childhood and adult peaks. The female are more frequently affected compared to male, sex ratio being 2.5:1 [2-4].

The diagnosis of inflammatory myopathies is based usually on clinical criteria, laboratory analyses, EMG (electromyography) changes, imaging investigations and muscle biopsy, in order to assess muscle involvement and other target-organs [1,4,5]. Imaging investigations represent useful methods to identify the presence of muscle abnormality due to the heterogeneity of distribution of muscle inflammation. Moreover, imaging investigations might be an alternative for guiding biopsy, reducing the sampling error of untargeted biopsies [4-8].

Ultrasound is the preferable imaging method for assessment of superficial muscles, due to its noninvasive characteristic as diagnostic method. The ultrasound is widespread available, easy to apply, offering a high spatial resolution and the possibility of real-time imaging without exposure to ionizing radiation [3-5].

Ultrasonic elastography (Sonoelastography) measures tissue deformation as a response to an external force, assuming that the deformation is lower in rigid tissues, compared with the elastic, soft tissues [9,10]. This method is based on comparing the radiofrequency of ultrasonic waves obtained before and after an easy made compression with a conventional transducer, using a free hand technique [9,10]. Even there are only a few studies in the literature which have attempted to present the muscular appearance of the muscle structures' elasticity, it is known that the muscular elasticity is modified in myopathies and sonoelastography. Nevertheless, the sonoelastography can be a useful method for assessment of muscular elasticity [9,10].

The aim of this research was to assess the usefulness of sonoelastography in diagnosis of inflammatory myopathies by processing sonoelastographic images using an image processing dedicated software.

Material and Method

Patients

A prospective longitudinal study was conducted to assess the role of sonoelastography in evaluating patients with inflammatory myopathies, using qualitative and quantitative evaluation. The studied population was represented by patients hospitalized or under investigation in Rheumatology Department and evaluated by ultrasound at Radio-Imaging Department of Cluj District University Hospital from May 2007 to July 2010. The following inclusion criteria were applied for case group:

- Patients with inflammatory muscle disease in assessment and/or follow-up in Rheumatology Clinic of Cluj District University Hospital from May 2007 to July 2010, with findings at history and physical examination of symmetric proximal muscular weakness for presented myopathies and plus typical rash in case of DM.
- Clinical and biochemical suspicion of inflammatory myopathies (symmetrical proximal muscle weakness; elevated serum creatin kinase – CK (values over 170 U/l) and lactate dehydrogenase – LDH (values over 460 UI));
- Recommendation for sonoelastographic examination addressed to Radio-Imaging Department.

Patients with extramuscular symptoms, patients whose health did not permit movement to Radio-Imaging Department for ultrasound investigations, patients without muscle biopsy and patients whose sonoelastographic images quality were excluded from case group.

The sample size of control group was imposed to be 30 due to the financial limitations of the research. The control group does not present any findings at history and physical examination of symmetric proximal muscular weakness or other clinical suspicion of inflammatory miopathies. The control group was chosen with no significant differences regarding age and gender distribution compared to the case group.

All the patients in case group presented clinical evaluation and laboratory tests for muscular inflammatory disease: symmetric and proximal muscular weakness, increased values of the nonspecific inflammatory markers (The erythrocyte sedimentation rate (ESR) > 10 mm at 1 hour; positive C-reactive protein, positive antinuclear antibodies) and increased levels of serum muscle enzymes (CK, LDH). Surgical or ultrasound guided muscular biopsy was performed for golden diagnosis of idiopathic inflammatory myopathies. The patients in control group were also clinical evaluated.

The study was approved by the institutional ethical board. Informed consent was obtained from both groups.

Elastography Imaging Technique

Both groups were examined using Hitachi EUB 8500 equipment with 6.5-13 MHz transducer. Sonoelastographic examinations were performed in real time, using transversal sections, with graduated compression of the muscular structures and the transducer perpendicular on the skin. The box of elastography was set to include interested muscle structure and adjacent structures. Slight compression was achieved with a frequency vibration maintained at 3-4 scale displayed on the monitor. The color gain was set at 26%, the density at 2 lines of information and the frequency of the images to "high".

Elastography image color scale ranges from red (soft parts) from blue (rigid elements). Green indicates the average elastic structures on elastography image.

The patients were assessed by elastography of the superior and medium muscle structures of the thighs and arms, left-right comparative. The sonoelastographic images with the most significant changes from rectus femoris in the thigh, and from the biceps brachii muscle in the arm were acquired and stored.

Study Protocol

Sonoelastographic images obtained were analyzed using a dedicated software in order to obtain objective and quantifiable data, useful for establishing an exact imaging diagnosis and for monitoring of this disease. Image Processing software version 2.8, developed by Technical University of Cluj-Napoca was used. The quantitative parameters followed on the selected sonoelastographic images were represented by the average numerical values of colors, color intensity, color dispersion, hue and hue dispersion.

Statistical Analysis

Quantitative continuous variables were summarized using descriptive statistic parameters while qualitative variables were summarized using relative frequencies. Kolmogorov-Smirnov statistics was used to test the normality of experimental data at a significance level of 5%. Student t-test assuming equal or unequal variances (according to Levene test) was used to compare two means (the mean obtained in case group and the mean obtained in control group). Whenever the experimental data proved not to be normal distributed the comparison were performed using a non-parametric test (e.g. Kolmogorov-Smirnov test) at a significance level of 5%. The SPSS v. 16.0 was used to analyze the experimental data.

The diagnostic performance of a test (accuracy of a test) to discriminate diseased cases from normal cases was evaluated using Receiver Operating Characteristic (ROC) curve analysis [11-16]. The ROC curve analysis was performed with SPSS software v. 16 using the following criteria: classification – includes cutoff value for positive classification; test direction – largest/smaller test result indicates more positive text; parameters for standard error of area – distribution assumptions = nonparametric & confidence level = 95%.

Results

Six hundred and thirty-eight muscles were investigated in 74 patients included in case group (55 female and 19 male). One hundred and twenty muscles were evaluated in 30 persons included in the control group (21 female and 9 male). The age of patients included in the case group varied from 24 to 78 years with a mean of 50.92±11.59 (95% CI [48.23-53.60]). The age of persons included in the control group varied from 33 to 63 years with a mean of 46.73±9.81 (95%CI [43.07-50.40]). The mean age in case group proved not to be significantly different compared to the mean age in control group (mean difference = 4.19, standard error of difference = 2.40, t-value = 1.741, df = 102, p = 0.085).

The distribution of the final diagnosis for patients included in case group is presented in Figure 1.

The distribution of the investigated sites according to left and right of the body and with region for both groups is presented in Table 1.

Descriptive statistics of the following sonoelastographic parameters for case and control groups are presented in Table 2: AvgRed, AvgGreen, AvgBlue, AvgIntensity, AvgHue, DispRed, DispGreen, DispBlue, DispIntensity, and DispHue.

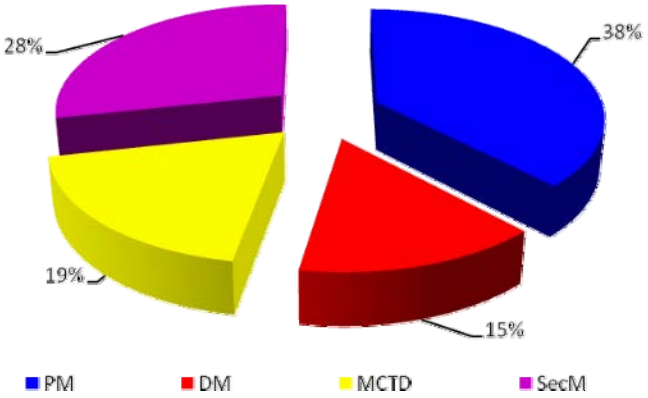

Figure 1. Final diagnosis in case group (PM = polymyositis, DM = dermatomyositis, MCTD = mixed conjunctive tissue disease, SecM = secondary myopathies)

Table 1. Investigated sites: case versus control group

Location	Side	Region		Total
		Superior	Medium	
Case group				
Thigh	Right	68	134	202
	Left	68	134	202
Sub-Total		*136*	*268*	*404*
Arm	Right	19	38	57
	Left	19	38	57
Sub-Total		*38*	*76*	*114*
Total		***174***	***344***	***518***
Control group				
Thigh	Right	31	31	62
	Left	29	29	58
Total		***60***	***60***	***120***

Table 2. Sonoelastographic parameters: descriptive statistics

Parameter	Mean [95% CI]	Standard Deviation	Minimum	Maximum
Case group (n=518)				
AvgRed	61.45 [59.75-63.15]	16.08	24.13	110.91
AvgGreen	97.42 [95.86-98.98]	14.74	62.70	141.02
AvgBlue	77.44 [75.50-79.39]	18.40	39.93	143.88
AvgIntensity	78.77 [77.36-80.18]	13.32	48.33	122.62
AvgHue	141.71 [139.11-144.31]	24.57	69.50	230.55
DispRed	33.31 [32.77-33.84]	5.05	15.80	45.13
DispGreen	38.76 [38.14-39.38]	5.83	26.38	65.83
DispBlue	42.85 [42.24-43.45]	5.71	22.93	62.84
DispIntensity	38.30 [37.86-38.75]	4.20	25.35	53.62
DispHue	64.78 [63.69-65.88]	10.37	31.47	90.17
Control group (n=120)				
AvgRed	59.20 [57.59-60.82]	9.05	37.58	88.12
AvgGreen	100.47 [98.36-102.57]	11.79	73.30	144.71
AvgBlue	63.84 [62.29-65.39]	8.68	45.87	84.29
AvgIntensity	74.50 [72.89-76.12]	9.05	52.25	98.26
AvgHue	125.16 [124.74-125.58]	2.33	120.31	130.67
DispRed	35.27 [34.71-35.84]	3.15	28.30	42.55
DispGreen	34.94 [33.97-35.92]	5.47	23.74	52.80
DispBlue	42.85 [41.96-43.75]	5.03	35.47	66.03
DispIntensity	37.69 [37.04-38.35]	3.67	29.21	53.52
DispHue	61.03 [59.60-62.47]	8.05	36.81	75.91

95% CI = 95% confidence interval associated to the mean

The result of comparison between the values of sonoelastographic parameters of case and control group, for normal distributed variables, are presented in Table 3.

Table 3. Sonoelastographic parameters for normal distributed variable: results of comparison between case and control group

Param	t-test for Equality of Means						
						95% CI of the Difference	
	t	df	p	MeanDiff [95%CI]	StdErrDiff	Lower	Upper
AvgRed	1.640	373.043	0.102	1.95	1.19	-0.39	4.29
AvgGreen	-2.506	257.183	$1.29 \cdot 10^{-2}$	-3.35	1.34	-5.98	-0.72
DispHue	4.04	261.76	$6.93 \cdot 10^{-5}$	3.76	0.93	1.93	5.59

t = t-value; df = degrees of freedom; MeanDiff = mean of difference;
95%CI = 95% confidence interval for mean difference; StdErrDiff = standard error of difference

The result of comparison between the values of sonoelastographic parameters of case and control group, for not normal distributed variables, are presented in Table 4.

Table 4. Sonoelastographic parameters for not normal distributed variable: results of comparison between case and control group

		AvgBlue	AvgIntensity	AvgHue	DispRed	DispGreen	DispBlue	DispIntensity
Most Extreme Differences	Absolute	0.429	0.230	0.694	0.253	0.348	0.106	0.176
	Positive	0.031	0.062	0.156	0.253	0.000	0.079	0.044
	Negative	-0.429	-0.230	-0.694	-0.027	-0.348	-0.106	-0.176
Kolmogorov-Smirnov Z		4.088	2.187	6.608	2.407	3.312	1.011	1.677
p		< 0.001	$1.41 \cdot 10^{-4}$	< 0.001	$1.86 \cdot 10^{-5}$	< 0.001	0.258	0.007

The results obtained from ROC curve analysis of sonoelastographic parameters are presented in Table 5.

Table 5. ROC curve analysis: sonoelastographic parameters

Param.	… [a]	Area [95%CI]	StdErr	p[b]
AvgRed	Larger	0.532 [0.480-0.583]	0.026	0.302
AvgGreen	Smaller	0.568 [0.512-0.623]	0.029	$2.70 \cdot 10^{-2}$
AvgBlue	Larger	0.742 [0.698-0.787]	0.023	$2.37 \cdot 10^{-15}$
AvgIntensity	Larger	0.595 [0.541-0.649]	0.028	$1.84 \cdot 10^{-3}$
AvgHue	Larger	0.772 [0.730-0.814]	0.022	$6.13 \cdot 10^{-19}$
DispRed	Smaller	0.613 [0.560-0.665]	0.027	$2.31 \cdot 10^{-4}$
DispGreen	Larger	0.691 [0.636-0.747]	0.028	$4.16 \cdot 10^{-10}$
DispBlue	Larger	0.516 [0.459-0.574]	0.029	0.5930
DisIntensity	Larger	0.560 [0.502-0.617]	0.029	0.0510
DispHue	Larger	0.615 [0.561-0.669]	0.028	$1.76 \cdot 10^{-4}$

[a] values of the test result variable indicate stronger evidence for a positive actual state
[b] Null hypothesis: true area = 0.5

The cutoff values and associated sensibility and specificity are presented in Table 6.

The ROC curve for four sonoelastographic parameters with performances in diagnosis (two with smaller values of the test result variable indicate stronger evidence for a positive actual state and two with larger values of the test result variable indicate stronger evidence for a positive actual state) are presented in Figure 2.

Discussion

Most patients included in the study were women (F:M ~ 3:1), which is within the existing data in the literature, according to which the disease is more common in women [2-4]. For a good comparison in terms of statistics, in the control group included more women (F: M = 2.3:1).

Table 6. ROC curve analysis: sonoelastographic parameters

Param.	Cutoff for positive	TP	FN	FP	TN	Se	Sp
AvgRed	≥ 33	343	6	120	0	0.9828	0.0000
	<40	29	1	634	238	0.0437	0.9958
AvgGreen	≤ 140	345	119	2	2	0.9942	0.0165
	< 80	45	5	602	230	0.0696	0.9787
AvgBlue	≥ 40	345	120	2	0	0.9942	0.0000
	≥ 84	111	1	470	238	0.1910	0.9958
AvgIntensity	≥ 50	344	120	4	0	0.9885	0.0000
	≥ 98	28	1	636	238	0.0422	0.9958
AvgHue	≥ 70	345	120	2	0	0.9942	0.0000
	≥ 130	242	3	208	234	0.5378	0.9873
DispRed	≥ 20	345	120	2	0	0.9942	0.0000
	≥ 42	11	1	670	238	0.0162	0.9958
DispGreen	≥ 27	345	113	2	14	0.9942	0.1104
	≥ 46	37	5	618	230	0.0565	0.9787
DispBlue	≥ 24	344	120	4	0	0.9885	0.0000
	≥ 62	3	2	686	236	0.0044	0.9916
DisIntensity	≥ 26	343	120	6	0	0.9828	0.0000
	≥ 47	12	3	668	234	0.0178	0.9873
DispHue	≥ 36	342	119	8	2	0.9771	0.0165
	≥ 75	51	3	590	234	0.0796	0.9873

TP = true positive; FP = false positive; TN = true negative; FN = false negative

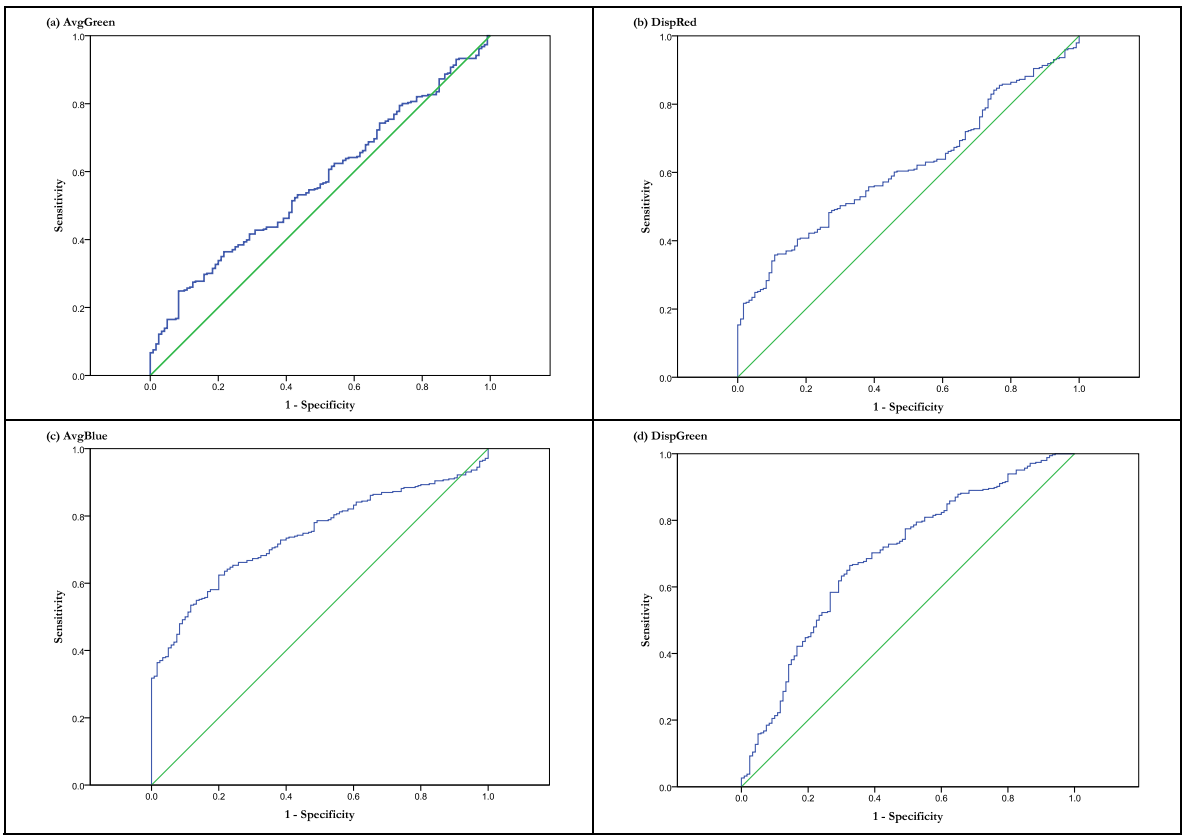

Figure 2. ROC curves: sonoelastographic parameters: (a) & (b) - smaller values of the test result variable indicate stronger evidence for a positive actual state; (c) & (d) – larger values of the test result variable indicate stronger evidence for a positive actual state.

The mean age in case group proved not to be significantly different compared to the mean age in control group, an expected result for a correct assignment of subjects in case and control groups.

The final diagnoses of patients included in the study proved to be PM, DM, mixed connective tissue disease (MCTD), and a group of secondary myopathies (Figure 1). MCTD is a special group of inflammatory muscle diseases that can present symptoms of other connective tissue diseases and can steer from one point to the PM or DM. In secondary myopathies group were included the conditions that present in evolution muscular symptoms (thyroid disease, lupus erythematosus or systemic vasculitis). Most patients were those with PM, followed by DM and MCTD. This finding is in part covered by the existing data in the literature, PM being more common. Percentage of patients with MCTD than in our study show the presence of a large number of patients who have general signs of muscle damage, which have migrated permanently to one clearly defined types of inflammatory myopathies.

In terms of examined regions (Table 1), the most important muscle structural changes were observed in the third medium, both in the thigh, and arm. This result revealed that in this class of diseases are affected the proximal regions of the thigh and arm.

Investigation of the descriptive parameters associated to numerical sonoelastographic parameters (Table 2) revealed the following aspects:

- The mean of red color averages was higher in the case group compared to the control group. The range of values obtained in control group proved to be contained in the range of values obtained in case group. Moreover, since the confidence intervals are overlap on each other, it is expected not to have a significant difference for this parameter between case and control groups. These observations sustain the useless of interpretation of average red parameter as possible diagnosis parameter.
- The mean of green color averages was lower in the case group compared to the control group. The range of values obtained in case group prove to be close with the range of values obtained in control group. Since the confidence intervals are slightly overlapped on each other for a small range, this parameter could have its usefulness as diagnosis parameter.
- The mean of blue color averages was higher in the case group compared with the control group. The confidence intervals proved not to be overlap on each other; it is expected to have a significant difference for this parameter between case and control group. These observations sustain the possible useful of average blue parameter as diagnosis parameter.
- The mean of color intensity was higher in the case group compared to the control group. The range of values obtained in control group proved to be contained in the range of values obtained in case group. Moreover, since the confidence interval of case group is not overlap on the confidence interval in control group it is expected to have a significant difference for this parameter between case and control groups. These observations sustain the usefulness of interpretation of color intensity parameter as possible diagnosis parameter.
- The mean of hue is higher in case group compared with the control group. The confidence interval obtained in case group is not overlap on the confidence interval obtained in control group. Thus, it is expected to have a significant difference for this parameter between case and control groups. This parameter could be useful as possible diagnosis parameter.
- It is not expected to saw a significant difference of mean of average dispersion of blue color and mean of average dispersion of intensity since the 95% confidence intervals are overlap on each other.
- The average of dispersion of red and green and also the average values of dispersion of hue have high potential to be useful parameters for diagnosis (the confidence intervals are not overlap on each other even if the data are in the same range of values).

The above observations attest that muscle structures lose their normal elasticity, becoming more rigid, in inflammatory myopathies.

A statistically significant difference between mean values of average green color (AvgGreen) which proves the appearance of medium elasticity has been identified between case and control group (Table 3). This observation can be explained by the appearance of medium elasticity that characterizes the normal muscle and is altered in inflammatory myopathies. Average dispersion of color shades (DispHue) proved also to be significantly different in the case group compared to the control group, supporting the changes of elasticity found in these pathologies.

The analysis of results of studying the sonoelastographic parameters comparative to the case and control groups for variables not normally distributed (Table 4) revealed the following statistically significant differences:

- The values of average blue color (AvgBlue) proved to be statistically different in terms of extreme values in case group compared to control group. This is explained by the reduction of elasticity in patients with inflammatory myopathies, due to the appearance of fibrosis or amyloid deposition in these diseases.
- The values of average intensity (AvgIntensity) and dispersion of colors proved to be statistically different in terms of extreme values in case group compared with control group. This is explained by the changes in muscles elasticity in inflammatory myopathies.
- The values of average of hue (AvgHue) proved to be statistically different in terms of extreme values in case group compared with control group, also, being higher in case group. This observation confirms the reduction of elasticity in inflammatory myopathies.
- The values of red color dispersion proved to be statistically different in case group compared to the control group, being higher in the control group. This observation supporting also the observation that in inflammatory myopathies reduction of normal muscle elasticity occurs.

Analysis of ROC curves statistics for elastography parameters (Table 5) show significant values for these items: average green color value, average blue color value, average intensity of color value, dispersion of red colors, green color, and of hue. These observations revealed that the parameters listed can be used as diagnostic factors for inflammatory myopathies. In addition, the cut off must be chose according with the aim of the elastography. Therefore, if the aim is to identify as more as possible positive persons the cutoff that provides the higher sensibility will be the best solution; otherwise the cutoff that is able to provide a higher value of specificity will be chose is the elastography is used as screening test.

There are certain limitations of the present study. One limitation is the lack of interobserver and intraobserver variability in sonoelastography evaluation, this exploration being generally recognized as operator dependent. Another limitation is that sample size of case group as well as the sample size of control group; a larger group of patients would probably have strengthened the results.

Conclusions

After our knowledge, there are not sufficient studies in the literature to prove or disprove the usefulness of elastography in the evaluation of inflammatory myopathies. Our study showed the usefulness of some parameters elastography in the diagnosis of inflammatory myopathy. However, standardization of sonoelastography and larger studies are required to ensure accurate diagnosis, reproductibility and reliability.

Ethical Issues

The study was approved by the ethical committee of the university as well as by the ethical committee of the hospital.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgements

The research was partly supported by UEFISCSU thought project CERIS, PNCDI 2 (42-102/2008).

References

1. Dalakas MC. Polymyositis. dermatomyositis, and inclusion-body myositis. N Engl J Med 1991;325:1487-98.
2. Amato AA, Barohn RJ. Idiopathic inflammatory myopathies. Neurol Clin 1997;15:615-648.
3. Ashok Kumar. Idiopathic Inflammatory Myopathies; Suppliment to Japi 2006;54:62-66.
4. Walker U. Imaging Tools for the Assessment of Idiopathic Inflammatory Myositis. Curr Opin Rheumatol 2008;20(6):656-661.
5. Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. Lancet 2003;362:971-982.
6. Weber MA. Ultrasound in the inflammatory myopathies. Ann NY Acad Sci 2009;1154:159-70.
7. O'Sullivan PJ, Gorman GM, Hardiman OM, Farrell MJ, Logan MP. Sonographically Guided Percutaneous Muscle Biopsy in Diagnosis of Neuromuscular Disease A Useful Alternative to Open Surgical Biopsy. J Ultrasound Med 2006;25:1-6.
8. Connor A, Stebbings S, Anne Hung N, Hammond-Tooke G, Meikle G, Highton J. STIR MRI to direct muscle biopsy in suspected idiopathic inflammatory myopathy. J Clin Rheumatol 2007;13:341-345.
9. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006;239:341-350.
10. Botar-Jid C, Vasilescu D, Dudea S. Ecografia tridimensionala si elastografia in patologia aparatului locomotor. In: Daniela Fodor. Ecografie clinica musculoscheletala. Editura Medicala Bucuresti 2009, p. 381-396.
11. Metz CE. Basic principles of ROC analysis. Seminars in Nuclear Medicine 1978;8:283-298.
12. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. Clinical Chemistry 1993;39:561-577.
13. Griner PF, Mayewski RJ, Mushlin AI, Greenland P. Selection and interpretation of diagnostic tests and procedures. Annals of Internal Medicine 1981;94:555-600.
14. Martin JM, Jabot F, Marrel P. How to Organise the Medical Data of Chronically III Patients in the Computer. Meth Inform Med 2001;24:5-12.
15. Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, et al, (Editors). Harrison's principles of internal medicine. 14th ed. New York: McGraw Hill, Health Professions Division; 1998.
16. Serena C, Pastor FJ, Gilgado F, Mayayo E, Guarro J. Efficacy of Micafungin in Combination with Other Drugs in a Murine Model of Disseminated Trichosporonosis Antimicrob. Agents Chemother [serial online] 2005 [cited 2009 September];49:497-502. Available from: URL: http://aac.asm.org/cgi/content/full/49/2/497.