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Portal hemodynamics disorders severity in liver cirrhosis assessment by duplex ultrasound

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Abstract

Background: The need to evaluate hemodynamics in case of portal hypertension syndrome is a current problem. Identification of portal hypertension by invasive methods is difficult, hence the logical conclusion of the need to optimize the portal hypertension diagnosis by non-invasive methods. This study aims: to identify a system of non-invasive measurements, which will permit to develop a scoring system for portal hemodynamics disorders severity in liver cirrhosis assessment by duplex ultrasound and a scoring interpretation, which allows the classification as: low severity, middle severity and high severity.
Material and methods: One hundred eleven patients who were diagnosed with cirrhosis formed the research cohort. The patients had an enhanced clinical and biological evaluation. Ultrasound examination was done by Logiq E9, Voluson E8 equipment, using linear probe of 7-10 MHz frequency and convex probe of 3.5-5 MHz frequency by the transabdominal access, in real time two-dimensional (B) regimen, with the subsequent use of color Doppler and spectral Doppler techniques. Obtained data was processed using case-based reasoning, data segmentation and clusterization.
Results: A scoring for portal hemodynamics disorders severity in liver cirrhosis assessment, based on five non-invasive measurements, obtained by doppler ultrasound imaging, was developed.
Conclusions: The scoring system can be used for a differential diagnosis of liver cirrhosis. The decision rules in the form of productions, obtained during the data clustering stage, can be used to develop medical information systems.
Key words: liver cirrhosis, portal hemodynamics, doppler ultrasound imaginghepatic.

Introduction

Liver cirrhosis is the final stage of chronic liver diseases and is usually complicated by portal hypertension, which becomes the most important cause of morbidity and mortality in these patients. Portal hypertension as a complication of liver cirrhosis, being a clinical / hemodynamic syndrome defined by gradient increase of portal venous pressure, conditions upon a positive diagnosis, the imaging examination being credited as having greater accuracy in detection of the structural hepatosplenic and hemodynamics changes on splenoportal axis.

The need to evaluate hemodynamics on splenoportal axis in case of portal hypertension syndrome is a current problem, due to the increased incidence of the given pathology and specific pathogenetic aspects. The early diagnosis and appropriate management of pathology can certainly improve the prognosis and life expectancy of patients with chronic liver diseases.

Identification of portal hypertension by invasive methods is difficult, both because of laborious processes and serious condition of the patients. Hence the logical conclusion of the need to optimize the portal hypertension diagnosis by non-invasive methods, a complicated problem recognized in numerous studies.

HVPG measuring through the hepatic veins catheterization is the gold standard for evaluation of portal pressure in cirrhosis, but it is an invasive method [1]. HVPG changes provide important information not only for positive diagnosis, but also during treatment have an important significance in guiding cirrhotic patients. However, the technique has limi-

tations in clinical practice to be invasive, with complications' potential and requires a technical expertise with limited availability and did not find a widespread use in medical practice.

It must be emphasized that none of the non-invasive methods replaces the measurement of pressure gradient in hepatic veins and endoscopic screening of esophageal varices, but they certainly facilitate clinical management of patients with liver cirrhosis and provide valuable prognostic information. Traditionally these techniques are based on scoring systems (e.g. Child-Pugh Score [2,3]), or on imaging signs analysis. The sequence of these diagnostics methods, conventional ultrasound (2D) and color duplex Doppler regimen has a number of advantages, being an accessible, non-irradiating, repeatable method it can be performed even at the patient's bedside.

Despite the fact that some techniques became conventional instruments in the estimation of portal hypertension, the search for non-invasive markers for predicting the portal hemodynamic disease severity continues and presents an interest in medical diagnostics, as well as social and economic.

In the study [4] a system of 6 criteria (sonographic signs) was proposed, which allows a differential diagnosis of liver cirrhosis and its classification into: minimal portal hemodynamic disturbances, moderate portal hemodynamic disturbances and severe portal hemodynamic disturbances.

Later this system was subjected to a complex analysis using segmentation and clusterization methods and algorithms, as well as techniques typical for case-based reasonong.

In this paper we propose a scoring system for portal hemodynamics disorders severity in liver cirrhosis assessment by duplex ultrasound and a scoring interpretation, which allows the classification of these disturbances as: low severity, middle severity and high severity.

Material and methods

It is a retrospective study realized at the Republican Clinical Hepatology Department of the University Hospital. The medical records of 111 patients in the last 36 months were studied, who were diagnosed with cirrhosis of the liver of various aetiologies (97.8% mainly of viral origin). The average age of the selected patients was 48.4 years old. The study group consisted of 46 (41.4%) men and 65 (58.6%) women, aged 20-70 years). The exclusion criteria of the research: children, pregnant women, patients with pre- and posthepatic portal hypertension, the presence of hepatocellular carcinoma.

The patients had an enhanced clinical and biological evaluation. The cytolytic, cholestatic, hepatoprive syndromes were assessed. The esophageal varices were diagnosed by upper endoscopy and classified as absent or present, and the severity of varices was described in degrees. The evaluation of severity of hemodynamic disorders was studied by duplex ultrasound, using linear probe of 7-10 MHz frequency and convex probe of 3.5-5 MHz frequency by the transabdominal access. All the patients were examined at the beginning in real time two-dimensional (B) regimen, with the subsequent use of color Doppler and spectral Doppler techniques. Through the two-dimensional exam the morphological appearance of the liver, spleen was studied, highlighting parenchymal structure, homogeneity. Dopplerography in color and power regimen was used to emphasize the portosystemic collaterals. Dopplerography in spectral regimen allowed to describe hemodynamic changes both on arterial and venous side, which included the features of the arterial and venous flows in the hepatolienal basin, by assessing the indices of impendance, congestion (CI), splenoportal (SPI), portal vascular (PVI), portal hypertension index (PHI).

From the cohort of 111 patients those with splenectomy were excluded. The remaining 101 cases were divided into three groups – patients with low, middle and high portal hemodynamics disorders severity.

The overall assessment of patients with portal hemodynamics disorders was based on 16 ultrasound and dopplerography parameters system [5, 6]. The selection of these 16 parameters was performed on the basis of statistical analysis. A set of operations carried out by specific working processes and techniques was applied during statistical processing:

- Measurement of intensity degree of statistical regularities was performed using correlation coefficient (Spearman correlation);
- Sensitivity, specificity indicators, positive and negative likelihood ratios, confidence levels, area under the ROC (AUROC) curvatures and diagnostic accuracy were calculated;
- Parameters estimation and verification of statistical hypotheses were performed by calculating errors, using t-criterion and the degree of veracity of "p".

A further analysis based on all 16 criteria segmentation [4], allowed the reduction of parameters to six: spleen area, congestion index, PHI, portal vascular index, splenoportal index, portosystemic collaterals' presence.To achieve the main aim of this research we decided to use the methods and algorithms used previously to formalize the field of ultrasound examination for pathologies of hepato-pancreato-biliary region [7, 8] and diagnosis of early stages of non-alcoholic fatty liver disease [9].

Results and discussion

Both segmentation and cluster analysis used in this research are based on the hypothesis that liver condition worsening acts specifically on each parameter. Each of the six parameters was subjected to the segmentation procedure. Initially the data about 101 patients were divided into three groups: 21 with low severity portal hemodynamics disorders; 45 with middle severity portal hemodynamics disorders; 35 with high severity portal hemodynamics disorders. Subsequently, data were selected for each parameter and arranged in increasing sets as follows:

Low_Ai = [v1, ..., Vj_low], where i = 1 ... 6; j_low = 21; V1, ..., Vj_low – i parameter values for 21 patients with low severity portal hemodynamics disorders and V1 is the minimum value, but Vj_low – maximum value.

Middle_Ai = [v1, ..., Vj_middle], where i = 1 ... 6; j_mi-

ddle = 45; V1, ..., Vj_middle - parameter values of 45 patients with portal hemodynamics middle severity disorders and V1 is the minimum value and Vj_middle – maximum value.

High_Ai = [V1, ..., Vj_high], where i = 1 ... 6; j_high = 35; V1, ..., Vj_high – i parameter values of 35 patients with portal hemodynamics high severity disorders and V1 is the minimum value and Vj_middle – maximum value.

Taking into consideration that Low_Ai, Middle_Ai, High_Ai sets are arranged in ascending order, for each parameter 2, 3 or 4 values can be emphasized, which are cut-offs:

1. Middle_Ai.V1;
2. High_Ai.V1;
3. Low_Ai.Vj_low, IF Low_Ai.Vj> High_Ai.V1;
4. Middle_Ai.Vj_low, IF Middle_Ai.Vj> High_Ai.V1;

Respectively, each range of values of six parameters can be divided into 3, 4 or 5 sub-segments.

For each sub-segment the confidence level in one of three conclusions was calculated. This confidence level corresponds to the probability of presence of one of the three conclusions, if the corresponding parameter has any value in this subsegment. This model has been used in many applications in domain of image processing and medical data processing, as well as segmentation of medical video sequences.

At the stage of clustering, from the sub-segments, which can be described by a logical reasoning and a general conclusion, clusters were formed, but the reasonings were formalized in the form of production rules of IF <condition> THEN <conclusion> type. The condition is made of the characteristics of the sub-segments, which form the given cluster.

The production rules are among the most popular methods of knowledge presentation in medical informatics field.

Using the proposed principle of segmentation, "Spleen area", "Congestion index", "Splenoportal index", "PHI", "Por-

Table 1

Results of six imaging diagnostic criteria segmentation

Spleen aria	**x<57**	**57<=x<113**	**113<=x<206**	**206<=x**
Low*	66.67%	17.91%	0	0
Middle*	33.33%	52.24%	36.36%	0
High*	0	29.85%	63.64%	100%
Congestion index	**x<0.07**	**0.07<=x<0.11**	**0.11<=x<0.18**	**0.18<=x**
Low*	80.00%	29.79%	0	0
Middle*	20.00%	61.70%	38.89%	0
High*	0	8.51%	61.11%	100%
Splenoportal index	**x<29%**	**29%<=x<=60%**	**60%<x<=67%**	**67%<x**
Low*	100%	24.29%	0	0
Middle*	0	52.86%	35.00%	0
High*	0	22.86%	65.00%	100%
Portal vascular index	**9<=x**	**7<=x<9**	**x<7**	
Low*	28.57%	0	0	
Middle*	61.90%	29.41%	0	
High*	9.52%	70.59%	100%	
PHI	**x<1.5**	**1.5<=x<1.6**	**1.6<=x<2.7**	**2.7<=x**
Low*	100%	64.29%	0	0
Middle*	0	35.71%	68.42%	0
High*	0	0	31.58%	100%
Portosystemic collaterals' presence	**0**	**1**	**2**	**3**
Low*	62.50%	38.10%	10.53%	3.57%
Middle*	37.50%	47.62%	52.63%	39.29%
High*	0	14.29%	36.84%	57.14%

* Low - confidence level of conclusion: low severity of portal hemodynamics disorders.
Middle - confidence level of conclusion: middle severity of portal hemodynamics disorders.
High - confidence level of conclusion: high severity of portal hemodynamics disorders.

Table 2

Scoring for portal hemodynamics disorders severity in liver cirrhosis assessment by duplex ultrasound

Measure	1 point	2 points	3 points	4 points	5 points	6 points
Spline area		x<57	57<=x<113		113<=x<206	206<=x
Congestion index		x<0.07	0.07<=x<0.11		0.11<=x<0.18	0.18<=x
PHI	x<1.5	1.5<=x<1.6		1.6<=x<2.7		2.7<=x
Portal vascular index			9<=x		7<=x<9	x<7
Splenoportal index	x<29%		29%<=x<60%		60%<=x<67%	67%<x

tosystemic collaterals' presence" parameters were divided into four sub-segments, and "Portal vascular index" in 3. For each sub-segment the confidence level in one of those three conclusions was calculated (tab. 1).

Analyzing the obtained results, it was found that the parameter "Portosystemic collaterals' presence" was less informative to differentiate portal hemodynamics disorders severity in liver cirrhosis. As a result, the six parameter system has been reduced to five.

At the next stage there was realized clustering of portal hemodynamic disorders severity assessment domain based on results of five imaging diagnostic criteria segmentation. Cluster analysis (or clustering) is the task of grouping a set of patients with portal hemodynamics disorders in such a way that patients in the same group (called a cluster) are more similar to each other than to those in other groups. More similar in the sense of disorder severity description based on five imaging diagnostic criteria. Seven clusters were identified. Taking into consideration the logical reasoning of each cluster expressed in the production rules and their role in the overall assessment of portal hemodynamics severity disorders, a scoring system was developed and the way of its interpretation was proposed (tab. 2).

Portal hemodynamics disorders severity was classified in: low severity, middle severity and high severity (tab. 3).

Table 3

Scoring interpretation

Total points	Portal hemodynamics disorders severity	Confidence level
9-10	Low	More than 90%
11-12	Low to Middle	Up to 70%
13-16	Middle	Up to 68%
17-24	Middle to High	Up to 65%
25-30	High	More than 95%

Two ways of applying the obtained results in this research can be pointed out:

1. The scoring system can be used directly as a means of differential diagnosis of liver cirrhosis;

2. The decision rules in the form of productions, obtained during the clustering stage, represent for computer scientists a formalized knowledge that can be used to develop medical information systems;

The obtained scoring system and its way of interpretation were validated in actual clinical practice. This process demonstrated their efficacy and veracity. In addition, the possibility of their use in assessing the dynamics of liver cirrhosis was observed.

Conclusions

For a broader test the authors intend to use the obtained results to develop computer-aided tools (desktop, web and mobile versions) for the evaluation and classification of portal hemodynamics disorders severity.

At the moment, a condition for the utilization of the proposed approach is that all five parameters of the scoping system should indicate any deviations from the norm. The proposed methodology is foreseen to be used in future in cohorts of patients with some additional restrictions as: patients with one or more normal parameters, patients after splenectomy, etc.

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