REPRODUCIBILITY OF ULTRASONOGRAPHY IN THE ASSESSMENT OF PERIPORTAL FIBROSIS ACCORDING TO NIAMEY CRITERIA IN PATIENTS WITH SCHISTOSOMIASIS MANSONI*

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Abstract **OBJECTIVE: To determine the intra- and interobserver agreement in the classification of periportal fibrosis, according to the criteria defined at the Niamey Workshop of 1996. MATERIALS AND METHODS: A prospective, observational and transverse study was developed in the period between February, 2005 and March, 2006, in 30 schistosomal patients with no other hepatic findings associated, submitted to abdominal ultrasound. Ultrasonographic studies were independently performed and reviewed by two radiologists at three different moments: the dynamic examination itself (first moment), 30 and 90 days later (second and third moments), by means of the images review performed in a workstation. Intra- and interobserver agreement was evaluated by means of the kappa test. RESULTS: Intraobserver agreement was 0.43 for the first, and 0.57 for the second observer. Interobserver agreement as regards the dynamic examination and images review was respectively 0.46 and 0.71. CONCLUSION: Ultrasonography demonstrated moderate to substantial reproducibility in the classification of periportal fibrosis according to the Niamey criteria.**

Keywords: Ultrasonography; Reproducibility of results; Fibrosis; Schistosomiasis.

Resumo *Reprodutibilidade da classificação ultra-sonográfica de Niamey na avaliação da fibrose periportal na esquistossomose mansônica.*

OBJETIVO: Medir a concordância intra- e interobservador da classificação ultra-sonográfica qualitativa para graduar a fibrose periportal adotada no encontro de Niamey em 1996. MATERIAIS E MÉTODOS: No período de fevereiro de 2005 a março de 2006 foi realizado estudo prospectivo, observacional e transversal em 30 pacientes esquistossomóticos, sem outras hepatopatias associadas, submetidos a ultra-sonografia abdominal e classificados segundo os critérios de Niamey. Os exames foram realizados por dois radiologistas de forma independente em diferentes momentos: durante o exame dinâmico (primeiro momento) e 30 e 90 dias depois (segundo e terceiro momentos) do exame, por meio da documentação fotográfica analisada em estação de trabalho. A concordância intra- e interobservador foi avaliada pelo teste kappa. RESULTADOS: A concordância intra-observador medida pelo teste kappa foi 0,43 para o observador 1 e 0,57 para o observador 2. A concordância interobservador durante o estudo dinâmico e na avaliação fotográfica foi, respectivamente, de 0,46 e 0,71. CONCLUSÃO: O uso do ultra-som para classificar a fibrose periportal segundo o protocolo de Niamey apresentou uma reprodutibilidade que variou de moderada a substancial.

Unitermos: Ultra-sonografia; Reprodutibilidade dos testes; Fibrose; Esquistossomose.

INTRODUCTION

Periportal fibrosis and splenomegaly are the causes of portal hypertension, most of times a condition responsible for the morbidity and mortality in cases of *Schistosoma mansoni* infection[1]. The disease progression is clinically insidious and asymptomatic. Ultrasonography (US) allows the evaluation of the extent, progression and possible regression of the disease after treatment[2]. In 1989, Homeida et al. demonstrated that the periportal thickening detected at US correlates with the periportal fibroses found in biopsies em 100% of cases[1].

Periportal fibrosis is directly correlated with clinical conditions and risks for complications as a result of the disease. Most frequently, hematemesis, sclerotherapy, blood transfusion, and lower limbs edema occur in patients with a more significant periportal thickening. Other parameters related to periportal fibrosis intensity are splenomegaly, portal and splenic veins caliber, the presence of collateral circulation,

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and the number and size of esophageal varices found at endoscopy[3].

The sonographic aspects of schistosomiasis have been described in different endemic areas like Brazil[4], Sudan[1] and Egypt[3]. Different methodologies were utilized in these studies to evaluate periportal fibrosis, so the resulting data could not be compared with each other. Then, a standardization of protocols was developed and published by the Cairo Working Group in 1992, with the aim at standardizing the sonographic evaluation, rating the affected population, evaluating their progression, and allowing comparisons among several research centers[5].

This protocol was reviewed in Niamey[6], and a qualitative analysis was added to classify periportal fibrosis; so its sonographic evaluation in schistosomotic patients included a subjective rating (qualitative analysis, comparing the liver with determined patterns of involvement by periportal fibrosis), and an objective rating (quantitative analysis, measuring the periportal fibrosis thickness).

Despite its evident advantages, US is known as a highly operator-dependant method, and that, in association with the highly subjective nature of the criteria adopted for rating periportal fibrosis, may lead to a low reproducibility of the method in the fibrosis gradation, compromising the utility of the Niamey scoring criteria.

Two studies have been published, demonstrating the interobserver variability in the grading of periportal fibrosis according to the Cairo criteria and according to specific criteria for children[7]. However, in the present literature review, no study was found measuring the US reproducibility according to the Niamey criteria.

Therefore, the present study was aimed at evaluating the intra- and interobserver agreement in the qualitative sonographic classification for grading periportal fibrosis adopted in the Niamey meeting.

MATERIALS AND METHODS

A prospective, transverse and observational study was developed in the period between February 2005 and March 2006, in 30 patients referred by the infirmary of schistosomiasis of the Discipline of Gastroenterology at Universidade Federal de São Paulo/Escola Paulista de Medicina (Unifesp/EPM) and submitted to US in the Department of Imaging Diagnosis (DID) of this institution.

Sixteen men and 14 women in the age range between 23 and 59 years (mean age 39.5 years) were studied. The group included patients with hepatosplenic-type schistosomiasis with no other associated pathology.

Inclusion criteria were: patients above 18 years of age, with diagnosis of schistosomiasis achieved by means of rectal biopsy or strong clinical-laboratory evidence (signs of portal hypertension and/or positive fecal parasitologic examination) and positive epidemiological history (contact with river or pond waters in endemic areas).

Exclusion criteria were: Previous history of alcoholism (ingestion of more than 160 g of ethanol/week), positive serology for hepatitis B or C viruses, with a previous history of proven autoimmune disease, and use of hepatotoxic drugs.

The project of the present study was approved by the Committee for Ethics in Research of Hospital São Paulo.

Ultrasonography technique

A Philips EnVisor US equipment (Philips Medical Systems do Brasil) with a convex multifrequency transducer. Examinations were performed by two radiologists, one of them with six-year experience (observer 1), and the other with two-year experience (observer 2) after conclusion of medical residence in imaging diagnosis and familiarized with the grading of periportal fibrosis according to the Niamey protocol.

Intentionally, the examinations results were not discussed by the observers during the study. The examinations were performed according to the sonographic standards proposed by the Niamey Working Group consisting of seven standard views: three longitudinal (left parasternal, right middle-clavicular, and right anterior axillary views), transverse substernal, transhepatic subcostal, right oblique and right oblique intercostal views[6].

Images analysis

Periportal fibrosis was classified by the qualitative method described in the Niamey meeting[6]. The results were compared with A to F patterns (Chart 1; Figures 1 to 5).

The examinations were independently performed by both observers, and the classification was defined at different moments: a) during the dynamic examination (called moment 1); b) 30 days after the dynamic examination, that is to say, only by the analysis of the photographic records obtained at the moment 1 (called moment 2); c) 90 days after the dynamic examination, also by means of the analysis of the photographic records (called moment 3).

The intra- and interobserver agreement were evaluated by the kappa test as follows: non-significant agreement for kappa between 0 and 0.2; median, for kappa between 0.21 and 0.4; moderate for kappa between 0.41 and 0.6; substantial, for kappa between 0.61 and 0.8; and almost-perfect, for kappa between 0.81 and 1.0[8].

RESULTS

The 30 patients were classified by both observers as C, D, E or F patterns. None of the patients was classified as A or B pattern of hepatic fibrosis.

The results from the analysis of the 30 patients assessed by the observers 1 and 2 are shown on Table 1. A tendency of ob-

Chart 1 Hepatic parenchyma patterns according to the Niamey classification.

Pattern	Sonographic image
A	Normal.
B	Starry sky (diffuse echogenic foci).
C	Ring echoes and pipe-stems.
D	Echogenic ruff around portal bifurcation.
E	Hyperechoic patches expanding from the portal vessels into the parenchyma.
F	Highly echogenic bands extending to the liver periphery and retracting the subjacent parenchyma.

Source: Niamey Working Group 2000[6].

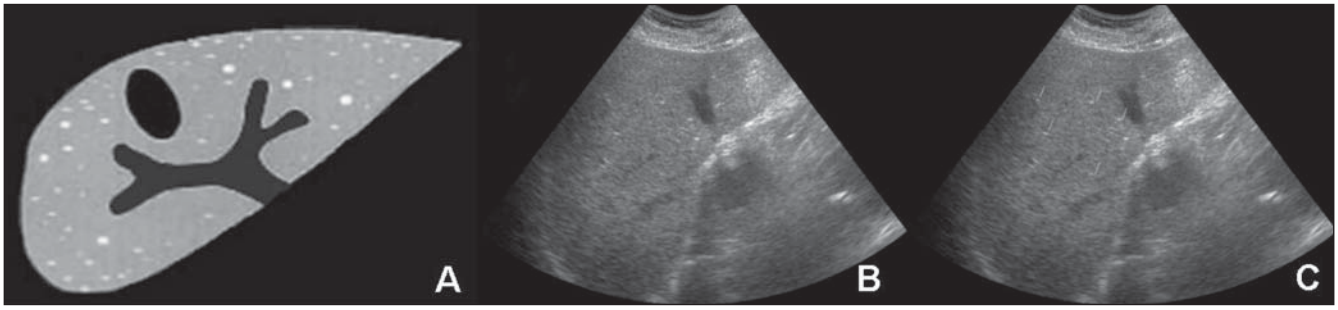

Figure 1. Image pattern B. Starry sky (sparse hyperechoic foci in the hepatic parenchyma). Figure 1A source: Niamey Working Group 2000[6].

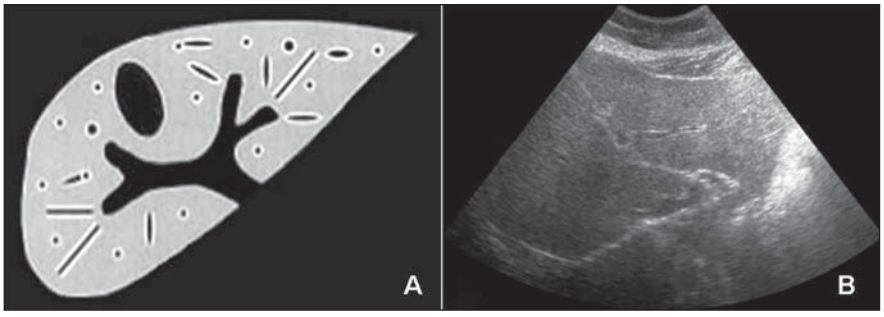

Figure 2. Image pattern C. Fibrosis in intraparenchymal branches of portal vein saving the central region presenting like ring echoes (transverse view of the vessel) and pipe-stems (longitudinal view). Figure 2A source: Niamey Working Group 2000[6].

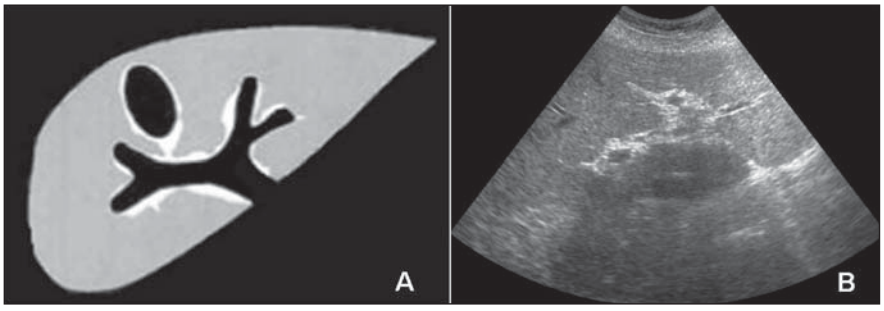

Figure 3. Image pattern D. Fibrosis bands adjacent to the portal vein, its main branches, and perivesicular region. Figure 3A source: Niamey Working Group 2000[6].

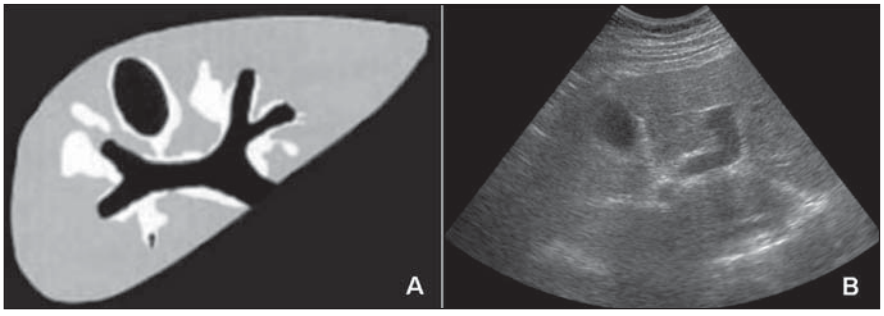

Figure 4. Image pattern E. Focal pattern in patches, predominantly in the central region, expanding into parenchyma, without reaching the hepatic surface. Figure 4A source: Niamey Working Group 2000[6].

Table 1 Distribution of the 30 patients with mansoni schistosomiasis, according to the periportal fibrosis patterns defined by the Niamey protocol, for observers 1 and 2 during the dynamic examination.

	Fibrosis patterns				
Observer	C	D	E	F	Total
1	1	4	13	12	30
2	1	2	14	13	30

server 2 to overestimate the periportal fibrosis in relation to observer 1 was noted.

The interobserver agreement measured by the kappa test for the dynamic study was 0.46 (moderate agreement), and for the photographic records (comparison between examinations on the second and third moments) was 0.71 (substantial agreement).

The intraobserver agreement measured by the kappa test for evaluating the static examinations (moments 2 and 3) was 1.0 for both observers (perfect agreement). On the other hand, the comparison between the analysis of the dynamic (moment 1) and static (moment 2) examinations, resulted in an intraobserver agreement in the range between 0.43 and 0.57 (Table 3).

DISCUSSION

A remarkable decrease in the incidence of severe schistosomiasis presentations has been observed since the treatment with appropriated drugs was introduced[9], with the mild presentations of the disease being more frequently observed. Therefore, the clinical examination has shown to be insufficient to the diagnosis of schistosomiasis in endemic areas, highlighting the necessity of subsidiary examinations to confirm

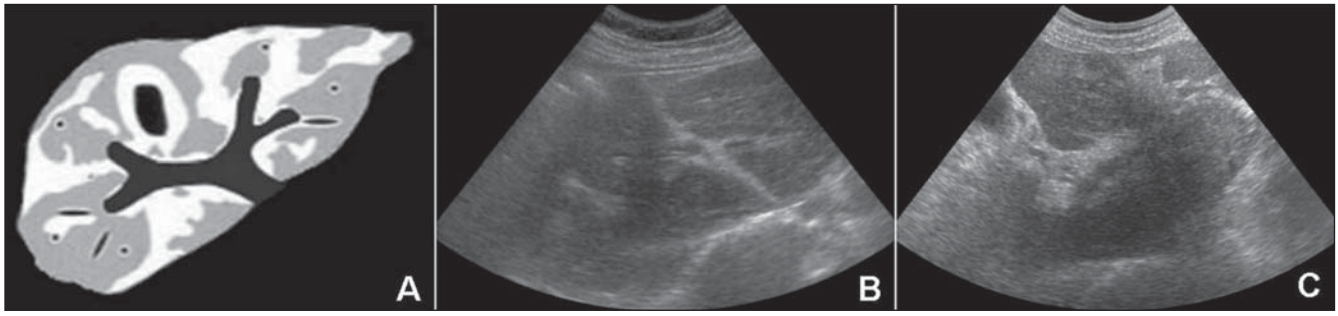

Figure 5. Image pattern F. Bird´s claw pattern. Echogenic bands and fibrosis extending towards the liver periphery, with retraction of the organ contour, not considering the hepatic fissures. Figure 5A source: Niamey Working Group 2000[6].

Table 2 Interobserver agreement for moment 1 (during dynamic examination) and moments 2 and 3 (30 and 90 days after the dynamic examination).

Moment	Agreeing cases				Agreement	Kappa
	C	D	E	F		
1	1	1	8	10	66.6%	0.46
2	1	1	10	13	83.3%	0.71
3	1	1	10	13	83.3%	0.71

Table 3 Intraobserver agreement (dynamic examination x static photographic images).

Observer	Agreeing cases				Agreement	Kappa
	C	D	E	F		
1	1	2	9	9	70.0%	0.57
2	1	1	7	11	66.6%	0.43

the diagnosis and mainly to evaluate the response of the patient to the therapy[10]. Ultrasonography (US) has been the method most frequently utilized in this group of patients, demonstrating a typical pattern of abnormalities[3,4].

One of the first sonographic classifications of periportal fibrosis was described by Homeida et al. in 1988, defining a classification based on periportal thickening that later was adopted by other authors[1]. A standard method to be adopted for children was proposed by Doehring-Schwerdtfeger et al. in 1989[7]. Later on, a protocols standardization was developed and published by the Cairo Working Group in 1992[11,12].

When a diagnosis method is proposed to evaluate determined diseases, not only the method effectiveness, but also its accuracy should be established. A method accuracy is measured by means of the calculation of intra- and interobserver reproducibility. Very few studies in the literature have been focused on the US reproducibility in the assessment of periportal fibrosis in schistosomotic patients.

In 1992, Doehring-Schwerdtfeger et al. developed a study about the interobserver variability based on a three-level classification[13] previously explained in another study of the same authors[7], and applied in Sudanese schistosomotic children. The authors observed an interobserver agreement in 38 of 49 cases studied (77.5%). In 10 cases, the observers disagreed on the definition of which patients were rated as normal and those rated as grade I. There was no disagreement on patients in grades I and II. In this study, the author included exclusively a pediatric population, where the disease manifestations are different from the manifestations found in the adult population[1]. More severe cases of fibrosis were not found, since only two of their patients were rated as grade II, and no patients was rated as grade III. Despite the reasonable agreement found in this study, it is important to note that the patients were categorized only into three groups (differently from the Niamey criteria establishing the classification of patients into six groups). Additionally, the authors utilized a handheld, low-definition equipment (possibly difficulting the images analysis), and do not mention the experience of the observers involved in this study.

In 1997, Thomas et al. studied the interobserver agreement for US utilizing the method developed in Cairo. The variation found was considerable. For the first observer, 31% (84/268) had hepatic periportal thickening, and for the second observer, 79% (200/253) had hepatic periportal thickening. In this study, for the first observer only two patients, and for the second observer four patients presented grade II periportal fibroses, and none, grade III[2].

Maharaj et al., in 1988, evaluated the US accuracy for the diagnosis of focal and diffuse hepatic diseases including schistosomiasis. The sensitivity and specificity of the US diagnosis were lower in the diffuse hepatic diseases than in the focal ones. The interobserver reproducibility only was evaluated in the focal diseases, demonstrating a 77% agreement rate[14].

In the present literature review, studies either measuring the US reproducibility according to the Niamey qualitative classification, or evaluating also the intraobserver variability were not found. This is the reason for the development of the present study.

One of the limitations in the present study is related to the fact that the authors could not cover the whole Niamey classification, including cases of lower levels of disease. Differently from the above mentioned studies, the cases included in this study are concentrated in the moderate and

severe presentations of schistosomiasis, probably because the criteria for selection of patients, only involving the hepatosplenic presentation of the disease. It should be taken into consideration that the patients referred to our institution are those affected by the hepatosplenic presentation were only the more advanced presentation of periportal fibrosis is observed[15]. It would be important to validate the results from the present study in a more diversified group of patients covering the six degrees of fibrosis according the Niamey criteria.

The analysis of the US reproducibility in this group of patients demonstrated an agreement ranging between moderate and substantial, and, surprisingly, with better results in the analysis of static images as compared with the dynamic evaluation. A hypothesis to explain this result would be related to the selection of images stored and considered as the most representative of the disease, contrarily to the dynamic evaluation, where subjective aspects may have a higher weight.

It was interesting to observe that the intraobserver agreement was higher for the observer 1 who was more experienced than the observer 2 (Table 3). This suggests that the classification tends to be more accurate as the observers' experience increases.

A possible contribution of the present study would be to aid in the diffusion of this classification, considering that periportal fibrosis is directly correlated with clinical conditions and risks of complication for patients[3]. Probably because of the lack of a specific training for sonographists and also the uncertainties about the method reproducibility, the Niamey classification has not been underutilized. US examinations in schistosomotic patients, in our environment, have been restricted to the evaluation of portal and splenic veins, organometry, and fluxometry of portal vein[16].

For a diagnostic test to be considered as useful, it must present, among other features, a high reproducibility. Analyzing the results from the present study demonstrating an agreement ranging between moderate and substantial, some may consider such agreement as undesirable or insufficient. On the other hand, it is important to consider that other recognized and widely adopted diagnostic tests, like mammography in the BIRADS classification, have demonstrated agreement indices (kappa) ranging between 0.28 and 0.75 for describing mammographic findings, and 0.37 in cases a procedure for the lesion is suggested[17], allowing, by analogy, a valorization of US in the evaluation of periportal fibrosis whose agreement rate is similar.

Finally, it should be remembered that, as already demonstrated[18], magnetic resonance imaging may contribute in those cases where discrepancies are observed between the sonographic evaluation and the clinical condition of patients with chronic schistosomiasis mansoni.

The results from the present study suggest that US is reliable method for classifying periportal fibrosis according to the Niamey criteria in patients with severe presentations of schistosomiasis.

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