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LETTER TO THE EDITOR

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Platelet count/spleen diameter ratio as a predictor of esophageal varices in cirrhotic patients

DEAR EDITOR,

This letter regards the very interesting paper published in Annals of Hepatology 2009; 8(4): 325-30 by Barrera, *et al*.[1] The authors emphasize an important matter, which is the burden of frequently endoscopying cirrhotic patients in order to verifying for the presence of esophageal varices (EV) and indicating the proper prophylaxis to avoid bleeding. They evaluate the platelet count/spleen diameter ratio (PC/SD)[2-4] in 67 patients as a non-invasive parameter to predict the presence of high risk esophageal varices (HREV), defined by them as those classified as large or with red wale signs. We conducted a quite similar study, currently in press in Arquivos de Gastroenterologia, with 164 cirrhotics from Santa Casa Hospital, Porto Alegre, Brazil.

In the paper by Barrera, *et al*., PC/SD had a sensitivity of 76.9%, a specificity of 74.2%, a positive predictive value (PPV) of 71.4% and a negative predictive value (NPV) of 77.8% for the diagnosis of HREV, using a cut-off point of 830.8. In our study, on the other hand, PC/SD had a sensitivity of 77.5%, a specificity of 45.5%, a PPV of 79.5%, a NPV of 42.6% and an accuracy of 68.9% for the diagnosis of EV, using the cut-off point of 909. Another difference between the results of the studies is that, even being significantly different between the 2 groups in the univariate analysis in both studies, PC/SD did not prove to be an independent marker of EV in the multivariate analysis we made, while PC/SD and age were associated to HREV in the multivariate analysis of the paper published by Barrera, *et al*. In our study, the only independent variable associated to EV in the multivariate analysis was platelet count ($p<0.05$).

The previous differences in results may be explained by differences in the design of the studies. The major difference in their designs probably is that we evaluated PC/SD for the prediction of varices of any kind, since the latest AASLD guideline,[5] which took place after Baveno IV,[6] recommends prophylaxis with beta-blockers even for patients with small varices and without red wale signs, as long as in patients with Child B or C classes. On the other hand, Barrera, *et al*., evaluated the index for the diagnosis of HREV. The other important difference in design is that we used the 909 cut-off point proposed by Giannini, *et al*., for the PC/SD in the analysis, while Barrera, *et al*., calculated their own cut-off point in a ROC-curve.

Besides, there were some differences in the studied samples that could have contributed to explain the differences found in some of the results. Barrera, *et al*., used a sample composed by men in only 43.3%, with a mean age of 66 years and a Child class distribution of A – 46.2%, B – 38.8% and C – 15%. We had a sample with a 56.7% male proportion, with a mean age of 56.6 years and with a Child class distribution of A – 57.6%, B – 37.7% and C – 4.6%. In our study, cirrhosis was caused by viral hepatitis in 43.9% of cases, by alcohol abuse in 29.3%, by viral hepatitis and alcohol in 10.4% and by other causes in 16.5%; Barrera, *et al*., found only 7.5% of viral hepatitis as cause of cirrhosis, while alcohol abuse was its cause in 26.9%, autoimmune hepatitis in 11.9%, primary biliary cirrhosis in 14.9%, non-alcoholic steatohepatitis in 14.9% and cryptogenic cirrhosis in 26.9%, which suggests a somewhat different population in the studies. We found EV on endoscopy in 73.2% of our cases, while Barrera, *et al*., found them in 85%.

Despite the mentioned differences between both studies, they agree in the most important, their conclusion: PC/SD cannot replace endoscopy in the screening of EV or of HREV in cirrhotic patients.

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Reply:

We thank Dr. De Mattos for their interest in our study. Many attempts have been performed to find comfortable and cost-effective methods different from endoscopy for diagnosing esophageal varices. These non-invasive approaches include, among others, the following: platelet count; spleen diameter; platelet count and Child-Pugh score; spider angiomata, ALT and albumin; CT esophageal study; fibrotest ((c-glutamyltranspeptidase, haptoglobin bilirubin, apolipoprotein A, alpha-2-macroglobulin); and fibroscan (transient elastography).[1] We are fully aware of the limitations of these predictors, but among all of these methods, platelet count/spleen diameter ratio has been one of the most consistently evaluated.[2-4] This ratio has been developed by Gianini, *et al.*[2] by combining 2 portal hypertension-dependent variables that can potentiate its accuracy on predicting esophageal varices. The problem of this ratio is that platelet count is a sensible parameter that can be easily modified by acute events such as bleeding, infection, medications, alcohol, etc. It has also been described that cirrhosis can be associated with lower thrombopoetin levels and increased antibody mediated platelet destruction,[5] both of them variables that are not dependent of the presence of portal hypertension. On the other hand, spleen bipolar diameter in most of the studies is measured by ultrasound. This is an operator-dependent method that could have low reproducibility if it is not performed with a proper technique. All the above-mentioned factors could explain the variability of the positive predictive value (PPV) and negative predictive value (NPV) among different studies. In spite of this, there are many publications on different populations that support the utility of this ratio on predicting presence of esophageal varices, many of them with similar or superior PPV and NPV to our findings.[2-4] An ongoing Cochrane database meta-analysis will help us to clarify the real value of laboratory and ultrasonography parameters on predicting esophageal varices.

With current data, we think that platelet count, spleen diameter and platelet count/spleen diameter ratio are a useful tool on approaching to portal hypertension, esophageal varices and cirrhosis diagnosis, especially when there is limited access to endoscopy examination. Another utility of these parameters is to help to suspect the diagnosis when clinical history and physical examination findings suggest the presence of initial cirrhosis. In our opinion, endoscopy will never be fully replaced by non-invasive parameters for esophageal varices final diagnosis. Hopefully, non invasive parameters could help to categorize patients on high probability, intermediate probability or low probability of esophageal varices. With this categorization, we could expect to give priority for endoscopy exam for intermediate-risk patients. High-risk patients could choose to begin empiric therapy or perform an endoscopy exam for diagnosis according to patient's preference and access to endoscopy. Low-risk patients could be given a lower priority for endoscopy exam, as suggested by Burton, *et al.*[6] The indication of prophylaxis on small esophageal varices is to prevent development of high risk esophageal varices.[7] Non-invasive method allows very frequent screening so we decided to focus directly on predicting HREV where beta blocking therapy has demonstrated to improve survival.

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