Usefulness of serum-ascites albumin gradient and fluid cholesterol determination in the differential diagnosis of ascites in Ivorian hospitals

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ABSTRACT

The aim of this cross-sectional study was to compare serum-ascites albumin gradient (SAAG), serum-ascites protein gradient (SAPG) and cholesterol in ascitic fluid to Rivalta test and total protein in the ascitic fluid (TPA) to assess their diagnostic value in the classification of transudative and exudative ascites. The study examined 98 patients suffering from ascites recruited at university teaching hospitals in Abidjan. The diagnostic concordance between SAAG and Rivalta test and between SAAG and TPA was moderate (69% and 73%, respectively), while it was better between Rivalta test and TPA (88%). Results showed a higher sensitivity of SAAG (86.8%), with low specificity (40%). Cholesterol concentrations in the ascitic fluid provided the best diagnostic accuracy in the classification of ascitic fluids into exudates and transudates, with a sensitivity of 64.2% and a specificity of 86.7% (threshold value, 0.183 g/L). Given the high sensitivity of SAAG, fluid cholesterol and SAAG should be associated for a better differential diagnosis of ascites.

INTRODUCTION

Ascites is an effusion in the abdominal cavity. Its pathophysiology varies depending on the etiology (1-3). Clinical diagnosis is easy in most cases. However, etiological diagnosis is often difficult and requires the implementation of diagnostic tests including, among others, biochemical analyses according to the clinical and radiological guidance (1). In Côte d'Ivoire, Rivalta test and total protein determination are widely used to classify ascites into transudates and exudates. However, this approach is outdated. Indeed, ascites of cirrhotic origin and ascites of cardiac origin in their initial phase may exhibit high concentrations of proteins, but they are not necessarily exudative ascites (4, 5).

Runyon et al. (6) have shown a higher diagnostic performance of serum-ascites albumin gradient (SAAG) when compared to total protein concentrations in ascitic fluid (TPA). More recently, ascitic fluid cholesterol was used to distinguish between neoplastic and non neoplastic ascites (7). In addition, several Authors have reported ascites of malignant origin as exudative ascites (8, 9). Taken together, these studies suggest that cholesterol concentrations in the ascitic fluid can also differentiate exudative from transudative ascites.

This study aims to compare the diagnostic value of SAAG, serum-ascites protein gradient (SAPG) and fluid cholesterol concentrations to Rivalta test and TPA in the classification of ascites according to transudate-exudate concept.

MATERIAL AND METHODS

Patients

98 patients with ascites (median age, 41 years; range 16 to 70) were consecutively recruited at the Service of Hepato-Gastroenterology of the University Hospital of Yopougon and at the Service of Internal Medicine of the University Hospital of Treichville from January to September 2006.

The classification of ascites was based on clinical findings and on their etiology (6, 7, 9). Thus, two groups of patients were formed according to this classification. Those with exudative ascites represented 54% and those with transudative ascites 46%. Characteristics of the study population are presented in Table 1. For each patient included, ascitic fluid was aspirated prior to initiation of treatment including antibiotics and diuretics. All patients gave informed consent.

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Methods

The ascitic fluid was aspirated into two sterilized tubes. One was used to carry out biochemical analyses and the other for cytologic analysis. Simultaneously, venous blood samples were drawn into 5 mL Vacutainer dry tube (Becton Dickinson) for the determination of total proteins and albumin. Serum was separated by centrifugation at 1300g for 10 min, divided into 0.5 mL aliquots and stored at -80 °C, if not immediately processed.

The quantitative determination of total proteins, albumin and total cholesterol in the ascitic fluid or serum was performed by Roche Cobas Integra 400 Plus analyzer. Total proteins were assayed using Biuret colorimetric method and albumin by a bromo-cresol green colorimetric method. Rivalta test was performed on each sample of ascitic fluid as previously described (1). Ascites was exudative or inflammatory when TPA was ≥30 g/L or when the Rivalta test was positive. On the contrary, ascites was qualified as transudative or non-inflammatory when the protein concentration was <30 g/L or when the Rivalta test was negative (10).

SAAG was determined by the following formula: (albumin concentration in serum) – (albumin concentration in ascites) in g/L. SAAG ≥11 g/L defines a non-inflammatory or transudative ascites (9). On the contrary, a SAAG <11 g/L reflects an inflammatory or exudative ascites.

SAPG was determined by the following formula: (protein concentration in serum) – (protein concentration in ascites) in g/L.

Statistical analysis

Quantitative variables were compared using Student's t test or Wilcoxon U test and qualitative variables by a chi-square test. A P-value <0.05 was considered statistically significant. Threshold values, sensitivity, and specificity of fluid cholesterol and SAPG were determined after analyzing the area under the ROC curve (AUROC). Statistical analysis was performed using SAS 9.1 by SAS Institute Inc. AUROC analysis was performed by the software MedCalc 8.2.0.1 demo.

RESULTS

Cellularity analysis of ascitic fluids showed that white blood cells, lymphocytes, neutrophils, and mesothelial cells were significantly more elevated (P <0.0001) in patients with exudative ascites as compared to those with transudative ascites (results not shown). Concerning biochemical analysis of ascitic fluid, concentrations of total protein, cholesterol and albumin were higher (P <0.0001) in subjects suffering from exudative ascites when compared to those with transudative ascites (Table 2). On the other hand, the SAAG and SAPG gradients were significantly higher (P <0.01) in patients with transudative ascites than in those with exudative ascites (Table 2).

Based on threshold values of Rivalta test, SAAG, and TPA, distribution of samples into exudates and transudates was examined (Table 3). In the group with transudative ascites (n=45), 22 patients showed a Rivalta positive test and 25 showed TPA ≥30 g/L. Among patients with exudates, 83% had their TPA ≥30 g/L and 77% had a positive Rivalta test. The analysis of diagnostic concordance revealed a good agreement between the test of Rivalta and TPA (k=0.72 or 88%). On the contrary, the concordance between SAAG and Rivalta (k=0.29, 69%) and SAAG and TPA (k=0.34, 73%) was moderate.

The analysis of the diagnostic value of SAAG, Rivalta test, and TPA showed that, out of 53 patients with exudative ascites, 46 were correctly classified by SAAG, 41 were correctly classified by the test of Rivalta and 44 were correctly classified by TPA, respectively (Table 4). SAAG had the highest sensitivity (86.8%) with the lowest specificity (40%) (Table 4). Similarly, Rivalta test and TPA showed good sensitivity and low specificity (Table 4). There were seven patients of the study population, whose ascites was caused by kidney failure. In these cases, SAAG is low (<11 g/L) because of lower albumin concentrations in serum, so the ascitic fluids are erroneously classified as exudates, while in reality they are transudates. However, by eliminating these patients from the evaluated population, the indices of performance of SAAG did not significantly improve.

Table 1
Characteristics of the study population

	Subjects suffering from transudative ascites (n=45)	Subjects suffering from exudative ascites (n=53)
Age (years)	48 (16-70)[a]	38 (17-70)[a]
Female	21 (46.7%)	28 (52.8%)
Male	24 (53.3%)	25 (47.2%)
Etiology of ascites	Non infected cirrhosis: 38 (84.4%)	Tuberculosis: 29 (54.7%)
	Kidney disease: 7 (15.6%)	Cancer: 18 (34.0%)
		Infected cirrhosis: 5 (9.4%)
		Acute pancreatitis: 1 (1.9%)

[a] *median (range).*

Table 2
Biochemical parameters studied in transudative and exudative ascites

	Transudative ascites	Exudative ascites
Serum proteins, g/L	58.9±12.5	63.6±11
Serum albumin, g/L	34.2±8.2	38.6±9.2[a]
Total proteins (ascites), g/L	28 (17.7-36.3)	40.7 (30-47.2)[b]
Albumin (ascites), g/L	20.2 (17.7-36.3)	29 (21-36)[b]
Cholesterol (ascites), g/L	0.038 (0.023-0.105)	0.290 (0.093-0.600)[b]
Serum-ascites albumin gradient, g/L	9.9 (8.4-13.9)	8.7 (6.3-10.2)[c]
Serum-ascites protein gradient, g/L	29.2 (24.1-35.3)	22.8 (14.7-30.4)[c]

Values expressed as mean±SD and, when data distribution was not Gaussian, as median (interquartile interval).
[a] P <0.05 (Student's t test); [b] P <0.0001 (Wilcoxon U test); [c] P <0.01 (Wilcoxon U test).

Table 3
Results of studied tests according to exudate-transudate classification

	Threshold	Transudative ascites	Exudative ascites	n
SAAG	<11g/L	27	46	73
	≥11g/L	18	7	25
Rivalta test	Positive	22	41	63
	Negative	23	12	35
TPA	≥30 g/L	25	44	69
	<30 g/L	20	9	29

n, number of patients according to test results; SAAG, serum-ascites albumin gradient; TPA, total protein concentration in the ascitic fluid.

Table 4
Diagnostic value of studied tests in the classification of ascites into exudates and transudates

	Sensitivity	Specificity	TP	TN	FP	FN	PPV	NPV
SAAG	0.86	0.40	46	18	27	7	63.0%	72.0%
Rivalta test	0.79	0.51	41	23	22	12	67.6%	65.7%
TPA	0.83	0.44	44	20	25	9	63.8%	69.0%

TP, true positives; TN, true negatives; FP, false positives; FN, false negatives; PPV, positive predictive value; NPV, negative predictive value; SAAG, serum-ascites albumin gradient; TPA, total protein concentration in the ascitic fluid.

The diagnostic value of total cholesterol in the ascitic fluid and SAPG was investigated using ROC curves. In particular, Figure 1 displays the ROC curve for cholesterol, showing an AUROC of 0.79. Table 5 shows the diagnostic performance of the two tests at three different threshold values. A SAPG less than or equal to the indicated cut-off indicates an exudative ascites, a greater value indicates a transudative ascites. A cholesterol concentration in the ascitic fluid greater than the cut-off indicates an exudate and otherwise a transudate. The concentration of cholesterol in the ascitic fluid (threshold, 0.183 g/L) provided the best diagnostic performance in the classification of transudative and exudative ascites, with a sensitivity of 64.2%, a specificity of 86.7%, a positive predictive value of 85.0% and a negative predictive value of 67.2% (Table 5).

DISCUSSION

This study focused on the classification of ascitic fluids into exudates and transudates through the determination of laboratory indices. According to cytologic analysis, the number of cells was higher in exudative ascites. Similarly, concentrations of proteins, albumin, and cholesterol were higher in exudative than in transudative ascites, while SAAG and SAPG were higher in transudative ascites. The elevation of cells, proteins, and albumin in exudative ascites fluids could be explained by the role of defense of the peritoneum (11-13). Analysis of diagnostic values showed a good sensitivity of Rivalta test, SAAG, and TPA, but with low specificity. The good concordance between Rivalta test and TPA is a convincing reason in favor of the common practice in which the operator performs protein assay on

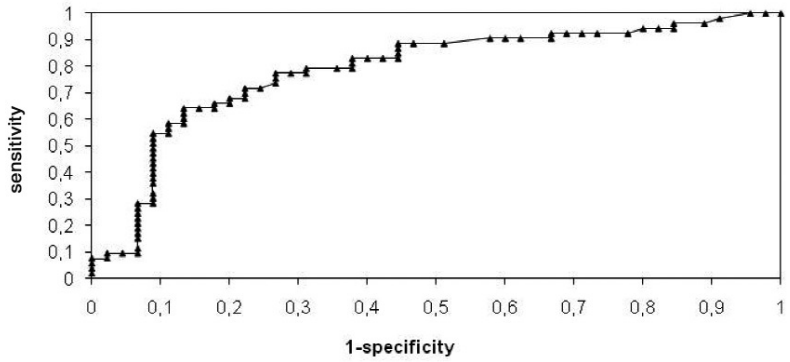


Figure 1
Diagnostic efficiency of the cholesterol concentration in ascitic fluid determined using the ROC curve. The area under ROC curve was 0.79, with a 95% confidence interval of 0.69-0.86.

Table 5
Diagnostic performance of serum-ascites protein gradient (SAPG) and of concentrations of cholesterol in the ascitic fluid at different cut-offs

	Cut-off	Sensitivity	Specificity	PPV	NPV
SAPG, g/L	≤23.5	0.55	0.78	74.4%	59.3%
	≤23.7	0.57	0.78	75.0%	60.3%
	≤23.8	0.57	0.76	73.2%	59.6%
Cholesterol, g/L	>0.180	0.64	0.84	82.9%	66.7%
	>0.183	0.64	0.87	85.0%	67.2%
	>0.200	0.62	0.87	84.6%	66.1%

PPV, positive predictive value; NPV, negative predictive value.

the basis of the Rivalta test results. Measurement of fluid total cholesterol provided the best diagnostic values, including fairly good sensitivity and good specificity. These results are in agreement with those obtained by Gupta et al. (5).

Regarding gradient values, subjects suffering from exudative ascites showed a lower SAAG than those with transudative ascites. These results agree with those of previous studies (5, 9, 14). Similarly, SAPG is also lower in patients with exudative ascites. However, the diagnostic ability of this parameter in the classification of ascitic fluids into exudates and transudates is not sufficiently documented, even if it is often used by clinicians in hospitals in Côte d'Ivoire. The diagnostic value of SAAG with a threshold value of 11 g/L proved to be fairly good, contrary to previous studies (4, 9, 15). The discrepancy observed could be attributed to the fact that the threshold value set at 11 g/L is not suitable for an optimal classification of ascites fluid in our study population. One could then propose a new cut-off that performs better for specific populations. The study conducted by Goran et al. (16) reported high sensitivity (97.6%), but low specificity (46.3%), results that are consistent with ours. The Authors concluded that it is probably necessary to determine another cut-off that would give a better balance between sensitivity and specificity.

High concentrations of cholesterol were found in exudative ascitic fluid. These results are consistent with those of Gupta et al. (5) and Pfalzer et al. (17). These findings support our hypothesis that the concentration of cholesterol in the ascitic fluid could be used to classify ascites according to the transudate-exudate concept, using a threshold value of 0.183 g/L. This threshold value differs from that reported by Pfalzer et al. (0.60 g/L) (17). The difference could be explained by their focus on both ascitic fluids and pleural effusions of patients. Gupta et al. (5) reported a threshold value of 0.55 g/L; notably, their study was limited to patients showing ascites from tuberculosis, malignant or non-infected cirrhotic origin. In 2002 Paramothayan et al. (8) evaluated the efficacy of cholesterol concentrations in ascitic fluid in the classification of ascites into exudates and transudates. They concluded that the measurement of lactate dehydrogenase activity and the ratio of serum/ascites protein concentrations, isolated or simultaneously applied, were more effective than concentrations of cholesterol in ascitic fluid.

CONCLUSIONS

Our study focussed on the usefulness of SAAG and fluid cholesterol in the differential diagnosis of ascites. The evaluation of the diagnostic performance of different tests showed a high sensitivity for SAAG, but with low

specificity. Cholesterol in the fluid provided the best diagnostic performance in the classification of ascites into transudate and exudate. However, given the high sensitivity of SAAG, it should be associated with this test for a better differential diagnosis of ascites.

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