Original Article

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Primary Prevention of Variceal Bleeding in Patients with Serum Ascites Albumin Gradient ≥ 1.5 g/dL

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ABSTRACT

Background & Aim: Correlations between serum ascites albumin gradient (SAAG) and presence of esophageal varices (EV), prevalence of EV, variceal size, incidence of esophageal variceal bleeding (EVB) and mortality were compared between the group of cirrhotic patients with SAAG <1.5 g/dL and the group with SAAG ≥1.5 g/dL. The predictive value of SAAG with regard to the presence of EV and variceal complications was also determined.

Methods: This prospective cohort study was conducted in cirrhotic patients with portal- type ascites with EV. Variceal size and incidence of EVB were recorded and compared between two groups. All patients were followed up to the study end-point, which was occurrence of EVB, or death or intolerance to the treatment prescribed.

Results: Thirty-five patients were enrolled, 4 patients with SAAG <1.5 g/dL and 31 patients with SAAG ≥1.5 g/dL. The prevalence and the size of EV were higher and larger in the SAAG ≥1.5 g/dL group. The sensitivity and specificity of SAAG >1.65 for predicting the presence of EV were 96.4% and 71.4%, while those of SAAG >2.05 for predicting the presence of large EV were 87.5% and 66.7%, respectively. The prevalence of EVB was also higher in the SAAG ≥1.5 g/dL group than SAAG <1.5 g/dL group, with no statistically significant difference.

Conclusion: The SAAG appeared useful in predicting the presence of EV and EVB. The higher value of SAAG was associated with a higher prevalence of large EV. The incidence of EVB was also higher in patients with higher SAAG. However, there is no statistically significant difference due to the relatively small sample size.

Key words : Serum ascites albumin gradient, SAAG, esophageal varices

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Esophageal variceal bleeding (EVB) is the most common and potentially lethal complication of liver cirrhosis, occurring with an incidence of 30-40% and carrying a mortality rate of 30-50%[1]. EVB usually occurs when the hepatic venous pressure gradient (HVPG) is higher than 12 mmHg[2]. In cirrhotic patient, the prevalence of EV at the first upper endoscopy is 40%, while the yearly incidence of newly developed EV is 6%. Small EV (size ≤5 mm.) progress to large EV at the rate of 12% per year. The incidence of bleeding from large EV is 30% in 2 years after diagnosis, while that from small EV is around 7-10%. EVB prevention by means of endoscopic surveillance followed by primary medical prophylaxis with non-selective beta blocker[3-5] is recommended. This approach can lower the rate of EVB from 30% to 15% at the second year[6].

A high HVPG is associated with EV, EVB, and death[2,7,8], and also with a high serum-ascites albumin gradient (SAAG ≥1.1 g/dL). Thus, ascites with a high SAAG is indirectly related to the presence of EV. Moreover, SAAG ≥1.435 ± 0.015 g/dL has been reported to predict the presence of EV[9]. In addition, a high SAAG is associated with EVB, although it is not associated with variceal size[10,11].

In our previous study at Maharaj Nakorn Chiangmai Hospital, a significantly higher incidence of EVB was seen in patients with SAAG ≥1.5 g/dL. We compared the prevalence of EV and the incidence of EVB in patients with SAAG ≥1.5g/dL and those with SAAG <1.5 g/dL. Primary prophylaxis of EVB in such patients may be cost effective as further endoscopic surveillance with associated potential complications and discomfort can be avoided.

METHODS

Patients

The objective of this prospective cohort study was to compare the prevalence of EV, variceal size, and the incidence of bleeding from small EV and large EV in cirrhotic patients with SAAG <1.5 g/dL. and those with SAAG ≥1.5g/dL. Patients with liver cirrhosis and ascites at the Gastrointestinal Unit of Maharaj Nakorn Chiangmai Hospital from October 2007 to January 2009 were recruited for the study. The inclusion criteria were 1) male and female with portal-type ascites (SAAG >1.1 g/dL), 2) age 18 to 80 years, and 3) agreement for an informed consent.

The exclusion criteria were 1) patients with history of EVB or gastric variceal bleeding, 2) patients with contraindication to esophagogastroduodenoscopy (EGD), 3) patients with hypotension, (BP <90/60 mmHg), and 4) prior treatment with non-selective beta blocker or esophageal variceal ligation before enrollment.

Following calculation of SAAG, all patients underwent a surveillance EGD. Patients were then placed into one of two groups, the SAAG ≥1.5 g/dL and the SAAG <1.5 g/dL groups, with subgroups by variceal size [no EV, small EV (size ≥5 mm), and large EV (size >5 mm)]. For patients with large EV, either non-selective beta blocker therapy or EVL was chosen for primary prophylaxis, after discussion with the patients on the risk and benefit issue. All patients were followed up to the study end-point, which was occurrence of EVB, or death or intolerance to the treatment prescribed.

Statistical analyses

The main analyses were conducted using the Fisher's Exact test to compare the incidence and the prevalence of EBV and variceal size. ROC curve was used to determined the cut-off point of SAAG for diagnosis of EV or large EV. The sensitivity and specificity of SAAG in predicting the presence of EV, large EV and EVB, were calculated.

RESULTS

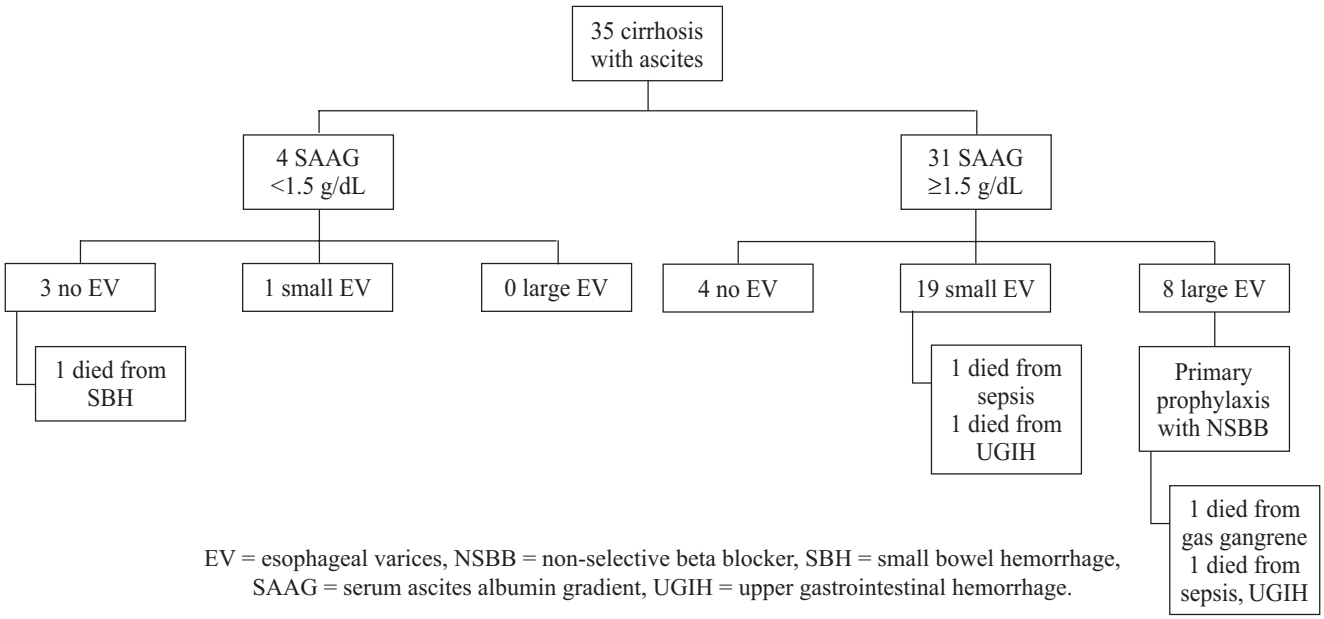
Thirty-five patients were enrolled to the study, 4 patients with SAAG <1.5 g/dL and 31 patients with SAAG ≥1.5 g/dL. The mean age was not different in both groups, most patients were male. There was only one patient with Child A cirrhosis. Child-Pugh B and C did not differ in the two groups ($p = 0.363$). Levels of serum AST, ALT and AP were not significantly different ($p = 0.146$, 0.108 and 0.736). The presence of EV (both small and large EV) and the size of EV were both statistically significant different in the two groups ($p = 0.019$ and $p = 0.039$). The baseline demographic data of both groups are shown in the Table 1.

In patients with SAAG <1.5 g/dL, 3 patients had no EV and 1 patient had small EV. In patients with SAAG ≥1.5 g/dL, 4 patients had no EV, 19 patients had small EV, and 8 patients had large EV (Figure 1). Four patients died. In the SAAG ≥1.5 g/dL group, 2 patients died from UGIH, 1 patient from spontaneous

Table 1. Baseline characteristics.

Characteristics	SAAG <1.5 group (n = 4)	SAAG ≥1.5 group (n = 31)	*p*-value
Mean age (SD) year	55 (18.1)	52.9 (12.4)	0.768
% male	50	61.3	
Present of EV			0.019
No EV	3	4	
Small EV	1	19	
Large EV	0	8	
CTP score			0.363
Child A	0	1	
Child B	2	7	
Child C	2	23	
Mean AST (range)	83.7 (17-224)	121.1 (1-358)	0.146
Mean ALT (range)	30 (2-58)	57.8 (23-171)	0.108
Mean AP (range)	152.5 (77-233)	220.3 (67-2566)	0.736
Death	1	4	1.0
UGIH with small EV	0	1	
UGIH with large EV	0	1	
Other causes	1	2	

ALT = alanine transaminase, AP = alkaline phosphatase, AST = aspatate transaminase, CTP = Child Turgot Pugh score, SD = standard deviation



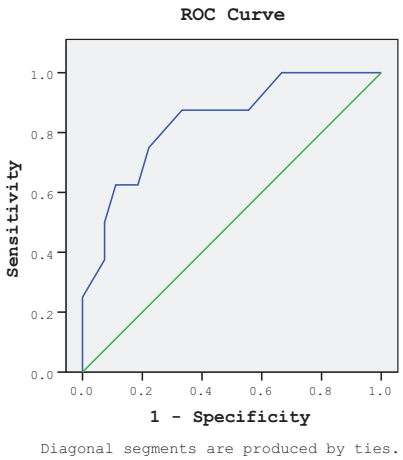
EV = esophageal varices, NSBB = non-selective beta blocker, SBH = small bowel hemorrhage, SAAG = serum ascites albumin gradient, UGIH = upper gastrointestinal hemorrhage.

Figure 1. Patients flow during the study from enrollment.

bacterial peritonitis (SBP) with newly diagnosed hepatocellular carcinoma, and 1 patient from gas gangrene infection. Only 1 patient in the SAAG <1.5 g/dL group died from a septicemic illness.

EVB occurred only in patients with SAAG ≥1.5 g/dL, although no statistically significant difference was evident between the two groups. The prevalence of small and large EV in the SAAG <1.5 g/dL group were 25% and 0%, and in the SAAG ≥1.5 g/dL group were 61.3% and 25.8%, respectively.

The ROC curve for the presence of small and large EV (Figure 2) showed that at the cut-off point of SAAG

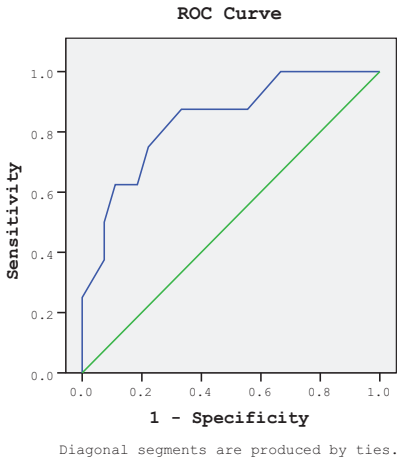


Coordinates of the curve

Test result variable(s): SAAG

Positive if greater than or equal to (a)	Sensitivity	1-specificity
.3000	1.000	1.000
1.3500	.964	1.000
1.4500	.964	.571
1.5500	.964	.429
1.6500	.964	.286
1.7500	.857	.286
1.8500	.714	.286
1.9500	.643	.143
2.0500	.536	.143
2.1500	.429	.000
2.2500	.357	.000
2.3500	.286	.000
2.5000	.214	.000
2.6500	.179	.000
2.8500	.071	.000
4.0000	.000	.000

Figure 2. The ROC curve for presence of EV.



Coordinates of the curve

Test result variable(s): SAAG

Positive if greater than or equal to (a)	Sensitivity	1-specificity
.3000	1.000	1.000
1.3500	1.000	.963
1.4500	1.000	.852
1.5500	1.000	.815
1.6500	1.000	.778
1.7500	1.000	.667
1.8500	.875	.556
1.9500	.875	.444
2.0500	.875	.333
2.1500	.750	.222
2.2500	.625	.185
2.3500	.625	.111
2.5000	.500	.074
2.6500	.375	.074
2.8500	.250	.000
4.0000	.000	.000

Figure 3. The ROC curve for large EV.

>1.65, the sensitivity and specificity were 96.4% and 71.4%. At the cut-off point of SAAG >2.05 (Figure 3), the sensitivity and specificity for diagnosing of large EV were 87.5% and 66.7%, respectively.

DISCUSSION

This study demonstrated that higher SAAG was associated with the presence of EV and a larger variceal size. Although the incidence of bleeding from EV was higher in patients with higher SAAG, the difference was not statistically significant. There was likely related to the small sample size, as we could enroll only one-third of the pre-determined sample size. However, the prevalence of EV and of large EV in patients with SAAG ≥1.5 g/dL were both significantly

higher than that in patients with SAAG <1.5 g/dL. Moreover, at the cut-off point of SAAG >1.65, the sensitivity and specificity for diagnosis of EV were 96.4% and 71.4% and at the cut-off point of SAAG >2.05, the sensitivity and the specificity for diagnosing large EV (Figure 3) were 87.5% and 66.7% respectively. Thus, the SAAG can be used as a convenient, less expensive, more readily available and a less invasive tool for diagnosing EV and large EV. In addition, the SAAG appears to be useful in the prediction of EVB, which is the ultimate end-point for EVB screening. We believe that continuation of this study to the predetermined sample size is likely to demonstrate the statistical difference. The cost effectiveness of using SAAG as a screening tool for the presence of EV, large EV, the prediction of EVB and related to primary prophylaxis requires further study to evaluate this attractive low-cost approach.

REFERENCES

1. Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. Gastroenterology 2001;120:726-48.
2. Garcia-Tsao G, Groszmann RJ, Fisher RL, *et al*. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology 1985;5:419-24.
3. Sharara AI, Rockey DC. Gastroesophageal variceal hemorrhage. N Engl J Med 2001;345:669-81.
4. Lowe RC, Grace ND. Primary prophylaxis of variceal hemorrhage. Clin Liver Dis 2001;5:665-76.
5. Feu F, Garcia-Pagan JC, Bosch J, *et al*. Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal haemorrhage in patients with cirrhosis. Lancet 1995;346:1056-9.
6. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. Semin Liver Dis 1999;19:475-505.
7. Rigau J, Bosch J, Bordas JM, *et al*. Endoscopic measurement of variceal pressure in cirrhosis: correlation with portal pressure and variceal hemorrhage. Gastroenterology 1989;96:873-80.
8. Groszmann RJ, Bosch J, Grace ND, *et al*. Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. Gastroenterology 1990;99:1401-7.
9. Torres E, Barros P, Calmet F. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Am J Gastroenterol 1998;93: 2172-8.
10. Mene A, Sharma D, Raina VK. Correlation between serum-ascites albumin concentration gradient with gastrointestinal bleeding in patients of portal hypertension. Trop Doct 2003;33: 39-41.
11. Gurubacharya DL, Mathura KC, Karki DB. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Kathmandu Univ Med J (KUMJ) 2005;3:327-33.