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Von Willebrand Factor and VITRO Score as Predictors for Variceal Bleeding in Egyptian Patients with Liver Cirrhosis

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Abstract

Background: Variceal bleeding isa majorcause of death in patients with cirrhosis. Von Willebrand factor (vWF) is a protein released by endothelial cells (ECs), reflects EC activation. Levels of vWF had been discovered to be higher in people with liver cirrhosis; however, there is a scarcity of information about its role in prediction of portal hypertensive bleeding. Blood test measuring Von Willebrand factor-Ag level (vWF-Ag) combined with platelet count allowed the development of a novel prediction score, the von Willebrand factor/thrombocyte ratio (the VITRO score).

Aim of Study: To assess the relationship between the von Willebrand factor and the VITRO score with variceal bleeding in cirrhotic patients.

Patients and Methods: 42 cirrhotic patients and 19 healthy controls were included in the study. The patients were categorized into two groups: 21 cirrhotic patients with recent variceal bleeding and 21 cirrhotic patients without variceal bleeding. All patients underwent Laboratory tests including vWF/Ag and upper endoscopy. vWF level andVITRO scorewere comparedbetween both groups and 19 normal controls.

Results: Patients with variceal bleeding had significantly higher level of vWF (12ng/ml) compared to patients without bleeding (9.2ng/ml) and normal controls (9.6ng/ml). Patients with variceal bleeding also had higher VITRO score (0.174), compared to patients without bleeding (0.058) and normal controls (0.037), the difference was statistically significant.

Conclusion: We suggest that the vWF and VITRO score can be used as noninvasive biomarkers for the prediction of variceal bleeding in patients with liver cirrhosis with high sensitivity and specificity.

Key Words: Cirrhosis – PHT – Variceal Bleeding – VWF – The Vitro Score.

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Introduction

VARICEAL bleeding is a leading cause of death in cirrhotic patients. Patients with variceal bleeding have a better chance of survival if adequate hemostasis was achieved. Up to 20% mortality is related to each bleeding episode **[1].** In addition, 70 % are liable to a second bleeding episode in one year **[2].**

Portal hypertension (PHT) is related to increased blood flow as well as increased vascular resistance in relation to cirrhotic changes. Portosystemic shunts, ascites (AS), and hepatic encephalopathy (HE) are all serious complications of PHT that increase mortality **[3].**

The hepatic venous pressure gradient (HVPG) is the 'gold standard' for determining PHT, however, HVPG testing is invasive and only accessible at certain facilities **[4].** Therefore, there is an increasing need for noninvasive measures of portal hypertension and prediction of variceal bleeding.

Predictors of portal hypertension (PHT) have been identified like ascites, splenomegaly, caput medusa, and low platelet count; however, they are unable to identify early PHT, nonspecific and have limited sensitivity in compensated cirrhosis **[5].** Transient elastography (TE) measures of liver stiffness is correlated with liver fibrosis severity. Evidence on the usefulness of TE in the prediction of variceal bleeding are few and inconclusive, however it has been shown to detect fibrosis, HVPG, and the presence of esophageal varices (OV) with varying sensitivities and specificities **[6].**

During initial hemostasis, stimulated endothelial cells produce a multimeric sticky protein called von Willebrand factor (vWF) **[7].** Patients with cirrhosis have been shown to have abnormally high amounts of vWF **[8].** Additionally, it has been shown that vWF levels are related to other conditions like bacterial translocation, inflammation, and coagulopathy **[7].**

There is a lack of information on the usefulness of the VITRO score (the vWF-/platelet ratio) in predicting variceal bleeding in hepatitis C virus (HCV) patients, for whom it has been studied as a noninvasive biomarker for cirrhosis/fibrosis **[9]**. In the current study, we aimed to explore the role of vWF and the VITRO score in the prediction of variceal bleeding in patients with cirrhosis.

Patients and Methods

This cross-sectional study included 42 cirrhotic patients with or without history of variceal bleedingand 19 control subjects recruited from Endemic Medicine Department and Outpatient Clinic, Faculty of Medicine, Kasr Al-Aini Hospital, Cairo University from November 2021 to April 2022. They were selected after fulfilling the inclusion criteria, obtaining an informed consent and ethical committee approval (MS-5232021).

Inclusion criteria included patients 18 years old or more from both sexes with a confirmed diagnosis of liver cirrhosis with or without history of variceal bleeding. Apparently healthy adults were selected from subjects presenting to outpatient clinic for non-liver related complaints and served as controls.

Exclusion criteria included patients with factors affecting levels of von Willebrand factor like history of alcohol intake, evidence of hepatocellular carcinoma (HCC), renal impairment or any source of infection or under treatment for infection, including spontaneous bacterial peritonitis. Moreover, patients on anticoagulants or antiplatelet therapyand those presenting with non-variceal bleeding were also excluded.

Study populations were divided into three groups:

- Group A: Cirrhotic patients presenting with recent variceal bleeding.
- Group B: Cirrhotic patients without history of variceal bleeding.
- Group C: Healthy controls.

All participants fulfilling the criteria signed Informed consent, clinical history was taken focusing on recent history variceal bleeding, laboratory assessment including complete blood count, Liver function tests as well as creatinine and urea.

Liver cirrhosis was diagnosed based onclinical criteriaof liver cell failure and portal hypertension e.g. ascites, splenomegaly, spider naevi, palmar erythema, as well as biochemical and hematological parameters including increased bilirubin, decreased albumin, coagulopathy, Increased AST/ALT ratio and thrombocytopeniaand Imaging criteria by ultrasound like liver surface nodularity, coarseness of texture and attenuation of hepatic veins and imaging features of portal hypertension e.g splenomegaly, ascites and collaterals. Transient elastography was done in selected cases to determine the stage of fibrosis in patients and to confirm healthy liver in controls.

Upper gastrointestinal endoscopy was performed for all cirrhotic patients at the gastrointestinal endoscopy unit, Kasr Al-Ainy University Hospital, Cairo University for the assessment of the presence of esophageal/gastric varices and/or portal hypertensive gastropathy. Variceal ligation was done for patients for patients with active bleeding.

Human von Willebrand factor was measured by vWF-Ag test for all participants by ELISAkit (cat. No E1140Hu) (Bioassay Technology Laboratory). Three to five ml of blood samples were withdrawn in a red topped plain vacutainer under complete aseptic precautions. Samples left undisturbed to clot at room temperature for 10-20 minutes, then centrifuged at 2000-3000 RPM to use the serum. Samples were then stored at –200C until used.

Inpatients with active variceal bleeding at time of enrollment, serum samples were collected at least 1 week after stabilization of the patient generacondition and control of variceal bleeding (to avoidfalse increase in the serum level of vWF and platelet count as a hemostatic response to bleeding. VITRO score was calculated by dividing VWF levels by the platelet number (vWF/PLT).

Sample size calculation:

The aim of this study was to compare the VITRO score between cirrhotic cases with variceal bleeding and without it. Based on the previous study by Ibrahim et al., **[10]** the difference in VITRO score between the 2 groups was 0.8±0.6; using power 95% and 5% significance level. A minimum number of 16 patients in each group is required. This number is to be increased to a sample size of 19 to adjust for using a nonparametric test. Sample size calculation was achieved using PS: Power and Sample Size Calculation softwareVersion 3.1.2 (Vanderbilt University, Nashville, Tennessee, USA.

Statistical analysis:

Data management and statistical analysis were performed using Statistical Package for Social Sciences (SPSS) version 25.

Numerical data were summarized using means and standard deviations or medians and ranges. Categorical data were summarized as percentages. Comparisons between the 2 groups with respect to normally distributed numeric variables were done using the independent *t*-test. Non normally distributed numeric variables were compared by Mann-Whitney test. Comparisons between 3 groups were done by Kruskal Wallis test followed by Dunn test for pairwise comparison. For categorical varia-

bles, differences were analyzed with chi square test and Fisher's exact test when appropriate. Pearson correlation coefficient was done to assess the correlation between numerical variables. Stepwise logistic regression was done to determine the predictors for esophageal bleeding. Roc Curve were used to assess the diagnostic performance of all *p*-values are two-sided. *p*-values <0.05 were considered significant.

Results

This prospective study included 42 Egyptian cirrhotic patients who were admitted to the Endemic Medicine Department, Faculty of Medicine, Kasr Al-Ainy, Cairo University fromOctober 2021 to May 2022. They were 26 males (61.9%) and 16 females(38.1%). Their age ranged from 17 to 81 years with a mean value of (51.45±15.79) years. Nineteen age and sex matched normal subjects were included in the study as a healthy control group. Participants in the control group were recruited from the outpatient clinics without symptoms suggestive of liver affection. They were 5 males and 14 Females. Their age ranged between 25 and 54 years with a mean value of 31.8±8.9 years (Table 1).

Table (1): Demographics data of patients and control subjects.

Studied Patients (no=42)		
	Mean ± SD	Range
Age (years)	51.45 ± 15.79	(17.00-81.00)
	Count	%
Sex:		
Male	26	61.9
Female	16	38.1
Control subjects (no=19)		
	Mean ± SD	Range
Age (years)	31.8 ± 8.9	(25.00-54.00)
	Count	%
Sex:		
Male	5	26.3
Female	14	73.6

SD: Standard deviation.
p-value: Not significant.

Patients were categorized according to history of variceal bleeding into two groups:

Group A: 21 (50%) cirrhotic patients presenting with variceal bleeding. Group B: 21 (50%) cirrhotic patients without history of variceal bleeding.

Child score was calculated for patients. Most patients in bleeding group was Child C (47.6%) while most non-bleeders were Child B (42.9%) (Table 2).

Table (2): Comparison between group A and group B regarding demographic and clinical data.

Item	Group A n=21 (%)	Group B n=21 (%)	*p*-value
Age (yrs.):			
Mean ± SD	51.5±15.0	51.3±16.8	0.962
Range	17-75	20-81	
	N (%)	N (%)	*p*-value
Sex:			
Male	11 (52.4)	15 (71.4)	0.204
Female	10 (47.6)	6 (28.6)	
Child Score:			
A	3 (14.3)	7 (33.3)	0.190
B	8 (38.1)	9 (42.9)	
C	10 (47.6)	5 (23.8)	

- Analysis done by Chi square test, $p<0.05$ is statistically significant.

Patients with variceal bleeding had significantly lower hemoglobin (10.0±1.6 mg%) and platelet count ($81x10^3$/ml), compared to patients without bleeding (11.4±2.1mg% and 150×10^3/ml) respectively.

No statistically significant differences were detected between patients with and without variceal bleeding regarding the TLC, the mean ALT levels, the mean AST levels, total and direct bilirubin levels, serum albumin levels, serum creatinine, INR, CRP and the mean spleen size (Table 3).

Patients with variceal bleeding had significantly higher level of vWF (12ng/ml ranging from 7.1-48.5ng/ml), compared to patients without bleeding (9.2ng/ml) and normal controls (9.6ng/ml) ($p=0.003$). They also had a higher VITRO score (0.174 ranging from 0.045 to 0.866), compared to patients without bleeding (0.058ng/ml) and normal controls (0.037ng/ml), the difference was statistically significant ($p<0.001$) (Table 4).

Table (3): Laboratory data of both groups.

	Group A n=21 Mean ± SD	Group B n=21 Mean ± SD	*p*-value
Hb (mg/dl)	10.0±1.6	11.4±2.1	0.024
TLC	6.0±2.7	6.7±2.1	0.349
PLT *x 10^3	81 (44-406)	150 (54-327)	0.011
ALT*	45 (6-232)	35 (10-270)	0.743
AST*	59.5 (9-461)	62.0 (23-324)	0.308
B_Total*	1.7 (0.41-16.42)	1.6 (0.1-14.8)	0.504
B_Direct*	0.80 (0.02-10.76)	0.83 (0.05-16)	0.801
ALP*	104.5 (65-1368)	139 (47-1150)	0.166
Albumin	2.8±0.5	2.8±0.7	0.470
Creatinine	0.8±0.3	0.9±0.3	0.677
INR	1.5±0.3	1.3±0.2	0.087
CRP	7.5±2.8	8.2±2.9	0.402

Table (4): Level of serum vWF and VITRO score in different groups.

	Group A (Bleeders)			Group B (Non-bleeders)			Control			*p*-value
	Median	Min.	Max.	Median	Min.	Max.	Median	Min.	Max.	
vWf (ng/ml)	12	7.1	48.5	9.2 [A]	0.6	15.4	9.6 [A]	0	31.3	0.003
Vitro score	0.174	0.045	0.866	0.058 [A]	0.008	0.195	0.037 [A]	0.000	0.111	<0.001

On plotting areceiver operating characteristic (ROC) curve, the best cut off value For vWF was 9.8 with 81% sensitivity and 61.9% specificity for variceal bleeding so vWF can significantly correlated with occurrence of bleeding with AUC=0.781 and standard error 0.07. While the best cut off value For VITRO score was 0.091 with 90.5% sensitivity and with 81% specificity for variceal bleeding (AUC=0.88 and standard error 0.053) (Fig. 1).

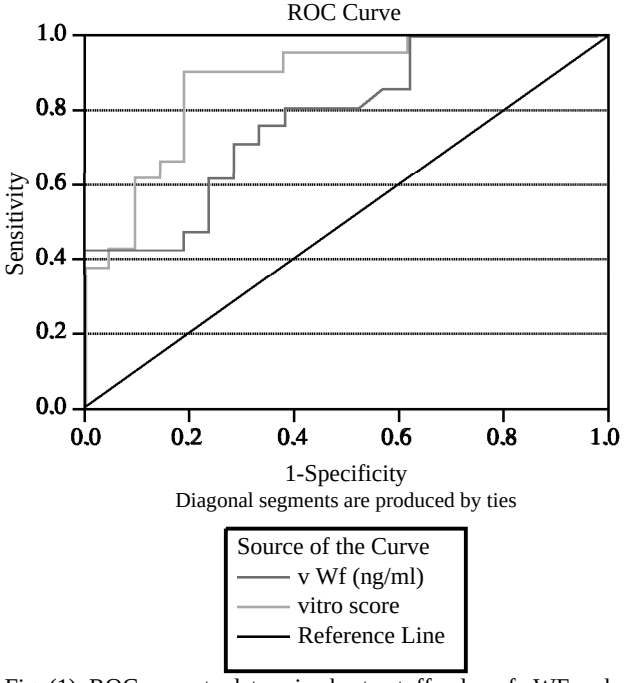

Fig. (1): ROC curve to determine best cutoff value of vWF and VITRO score.

It had been shown that the mean hemoglobin level among patients without varices (11.7±2.5mg/dl) was significantly higher than that of patients with varices (10.2±1.7mg/dl) (p=0.023). The mean platelet count was 187 and 90.5 in cirrhotic patients without and patients with varices, respectively, the difference was statistically significant (p=0.007). There was significant difference between the two groups regarding the mean serum albumin level, with higher level in patients without varices (3.3±0.7g/dl), compared to those with varices (2.8±0.5g/dl). (p=0.007). No statistically significant difference between the two groups was found as regards TLC, ALT, AST, total and direct bilirubin, ALP, Creatinine, INR, CRP and spleen size (Table 5).

Cirrhotic patients with varices had significantly higher vWF level and VITRO score (11.8ng/ml and 0.12, respectively), compared to those without varices (8.7ng/ml and 0.05, respectively) (p=0.020), (p<0.001) (Table 6).

Table (5): Comparison between patients with and without varices regarding laboratory findings.

	No Varices n=9 Mean ± SD	Varices n=33 Mean ± SD	*p*-value
Hb (mg/dl)	11.7±2.5	10.2±1.7	0.023
TLC	6.7±1.9	6.2±2.5	0.574
PLT *	187 (61-327)	90.5 (44-406)	0.007
ALT*	33 (16-270)	37.5 (6-232)	0.567
AST*	38 (21-324)	61 (9-461)	0.559
B_Total*	1.06 (0.36-11.7)	1.525 (0.1-16.42)	0.152
B_Direct*	0.75 (0.15-16)	0.8 (0.02-10.76)	0.748
ALP*	119.5 (65-1150)	112 (47-1368)	0.784
Albumin	3.3±0.7	2.8±0.5	0.007
Creatinine	0.8±0.2	0.9±0.3	0.767
INR	1.3±0.2	1.4±0.3	0.079
CRP	7±2.9	8.5±3.5	0.191

Table (6): Univariate analysis of lab parameters to detect possible predictors of esophageal varices.

	No Varices n=9 Mean ± SD	Varices n=33 Mean ± SD	*p*-value
v Wf (ng/ml) *	8.7 (0.6-13.2)	11.8 (1.3-48.5)	0.020
Vitro score*	0.05 (0.01-0.09)	0.12 (0.01-0.9)	<0.001

SD: Standard deviation, p<0.05 is statistically significant.

The mean vWF among the studied patients differed significantly according to the grade of varices with median value of 8.7ng/ml, 11.6ng/ml, 12.1ng/ml and 18.6ng/ml in cirrhotic patients with no varices, grade 1, 2 and 3 esophageal varices, respectively.

In addition, VITRO score showed statistically significant difference according to the grade of varices with median value of 0.05, 0.11, 0.15 and 0.23 in cirrhotic patients with no varices, grade 1, 2 and 3 esophageal varices, respectively (Table 7) (Fig. 2).

Table (7): Comparison of mean serum von Willebrand factor and vitro score with grades of varices.

	No Varices n=9 Median (Range)	Grade 1 C (n=16) Median (Range)	Grade 2 (n=13) Median (Range)	Grade 3 (n=4) Median (Range)	*p*-value
vWf (ng/ml)	8.7 (0.6-13.2)	11.6 (3.1-48.5)	12.1 (1.3-35.7)	18.6 (8.2-27.3)	0.049
Vitro score	0. 05 (0.01-0.09)$^{a-b}$	0.11 (0.01-0.42)	0.15 (0.05-0.87)^{a}	0.23 (0.090.49)^{b}	0.002

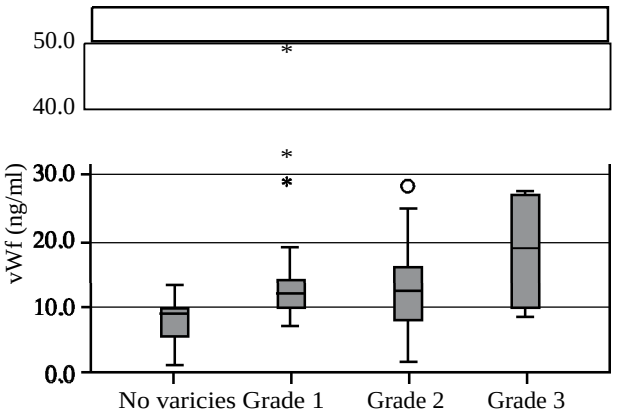

Fig. (2): Comparison of mean serum von Willebrand factor with grades of varices.

Discussion

It is still difficult to determine which cirrhotic patient will have variceal bleeding or other fatal complications. Early identification of those with clinically significant portal hypertension CSPH and prompt management is essential to avoid variceal bleeding which could be lethal *[11]*. Therefore, the hepatic venous pressure gradient (HVPG) should be measured for diagnostic and therapeutic purposes according to current standards, yet it is not practical being costly and invasive *[12]*. Therefore, we need a more practical marker for prediction of variceal bleeding in patients with portal hypertension.

The VITRO score is a simple method for diagnosing CSPH apart from the Child-Pugh score (CPS) inclinical practice, and it has the potential to enhance the care given to patients with cirrhosis *[10]*.

Thus, in the current study we assessed the relationship of the von Willebrand factor and the VITRO score with variceal bleeding in cirrhotic patients. Hemoglobin levels and platelet counts werelower in individuals with variceal bleeding compared to those without bleeding. Additionally, patients who did not have varices had a substantially higher mean hemoglobin level than those who did have varices. In other words, the mean hemoglobin level was a reliable indicator of advanced illness as measured by the presence of varices and the occurrence of variceal bleeding. Umar et al. *[14]* found that thrombocytopenia was present in 88% of cirrhotic patients with upper GI bleed (mean platelet count of 85 x 10^{6}/L) compared to 66% of patients without a previous history of upper gastrointestinal bleeding (*p*-value: 0.014). The degree of thrombocytopenia was shown to be correlated with increased bleeding risk in individuals with chronic liver disease. The risk of bleeding decreases by 1.5% for every unit of platelets that are added to the blood. Drolz et al. *[15]* also found that platelet count was linked to significant bleeding in cirrhosis patients, which is consistent with the present study's findings.In contrast, prospective research conducted by Basili et al. *[16]* found that platelet count is not indicative of overall bleeding risk in cirrhotic patients with varying degrees of liver failure. As severe thrombocytopenia was very uncommon (8.2%) in the research by Basili et al., this may explain the absence of connection between severe thrombocytopenia and the risk of bleeding events.

According to current study, patients with variceal bleeding had a significantly higher level of vWF with a mean value of 12ng/ml and a higher VITRO score with a mean value of 0.174 compared to patients without bleeding and healthy controls who had lower levels of vWF and VITRO score and the difference was statistically significant. The best cut off value for vWF was 9.8 with 81% sensitivity and 61.9% specificity for variceal bleeding (AUC=0.781 and standard error 0.07). While the best cut off value For VITRO score was 0.091 with 90.5% sensitivity and with 81% specificity for variceal bleeding (AUC=0.88 and standard error 0.053).

Another study corroborated the findings of our study where patients with variceal bleeding had a substantially higher mean blood level of vWF than patients without variceal bleeding or healthy individuals (115.75±8.33ng/ml vs. 78.15±17.20ng/ml, respectively; *p*: 0.001). Additionally, patients with variceal bleeding had a significantly greater mean VITRO score than patients without variceal bleeding or healthy participants (1.404±0.78 +vs. 0.60±0.33 F=51.52, *p*:0.001), and patients without variceal bleeding had a significantly greater mean VITRO score than healthy participants (0.2580.08) *[10]*.

It also found that vWF cutoff value of 100.1ng/ml had a sensitivity and specificity of 92% and 99.9%, respectively [area under the curve (AUC)=0.982], in predicting variceal bleeding among patients with HCV-related liver cirrhosis, while VITRO score cutoff value of 0.732 had a sensitivity and specificity of 80% and 68.3%, respectively *[10]*.

Ghweil et al. [17] came to the same conclusion we did, namely that vWFlevels were considerably higher in patients with PHT bleeding compared with non-bleeders, and thatvalues greater than 187.1 IU/dl increased the sensitivity of vWF measurement to 82.5% and the specificity to 65%.

In addition, Ferlitsch et al. [18] examined vWF in predicting CSPH (HVPG 10 mmHg), finding that a cutoff value of larger than 241 had a sensitivity of 85.7% and a specificity of 81.3%. Our findings are consistent with these results.

On the other hand, the VITRO score did not predict variceal bleeding in the research by Schwarzer et al. [19] due to small sample size (n = 5). As a result, it's possible that the study didn't have enough participants to reliably identify a clinically significant difference.

Both the vWF level and the VITRO score were substantially greater in our study population of Cirrhotic patients with varices than in those without varices (11.8ng/ml vs. 8.7ng/ml and 0.12 vs. 0.05, respectively). Wu et al. [20] found similar results, showing that vWF is a credible new noninvasive predictor of PHT in patients with liver cirrhosis. Also, vWF has been shown to be a reliable predictor of PH in cirrhotic patients by Ferlitsch et al., [18].

Moreover, In the present study VITRO score found to be a good predictor of the grading of varices with median values of 0.05, 0.11, 0.15 and 0.23 in cirrhotic patients with no varices, grade 1, 2 and 3 varices, respectively. Ibrahim et al. [10] found substantial positive relationships between serum vWFlevels and esophageal varices grade in individuals with variceal bleeding, corroborating the findings of the current study. Hassan et al. [21] also found a significant relationship between the VITRO score and the severity of esophageal varices (*p*: 0.001).

Furthermore, Serum vWF levels were positively correlated with OV severity across all patients, which may be due to the fact that those who suffer from variceal bleeding tend to have higher vWF levels to begin with. It seems that vWF would be linked with OV grade given the known relationship between OV grade and PHT. This direct relationship may be explained by the fact that increasing portal pressure stretches the varix wall, which in turn releases more vWF.

Conclusion:

We suggest that vWF and the VITRO score can be used as noninvasive biomarkers for the prediction of variceal bleeding in patients with liver cirrhosis with high sensitivity and specificity. This will help to avoid invasive procedures in patients who have low risk to bleed and to intervene early in patients with a high risk for bleeding. Also, vWF and VITRO score can be used as a noninvasive measure of esophageal variceal grade if present.

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معرفة دور Vin Willebrand Factor and Vitro Score كمتنبئين لنزيف فى مرضى التليف الكبدى الدوالى

نزيف الدوالى هو حالة طارئة فى الجهاز الهضمى وهى واحدة من الأسباب الرئيسية للوفيات لدى مرض تليف الكبد. ترتبط كل نوبة من نزيف الدوالى النشط بنسبة تصل إلى ٢٠-٣٠٪ من الوفيات.

تؤدى زيادة المقاومة و/أو زيادة تدفق الدم فى الدورة الدموية البابية إلى ارتفاع ضغط الدم البابى ويؤدى ذلك إلى نزيف الدوالى. مازال إلى الأن قياس ضغط اوردة الكبد المقياس الادق للتنبؤ بارتفاع ضغط الدم البابى لكنه اجراء تدخلى متاح فقط فى المعاهد المتخصصة لذا توجد حاجه الي وجود اجرائات اخرى غير باضعة لتقييم ضغط الدم البابى. وقد وجد أن الاستسقاء، وتضخم الطحال، ورأس المدوسة، علامات غير باضعة للكشف عن ارتفاع ضغط الدم البابى ومع ذلك، لا يمكنهم الكشف المبكر.

عامل الفون ويلبراند هو بروتين تفرزه الخلايا البطانية وقد تم اكتشاف وجوده بمستويات اعلى فى المرضى المصابين بتليف الكبد كما لوحظ ايضا ان هؤلاء المرضى يوجد لديهم درجة عالية من درجة الفيترو. ولكن لا توجد بيانات عن فعاليتهم فى التنبؤ بنزيف الدوالى.

هدفنا فى هذه الدراسة إلى النظر فى تأثير عامل فون ويلبراندو درجة فيترو فى التنبؤ بنزيف الدوالى فى المرضى المصريين الذين يعانوا من تليف الكبد.

شملت هذه الدراسة بأثر رجعى ٤٢ مريضًا مصرياً مصاباً بالتليف الكبدى تم قبولهم فى قسم الأمراض المتوطنة بكلية الطب، قصر العينى، جامعة القاهرة، بمتوسط عمر ٥١,٤٥ عامًا.

تم تصنيف المرضى إلى مجموعتين؛ ٢١ مريضاً بالتليف الكبدى يعانون من نزيف الدوالى (المجموعة أ) و٢١ مريضاً بالتليف الكبدى بدون تاريخ لنزيف الدوالى (المجموعة ب). تمت مطابقة المجموعتين فيما يتعلق بالعمر والجنس ودرجة وأسباب تليف الكبد. ويأتى هذا لصالح إلغاء آثار العوامل المربكة المحتملة.

لاحظنا أن المرضى الذين يعانون من نزيف الدوالي لديهم عدد أقل بكثير من الهيموجلوبين والصفائح الدموية مقارنة بالمرضى الذين لا يعانون من نزيف. كان عدد الصفائح الدموية متناسباً عكسياً مع نزيف الدوالى فى هذه الدراسة: مع كل زيادة فى عدد الصفائح الدموية بمقدار وحدة واحدة؛ هناك انخفاض فى ميل النزيف بنسبة ١,٥٪.

بالمقارنة مع المرضى الذين لا يعانون من نزيف، لوحظ ان المرضى الذين يعانون من نزيف الدوالى لديهم مستوى أعلى بكثير من عامل فونفيلبراندو درجة فيترو.

فى الختام، نقترح أن يكون عامل فون ويلبراندودرجة فيترو بمثابة مؤشرات حيوية غير باضعة لارتفاع خطر نزيف الدوالى لدى المرضى الذين يعانون من تليف الكبد مع حساسية ونوعية عالية. سيساعد ذلك على تجنب الإجراءات التدخلية لدى المرضى الذين لديهم خطر منخفض للنزيف والتدخل المبكر فى المرضى الذين لديهم خطر كبير للنزيف.