ROLE OF CONTRAST ENHANCED COMPUTED TOMOGRAPHY IN DETECTION AND GRADING OF ESOPHAGEAL VARICES IN PATIENTS WITHLIVER CIRRHOSIS.

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ABSTRACT

Background:Purpose is to evaluate the role of contrast enhanced CT in the detection of esophageal varices (OV) and the differentiation of the varices at low risk and those at high risk of bleeding compared to upper GIT endoscopy.

Patients and Methods: This study includes 32 patients with liver cirrhosis. These patients were selected from outpatient clinic and inpatient section of internal medicine department, Zagazig university hospitals. Patients with active or previous variceal bleeding, or with history of previous variceal ligation or injection were excluded. OV were best visualized on axial multidetector-CT (MD-CT) images in the post-contrast portal venous phase. upper GIT endoscope and contrast enhanced CT was done to all the patients .

Results:The study was conducted on 32 patients with liver cirrhosis; 23 males and 9 females with a mean age 55.97 +/- 9.04 years They were classified according to the CT findings into 3 groups Group I: included (3) patients (9.4%) with no esophageal varices (2) males, (1) female with a mean age (60.5 +/-4.5) years. Group II: included (12) patients (37.5%) with small varices (low risk varices) (8) males, (4) females with a mean age (56.08 +/- 12.7) years Group III: included (17) (53.1%) patients with large varices (high risk varices) (13) males, (4) females with a mean age (55.12 +/- 6.5) years. The overall CT sensitivity for detection of OV was 96.7%, specificity 100%, positive predictive value 100% and negative predictive value 66.7%.The CT sensitivity for the high risk OV cases (100%) was higher than that for those with low risk OV (92.3%).There was no significant statistical difference in the distribution of age, sex and extra-esophageal CT findings between the low and high risk OV cases (P-value >0.05).

Conclusion: contrast enhanced Computed Tomography is a good alternative diagnostic tool to conventional upper G.I.T endoscopy for detecting and grading of esophageal varices in patients with liver cirrhosis.

Key words: esophageal varices-contrast enhanced CT-detection and grading of the OV.

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INRTODUCTION

Esophageal varices are the most common source of upper gastrointestinal bleeding in liver cirrhosis. Considering the discrepancy in the management among the sources of upper gastrointestinal bleeding, early identification of esophageal varices is very important for the physicians to initiate the accurate prophylactic and therapeutic strategy of variceal bleeding as soon as possible ([1]).

- Upper gastrointestinal endoscopy is the gold standard for esophageal varices detection in liver cirrhosis. If varices were not found at the initial endoscopy, cirrhotic patients would undergo endoscopic examinations every 2-3 years ([2]).

- Currently, upper gastrointestinal endoscopy is the gold standard for the diagnosis of esophageal varices, however nearly all patients are poorly tolerated with upper gastrointestinal endoscopy and even a majority of cirrhotic patients without any previous history of portal hypertension-related complications refuse the routine examinations in our clinical practice ([3]).

- Several alternative methods for predicting the presence of EVs in liver cirrhosis have been proposed, including computed tomography (CT), magnetic resonance (MR), serum markers, ultrasonographic parameters, liver stiffness measurement (LSM), spleen stiffness measurement(SSM) platelet count to spleen diameter ratio (PSR) and capsule endoscopy([4]).

- With new advances in multi-detector CT imaging, spontaneous portosystemic shunts, esophageal and gastric varices, and peri-luminal varices are progressively discovered in patients with cirrhosis. As CT imaging is non-invasive, doesn't require sedation, and permit survey and precise estimation of variceal size, it is reasonable to believe that CT would be better endured than endoscopy by most patients ([5]).

- Moreover, if the accuracy of CT in detection of esophageal varices is significant, a careful assessment of high risk esophageal varices on a liver multi-detector CT examination may be useful to prevent the patients from performing endoscopy ([6]).

-Thus, the aim of our study is to evaluate the use of contrast-enhanced CT to detect and grade esophageal varices and differentiate between varices at low risk (<3mm) and those at high risk (>3mm) for bleeding, in comparison to endoscopy as reference standard ([7]).

PATIENTS AND METHODS

The present study was conducted between March 2017 and September 2017 upon 32 patients with liver cirrhosis. These patients were selected from outpatient clinic and inpatient section of internal medicine department, Zagazig university hospitals. They were 23 males and 9 females with a mean age 55.97 +/- 9.04 years.

Patients were previously informed of the research details and informed consent was obtained from all patients.

- **Inclusion criteria:**

Patients presented with liver cirrhosis diagnosed by clinical and radiological parameters, and presented with esophageal varices that staged with endoscopy.

- **Exclusion criteria:**

1. Active gastrointestinal bleeding on admission.
2. Patients with previous variceal bleeding, ligations or porto-systemic shunts.
3. Patients who have contraindications to contrast as patients presented with renal impairment (not on dialysis), or patients who have hypersensitivity to intravascular contrast agent or pregnant patients.
4. Patients who refused to be enrolled in the study.

All patients were subjected to the following:

1) History taking: with special emphasis on symptoms suggestive of chronic liver disease, attacks of hematemesis, and melena and history of hepatic encephalopathy. Past history of schistosomal infection and anti-schistosomal treatment.

2) Clinical examination:

i. **Signs suggestive of chronic liver disease as:** weight loss, vitamin deficiency, jaundice, spider naevi, palmar erythema, ascites and lower limbs edema.

ii. **Abdominal examination:** with special emphasis on:

- Liver size, consistency, edge and surface. – Splenomegaly - Ascites. - Dilated veins.

3) Upper endoscopy: was done for all patients using Olympus 2 channels vidioscope (Gif2T200) to detect and grade varices if present. Esophageal varices were graded according to **Thakeb et al., (1988)**, which was based on **Degradi et al., (1966)** classification.

■ **Grade I:** Small straight varices confined to the lower third of the esophagus.

■ **Grade II:** Moderate sized clubbed varices, with thin well defined areas of normal mucosa between them and confined to the lower half of the esophagus.

■ **Grade III:** Gross varices, extending into the proximal half of the esophagus. Normal mucosa might not be visible between them unless esophagus is fully distended with air.

■ **Grade IV:** Varices like those of grade III, but with dilated capillaries on top of varices

4) CT scan: was done for all patients using a 128-detector Philips CT , Zagazig University Hospital, to detect and grade varices if present.

❖ EQUIPMENT

For each patient, the following equipment was used:

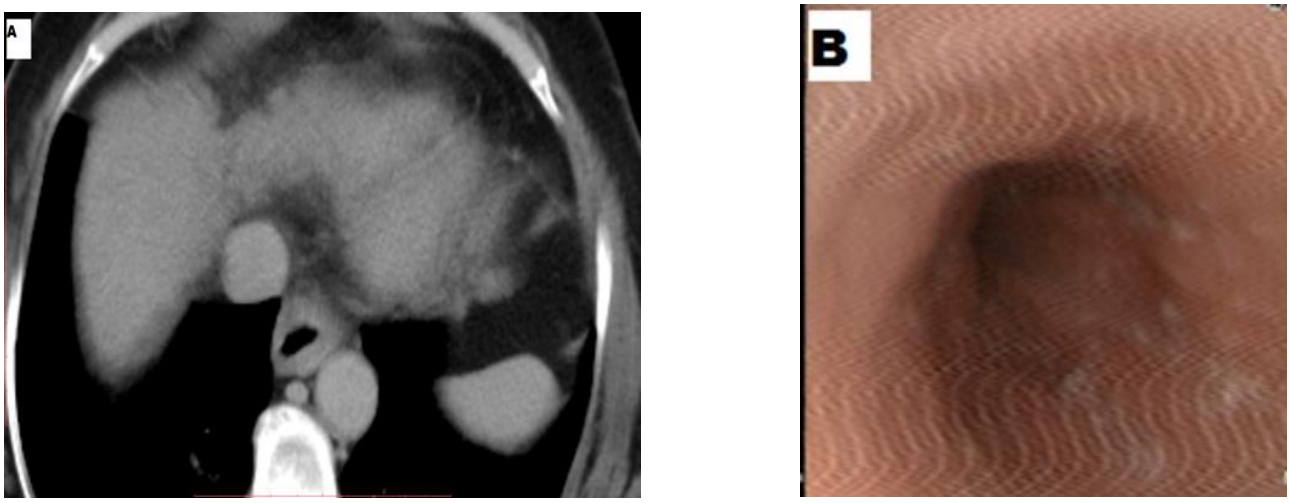
1. An injector syringe and set.
2. A cannula.
3. Intravenous 100-150ml of nonionic contrast material (iopromide, Ultravist 300; Schering, Berlin, Germany).

PATIENTS' GROUPS:

According to CT findings, the patients were classified into 3 groups:

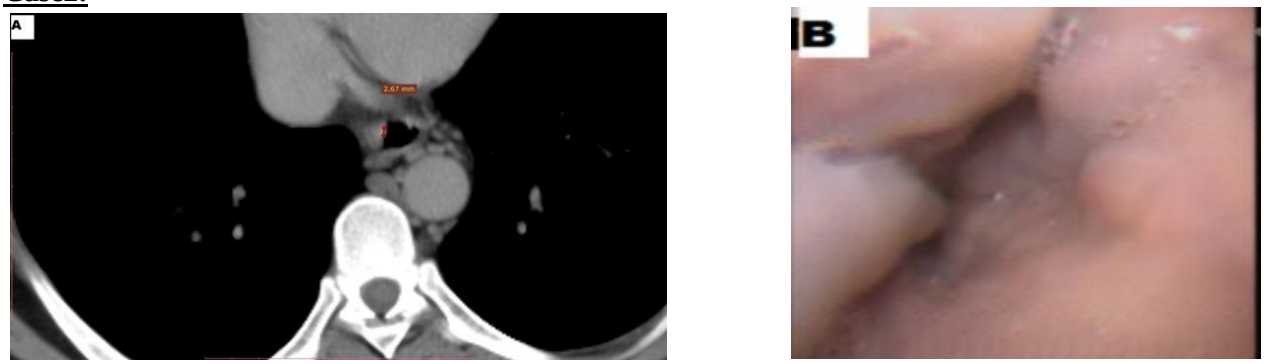
- **Group I**: included (3) patients (9.4%) with **no esophageal varices** (2) males, (1) female.(case1)
- **Group II:** included (12) patients (37.5%) with **small varices** (low risk varices) (grade I & grade II) (8) males, (4) females with a mean age (56.08 +/- 12.7) years.(case2)
- **Group III:** included (17) (53.1%) patients with **large varices** (high risk varices) (grade III,IV) (13) males, (4) females with a mean age (55.12 +/- 6.5) years.(case3)

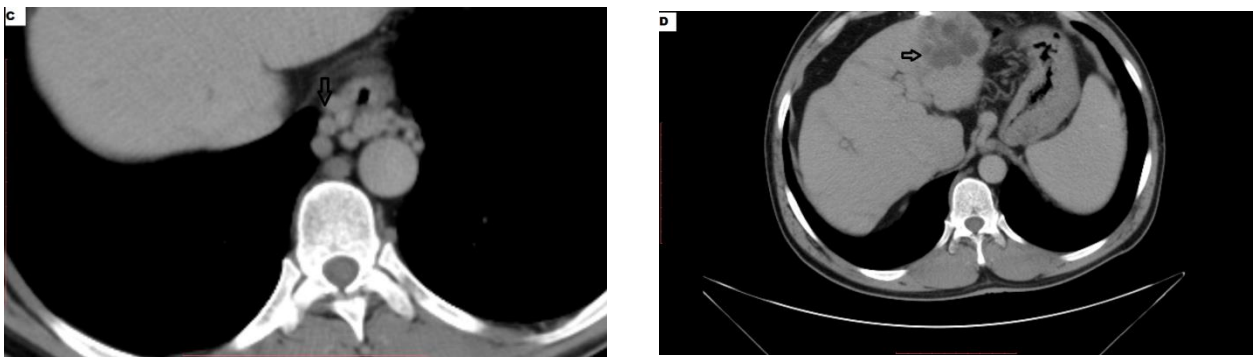
Case1:



Picture A, CT section through the lower esophagus during the porto-venous phase, showing no evidence of esophageal varices, picture (B) the same patient's endoscopic picture showing no varices.

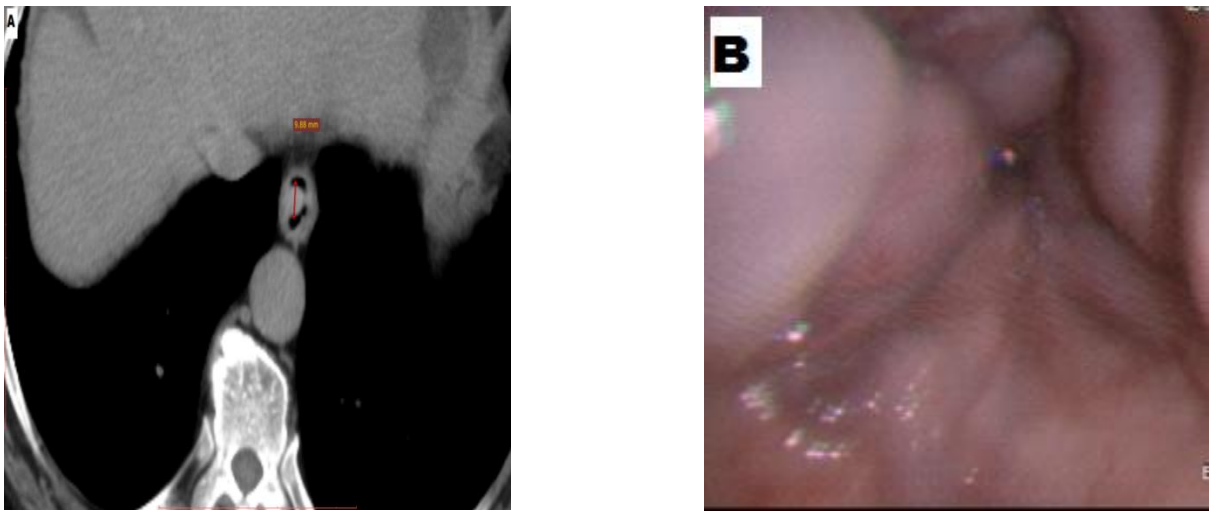
Case2:





CT section through the lower esophagus during the porto-venous phase picture (A) showing a 2.67mm varix (measured), (B) the same patient's endoscopic picture showing a grade I-II varix, (C)shows paraoseophgeal varies accidental finding (arrow) and (D) a hepatic focal lesion also noted(arrow).

Case3:



CT section through the lower esophagus during the porto-venous phase showing (A) 9.88mm varix (measured), (B) the same patient's endoscopic picture showing a grade IV varix.

STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for Social Sciences version 16.0 (SPSS for Windows 16.0, Inc., Chicago, IL, USA).

Regarding quantitative parameters, the data were presented with mean and standard deviation. Comparison between two groups was done using independent t test

Categorical data are presented as absolute numbers and percentages within brackets. A $\chi 2$ analysis or Fisher exact test was used to compare these variables when expected cell frequency was less than five.

Correlation between age and Varices size was done using Pearson correlation coefficient.

All P values were based on a 2-tailed distribution, and the corresponding P value:

- Non-significant (NS) difference if $P > 0.05$.
- Significant(S) difference if $P < 0.05$.
- Highly significant (HS) difference if $P< 0.001$

The statistical analysis was based on the intention-to-treat population.

RESULTS

The study was conducted on 32 patients with liver cirrhosis; 23 males and 9 females with a mean age 55.97 +/- 9.04 years.

All of the patients were subjected to upper GI endoscopy and triphasic CT study of the lower third of the esophagus (CT esophagography) for detection and grading the esophageal varices.

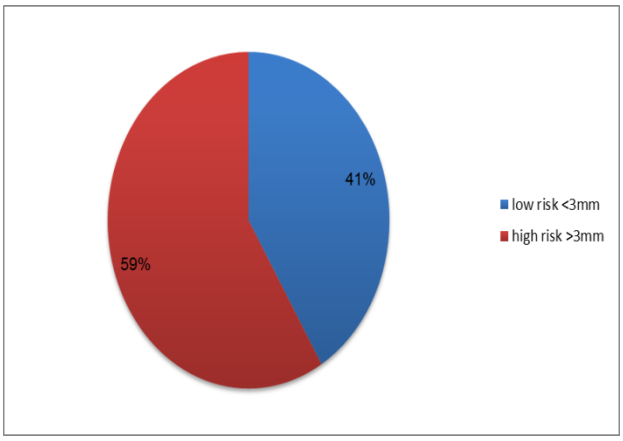
By analyzing the results obtained by the CT, the patients were divided into three groups; 3 patients showing no esophageal varices (controls), 12 patients with small low risk esophageal varices and 17 patients with large high risk esophageal varices.(table1)(figure1)

Comparing the results obtained by the CT esophagography to that obtained by endoscopy, the following was found:

- The 2 patients who were free by endoscopy (controls), all turned out to be free by CT esophagography.
- Of the 13 patient with low risk esophageal varices, 12 patients were detected by the CT esophagography, and 1 were missed (1 false negative by CT scan) with a sensitivity reaching 96.7 %.
- 17 patients with high risk esophageal varices.(table1)(figure1)

Table (1): Level of risk of OV as among cirrhosis cases.

	No.	%
low risk " size < 3 mm"	12	41.3 %
high risk " size > 3 mm"	17	58.6 %

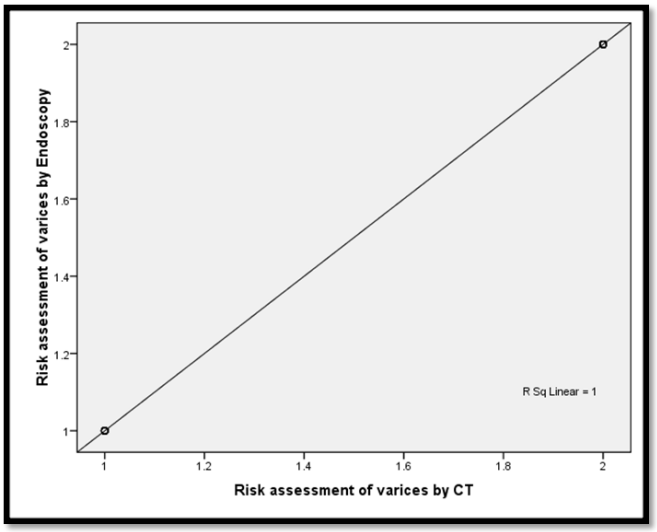


(Figure 1)Level of risk of OV among cirrhosis cases

Table (2): Measures of sensitivity and specificity of CT among studied group.

Endoscopy / CT	Esophageal varices	No esophageal varices
Positive	**29** "True positive results"	**0** "False positive results"
Negative	**1** "False negative results"	**2** True negative results"

The overall CT sensitivity was 96.7%, specificity 100%, accuracy 100%, PPV 100% and NPV 66.7% in comparison to the gold standard upper endoscopy. CT sensitivity among the cases with low risk OV (Group II) was 92.3%, while that among those with high risk OV (Group III) 100% .

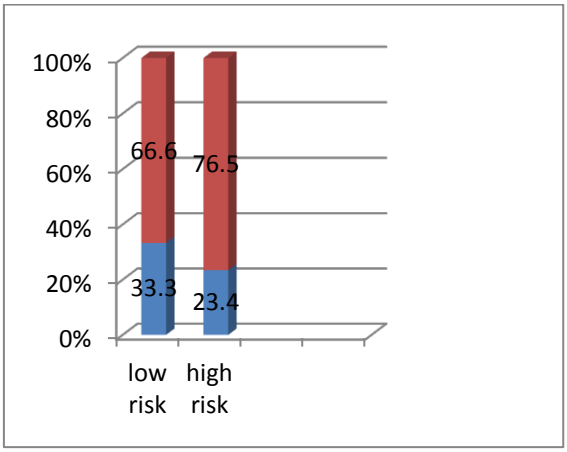


There was 12 patients (37.5%) graded as low risk by CT scan, and 17 patients (53.1%) graded as high risk, there was a close correlation and substantial agreement between endoscopic and CT findings (P value <0.05).(figure 2)

Figure 1: Correlation between risk assessment by CT and upper endoscopy

The mean age in the low risk and high risk cases was 56.08± 12.7and 55.12± 6.5 years respectively. The P-value between the patients' age and the OV size was 0.790 (non-significant).table (3).

There was no significant difference in the sex distribution among the low and high risk OV cases (P-values = 0.561).table (3) figure (3)



Figure(3) Sex distribution among low and high risk esophageal varices cases.

(Table 3) Age and gender in low and high risk groups

Parameter		Low risk group N=12	Highrisk group N=17	Test value	P value
Age (years) Mean ± SD		56.08 ± 12.7	55.12 ± 6.5	0.270^{t}	0.790 (NS)
Gender	Male	8 (66.7%)	13 (76.5%)	0.338^{X2}	0.561 (NS)
	Female	4 (33.3%)	4 (23.5%)		

(Table 3) Age and gender in low and high risk groups

The extra- esophageal CT findings detected among cirrhosis cases are summarized in Table 4 figure 4.

Findings	Gender Male	Female	total	%
Splenomegally	16	6	22	68.7%
Splenic varices	9	4	13	40.6%
Hepatic focal lesions	10	5	15	21.8%
Hepatomegally	4	3	7	21.8%
Ascitis	12	3	15	46.8%
GB stones	5	1	6	18.7%
Peri-GB collections	11	3	14	43.7%
Portal vein thrombosis	4	1	5	15.6%

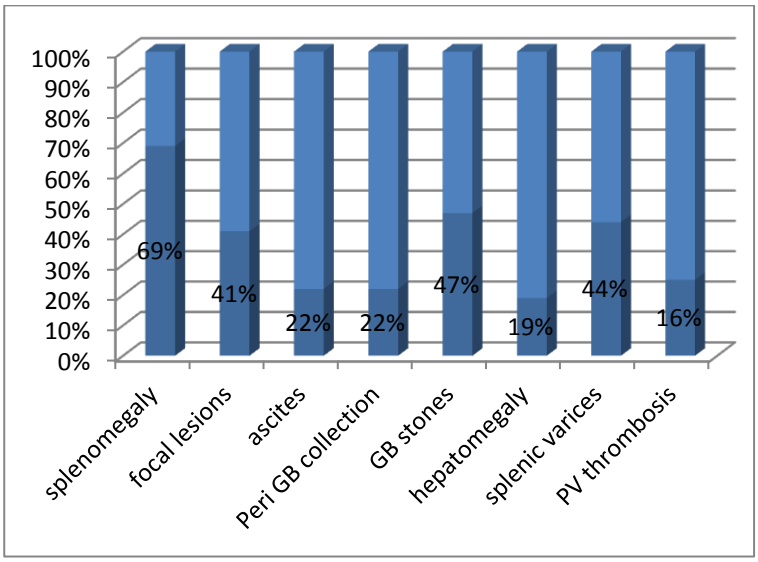
There was no significant difference in the presence of hepatic focal lesions table (5) figure (5) [i.e., hepatocellular carcinoma (HCC) as proved by CT criteria ± biopsy] and hepatomegaly table(6) figure(6) among the

low and high risk OV cases (P-values =0.176 and 0.927, respectively).

There was no significant difference in the presence of splenomegaly table(7)figure (7) and splenic varices table(8) figure(8) among the low and high risk OV cases (P-values =0.544 and 0.295, respectively).

There was no significant difference in the presence of ascites table(9)figure (9) and gallbladder stones table(10) figure(10) among the low and high risk OV cases (P-values =0.176 and 0.167, respectively).

There was no significant difference in the presence of portal vein thrombosis table(11)figure (11) and peri-gallbladder collection table(12) figure(12) among the low and high risk OV cases (P-values =0.054 and 0.875, respectively).



Figure(4)Extra-luminalCTfindings among cases.

Table (5): Hepatic focal lesions among low and high risk esophageal varices case

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	8	66.6	7	41	0.176
No	4	33.3	10	59	

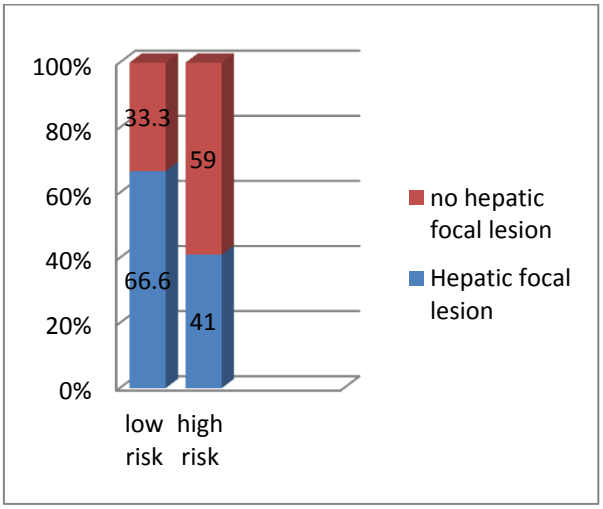


Figure (5): Hepatic focal lesions among low and high risk esophageal varices cases.

Table (6): Hepatomegaly among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	3	25	4	23.5	
No	9	75	13	76.5	0.927

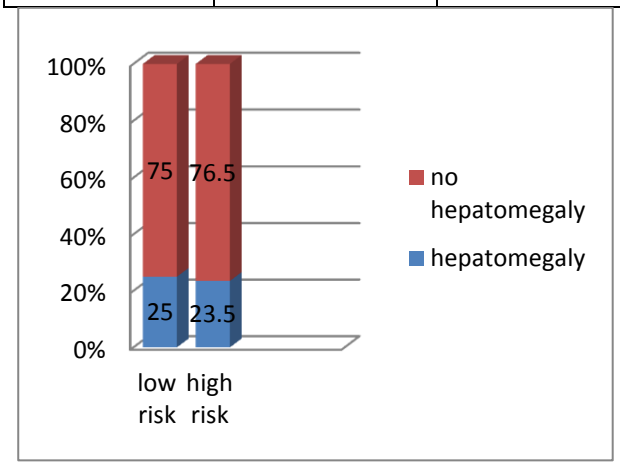


Figure (6): Hepatomegaly among low and high risk esophageal varices cases.

Table (7): Splenomegaly among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	8	66.6	14	82.3	0.544
No	3	33.4	3	17.6	

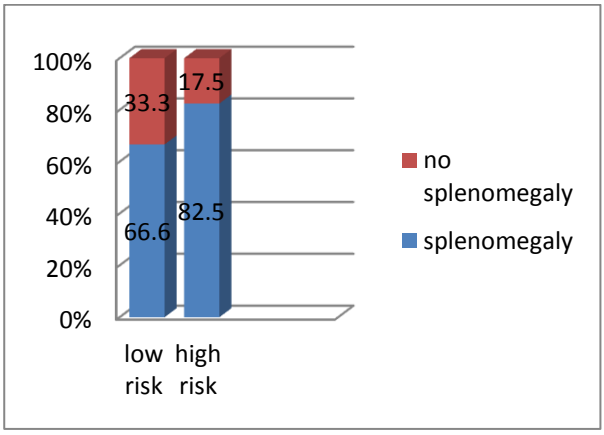


Figure (7): Splenomegaly among low and high risk esophageal varices cases.

Table (8): Splenic varices among low and high risk esophageal varices cases

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	4	33.3	9	52.9	٠.٢٩٥
No	8	66.6	8	47.1	

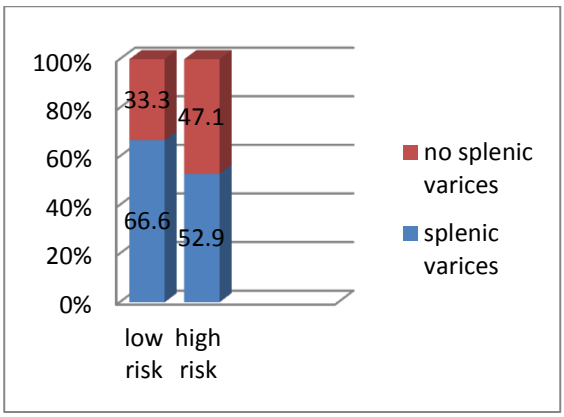


Figure (8): Splenic varices among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	8	66.6	7	41.1	0.١٧٦
No	4	33.3	10	58.8	

Table (9): Ascites among low and high risk esophageal varices cases.

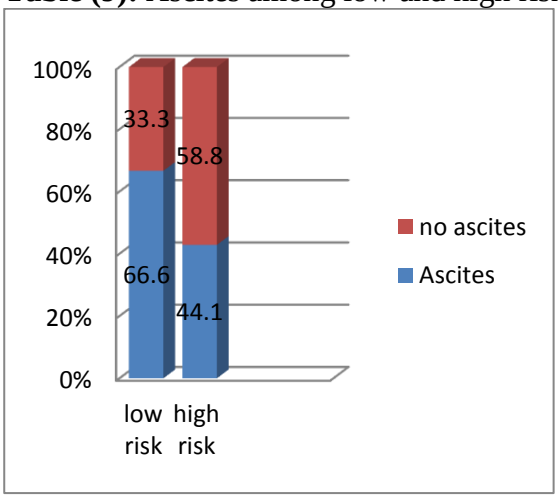


Figure (9): Ascites among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	1	8.3	5	29.4	0.167
No	11	91.6	12	70.5	

Table (10): Gall bladder stones among low and high risk esophageal varices cases

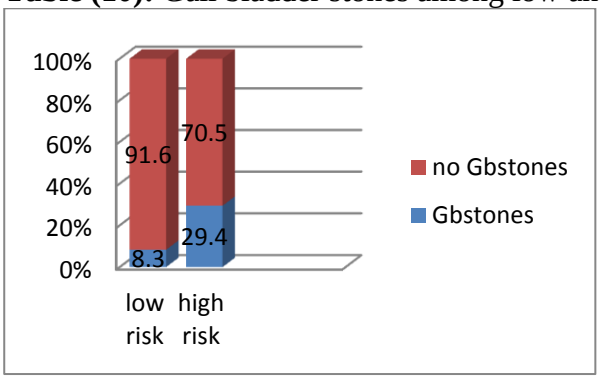


Figure (10): Gall bladder stones among low and high risk esophageal varices cases.

Table (11): Portal vein thrombosis among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	4	33.3	1	5.8	0.054
No	8	66.6	16	94.1	

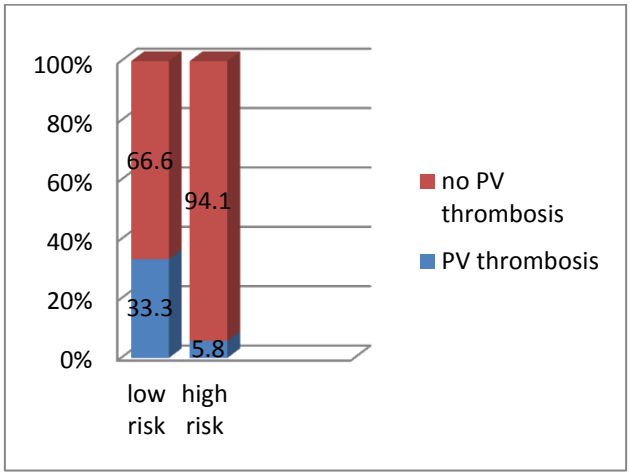


Figure (11): Portal vein thrombosis among low and high risk esophageal varices cases.

	Low risk N.=12		High risk N.=17		P value
	No.	%	No.	%	
Yes	6	50	8	47	0.875
No	6	50	9	53	

Table (12): Peri GB collections among low and high risk esophageal varices cases.

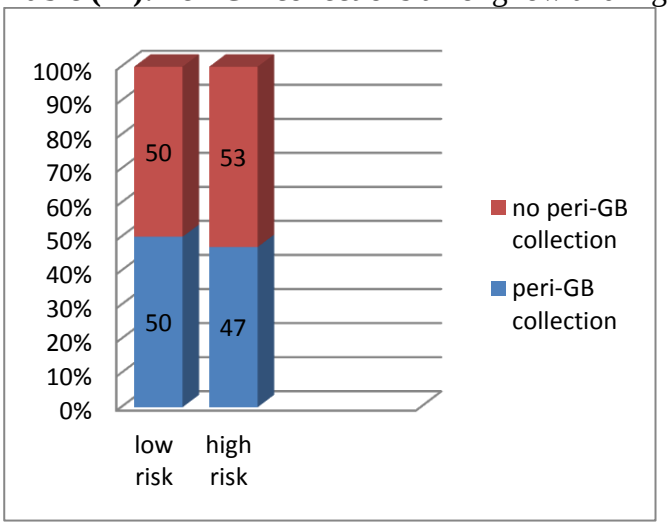


Figure (12): Peri GB collections among low and high risk esophageal varices cases.

DISCUSSION

Cirrhosis is the result of chronic liver disease that causes scarring of the liver (fibro-nodular regeneration) and liver dysfunction [8].

(Sherlock and Dooley,)[9] stated that cirrhosis apart from other features peculiar to the cause, results in two major events, hepatocellular failure and portal hypertension. Development of the portal hypertension was attributed to many factors; diffuse fibrosis, compression of intrahepatic vasculature by regenerative nodules, hepatocyte enlargement,

various dynamic phenomena including contraction of fibromyoblasts and development of hyperdynamic circulation. Reported that prevalence of esophageal varices in patients with decompensated cirrhosis is higher than in those with compensated cirrhosis.

It is estimated that approximately 60%–80% of patients with cirrhosis develop esophageal varices during their life at a rate of 5% per year, and the progression from small to large varices occurs in 5%–10% of patients after the first year [(10).]

There is a considerable mortality risk after the first event of bleeding; hence, prophylactic measures are mandatory .

Prevention of variceal bleeding is an important goal both for cirrhotic patients and for the physicians dealing with them. The first crucial step in prevention is to identify the patients at risk of bleeding, in order to select them for prophylactic treatment including beta-blockers, variceal sclerotherapy and variceal band ligation, thus reducing the risk of variceal bleeding and related mortality [(**11,12,13,14,15**,).]

Current guidelines ([2]) recommend screening all cirrhotic patients by upper GI endoscopy. Even patients with no varices at screening should undergo endoscopic surveillance every 2–3 years. Those with low-risk varices at screening should be re-endoscoped every 1–2 years. Those with decompensated disease, with or without varices, should be re-endoscoped in 1 year. Thus, screening all cirrhotic patients with upper GI endoscopy to detect the presence of varices implies a number of unnecessary endoscopies to the patients and this increases the workload of endoscopy units.

In addition, the invasiveness, requirement of sedation and risk of complications have made the application of the recommendations hampered by suboptimal patient acceptance of upper GI endoscopy [(16–17)]

The availability of less invasive screening tools could improve the patient acceptance and thus adherence to recommendations and restrict the performance of endoscopy to those patients who may need endoscopic therapies. The aim of the present study is to evaluate the use of contrast enhanced CT to detect esophageal varices, differentiate between varices at low risk (<3 mm) and those at high risk (> 3 mm) for bleeding and to determine its cost-benefit, with endoscopy as the reference standard. All studied subjects were subjected to thorough history taking, clinical evaluation, standard upper GI endoscopy performed by a gastroenterologist of at least 10 year experience and standard abdominal triphasic CT scanning. The findings obtained from the abdominal triphasic CT pictures as regards the presence or absence and the size of esophageal varices were compared to the results obtained from the upper GI endoscopy. Using the multidetector CT esophagography - not only in detection of presence of esophageal varices but also in accurately measuring their sizes- was found to be worth noting. Multidetector CT esophagography has sensitivity of 96.7 %, specificity 100%, positive predictive value 100%, negative predictive value 66.7% and accuracy 100%. One case of the low risk group was false negative detected by endoscope and missed by the CT can be attributed to several factors. First, small esophageal varices are presumably more susceptible to hemodynamic and respiratory factors, so they may at times be collapsed and not visible on CT; for example, some small varices are detectable only during the Valsalva maneuver [**(17).**] Second, it is sometimes difficult to visualize small enhancing varices almost embedded in the wall of esophagus [**(18)**] because the wall itself enhances to variable degrees.

These results are much better than the results of previous similar studies as in: (Jun et al., 2007)[**(19),**] (Ba-Ssalamah et al., 2009) [**(20)**]

Jun et al. 2007 [(19),] who use contrast enhanced CT and got results as follow; sensitivity 92%, specificity 84%, positive predictive value 55%, negative predictive value 98% and accuracy 85%. In these studies esophageal lumen was insufflated in order to clearly visualize the varices. For air insufflation, a 16-F end-hole catheter, which was connected to a mechanical inflator (Enema Teleflator CK-85; Kaigen, Osaka, Japan) beside the CT console with a long

plastic connector, was inserted into the upper esophagus through the mouth. Air injection was performed by one radiologist at a rate of 700 mL/30 sec from 12 seconds before scanning to the time the scanner passed the gastroesophageal junction during the arterial and portal phases. This procedure had a negative effect on the ability to visualize and accurately measure small varices.

According to Kim SH etal [5] and Perri RE, Chiorean MV etal [21]. The reported overall sensitivities for detecting EVs of any size were <70% due to the unsatisfactory detection of small varices. This could be due to the conventional liver CT protocol and the slice thickness they used, which was not optimal for the detection of lesions <5 mm. In addition, variceal enhancement may have been suboptimal because they used a fixed time delay rather than a bolus- tracking technique, which would allow more accurate timing of arterial and portal venous phases. Moreover, this poor sensitivity for low-grade disease can be attributed to the use of positive oral contrast agent; hence, residual contrast material coating the luminal surface may have interfered with the detection of some small varices. They also applied nonspecific definition for EVs as dilated vessels in or adjacent to the wall of the oesophagus, thus likely resulting in inclusion of some paraoesophageal varices. Further, the time interval between endoscopy and MDCT was up to 4 weeks; therefore, some interval changes of variceal size and shape cannot be ruled out.

Furthermore, one of the studies Kim YJ etal [22] was retrospective and the patient population did not represent a consecutive group in a screening setting.

In a recent report, one of the reasons that hampered patient compliance to MDCT was the use of intubation and a mechanical inflator to distend the oesophagus. As the authors mentioned, the technique required considerable patient cooperation to achieve optimal distension of the oesophagus and they suggested that the use of an effervescent agent will further increase patient compliance.

According to Dessouky etal 2013 [7] used an efficient and well-tolerated technique for distending the esophagus that was achieved by the administration of effervescent powder combined with visceral hypotonia(as we did in our study). The slow passage of the effervescent powder through the esophagus, favoured by hypotonia and the supine position of the patient, retains the developed gas within the esophageal lumen longer, thus causing a more effective wall distension. As a result, the esophageal segments, in particular the lower oesophagus, in which most EVs developed were adequately distended.

In conclusion, our results suggest a potential role for CT in the evaluation of esophageal varices. The use of an optimized CT protocol may yield increased CT accuracy and allow CT to function as an important alternative or adjuvant to endoscopic screening and surveillance.

We had limitations relating to CT as compared to qualitative endoscopic appearances including the presence of red signs such as cherry-red spots, red wale markings, and diffuse redness, which cannot be demonstrated on CT. The presence of a red sign on endoscopy can be one of the predictors of variceal bleeding Fortunately, endoscopic red signs were rarely observed in the patients with low-risk (grade 1) esophageal varices.

Conclusion: contrast enhanced CT is a good alternative diagnostic tool to conventional upper G.I. endoscopy for detecting and grading of esophageal varices in patients with liver cirrhosis. Also, considering the need of patients to undergo a complimentary abdominal contrast enhanced CT after endoscopy to assess liver, and also CT could also be a low cost-high benefit.

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