PREVALENCE AND RISK FACTORS FOR GASTROESOPHAGEAL VARICES AND BLEEDING IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE – A PROPENSITY MATCHED ANALYSIS.

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Background

- Gastric varices (GV, seen in ~20% patients with cirrhosis) have a higher propensity to bleed severely in comparison to esophageal varices (EV).
- Higher portal pressures in patients with acute-on-chronic liver failure (ACLF) portends higher risk of esophageal varices bleed, often associated with poor patient outcomes.
- Data regarding the prevalence and risk factors for GV and GV bleed in ACLF is limited.

Methods

- Consecutive patients with ACLF were evaluated for presence and location of GV on screening endoscopy.
- We analyzed the correlation of GV with -

➢ ACLF severity
➢ liver and splenic stiffness (LSM and SSM) measurements
➢ hepatic venous pressure gradients (HVPG) presence of portal venous thrombosis (PVT)
➢ gastro-lienorenal shunts (GRS).

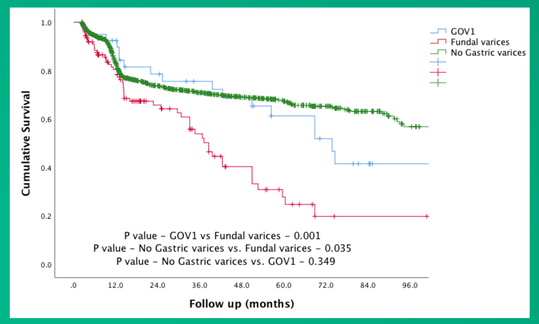
- We also evaluated the incidence and predictors of GV bleed, EV bleed and ACLF related outcomes on follow-up.

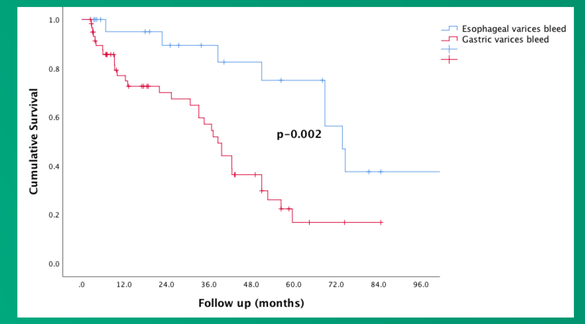
Results

Comparison of ACLF patients with or without presence of gastric varices on endoscopy.

Variable	ACLF patients with Gastric Varix (n=175)	ACLF patients without Gastric Varix (n=1408)	P value	OR (95%CI)
Age (in years) [mean ±SD]	43.1 +11.5	42.8 + 11.1	0.802	
Sex (Male %)	166 (94.9)	1263 (89.7)	0.03	2.118 (1.059-4.232)
BMI (Kg/m2) [mean ±SD]	25.26 + 3.5	25.1 + 3.6	0.563	
Alcohol related ACLF- n (%)	125 (71.4)	1037 (73.7)	0.844	
Esophageal Varices- n (%)	162 (92.6)	1311 (93.1)	0.791	
Gastric varix - n (%)				
GOV1	40 (22.9)	0	<0.001	
GOV2	108 (61.7)	0		
IGV1	24 (13.7)	0		
GOV1 + GOV2	3 (1.7)	0		
Porto-systemic shunt - n (%)	77 (44)	417 (29.6)	<0.001	1.867 (1.356-2.571)
Leino-renal shunt	72 (41.1)	287 (20.4)	<0.001	2.731 (1.967-3.790)
Transhepatic apex shunt	5 (2.9)	104 (7.4)		
Arterio-portal shunt	0	6 (0.4)		
Mesocaval shunt	0	15 (1.1)		
Shunt diameter (mm) [mean ±SD]	9.4 + 3.3	9.8 + 3.5	0.593	
Spleen longitudinal length (cms) [mean ±SD]	14.6 + 2.9	14.3 + 2.6	0.312	
Vascular thrombosis - n (%)	11 (6.3)	38 (2.7)	0.010	2.418 (1.213-4.823)
Hemoglobin (g/L) [mean ±SD]	9.98 + 2.27	10.55 + 2.11	0.002	
Total leucocyte count (X10^3/mm) [median ±IQR]	10.1 (7.6-14.5)	10.5 (7.3-15.3)	0.456	
Platelet count (X10^3/mm) [median ±IQR]	131 (80-170)	136 (90-201)	0.222	
Bilirubin (mg/dl) [median (IQR)]	14.05 (7.44-25.3)	16.5 (8.5-25.2)	0.082	
AST (U/L) [median (IQR)]	137 (88-200)	142 (96-215)	0.880	
ALT (U/L) [median (IQR)]	45 (29-79)	50 (32-87)	0.115	
Serum albumin (g/dl) [mean ±SD]	2.5 + 0.4	2.5 + 0.3	0.059	
Blood Urea Nitrogen (mg/dl) [median (IQR)]	31 (17.6-48)	24.9 (16.4-43.3)	0.099	
Serum creatinine (mg/dl) [median (IQR)]	0.83 (0.66-1.23)	0.78 (0.58-1.16)	0.147	
INR [median (IQR)]	2.17 + 0.86	2.05 + 0.07	0.049	
Baseline HVPG (mmHg) [mean ±SD] (n=737)	17.13 + 3.8	17.08 + 4.2	0.918	
Liver stiffness measurement (kPa) (n=614)	67.7 + 15.5	57.2 + 19.8	<0.001	
Spleen stiffness measurement (kPa) (n=472) [	82.03 + 15.2	63.3 + 15.5	<0.001	
MELD [mean ±SD]	24.9 + 3.6	24.5 + 5.9	0.344	
MDF (n=1088) [median ±IQR]	70.9 (48.2 -91)	65.9 (47.8 -87.6)	0.324	
AARC score [mean ±SD]	8.5 +2.9	8.46 + 1.87	0.458	
Esophageal varices bleed - n (%)	48 (27.4)	201 (14.3)	<0.001	2.27 (1.57-3.26)
Gastric varices bleed - n (%)	60 (34.3)	0	<0.001	
GOV1	13 (21.7)	0		
GOV2	37 (61.7)	0		
IGV1	7 (11.7)	0		
GOV1 + GOV2	3 (5)	0		
EVL Session - n (%)	77 (44)	401 (28.5)	<0.001	1.973 (1.433-2.718)
TIPS- n (%)	4 (2.3)	13 (0.9)	0.099	
PARTO - n (%)	0	2 (0.1)	0.618	
Hepatic encephalopathy - n (%)	64 (36.6)	485 (34.4)	0.577	
Acute kidney injury - n (%)	54 (30.9)	393 (27.9)	0.414	
SBP - n (%)	6 (3.4)	84 (6)	0.172	
HCC - n (%)	2 (1.1)	15 (1.1)	0.925	
Mortality - n (%)	73 (41.7)	420 (29.8)	<0.001	1.681 (1.225-2.320)

Cumulative survival based on (1) type of gastric varices and (2) presence of gastric or esophageal variceal bleeding

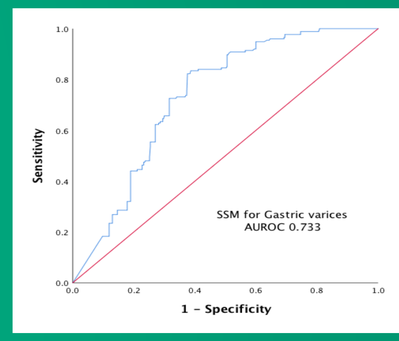




Predictors of GV

	Univariate analysis		Multivariate analysis	
Variable	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Male gender	2.118 (1.059-4.232)	0.034		
Leino-renal shunt	2.730 (1.967-3.790)	<0.001	2.491 (1.623-3.823)	<0.001
PVT	2.418 (1.213-4.823)	0.012		
HB	0.884 (0.822-0.952)	<0.001	0.885 (0.803-0.975)	0.014
INR	1.188 (0.993-1.421)	0.060		
Platelet count	0.998 (0.996-1.000)	0.039		
LSM	1.046 (1.032-1.060)	<0.001		
SSM	1.044 (1.034-1.055)	<0.001	1.046 (1.035-1.057)	<0.001
Serum Albumin	0.740 (0.551-0.993)	0.045		

AUROC of SSM for predicting Gastric varices



Comparison of ACLF patients having GV based on presence or absence of gastric variceal bleeding on follow up.

Variable	Esophageal Varices bleed (n=249)	No Esophageal Varices bleed (n=1334)	P value	OR (95%CI)
Age (in years) [mean ±SD]	41.45 + 9.9	43.1 + 11.3	0.016	
Sex (Male %)	246 (98.8)	1183 (88.7)	0.001	10.46 (3.31-33.09)
Alcohol related ACLF- n (%)	208 (83.5)	954 (71.5)	<0.001	
Porto-systemic shunt - n (%)	94 (37.8)	400 (30)	0.015	1.416 (1.068-1.877)
Spleen longitudinal length (cms) [mean ±SD]	14.7 + 2.7	14.3 + 2.6	0.014	
Vascular thrombosis - n (%)	9 (3.6)	40 (3)	0.606	
Hemoglobin (g/L) [mean ±SD]	9.8 + 2.2	10.6 + 2.1	<0.001	
Platelet count (X10^3/mm) [median ±IQR]	116 (73-179)	139 (92-201)	0.005	
Bilirubin (mg/dl) [median (IQR)]	12.9 (7.3-23.5)	16.8 (8.6-25.3)	<0.001	
Serum albumin (g/dl) [mean ±SD]	2.5 + 0.5	2.5 + 0.4	0.946	
Blood Urea Nitrogen (mg/dl) [median (IQR)]	28.9 (17.9-51.1)	24.8 (16.3-43)	0.049	
Serum creatinine (mg/dl) [median (IQR)]	0.84 (0.61-1.34)	0.77 (0.58-1.14)	0.028	
INR [median (IQR)]	2.13 + 0.56	2.05 + 0.71	0.209	
Baseline HVPG (mmHg) [mean ±SD] (n=737)	19.4 + 3	16.8 + 4.3	<0.001	
Liver stiffness measurement (kPa) (n=614) [mean ±SD]	63.3 + 17.4	58.5 + 19.9	0.016	
Spleen stiffness measurement (kPa) (n=472) [mean ±SD]	86.6 + 12.1	67.5 + 14.1	<0.001	
MELD [mean ±SD]	25.1 + 3.6	24.4 + 2.9	<0.001	
MDF (n=1088) [median ±IQR]	69.7 (48-90)	65 (47-87)	0.037	
AARC score [mean ±SD]	8.84 + 2	8.41 + 1.95	0.117	
TIPS- n (%)	4 (1.6)	13 (1)	0.374	
PARTO - n (%)	0	2 (0.1)	0.541	
Hepatic encephalopathy - n (%)	104 (41.8)	445 (33.4)	0.010	1.433 (1.087-1.889)
Acute kidney injury - n (%)	88 (35.3)	359 (26.9)	0.007	1.484 (1.115-1.977)
SBP - n (%)	18 (7.2)	72 (5.4)	0.252	
Mortality - n (%)	96 (38.6)	397 (29.8)	0.05	1.481 (1.118-1.961)

Comparison of ACLF patients with or without presence of esophageal varices bleeding.

Variable	Esophageal varices bleed (n=225)	Gastric varices bleed (n=60)	P value
Age (in years) [mean ±SD]	41.4 + 9.8	45.2 + 11.1	0.019
Sex (Male %)	222 (98.7)	57 (95)	0.079
BMI (Kg/m2) [mean ±SD]	24.96 + 3.4	24.9 + 4	0.987
Alcohol related ACLF- n (%)	1037 (73.7)	73 (41.7)	0.004
Porto-systemic shunt - n (%)	81 (36)	29 (48.3)	0.081
Lienorenal shunt - n (%)	64 (28.4)	26 (43.3)	0.027
Spleen longitudinal length (cms) [mean ±SD]	14.7 + 2.7	14.6 + 2.57	0.660
Vascular thrombosis - n (%)	9 (3.6)	3 (5)	0.606
Hemoglobin (g/L) [mean ±SD]	9.8 + 2.2	10.23 + 2.18	0.225
Total leucocyte count (X10^3/mm) [median ±IQR]	11.2 (7.8-16.3)	11.25 (8.6–14.7)	0.787
Platelet count (X10^3/mm) [median ±IQR]	116 (73-179)	140 (85-163)	0.048
Bilirubin (mg/dl) [median (IQR)]	12.9 (7.3-23.5)	14.4 (7.4-27.2)	0.641
Serum albumin (g/dl) [mean ±SD]	2.5 + 0.5	2.42 + 0.55	0.239
Serum creatinine (mg/dl) [median (IQR)]	0.84 (0.61-1.34)	0.93 (0.71-1.4)	0.813
INR [median (IQR)]	2.13 + 0.56	2.26 + 1	0.270
Baseline HVPG (mmHg) [mean ±SD] (n=737)	19.4 + 3	16.47 + 3.3	<0.001
Liver stiffness measurement (kPa) (n=614) [mean ±SD]	63.3 + 17.4	68.3 + 11.2	0.007
Spleen stiffness measurement (kPa) (n=472) [mean ±SD]	73.3 + 9.9	86.3 + 10.1	<0.001
MELD [mean ±SD]	25.1 + 3.6	24.8 + 3.3	0.785
MDF (n=1088) [median ±IQR]	69.7 (48-90)	73.2 (42.9-91.4)	0.711
AARC score [mean ±SD]	8.84 + 2	8.3 + 1.4	0.274
Hepatic encephalopathy - n (%)	92 (40.9)	24 (40)	0.901
Acute kidney injury - n (%)	78 (34.7)	24 (40)	0.444
SBP - n (%)	17 (7.6)	3 (5)	0.298
HCC - n (%)	3 (1.3)	2 (3.3)	0.294
Mortality - n (%)	83 (36.9)	33 (55)	0.011

Conclusions

- Almost **10% of ACLF patients have gastric varices**, most frequently located as **cardio-fundal varices**.
- **One-third of patients with gastric varices bleed** on follow-up, associated with **high mortality.**
- **Splenic stiffness measurement** is an important non-invasive tool to **predict presence of gastric varices** and risk of future gastric variceal bleeding.

No conflict of interest

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