Outcomes for Patients on DOACs in Compensated and Decompensated Cirrhosis

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Background

- Cirrhotic patients are prone to thromboembolism as well as bleeding.
- Use of novel anticoagulants is well established in patients with compensated cirrhosis (CTP class A)
- Data on the efficacy and safety profile of DOACs in decompensated cirrhotic patients are limited

AIM

- Our AIM was to determine if clinical outcomes differed in those with compensated cirrhosis receiving DOACS (apixaban, rivaroxaban, edoxaban, and dabigatran) compared to those with decompensated cirrhosis in terms of thromboembolic events, atrial fibrillation (a fib), bleeding events, and TPA administration

Methods

- Single center review from 2015-present in all subjects with cirrhosis with/without decompensation at time of DOAC administration.
- Patients were required to have 90 days of history prior to the DOAC and at least 1 year of follow-up
- Decompensation was identified based on ICD codes (ascites, jaundice, gastric and esophageal varices, portal hypertension, hepatorenal syndrome, hepatic encephalopathy)
- We performed sensitivity analysis for MELD < 11, 11-14 and >14.
- The cohorts were compared for new onset a fib, bleeding (GI bleed, hemorrhagic stroke, retroperitoneal bleed), new onset thrombotic events (PVT, pulmonary embolism, DVT, occlusive stroke) and new administration of TPA before and after matching for all observable confounders using high dimensionality propensity score matching (Schuler, 2018) (Table 2)

Results

Table 1. Baseline Characteristics in subjects with compensated and decompensated cirrhosis

Demographics Table		
	Compensated cirrhosis	Decompensated cirrhosis
N	321	452
Females	116 (36.1%)	149 (33%)
Mean age (sd)	67.2 (12.8%)	63.6 (13%)
18-30 yr	7 (2.2%)	10 (2.2%)
30-40 yr	7 (2.2%)	18 (4%)
40-50 yr	19 (5.9%)	34 (7.5%)
50-60 yr	38 (11.8%)	88 (19.5%)
60-70 yr	106 (33%)	149 (33%)
70-80 yr	100 (31.2%)	119 (26.3%)
80-90 yr	44 (13.7%)	34 (7.5%)
Race (%)		
White	208 (64.8%)	242 (53.5%)
Other	45 (14%)	128 (28.3%)
Asian	44 (13.7%)	62 (13.7%)
Black	24 (7.5%)	20 (4.4%)
Hispanic	40 (12.5%)	102 (22.6%)
Index year (%)		
2015-2019	190 (59.2%)	227 (50.2%)
2020-Present	131 (40.8%)	225 (49.8%)
Mean Pre-index days (sd)	3746 (2352.2)	3452.3 (2493.6)
Mean follow up days (sd)	999.1 (646.7)	854 (500.4)
Number of encounters (sd)	33.3 (37.7)	40.5 (37.3)
Baseline labs (sd or %)		
Hb	12.6 (2.2)	11.8 (2.5)
INR	1.6 (0.5)	1.5 (0.4)
Platelet count	191.6 (65.7)	162.4 (113.1)
PT	15.1 (5.1)	14.6 (4.8)
Co morbidity score (sd)	7.5 (3.5)	10.5 (4.2)
Malignancy	98 (31%)	192 (42.48%)
Metastatic solid tumor	27 (8.41%)	70 (15.49 %)
Diabetes	109 (34%)	206 (45.58%)
Diabetes with complications	58 (18%)	139 (30.75%)
Congestive heart failure	153 (47.6%)	217 (48.01%)
Myocardial infarction	54 (16.82%)	84 (18.58%)
Peripheral vascular disease	75 (23.36%)	101 (22.35%)
Chronic pulmonary disease	137 (42.68%)	162 (35.84%)
Cerebrovascular disease	59 (18.38%)	90 (19.91%)
Dementia	13 (4.05%)	22 (4.87%)
Hemiplegia	13 (4.05%)	18 (3.98%)
Mild liver disease	319 (99.38%)	450 (99.56%)
Severe liver disease	11 (3.43%)	308 (68.14%)
Renal disease	112 (34.89%)	232 (51.33%)
Peptic ulcer disease	20 (6.23%)	50 (11.06%)
Rheumatic disease	15 (4.67%)	27 (5.97%)
HIV	2 (0.62%)	5 (1.11%)
Outcomes (sd or %)		
Atrial fibrillation	161 (50.16%)	198 (43.81%)
Bleeding event	35 (10.9%)	91 (20.13%)
Thrombotic event	63 (19.63%)	144 (31.86%)
TPA	2 (0.62%)	5 (1.11%)

Table 2. Event analysis in matched and unmatched cohorts in compensated and decompensated cirrhosi

Event	Negative	Positive	OR (95% CI)	P value
Thrombosis				
Decompensated (unmatched)	308	144	1 (1.000, 1.000)	NA
Compensated (unmatched)	258	63	0.522 (0.372, 0.733)	0.000128
Decompensated (propensity score matched)	111	39	1 (1.000, 1.00)	NA
Compensated (propensity score matched)	112	38	0.966 (0.575, 1.62)	0.895
TPA Administration				
Decompensated (unmatched)	447	5	1 (1.0000, 1.00)	NA
Compensated (unmatched)	319	2	0.561 (0.0531, 3.45)	0.706
Decompensated (propensity score matched)	148	2	1 (1.00000, 1.00)	NA
Compensated (propensity score matched)	149	1	0.498 (0.00837, 9.66)	1
Atrial Fibrillation				
Decompensated (unmatched)	254	198	1 (1.000, 1.00)	NA
Compensated (unmatched)	160	161	1.291 (0.969, 1.72)	0.0811
Decompensated (propensity score matched)	65	85	1 (1.000, 1.00)	NA
Compensated (propensity score matched)	78	72	0.706 (0.448, 1.11)	0.133
Bleeding events				
Decompensated (unmatched)	361	91	1 (1.000, 1.000)	NA
Compensated (unmatched)	286	35	0.485 (0.319, 0.739)	0.000481
Decompensated (propensity score matched)	129	21 1	(1.000, 1.00)	NA
Compensated (propensity score matched)	0.867	20	0.945 (0.489, 1.83)	

Summary

- In a single site observational analysis, we identified no difference in thrombotic events, a fib, bleeding complication , or administration of TPA when comparing compensated and decompensated liver cirrhosis patients who were receiving DOAC therapy
- We matched patients on all baseline observable confounders at the time they began DOAC administration. For sensitivity analysis we stratified presenting MELD into low, medium, high and for each subgroup the findings were consistent.

Limitations

- We reported a single center and retrospective data
- Sample size limited power in this study

Future Directions

- Performing a prospective study
- Performing a larger sample size/multicenter study to increase the statistical power and validate these results