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ORIGINAL ARTICLE

Observational Study

Novel CABIN score outperforms other prognostic models in predicting in-hospital mortality after salvage transjugular intrahepatic portosystemic shunting

Jake Krige, Eduard Jonas, Chanel Robinson, Steve Beningfield, Urda Kotze, Marc Bernon, Sean Burmeister, Christo Kloppers

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Abstract

BACKGROUND

Transjugular intrahepatic portosystemic shunt (TIPS) is now established as the salvage procedure of choice in patients who have uncontrolled or severe recurrent variceal bleeding despite optimal medical and endoscopic treatment.

AIM

To analysis compared the performance of eight risk scores to predict in-hospital mortality after salvage TIPS (sTIPS) placement in patients with uncontrolled variceal bleeding after failed medical treatment and endoscopic intervention.

METHODS

Baseline risk scores for the Acute Physiology and Chronic Health Evaluation (APACHE) II, Bonn TIPS early mortality (BOTEM), Child-Pugh, Emory, FIPS, model for end-stage liver disease (MELD), MELD-Na, and a novel 5 category CABIN score incorporating Creatinine, Albumin, Bilirubin, INR and Na, were calculated before sTIPS. Concordance (C) statistics for predictive accuracy of inhospital mortality of the eight scores were compared using area under the receiver operating characteristic curve (AUROC) analysis.

RESULTS



Thirty-four patients (29 men, 5 women), median age 52 years (range 31-80) received sTIPS for uncontrolled (11) or refractory (23) bleeding between August 1991 and November 2020. Salvage TIPS controlled bleeding in 32 (94%) patients with recurrence in one. Ten (29%) patients died in hospital. All scoring systems had a significant association with in-hospital mortality (P < 0.05) on multivariate analysis. Based on in-hospital survival AUROC, the CABIN (0.967), APACHE II (0.948) and Emory (0.942) scores had the best capability predicting mortality compared to FIPS (0.892), BOTEM (0.877), MELD Na (0.865), Child-Pugh (0.802) and MELD (0.792).

CONCLUSION

The novel CABIN score had the best prediction capability with statistical superiority over seven other risk scores. Despite sTIPS, hospital mortality remains high and can be predicted by CABIN category B or C or CABIN scores > 10. Survival was 100% in CABIN A patients while mortality was 75% for CABIN B, 87.5% for CABIN C, and 83% for CABIN scores > 10.

Key Words: Transjugular intrahepatic portosystemic shunt; Risk score; Portal hypertension; Variceal bleeding; Mortality

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Core Tip: This study compared the performance of a new CABIN score with seven existing risk scores to predict in-hospital mortality after salvage transjugular intrahepatic portosystemic shunt (TIPS) placement in 34 patients with uncontrolled variceal bleeding after failed medical treatment and endoscopic intervention. Using concordance statistics for predictive accuracy of in-hospital mortality the novel 5 category CABIN score incorporating Creatinine, Albumin, Bilirubin, INR and Na outperformed the APACHE II, BOTEM, Child-Pugh, Emory, FIPS, MELD and MELD-Na scores when compared by area under the receiver operating characteristic curve (AUROC) analysis. Survival was 100% in CABIN A patients while mortality was 75% for CABIN B, 87.5% for CABIN C, and 83% for CABIN scores > 10.

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INTRODUCTION

Transjugular intrahepatic portosystemic shunt (TIPS) is now established as the salvage procedure of choice in patients who have uncontrolled or severe recurrent variceal bleeding despite optimal medical and endoscopic treatment[1]. Key clinical distinctions exist in the spectrum of patients undergoing TIPS, ranging from high-risk cirrhotic patients with liver decompensation and uncontrolled variceal bleeding necessitating an emergent salvage TIPS (sTIPS) to those with well-preserved liver function undergoing an elective TIPS for refractory bleeding. Current risk stratification of patients who have refractory variceal bleeding and require sTIPS is however imperfect. Although TIPS is a minimally invasive procedure, appropriate patient selection is crucial to identify patients who would benefit from the procedure, considering the substantial risks of hepatic encephalopathy, liver failure and increased overall morbidity and mortality in high-risk individuals[2,3].

Several prognostic and risk scores have been developed to identify patients at risk for a poor clinical outcome after sTIPS. These include the Acute Physiology and Chronic Health Evaluation (APACHE) II [4], Bonn TIPS early mortality (BOTEM)[5], Child-Pugh (C-P)[6], Emory[7], Freiburg index of post-TIPS survival (FIPS)[8], model for end-stage liver disease (MELD)[9], and Model for End-Stage Liver Disease sodium (MELD-Na)[10] scores. In this study the accuracy of a novel CABIN score, which was developed to overcome limitations of existing scoring systems, was compared to established risk scores for the prediction of in-hospital mortality following sTIPS.

MATERIALS AND METHODS

In this retrospective observational analysis, eight risk scores were evaluated in a cohort which included all adult patients who underwent sTIPS for uncontrollable or life-threatening refractory variceal



bleeding in the Surgical Gastroenterology Unit at Groote Schuur Hospital and the University of Cape Town Private Academic Hospital between August 1991 and November 2020. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies[11]. Baseline demographic, clinical and endoscopic data and biochemical variables were collected on admission. The anonymized and de-identified information were retrieved from a prospectively maintained ethics approved registry for patients treated for esophageal varices (Table 1).

Details of the acute bleeding management protocol and the endoscopic interventional techniques used in our unit have been published previously [12-15]. In patients who had endoscopically uncontrolled bleeding a Minnesota balloon tube or a Danis esophageal stent (Ella-CS, Hradec Kralove, Czech Republic) was inserted to tamponade variceal bleeding and endotracheal intubation was used for airway protection when indicated^[16]. In this high-risk group with uncontrolled variceal bleeding and those with refractory life-threatening bleeding despite endoscopic intervention and somatostatin infusion, sTIPS was performed as an emergency procedure under general anaesthesia with placement of an expandable uncovered 10 mm Wallstent (Boston Scientific, Marlborough, MA, United States)[15].

The study protocol followed the Baveno recommendations and defined uncontrolled or persistent variceal bleeding as the need for a transfusion of 4 units of blood or more within 6 h and the inability to achieve an increase in systolic blood pressure to 70 mmHg or more or a pulse reduction to less than 100/min. Contraindications to sTIPS in our unit were severe pulmonary hypertension, severe tricuspid regurgitation, congestive heart failure, fibropolycystic liver disease, uncontrolled systemic sepsis and unrelieved biliary obstruction. Relative contraindications were congenital hepatic fibrosis, portal vein thrombosis, obstruction of all hepatic veins and severe coagulopathy (INR > 5).

Details of the newly developed five component CABIN score are given in Supplementary Table 1. Each CABIN variable is scored from one to five and the cumulative total is calculated by adding the individual values of the five biochemical components (Creatinine, Albumin, Bilirubin, INR (international normalized ratio) and Na (sodium). The best total CABIN score computes at 5 points and the worst at 25 points. Four CABIN categories (A-D) were established (A: 5-10 points, B: 11-15, C: 16-20, D: 21-25).

The CABIN score and seven previously described scoring systems, APACHE II, BOTEM, Child-Pugh, Emory, FIPS, MELD, and MELD-Na scores were calculated based on clinical evaluation and laboratory values obtained before the sTIPS procedure. The primary study outcome measure was prediction of inhospital mortality after sTIPS and compared the relative performances of the seven established scoring models and the new CABIN score.

Statistical analysis

All clinical data and variables were collected and managed using the REDCap electronic data capturing software licensed to the University of Cape Town[17]. Statistical computations were made using IBM SPSS statistics (version 26.0, IBM, United States). Statistical significance was set at P < 0.05. Continuous data were reported as mean ± SD or medians and range and discrete data as percentages. To evaluate the performance of the various scoring systems to predict in-hospital mortality the concordance Cstatistic [area under the curve (AUC) of the receiver operating characteristic (ROC) curves] was used.

Ethical considerations

The study protocol was approved by the Human Research Ethics Committee (HREC Ref No. 120/2019) of the University of Cape Town and the research was conducted in accordance with the Declaration of Helsinki.

RESULTS

A total of 564 patients with variceal bleeding were treated during the study period. In 530 patients (94%), bleeding was controlled by endoscopic intervention and medication. In 34 patients (6%) who constitute the study population and underwent sTIPS, bleeding was either uncontrollable *ab initio* (*n* = 11) or life-threatening refractory (n = 23) despite optimal endoscopic and pharmacological management.

The demographic and clinical data of the patients are summarized in Table 1. No patients had a concomitant HCC or portal vein thrombosis at the time of TIPS insertion. Before sTIPS 19 patients had a median of three (1-9) injection sclerotherapy treatment (IST) sessions and 20 had a median of two (1-6) endoscopic variceal ligation (EVL) sessions with a median of 10 bands placed per session. Five patients had both IST and EVL. Median units of blood transfused before sTIPS was six (3-12), and 14 patients required either Minnesota balloon tamponade (n = 12) or placement of a Danis stent (n = 2) for temporarily control of bleeding before the sTIPS procedure. Eleven patients required endotracheal intubation and mechanical ventilation and nine required inotropic support.

Technical success for sTIPS was 100% and therapeutic success (control of bleeding) was achieved in 31 of 34 (91%) patients. Bleeding persisted in two patients (6%) despite a patent sTIPS on repeat USdoppler examination and one patient developed recurrent bleeding in hospital during the index



Table 1 Demographic, clinical characteristics and risk prediction scores of 34 patients undergoing salvage transjugular intrahepatic portosystemic shunt, *n* %

portosystemic snunt, n %				
Variable	Total cohort (<i>n</i> = 34)	Survived (<i>n</i> = 24)	In-hospital death (<i>n</i> = 10)	P value
Demographics				
Age (mean ± SD)	52 ± 11.6	50 ± 10.5	57 ± 12.9	0.107
Sex				
Male	29 (85)	22 (92)	7 (70)	0.104
Female	5 (15)	2 (8)	3 (30)	
Cause of cirrhosis				
Alcohol related	22 (65)	15 (63)	7 (70)	0.938
Non-alcohol related	12 (35)	9 (37)	3 (30)	
Child-Pugh grade				
А	3 (9)	3 (12)	0	0.022
В	19 (56)	16 (67)	3 (30)	
С	12 (35)	5 (20)	7 (70)	
Risk prediction scores				
APACHE II (mean ± SD)	13.4 ± 4.7	11.4 ± 3.3	18.3 ± 3.8	0.196
BOTEM (mean ± SD)	5.4 ± 1.1	5.0 ± 0.9	6.3 ± 0.7	0.964
CABIN (mean ± SD)	10.9 ± 5.0	8.3 ± 1.8	17.0 ± 3.8	0.133
CHILD-PUGH (mean ± SD)	8.9 ± 1.8	8.2 ± 1.8	10.6 ± 2.0	0.001
EMORY (mean ± SD)	3.2 ± 0.9	2.8 ± 0.7	4.3 ± 0.5	0.497
FIPS (mean ± SD)	-0.3 ± 0.9	-0.6 ± 0.9	0.5 ± 0.5	0.205
MELD (mean ± SD)	15.0 ± 6.2	13 ± 4.8	19.8 ± 6.7	0.007
MELD-Na (mean ± SD)	16.9 ± 7.4	14 ± 5.3	23.9 ± 7.1	< 0.001

SD: Standard deviation; APACHE II: Acute physiology and chronic health evaluation II; BOTEM: Bonn TIPS early mortality; CABIN: Creatinine, Albumin, Bilirubin, INR, Sodium score; FIPS: Freiburg index of post-TIPS survival; MELD: Model for end-stage liver disease; MELD-Na: Model for end-stage liver disease sodium.

admission after initial control of bleeding by sTIPS.

Ten patients (29.4%) died in hospital at a median of 5 d following the procedure (range 1-10 d) of progressive liver failure (n = 4), MOF (2), alcoholic cardiomyopathy (n = 2) or uncontrolled variceal bleeding (n = 2). Mortality in C-P grade A patients was 0%, in C-P grade B patients 16% and C-P grade C patients 58%. In patients who died the median C-P score was 11, (range 7-13), median MELD score was 18 (range 11-29) and median MELD Na score was 25 (range 11-33). Nine of the 12 (75%) patients who required pre-sTIPS balloon tamponade died, while all nine (100%) patients who were hypotensive (systolic blood pressure < 70 mmHg) and with the combination of > 8 unit blood transfusion, inotropic support, balloon tamponade and mechanical ventilation died.

The two patients with persistent bleeding after TIPS underwent repeat endoscopy and ultrasoundguided Histoacryl and coil injection of residual gastric varices with resolution. The patient with recurrent bleeding in hospital underwent a gastric devascularization for control of gastric varices.

Figure 1 shows the graphic representation of the comparative performances of the eight risk scores in predicting in-hospital death following sTIPS. The CABIN score (AUROC 0.967) had the highest discriminative ability in predicting in-hospital death compared to the APACHE II (AUROC 0.948), BOTEM (AUROC 0.877), C-P (AUROC 0.802), EMORY (AUROC 0.942), FIPS (AUROC 0.892), MELD (AUROC 0.792), and MELD-Na (AUROC 0.865) scores as detailed in Table 2. The median CABIN score in the 24 in-hospital TIPS survivors was 8 (range 5-18) compared to a median of 17 (range 11-22) in the 10 deaths. CABIN A patients had a 100% survival, compared to 25% and 12.5% survival in CABIN B and CABIN C category patients respectively. CABIN points of 11 or more provided a clear survival cut-off. No patients with CABIN scores < 10 died while 83% of patients with CABIN scores of > 11 died.

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Table 2 Performance of various risk prediction scores in predicting in-hospital death following salvage transjugular intrahepatic portosystemic shunt

	In-hospital deaths				
	AUC	STD error	<i>P</i> value	95% confidence interval	
APACHE II	0.948	0.035	0	0.879-1.000	
BOTEM	0.877	0.059	0.001	0.762-0.992	
CABIN	0.967	0.028	0	0.912-1.000	
CHILD-PUGH	0.802	0.084	0.006	0.638-0.967	
EMORY	0.942	0.038	0	0.868-1.000	
FIPS	0.892	0.055	0	0.783-1.000	
MELD	0.792	0.082	0.008	0.631-0.952	
MELD Na	0.865	0.077	0.001	0.713-1.000	

AUC: Area under the curve; SD: standard deviation; APACHE II: Acute physiology and chronic health evaluation II; BOTEM: Bonn TIPS early mortality; CABIN: Creatinine albumin bilirubin INR sodium score; FIPS: Freiburg index of post-TIPS survival; MELD: Model for end-stage liver disease; MELD-Na: Model for end-stage liver disease sodium.

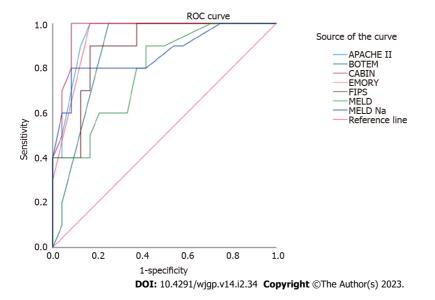


Figure 1 Performance of various risk prediction scores in predicting in-hospital death following salvage transjugular intrahepatic portosystemic shunt. APACHE II: Acute physiology and chronic health evaluation II; BOTEM: Bonn TIPS early mortality; CABIN: Creatinine, Albumin, Bilirubin, INR, Sodium score; FIPS: Freiburg index of post-TIPS survival; MELD: Model for end-stage liver disease; MELD-Na: Model for end-stage liver disease sodium; TIPS: Transjugular intrahepatic portosystemic shunt; ROC: Receiver operating characteristic.

DISCUSSION

The unique safety profile and minimally invasive characteristics conferred by TIPS provide an effective reduction in portal pressure and make the procedure the ideal rescue intervention for variceal bleeding not controlled by endoscopic intervention and pharmacological therapy[18]. In this study we compared the relative performances of eight scoring models, including the novel CABIN score, in predicting inhospital mortality in a high-risk cohort of patients who underwent sTIPS placement. Although sTIPS controlled variceal bleeding in 94% of patients, over-all in-hospital mortality was 29.4% and increased exponentially in those who required > 8 unit blood transfusion, inotropic support, esophageal balloon tamponade and mechanical ventilation. Log-rank comparisons of survival curves showed that of the eight scores evaluated, the CABIN, APACHE II and Emory scores had the highest AUROC values and the best discriminatory ability with C-statistic values all exceeding 0.9. Of these three top contenders, the CABIN score (0.967) had the best discriminatory and predictive capability. As a collorary, this study also demonstrates the predictive ability of the CABIN score with 100% survival observed in patients in the CABIN A category (< 10 points) after sTIPS.



The reported mortality rate after TIPS placement varies widely due to differing inclusion criteria, timing of TIPS placement, the spectrum and severity of the underlying liver disease and inclusion in some reports of patients with active bleeding during urgent TIPS as well as stable patients undergoing elective TIPS[19-21]. In the 22 studies exclusively reporting salvage or rescue TIPS in patients with uncontrolled life-threatening or endoscopically unmanageable variceal bleeding, as in this study, inhospital mortality rates range from 17% to 56% which are significantly higher than for elective TIPS[22-43] (Table 3). Accurate prediction of outcome following sTIPS is thus a crucial element of management and the optimal prognostic score should ideally be able to distinguish two groups, patients with a better prognosis and likely to survive and those with a high or prohibitive risk of death.

Most of the current prognostic scores used in sTIPS patients have intrinsic limitations due to the selection and weighting of the constituent components. The MELD score, which was initially created to predict survival following elective placement of TIPS, is currently the most widely used liver-related prognostic score both in clinical practice and research and especially as a tool for organ allocation[9]. Although the MELD score was a prospectively developed and validated indicator of the severity of endstage liver disease that utilizes quantitative and objective measures, including bilirubin, creatinine and INR values, the score has potential limitations. A further caveat is the maximum assigned value of serum creatinine which is capped at four even when the measured serum level is higher. Modifications to overcome MELD shortcomings have included reweighting the model's coefficients, altering the laboratory components and the addition of new variables including serum sodium ('MELD-Na'), albumin [termed '5-variable MELD' (5vMELD)][44] and female gender (MELD 3.0)[45]. These modifications are more discriminative than either MELD or MELD-Na in transplant assessment and use similar elements as the CABIN score.

The inclusion of subjective clinical components in other proposed prognostic models may also limit precision and reproducibility of score assignments. The C-P, Emory and BOTEM scores all have at least one component that may be perceived as subjective while the APACHE II and BOTEM scores lack specificity for liver disease which limits their capacity to predict outcomes after liver interventions such a sTIPS. In addition the C-P, Emory, and BOTEM scores are limited by a ceiling effect in which laboratory values above a particular cut-off level are not distinguished from one another in terms of higher scoring[4-7,9,10]. The FIPS overcomes some of these limitations by using four objective components, age, bilirubin, albumin, and creatinine levels^[8].

In a meta-analysis, which included 11 studies and 2037 patients Zhou et al[46] found that MELD was superior to the C-P score in predicting 3-mo survival after TIPS but not 1-mo, 6-mo or 12-mo survival. Zhang et al[47] found that C-P grade C and MELD > 10 but not the Emory, BOTEM or SB/PLT scores were predictors of survival in Chinese cirrhotic patients treated with TIPS. Gaba et al[48] reported that MELD and MELD-Na scores had the best capability to predict early mortality in an American population compared with bilirubin and the C-P, Emory, PI, APACHE II, and BOTEM scores. In a comparison of the MELD, C-P and Emory scores Schepke et al[49] found that all three models predicted 3-mo survival with similar accuracy, but the MELD score was marginally superior to the C-P score for both 12- and 36-mo survival. In patients with refractory variceal bleeding Rubin et al[39] found that survival was inversely proportional to C-P class and APACHE II scores. The single determinant most closely associated with decreased survival in the first month following TIPS was the APACHE II score, with a score of 18 stratifying patients into low and high mortality risk groups (Table 3). Only one of 13 patients with C-P class C cirrhosis and an APACHE II score exceeding 18 survived > 30 d[39]. In the Hermie study early mortality was associated with a MELD score of at least 19 and hemodynamic instability at the time of admission[32] (Table 3). If hemodynamic instability was combined with a high MELD score, the 6-week mortality peaked at 77.8% [32]. In a multicentre French study Walter et al [50] reported that sTIPS mortality was > 90% in patients who had lactate levels ≥ 12 mmol/L and/or a MELD score \geq 30.

In view of these differing outcomes, the development of a prognostic model to accurately stratify the risk profile of patients undergoing sTIPS may be invaluable in guiding treatment. The novel CABIN score used in this study was developed as a point-based tool to improve prognostic prediction specifically for patients undergoing emergent sTIPS and circumvents the complex computations of the MELD and other scores. This new score avoids subjective elements and can be calculated at the bedside providing a refined, granular grading system from a minimal laboratory dataset with scores ranging from 5 to 25. The CABIN score achieved significant prognostic discrimination reflected by in-hospital survival of 100% in patients in the CABIN A category (5-10 points), while patients in the CABIN B category (11-15) score had a 25% and those in the CABIN C category (16-20) a 12.5% survival. Our model predicted in-hospital mortality with high accuracy and showed statistical superiority over the other seven contenders, including MELD and C-P scores. Moreover, of all the examined models, only the CABIN, APACHE II and Emory scores exceeded a C-statistic value of 0.9.

There are inevitable and specific limitations to our study. Firstly, this investigation is limited by its small sample size, retrospective design, and lack of a control group. Secondly, the study has a clear selection bias which restricts universal applicability as these patients were treated in a single, wellresourced tertiary care referral center with round the clock skilled endoscopic and TIPS access. Thirdly, because patients were accrued over three decades, technical differences in TIPS placement and improvements in medical care during the study period would have contributed to differences in clinical



Table 3 Published series of salvage transjugular intrahepatic portosystemic shunt for uncontrolled variceal bleeding

Ref.	Country	No. of patients	C-P grade A/B/C	Initial control of bleeding %	30-d mortality %	Persistent/Recurrent rebleeding	Survival %	Prognostic factors
Azoulay <i>et al</i> [22], 2001	France	58	3/8/47	90	29	17	51.7 (12 mo)	Sepsis, vasoactive drugs, balloon tamponade
Bañares <i>et al</i> [<mark>23</mark>], 1998	Spain	56	11/22/23	95	28	22 (1 mo)	72 (30 d)	Ascites, HE, albumin
Barange <i>et al</i> [<mark>24</mark>], 1999	France	32	3/14/15	90	25	14	75 (30 d)	ND
Bizollon <i>et al</i> [<mark>25]</mark> , 2001	France	28	0/11/17	96	25 (40 d)	18	52 (2 yr)	↑Creatinine, ↑bilirubin
Casadaban <i>et al</i> [<mark>26</mark>], 2015	United States	101	2/46/52	89	31	21	44 (12 mo)	†Bilirubin, †creatinine, †INR, non-alcoholic liver disease
Chau <i>et al</i> [<mark>27</mark>], 1998	England	84	4/17/63	98	34	30 (30 d)	66 (30 d)	ND
Encarnacion <i>et</i> al[28], 1995	United States	64	2/32/31	98	19	29 (6 mo)	56 (12 mo)	Haemodynamic instability
Gazzera <i>et al</i> [<mark>29]</mark> , 2012	Italy	82	ND	94	25.6	13.4	74.4 (30d)	Child-Pugh C, ↑ creatinine, ↑PT
Gerbes <i>et al</i> [<mark>30]</mark> , 1998	Germany	11		91	27	27	73 (12 mo)	ND
Helton <i>et al</i> [<mark>31</mark>], 1993	United States	23	0/15/18	74	56 (in hospital)	39	ND	Emergency TIPS, active bleeding
Hermie <i>et al</i> [32], 2018	Belgium	32	ND/ND/14	97	31	0	69	MELD > 19, Haemodynamic instability
Jabbour <i>et al</i> [<mark>33</mark>], 1996	United States	25	ND/ND/8	96	44	ND	56 (30 d)	Child-Pugh C, urgent TIPS
Jalan <i>et al</i> [<mark>34</mark>], 1995	Scotland	19	3/3/13	100	42	15.6	58 (30 d)	Liver failure, sepsis
Maimone <i>et al</i> [36], 2019	England	144	11/55/78	ND	36 (6 wk)	29	64 (6 wk)	↑MELD, ↑Child-Pugh score
Le Moine <i>et al</i> [<mark>35</mark>], 1994	Belgium	24	3/13/9	96	17	25	29 (5 mo)	ND
McCormick <i>et al</i> [37], 1994	England	20	1/7/12	100	60 (40 d)	40	30	ND
Patch <i>et al</i> [<mark>38</mark>], 1998	England	54	5/20/29	91	48 (6 wk)	11	53 (6 mo)	Ventilation, ↑WBC, platelets, ↑creatinine
Rubin <i>et al</i> [<mark>39</mark>], 1995	United States	49	3/23/23	84	40%	16	ND	C-P grade C, APACHE II > 18
Sanyal <i>et al</i> [40], 1996	United States	30	1/7/22	100	37	7	60 (6 wk)	> 70 yr, bilirubin >6 mg/dL, creatinine > 3 mg/dL, HE, ARDS
Tyburski <i>et al</i> [<mark>41</mark>], 1997	United States	33	0/5/28	ND	27	15	58 (12 mo)	Albumin < 2.5 g/dL, bilirubin > 3 mg/dL, PT > 15 s
Tzeng <i>et al</i> [42], 2009	Taiwan	107	ND	ND	28	ND	50 (12 mo)	C-P score > 11, MELD > 20
Zhu <i>et al</i> [<mark>43</mark>], 2019	China	58	5/36/7	91.2	12.3 (6 wk)	10.5 (6 wk)	81.8 (12 mo)	Ventilation, ICU

APACHE: Acute Physiology and Chronic Health Evaluation; ARDS: Adult Respiratory Distress Syndrome; C-P: Child-Pugh; INR: International normalized ratio; TIPS: Transjugular intrahepatic portosystemic shunt; MELD: Model for end-stage liver disease; HE: Hepatic encephalopathy; ND: No data; ICU: Intensive care unit; WBC: White blood cells.

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outcomes over time. Fourthly, this new score has been developed using a derivation dataset and requires confirmation and external validation in a similar sTIPS patient group. The robustness of this study is enhanced by the prospective data collection, supervision by the same investigators during the study period, restriction of subjects to a well-defined cohort of cirrhotic patients with uncontrolled exsanguinating bleeding and complete follow-up. The use of all-cause mortality as the primary outcome provided a consistent and objective end point.

CONCLUSION

In conclusion, the novel CABIN prognostic score, which is objective, quantitative, and reproducible, combines five easily obtained laboratory test results and provides improved statistical power predicting in-hospital mortality in patients with uncontrolled variceal bleeding undergoing sTIPS. The CABIN score identified high-risk patients and outperformed other scoring systems in predicting in-hospital mortality. Despite the fact that mortality was 75% for CABIN B, 87.5% for CABIN C, and 83% for CABIN scores > 10 in this study, this high-risk category should not be denied consideration for an emergency TIPS and should be assessed on a case-by-case basis especially in units where there is prompt access to liver transplantation after sTIPS. This study was based on a small defined cohort of predominantly alcoholic decompensated cirrhotic patients undergoing emergent TIPS and this newly developed derivative CABIN score will need further prospective external validation before being considered for general clinical application.

ARTICLE HIGHLIGHTS

Research background

Transjugular intrahepatic portosystemic shunt (TIPS) is now established as the salvage procedure of choice in patients who have uncontrolled or severe recurrent variceal bleeding despite optimal medical and endoscopic treatment.

Research motivation

Although TIPS is a minimally invasive procedure, appropriate patient selection is crucial to identify patients who would benefit from the procedure, considering the substantial risks of hepatic encephalopathy, liver failure and increased overall morbidity and mortality in high-risk individuals.

Research objectives

In this study the accuracy of a novel CABIN score, which was developed to overcome limitations of existing scoring systems, was compared to established risk scores for the prediction of in-hospital mortality following sTIPS.

Research methods

Eight risk scores were evaluated in a cohort which included all adult patients who underwent sTIPS for uncontrollable or life-threatening refractory variceal bleeding. A new five component CABIN score was devised in which each CABIN variable was scored from one to five and the cumulative total is calculated by adding the individual values of the five biochemical components (Creatinine, Albumin, Bilirubin, INR (international normalized ratio) and Na (sodium). The best total CABIN score computes at 5 points and the worst at 25 points. Four CABIN categories (A-D) were established (A: 5-10 points, B: 11-15, C: 16-20, D: 21-25). The CABIN score and seven previously described scoring systems, Acute Physiology and Chronic Health Evaluation (APACHE) II, Bonn TIPS early mortality (BOTEM), Child-Pugh, Emory, FIPS, model for end-stage liver disease (MELD), and MELD-Na scores were calculated based on clinical evaluation and laboratory values obtained before the sTIPS procedure. The primary study outcome measure was prediction of in-hospital mortality after sTIPS and compared the relative performances of the seven established scoring models and the new CABIN score.

Research results

In 34 patients (6%) who underwent sTIPS, bleeding was either uncontrollable *ab initio* (n = 11) or lifethreatening refractory (n = 23) despite optimal endoscopic and pharmacological management. Ten patients (29.4%) died in hospital at a median of 5 d following the procedure (range 1-10 d). Nine of the 12 (75%) patients who required pre-sTIPS balloon tamponade died, while all nine (100%) patients who were hypotensive (systolic blood pressure < 70 mmHg) and with the combination of > 8 unit blood transfusion, inotropic support, balloon tamponade and mechanical ventilation died. The CABIN score [area under the receiver operating characteristic curve (AUROC) 0.967] had the highest discriminative ability in predicting in-hospital death compared to the APACHE II (AUROC 0.948), BOTEM (AUROC



0.877), C-P (AUROC 0.802), EMORY (AUROC 0.942), FIPS (AUROC 0.892), MELD (AUROC 0.792), and MELD-Na (AUROC 0.865) scores. The median CABIN score in the 24 in-hospital TIPS survivors was 8 (range 5-18) compared to a median of 17 (range 11-22) in the 10 deaths. CABIN A patients had a 100% survival, compared to 25% and 12.5% survival in CABIN B and CABIN C category patients respectively. CABIN points of 11 or more provided a clear survival cut-off. No patients with CABIN scores < 10 died while 83% of patients with CABIN scores of > 11 died.

Research conclusions

The novel CABIN prognostic score, which is objective, quantitative, and reproducible, combines five easily obtained laboratory test results and provides improved statistical power predicting in-hospital mortality in patients with uncontrolled variceal bleeding undergoing sTIPS. The CABIN score identified high-risk patients and outperformed other scoring systems in predicting in-hospital mortality. Despite the fact that mortality was 75% for CABIN B, 87.5% for CABIN C, and 83% for CABIN scores > 10 in this study, this high-risk category should not be denied consideration for an emergency TIPS and be assessed on a case by case basis especially in units where there is prompt access to liver transplantation after sTIPS.

Research perspectives

This study was based on a small defined cohort of predominantly alcoholic decompensated cirrhotic patients undergoing emergent TIPS and this newly developed derivative CABIN score will need further prospective external validation before being considered for general clinical application.

FOOTNOTES

Author contributions: Krige J, Jonas E and Robinson C designed the research study; Krige J, Jonas E, Robinson C and Kotze U collected the data and performed the research; Krige J, Jonas E, Robinson C, Kotze U, Beningfield S, Bernon M, Burmeister S, and Kloppers C analyzed the data and wrote the manuscript; All authors have read and approve the final manuscript.

Institutional review board statement: The study protocol was approved by the Human Research Ethics Committee (HREC Ref No. 120/2019) of the University of Cape Town and the research was conducted in accordance with the Declaration of Helsinki.

Informed consent statement: Since this was a retrospective observational study using existing anonymized data, the requirement for informed consent from the study participants was waived by the Institutional Review Board.

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