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ORIGINAL ARTICLE

Design and validation of a tool for the prediction of adverse outcomes in patients with adhesive small bowel obstruction: The HALVIC score

Diseño y validación de una herramienta para la predicción de desenlaces adversos en pacientes con obstrucción intestinal por bridas: La escala HALVIC

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Abstract

Introduction. Adhesive Small Bowel Obstruction (ASBO) represents a common cause of consultation to the emergency department. Currently there is little clarity about which patients with ASBO are at increased risk of developing complications, potentially benefiting from early surgical management. The present study aims to design and validate a risk prediction scale for adverse outcomes in patients with ASBO.

Methods. Retrospective cohort study performed from the MIMIC-IV database between 2008 and 2019. Adult patients admitted to the emergency department with a diagnosis of ASBO were included. The primary outcome was the combined of bowel resection, intensive care unit admission, and all-cause mortality. A risk prediction scale was designed by assigning a score to each variable according to the measure of association obtained in the logistic regression model. All analyses were performed in R statistical software (version 3.5.3).

Results. Five-hundred-thirteen patients were included (men 63.7%, median age: 61 years). Composite outcome was present in 25.7% of cases. Age, history of heart failure and peripheral arterial disease, hemoglobin level, leukocyte count, and INR were the best predictors of these outcomes (AUC 0.75). Based on this model, the simplified HALVIC score was created, classifying the risk of the composite outcome as low (0-2 points), medium (3-4 points) and high (5-7 points).

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Discussion. The HALVIC scale is presented as a simple and easily applicable predictive tool in the clinical setting, which can accurately identify patients with ASBO at high risk of complications, allowing the surgeon to adjust management strategies individually and potentially improving the outcomes of these patients.

Keywords: intestinal obstruction; tissue adhesions; Ischemia; mortality; predictive value; surgery.

Resumen

Introducción. La obstrucción intestinal por bridas representa una causa común de consulta a los servicios de urgencias, pero hay poca claridad sobre qué pacientes tienen mayor riesgo de desarrollar complicaciones. El objetivo de este estudio fue diseñar y validar una escala de predicción de riesgo de desenlaces adversos en pacientes con obstrucción intestinal por bridas.

Métodos. Estudio de cohorte retrospectivo realizado a partir de la base de datos MIMIC-IV. Se incluyeron pacientes adultos admitidos al servicio de urgencias entre 2008 y 2019, con diagnóstico de obstrucción intestinal por bridas. El desenlace principal fue el compuesto de resección intestinal, ingreso a unidad de cuidados intensivos y mortalidad por cualquier causa. Se diseñó una escala de predicción de riesgo asignando un puntaje a cada variable.

Resultados. Se incluyeron 513 pacientes, 63,7 % hombres. El desenlace compuesto se presentó en el 25,7 % de los casos. La edad, historia de insuficiencia cardíaca y enfermedad arterial periférica, nivel de hemoglobina, recuento de leucocitos e INR constituyeron el mejor modelo de predicción de estos desenlaces (AUC 0,75). A partir de este modelo, se creó la escala simplificada HALVIC, clasificando el riesgo del desenlace compuesto en bajo (0-2 puntos), medio (3-4 puntos) y alto (5-7 puntos).

Conclusión. La escala HALVIC es una herramienta de predicción simple y fácilmente aplicable. Puede identificar de manera precisa los pacientes con obstrucción intestinal por bridas con alto riesgo de complicaciones, permitiendo el ajuste individualizado de las estrategias de manejo para mejorar los desenlaces.

Palabras clave: obstrucción intestinal; adherencias tisulares; isquemia; mortalidad; valor predictivo; cirugía.

Introduction

Small bowel obstruction represents one of the most common causes of surgical admissions to emergency departments worldwide and its most frequent etiology is adhesions in up to 75% of cases [1-7]. Although most patients evolve favorably with medical management, timely surgical intervention represents in some cases the treatment of choice, to prevent the progression of intestinal ischemia or abdominal sepsis, the establishment of which leads to increased morbidity and mortality [4,6,8,9]. Delay in surgical intervention has been associated with a significantly increased risk of bowel resection, hospital stay, intensive care unit admission, and mortality. [1,4,6,7,10,11]. Small bowel obstruction has been associated with a mortality incidence of up to 8%. Therefore, the early recognition of patients most prone to adverse outcomes becomes a challenge for surgeons. [11-13].

Multiple studies have suggested that clinical, paraclinical, and imaging findings may be helpful in determining the need for early operative management [4,6,8,9]. One of the most frequently mentioned clinical aspects is advanced age, since it is frequent that in this population there is a delay in the diagnosis due to atypical symptoms [4,6]. Additionally, comorbidities such as diabetes mellitus could represent an alarm sign for earlier surgical management, since its delay has been associated with a higher incidence of acute kidney injury (7.5%) and acute myocardial infarction (4.8%) [9]. Other comorbidities that are suggested to have an impact on the torpid evolution of intestinal obstruction due to adhesions are heart failure, coronary disease, renal failure, chronic lung disease, and malignancy [2].

On the other hand, some laboratory tests have shown diagnostic utility to assess the risk of intes-

intestinal involvement.

tinal involvement. For example, C-reactive protein, leukocyte count, and serum lactate have been the most widely studied tests, evidencing their potential utility to predict adverse outcomes secondary to intestinal ischemia and perforation [4,6,14]. Although management guidelines and recent literature have suggested the use of some of these parameters together to predict the need for surgical management, to date there is no practical tool that integrates widely available clinical and laboratory variables to objectively stratify the risk of adverse outcomes associated with this condition [1,8,12–17]. Its application could help to dynamically establish the need for adjustments in medical management and early surgical intervention in patients at higher risk. Therefore, the aim of this study is to design and validate a risk scale for adverse outcomes in patients with intestinal obstruction due to ahesions that is applicable in daily surgical practice.

Methods

About the Medical Information Mart for Intensive Care IV (MIMIC IV)

The Medical Information Mart for Intensive Care (MIMIC)-IV database corresponds to a registry of more than 40,000 patients admitted to the Beth Israel Deaconess Medical Center, located in Boston, Massachusetts, United States, during the period of 2008-2019. This database is a pioneer in the automatic use of clinical history records, making a wide range of de-identified data derived from hospital care openly available to the international scientific community with minimal human intervention, thanks to machine learning tools developed by team members of the Laboratory for Computational Physiology at the Massachusetts Institute of Technology.

Data source and patients

Data were obtained from the MIMIC-IV and included sociodemographic (age, sex, race, marital status), administrative (medical insurance), clinical (diagnoses, comorbidities, vital signs on admission), laboratory (complete blood count, serum creatinine, coagulation tests), and outcomes (hospital stay, bowel resection, ICU admission, and mortality). Hospital admissions through the emergency department associated with a primary diagnosis of intestinal obstruction secondary to postoperative peritoneal adhesions were identified using the International Classification of Diseases in its ninth and tenth editions (ICD-9 and ICD-10). The codes used were: 560.81 ("Intestinal or peritoneal adhesions with (postoperative) obstruction (postinfection)") and K56.5 ("Intestinal adhesions [bands] with obstruction (postinfection)"), respectively. We included only those patients in whom the primary diagnostic code was intestinal obstruction due to adhesions, being only the first admission for this cause considered. The above was done in order to promote the homogeneity of the individuals and data. Patients under 18 years of age were excluded, as were repeated admissions for the same cause and those patients who presented incomplete information on relevant components such as sociodemographic or follow-up parameters.

Outcomes

The main outcome of the present study corresponded to a composite outcome of resection of a bowel segment, admission to the intensive care unit, and all-cause mortality during the hospital stay. Patients who underwent intestinal resection were identified using the following ICD procedure codes (ICD-9: 4561, 4562, 4563; ICD-10: 0DT80ZZ, 0DT87ZZ, 0DT88ZZ). On the other hand, the length of hospital stay in days was analyzed as a secondary outcome.

Statistical analysis

The evaluated variables were described according to their nature, presenting the categorical ones as absolute values and proportions (%) and the quantitative ones as medians and quartiles 1 and 3. Initially, variables in which missing data were less than 20% were imputed through a multiple imputation approach using the statistical package mice available in the statistical software R, version 3.6 (R Core Team). Subsequently, the sample was divided into a training group and a validation group with a 70%-30% distribution, respectively, using the dplyr package. The random assignment of the participants in both groups was verified by comparing the variables evaluated through the Chi-square test for categorical variables and the Mann-Whitney U test for quantitative variables (Table 1).

Table 1. Sociodemographic and clinical characteristics of patients with a diagnosis of adhesive small bowel obstruction in MIMIC IV.

	Design Cohort (n=359)	Validation Cohort (n=154)	Total (n=513)	p-value
Sociodemographic data				
Age	62 (50, 74.5)	58.5 (48, 72)	61 (49, 74)	0.220
Women	121 (33.7%)	65 (42.2%)	186 (36.3%)	0.066
Race				
Native-American	0 (0.0%)	1 (0.6%)	1 (0.2%)	0.696
Asian	12 (3.3%)	4 (2.6%)	16 (3.1%)	
African-American	58 (16.2%)	25 (16.2%)	83 (16.2%)	
Hispanic/Latino	17 (4.7%)	7 (4.5%)	24 (4.7%)	
White	266 (74.1%)	113 (73.4%)	379 (73.9%)	
Other	5 (1.4%)	4 (2.6%)	9 (1.8%)	
Unspecified	1 (0.3%)	0 (0.0%)	1 (0.2%)	
Marital Status				
Divorced	37 (10.3%)	11 (7.1%)	48 (9.4%)	0.558
Married	170 (47.4%)	74 (48.1%)	244 (47.6%)	
Single	114 (31.8%)	56 (36.4%)	170 (33.1%)	
Widow/widower	36 (10.0%)	13 (8.4%)	49 (9.6%)	
Unspecified	2 (0.6%)	0 (0.0%)	2 (0.4%)	
Health insurance				0.401
Medicaid	19 (5.3%)	13 (8.4%)	32 (6.2%)	
Medicare	131 (36.5%)	54 (35.1%)	185 (36.1%)	
Other	209 (58.2%)	87 (56.5%)	296 (57.7%)	
Clinical Data				
Charlson Comorbidity Index	4 (2, 5)	3 (2, 5)	4 (2, 5)	0.670
Heart failure	38 (10.6%)	10 (6.5%)	48 (9.4%)	0.145
Peripheral arterial disease	22 (6.1%)	7 (4.5%)	29 (5.7%)	0.477
Myocardial infarction	10 (2.8%)	9 (5.8%)	19 (3.7%)	0.093
Cerebrovascular disease	8 (2.2%)	3 (1.9%)	11 (2.1%)	0.841
Dementia	4 (1.1%)	1 (0.6%)	5 (1.0%)	0.623
Chronic obstructive pulmonary disease	65 (18.1%)	30 (19.5%)	95 (18.5%)	0.713
Rheumatic disease	17 (4.7%)	5 (3.2%)	22 (4.3%)	0.446
Peptic ulcer	3 (0.8%)	0 (0.0%)	3 (0.6%)	0.255
Mild Liver Disease	25 (7.0%)	15 (9.7%)	40 (7.8%)	0.282
Uncomplicated diabetes	45 (12.5%)	25 (16.2%)	70 (13.6%)	0.263
Diabetes with complications	8 (2.2%)	4 (2.6%)	12 (2.3%)	0.800
Paraplegia	3 (0.8%)	3 (1.9%)	6 (1.2%)	0.283
Renal disease	34 (9.5%)	12 (7.8%)	46 (9.0%)	0.542
Cancer	22 (6.1%)	8 (5.2%)	30 (5.8%)	0.680
Severe Liver Disease	8 (2.2%)	5 (3.2%)	13 (2.5%)	0.501
Solid Metastatic Neoplasms	16 (4.5%)	11 (7.1%)	27 (5.3%)	0.212
HIV/AIDS	2 (0.6%)	0 (0.0%)	2 (0.4%)	0.353

Table 1 Continued

	Design Cohort (n=359)	Validation Cohort (n=154)	Total (n=513)	p-value
Vital Signs on Admission				
Temperature (°C)	36.7 (36.6, 36.9)	36.7 (36.6, 36.9)	36.7 (36.6, 36.9)	0.341
Heart rate (bpm)	81 (73.5, 91)	80.5 (72.5, 93)	81 (73, 91)	0.510
Respiratory rate (bpm)	17 (16, 18)	17 (16, 18)	17 (16, 18)	0.814
Oxygen saturation (%)	98 (96, 99)	98 (97, 99)	98 (96, 99)	0.185
SBP (mmHg)	130 (116.5, 147)	126.5 (112, 138)	128 (115, 146)	0.087
DBP (mmHg)	76 (66, 86)	76 (64, 85)	76 (65, 86)	0.882
Laboratory Data on Admission				
Hemoglobin (g/dl)	10.8 (9.4, 12.1)	10.6 (9.1, 11.9)	10.7 (9.3, 12)	0.273
Leukocytes (/ml)	7.1 (5.5, 9.4)	7.3 (5.6, 9.1)	7.2 (5.5, 9.2)	0.982
Mean Corpuscular Hemoglobin (pg)	29.8 (28.4, 31.3)	30 (28.3, 31.3)	29.9 (28.4, 31.3)	0.979
Mean Corpuscular Hemoglobin Concentration (g/dl)	32.9 (32, 33.9)	33.1 (32, 34.1)	33 (32, 33.9)	0.584
Medium corpuscular volume (fl)	90 (87, 94)	90 (86, 94)	90 (87, 94)	0.360
Platelets (/µl)	253 (202, 331)	265.5 (204.3, 354.5)	258 (203, 341)	0.246
Red Blood Cell Count (/µl)	3.6 (3.2, 4.1)	3.5 (3.2, 3.9)	3.6 (3.2, 4.0)	0.291
Red Cell Distribution Width (%)	14 (13.1, 15.2)	14.1 (13.2, 15.4)	14 (13.1, 15.3)	0.491
Serum Creatinine (mg/dl)	0.6 (0.5, 0.8)	0.6 (0.5, 0.8)	0.6 (0.5, 0.8)	0.324
INR	1.1 (1.1, 1.2)	1.2 (1.1, 1.3)	1.1 (1.1, 1.3)	0.112
PT (sec)	12.9 (11.8, 14)	13.1 (12, 14.1)	12.9 (11.9, 14)	0.312
PTT (sec)	30 (26.9, 34.5)	30.1 (26.8, 33.1)	30 (26.9, 34.3)	0.535
Outcomes				
Hospital stay (Days)	6.9 (4.2, 9.9)	7.1 (4.4, 11.7)	7.3 (4.3, 10.6)	0.418
Mortality	4 (1.1%)	3 (1.9%)	7 (1.4%)	0.456
Bowel resection	45 (12.5%)	23 (14.9%)	68 (13.3%)	0.462
ICU admission	61 (17.0%)	26 (16.9%)	87 (17.0%)	0.976
composite outcome	92 (25.6%)	40 (26.0%)	132 (25.7%)	0.934

Source: Authors.

Subsequently, a bivariate analysis was performed in the training group through simple logistic regression models, in which all the variables potentially associated with the composite outcome were evaluated. Quantitative variables were analyzed using the LOESS (locally weighted smoothing) technique. This represents a non-parametric technique that allows visualizing the relationship between the quantitative independent variables and the dependent variable, as long as the latter has a binomial distribution. Through the visualization of the LOESS curves, the potential cut-off points were identified and the categorization of the quantitative variables with a significant association with the composite outcome was directed. These cut-off points were subsequently validated using the Youden index. The area under the curve (AUC) of the models was calculated as a discriminatory parameter and the Hosmer-Lemeshow test as a calibration measure.

Subsequently, the predictor with the highest discriminative capacity for the composite outcome was identified and included first in the multivariate model; From then on, variables with a p-value of < 0.2 were included in the bivariate analysis based on their AUC value. A variable was conserved in the multivariate model if its inclusion in it was associated with a significant increase in AUC and the p-value remained below 0.1. The inclusion of variables in the multivariate model ended when adding a new one to it was not associated with a significant increase in the AUC of the model. The performance of the final model was validated in the validation group by recording the AUC values and the result of the Hosmer-Lemeshow test.

For the scale design, the coefficients of the final logistic regression model were converted into points to simplify its use: the individual score of each variable was calculated by subtracting the value of each category from the reference category and then multiplying the result by the value of the global regression coefficient of the variable according to what was suggested by Sullivan et al [18]. The resulting value for each variable was rounded to the nearest integer. Finally, the incidence of the composite outcome was evaluated according to the total score per patient, calculating the sensitivity, specificity, likelihood ratios (positive and negative), and the proportion of cases correctly classified in the validation cohort, according to this design risk groups. An α level of 0.05 (two-sided) was considered statistically significant. The data set was built using the Google BigQuery® tool and analyzed using R, version 3.6 (R Core Team).

Results

Characteristics of the included patients

The search process in the MIMIC IV database allowed the identification of 753 patients with a diagnosis of intestinal obstruction due to adhesions, of which 513 were finally included after applying the exclusion criteria (Figure 1).

Of the total number of patients included, 359 were assigned to the design cohort and 154 to the validation one. The design group was used for the internal validation of the model, while the validation group was used for its external validation. The characteristics of the patients, including sociodemographic, clinical, and laboratory aspects, are presented in Table 1. There were no significant differences in any of the variables evaluated

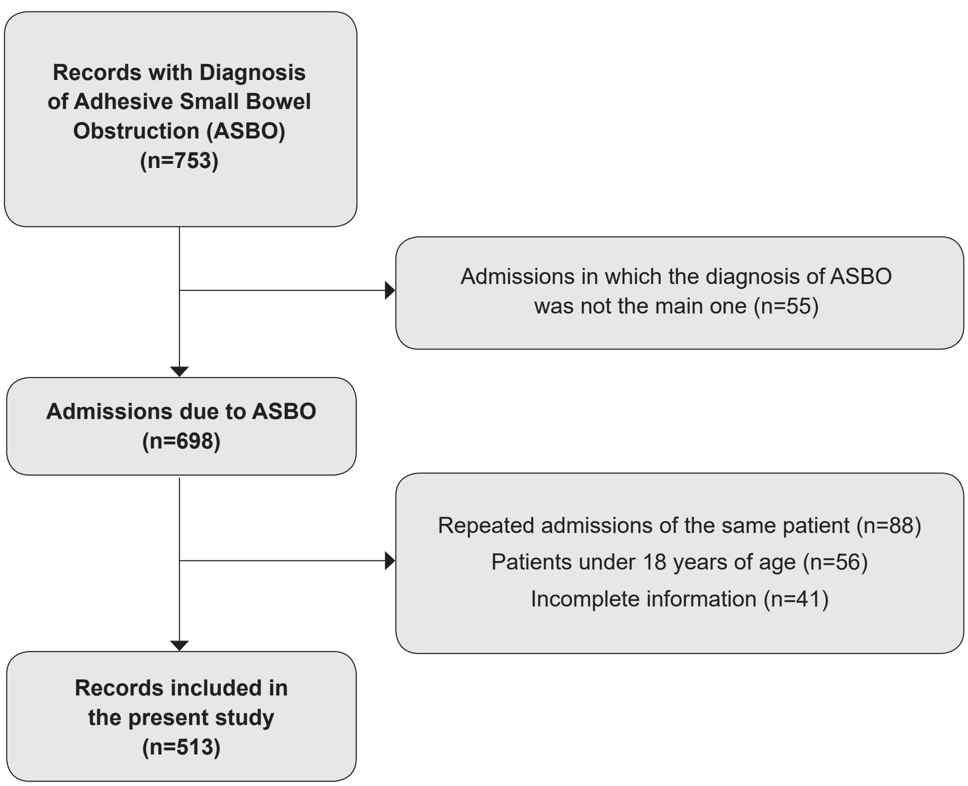

Figure 1. Flowchart summarizing the selection process of patients diagnosed with SBO in the MIMIC-IV database. Source: Authors.

between the two study groups, which suggested that the randomization process was carried out properly.

In the global cohort, the median age of presentation of intestinal obstruction due to ahesions was 61 years (Q1: 49, Q3: 74), with men developing this pathology more frequently during the period evaluated (63.7%). Caucasians (73.9%) and African-Americans (16.2%) were the most prevalent, as well as the married marital status (47.6%). Regarding comorbidities, chronic obstructive pulmonary disease was the most prevalent (18.5%), followed by diabetes mellitus (15.9%), heart failure (9.4%), and kidney disease (9.0%). Notable by groups of comorbidities, 16.3% of the patients suffered from some cardiovascular pathology, while 11.1% had a history of some neoplastic disease.

Although the median of the values of the vital signs at the time of admission were within normal ranges, the dispersion of the measurements included some abnormal values (Table 1). Similarly, the median of most laboratory test results was in the normal range, except for the hemoglobin level, whose median was in the range of mild anemia (10.7 g/dl).

Regarding the adverse outcomes associated with intestinal obstruction by adhesions, it was found that 298 (58%) underwent surgical management, of which 68 (13.3%) required intestinal resection. The second most frequent outcome was the need for management in the Intensive Care Unit (ICU) in 17% of cases. Additionally, 1.4% of the patients died during medical care and the composite outcome occurred in more than a quarter of the cases (25.7%). Finally, the median hospital stay was 7.3 days (Q1: 4.3, Q3: 10.6).

Factors associated with the composite outcome and design of the prediction model

Multiple factors significantly associated with the composite outcome were identified in the bivariate analysis (Table 2). Subsequently, the construction of the multivariate model started with the inclusion of Peripheral Arterial Disease

Table 2. Bivariate analysis evaluating factors associated with the composite outcome in the design cohort.

	No Combined Endpoint (n=267)	With Combined Endpoint (n=92)	Total (n=359)	p-value
Sociodemographic data				
Age	59 (48, 72)	72.5 (57, 82)	62 (50, 74.5)	< 0.001
Women	174 (65.2%)	64 (69.6%)	238 (66.3%)	0.442
Race				
Asian	11 (4.1%)	1 (1.1%)	12 (3.3%)	0.198
African-American	45 (16.9%)	13 (14.1%)	58 (16.2%)	
Hispanic/Latino	13 (4.9%)	4 (4.3%)	17 (4.7%)	
White	193 (72.3%)	73 (79.3%)	266 (74.1%)	
Other	5 (1.9%)	0 (0.0%)	5 (1.4%)	
Unspecified	0 (0.0%)	1 (1.1%)	1 (0.3%)	
Marital Status				
Divorced	31 (11.6%)	6 (6.5%)	37 (10.3%)	0.018
Married	127 (47.6%)	43 (46.7%)	170 (47.4%)	
Single	89 (33.3%)	25 (27.2%)	114 (31.8%)	
Widow/widower	19 (7.1%)	17 (18.5%)	36 (10.0%)	
Unspecified	1 (0.4%)	1 (1.1%)	2 (0.6%)	

Table 2 Continued

	No Combined Endpoint (n=267)	With Combined Endpoint (n=92)	Total (n=359)	p-value
Health insurance				< 0.001
Medicaid	12 (4.5%)	7 (7.6%)	19 (5.3%)	
Medicare	83 (31.1%)	48 (52.2%)	131 (36.5%)	
Other	172 (64.4%)	37 (40.2%)	209 (58.2%)	
Clinical Data				
Charlson Comorbidity Index	3 (2, 5)	5 (3, 6)	4 (2, 5)	< 0.001
Heart failure	15 (5.6%)	23 (25.0%)	38 (10.6%)	< 0.001
Peripheral arterial disease	8 (3.0%)	14 (15.2%)	22 (6.1%)	< 0.001
Myocardial infarction	9 (3.4%)	1 (1.1%)	10 (2.8%)	0.251
Cerebrovascular disease	6 (2.2%)	2 (2.2%)	8 (2.2%)	0.967
Dementia	2 (0.7%)	2 (2.2%)	4 (1.1%)	0.262
Chronic obstructive pulmonary disease	44 (16.5%)	21 (22.8%)	65 (18.1%)	0.173
Rheumatic disease	16 (6.0%)	1 (1.1%)	17 (4.7%)	0.056
Peptic ulcer	1 (0.4%)	2 (2.2%)	3 (0.8%)	0.102
Mild Liver Disease	13 (4.9%)	12 (13.0%)	25 (7.0%)	0.008
Uncomplicated diabetes	30 (11.2%)	15 (16.3%)	45 (12.5%)	0.205
Diabetes with complications	5 (1.9%)	3 (3.3%)	8 (2.2%)	0.437
Paraplegia	2 (0.7%)	1 (1.1%)	3 (0.8%)	0.759
Renal disease	18 (6.7%)	16 (17.4%)	34 (9.5%)	0.003
Cancer	18 (6.7%)	4 (4.3%)	22 (6.1%)	0.409
Severe Liver Disease	4 (1.5%)	4 (4.3%)	8 (2.2%)	0.110
Solid Metastatic Neoplasms	12 (4.5%)	4 (4.3%)	16 (4.5%)	0.953
HIV/AIDS	2 (0.7%)	0 (0.0%)	2 (0.6%)	0.405
Vital Signs on Admission				
Temperature (°F)	36.7 (36.6, 36.9)	36.7 (36.6, 37)	36.7 (36.6, 36.9)	0.874
Heart rate (bpm)	80 (72, 89)	87 (74, 94.3)	81 (73.5, 91)	0.002
Respiratory rate (bpm)	17 (16, 18)	16.5 (16, 18)	17 (16, 18)	0.913
Oxygen saturation (%)	98 (96, 99)	97 (96, 99)	98 (96, 99)	0.079
SBP (mmHg)	130 (117, 146.5)	128 (112, 149)	130 (116.5, 147)	0.753
DBP (mmHg)	77 (67, 87)	70.5 (62, 81.3)	76 (66, 86)	0.019
Laboratory Data on Admission				
Hemoglobin (g/dl)	11.2 (9.9, 12.6)	9.6 (8.5, 10.7)	10.8 (9.4, 12.1)	< 0.001
Leukocytes (/ml)	6.9 (5.4, 8.9)	8.1 (5.9, 10.1)	7.1 (5.5, 9.4)	0.004
Mean Corpuscular Hemoglobin (pg)	29.8 (28.4, 31.3)	29.8 (28.5, 31.4)	29.8 (28.4, 31.3)	0.873
Mean Corpuscular Hemoglobin Concentration (g/dl)	33.1 (32.2, 33.9)	32.5 (31.7, 33.5)	32.9 (32, 33.9)	0.004
Medium corpuscular volume (fl)	89 (87, 94)	91 (87, 96.250)	90 (87, 94)	0.039
Platelets (/µl)	253 (203, 327.5)	254 (199.3, 346.3)	253 (202, 331)	0.824
Red Blood Cell Count (/µl)	3.8 (3.4, 4.2)	3.3 (2.9, 3.6)	3.6 (3.2, 4.1)	< 0.001
Red Cell Distribution Width (%)	13.8 (13, 14.8)	15 (13.8, 16.5)	14 (13.1, 15.2)	< 0.001
Serum Creatinine (mg/dl)	0.6 (0.5, 0.8)	0.6 (0.5, 0.8)	0.6 (0.5, 0.8)	0.120
INR	1.1 (1.1, 1.2)	1.2 (1.1, 1.325)	1.1 (1.1, 1.2)	0.104
PT (sec)	12.7 (11.8, 13.8)	13.2 (11.975, 15.225)	12.9 (11.8, 14)	0.033
PTT (sec)	29.6 (26.6, 34.2)	31.4 (28.2, 36.4)	30 (26.9, 34.5)	0.053

Source: Authors.

(PAD) variable, since the bivariate model with this variable presented the highest predictive power (15.98; 95% CI 5.21-48.99; p<.001; AUC 0.602). The sequence of adding variables to the model was carried out following the process described in the methodology section. As a result, six factors were the best predictors of these outcomes in the multivariate analysis: age, three laboratory parameters measured on admission (hemoglobin (Hb) level, leukocyte count, and INR), history of congestive heart failure (CHF) and PAD (Table 3).

Of these factors, PAD diagnosis had the greatest association with the risk of bowel resection, ICU admission, and mortality compared with patients without this condition (OR 10.23; 95% CI 3.03-34.47; p<.001). Second, anemia with Hb levels ≤11.3 was associated with a more than three-fold increased risk of these outcomes (OR 3.46; 95% CI 1.89-6.31; p<.001). For its part, a history of CHF was associated with more than double the risk (OR 2.28; 95% CI 1.01-5.15; p=.047). Finally, a white blood cell count > 9000/mL, INR > 1.2, and age greater than 70 years were associated with an increased risk of adverse outcomes in this setting by 83%, 76%, and 72%, respectively (Table 3). Although age did not have a statistically significant p-value, it was included in the multivariate model because its addition to the model significantly increased its discriminative capacity (AUC of the model without age = 0.739 vs. AUC of the model with age = 0.750; p<0.001) (Figure 2A). Finally, the result of the Hosmer-Lemeshow test did not suggest an inadequate adjustment of the model to the evaluated population (p=0.965). It is worth noting that these last measures of discrimination and calibration of the model (AUC and the Hosmer-Lemeshow test) are taken from their application in the validation cohort.

As a sensitivity analysis, we evaluated the performance of the multivariate model for the prediction of individual outcomes, observing an acceptable predictive capacity for the outcome of intestinal resection (AUC 0.679) (Figure 2B), outstanding for the prediction of ICU admission (AUC= 0.783) (Figure 2C), and excellent for the outcome of in-hospital mortality (AUC = 0.856) (Figure 2D).

Simplified score

Once the factors independently associated with the composite outcome were identified, these variables were used in the model to generate a clinically applicable risk scale. As described in the methods section, an individual score was assigned to each of the levels of the variables included in the final multivariate model based on the measure of the effect of association with the composite outcome. A score of 1 was assigned to age > 70 years, diagnosis of CHF, admission Hb level ≤ 11.3 g/dl, leukocyte count > 9000/ml, and INR value > 1.2. On the other hand, a score of 2 was assigned to the diagnosis of PAD. Therefore, a patient can have a score on the HALVIC scale from 0 to 7 (Table 3).

As a result, the median score for this scale in the design cohort was 2 points (Q1: 1 point, Q3: 2 points, range 0-7 points). A significant association was observed between the scale value and the composite outcome, with a significantly higher risk as the score increased (OR 2.23; 95% CI 1.79-2.79; p<0.001) (Figure 3). From this, three risk groups were identified: those patients with a HALVIC score ≤ 2 points (low risk: CO incidence

Table 3. Multivariate analysis of the factors associated with the composite outcome in the design cohort.

Variable	OR and 95% CI (Univariate)	OR and 95% CI (Multivariate)	Assigned score
Age (>70 vs ≤70)	2.82 (1.71-4.63; p<.001)	1.72 (0.97-3.05; p=.061)	1
Heart failure	4.39 (2.18-8.85; p<.001)	2.28 (1.01-5.15, p=.047)	1
Peripheral arterial disease	15.98 (5.21-48.99; p<.001)	10.23 (3.03-34.47; p<.001)	2
Hemoglobin (≤11.3 vs >11.3 g/dl)	3.63 (2.09-6.31; p<.001)	3.46 (1.89-6.31; p<.001)	1
Leukocytes (>9000 vs ≤9000/ml)	2.42 (1.44-4.07; p<.001)	1.83 (1.01-3.32; p=.048)	1
INR (>1.2 vs. ≤1.2)	1.71 (1.05-2.79; p=.031)	1.76 (1.02-3.05; p=.043)	1

Source: Authors.

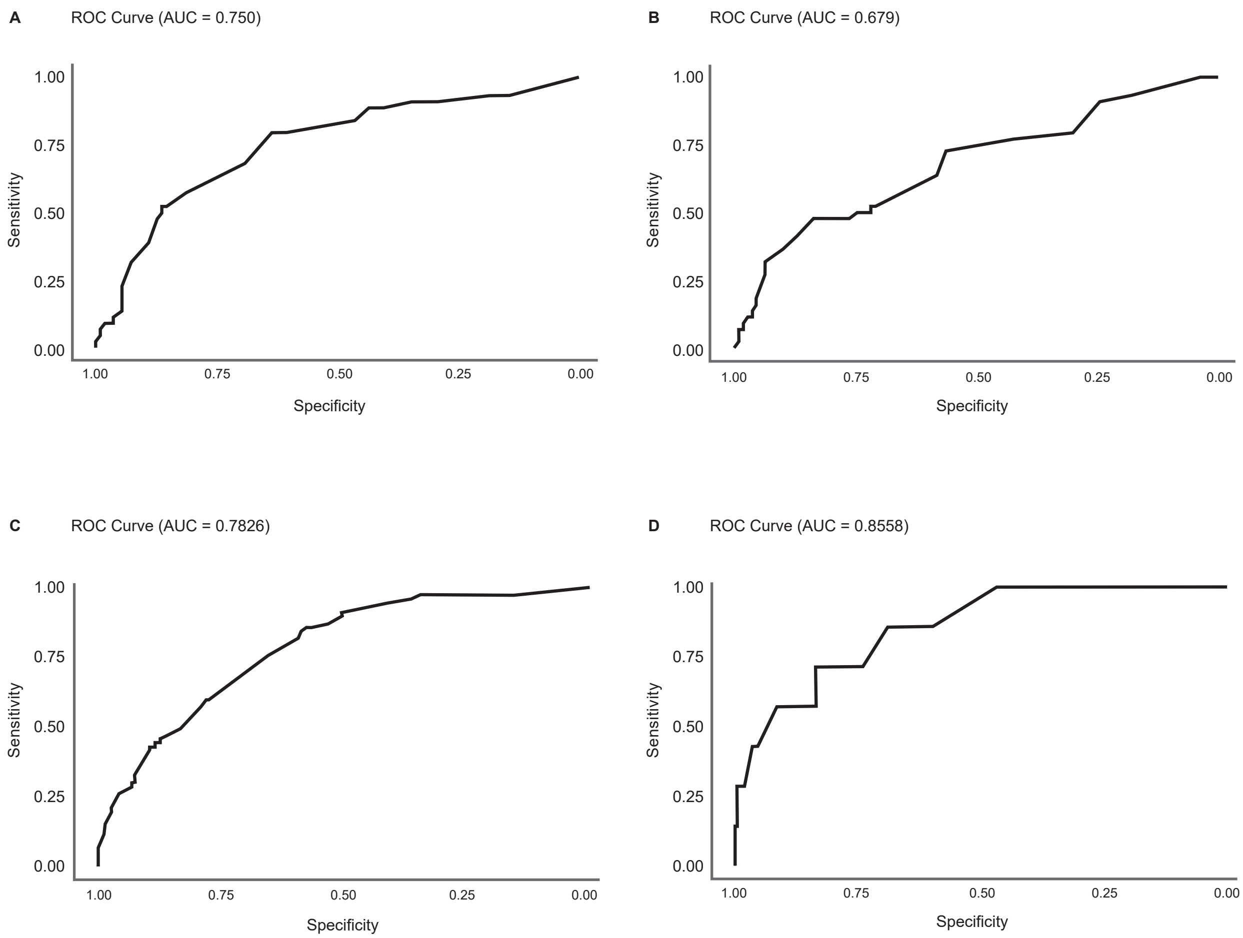

Figure 2. ROC curves and their respective areas under the curve (AUC) summarizing the discriminative capacity of the multivariate model to predict the following outcomes: A) Composite Outcome (CO); B) Intestinal resection; C) ICU admission; D) Mortality. Source: Authors.

= 16.2%), score 3-4 points (intermediate risk: DC incidence = 41.7%) and score ≥ 5 (high risk: DC incidence = 87.5%) (Table 4, Figure 4).

Validation of the scale

Finally, these results were validated in the validation cohort, whose median score on this scale was 2 points (Q1: 1 point, Q3: 3 points, range: 0-6 points). The significant association between the value of the scale and the composite outcome was confirmed (OR 2.06; 95% CI 1.47-2.89; $p<0.001$). In a similar way, the three risk groups were characterized: those patients with a HALVIC score ≤ 2 points (low risk: CO incidence = 17.2%), score of 3-4 points (intermediate risk: DC incidence = 48.9%) and score ≥ 5 (high risk: DC incidence = 72.8%).

Discussion

In this study, the HALVIC score for predicting the risk of adverse outcomes in patients with intestinal obstruction SBO was designed and validated. This score is In this study, the HALVIC scale for predicting the risk of adverse outcomes in patients with intestinal obstruction SBO was designed and validated, which is composed of six easily evaluable variables (age, heart failure, peripheral arterial disease, hemoglobin level, leukocyte count, and INR). We highlight that the performance of the scale for the prediction of the composite outcome of intestinal resection, admission to the intensive care unit, and mortality was outstanding, being less precise for the individual outcome of intestinal resection and more precise for the mortality outcome. Therefore, it is necessary to analyze the potential pathophysiological mechanisms that may explain the relationship between the variables that make up the HALVIC scale and the progression of SBO. Additionally, the performance of this scale will be compared with other similar tools published in the literature.

Regarding age, it has been reported that intestinal obstruction is a relatively frequent diagnosis in people over 65 years of age, representing approximately 10-12% of diagnoses in patients of this age group who attend the emergency de-

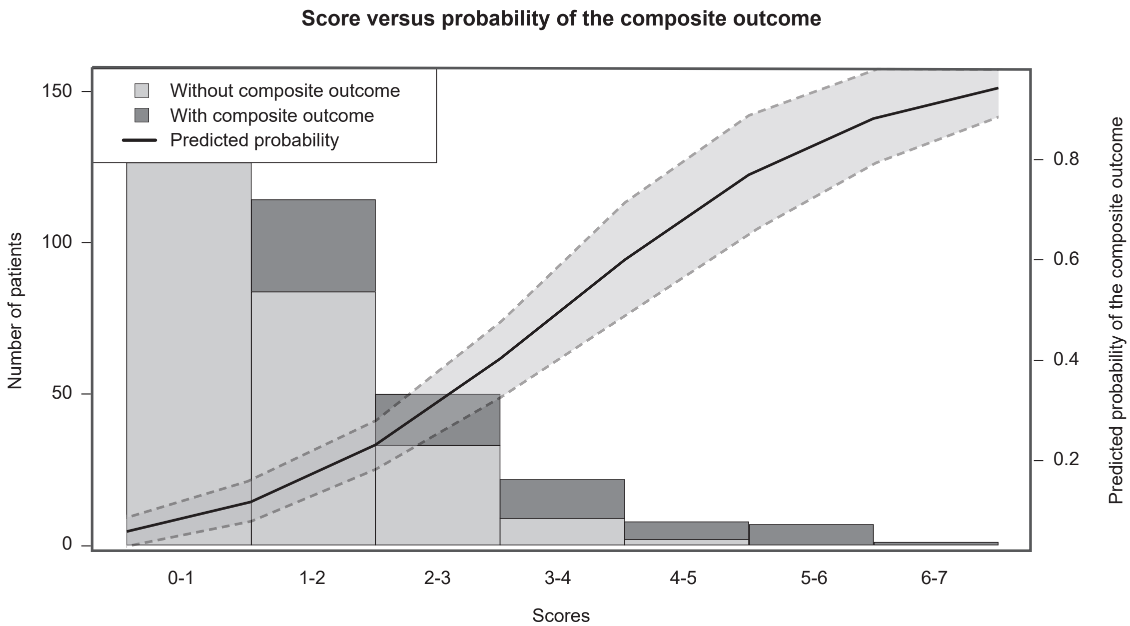

Figure 3. Probability of the composite outcome according to the HALVIC score in patients with a diagnosis of ASBO. Source: Authors.

Table 4. Detailed report of sensitivity and specificity of the score in the validation cohort.

Cutoff point	Sensitivity	Specificity	Correctly classified	Likelihood ratio (+)	Likelihood ratio (-)
(> 0)	100.00%	0.00%	25.73%	1.0000	
(> 1)	94.70%	17.06%	37.04%	1.1418	0.3108
(> 2)	84.85%	51.71%	60.23%	3.0726	0.2930
(> 3)	50.00%	83.73%	75.05%	6.3139	0.5972
(> 4)	26.52%	95.80%	77.97%	12.9886	0.7671
(> 5)	13.64%	98.95%	77.00%		0.8728
(> 6)	6.82%	100.00%	76.02%		0.9318
(> 7)	0.76%	100.00%	74.46%		0.9924
(> 7)	0.00%	100.00%	74.27%		1.0000

Source: Authors.

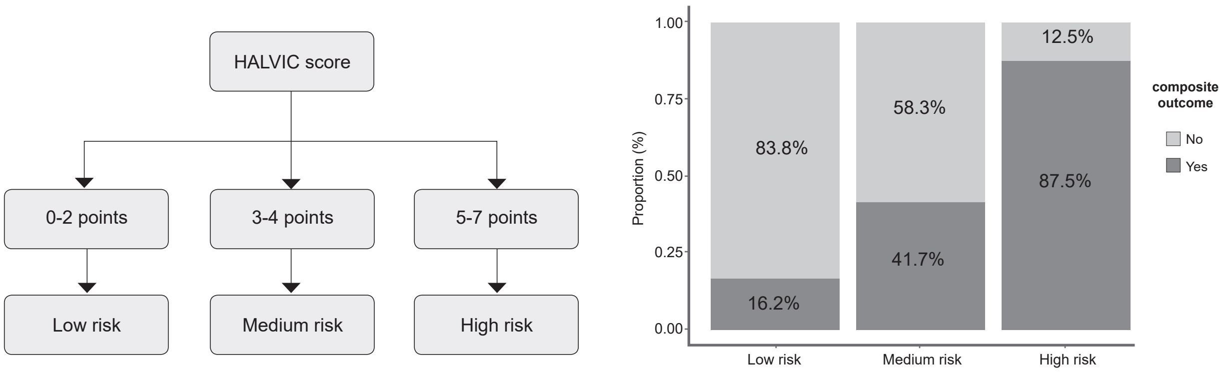

Figure 4. Descriptive diagrams summarizing the risk classification of the composite outcome according to the HALVIC score (left) and the proportion of patients with the composite outcome in each of the risk groups (right). Source: Authors.

partment [19]. Consistent with our study, advanced age has been pointed out in the literature as a predictor of major complications and mortality [20]. However, so far there is no clear association between advanced age and the risk of bowel resection [21]. Among the main approaches that support the findings of our study, it is proposed that the decrease in physiological reserve and frailty, both associated with the presence of comorbidities in this age group, are the main factors that could explain the torpid clinical evolution of this population in the emergency context [20]. Additionally, it has been proposed that elderly patients present an atypical clinical picture characterized by less intensity of pain, lower basal temperatures, and mild changes in the leukocyte response. These changes can lead to late consultation and delay in diagnosis, limiting timely medical and/or surgical management [19,22,23].

On the other hand, anemia as an independent risk factor for worse clinical and surgical outcomes has already been suggested in the area of gastrointestinal Surgery [24,25]. Specifically, a recent case-control study that evaluated the utility of the nasoenteral tube in intestinal obstruction suggests that anemia is a risk factor for failure in medical management because the drop in hemoglobin level could be an indicator of tissue hypoxia, and secondary intestinal ischemia [26]. The mechanism underlying this association corresponds to the lower oxygen supply to the tissue that is subjected to mechanical compression by adhesions in the anemic patient, which exposes them to a greater risk of ischemia in this condition [27]. For its part, the association between a higher leukocyte count and the risk of adverse outcomes is more complex, having a potential multifactorial origin. In principle, mechanical stress on the intestinal wall has been associated with an increase in the production of proinflammatory markers such as interleukin-6 and monocyte chemoattractant protein 1 at the level of the segment proximal to the obstruction [28]. In addition, tissue hypoperfusion, present in more advanced stages of the disease, causes an increase in oxygen free radicals, which in turn promotes the permeability of the intestinal mucosa. As a consequence, a translocation of both bacterial and inflammatory components is generated, which translates into greater recruitment and circulation of leukocytes [29].

This proinflammatory state can also favor the development of a coagulopathy process, which can vary from subclinical activation of the coagulation cascade to advanced conditions of disseminated intravascular coagulation [30,31]. Similarly, in addition to the activation of the immune system, the cell damage present in intestinal ischemia promotes the release of DNA and nuclear proteins, also with procoagulant effects. However, perpetuation of these conditions promotes dysregulation of the coagulation cascade through aberrant expression of tissue factor by monocytes/macrophages and endothelial dysfunction that can result in prolongation of the INR [32–35]. Therefore, elevated values of this parameter have been identified as early markers of severe compromise and adverse outcomes in patients with sepsis [36–38].

In particular, PAD was the single variable most strongly associated with the composite outcome in the present study. Currently, more than 200 million people are estimated to have this pathology worldwide, with only 10-30% of these cases having typical symptoms of intermittent claudication, while 20-50% of the cases are asymptomatic [39]. It is necessary to understand PAD as a systemic disease, characterized by the loss of elasticity of the arterial walls and secondary luminal narrowing that conditions a reduced oxygen supply in the different tissues, which also include those irrigated by the splanchnic circulation. Despite the compensatory processes of neovascularization, the tissue demand in stress situations ends up exceeding the supply of oxygen, forcing an anaerobic metabolism with acid metabolic products, which will affect intraerythrocytic ATP, decreasing the flexibility of its membrane and thus leading to an increase in blood viscosity and an increase in platelet aggregation, concluding in an even greater condition of the tissue oxygenation process [39,40] added to a permanent proinflammatory state of the affected vascular segment [41]. This combination of sub-optimal perfusion and baseline hypo-oxygenation could favor hypoperfusion and tissue ischemia secondary to mechanical stress in the SBO, exposing the patient with PAD to a greater risk of complications.

Lastly, the association between CHF and increased morbidity and mortality in patients undergoing non-cardiac surgery is well established [42]. In addition, previous studies conducted have shown a statistically significant relationship between CHF and the increased risk of postoperative complications in patients diagnosed with intestinal obstruction [13,43–45]. The mechanisms underlying this association are multiple, highlighting the changes at the intestinal level in the patient with CHF secondary to the chronic hypoperfusion characteristic of this entity. This results in the disproportionate growth of bacterial populations and mucosal edema, which can reduce its tolerance to ischemia under stress conditions [46–48].

Despite the importance of this phenomenon in terms of morbidity and mortality worldwide, the current literature on factors associated with adverse outcomes in intestinal obstruction due to adhesions is relatively scarce. However, there are two studies that have proposed prediction scales similar to the one described in the present study and that require mention in this section. Among these, the study by Hernández et al stands out, in which the prognostic value of the anatomical severity classification system of the American Association for the Surgery of Trauma (AAST) was evaluated in patients diagnosed with SBO [15]. This scale uses radiographic and intraoperative features to classify patients into five stages: I (partial SBO), II (complete SBO with bowel viability), III (complete SBO with compromised bowel viability), IV (SBO with evidence of non-viable intestine or perforation with localized contamination), and V (SBO with intestinal perforation and diffuse peritoneal contamination). The authors of this study noted that as the severity of the scale increased, there was an increased risk of the need for conversion from laparoscopic to open surgery, bowel resection, open abdomen, and stoma creation, in addition to a longer length of in-hospital stay and need for ICU admission. Finally, the model composed of the AAST scale presented an outstanding discriminative capacity to predict the development of any postoperative complication (AUC 0.76) [15]. Similarly, the study by Morris et al evaluated the prognostic performance of the so-called "bowel ischemia score" (BIS) in patients diagnosed with SBO. This scale was based on the tomographic findings suggested by the Eastern Association for the Surgery of Trauma (EAST) guidelines for SBO, assigning one point for each of these findings [14]. The authors noted that the BIS score was an excellent predictor of early surgery (AUC 0.812), an outstanding predictor of need for any surgery (AUC 0.705), and a fair predictor of bowel resection outcome (AUC 0.614) [14].

Therefore, we can conclude that, in the absence of information on imaging characteristics, the HALVIC score performance was comparable to the AAST scale for the prediction of any adverse outcome and superior to the BIS for the prediction of bowel resection. This represents a relevant advantage, since the aforementioned scales depend on the availability of a tomographic image, which may not be available to the physician in all contexts, especially in developing countries. Furthermore, the tomographic findings reflect the presence of an incipient or already established ischemia process, but they do not allow us to identify the patient who at the time of the evaluation does not present signs of intestinal compromise but who will develop this process in the short term. Additionally, the AAST scale also depends on intraoperative criteria, which significantly limits its use as a prognostic tool to define therapeutic behavior in the patient with ASOB at the time of hospital admission. Finally, we highlight the possibility of improving the performance of HALVIC by including tomographic data, which makes it necessary to carry out future studies integrating the information on laboratory variables used in this scale with the relevant imaging findings.

Strengths and limitations of the study

Among the strengths of our study, the sample size evaluated stands out, which is superior to a good part of the published studies evaluating factors associated with adverse outcomes in ASBO. On the other hand, the availability of detailed physiological information made it possible to evaluate variables usually excluded from analyzes in this area, such as vital signs on admission and laboratory tests. Additionally, we highlight the completion of a validation of the scale using a standard statistical approach, which allows the reproducibility of the study.

However, it is important to mention some relevant limitations of this study. Firstly, the absence of imaging information limited the possibility of developing a comprehensive model/scale, given the great importance of tomographic findings for the comprehensive assessment of the patient with SBO. Therefore, additional studies are required to evaluate the benefit of integrating the predictive sociodemographic and clinical variables described in the HALVIC scale with imaging findings suggestive of intestinal loop compromise requiring surgical intervention, which will possibly allow more precise tools to be available for the prediction of adverse outcomes and early decision making in these patients. Cambiar por: Despite this limitation, we also want to highlight the adequate performance of our scale, which, in the absence of a comprehensive tool, makes it relevant for the surgeon even in its current state.

In addition, information related to the duration of obstructive symptoms is not disclosed, which is directly related to the degree of compromise at the time of hospital admission. On the other hand, due to the lack of information on the time from admission to surgical intervention in the patients who underwent surgery, it was not possible to adjust the variables evaluated for this highly relevant factor. Finally, despite the sample size being relatively large, the number of patients with HALVIC scores of 6 and 7 points was low, which limited the evaluation of the model in these patients. Despite this, the very high proportion of patients with elevated HALVIC scores who had any of the outcomes strongly suggests an increased risk in these individuals.

Conclusions

The HALVIC score is presented as a simple and easily applicable prediction tool in the clinical context, which can accurately identify patients with ASOB at high risk of complications using widely available clinical and laboratory data. The identification of patients at high risk of adverse outcomes has the potential to promote individualized adjustment of management strategies, potentially improving their outcomes. Finally, the need to validate the findings of this study in other populations and include additional imaging parameters and other important clinical data to improve its performance is highlighted.

Compliance with ethical standards

Ethical considerations: This study was developed from an analysis of de-identified data from MIMIC IV, for which reason it was exempt from approval by an ethics committee. The authors who developed the analysis performed the CITI Data of Specimens Only Research of the National Institutes of Health, receiving the necessary certification and credentials for the access and use of the MIMIC-IV data.

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Author's contributions

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- Data analysis and interpretation: Andrea Carolina Quiroga-Centeno y Sergio Alejandro Gómez-Ochoa.
- Writing the manuscript: Andrea Carolina Quiroga-Centeno, Katherine Hoyos-Rizo, Diego Fernando Chaparro-Zaraza, Pedro Felipe Pinilla-Merchán, María Camila Pinilla-Chávez, Juan Paulo Serrano-Pastrana, Sergio Alejandro Gómez-Ochoa.
- Critical review: Andrea Carolina Quiroga-Centeno, Katherine Hoyos-Rizo, Diego Fernando Chaparro-Zaraza, Pedro Felipe Pinilla-Merchán, María Camila Pinilla-Chávez, Juan Paulo Serrano-Pastrana, Sergio Alejandro Gómez-Ochoa.

References

1 Maung AA, Johnson DC, Piper GL, Barbosa RR, Rowell SE, Bokhari F, et al. Evaluation and management of small-bowel obstruction: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg. 2012;73(5 Suppl. 4):S362-9. https://doi.org/10.1097/TA.0b013e31827019de

2 Vercruysse G, Busch R, Dimcheff D, Al-Hawary M, Saad R, Seagull FJ, et al. Evaluation and management of mechanical small bowel obstruction in adults. Ann Arbor (MI): Michigan Medicine University of Michigan. 2021. Fecha de consulta: 10 de septiembre de 2022. Disponible en: http://www.ncbi.nlm.nih.gov/books/NBK572336/.

3 Behman R, Nathens AB, Haas B, Look-Hong N, Pechlivanoglou P, Karanicolas P. Surgery for adhesive small-bowel obstruction is associated with improved long-term survival mediated through recurrence prevention: A population-based, propensity-matched analysis. J Trauma Acute Care Surg. 2019;87:636-44. https://doi.org/10.1097/TA.0000000000002366

4 Ten Broek RPG, Krielen P, Di Saverio S, Coccolini F, Biffl WL, Ansaloni L, et al. Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2017 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg. 2018;13:24. https://doi.org/10.1186/s13017-018-0185-2

5 Catena F, De Simone B, Coccolini F, Di Saverio S, Sartelli M, Ansaloni L. Bowel obstruction: a narrative review for all physicians. World J Emerg Surg. 2019;14:20. https://doi.org/10.1186/s13017-019-0240-7

6 Tong JWV, Lingam P, Shelat VG. Adhesive small bowel obstruction - an update. Acute Med Surg. 2020;7:e587. https://doi.org/10.1002/ams2.587

7 Aquina CT, Fleming FJ. Who should manage patients with adhesive small bowel obstruction? Adv Surg. 2017;51:125-40. https://doi.org/10.1016/j.yasu.2017.03.010

8 Tanaka S, Yamamoto T, Kubota D, Matsuyama M, Uenishi T, Kubo S, Ono K. Predictive factors for surgical indication in adhesive small bowel obstruction. Am J Surg. 2008;196:23-7. https://doi.org/10.1016/j.amjsurg.2007.05.048

9 Karamanos E, Dulchavsky S, Beale E, Inaba K, Demetriades D. Diabetes mellitus in patients presenting with adhesive small bowel obstruction: Delaying surgical intervention results in worse outcomes. World J Surg. 2016;40:863-9. https://doi.org/10.1007/s00268-015-3338-4

10 Bower KL, Lollar DI, Williams SL, Adkins FC, Luyimbazi DT, Bower CE. Small bowel obstruction. Surg Clin North Am. 2018;98:945-71. https://doi.org/10.1016/j.suc.2018.05.007

11 Musiienko AM, Shakerian R, Gorelik A, Thomson BNJ, Skandarajah AR. Impact of introduction of an acute surgical unit on management and outcomes of small bowel obstruction. ANZ J Surg. 2016;86:831-5. https://doi.org/10.1111/ans.13238

12 Mu JF, Wang Q, Wang SD, Wang C, Song JX, Jiang J, Cao XY. Clinical factors associated with intestinal strangulating obstruction and recurrence in adhesive small bowel obstruction: A retrospective study of 288 cases. Medicine (Baltimore). 2018;97:e12011. https://doi.org/10.1097/MD.0000000000012011

13 Asuzu D, Pei KY, Davis KA. A simple predictor of post-operative complications after open surgical

adhesiolysis for small bowel obstruction. Am J Surg. 2018;216:67-72. https://doi.org/10.1016/j.amjsurg.2018.02.031

14 Morris RS, Murphy P, Boyle K, Somberg L, Webb T, Milia D, et al. Bowel ischemia score predicts early operation in patients with adhesive small bowel obstruction. Am Surg. 2022;88:205-11. https://doi.org/10.1177/0003134820988820

15 Hernandez MC, Haddad NN, Cullinane DC, Yeh DD, Wydo S, Inaba K, et al. The American Association for the Surgery of Trauma Severity Grade is valid and generalizable in adhesive small bowel obstruction. J Trauma Acute Care Surg. 2018;84:372-8. https://doi.org/10.1097/ta.0000000000001736

16 Zielinski MD, Eiken PW, Heller SF, Lohse CM, Huebner M, Sarr MG, Bannon MP. Prospective, observational validation of a multivariate small-bowel obstruction model to predict the need for operative intervention. J Am Coll Surg. 2011;212:1068-76. https://doi.org/10.1016/j.jamcollsurg.2011.02.023

17 Deng Y, Wang Y, Guo C. Prediction of surgical management for operated adhesive postoperative small bowel obstruction in a pediatric population. Medicine (Baltimore). 2019;98:e14919. https://doi.org/10.1097/MD.0000000000014919

18 Sullivan LM, Massaro JM, D'Agostino RB. Presentation of multivariate data for clinical use: The Framingham Study risk score functions. Stat Med. 2004;23:1631-60. https://doi.org/10.1002/sim.1742

19 Ozturk E, van Iersel M, Stommel MM, Schoon Y, Ten Broek RR, van Goor H. Small bowel obstruction in the elderly: a plea for comprehensive acute geriatric care. World J Emerg Surg. 2018;13:48. https://doi.org/10.1186/s13017-018-0208-z

20 Quero G, Covino M, Laterza V, Fiorillo C, Rosa F, Menghi R, et al. Adhesive small bowel obstruction in elderly patients: a single-center analysis of treatment strategies and clinical outcomes. Scand J Gastroenterol. 2021;56:784-90. https://doi.org/10.1080/00365521.2021.1921256

21 Krause WR, Webb TP. Geriatric small bowel obstruction: an analysis of treatment and outcomes compared with a younger cohort. Am J Surg. 2015;209:347-51. https://doi.org/10.1016/j.amjsurg.2014.04.008

22 Liang SY. Sepsis and other infectious disease emergencies in the elderly. Emerg Med Clin North Am. 2016;34:501-22. https://doi.org/10.1016/j.emc.2016.04.005

23 Springer JE, Bailey JG, Davis PJB, Johnson PM. Management and outcomes of small bowel obstruction in older adult patients: a prospective cohort study. Can J Surg. 2014;57:379-84. https://doi.org/10.1503/cjs.029513

24 Sincavage J, Robinson B, Msosa VJ, Katete C, Purcell LN, Charles A. Preoperative anemia and surgical outcomes following laparotomy in a resource-limited setting. Am J Surg. 2021;222:424-30. https://doi.org/10.1016/j.amjsurg.2020.12.032

25 Michailidou M, Nfonsam VN. Preoperative anemia and outcomes in patients undergoing surgery for inflammatory bowel disease. Am J Surg. 2018;215:78-81. https://doi.org/10.1016/j.amjsurg.2017.02.016

26 Wang H, Zhang JR, Chen S, Hou P, Chen QF, Weng ZQ, et al. Who would avoid severe adverse events from nasointestinal tube in small bowel obstruction? A matched case-control study. BMC Gastroenterol. 2022;22:332. https://doi.org/10.1186/s12876-022-02405-8

27 Kärkkäinen JM. Acute mesenteric ischemia: A challenge for the acute care surgeon. Scand J Surg. 2021;110:150-8. https://doi.org/10.1177/14574969211007590

28 Lin YM, Li F, Shi XZ. Mechanical stress is a pro-inflammatory stimulus in the gut: in vitro, in vivo and ex vivo evidence. PLoS One. 2014;9:e106242. https://doi.org/10.1371/journal.pone.0106242

29 Vaishnavi C. Translocation of gut flora and its role in sepsis. Indian J Med Microbiol. 2013;31:334-42. https://doi.org/10.4103/0255-0857.118870

30 Lipinska-Gediga M. Coagulopathy in sepsis - a new look at an old problem. Anaesthesiol Intensive Ther. 2016;48:352-9. https://doi.org/10.5603/AIT.a2016.0051

31 Semeraro N, Ammollo CT, Semeraro F, Colucci M. Coagulopathy of acute sepsis. Semin Thromb Hemost. 2015;41:650-8. https://doi.org/10.1055/s-0035-1556730

32 Iba T, Levy JH. Sepsis-induced coagulopathy and disseminated intravascular coagulation. Anesthesiology. 2020;132:1238-45. https://doi.org/10.1097/ALN.0000000000003122

33 Dorgalaleh A, Daneshi M, Rashidpanah J, Yasaghi ER. An overview of hemostasis. En: Dorgalaleh A, ed. Congenital bleeding disorders. Diagnosis and management. Cham: Springer International Publishing; 2018. p. 3-26.

34 Levi M, Schultz MJ. What do sepsis-induced coagulation test result abnormalities mean to intensivists? Intensive Care Med. 2017;43:581-3. https://doi.org/10.1007/s00134-017-4725-0

35 Lyons PG, Micek ST, Hampton N, Kollef MH. Sepsis-associated coagulopathy severity predicts hospital mortality. Crit Care Med. 2018;46:736-42. https://doi.org/10.1097/CCM.0000000000002997

36 Zhang J, Du HM, Cheng MX, He FM, Niu BL. Role of international normalized ratio in nonpulmonary sepsis screening: An observational study. World J Clin Cases. 2021;9:7405-16. https://doi.org/10.12998/wjcc.v9.i25.7405

37 Winer LK, Salyer C, Beckmann N, Caldwell CC, Nomellini V. Enigmatic role of coagulopathy among sepsis survivors: a review of coagulation abnormalities and their possible link to chronic critical illness. Trauma Surg Acute Care Open. 2020;5:e000462. https://doi.org/10.1136/tsaco-2020-000462

38 Liu J, Bai C, Li B, Shan A, Shi F, Yao C, et al. Mortality prediction using a novel combination of biomarkers in the first day of sepsis in intensive care units. Sci Rep. 2021;11:1275. https://doi.org/10.1038/s41598-020-79843-5

39 Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. Circ Res. 2015;116:1509-26. https://doi.org/10.1161/CIRCRESAHA.116.303849

40 Emma LA. Chronic arterial occlusive disease. J Cardiovasc Nurs. 1992;7:14-24. https://doi.org/10.1097/00005082-199210000-00004

41 Moore KJ, Sheedy FJ, Fisher EA. Macrophages in atherosclerosis: a dynamic balance. Nat Rev Immunol. 2013;13:709-21. https://doi.org/10.1038/nri3520

42 Smilowitz NR, Banco D, Katz SD, Beckman JA, Berger JS. Association between heart failure and perioperative outcomes in patients undergoing non-cardiac surgery. Eur Heart J Qual Care Clin Outcomes. 2021;7:68-75. https://doi.org/10.1093/ehjqcco/qcz066

43 Margenthaler JA, Longo WE, Virgo KS, Johnson FE, Grossmann EM, Schifftner TL, et al. Risk factors for adverse outcomes following surgery for small bowel obstruction. Ann Surg. 2006;243:456-64. https://doi.org/10.1097/01.sla.0000205668.58519.76

44 Sharma R, Reddy S, Thoman D, Grotts J, Ferrigno L. Laparoscopic versus open bowel resection in emergency small bowel obstruction: Analysis of the National Surgical Quality Improvement Program Database. J Laparoendosc Adv Surg Tech A. 2015;25:625-30. https://doi.org/10.1089/lap.2014.0446

45 Chang E, Chung PJ, Smith MC, Lee MJ, Gross DJ, Kao E, Sugiyama G. Can the laparoscopic approach for adhesive small bowel obstruction be used in octogenarians? An observational study using ACS NSQIP. J Surg Res. 2019;233:345-50. https://doi.org/10.1016/j.jss.2018.07.064

46 Sandek A, Bauditz J, Swidsinski A, Buhner S, Weber-Eibel J, von Haehling S, et al. Altered intestinal function in patients with chronic heart failure. J Am Coll Cardiol. 2007;50:1561-9. https://doi.org/10.1016/j.jacc.2007.07.016

47 Romeiro FG, Okoshi K, Zornoff LAM, Okoshi MP. Gastrointestinal changes associated to heart failure. Arq Bras Cardiol. 2012;98:273-7. https://doi.org/10.1590/S0066-782X2012000300011

48 Sandek A, Swidsinski A, Schroedl W, Watson A, Valentova M, Herrmann R, et al. Intestinal blood flow in patients with chronic heart failure: A link with bacterial growth, gastrointestinal symptoms, and cachexia. J Am Coll Cardiol. 2014;64:1092-102. https://doi.org/10.1016/j.jacc.2014.06.1179