ORIGINAL ARTICLE

Shock Index and Age-Adjusted Shock Index as Predictors of Mortality in Decompensated Heart Failure

El índice de shock e índice de shock ajustado por edad como predictores de muerte en la insuficiencia cardíaca descompensada

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ABSTRACT

Background: Shock index (SI), calculated as the ratio of heart rate (HR) to systolic blood pressure (SBP) obtained on admission, and age-adjusted SI are tools that have already demonstrated prognostic value in some clinical contexts, but their prognostic value in decompensated heart failure (DHF) is unknown.
Objective: The aim of this study was to evaluate the prognostic ability of both indices for total in-hospital mortality in patients admitted to the coronary unit for DHF.
Methods: We conducted a retrospective study of consecutive patients admitted to 2 coronary care units between January 2010 and August 2020. Both indices and their respective predictive values were calculated. The cutoff point values with the best combination of sensitivity and specificity were defined using the ROC curve. Multivariate analysis was performed to identify independent predictors of in-hospital mortality.
Results: Population: 1472 patients. Median age was 81 years, 50 had left ventricular ejection fraction < 40% and 50% had a history of DHF. In-hospital mortality 6.2%. Youden's index identified SI ≥ 0.58 and age-adjusted SI ≥ 45.6 as predictors of mortality. On multivariate analysis including age, systolic blood pressure (SBP) < 115 mmHg, blood urea nitrogen (BUN) > 43 mg/dL, creatinine level > 2.75 mg/dL, Hemoglobin (Hb) < 10 g/dL and SI ≥ 0.58, only age, BUN > 43 mg/dL and anemia remained as independent predictors of in-hospital mortality. On multivariate analysis, when age-adjusted SI ≥ 45.6 was analyzed with the other variables (but not with age), the independent predictors were age-adjusted SI ≥ 45.6 (OR 2.41; 95% CI, 1.37-4.2; p < 0.01), BUN > 43 mg/dL and anemia.
Conclusion: A simple calculation as age-adjusted SI is highly useful to predict in-hospital mortality in patients hospitalized with DHF and provides additional information to the classic prognostic variables.

Key words: Heart Failure – Mortality - Prognosis

RESUMEN

Introducción: El índice de shock (IShock), calculado a partir de los valores al ingreso de la frecuencia cardíaca (FC) y tensión arterial sistólica (TAS) y el IShock ajustado por edad, son herramientas que han demostrado utilidad pronóstica en algunos contextos clínicos; sin embargo, su valor pronóstico en la insuficiencia cardíaca aguda descompensada (ICD) es desconocido. Objetivo: evaluar la capacidad pronóstica para mortalidad total intrahospitalaria de ambos índices en pacientes ingresados a unidad coronaria por ICD.
Material y métodos: Estudio retrospectivo de pacientes consecutivos ingresados en 2 unidades coronarias durante el periodo enero 2010/agosto 2020. Se calcularon ambos índices, se determinó su valor predictivo y mediante curva ROC se definieron los valores de corte con mejor combinación de sensibilidad y especificidad. Se efectuó análisis multivariado para encontrar los predictores independientes de mortalidad intrahospitalaria.
Resultados: Población: 1472 pacientes. Edad (mediana) 81 años, 50% con fracción de eyección ventricular izquierda <40%, y 50% con antecedentes de ICD previa. Mortalidad intrahospitalaria 6,2%. Un IShock ≥0,58 e IShock ajustado por edad ≥45,6 (definido por el índice de Youden) fueron predictores de mortalidad. En el análisis multivariado que incluyó edad, tensión arterial sistólica (TAS) <115 mmHg, nitrógeno ureico en sangre (BUN) >43 mg/dL, creatinina >2,75 mg/dL, hemoglobina <10 g/dL y el ISHock ≥0,58, solo mantuvieron su valor predictivo la edad, el BUN >43 mg/dL y la anemia. En un modelo multivariado donde se evaluó al IShock ajustado por edad ≥45,6 junto a las otras variables (excepto edad), éste fue predictor independiente (OR 2,41 IC95% 1,37-4,2 p <0,01) al igual que el BUN >43 mg/dL y la anemia.
Conclusión: Un cálculo sencillo como el IShock ajustado por edad es de gran utilidad en la predicción de la mortalidad hospi¬talaria de los pacientes internados con ICAD y agrega información adicional a las variables pronósticas clásicas.

Palabras clave: Insuficiencia cardiaca - Mortalidad – Pronóstico

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INTRODUCTION

Decompensated heart failure (DHF) is one of the most common causes of hospital admissions in the coronary care unit (especially in elderly patients) (1) and is associated with high risk of in-hospital mortality, between 4 and 12 %, depending on the populations analyzed. (2-4) The ability to predict which patients are most likely to die using parameters present when the patient is admitted to the institution is a clinical challenge.

Shock index (SI), calculated as the ratio of heart rate (HR) to systolic blood pressure (SBP) obtained on admission, is a tool that has already demonstrated prognostic usefulness in other contexts such as myocardial infarction, (5) severe sepsis, (6) pulmonary embolism. (7) hypovolemia and trauma, (8) even in patients admitted with normal BP and HR values. (9) Yet, the usefulness of SI in the setting of DHF is unknown. Furthermore, age-adjusted SI provides better prognostic information. (10)

The aim of the present study was to evaluate the prognostic ability of SI and age-adjusted SI for overall in-hospital mortality in patients admitted to the coronary unit for DHF.

METHODS

WE conducted a retrospective study of patients consecutively included in our heart failure database. On admission, HR and SBP were recorded. SI was calculated using the formula: HR/SBP and adjusted SI was estimated as SI × age. Both indices were analyzed using ROC curve and Youden's index to find the most sensitive and specific value to predict in-hospital mortality. The positive predictive value (PPV) and negative predictive value (NPV) were also calculated for both indices.

We analyzed the prognostic value of both indices for mortality in the total population and discriminated by ventricular function (preserved vs. reduced) and examined whether SI provided additional prognostic value to patients who were admitted with hypotension (with SBP <90 mm Hg) or tachycardia (HR > 100 beats/min). Patients with no records of SBP or HR on admission were excluded. In-hospital mortality was correlated with different values of SI and age adjusted-SI.

Univariate and multivariate logistic regression analyses were performed to identify independent predictors of in-hospital mortality.

Statistical analysis

Qualitative variables are presented as frequencies and percentages with their corresponding confidence intervals. Quantitative variables are expressed as mean ± standard deviation (SD), or median and interquartile range (IQR 25-75), according to their distribution.

Discrete variables were analyzed using the chi square test or Fisher's exact test, as applicable. For continuous variables, the t test or the Mann-Withney test were used, as applicable; and in case or 3 groups or greater, ANOVA or the Kruskall-Wallis test were used, as applicable. Univariate and multivariate logistic analyses were used to identify the independent predictors of in-hospital mortality. A p value < 0.05 was considered statistically significant.

Shock index and age-adjusted SI were analyzed using ROC curve and Youden's index to find the most sensitive and specific value to predict in-hospital mortality.

All the calculations were performed using Epi-Info 7.2.2.6 and IBM SPSS Statitics 23 software package.

RESULTS

A total of 1472 patients admitted to 2 coronary care units in the city of Buenos Aires due to DHF between January 2010 and August 2020 were included. Median age was 81 (IQR 25-75 73-87) years and 54% were men. Eighty percent had hypertension, 27% diabetes, 13% were smokers, 22% had chronic kidney failure, 9% had history of stroke, 22% of myocardial infarction and 50% of heart failure. Left ventricular ejection fraction was < 40% in 50% of the patients. The etiology of heart failure was ischemic heart disease in 26%, valvular heart disease in 20%, hypertension in 15%, idiopathic in 24.5% and other causes in 14.5%.

Inotropic requirement was observed in 12.2% of the patients and 5.5% required mechanical ventilation. Length of hospital stay was prolonged (> 7 days) in 35% of the patients and in-hospital mortality was 6.2%.

Median SI was 0.6 (IQR 25-75: 0.5-0.75) and median age-adjusted SI was 47 (IQR 25-75; 38.2-60). Figure 1 represents the relationship between the different values of the SI and age-adjusted SI and in-hospital mortality.

Figure 2 shows the ROC curves of both indices for in-hospital mortality. According to the Youden's index, a SI of 0.58 was the best value with a sensitivity of 70% and specificity of 46% (PPV of 8% and NPV of 96%), and age-adjusted SI of 45.6 was the best value with a sensitivity of 76% and specificity of 48%, PPV of 9% and NPV of 97%. Different cutoff point values were considered for the SI and age-adjusted SI to increase specificity. Table 1 describes the prevalence, sensitivity, specificity, NPV and PPV for each index. When the index value increases, specificity is higher, the PPV is slightly higher, and although sensitivity decreases, the NPV remains high (94-95%).

Different variables were considered on univariate analysis for in-hospital mortality (Table 2); in some of them (BUN, creatinine, hemoglobin, BP) the cutoff point values used in the ADHERE study were considered. (11) Age, chronic kidney failure, anemia, hypotension, SI ≥ 0.58 and age-adjusted SI ≥ 45.6 resulted independent predictors of mortality.

On multivariate analysis including age, SBP < 115 mm Hg, BUN > 43 mg/dL, creatinine level > 2.75 mg/dL, Hb < 10 g/dL and SI ≥ 0.58, only age (OR 1.02; 95% CI, 1.00-1.065; p < 0.01), BUN > 43 mg/dL (OR 2.36; 95% CI, 1.17-4.74; p<0.01) and anemia (OR 2.42; 95% CI 1.44-4.07; p < 0.001) remained as independent predictors of in-hospital mortality (Model 1. Table 3). But on multivariate analysis, when age-adjusted SI ≥ 45.6 was analyzed with the other variables (but not with age), the independent predictors were age-adjusted SI ≥ 45.6 (OR 2.41; 95% CI, 1.37-4.2; p < 0.01), BUN > 43 mg/dL (OR 2.46; 95% CI, 1.22-4.95; p < 0.01) and

Fig. 1. In-hospital mortality according to different range values of SI and age-adjusted SI

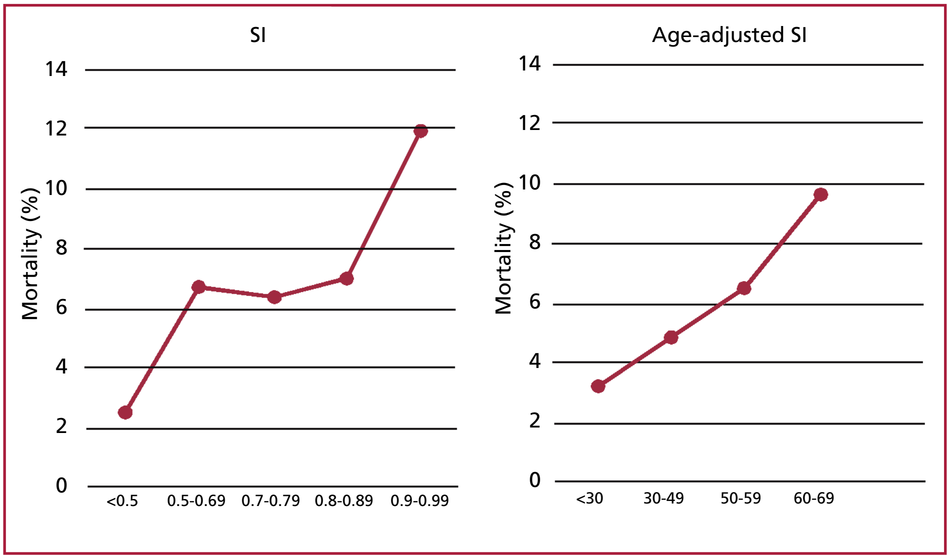
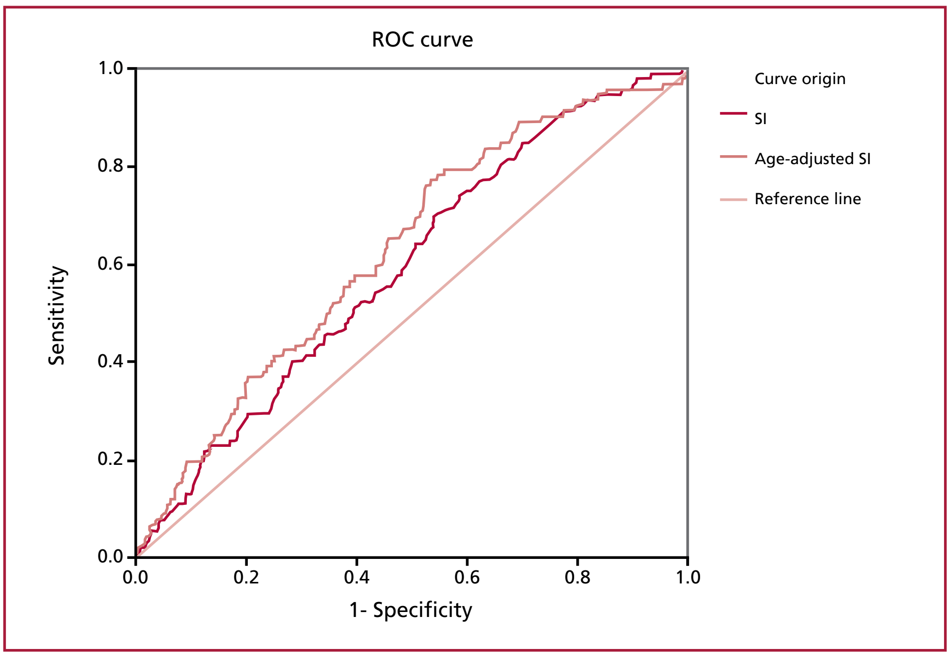


Fig. 2. ROC curve of SI and age-adjusted SI for in-hospital mortality



SI: Shock index

Area under the curve

Variables	Area	Standard error	p	95% CI	
				Lower limit	Upper limit
SI	0.592	0.028	0.003	0.536	0.648
Age-adjusted SI	0.628	0.028	< 0.0001	0.572	0.683

anemia (OR 2.48; 95% CI, 1.47-4.19; p < 0.01). (Model 2. Table 4).

DISCUSSION

The ability to predict which patients are most likely to develop in-hospital complications or die before hospital discharge using simple variables present on admission is a clinical challenge in all the diseases. Decompensated heart failure, one of the main causes of admission in coronary care units worldwide, is not an exception.

The concept of SI was introduced in 1967 by Allgower and Burri who studied its value in the context of hypovolemic shock. (12) Subsequently, experimen-

Table 1. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) negative likelihood ratio (LR-) and positive likelihood ratio (LR+) of different SI and age-adjusted SI cutoff points for mortality

Value	Prevalence (%)	Sensitivity (%)	Specificity (%)	NPV	PPV	LR-	LR+
SI							
≥0.7	33	41	68	95	8	0.87	1.28
≥0.8	20	28	80	94	8	0.9	1.4
≥0.9	13	20	88	94	10	0.91	1.67
Age-adjusted SI							
≥50	43	57	60	95	8	0.72	1.38
≥60	25	39	76	95	10	0.9	1.63

Table 2. Univariate analysis for in-hospital mortality

Baseline characteristics	Deceased n = 92	Alive n = 1380	p	OR	95% CI
Age, median (IQR)	85 (79-90)	81 (73-87)	<0.01	3.5	1.0-6.0
Male gender, n (%)	46 (50)	748 (54)	NS	-	-
Hypertension, n (%)	76 (83)	1108 (80)	NS	-	-
Diabetes, n (%)	29 (31)	370 (27)	NS	-	-
Smoking habits, n (%)	13 (14)	174 (13)	NS	-	-
History of stroke, n (%)	6 (6)	126 (9)	NS	-	-
History of myocardial infarction, n (%)	16 (17)	316 (23)	NS	-	-
History of HF, n (%)	53 (58)	685 (50)	NS	-	-
LVEF < 40%	47 (53)	674 (50)	NS	-	-
Positive natriuretic peptides (n=988) n (%)	70 (97)	878 (96)	NS	-	-
Positive troponin levels (n = 1324), n (%)	78 (93)	1087 (88)	NS	-	-
BUN > 43 mg/dL, n (%)	70 (87)	792 (68)	<0.01	3.3	1.7 – 6.5
Creatinine levels >2.75 mg/dL, n (%)	13 (16)	81 (7)	<0.01	2.6	1.4 – 4.9
Anemia (Hb<10 g/dL), n (%)	29 (33)	197 (17)	<0.01	2.5	1.6 – 4.0
Normal BP and normal HR, n (%)	63 (68)	1048 (76)	NS	-	-
SBP < 115 mm Hg, n (%)	20 (22)	189 (14)	0.02	1.75	1.0- 2.94
HR > 100, n (%)	28 (30)	323 (23)	NS	-	-
Sodium <136 mEq/L, n (%)	31 (40)	437 (37)	NS	-	-
Median SI (IQR)	0.64 (0.55 – 0.81)	0.6 (0.5 – 0.75)	<0.01	0.06	0.017-0.1
SI ≥ 0,58, n (%)	62 (67)	738 (53)	<0.01	1.79	1.14-2.81
Median age x SI (IQR)	53 (45 – 67)	46 (37 – 59)	<0.01	7.7	3.8-11
Age x SI ≥ 45,6, n (%)	70 (76)	723 (52)	<0.01	2.89	1.77-4.72
MV, n (%)	52 (5)	30 (6.5)	NS	-	-

HF: heart failure; LVEF: left ventricular ejection fraction; Hb: hemoglobin, HR: heart rate, SBP: systolic blood pressure; MV: mechanical ventilation BUN: blood urea nitrogen

tal and clinical studies demonstrated that SI was inversely related to physiologic parameters as cardiac index, stroke volume, left ventricular stroke work and mean arterial pressure. (13)

SI reflects the integrated response of the cardiovascular and nervous systems. Higher SI may reflect hyperactivity of the sympathetic nervous system, which is associated with fatal ventricular arrhythmias or may be a simple marker of more severe cardiac dysfunction and myocardial damage. Normal SI values range between 0.5 and 0.7 in healthy adults (14) and its prognostic usefulness depends on the cutoff values used, which provide different sensitivity and specificity to predict events. Most studies use a cutoff point value > 0.7. Higher values are associated with greater mortality, and the cutoff point value with the highest specificity is > 0.9. Values close to 1 indicate worse hemodynamic status and shock (15) and also predict 30-day mortality.

In our study, Youden's index identified SI ≥ 0.58 and age-adjusted SI ≥ 45.6 as the most sensitive and specific values. Both indices, based on these values, provide a very high NPV for mortality, so that values lower than 0.58 or 45.6 would indicate favorable clinical outcome. Greater values indicate greater mortality.

Some authors suggest that the elderly population tends to have lower HR in response to physiologic changes (15) or use medications such as beta-blockers or calcium channel blockers that can affect HR in response to lower cardiac output. (16) Therefore, the prognostic power of SI in this subgroup of patients is reduced and the use of age-adjusted SI (SI x age) is recommended (13) to achieve greater sensitivity and specificity. (17,18) Age-adjusted SI has recently proved to be an even better predictor of mortality than classic SI in patients admitted to emergency departments. (19,20) Its high negative predictive value (>95%) in prognostic stratification is similar to that of other biomarkers, such as troponin or BNP, in conditions such as pulmonary embolism. (21) Indices are primarily useful to ensure favorable outcome when they are low, because of their very high NPV; they are less useful for risk prediction when they are high, because their PPV, as we can see, is low.

There is little information in the literature about the value of SI and age-adjusted SI in decompensated heart failure and the results are even contradictory. In an Arab registry (22) including 5005 patients, SI, modified SI (HR/mean blood pressure) and age-adjusted SI were independent predictors of events. For Pourafkari et al., SI did not present prognostic value (23) in a sample of 550 patients but they suggested that age-adjusted SI might play some role.

In the Arab registry, median SI was 0.74 and a SI of 0.9 was the best cutoff point value to predict mortality (based on ROC curves and present in 23% of the population with median age of 57 years). However, when they analyzed the relationship between SI and age, they noticed that for patients >75 years (like in the study by Pourafkari's and in ours) the median value was similar to that of our population (0.69 vs. 0.6) respectively. In our study, both indices were predictors of mortality, but age-adjusted SI provided better prognostic discrimination. Patients in the study by Pourafkari et al. and in our study were much older than those in the Arab registry (77 ± 11 years and 81 years, respectively versus 57 years), which could justify the difference in the performance of both indices.

Hypotension on admission is an independent predictor of complications and mortality during hospitalization and in the long-term in heart failure patients (24), but its prognostic value is lower than that of SI, as we observed in our study. The SI provides additional prognostic information besides that provided by the individual vital signs (HR and BP), even when these are within normal values (25,9), and for this reason its prognostic value has been tested in different clinical scenarios with favorable results.

In our model, renal failure and anemia on admission and age-adjusted SI kept their prognostic value of higher mortality. The ADHERE registry included nearly 33,000 patients with a mean age of 72.5 years (almost 8 years younger than ours); compared with our study, the prevalence of patients with diabetes (44% vs 27%) and chronic renal failure (29% vs 22%) was higher. That study reported the prognostic value of a risk assessment tool that included BUN level > 43 mg/dL, serum creatinine level > 2.75 mg/dL, and SBP < 115 mm Hg to discriminate populations with different in-hospital mortality (from 9 to 21%, depending on the association of factors). (26). Kidney failure is a prevalent condition in the elderly population, but its prevalence can vary considerably according to the definition used (estimation of glomerular filtration

Table 3. Multivariate logistic regression analysis for mortality. Model 1

Predictor	OR	95% CI	p
Age	**1.02**	**1.00-1.05**	**0.03**
Creatinine levels > 2.75 mg/dL	1.75	0.88-3.46	0.10
BUN > 43mg/dL	**2.36**	**1.17-4.74**	**0.01**
Hb < 10 g/dL	**2.42**	**1.44-4.07**	**<0.01**
SBP < 115 mm Hg	1.11	0.59-2.08	0.72
SI ≥ 0.58	1.52	0.89-2.5	0.11

BUN: blood urea nitrogen. Hb: hemoglobin. SBP: systolic blood pressure. SI: Shock Index

Table 4. Multivariate logistic regression analysis for mortality. Model 2

Predictor	OR	95% CI	p
Creatinine levels > 2.75 mg/dL	1.70	0.86-3.39	0.12
BUN > 43 mg/dL	**2.46**	**1.22-4.95**	**<0.001**
Hb < 10 g/dL	**2.48**	**1.47-4.19**	**<0.001**
SBP < 115 mm Hg	1.00	0.54-1.85	0.99
Age-adjusted SI > 45.6	**2.41**	**1.35-4.28**	**<0.001**

BUN: blood urea nitrogen. Hb: hemoglobin. SBP: systolic blood pressure. SI: Shock Index rate with formulas or simply absolute value above the reference parameters).

Study limitations

Although the sample size is significant, we cannot rule out the possibility that our findings may have occurred by chance because of the retrospective nature of the study. Nevertheless, there are no prospective studies in this context. Age is a preeminent variable in the prognosis of patients associated with their comorbidities, so differences in its prevalence will determine the weight of the prognostic variables. In our study, as most patients were > 80 years, heart rate and blood pressure probably express the significant role of dysautonomia, which determine a greater lability on admission and even a lower response to treatment with vasoactive drugs. The absence of differences between survivors and deceased patients in the prevalence of humoral markers of heart failure (BNP), necrosis (troponins) or cardiac function express pathophysiological mechanisms of different relevance, especially in the elderly population.

CONCLUSIONS

It is important to emphasize that registries are made up of heterogeneous populations in terms of age, past medical history and types of presentation, which may determine the results of the studies. We believe that simple variables that can be recorded on hospital admission allow calculation of the age-adjusted shock index, a very useful parameter for predicting in-hospital mortality in patients hospitalized with decompensated heart failure and that adds additional information to the classic prognostic variables.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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