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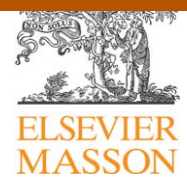

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CLINICAL RESEARCH

Usefulness of serum albumin and serum total cholesterol in the prediction of hospital death in older patients with severe, acute heart failure

Utilité de l'albumine sérique et du cholestérol total dans le pronostic hospitalier des patients âgés en insuffisance cardiaque aiguë sévère

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KEYWORDS
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Serum total cholesterol

Summary
Background. — Acute heart failure (HF) carries high hospital mortality rates in older patients; a multimarker strategy may help identify patients at high risk.
Aims. — To investigate prospectively the prognostic relevance of serum albumin and serum total cholesterol (TC) in older patients with severe, acute HF.
Methods. — Usual prognostic variables were collected on admission in 207 consecutive patients aged > 70 years with severe, acute HF. Serum albumin and serum TC were obtained soon after clinical improvement.
Results. — Hospital mortality rate was 19%. Patients who died were similar to patients who survived in terms of age, sex, heart rate, serum haemoglobin and left ventricular ejection fraction. Patients who died had higher concentrations of B-type natriuretic peptide (BNP), blood urea nitrogen, serum creatinine, C-reactive protein and serum troponin I, lower systolic blood pressure, and lower concentrations of serum albumin and serum TC than patients who survived ($P < 0.01$ for all). Serum albumin was the best independent predictor of hospital death (odds ratio

Abbreviations: BNP, B-type natriuretic peptide; HF, heart failure; LV, left ventricular; ROC, receiver operating characteristic; TC, total cholesterol.

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0.82 [0.74—0.90], $P < 0.001$), with blood urea nitrogen ($P = 0.02$) and log (BNP) ($P = 0.02$). A simple risk score based on serum albumin (< 3 g/dL; 2 points), BNP (> 840 pg/mL; 1 point) and blood urea nitrogen (> 15.3 mmol/L; 1 point) discriminated patients without (score 0 to 1, hospital death 4%) from patients with (score 2 to 4, hospital death 35%, $P < 0.001$) a high risk of death.
Conclusion. — Hypoalbuminaemia offers powerful additional prognostic information to usual prognostic variables in older patients with severe, acute HF, and deserves further attention in multimarker strategies.

MOTS CLÉS
Albumine sérique ;
Cholestérol total ;
Insuffisance cardiaque aiguë ;
Pronostic ;
Sujet âgé

Résumé
Contexte. — Le taux de mortalité hospitalière est particulièrement élevé dans l'insuffisance cardiaque aiguë (ICA) du sujet âgé, et une stratégie basée sur plusieurs marqueurs biologiques pourrait contribuer à l'identification des sujets les plus à risque.
Objectif. — Évaluer la valeur pronostique de l'albumine sérique et du cholestérol total chez le sujet âgé en ICA sévère.
Méthodes. — Les paramètres biologiques usuels ont été dosés à l'admission chez 207 patients consécutifs de plus de 70 ans. L'albumine sérique et le cholestérol total ont été dosés lors de la stabilisation clinique.
Résultats. — La mortalité hospitalière était de 19 %. Les patients décédés et survivants étaient similaires en terme d'âge, de sexe, de fréquence cardiaque, d'hémoglobine sérique et de fraction d'éjection. Les patients décédés avaient des concentration en peptide natriurétique de type B (BNP), urée plasmatique, créatinine sanguine, protéine C réactive et troponine I plus élevées, d'albumine sérique et de cholestérol total plus basses ($p < 0{,}01$). L'albumine sérique était le facteur prédictif indépendant de mortalité le plus puissant (OR 0,82 [0,74—0,90], $p < 0{,}001$), avec l'urée ($p = 0{,}02$) et le BNP ($p = 0{,}02$). Un score de risque basé sur l'albumine sérique (< 3 g/dL ; 2 points), le BNP (> 840 pg/mL ; 1 point) et l'urée (> 15,3 mmol/L ; 1 point) séparait les patients à bas risque (score 0 à 1, mortalité de 4 %) des patients à haut risque (score 2 à 4, mortalité de 35 %).
Conclusion. — L'albumine sérique offre une information pronostique pertinente chez le sujet âgé hospitalisé en ICA sévère, et mérite d'être intégré plus largement dans les algorithmes pronostiques.

Background

Acute HF syndromes are one of the most frequent causes of admission to community hospitals in developed countries. This epidemic medical condition primarily affects older patients and carries high hospital mortality rates [1,2]. Many elderly patients hospitalized with HF do not benefit from cardiologist care [3], and may therefore experience poorer outcomes [4]. Severe symptoms and high concentrations of BNP are well-established landmarks of severe, acute HF at hospital admission [5]. A targeted multimarker strategy may, however, be helpful in improving the identification of older patients at high risk of hospital death, who are candidates for cardiologist care and tailored unloading therapy.

Serum albumin and serum TC are two simple and inexpensive markers of malnutrition-inflammation syndrome, which have been recently proposed for the identification of patients with acute HF at risk of adverse outcome [6—11]; however, it is unknown whether these two biomarkers offer relevant prognostic information incremental to usual prognosticators in older patients with severe, acute HF. The present study addressed the prognostic relevance of serum albumin and serum TC in the prediction of hospital death in older patients identified as having severe, acute HF at admission to a French community hospital.

Methods

Study population

This prospective, observational study included consecutive elderly patients aged > 70 years, who were admitted to the Department of Cardiology of our institution from January 2009 to February 2011 with the primary diagnosis of acute HF. All the patients had acute dyspnoea at rest, clinical and radiographic signs of pulmonary oedema, which responded favourably to intravenous furosemide therapy, and abnormal concentrations of BNP. Comprehensive Doppler echocardiography was performed in all patients within 24 h of admission. Because low and intermediate BNP concentrations indicate good prognosis at the time of admission, all patients with BNP concentrations < 300 pg/mL associated with a LV ejection fraction > 50%, as well as all patients with BNP concentrations < 600 pg/mL associated with a LV ejection fraction < 50%, were not included in the study [5]. Other exclusion criteria were acute coronary syndromes, acute myocardial infarction with ST-segment elevation, severe left-sided valve disease, neoplasia and liver cirrhosis. Finally, 207 consecutive patients with the final diagnosis of severe, acute HF were included in the study. All patients were managed by two HF specialists dur-

ing their hospital stay. Patients were discharged from the hospital provided that they were clinically stable under oral therapy for at least 2 days, without residual pulmonary and peripheral fluid overload. All patients were included after informed consent was obtained.

Baseline patient data

Baseline clinical data, serum sodium concentration (Dimension RXL system, Siemens, Munich, Germany; normal range 137 to 145 mmol/L), BNP concentration (Architect I1000 system, Abbott Diagnostics, Abbott Park, IL, USA; 10 to 5000 pg/mL), serum creatinine concentration (Dimension RXL system; normal range 71—115 μmol/L for men and 53—88 μmol/L for women), blood urea nitrogen concentration (Dimension RXL system; normal range 2.5 to 6.4 mmol/L), serum haemoglobin concentration (XE2100 system, Sysmex, Kobe, Japan; normal range 13 to 17 g/dL in men and 12 to 16 g/dL in women) and serum troponin I concentration (Dimension RXL system; normal value < 0.14 pg/mL) were collected on admission. Serum albumin concentration (Dimension RXL system; normal range 3.5 to 5 g/dL), serum TC concentration (Dimension RXL system; normal range 135 to 250 mg/dL) and C-reactive protein concentration (Dimension RXL system; normal value < 3 mg/L) were measured in the same blood sample within 3 days of admission, after clinical stabilization. Clinically relevant hypoalbuminaemia was defined by a value of < 3 g/dL [12]. Creatinine clearance (mL/minute) was calculated according to the MDRD formula, which integrates serum creatinine concentration, age and sex but not weight.

The Boston score for congestive HF was calculated by a cardiologist at admission. This score is based on symptoms (0—4 points), physical examination (0—4) and chest X-ray (0—4). As all of the patients presented with dyspnoea at rest and radiographic pulmonary oedema, their scores ranged from 7 to 12. All patients underwent comprehensive Doppler echocardiography at the bedside within 24 h of admission. LV ejection fraction was measured by Simpson's method; the combination of visual estimate and endocardial fractional shortening was used in patients with poor echogenicity. An LV ejection fraction ≥ 50% was used to define normal LV systolic function. Diastolic function was assessed in patients in sinus rhythm by the analysis of mitral filling and tissue Doppler imaging at the mitral annulus. Diastolic dysfunction was classified as abnormal relaxation of mitral filling, pseudonormal mitral filling and restrictive mitral filling.

Statistical analysis

Descriptive data with normal distribution are given as mean ± standard deviation. Descriptive data without normal distribution are given as median [interquartile range]. Intergroup comparison used the analysis of variance test, the Kruskal-Wallis test, the Chi^2 test and Fisher's exact test with bilateral formulation as appropriate. The prespecified endpoint was hospital death. The analysis of variables associated with length of hospital stay in patients discharged alive was designed retrospectively, at the end of the study. Multiple regression analysis was used to identify variables that were associated with serum albumin concentration and serum TC concentration, and the correlation coefficient (r) was provided for variables that achieved statistically significant results. Logistic regression analysis was used to determine predictors of hospital death, using hospital death as the dependent variable and age, sex, heart rate, systolic blood pressure, LV ejection fraction, log (BNP), serum troponin I, serum sodium, serum creatinine, creatinine clearance, blood urea nitrogen, serum albumin, serum TC and C-reactive protein as independent variables. Multivariable stepwise logistic regression analysis was used to determine variables that independently predicted hospital death; a variable was entered into the model if its associated significance level was < 0.05 and was removed if its associated significance level was > 0.1. The area under the ROC curve in the prediction of hospital death was given with its 95% confidence interval. Variables that were independently associated with hospital death were used to create a risk score by assigning a specific number of points proportional to regression coefficients. Multiple regression analysis was used to identify predictors of hospital length of stay in patients discharged alive. A P value < 0.05 was considered statistically significant. Medcalc® software, version 11.1.0.0 (Medcalc® Software, Mariakerke, Belgium) was used for the purpose of statistical analysis.

Results

Baseline characteristics of the study population

The mean age of the study population was 86 ± 7 (range 71—102) years. Median LV ejection fraction was 55% [40—65] and 144 patients (70%) had normal LV systolic function. Mean serum albumin concentration was 3.05 ± 0.5 (range 1.47—4.52) g/dL and median serum TC was 170 [140—200] (range 70—330) mg/dL. Ninety-seven patients (47%) had clinically relevant hypoalbuminaemia and 45 patients (22%) had hypocholesterolaemia. Among patients in sinus rhythm, 42% had a restrictive mitral filling pattern, 33% had pseudonormal mitral filling and 25% had abnormal relaxation mitral filling. Forty patients died during their hospital stay, soon after a short period of clinical improvement: 32 with refractory congestive HF and eight with sudden cardiac death. Twenty-seven patients (67%) who died had normal LV systolic function. None of the patients died from causes of extracardiac origin during their hospital stay. The length of hospital stay was significantly shorter in patients who died than in those discharged alive (P < 0.001). Baseline clinical characteristics of the patients are displayed in Table 1 according to outcome.

Variables associated with serum albumin and total cholesterol concentrations

There was a significant linear correlation between serum albumin concentration and serum TC concentration (r = 0.43 [0.31—0.53], P < 0.001). Serum albumin concentration was associated with a history of dementia (r = 0.17, P = 0.01), C-reactive protein (r = —0.53, P < 0.001), serum creatinine (r = —0.17, P = 0.01), log (BNP) (r = —0.15, P = 0.03) and serum haemoglobin (r = 0.14, P = 0.03). Serum albumin

Table 1 Baseline characteristics of patients according to hospital outcome.

Variable	Survivors ($n=167$)	Non-survivors ($n=40$)	p
Age (years)	86 ± 7	87 ± 7	0.4
Women	112 (67)	28 (70)	0.8
Presenting characteristics			
Boston score	10.1 ± 1.5	10 ± 1.7	0.8
Systolic blood pressure (mmHg)	152 ± 34	132 ± 36	< 0.01
Sinus rhythm	93 (56)	17 (43)	0.2
Heart rate (beats per minute)	83 [69—100]	90 [72—110]	0.09
LV ejection fraction (%)	55 [40—65]	55 [37—65]	0.8
BNP concentration (pg/mL)	919 [660—166]	1194 [757—2790]	< 0.01
Serum sodium (mmol/L)	138 [136—141]	140 [134—144]	0.2
Serum creatinine (μmol/L)	102 [84—134]	134 [89—203]	0.01
Creatinine clearance (mL/minute)	50 [37—63]	35 [25—56]	< 0.01
Blood urea nitrogen (mmol/L)	9.2 [7—12.6]	14.1 [9.6—23.5]	< 0.001
Serum haemoglobin (g/dL)	12.1 ± 1.8	12 ± 1.9	0.6
Positive serum troponin I	26 (15)	15 (38)	< 0.01
C-reactive protein (mg/L)	38 [14—85]	143 [41—208]	< 0.001
Serum albumin concentration (g/dL)	3.1 ± 0.5	2.6 ± 0.5	< 0.001
Serum total cholesterol concentration (mg/dL)	174 [143—204]	146 [119—172]	< 0.001
Medical history			
Congestive heart failure	70 (42)	14 (35)	0.5
Hypertension	111 (66)	22 (55)	0.2
Coronary artery disease	53 (32)	16 (40)	0.4
Stroke	31 (18)	5 (12)	0.5
Diabetes mellitus	35 (21)	13 (32)	0.1
Pulmonary disease	28 (17)	6 (15)	0.9
Dementia	39 (23)	14 (35)	0.2
Institutionalized status	80 (48)	21 (52)	0.7
Chronic medications			
Diuretics	93 (56)	24 (60)	0.7
ACE-I or ARB	75 (45)	17 (42)	0.9
Beta-blocker	65 (39)	17 (42)	0.8
Statin	23 (14)	6 (15)	0.9
Length of hospital stay (days)	10 [7—13]	6 [4—9]	< 0.001

Data are mean ± standard deviation, mean [interquartile range] or number (%). ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin-receptor blocker; BNP: B-type natriuretic peptide; LV: left ventricular.

concentration was not associated with age ($P=0.5$), sex ($P=0.3$), a history of HF ($P=0.6$), the institutionalized status ($P=0.07$), LV ejection fraction ($P=0.3$) or diuretic therapy ($P=0.9$). Variables that were independently associated with serum albumin concentration were C-reactive protein ($P<0.001$) and serum haemoglobin ($P=0.01$).

Serum TC concentration was associated with sex ($r=0.21$, $P=0.002$), LV ejection fraction ($r=0.16$, $P=0.02$), C-reactive protein ($r=-0.25$, $P<0.001$), serum creatinine ($r=-0.17$, $P=0.01$), log (BNP) ($r=-0.16$, $P=0.02$) and statin therapy ($r=0.27$, $P<0.001$). Serum CT was not associated with age ($P=0.8$), history of HF ($P=0.1$), institutionalized status ($P=0.055$), history of dementia ($P=0.07$), serum haemoglobin ($P=0.9$) or diuretic therapy ($P=0.09$). Variables independently associated with serum TC concentration were C-reactive protein ($P<0.001$), statin therapy ($P=0.002$) and sex ($P=0.02$).

Serum albumin, serum total cholesterol and hospital death

Serum albumin ($P<0.001$), serum TC ($P<0.001$), C-reactive protein ($P<0.001$) and blood urea nitrogen ($P<0.001$) were the best predictors of hospital death in the univariate model (Table 2). In the first step, all the significant variables, except for serum albumin, were entered into the multivariable model. C-reactive protein ($P=0.001$), blood urea nitrogen ($P=0.005$) and serum TC ($P=0.03$) were independent predictors of hospital death. In the second step, all the significant variables, except for serum TC, were entered into the multivariable model. Serum albumin ($P<0.001$), log (BNP) ($P=0.02$) and blood urea nitrogen ($P=0.02$) were independent predictors of hospital death. In the third step, all the significant variables were entered into the multivariable model. Serum albumin ($P<0.001$), log (BNP) ($P=0.02$) and

Table 2 Stepwise logistic regression analysis: predictors of hospital death.

Variable	Univariate model		Area under the ROC curve [95% CI]	Multivariable model	
	OR [95% CI]	*P*		OR [95% CI]	*P*
Age	1.02 [0.97—1.07]	0.4	0.54 [0.47—0.61]	—	
Sex	1.14 [0.54—2.52]	0.7	0.51 [0.44—0.58]	—	
Heart rate	1.01 [0.99—1.02]	0.1	0.58 [0.51—0.65]	—	
Systolic blood pressure	0.98 [0.97—0.99]	0.002	0.65 [0.58—0.71]	NS	
LV ejection fraction	1.00 [0.97—1.01]	0.5	0.51 [0.44—0.58]	—	
Serum sodium	1.05 [0.99—1.11]	0.07	0.56 [0.49—0.63]	—	
Log (BNP)	7.8 [2.13—28.6]	0.002	0.64 [0.57—0.70]	5.1 [1.2—21.7]	0.02
Serum creatinine	1.007 [1.003—1.01]	0.001	0.63 [0.56—0.70]	NS	
Creatinine clearance	0.97 [0.95—0.99]	0.009	0.61 [0.54—0.68]	NS	
Blood urea nitrogen	1.1 [1.05—1.15]	< 0.001	0.72 [0.65—0.78]	1.06 [1.009—1.1]	0.02
Serum troponin I	3.5 [1.6—7.83]	0.002	0.62 [0.55—0.70]	NS	
C-reactive protein	1.01 [1.005—1.013]	< 0.001	0.73 [0.66—0.78]	NS	
Serum albumin	0.79 [0.72—0.87]	< 0.001	0.78 [0.72—0.83]	0.82 [0.74—0.90]	< 0.001
Serum total cholesterol	0.51 [0.35—0.73]	< 0.001	0.69 [0.62—0.75]	NS	

BNP: B-type natriuretic peptide; CI: confidence interval; LV: left ventricular; OR: odds ratio; ROC: receiver operating characteristic.

blood urea nitrogen ($P = 0.02$) were independent predictors of hospital death (Table 2). Clinically relevant hypoalbuminaemia < 3 g/dL was 82.5% sensitive and 61.7% specific in the prediction of hospital death.

Serum albumin was a strong predictor of hospital death in patients with normal LV systolic function (odds ratio 0.77 [0.69—0.86], $P < 0.001$; area under the ROC curve 0.81 [0.73—0.87]) and in those with LV systolic dysfunction (odds ratio 0.83 [0.72—0.96], $P = 0.01$; area under the ROC curve 0.73 [0.60—0.83]). Serum TC predicted outcome in patients with normal LV systolic function (odds ratio 0.48 [0.31—0.76], $P = 0.001$; area under the ROC curve 0.71 [0.63—0.78]). However, serum TC did not clearly predict hospital death in patients with LV systolic dysfunction ($P = 0.08$).

Risk score in the prediction of hospital death

We assigned the following points to the independent predictors of hospital death in the multivariable model, using standard cut-off values from the ADHERE registry for BNP and blood urea nitrogen [5,13—17]: BNP concentration > 840 pg/mL (1 point), blood urea nitrogen > 15.3 mmol/L (1 point) and serum albumin concentration < 3 g/dL (2 points). Patients with a score of 0 to 1 ($n = 103$) had a hospital mortality rate of 4% compared with a hospital mortality rate of 35% in patients with a score of 2 to 4 ($n = 104$) ($P < 0.001$).

Serum albumin, serum total cholesterol and length of hospital stay

In patients discharged alive, the length of hospital stay was predicted by serum albumin ($r = -0.27$, $P < 0.001$), serum haemoglobin ($r = -0.24$, $P = 0.002$), serum TC ($r = -0.18$, $P = 0.02$) and C-reactive protein ($r = -0.15$, $P = 0.04$) (Table 3). Serum albumin ($P = 0.004$) and serum haemoglobin ($P = 0.01$) independently predicted the length of hospital stay in the multivariable analysis.

Discussion

Acute HF syndromes carry disturbing hospital mortality rates, which increase with advancing age and illness. The hospital mortality rate is reported to exceed 10—20% in octogenarians and nonagenarians hospitalized with HF [1,2]. As expected, the hospital mortality rate was high in the present study (19%), which focused on older patients with a severe clinical picture and elevated concentrations of BNP. Several contributors to adverse outcome have been recently identified in acute HF syndromes, including the specialty of the attending physician [4], in-hospital treatment delay [13] and residual fluid overload [14]. Accurately identifying older patients at high risk may help to improve the therapeutic management through cardiologist care and tailored unloading therapy. The landmark ADHERE registry has well established the prognostic relevance of several simple markers in the prediction of hospital death in acute HF syndromes, such as systolic blood pressure, BNP, troponin I and renal failure [5,15—17]. We addressed the clinical relevance of serum albumin and serum TC on top of the usual prognostic variables, because abnormal concentrations of these two biomarkers of malnutrition-inflammation syndrome are common in elderly patients and patients with HF, and indicate poor prognosis [6—11,18—20]. In the present study, the prevalence of clinically relevant hypoalbuminaemia was 47%, which is similar to that reported in a previous study [10]. A few retrospective works have previously suggested that serum albumin may predict adverse outcome in patients with HF, independent of natriuretic peptides. Hypoalbuminaemia was the strongest predictor of hospital death in 349 elderly patients hospitalized with HF, after adjusting for prior HF hospitalization, serum sodium, blood urea nitrogen and BNP [9]. Serum albumin was the sole, independent predictor of mid-term outcome in 146 nonagenarians hospitalized with HF, after adjusting for BNP and routine laboratory tests [11]. However, these two studies had a retrospective design and the relation of serum albumin and

Table 3 Multiple regression analysis: predictors of length of stay in patients discharged alive.

Variable	Univariate model *P* value	Multivariable model *P* value
Age	0.6	—
Sex	0.3	—
Systolic blood pressure	0.1	—
LV ejection fraction	0.1	—
Serum sodium	0.2	—
Log (BNP)	0.07	—
Serum haemoglobin	0.002	0.01
Serum creatinine	0.4	—
Creatinine clearance	0.5	—
Blood urea nitrogen	0.2	—
Serum troponin I	0.1	—
C-reactive protein	0.04	NS
Serum albumin	< 0.001	0.004
Serum total cholesterol	0.02	NS

BNP: B-type natriuretic peptide; LV: left ventricular.

serum TC to cardiac death was not studied. Furthermore, the influence of LV ejection fraction on the ability of serum albumin to predict outcome was not specifically addressed. This latter concern is of major importance because the prognostic usefulness of serum albumin has been recently questioned in patients with a preserved LV systolic function [10]. In the present study, median serum TC concentration was higher than that previously reported in patients with acute HF [8]. However, serum TC concentration is influenced by lipid-lowering medication, and such a chronic treatment was prescribed significantly less frequently in our patients (14% versus 46%). To the best of our knowledge, no study has addressed the prognostic relevance of serum TC in patients with HF and increased concentrations of BNP. In the present study, usual prognosticators at admission predicted hospital cardiac death in elderly patients with severe, acute HF. Serum albumin offered more relevant prognostic information incremental to all these usual variables than serum TC. Serum albumin predicted hospital cardiac death in systolic and diastolic HF. Hypoalbuminaemia was independently linked to longer length of hospital stay in patients discharged alive, which is consistent with other observational studies [18,21].

The prognostic relevance of serum albumin and serum TC probably refers to underlying malnutrition, inflammation and wasting syndrome [22,23]. The strong, independent prognostic value of serum albumin may, however, illustrate its contribution to the progression of HF. Serum albumin is an abundant plasma protein with multiple physiological properties, including colloid osmotic effect, antioxidant and anti-inflammatory functions, and binding capacity for many molecules and drugs [6]. Growing evidence suggests that severe hypoalbuminaemia exerts adverse pleiotropic effects on many organs and neurohumoral systems that are involved in the clinical syndrome of HF [6]. Hydrostatic capillary and plasma oncotic pressures are the main opposing forces that regulate fluid balance across the capillary membrane and there is definite evidence that severe hypoalbuminaemia promotes pulmonary oedema [6]. Serum albumin contributes to maintain the integrity of the myocardial microvasculature through its oncotic properties and its interaction with the endothelial glycocalyx [6]. Severe hypoalbuminaemia aggravates myocardial oedema, which is considered as a cause of myocardial dysfunction and electrophysiological instability in many heart diseases [6,24,25]. Serum albumin properties include antioxidant and anti-inflammatory functions [6,26,27], and severe hypoalbuminaemia may exacerbate oxidative stress and inflammation, which are involved in the global process of HF. Severe hypoalbuminaemia contributes to volume overload through the activation of baroreceptors and diuretic resistance [6], and residual fluid overload is linked to adverse outcome in the setting of congestive HF [14,28].

The present study highlights the relevance of a simple and inexpensive biomarker on top of usual prognostic variables, through a multimarker strategy, in older patients hospitalized with severe, acute HF. The combination of serum albumin, BNP and blood urea nitrogen through a simple risk score enabled the identification of a subgroup of patients at very high risk of hospital death (35%). Such patients may benefit from cardiologist care and tailored unloading therapy. Because severe hypoalbuminaemia potentially contributes to diuretic resistance and volume overload [6], further studies are needed to evaluate the safety and benefits of ultrafiltration and targeted albumin administration associated with furosemide therapy in hypoalbuminaemic patients with refractory congestive HF [12,28—30].

Study limitations

The major limitation of the present study is that clinical markers of malnutrition were not studied, while malnutrition and inflammation are the main determinants of hypoalbuminaemia. The prognostic value of body mass index was not addressed because the patient's weight was not available in patients with in-hospital fatal outcome as well as in bedridden patients. For the same reason, the Cockroft

formula was not used to calculate creatinine clearance in our study. The risk score in the prediction of hospital death should be validated in further prospective studies. Further studies are also needed in younger patient populations to determine the prognostic relevance of serum albumin and serum TC additional to usual prognostic markers.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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