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CLINIC, BIOLOGIC AND ECHOCARDIOGRAPHIC PARTICULARITIES WITH SHORT TIME PROGNOSIS VALUE IN SEVERE CLINICAL FORMS OF ACUTE HEART FAILURE

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SUMMARY

Introduction: Acute Heart Failure (AHF) is a clinical and paraclinical polymorphic syndrome, with high in hospital and early post discharge mortality. A few national and international registries have analysed, individually, the severe forms of AHF, Acute Pulmonary Edema (APE) or Chronic Decompensated Acute Heart Failure (CDAHF) IV NYHA Class.

Purpouse: Identifying clinical, biological and echocardiographic parameters with prognosis value for in hospital mortality (IHM) in a lot of patients with severe forms of AHF. Customizing them according to clinical form: APE without acute coronary syndrome (APE non ACS) or CDAHF IV NYHA class.

Methods: 228 patients with AHF severe clinical forms, admitted consecutively in our Cardiology department during 01.01-31.12.2013. The final diagnosis was established by clinic, biologic and echocardiographic data and vital status at discharge was collected. This data were analysed according to clinical form and in hospital mortality.

Results: Ninty two patients with APE non ACS and 136 patients with CDAHF IVNYHA Class. Similar average age for both forms (73.32 years). A slightly higher percentage of men for CDAHF (55.88%) and women for APE (54.35%), difference with no statistical value ($p=0.9$). Hypertension, type II diabetes and dyslipidemias are the most identified risk factor, with a higher percentage for APE vs CDAHF with statistical value ($p<0.05$). The ischemic etiology predominates in both clinical forms. There are statistically significant (SS) differences for pretherapeutic Systolic Blood Presure (SBP) and clinical form ($p<0.001$) with higher average values for APE vs CDAHF, with no significant correlation to IHM for SBP in APE ($p=0.9$), significant for CDAHF ($p<0.001$). There are no statistical differences between adminission heart rate and clinical form, neither correlations of this with IHM. There are SS correlations between Urea ($p<0.001$), Creatinine ($p=0.07$) and on admission sodium ($p=0.004$) with IHM for CDAHF, for APE just for sodium ($p<0.001$). There are o lot of echo parameters correlated with IHM for both APE and

RÉSUMÉ

Caractéristiques clinique, biologique et échocardiographique à valeur pronostique à court terme dans les formes cliniques sévères de l'insuffisance cardiaque aiguë

Introduction: L'insuffisance cardiaque aiguë est un syndrome polymorphe clinique et paraclinique à mortalité élevée dans l'hôpital et précoce après l'hospitalisation. Certain statistiques nationales et internationales ont analysé, individuellement, les formes sévères d'insuffisance cardiaque aiguë, Œdème Pulmonaire aign ou Insuffisance cardiaque aiguë décompensée chronique de classe IV NYHA.

But: Identification des paramètres cliniques, biologiques et échocardiographiques à valeur de pronostic de mortalité intra-hospitalière chez un groupe de patients aux formes sévères de ICA.

Méthodes: 228 patients avec des formes cliniques sévère d'ICA ont été admis dans notre Département de Cardiologie entre 01.01-31.12.2013. Le diagnostic final a été mis selon les données cliniques, biologiques et échocardiographiques et le statut vital a été recueilli à la sortie de l'hôpital. Ces données ont été analysées d'après la forme clinique et la mortalité intra-hospitalière.

Résultats: 92 patients avec insuffisance cardiaque aiguë sans syndrome coronarien aigu et 136 patients avec insuffisance cardiaque aiguë décompensée chronique de classe IV NYHA. Âge moyen similaire pour les deux formes (73,32 ans). L'hypertension, le diabète de type II et la dyslipidémie sont les facteurs de risque le plus fréquemment identifiés, à un pourcent plus grenal pour ICA vs ICADC à valeur statistique ($p<0,05$). L'étiologie ischémique prédomine dans les deux formes. Il ya des différences significatives du point de vue statistique pour la Pression Sanguine Systolique et la forme clinique ($p<0,001$) aux valeurs moyennes plus grandes pour ICA vs ICADC. Il n'y a pas de différences statistiques entre le taux cardiaque et la forme clinique, ni de corrélations avec la mortalite intra-hospitalière.

Conclusions: A l'admission à l'hôpital, bien que différentes, du point de vue clinique, l'ICA sans SCA et l'ICADC se présentent

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CDAHF, the values of these parameters change according to clinical form and etiology.
Conclusions: Clinically different on admission, APE nonACS and CDAHF present as much common elements as particular ones. The ischemic etiology is a common cause, with more cardiovascular risk factors and a cumulation of them for APE. Classic parameters: on admission SBP, Urea, Creatinine, Sodium maintain a positive prognostic value for IHM just in CDAHF patients, for APE patients echocardiographic parameters have proven prognostic value, and less clinical and biological ones
Key words: heart failure, pulmonary edema, echocardiography

avec des éléments communs et particuliers en égale mesure. L'étiologie ischémique est une cause commune, avec plus de facteurs de risque cardiovasculaires et un accumulation d'eux pour les ICA. Les paramètres classiques: la PSS à l'admission, l'urée, la créatinine, la sodium maintiennent une valeur pronostique positive pour MIH seulement pour les patients avec ICADC; pour les patients avec ICA les paramètres échocardiographiques ont démontré une valeur pronostic et dous une maindre mesure aux cliniques et biologiques.
Mots clefs: insuffisance cardiaque, œdème pulmonaire, échocardiographie

INTRODUCTION

Acute heart failure is a polymorph clinical and paraclinically syndrome, still with a high in-hospital mortality, unacceptably high at 1-12 months. Hospitalizations for AHF represent one of the most important predictors of after discharge early mortality and rehospitalization. Over one million hospitalizations yearly with acute heart failure as diagnosis occurring in the US and about the same number in Western European countries; as discharge diagnosis in the last three decades has tripled, and this trend is likely to continue due to the increasing life expectancy and the aging of population. But there is few data about two of the severe forms, namely APE and CDAHF IV NYHA, compared with the clinical forms and the prognostic parameters. Data coming from the register ALARM HF (1) (multinational register) and ROAHF (2) show that in the AHF syndrome, the two forms are the most common [76% of all patients in ALARM HF (1), 86% of those included in ROAHF (2)] having unacceptable high in-hospital mortality [7.4% vs 3.6% APE vs CDAHF in ROAHFS (2), 7.4% vs 6% in ALARM HF (1)].

Although forms of the same syndrome, between the two conditions, APE and CDAHF, there are differences both regarding etiopathogeny and patophysiology. CDAHF frequently represents an acute stage of a chronic heart failure, with varied etiopathogenic substrate: ischemic, nonischemic dilated, valvular, hypertensive or nonhipertensive hypertrophic, dysrhythmic, and rarely de novo AHF; while APE can be either de novo event in ischemic or non-ischemic context, or an acute decompensation of chronic heart failure. This distinction is important, as the pathophysiology and clinical presentation of the two types, de novo or chronic decompensated one, differ greatly. Patients with de novo AHF - the first manifestation of heart failure - have an important sympathetic adrenergic discharge, an increased capillary permeability with signs of pulmonary congestion presented and manifested in a dramatic and acute way, in turn may be missing signs of systemic congestion. At the CDAHF patients due to the adaptation neurohormonal and compensation mechanisms by activation of the renin angiotensin aldosterone system, there is an accumulation of excess fluid redistributed in pulmonary and systemic vascular bed with signs of systemic congestion and high tolerability for pulmonary capillary pressure increased, elements of pathophysiology that may justify clinical and laboratory differences between the two forms.

Purpose

Given these differences we aimed to analyze the clinic, biologic and echocardiographic parameters in relation to each form and how they correlate with prognosis.

MATERIALS AND METHODS

The study is a retrospective analysis of a group of 228 patients with severe AHF, CDAHF IV NYHA and APE non ACS, hospitalized in the Cardiology Department of St. Pantelimon Hospital in the period 01.01.2013 -31.12.2013, from were gathered which data about demographic, clinical, laboratory and vital status at hospital discharge. Patients were classified by diagnosis at discharge, established according to the ESC Guidelines (7, 8).

Differential diagnosis between the two clinical forms was based on the clinical data and anamnesis: sudden onset of symptoms, dyspnea at rest with orthopnoea, low oxygen saturation, therapeutic response and less on the paraclinical elements (pulmonary XR with typical appearance of edema in butterfly or biomarkers as NT pro BNP, available only in 28.6% of cases). We have analyzed demographic data, cardiovascular risk factors, comorbidities, vital parameters, systolic blood pressure at presentation (SBP) and heart rate before treatment (HR), biological (BUN, serum creatinine, and sodium on admission) and echocardiographic data and vital status at discharge in relation to clinical form. There have been identified elements with positive predictive value for in-hospital mortality (IHM).

The study was approved by the Ethics Committee of the "Sf.Pantelimon" Emergency Hospital and all patients signed an informed consent form for the use of their data.

For the statistical analysis we used SPSS 20.0 and EPIINFO7.0. The impact of clinical and laboratory variable on short term outcome was determined by using multiple regression equations,while the differences between variables were calculated by using the analysis of variance for continuous variables and chi – square test for categorical variables.

RESULTS

Two hundred twenty- eight (228) patients with AHF, divided as follows: 92 (40.35%) APE non ACS, 136 (59.64%) CDAHF IV NYHA. The average age is relatively equal for the two forms (73 years), with a higher percentage of men in the group CDAHF IV NYHA (55.89 vs 45.65%), statistically nonsignificant differences (p=0.1). The presence of the risk factors differs significantly between the two forms with a higher percentage for hypertension (89.13 vs 69.12%, p < 0.001), dyslipidemia (76.09 vs 39.71%, p <0.001) and diabetes mellitus type II (76.09 vs 32.35%, p <0.001) in APE non ACS; active smoking is found in relatively equal percentages for the two forms (Table 1).

The incidence of certain diseases, such fibrillation / atrial flutter rhythm on admission (permanent, persistent or paroxysmal) (33.82 vs. 19.56%, p = 0.006), and history of heart failure (100 vs. 80.43%, p <0.001) can be found in higher percentages, statistically significant, in CDAHF IV NYHA. Note that coronary ischemic disease exists in relatively equal percentages, important (51.47 vs 47.873%) in both forms, similar data for history of COPD(chronic obstructive pulmonary deasese) or stroke, too (Table 2).

Ischemic etiology is a common one (51.47% vs 47.83% CDAHF vs APE) with a higher incidence of hypertensive substrate in APE (28.26% vs 7.35%) and the valvular one in CDAHF IV NYHA(36.76% vs 23.91%), without statistically significant differences.

Among the clinical and biological parameters only SBP (systolic blood pressure) before treatment and creatinine make significant statistically differences between the two clinical forms, with lower values of SBP in group of CDAHF IV NYHA (p = <0.001) and values of creatinine on admission higher for APE non ACS (Table 3).

Among the echocardiographyic parameters only the left ventricular ejection fraction (LVEF), p=0.07, left atrial diameter (LA), p=0.04, right atrio- ventricular gradient (RA/RV gradient), p=0.02 and deceleration time of transmitral flow E wave (DTE), p = 0.07, differentiate statistically or are at the borderline of the two clinical forms.

In-hospital mortality for the whole AHF group was 17.54%, distributed as follows: 7.89% patients had CDAHF IV NYHA and 9.64% as APE non ACS. A Chi- square type analysis shows a higher risk for in-hospital death for APE, as the clinical form at presentation, statistically significant with a RR of 1.1403, 95% CI 0.9993 -1.3013, or 2.0603 95% CI 1.0339 -4.1058, p = 0.057.

Among the clinical and biological parameters, were significantly correlated with IHM in the subgroup of CDAHF IV NYHA: SBP at presentation (p <0.001), serum urea at presentation (p <0.001) and sodium or admission (p = 0.004). ROC curve analysis for these parameters had identified a prognostic threshold value, statistically significant for each of them (Table 5). For APE only serum sodium was

Table 1 - Demographics date and risk factors in relation to the clinical form

Parameter	CDAHF NYHA IV	APE non ACS	Differences with statistically value
Gender M(%)	55.89%(76)	45.65%(42)	p=0.1
Mean age	73.32	73.6	p=0.8
Hypertension	69.12%	89.13%	RR 1.51, 95%CI, 1.2489 – 1.9313, p<0.001
Dyslipidemia	39.71%	76.09%	RR 1.81, 95%CI, 1.4475 - 2.2646, p<0.001
DM type II	32.35%	76.09%	p< 0.001
Active smoking	14.71%	13.04%	p=0.7

Table 2 - Comorbidities in relation to clinical forms

Parameter	CDAHF NYHA IV	APE non ACS	Differences with statistically value
COPD	14.71%	15.22%	p=0.9,
Stroke history	10.29%	8.7%	p=0.6
Fibrillation / atrial flutter	33.82%	19.56%	p=0.006
pre-existing AHF	100%	80.43%	p<0.001
Documented coronary heart disease	51.47%	47.83%	p=0.5

Table 3 - Clinical and laboratory characteristics in relation to clinical forms

Clinical parameter	CDAHF IV NYHA	APE non ACS	Statistical value
SBP before treatment	145.33 +/- 33.37 mmHg	174.06 +/- 37.9 mmHg	p<0.001
Heart rate before treatment	94.54+/- 24.10 bpm	94.86+/-23.8 bpm	p=0.9
Serum urea on admission	55.74+/-33.73 mg/dl	61.82+/-35.12 mg/dl	p=0.1
Serum creatinine on admission	1.06+/-1.43 mg/dl	1.59+/-1.42 mg/dl	p=0.043
Serum Sodium on admission	131.82+/-23.54mEq/l	135.84 +/-5.70 mEq/l	p=0.4
Hemoglobin	12.92+/-2.08 g/dl	12.91+/-2.45 g/dl	p=0.9

Table 4 - Echocardiographic parameters in relation to clinical forms

Parameter	CDAHF IV NYHA	APE non ACS	Statistical value
LVEF	45.90+/11.99	48.72+/-11.57	p=0.07
LA diameter	47.32+/-7.68	45.36+/-6.47mm	p=0.046
DTE	187.73+/-69.82	204.95 +/- 73.58 ms	p=0.076
RA/RV gradient	38.18+/-17.39	32.29+/-13.84 mmHg	p=0.020

Table 5 - Clinical and biological parameters in relation to in-hospital mortality and clinical form (univariate analysis)

Clinical – biological parameter	APE non ACS		CDAHF IV NYHA	
	Prognosis value	Threshold value	Prognosis value	Threshold value
SBP on admission	p=0.9	-	p<0.001	100 mmHg
HR before treatment	p=0.4	-	p=0.5	-
Serum ureea on admission	p=0.8	-	p<0.001	66.9mg/dl
Serum creatinine on admission	p=0.7	-	p=0.07	1.25mg/dl
Seum sodium on admission	p<0.001	130 mEq/l	p=0.004	130.2mEq/l

statistically significantly correlated IHM ($p < 0.001$) (Table 5).

In-hospital mortality prognostic value (IHM) of the ecocardiographic parameters differs too, depending on the clinical form, such as, for CDAHF IV NYHA are positive predictive, in univariate analysis: LA diameter ($p = 0.03$), S wave velocity on tissue Doppler interrogation at the lateral mitral annulus side, S/TDI ($p = 0.01$), DTE ($p < 0.001$), the ratio between the E wave's flow transmitral and E' wave flow tissue Doppler at lateral mitral annulus side, E / E' ($p < 0.001$), tricuspid annular plane systolic excursion (TAPSE), $p < 0.001$, gradient RA/RV ($p = 0.003$); of these only the E/E' ratio and RA/RV gradient > 47 mmHg are independent predictors in multivariate analysis. For APE non ACS statistically significant correlation with IHM for LVEF ($p = 0.02$), left ventricle end diastolic diameter, LVd ($p = 0.006$), DTE ($p = 0.003$), E/E '($p = 0.009$), TAPSE ($p < 0.001$) acceleration time of pulmonary artery flow, ATAP ($p < 0.001$) and gradient RA/RV ($p < 0.001$). Of these, only DTE < 196 ms and LVd > 54 mm have proven independent prognostic value in multivariate analysis. Many of the evaluated echo parameters lose their predictive value in analysis per etiology. That may explain the small number of parameters remained with independent value.

Discussion

Similar to the literature data, in our analysis there were identified differences between the two clinical forms both in terms of risk factors and comorbidities and in terms of clinical and biological parameters. Most majority of registers [ADHERE (3), ROAHFS (2), ATTEND (4)] analyze the prognostic value of some clinical, biological and echo parameters, in the AHF syndrome and less for each form individually. In our analysis, clinical and biological parameters proven with prognostic value in the registers (2,3) and literature (5, 8) - lower systolic blood pressure, seric ureea at presentation, serum sodium, were independently and significantly associated only with CDAHF IV NYHA. APE non ACS, clinical entity with particular pathophysiological mechanisms and hemodynamic profile, has associated only serum sodium on admission with independent prognostic value, the rest of the predictive parameters being etiologic and echocardiographic, expressing left (LVEF) and right pump (TAPSE) dysfunction, left ventricular high filling pressures (E/E', DT) and increased lung vascular resistance (ATAP, gradient RA/RV); data that differ from the results of ALARM HF (1) where reduced LVEF, serum creatinine > 1.6 mg /dL and low systolic blood pressure were statistically significantly associated with in-hospital mortality in APE, however similar with the literature data, which analyze ultrasound prognostic parameters in APE (6). Differences can be explained through the small group of our analysis and that our analysis excluded acute coronary syndromes APE associated.

Conclusions

Different as clinical picture at presentation as well as the pathophysiological mechanisms, between the two clinical forms, CDAHF IV NYHA and APE non ACS , there are both differences and similarities as well. Ischemic etiology is a common denominator. Clinical and biological parameters with proven prognostic value in literature, low SBP at presentation, serum urea and serum sodium on admission were associated in our work, with in-hospital mortality only in CDAHF IV NYHA . APE non ACS patients presented had a 1.14 times greater risk, statistically significant ($p = 0.05$), of in-hospital mortality than those with CDAHF IV NYHA. Parameters associated with adverse prognosis in APE non ACS are rather ultrasonographically, expressing the right and left pump dysfunction, increased vascular resistance and high pressures of LV filling and less clinical and biological (sodium presentation).

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