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ORIGINAL ARTICLE
Rare diseases of the heart

Different biochemical profile of stable and decompensated systolic heart failure patients due to ischemic or dilated cardiomyopathy hospitalized in the tertiary cardiology center (RCD code: III-1)

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Abstract

Aim: This study aims to compare the extended biochemical profile of unselected and consecutive systolic heart failure (SHF) patients admitted electively and urgently to the tertiary cardiology center. **Methods:** This study is a retrospective analysis of the 310 consecutive SHF patients who were hospitalized between January 2011 till December 2013. Data about health status of the patients, medications, as well as laboratory data, including indicators of myocardial damage, such as high–sensitivity troponins (hs-Tn), MB isoform of creatin kinase (CK-MB), marker of myocardial strain (NT-proBNP) and inflammatory parameters [high-sensitivity C-reactive protein (hs-CRP) and white blood cell count (WBC)] were gathered from medical histories and documentations. **Results:** Out of 310 patients more than a half (n=172, 55%) were admitted electively. Urgent patients had higher heart rate, NYHA class, and lower left ventricular ejection fraction (EF). Elective ischemic cardiomyopathy (ICM) patients were more likely to be older male with higher EF, and increased level of hs-TnT and CK-MB. As for urgent admissions, the frequency of male sex was similar in both groups but ICM patients were significantly older, had worse kidney function, and increased level of hs-TnT and NT-proBNP than patients with dilated cardiomyopathy (DCM). **Conclusions:** Systolic HF patients admitted electively and urgently differ significantly. Moreover, patients with different HF etiologies, such as ischemic and dilated cardiomyopathy, admitted either electively or urgently have different profiles. The observed elevation of ischemic and inflammatory parameters in decompensated HF may indicate possible mechanisms of HF worsening, leading to the acute admissions. The true meaning of the observations as well as potential additional anti-inflammatory and/or anti-ischemic treatment in stable HF to prevent acute episodes could a subject for further studies. JRCD 2014; 1 (7): 7–12

Key words: management, laboratory findings, acute heart failure

Aim

Differences in the characteristics of stable and decompensated systolic heart failure (SHF) patients are expected. Nevertheless, the direction and magnitude of those differences are less clearly defined. This study aims to compare the extended biochemical profile of unselected and consecutive SHF patients admitted electively and urgently to the tertiary cardiology center. Furthermore, the direct comparison of biochemical profile between ischemic (ICM) and dilated (DCM) cardiomyopathy was performed.

Methods

This study is a retrospective analysis of the 310 consecutive SHF patients with who were hospitalized in the tertiary cardiac Center between January 2011 till December 2013. There were two main reasons for hospitalization: elective and urgent. Planned or elective hospitalizations served mostly for diagnostic purposes and/or optimization of the management, e.g. qualification for revascularization or valve surgery, heart transplantation, or cardiac resynchronization therapy. On the other spectrum were

Conflict of interest: none declared.

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Table 1. Baseline comparison of electively and urgently admitted systolic heart failure patients

Parameter	Elective admission n=172 (55% of total)	Urgent admission n=138 (45% of total)	p-value
Male sex	126 (73%)	113 (82%)	0.07
Age [years]	58.8 ± 13.4	61.4 ± 13.9	0.1
BMI [kg/m^2]	27.2 ± 6.3	27.6 ± 6.7	0.7
HR [bpm]	**75.4 ± 15.2**	**80.2 ± 18.4**	**0.02**
SBP [mmHg]	119 ± 20.5	121.3 ± 24.7	0.56
NYHA class	**2.6 ± 0.7**	**3.1 ± 0.9**	**< 0.001**
Leading cardiac rhythm: – sinus – atrial fibrillation – paced	 112 52 8	 82 48 8	 0.6
Ejection fraction [%]	**30.7 ± 11.2**	**27.8 ± 12.3**	**0.03**
Creatinine [umol/l]	96.1 ± 66.6	104 ± 53.1	0.2
eGFR [ml/min]	72.9 ± 17.1	71.2 ± 21.1	0.4
Hemoglobin [g/dl]	**14.2 ± 1.5**	**13.7 ± 1.9**	**0.02**
RBC [10^6/µl]	4.7 ± 0.5	4.6 ± 0.6	0.1
Sodium [mmol/l]	**140.7 ± 3**	**139.2 ± 3.4**	**0.001**
Potassium [mmol/l]	**4.5 ± 0.4**	**4.3 ± 0.5**	**0.005**
WBC [10^3/µl]	**7.7 ± 2.2**	**8.6 ± 3.4**	**0.01**
AlAt [U/l]	**30.2 ± 19.3**	**60.1 ± 105.1**	**0.001**
AspAt [U/l]	**26.9 ± 10.4**	**57.5 ± 105**	**0.001**
hs-CRP [mg/dl]	**5.7 ± 10.4**	**19.3 ± 39.7**	**0.01**
Troponin T [ng/ml]	**0.028 ± 0.022**	**0.21 ± 0.046**	**0.04**
CK [U/l]	**92.2 ± 48.6**	**249.6 ± 434.9**	**0.01**
CK-MB [U/l]	**14.6 ± 4.1**	**32.8 ± 40.3**	**0.03**
NT-proBNP [pg/ml]	**2172.2 ± 2645**	**4614.3 ± 5835.6**	**0.0003**

BMI – body mass index; HR – heart rate; SBP – systolic blood pressure; NYHA – New York Heart Association; eGFR – estimated glomerular filtration rate; RBC – red blood cells; WBC – white bllod cells; AlAt – alanine transaminase; AspAT – aspartate transaminase; hs-CRP – high sensitivity C-reactive protein; CK – creatinine kinase; CK-MB – MB creatinine kinaze; NT-proBNP – N-terminal of the prohormone brain natriuretic peptide

urgent hospitalizations for acutely or sub-acutely decompensated SHF. Only patients with clearly defined etiology of SHF were included and comprised two study groups of ischemic (ICM) and dilated (DCM) cardiomyopathy. Data about health status of the patients, medications, as well as laboratory data, including indicators of myocardial damage, such as high–sensitivity troponins (hs-Tn), MB isoform of creatin kinase (CK-MB), marker of myocardial strain (NT-proBNP) and inflammatory parameters [high-sensitivity C-reactive protein (hs-CRP) and white blood cell count (WBC)] were gathered from medical histories and documentations. Estimated GFR (eGFR) was calculated according to the Cockcroft-Gault formula.

Statistical analysis

Data were analyzed using SPSS 17.0 software. Continuous variables are presented as mean ± SD and are compared using Student's t test. Categorical variables are expressed as absolute numbers and percentages and are compared using the chi-square test or the Fisher exact test, as appropriate. Significance of differences was tested by Mann-Whitney U test. Differences between proportions were analyzed with the chi-square test. Differences were considered significant for $P < 0.05$.

Table 2. Comparison of electively and urgently admitted systolic heart failure patients within the groups of dilated and ischemic cardiomyopathy

Parameter	DCM (n = 172	group (55%)	p-value	ICM (n = 138)	group 45%)	p-value
	elective admission n=105 (61%)	urgent admission n=67 (39%)		elective admission n=67 (49%)	urgent admission n=71 (51%)	
Male sex	**71 (67%)**	**55 (82%)**	**0.03**	55 (82%)	58 (82%)	0.9
Age [years]	54.7 ± 14.2	55.1 ± 14.5	0.8	64.5 ± 9.4	67.1 ± 10.2	0.1
BMI [kg/m^2]	26.7 ± 6.5	27.8 ± 7.8	0.5	26.6 ± 5.9	26.2 ± 4.2	0.8
HR [bpm]	76.8 ± 16.2	82.5 ± 21.7	0.05	73.1 ± 13.5	77.7 ± 14.3	0.06
SBP [mmHg]	116.5 ± 20.7	121.6 ± 21.2	0.2	123.3 ± 19.6	120 ± 28.8	0.6
NYHA class	**2.6 ± 0.7**	**2.9 ± 1**	**0.05**	**2.6 ± 0.7**	**3.2 ± 0.8**	**0.02**
Rhythm:			0.4			0.7
– sinus	67	36		45	46	
– AF	34	27		18	20	
– paced	4	4		4	5	
Ejection fraction [%]	29.3 ± 10.3	26.9 ± 13.9	0.2	**32.8 ± 11.8**	**28.8 ± 10.5**	**0.04**
Creatinine [umol/l]	94.7 ± 82.6	94.7 ± 22.9	0.9	98.1 ± 30.9	114.7 ± 68.4	0.07
eGFR [ml/min]	86.9 ± 8.5	86.4 ± 16.8	0.8	82.8 ± 12	79.6 ± 24	0.6
Hemoglobin [g/dl]	13.8 ± 1.3	13.5 ± 1.8	0.17	13.7 ± 1.8	13.2 ± 2	0.15
RBC [10^6/µl]	4.3 ± 0.5	4.3 ± 0.6	0.9	4.2 ± 0.7	4.1 ± 0.7	0.3
Sodium [mmol/l]	**140.7 ± 3.1**	**139.1 ± 3.7**	**0.003**	**140.6 ± 3.1**	**138.9 ± 3**	**0.001**
Potassium [mmol/l]	4 ± 0.5	3.9 ± 0.6	0.3	**4.1 ± 0.4**	**3.9 ± 0.6**	**0.05**
WBC [10^3/µl]	7.4 ± 2.4	7.7 ± 2.4	0.5	**7.1 ± 2.1**	**8.5 ± 4.1**	**0.02**
AlAt [U/l]	**31.4 ± 18.7**	**73.8 ± 128.7**	**0.02**	**28.5 ± 20.4**	**49.5 ± 87.1**	**0.05**
AspAt [U/l]	**27.9 ± 10.5**	**55.3 ± 88.2**	**0.01**	**25.3 ± 10.3**	**60.7 ± 121.7**	**0.02**
hs-CRP [mg/dl]	**4.6 ± 8.1**	**15.6 ± 28.9**	**0.01**	**6.5 ± 13.5**	**21.7 ± 40.9**	**0.02**
Troponin T [ng/ml]	0.02 ± 0.01	0.1 ± 0.26	0.2	0.047 ± 0.03	0.29 ± 0.55	0.3
CK [U/l]	88.3 ± 50.8	201.3 ± 259	0.08	114 ± 31.2	282.5 ± 525.9	0.5
CK-MB [U/l]	**13.6 ± 3.1**	**28.8 ± 30.6**	**0.03**	20.7 ± 4	35.8 ± 46.5	0.6
NT-proBNP [pg/ml]	**2195 ± 2616**	**3259 ± 2675**	**0.05**	**2132 ± 2727**	**6119 ± 7673**	**0.004**

DCM – dilated cardiomyopathy; ICM – ischemic cardiomyopathy; BMI – body mass index; HR – heart rate; SBP – systolic blood pressure; NYHA – New York Heart Association; eGFR – estimated glomerular filtration rate; RBC – red blood cells; WBC – white bllod cells; AlAt – alanine transaminase; AspAT – aspartate transaminase; hs-CRP – high sensitivity C-reactive protein; CK – creatinine kinase; CK-MB: MB creatinine kinaze; NT-proBNP – N-terminal of the prohormone brain natriuretic peptide

Results

Out of 310 patients more than a half (n=172, 55%) were admitted electively (Table 1). Unsurprisingly urgent patients had higher heart rate, NYHA class, and lower left ventricular ejection fraction (EF). However, elective and urgent patients did not differ in terms of age, systolic blood pressure, and leading cardiac rhythm. Although it did not reach statistical significance, nevertheless, there was an obvious trend towards male sex prevalence in urgent admissions. The other unexpected findings were similar levels of kidney parameters in elective and urgent patients. Although both groups had normo-natremia and normo-kaliemia but urgent patients had significantly lower level of natrium and kalium. Moreover, there were significant differences in terms of liver function tests as well as inflammatory (WBC and hs-CRP) parameters. Additionally, cardiac markers of myocardial damage were much more elevated in the urgent group. Finally, NT-proBNP level was significantly increased in the urgent group but standard deviations (SD) in both groups were very wide.

Table 3. Direct comparison of DCM and ICM patients within the elective and urgent systolic heart failure patients

Parameter	Elective (n = 172)	admission (55%)	p-value	Urgent (n = 138)	admission (45%)	p-value
	ICM group n=67 (39%)	DCM group n=105 (61%)		ICM group n=71 (51%)	DCM group n=67 (49%)	
Male sex	**55 (82%)**	**71 (67%)**	**0.03**	58 (82%)	55 (82%)	0.9
Age [years]	**64.5 ± 9.4**	**55 ± 14.4**	**0.001**	**67.1 ± 10.2**	**55.3 ± 14.6**	**0.001**
BMI [kg/m^2]	26.5 ± 5.9	26.7 ± 6.5	0.9	26.1 ± 4.2	27.8 ± 7.9	0.4
HR [bpm]	73.1 ± 13.5	76.9 ± 16	0.1	77.7 ± 14.3	82.3 ± 22	0.1
SBP [mmHg]	123.3 ± 19.6	116.9 ± 20.8	0.2	119.9 ± 28.8	122.5 ± 21.4	0.6
NYHA class	2.6 ± 0.8	2.6 ± 0.8	0.6	3.2 ± 0.8	2.8 ± 1	0.1
Ejection fraction [%]	**32.8 ± 11.8**	**29.3 ± 11.3**	**0.04**	28.7 ± 10.5	26.9 ± 14	0.4
Creatinine [umol/l]	98.1 ± 30.9	94.5 ± 82.2	0.7	**114.7 ± 68.4**	**92.8 ± 26.2**	**0.01**
eGFR [ml/min]	82.8 ± 12	86.9 ± 8.5	0.1	79.6 ± 24	86.4 ± 16.8	0.3
Hemoglobin [g/dl]	13.7 ± 1.8	13.8 ± 1.2	0.7	13.2 ± 2	13.5 ± 1.8	0.4
RBC [10^6/µl]	4.2 ± 0.7	4.3 ± 0.5	0.6	4.1 ± 0.7	4.3 ± 0.6	0.1
Sodium [mmol/l]	140.6 ± 3	140.7 ± 3	0.9	138.9 ± 3	139 ± 3.7	0.7
Potassium [mmol/l]	4.1 ± 0.4	4 ± 0.5	0.2	3.9 ± 0.6	3.9 ± 0.5	0.9
WBC [10^3/µl]	7.1 ± 2	7.4 ± 2.4	0.4	8.5 ± 4.1	7.6 ± 2.3	0.1
AlAt [U/l]	28.5 ± 20.5	31.3 ± 18.7	0.4	49.5 ± 87.1	72.5 ± 128.9	0.2
AspAt [U/l]	25.3 ± 10.3	20.8 ± 10.5	0.1	60.7 ± 121.1	53.9 ± 82.3	0.7
hs-CRP [mg/dl]	6.5 ± 13.5	4.5 ± 8	0.2	21.7 ± 41.8	15.8 ± 21.2	0.4
Troponin T [ng/ml]	**0.047 ± 0.036**	**0.023 ± 0.02**	**0.03**	**0.295 ± 0.55**	**0.107 ± 0.27**	**0.05**
CK [U/l]	114 ± 31.2	88.3 ± 50.8	0.4	282.5 ± 526	204 ± 263	0.4
CK-MB [U/l]	**20.7 ± 10.4**	**13.6 ± 3.2**	**0.02**	35.8 ± 46.5	28.9 ± 31.1	0.4
NT-proBNP [pg/ml]	2132 ± 2727	2195 ± 2616	0.9	**6119 ± 7673**	**3186 ± 2669**	**0.02**

DCM – dilated cardiomyopathy; ICM – ischemic cardiomyopathy; BMI – body mass index; HR – heart rate; SBP – systolic blood pressure; NYHA – New York Heart Association; eGFR – estimated glomerular filtration rate; RBC – red blood cells; WBC – white bllod cells; AlAt – alanine transaminase; AspAT – aspartate transaminase; hs-CRP – high sensitivity C-reactive protein; CK – creatinine kinase; CK-MB – MB creatinine kinaze; NT-proBNP: N-terminal of the prohormone brain natriuretic peptide

The comparison of elective and urgent patients within the etiological groups of DCM and ICM is presented in the Table 2. Importantly, more DCM patients were admitted electively in contrast to ICM group where acute and planned hospitalizations were equally distributed. Although male sex was more frequent in both groups but there were more men in DCM patients admitted acutely, whereas the number of male patients did not differ in acute and stable ICM group. Interestingly, EF did not differ in elective and urgent DCM patients but was significantly lower in acute ICM patients. Although hs-CRP was significantly increased in both acute DCM and ICM patients in comparison to stable patients, WBC were only increased in acute ICM patients. There were not differences between acute and stable DCM and ICM patients in terms of troponins and CKs, however, CK-MB was significantly increased in acute DCM patients in contrast to stable DCM group. An anticipated findings were increased level of NT-proBNP in acute DCM and ICM patients.

The direct comparison was made between DCM and ICM patients dived according to the type of admission and presented in the Table 3. Elective ICM patients were more likely to be older male with higher EF, and increased level of hs-TnT and CK-MB. Importantly, although grossly elevated in both groups, nevertheless, NT-proBNP was comparable in ICM and DCM patients. As for urgent admissions, the frequency of male sex was similar in both groups but ICM patients were significantly older, had worse kidney function, and increased level of hs-TnT and NT-proBNP.

Lastly, the pre-admission therapy was analyzed in details (Table 4). Generally, both elective and urgent group were very well

Table 4. Comparison of the pre-hospital therapy in electively and urgently admitted systolic heart failure patients

Parameter	Elective admission n=172 (55%)	Urgent admission n=138 (45%)	p-value
Beta-blockers	157 (91%)	121 (87%)	0.4
–% of maximal dose	36 ± 28	33 ± 24	0.2
- type of beta-blocker			0.5
– carvedilol	82	74	
– bisoprolol	45	29	
– metoprolol succinate	18	12	
– nebivolol	6	3	
– others	6	2	
ACE-inhibitors	**148 (86%)**	**97 (70%)**	**0.03**
–% of maximal dose	45 ± 26	49 ± 36	0.2
- type of ACE-inhibitor			0.1
– ramipril	95	62	
– perindopril	47	25	
– lisinopril	0	2	
– enalapril	2	0	
– chinapril	1	0	
– others	6	8	
Mineralocorticoid antagonists	122 (71%)	96 (69%)	0.4
- spironolactone	97	68	0.2
– eplerenone	24	26	
Angiotensin receptor antagonists	9 (5%)	7 (5%)	0.8
Furosemide	95 (55%)	72 (52%)	0.9
– dose of Furosemide [mg]	75 ± 65	75 ± 80	0.95
Other diuretics (torasemide, indapamide, hydrochlorotiazide)	44 (25%)	41 (32%)	0.2
Digoxin	28 (16%)	26 (19%)	0.3
Vitamin K antagonists	46 (26%)	33 (24%)	0.8
Acetylosalicic acid	90 (52%)	80 (58%)	0.09
Statin	117 (68%)	79 (57%)	0.2
Amiodarone	17 (10%)	9 (6%)	0.3

ACE – angiotensin converting enzyme

treated with high penetration of beta-blockers, ACE-inhibitors, and aldosterone antagonists. Surprisingly, the only significant difference between elective and urgent patients was in the distribution of ACE-inhibitors, which were used more often in stable patients. All other medications, as well as mean dosages, were comparable between two groups. Although it did not reach statistical difference but prescription of acetylsalicylic acid was more prevalent in acutely admitted patients.

Discussion

Thanks to better management of most cardiac disorders the prevalence of SHF is constantly increasing [1]. Stable and unstable SHF patients are interchangeable and represent two sides of the coin as in most cases compensated, even long-term periods are interrupted with acute or sub-acute worsening. Once stable patient, who is improperly managed or develop acute complications, e.g. acute coronary syndrome, serious arrhythmia, infection, etc. can easily deteriorate [1]. Intuitively, we suspect that there should be numerous differences between stable and unstable SHF patients, nevertheless, the exact characterization of those two groups is less clear. Importantly, in this contemporary analysis systolic blood pressure of elective and acute patients did not differ. This finding may come as a kind of big surprise as we frequently associate decompensated SHF with low blood pressure or even cardiogenic shock [2]. Perhaps, our study group is not representative for the whole SHF population, nevertheless, this is an interesting and unexpected finding. This may be in line with the concept of 'vascular' mechanism of SHF decompensation rather than pure

'cardiac' mechanism where critical state of the heart drive patients into cardiogenic shock [3]. In the contemporary optimal management of SHF, and our study group is undoubtedly very well treated, there are rather uncontrolled blood pressure, chronic fluid overload, infection, arrhythmias as the primary reasons for decompensation. Fortunately, those patients are usually not in critical state as was found by Rudiger et al. in a relatively recent study where only 4% out of 312 acutely decompensated HF were in cardiogenic shock [4]. The other potential mechanism of decompensation could be chronic anemia common in SHF. Similar to other studies, our acute patients had significantly lower hemoglobin level [5, 6]. Similarly to previous studies, the unspecific marker of inflammation, namely C-reactive protein was elevated in stable SHF [7]. Furthermore, CRP was significantly higher in acute SHF, which may indicate into an inflammation as an important mechanism of decompensation. This finding should be probably interpreted in the wider context of chronic elevation of not only inflammatory parameters (CRP, WBC) but also cardiac necrotic parameters (troponins, CK-MB) and marker of myocardial strain (NT-proBNP) in chronic and compensated SHF. Consequently, those parameters significantly rise in sub-acute or acute SHF [8]. It may be that they are solely markers of decompensation or acute reason for exacerbation, e.g. fluid overload causing elevation of BNP or acute coronary syndrome in ICM and increase of troponins [8, 9]. Moreover, the comparison was made between patients with ICM and DCM admitted electively or acutely. Ischemic and dilated cardiomyopathy represent two different gross cardiac pathologies that eventually lead to the uniform definition of SHF. As the initial pathology as well as natural course, triggering mechanisms, response to therapy and survival differ between those two, therefore it is important to precisely understand those differences as they may affect our management [10, 11]. However, only few differences were actually found, such as the elective ICM patients were significantly older, had lower EF, elevated necrotic markers otherwise they were indistinguishable from DCM patients. On the other hand, acute ICM patients were older, had worse kidney function, and grossly elevated troponins and NT-proBNP but the rest of assessed parameters were comparable. These results could be important as it seems apparent that once cardiac pathology is so advanced that leads to SHF, the initial differences between ICM and DCM slowly diminish. Finally, it should be acknowledged that those SHF patients were well managed according to contemporary HF guidelines [1]. Of note, although this observation did not reach statistical difference, nevertheless, there was an obvious trend towards Aspirin prevalence in decompensated SHF. This finding is difficult to interpret as results of large-scale studies on the role of Aspirin are conflicting [12, 13]. The recent statement from the group of experts on the anticoagulation in HF urge to caution in the wide-spread use of Aspirin in HF [14]. Perhaps underutilization of ACE-I in urgently admitted patients (70% on ACE-I) is another important factor contributing to worsening of HF in this group.

Conclusions

Systolic HF patients admitted electively and urgently differ significantly. Moreover, patients with different SHF etiologies, such as ischemic and dilated cardiomyopathy, admitted either electively or urgently have different profiles. The observed elevation of ischemic and inflammatory parameters in decompensated HF may indicate possible mechanisms of HF worsening, leading to the acute admissions. The true meaning of the observations as well as potential additional anti-inflammatory and/or anti-ischemic treatment in stable HF to prevent acute episodes could a subject for further studies.

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