

# Of the X and the Y – sex-specific differences in patients presenting with acute myocarditis.

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## Background

Biological sex has a paramount influence on the pathophysiology of diseases, and thus on clinical presentation. In this study, we provide a comprehensive analysis of sex-specific differences in patients with myocarditis, with regards to laboratory parameters, abnormalities on the electrocardiogram (ECG) and transthoracic echocardiography (TTE), as well as diagnostic procedures and outcome.

## Methods

Patients with myocarditis who were admitted to our study center in the time-period of 2009 to 2019 were retrospectively enrolled in this study. Clinical data, laboratory parameters and measurements from transthoracic echocardiography were extracted from hospital records. Follow-up was acquired for 2 years after admission.

## Results

224 patients with myocarditis were enrolled in this study. Of these, 78% were males and 22% females. Female patients were older (median 50 years vs. 35 years,  $p < 0.0001$ ), had a higher prevalence of respiratory tract infections and less frequently ST-segment elevations on ECG (28% vs. 59%,  $p = 0.003$ ). Furthermore, C-reactive protein was lower in females (median 0.60 mg/dl vs. 3.90 mg/dl,  $p < 0.0001$ , see Table 1), but showed a less pronounced decrease within three days when compared to males (fold-change 1.00 vs. 0.80,

$p = 0.002$ , see Figure 1 and Table 1). Cardiac MRI was conducted less often in females, whereas time to coronary angiography was significantly longer. We found no difference in LV systolic function or all-cause-mortality between the two sexes (see Table 2).

## Conclusions

We observed sex-specific differences in laboratory parameters, abnormalities on ECG and diagnostic procedures conducted in patients with myocarditis. Understanding these differences, both at the cellular level and in regards to the clinical presentation of patients, could be helpful in the diagnosis and treatment of this disease and could further expand our understanding of its pathophysiology.

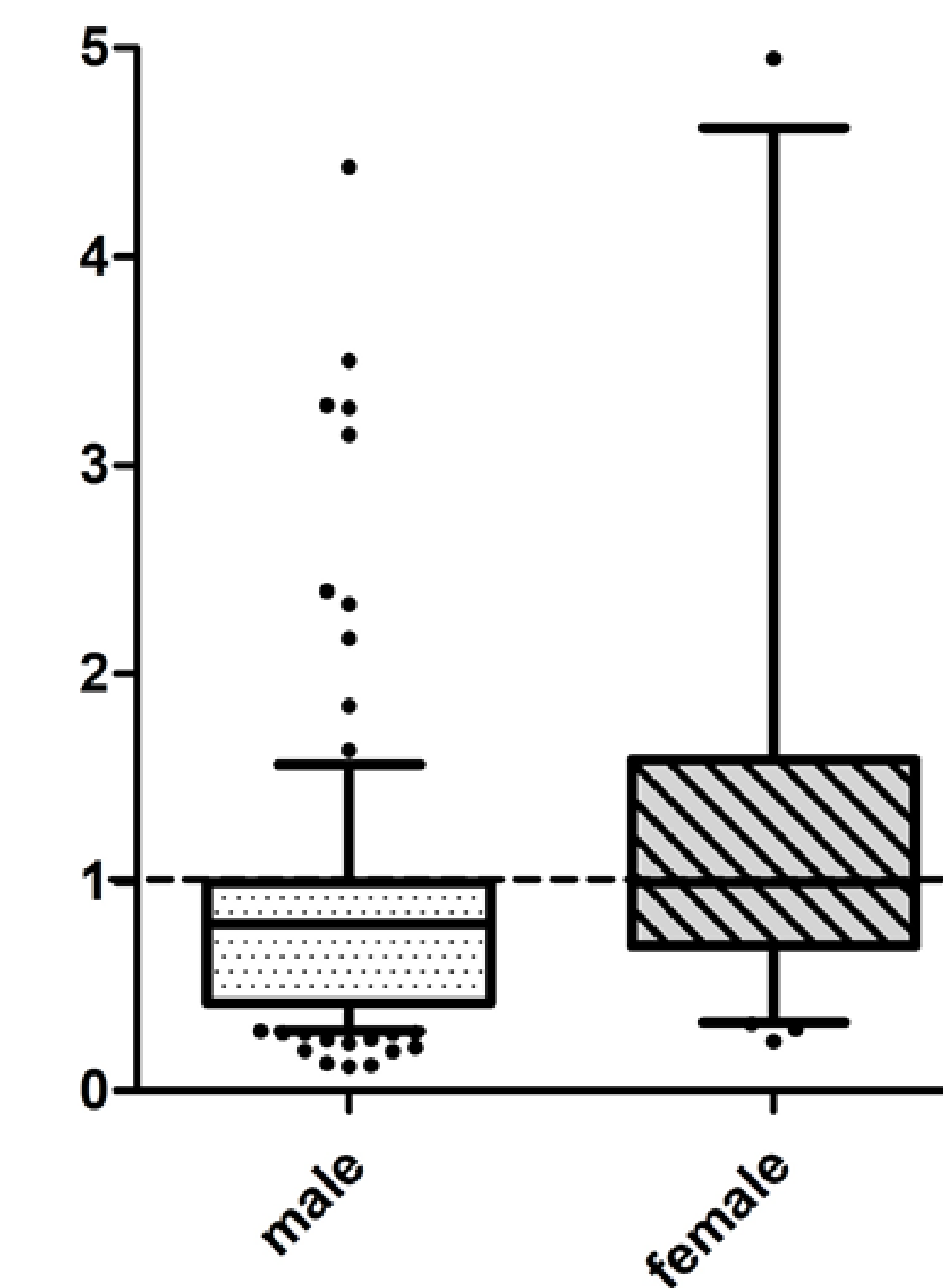


Figure 1: Sex-specific fold-change of C-reactive protein (CRP) within three days after hospital admission

	female (n= 50)		male (n= 174)		
Diagnostic procedures and outcome	%	n	%	n	p-value
Coronary angiography	40	20	43	75	0.747
Coronary CT	16	8	11	19	0.460
Myocardial scintigraphy	2	1	1	2	0.990
Cardiac MRI	61	30	79	136	0.015
Endomyocardial biopsy	16	8	5	9	0.019
All-cause-mortality (24 months)	2	1	2	3	0.990
	median	IQR	median	IQR	p-value
Δ EF to 3-6 months (%)	0.0	-9.0-5.0	0.0	-3.1-9.8	0.510
FC EF to 3-6 months	1.00	0.85-1.15	1.00	0.95-1.20	0.638
Time to coronary angiography	2	0-4	0	0-1	0.001
Time to cardiac MRI	8	2-17	6	3-16	0.864
Time to endomyocardial biopsy	11	1-238	3	2-23	0.536
Time to coronary CT	3	1-4	1	0-3	0.198
Time to myocardial scintigraphy	30	30-30	5	4-5	0.990

Table 2: Diagnostic procedures conducted and outcomes between males and females. Abbreviations: CT= computed tomography, MRI= magnetic resonance imaging, FC= fold-change, EF= ejection fraction.

	female (n= 50)		male (n= 174)		
Laboratory findings	median	IQR	median	IQR	p-value
Creatinine (mg/dl)	0.80	0.70-0.90	0.92	0.83-1.10	<0.0001
eGFR (ml/min/1.73m <sup>2</sup> )	70.0	68.0-70.0	70.0	70.0-70.0	0.098
C-reactive protein (CRP) (mg/dl)	0.60	0.60-3.98	3.90	0.60-8.30	<0.0001
Bilirubin (mg/dl)	0.30	0.40-0.50	0.60	0.40-0.80	<0.0001
AST (IU/l)	28.0	21.0-40.0	42.5	29.0-60.3	0.007
ALT (IU/l)	18.0	14.0-32.0	31.5	21.0-46.5	0.001
LDH (IU/l)	170.0	154.0-237.5	206.0	173.0-242.3	0.024
				106.0-	
Creatinine kinase (CK) (IU/l)	97.5	58.3-184.5	211.0	412.5	<0.0001
CK-MB (%)	10.1	8.3-19.4	10.2	7.1-13.5	0.386
High sensitivity troponin (hsTnT) (ng/l)	73.0	8.5-302.5	179.0	17.4-543.5	0.101
pro brain natriuretic peptide (pBNP) (ng/l)	287.8	129.0-2799.5	294.6	101.3-760.3	0.188
				312.0-	
Fibrinogen (mg/dl)	371.5	281.0-555.0	405.0	552.0	0.600
Hemoglobin (mg/dl)	12.9	12.2-13.6	14.9	14.0-15.7	<0.0001
Leukocyte count (G/l)	8.72	6.83-11.70	8.69	7.07-11.55	0.895
				174.3-	
Thrombocyte count (G/l)	261.5	217.3-299.8	215.0	247.8	<0.0001
Interleukin 6 (pg/ml)	54.3	7.2-74.3	27.7	8.0-83.0	0.990
Procalcitonin (µg/l)	0.15	0.10-0.20	0.20	0.10-0.40	0.324
Neutrophil to lymphocyte ratio	3.39	1.49-4.73	2.20	1.51-4.71	0.465
Eosinophil to lymphocyte ratio	0.05	0.03-0.13	0.07	0.02-0.16	0.967
Basophil to lymphocyte ratio	0.01	0.00-0.02	0.02	0.00-0.02	0.734
Monocyte to lymphocyte ratio	0.42	0.32-0.54	0.42	0.27-0.60	0.903
Deltas (Δ) and fold-changes (FC)	median	IQR	median	IQR	p-value
Δ CRP (mg/dl)	0.0	-0.7-0.8	-1.0	-3.6-0.0	0.001
FC CRP	1.00	0.70-1.58	0.80	0.42-1.00	0.002
				-77.3-	
Δ hsTnT (ng/l)	-4.0	-116.5-23.5	1.5	257.0	0.209
FC hsTnT	0.98	0.59-1.56	1.06	0.73-2.17	0.255
				-1169.3-	
Δ pBNP (ng/l)	-24.8	235.5	-28.0	92.8	0.720
FC pBNP	0.75	0.66-1.22	0.83	0.44-1.49	0.699
Δ CK (IU/l)	-30.0	-90.0--6.0	-87.0	-283.0--4.5	0.029
FC CK	0.70	0.46-0.90	0.57	0.31-0.94	0.177

Table 1: Laboratory findings between males and females. Abbreviations: IQR= interquartile range, eGFR= estimated glomerular filtration rate, AST= aspartate transaminase, ALT= alanine transaminase, CK-MB= creatine kinase myocardial band, FC= fold-change.