

SUPPLEMENTARY MATERIAL

Supplementary table 1. Demographic characteristics and maximal cardiopulmonary exercise testing indexes of patients with chronic heart failure of different severity based on predicted peak VO₂

Demographic characteristics	Group 1	Group 2
Number of patients (N)	25	24
Gender (<i>Males/Females</i>)	20 / 5	21 / 3
Age (years) ^a	51 ± 10	61 ± 7
Height (cm) ^a	175 ± 12	174 ± 8
Weight (kg) ^a	97 ± 27	82 ± 14
NYHA stage (class II/III)	16 / 9	18 / 6
EF (%) ^a	32 ± 9	33 ± 8
Type of CHF		
Dilated cardiomyopathy [n (%)]	8 (32%)	4 (17%)
Ischemic [n (%)]	12 (48%)	17 (71%)
Other (valvulopathy, etc) [n (%)]	5 (20%)	3 (12%)
Medication		
Diuretics [n (%)]	19 (76%)	13 (54%)
ACE inhibitors [n (%)]	12 (48%)	12 (50%)
ARBs [n (%)]	4 (16%)	3 (13%)
b Blockers [n (%)]	24 (96%)	24 (100%)
Aldosterone Antagonists [n(%)]	19 (76%)	18 (75%)
Cardiopulmonary exercise testing parameters		
Peak VO ₂ (ml/kg/min) ^a	15.7 ± 4.2	20.5 ± 3.2
Predicted peak VO ₂ (%) ^a	50 ± 9	77 ± 8
VE/VCO ₂ slope ^a	33 ± 4	34 ± 4
Peak WR (watts) ^a	86 ± 42	106 ± 36
Group 1: Predicted peak VO ₂ < 65.5%; Group 2: Predicted peak VO ₂ ≥ 65.5%		
NYHA, New York Heart Association; EF, ejection fraction; CHF, chronic heart failure; ACE, angiotensin-converting-enzyme; ARB, angiotensin II receptor blockers; VO ₂ , oxygen		

uptake; VCO_2 , carbon dioxide output; **WR**, work rate; **CPET**, cardiopulmonary exercise testing.

^a Values are expressed as mean \pm SD

Supplementary table 2. Demographic characteristics and maximal cardiopulmonary exercise testing indexes of patients with chronic heart failure of different severity based on VE/VCO₂ slope

Demographic characteristics	Group 1	Group 2
Number of patients (N)	27	22
Gender (<i>Males/Females</i>)	22 / 5	19 / 3
Age (years) ^a	54 ± 10	59 ± 9
Height (cm) ^a	177 ± 10	172 ± 9
Weight (kg) ^a	97 ± 25	80 ± 17
NYHA stage (class II/III)	16 / 9	12 / 10
EF (%) ^a	34 ± 8	30 ± 8
Type of CHF		
Dilated cardiomyopathy [n (%)]	10 (37%)	2 (9%)
Ischemic [n (%)]	13 (48%)	16 (73%)
Other (valvulopathy, etc) [n (%)]	4 (15%)	4 (18%)
Medication		
Diuretics [n (%)]	15 (56%)	17 (77%)
ACE inhibitors [n (%)]	14 (52%)	10 (46%)
ARBs [n (%)]	5 (19%)	2 (9%)
b Blockers [n (%)]	26 (96%)	22 (100%)
Aldosterone Antagonists [n(%)]	23 (85%)	14 (64%)
Cardiopulmonary exercise testing parameters		
Peak VO ₂ (ml/kg/min) ^a	17.9 ± 4.7	18.3 ± 4.2
Predicted peak VO ₂ (%) ^a	60 ± 15	67 ± 17
VE/VCO ₂ slope ^a	30 ± 2	38 ± 3
Peak WR (watts) ^a	102 ± 44	89 ± 33
Group 1: VE/VCO₂ slope < 32.5; Group 2: VE/VCO₂ slope ≥ 32.5		
NYHA, New York Heart Association; EF, ejection fraction; CHF, chronic heart failure; ACE, angiotensin-converting-enzyme; ARB, angiotensin II receptor blockers; VO ₂ , oxygen		

uptake; VCO_2 , carbon dioxide output; **WR**, work rate; **CPET**, cardiopulmonary exercise testing.

^a Values are expressed as mean \pm SD

Supplementary table 3. Demographic characteristics and maximal cardiopulmonary exercise testing indexes of patients with chronic heart failure of different severity based on EF

Demographic characteristics	Group 1	Group 2
Number of patients (N)	37	12
Gender (<i>Males/Females</i>)	32 / 5	9 / 3
Age (years) ^a	56 ± 10	56 ± 10
Height (cm) ^a	175 ± 10	174 ± 11
Weight (kg) ^a	87 ± 21	97 ± 29
NYHA stage (class II/III)	23 / 14	11 / 1
EF (%) ^a	29 ± 6	43 ± 3
Type of CHF		
Dilated cardiomyopathy [n (%)]	10 (27%)	2 (16%)
Ischemic [n (%)]	24 (65%)	5 (42%)
Other (valvulopathy, etc) [n (%)]	3 (8%)	5 (42%)
Medication		
Diuretics [n (%)]	25 (68%)	7 (58%)
ACE inhibitors [n (%)]	17 (46%)	7 (58%)
ARBs [n (%)]	5 (14%)	2 (17%)
b Blockers [n (%)]	36 (97%)	12 (100%)
Aldosterone Antagonists [n(%)]	28 (76%)	9 (75%)
Cardiopulmonary exercise testing parameters		
Peak VO ₂ (ml/kg/ min) ^a	18.1 ± 4.4	17.9 ± 4.5
Predicted peak VO ₂ (%) ^a	63 ± 16	62 ± 18
VE/VCO ₂ slope ^a	34 ± 5	33 ± 4
Peak WR (watts) ^a	96 ± 38	98 ± 46
Group 1: EF < 40%; Group 2: EF ≥ 40%		
<p>NYHA, New York Heart Association; EF, ejection fraction; CHF, chronic heart failure; ACE, angiotensin-converting-enzyme; ARB, angiotensin II receptor blockers; VO₂, oxygen uptake; VCO₂, carbon dioxide output; WR, work rate; CPET, cardiopulmonary exercise testing.</p>		

^a Values are expressed as mean \pm SD

Supplementary table 4. Acute mobilization of endothelial cellular populations after a symptom-limited cardiopulmonary exercise testing of 2 different severity groups according to the median value of predicted peak VO₂.

Endothelial cellular populations	Group 1 (25 patients) Predicted peak VO ₂ < 65.5%		Group 2 (24 patients) Predicted peak VO ₂ ≥ 65.5%		P value between groups
	<i>Before CPET</i>	<i>After CPET</i>	<i>Before CPET</i>	<i>After CPET</i>	
	CD34 ⁺ /CD45 ⁺ /CD133 ⁺	48 (25-75)	90 (43-103) ^a	46 (23-81)	
CD34 ⁺ /CD45 ⁺ /CD133 ⁺ /VEGFR ₂	1 (1-4)	5 (3-8) ^a	2 (1-3)	5 (3-9) ^a	0.821
CD34 ⁺ /CD133 ⁺ /VEGFR ₂	12 (8-16)	14 (11-29) ^b	11 (7-18)	14 (8-19)	0.333
CD34 ⁺ /CD45 ⁺ /CD133 ⁻	222 (155-312)	450 (219-658) ^a	198 (150-335)	352 (268-548) ^a	0.419
CD34 ⁺ /CD45 ⁺ /CD133 ⁻ /VEGFR ₂	1 (1-2)	3 (2-7) ^a	1 (1-2)	4 (2-5) ^a	0.610

VO₂, oxygen uptake; CPET, cardiopulmonary exercise testing.

Differences within each severity group ^aP<0.001 ^bP<0.05

Supplementary table 5. Spearman’s Rho correlations between numeric and percentage differences of cellular populations before and after cardiopulmonary exercise testing (CPET) and CPET parameters.

CELLULAR PARAMETERS		Ejection Fraction	Peak VO ₂	Predicted VO ₂	VE/VCO ₂ slope
Numeric difference in EPC₁ subgroup	<i>Correlation Coef.</i>	-.012	.127	.064	-.066
	<i>p value</i>	.935	.385	.664	.651
Numeric difference in CEC₁ subgroup	<i>Correlation Coef.</i>	.097	-.097	-.009	-.036
	<i>p value</i>	.508	.507	.951	.804
Numeric difference in EPC₂ subgroup	<i>Correlation Coef.</i>	.160	.252	.147	-.124
	<i>p value</i>	.273	.081	.315	.395
Numeric difference in CEC₂ subgroup	<i>Correlation Coef.</i>	.058	.088	.062	.176
	<i>p value</i>	.693	.549	.671	.228
Numeric difference in EPC₃ subgroup	<i>Correlation Coef.</i>	-.117	.013	-.004	.037
	<i>p value</i>	.424	.930	.978	.801
Percentage difference in EPC₁ subgroup	<i>Correlation Coef.</i>	-.233	.072	-.006	.166
	<i>p value</i>	.107	.625	.967	.254
Percentage difference in CEC₁ subgroup	<i>Correlation Coef.</i>	.129	-.070	-.003	-.044
	<i>p value</i>	.377	.633	.985	.763
Percentage difference in EPC₂ subgroup	<i>Correlation Coef.</i>	.151	.341*	.172	-.278
	<i>p value</i>	.300	.017	.237	.053
Percentage difference in CEC₂ subgroup	<i>Correlation Coef.</i>	.219	.191	.195	.173
	<i>p value</i>	.130	.188	.179	.234
Percentage difference in EPC₃ subgroup	<i>Correlation Coef.</i>	-.052	.045	.035	.051
	<i>p value</i>	.725	.760	.813	.726

VO₂, oxygen uptake; EPC₁, CD34⁺/CD45⁻/CD133⁺; EPC₂, CD34⁺/CD45⁻/
/CD133⁺/VEGFR₂; EPC₃, CD34⁺/CD133⁺/VEGFR₂; CEC₁, CD34⁺/CD45⁻/
/CD133⁻; CEC₂, CD34⁺/CD45⁻/CD133⁻/VEGFR₂

Supplementary table 6. Differences of demographics and CPET indexes between groups of CHF patients according to the median value of the percentage increase of each endothelial cellular population's acute mobilization after CPET.

Variables	EPC₁ (66,7%)	EPC₂ (150%)	EPC₃ (31,6%)	CEC₁ (78,4%)	CEC₂ (100%)
Age (p value)	0.862	0.020	0.575	0.859	0.608
Group 1	56 ± 11	59 ± 8	55 ± 10	56 ± 9	56 ± 10
Group 2	56 ± 9	53 ± 10	57 ± 9	56 ± 10	55 ± 9
Height (p value)	0.305	0.792	0.653	0.583	0.957
Group 1	173 ± 11	174 ± 10	174 ± 9	175 ± 9	175 ± 10
Group 2	176 ± 9	175 ± 10	175 ± 11	174 ± 11	174 ± 9
Weight (p value)	0.184	0.423	0.372	0.575	0.988
Group 1	85 ± 24	87 ± 21	86 ± 24	88 ± 21	89 ± 20
Group 2	94 ± 22	92 ± 25	92 ± 22	91 ± 25	90 ± 27
Peak VO₂ (p value)	0.591	0.006	0.997	0.612	0.559
Group 1	18.4 ± 4.3	16.4 ± 3.6	18.1 ± 3.6	17.8 ± 5	17.7 ± 4.7
Group 2	17.7 ± 4.6	19.8 ± 4.6	18.1 ± 5.2	18.4 ± 3.9	18.5 ± 4.1
Predicted peak VO₂ (p value)	0.559	0.178	0.964	0.569	0.699
Group 1	64 ± 15	60 ± 14	63 ± 16	61 ± 18	62 ± 17
Group 2	61 ± 18	66 ± 17	63 ± 17	64 ± 14	64 ± 15
VE/VCO₂ slope (p value)	0.230	0.007	0.860	0.938	0.104
Group 1	33 ± 4	35 ± 4	33 ± 4	34 ± 4	33 ± 5
Group 2	34 ± 5	32 ± 4	34 ± 5	33 ± 5	35 ± 4
Peak WR (p value)	0.901	0.013	0.992	0.780	0.589
Group 1	97 ± 42	82 ± 30	96 ± 35	95 ± 37	93 ± 42
Group 2	95 ± 38	111 ± 44	96 ± 45	98 ± 43	100 ± 37

CPET, cardiopulmonary exercise testing; CHF, chronic heart failure; VO₂, oxygen uptake; WR, work rate; EPC₁, CD34⁺/CD45⁻/CD133⁺; EPC₂, CD34⁺/CD45⁻/CD133⁺/VEGFR₂; EPC₃, CD34⁺/CD133⁺/VEGFR₂; CEC₁, CD34⁺/CD45⁻/CD133⁻; CEC₂, CD34⁺/CD45⁻/CD133⁻/VEGFR₂.

Supplementary figure 1. Plots representing the percentage difference in the mobilization of each endothelial cellular population after a symptom limited maximal cardiopulmonary exercise testing (CPET) between severity groups based on the median values of peak VO₂ (18.0 ml/kg/min) (A), predicted peak VO₂ (65.5%) (B) and VE/VCO₂ (32.5) (C), as well as the EF (< 40% and 40 - 49%) (D). No statistically significantly difference was observed between the 2 groups (p > 0.05).

