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Effect of a single maximal exercise bout on monocyte subsets in chronic kidney disease

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INTRODUCTION AND OBJECTIVES

- Monocytes, the key players in inflammation, consist of 3 functionally distinct subtypes[1]
  - Classical (Mon1) highly phagocytic
  - Intermediate (Mon2) pro-angiogenic, production of pro- and anti-inflammatory cytokines, antigen presentation
  - Nonclassical (Mon3) antigen presentation, patrolling endothelial-blood interface
- Chronic low-grade inflammation contributes to the high cardiovascular risk of CKD patients, which can be reduced by exercise training
- The response of monocyte subsets to a single exercise bout is blunted in the setting of chronic heart failure

AIM: to evaluate the response of monocyte subsets and Il-6 and MCP-1 to a single maximal exercise bout in CKD patients compared to healthy subjects

METHODS

Study design and clinical assessment

20 CKD patients
15 age-matched healthy subjects

PRE → CARDIOPULMONARY EXERCISE TESTING → 10 MIN POST

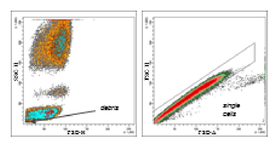
Echocardiography
Venous blood sampling

Venous blood sampling

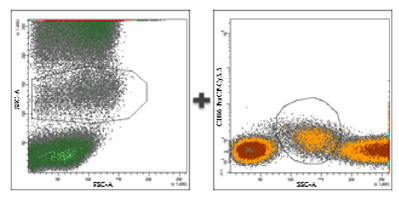
Laboratory assessment

Multiparametric flow cytometry[2]
Mon1: CD14++CD16-CCR2+
Mon2: CD14++CD16+CCR2+
Mon3: CD14+CD16++CCR2-

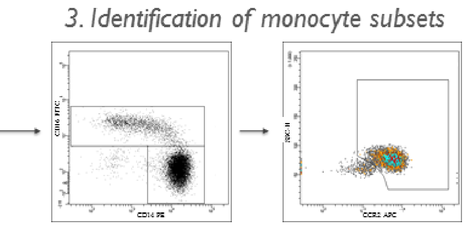
1. Exclusion of doublets & dead cells



2. Identification of monocytes



3. Identification of monocyte subsets



ELISA
MCP-1, IL-6

RESULTS

Baseline characteristics

Table 1. Baseline characteristics

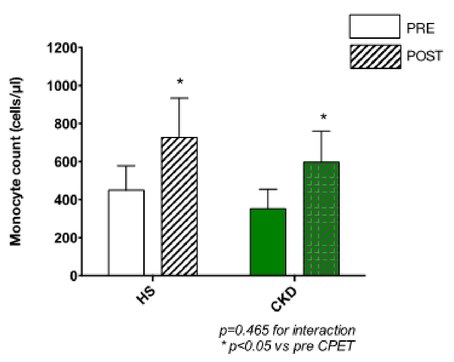
	HS (n=15)	CKD (n=20)	*P-value*
Age (yrs)	43.5 ± 5.0	51.3 ± 15.6	0.070
Sex (F/M)	6/9	12/8	0.200
Creatinin (mg/dl)	0.85 ± 0.19	1.73 ± 0.63*	<0.001
eGFR (ml/min/1.73m^2)	99.04 ± 11.31	44.42 ± 19.7*	<0.001
BMI	24.16 ± 2.26	26.12 ± 5.11	0.139
IL-6 (pg/mL)	1.04 ± 1.71	1.39 ± 1.45	0.526
MCP-1 (pg/mL)	330 ± 163	446 ± 95*	0.013
Systolic BP (mmHg)	123.5 ± 13.4	130.6 ± 15.9	0.180
Diastolic BP (mmHg)	77.4 ± 9.4	77.1 ± 10.3	0.924
EF (%)	65.0 ± 0	62.9 ± 8.2	0.287
VO_2peak (ml/min/kg)	37.20 ± 9.04	25.54 ± 7.53*	<0.001
Peak heart rate (bpm)	171 ± 14	153 ± 26*	0.017
Max workload (Watt)	249 ± 83	152 ± 50*	0.001

Table 2. Monocyte subset distribution

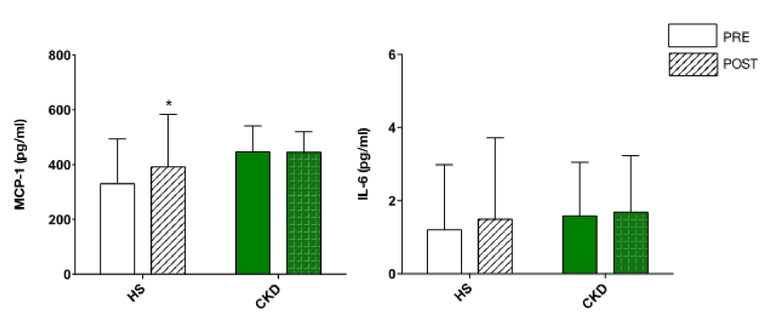
	HS (n=15)	CKD (n=20)	*P-value*
Monocyte count (cells/µl)	450.1 ± 128.1	352.1 ± 103.7	0.017
%Mon1	88.09 ± 4.73	88.48 ± 4.27	0.802
%Mon2	4.51 ± 2.05	3.55 ± 1.69	0.142
%Mon3	7.38 ± 3.17	7.95 ± 3.61	0.631

Effect of a single maximal exercise bout

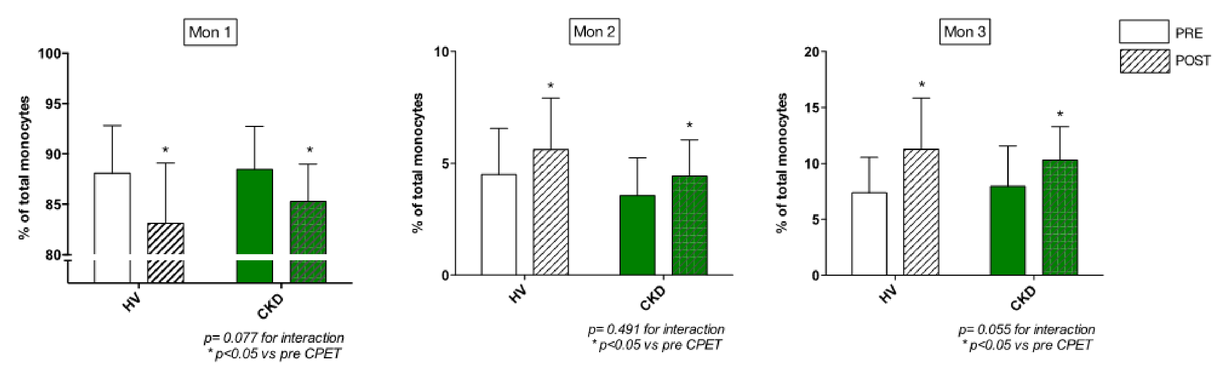
Monocyte count: comparable increase



MCP-1 & IL-6



Monocyte subsets: increase in %Mon2 and %Mon3 at the expense of %Mon1



Relation with VO_2peak

- %Change Mon1 r=0.503, p= 0.03
- %Change Mon3 r=0.509, p=0.002
- %Change in MCP-1 r=0.612, p<0.001 - no relation with monocyte subset response

CONCLUSION

- Despite a lower exercise capacity and low-grade inflammation at baseline, CKD patients showed a comparable acute exercise-induced change in monocyte subsets as healthy subjects
- Levels of MCP-1 increased significantly in healthy subjects but remained unchanged in patients with CKD
- The monocyte subset response is characterized by an increase in pro-angiogenic Mon2 and pro-inflammatory Mon3, at the expense of Mon1
- These observations add insight into the dynamic inflammatory response to acute exercise in CKD, which contributes to unravelling the mechanisms underlying the long-term beneficial effects of exercise training.

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H) Clinical Nephrology, CKD. H6) Nutrition, inflammation and oxidative stress in CKD 1-5.
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