

Intermediate monocytes are predictors of cardiovascular but not of renal events



Adam M. Zawada, Anne I. Michel, Kyrill S. Rogacev, Sarah Seiler, Insa E. Emrich, Kathrin Untersteller, Claudia S. Lennartz, Danilo Fliser, Gunnar H. Heine

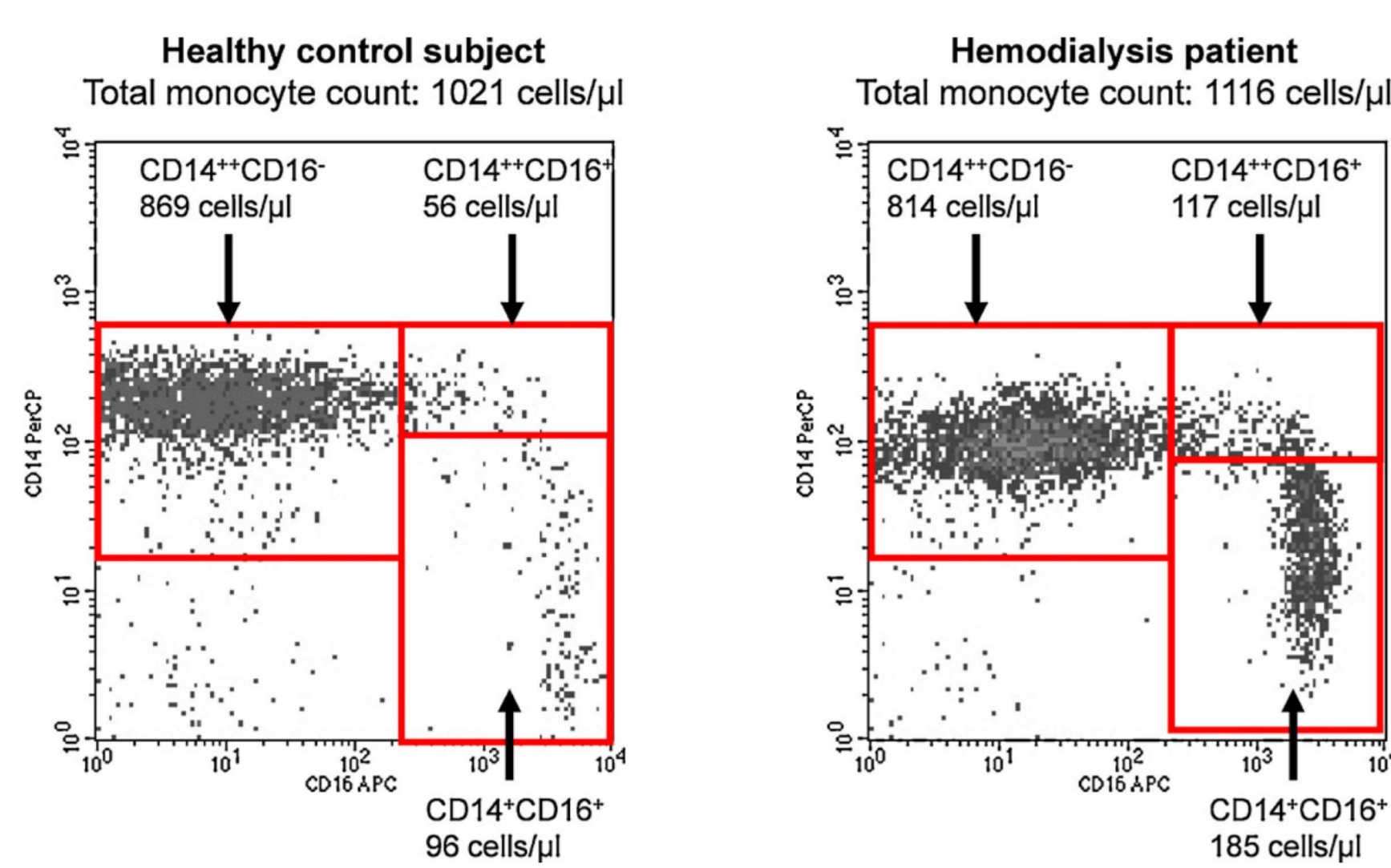
Department of Internal Medicine IV, Saarland University Medical Center, Homburg, Germany

Introduction

Monocytes and monocyte-derived macrophages and Dendritic cells (DC) play a central role in both atherogenesis as well as in renal fibrosis. Based on the expression of CD14 and CD16, three different monocyte subpopulations can be differentiated: classical CD14⁺⁺CD16⁻ monocytes, intermediate CD14⁺⁺CD16⁺ monocytes and nonclassical CD14⁺CD16⁺⁺ monocytes. In previous studies, intermediate monocytes have been characterized as independent predictors of cardiovascular events in chronic kidney disease (CKD) patients. However, until now no data exist whether distinct monocyte subsets also predict CKD progression.

Monocyte subsets:

Healthy subject
vs
CKD patient



Methods

- CARE FOR HOME study (438 CKD patients)
- Counts of monocyte subsets were determined flow-cytometrically on the day of study inclusion
- All patients were followed for the occurrence of cardiovascular (myocardial infarction, coronary, cerebrovascular and peripheral-arterial revascularization, amputation above the ankle, stroke and death) and renal events (reduction of eGFR \leq 50% or the onset of renal replacement therapy)

Results

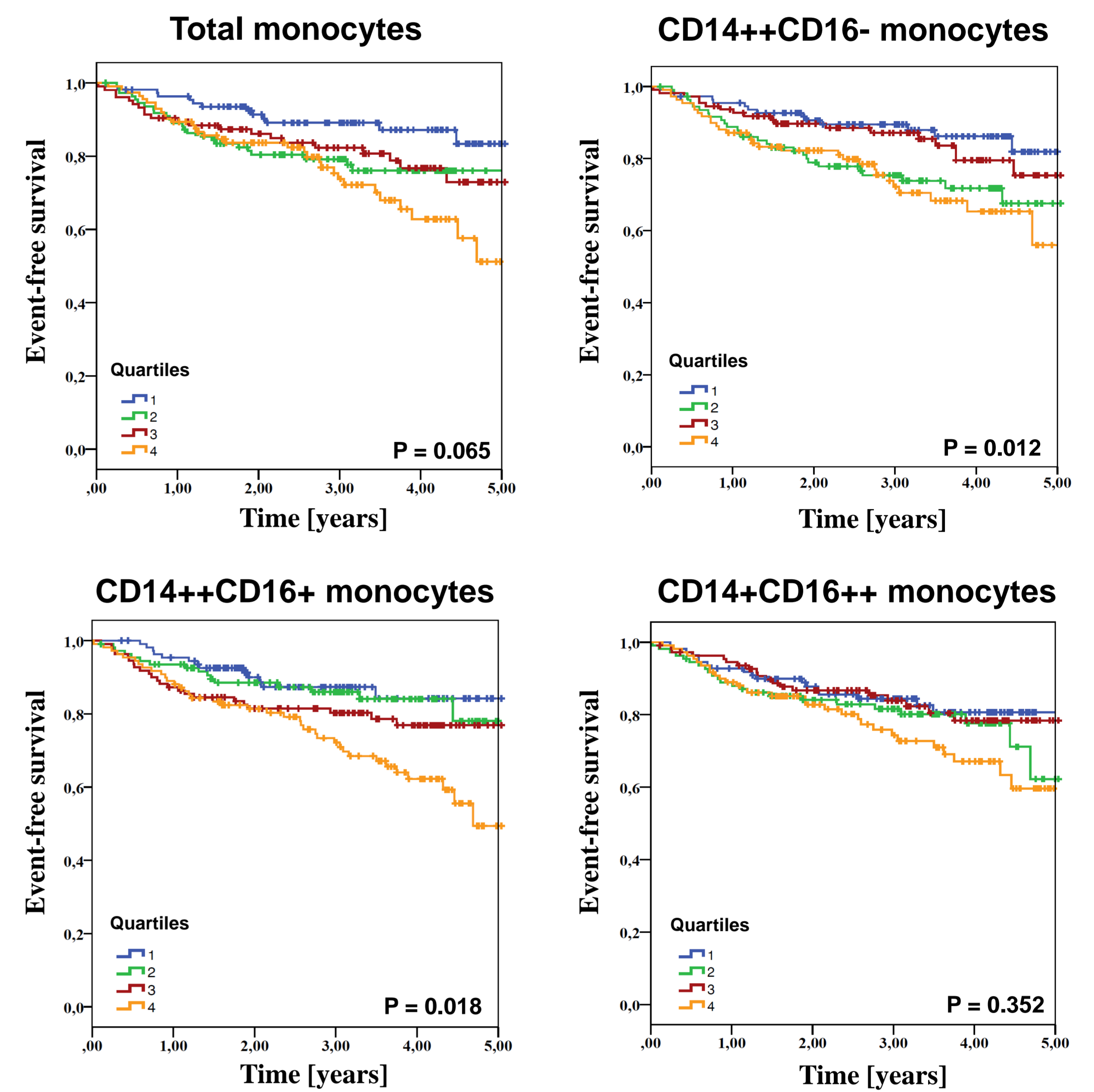
1. Baseline characteristics

	Total cohort (n = 438)	GFR category 2 (n = 86)	GFR category 3a (n=145)	GFR category 3b (n=121)	GFR category 4 (n=86)	P value
Sex (men)	263 (60%)	58 (67%)	82 (57%)	71 (59%)	52 (61%)	0.424
Prevalent CVD (yes)	134 (31%)	10 (12%)	45 (31%)	51 (42%)	28 (33%)	<0.001
Smoking (yes)	43 (10%)	14 (16%)	13 (9%)	10 (8%)	6 (7%)	0.152
Diabetes mellitus (yes)	167 (38%)	28 (33%)	56 (39%)	47 (39%)	36 (42%)	0.641
Age (years)	65.1±12.1	57.8±12.0	64.7±12.7	68.4±10.8	68.7±11.4	<0.001
BMI (kg/m ²)	30.1±5.4	30.3±5.6	30.5±5.7	30.4±5.5	29.3±4.8	0.226
Systolic BP (mmHg)	154±24	150±21	156±24	152±25	155±27	0.510
Diastolic BP (mmHg)	89±13	90±12	89±12	83±13	84±12	<0.001
Mean BP (mmHg)	109±15	110±14	112±14	106±15	108±15	0.028
eGFR (ml/min per 1.73 m ²)	45.3±16.0	65.0±5.9	51.5±4.3	37.8±4.4	22.4±4.2	<0.001
Albuminuria (mg/g creatinine)	36 (8-189)	26 (7-106)	19 (6-70)	46 (11-162)	128 (36-660)	<0.001
Total cholesterol (mg/dl)	193±42	198±37	191±40	191±44	192±47	0.423
HDL cholesterol (mg/dl)	48 (39-61)	48 (39-63)	49 (41-64)	47 (39-62)	46 (37-58)	0.240
LDL cholesterol (mg/dl)	116±35	122±32	113±34	114±36	116±39	0.395
Triglycerides (mg/dl)	135 (96-191)	136 (90-192)	127 (89-184)	133 (107-198)	151 (105-202)	0.116
Apo A-I (mg/dl)	161 (142-184)	161 (141-187)	161 (146-186)	158 (144-187)	161 (135-182)	0.579
hsCRP (mg/l)	2.7 (1.2-5.4)	2.4 (1.5-2.8)	2.6 (0.9-5.3)	2.9 (1.2-6.1)	3.4 (1.1-5.8)	0.454
Hemoglobin (g/dl)	13.4±1.6	14.2±1.3	13.8±1.5	13.2±1.6	12.3±1.5	<0.001
Leukocytes (per μ l)	6856±1998	6648±2115	6540±1665	7140±2234	7199±1857	0.008
Total monocytes (per μ l)	561±203	559±193	524±159	593±249	580±197	0.088
Classical monocytes (per μ l)	463±174	466±167	431±133	487±215	479±172	0.147
Intermediate monocytes (per μ l)	34±21	31±18	32±19	36±22	39±25	0.004
Nonclassical monocytes (per μ l)	64±32	61±31	61±34	70±32	62±28	0.319

Results

2. Monocyte subsets and cardiovascular events

Univariate analysis

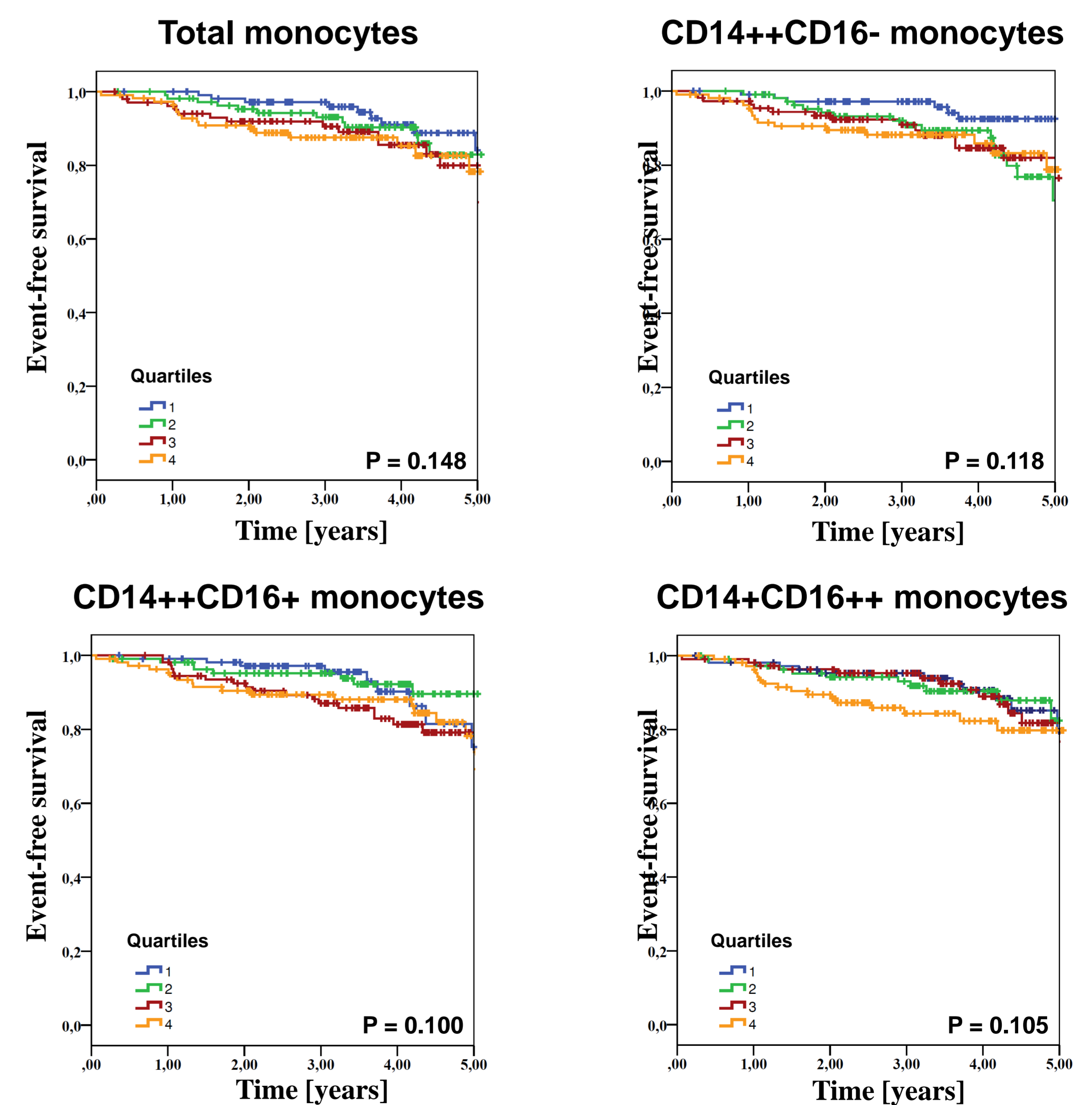


Multivariate analysis (adjusted for age, gender, Diabetes mellitus, prevalent CVD, smoking, total cholesterol, mean BP, eGFR, albuminuria)

	Exp (B)	95% CI	P value
Total monocytes	1.001	1.000 – 1.002	0.030
CD14 ⁺⁺ CD16 ⁻ monocytes	1.042	1.000 – 1.002	0.060
CD14 ⁺⁺ CD16 ⁺ monocytes	1.012	1.004 – 1.019	0.003
CD14 ⁺ CD16 ⁺⁺ monocytes	1.004	0.998 – 1.010	0.229

3. Monocyte subsets and renal events

Univariate analysis



Discussion

Intermediate monocytes were confirmed as independent predictors of cardiovascular events in CKD patients. However, despite the central role of monocytes and monocyte-derived macrophages and DCs in renal fibrosis, high counts of distinct monocyte subsets did not predict CKD progression.

Contact: Adam.Zawada@uks.eu