Table 1 Monocyte subset expression of study receptors

Receptor MFI	Day 1	Day 3	Day 7	Day 30	p value	CAD	p value STEMI day 1 vs CAD
IL6r Mon1	66 [16]	68 [15]	66 [17]	73 [17]	0.048	70 [16]	0.37
IL6r Mon2	56 [12]	60 [13]	60 [14]	64 [14]	0.012	62 [15]	0.028
IL6r Mon3	32 [11]	32 [9]	30 [8]	31 [9]	0.29	35 [26]	0.25
VCAM-1r Mon1	10 [3]	10 [3]	12 [3]	13 [4]	<0.001	11 [5]	0.002
VCAM-1r Mon2	20 [7]	23 [9]	25 [9]	26 [8]	0.009	23 [10]	0.007
VCAM-1r Mon3	30 [11]	38 [11]	37 [10]	40 [14]	0.003	39 [14]	0.005
ICAM-1r Mon1	44 [21]	39 [20]	47 [26]	32 [13]	0.001	36 [16]	0.27
ICAM-1r Mon2	76 [36]	69 [34]	80 [41]	64 [25]	0.10	65 [25]	0.47
ICAM-1r Mon3	34 [19]	35 [21]	40 [25	32 [13]	0.16	32 [16]	0.85

p < 0.05 vs day3, p,0.05 vs day7, p < 0.05 vs day 30. Data presented as mean [standard deviation]. MFI = median fluourescent intensity.

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EXPRESSION OF RECEPTORS TO INTERLEUKIN 6 AND ADHESION MOLECULES ON CIRCULATING MONOCYTE SUBSETS IN MYOCARDIAL INFARCTION

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Introduction Coronary artery disease (CAD) and myocardial infarction (MI) are diseases of inflammatory aetiology, in which monocytes have been implicated. However, monocytes may also have benefical roles in myocardial recovery after MI. This diversity of roles is thought to be due to functional heterogeneity of monocyte subsets. Adhesion molecules are a key component of the inflammatory process and the mechanism by which monocytes are recruited to activated endothelium and inflamed myocardium. Additionally, a growng body of evidence has implicated the interleukin-6 receptor (IL6r) in the pathogenesis of atherosclerosis. Monocytes are a major type of IL6r expressing cell in circulation. However, limited data are available on expression of receptors to adhesion molecules and IL6r by the three human monocyte subsets after MI. Having observed marked differences in expression of adhesion molecules and IL6r between monocyte subsets in healthy humans, we aimed to evaluate the dynamics of monocyte subset expression of receptors to vascular cell adhesion molecule (VCAM-1r), intercellular adhesion molecule (ICAM-1r), and IL6r after ST-elevation MI (STEMI), which has not been previously evaluated.

Methods Expression of VCAM-1r, ICAM-1r and IL6r was quantified by flow cytometry of venous blood on days 1, 3, 7 and 30 post STEMI (n=50). All STEMI patients were treated with primary percutaneous coronary intervention. STEMI patients were compared with an age and sex-matched control group with stable CAD (n=40). Monocyte subsets were defined as CD14++CD16 (Mon1), CD14++CD16+(Mon2) and CD14+CD16++(Mon3). Exclusion criteria comprised factors known to affect monocyte count. Expression of surface markers was quantified as median fluorescent intensity (MFI). Inter- and intra-assay reproducibility for surface marker assays in our laboratory is <10%.

Results On day1 after STEMI, VCAM-1r expression was reduced on Mon1 (p=0.002), Mon2 (p=0.007) and Mon3 (p=0.005). There was no change in monocyte ICAM-1r expression after MI, whilst its expression on Mon1 reduced by day 30 (p=0.001). IL6r expression by Mon2 was reduced on day1 after STEMI, with no differences seen for the other subsets. A gradual upregulation of IL6r expression was seen by Mon1 and Mon2 during follow-up.

Conclusions There are marked differences in expression of adhesion molecules and IL6r by monocyte subsets after STEMI. Monocyte subsets involved in inflammatory responses (Mon2) have reduced IL6r expression in the acute phase following STEMI. This may represent a regulatory feed-back mechanism aiming to re-balance the marked inflammation which is typically present after STEMI. There is also a decrease in VCAM-1r density on monocytes after STEMI. This may reflect the selective homing of monocytes with high VCAM-1r expression to damaged myocardium. Selective pharmacological modulation of monocyte subset expression of adhesion molecules and IL6r may represent a novel target for the treatment of MI and CAD.