

CD4⁺CD28⁻CX3CR1⁺ T cells: the CMV-specific troublemakers in patients with myocardial infarction?

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1 INTRODUCTION

Myocardial infarction (MI) caused by coronary artery disease has been the leading cause of mortality worldwide for decades.

More than 80,000 admissions of acute coronary syndrome (ACS) annually in the UK.

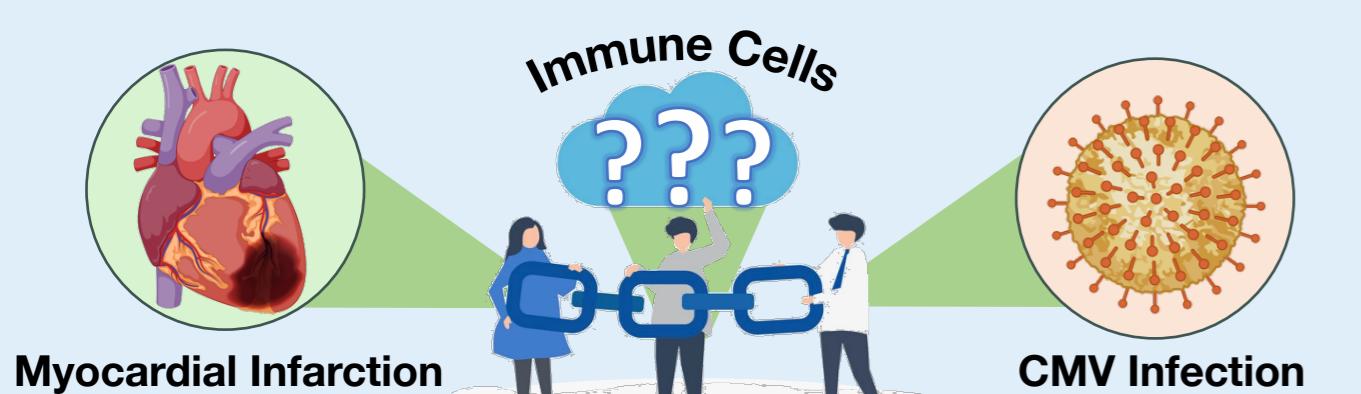
Despite reperfusion by primary percutaneous coronary intervention and optimisation of drug therapy (anti-platelets and lipid-lowering drugs), complications following MI are surprisingly high.

This suggests other mechanisms such as inflammation.

Cytomegalovirus (CMV) infection (global seroprevalence of 83%) has been implicated in the inflammatory process of vascular pathobiology in atherosclerosis (pathologic process preceding MI).

CMV-driven expansion of cytotoxic T cells has been studied in a number of diseases.

Nevertheless, how CMV infection links to immune cells in MI has not been fully explored.



2 AIMS

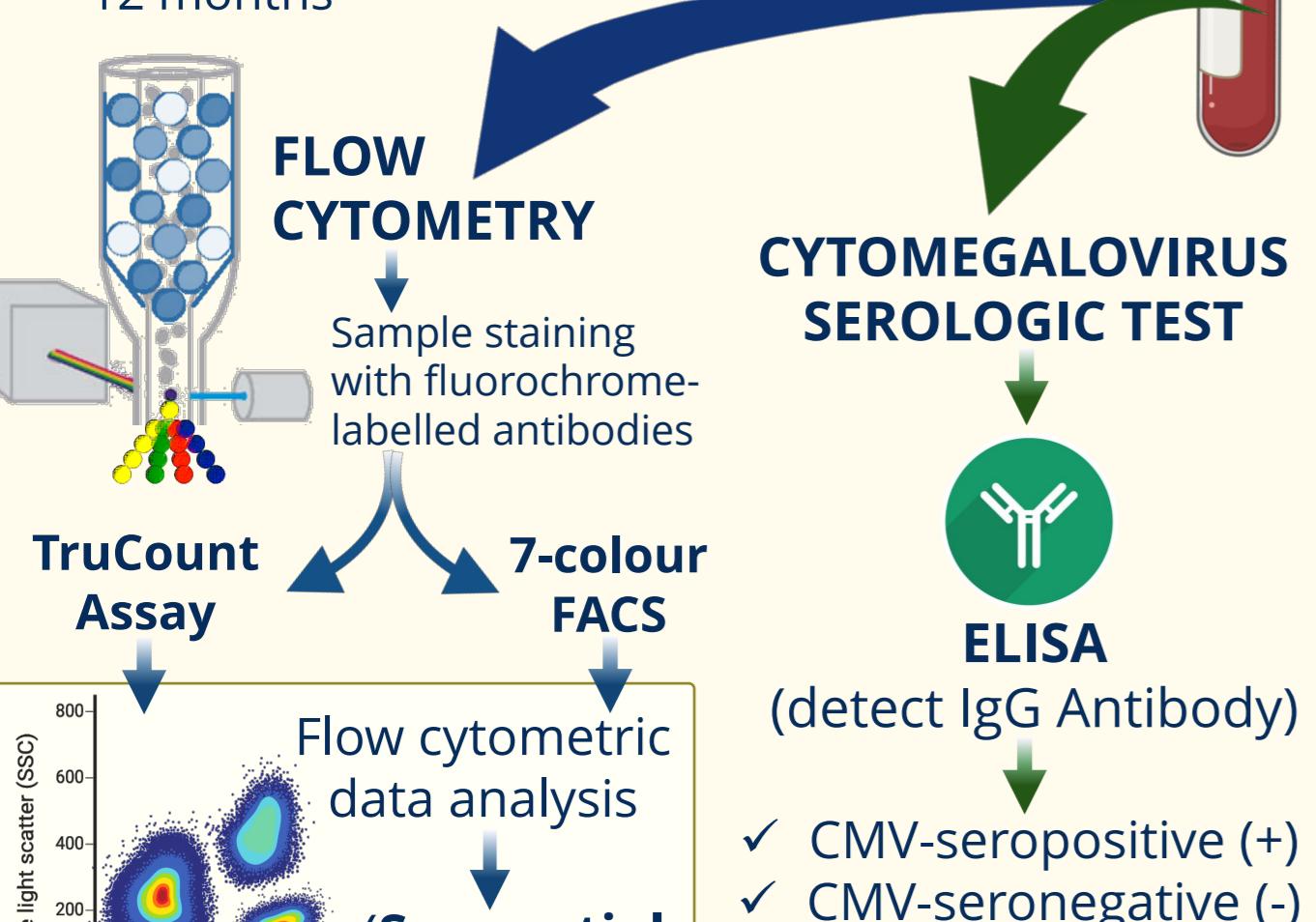
- To conduct immunophenotypic characterisation and investigate the temporal dynamics of peripheral blood leucocyte subpopulations
- To conduct comparative subgroup analysis between STEMI vs NSTEMI and CMV-seropositive vs CMV-seronegative
- To elucidate the link between CMV and immune cells in patients with myocardial infarction

3 METHODS

WHOLE BLOOD from TACTIC trial patients presenting with ACS (STEMI or NSTEMI)

Collected at 3 time points:

- Baseline (24-hour post-infarct)
- 6 months
- 12 months



- Absolute counts (number of cells/ μ L)
- Percentage of parent populations (%)

- Statistical analysis
 - Longitudinal analysis
 - STEMI versus NSTEMI
 - CMV (+) versus (-)

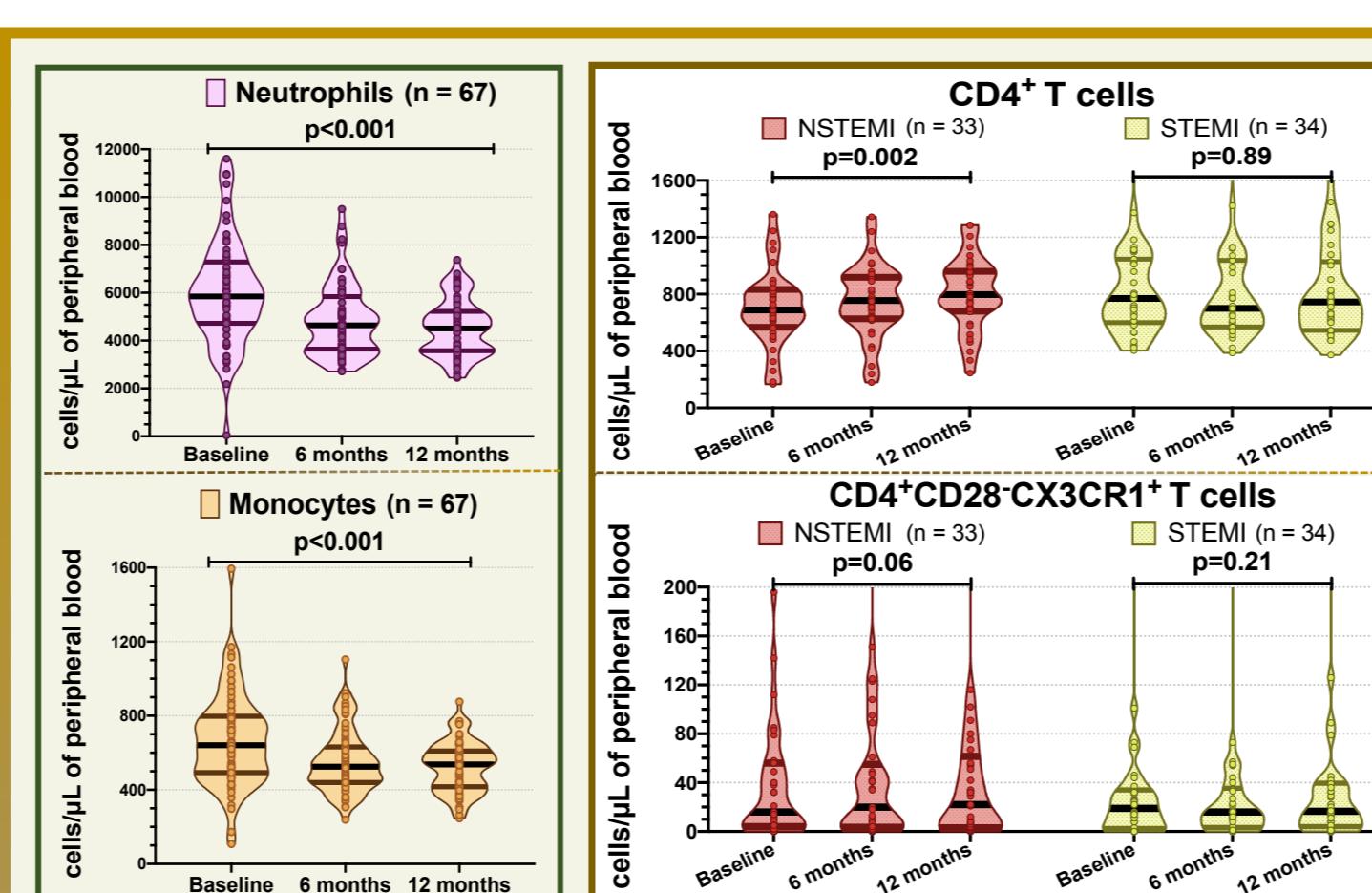


FIGURE 1. Violin plots of main temporal changes from the total patient population [Left box] and subgroup analysis based on the types of ACS (NSTEMI and STEMI) [Right box].

4 RESULTS & DISCUSSION

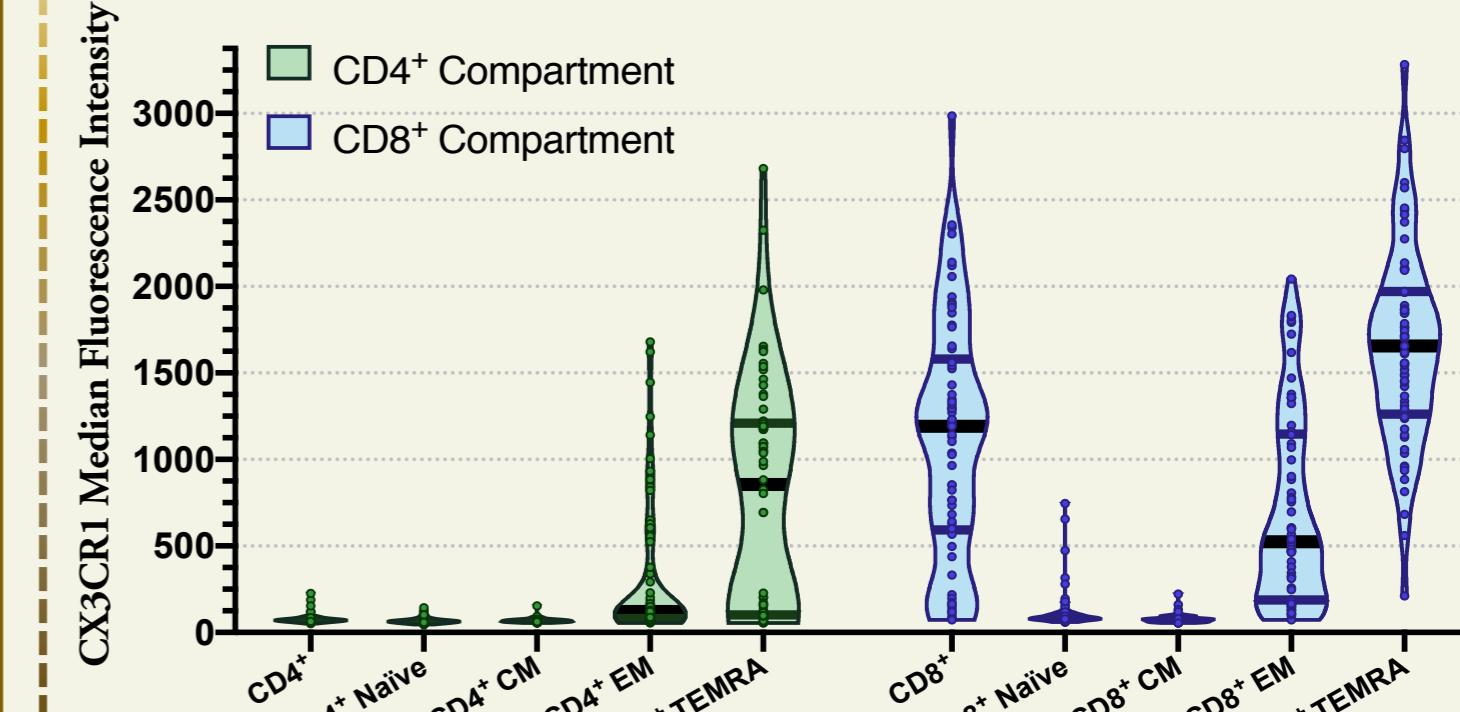


FIGURE 2. CX3CR1 receptor surface expression (median fluorescence intensity) of CD4⁺ and CD8⁺ T-cell subsets in patients with MI (n = 67) at baseline time point.

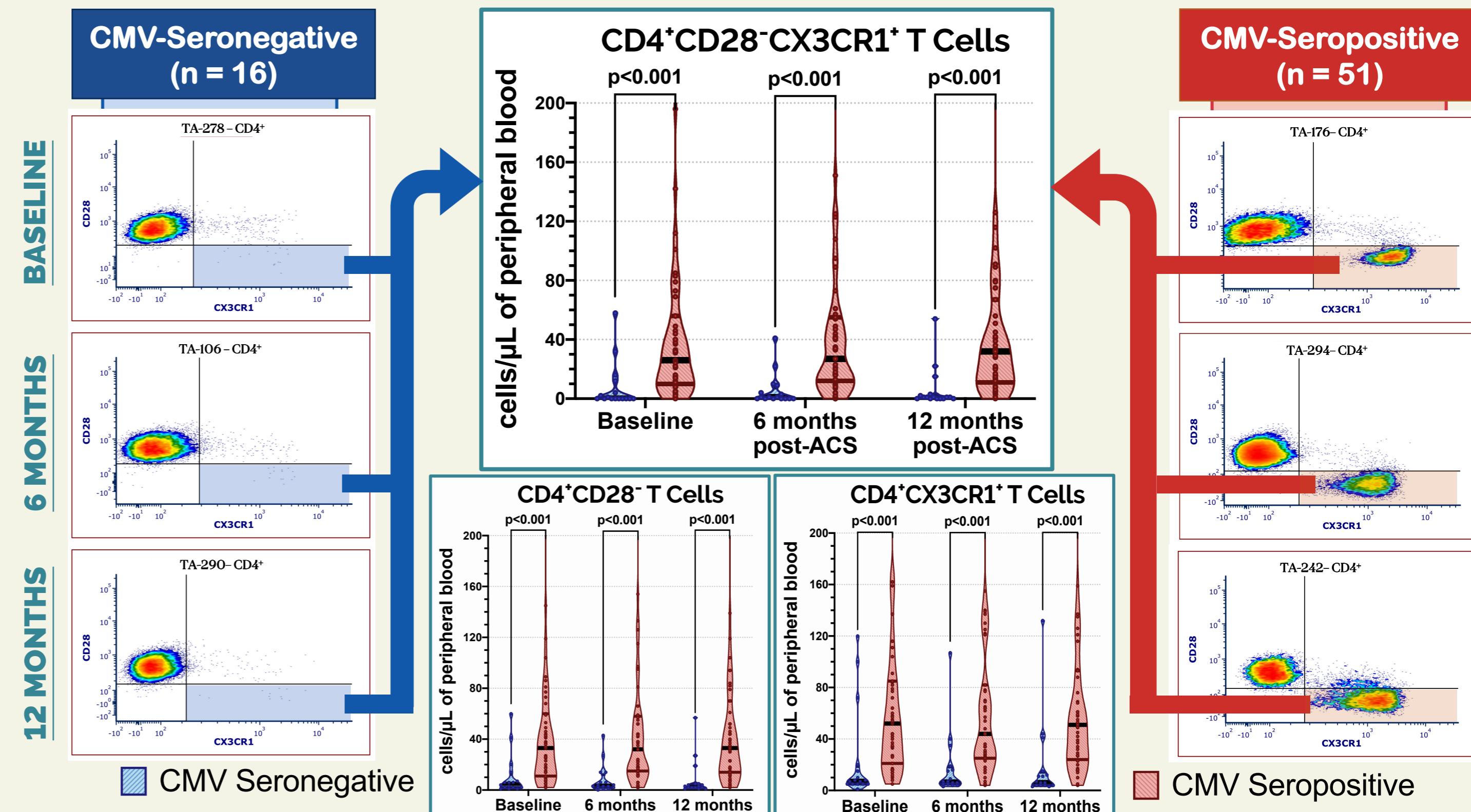
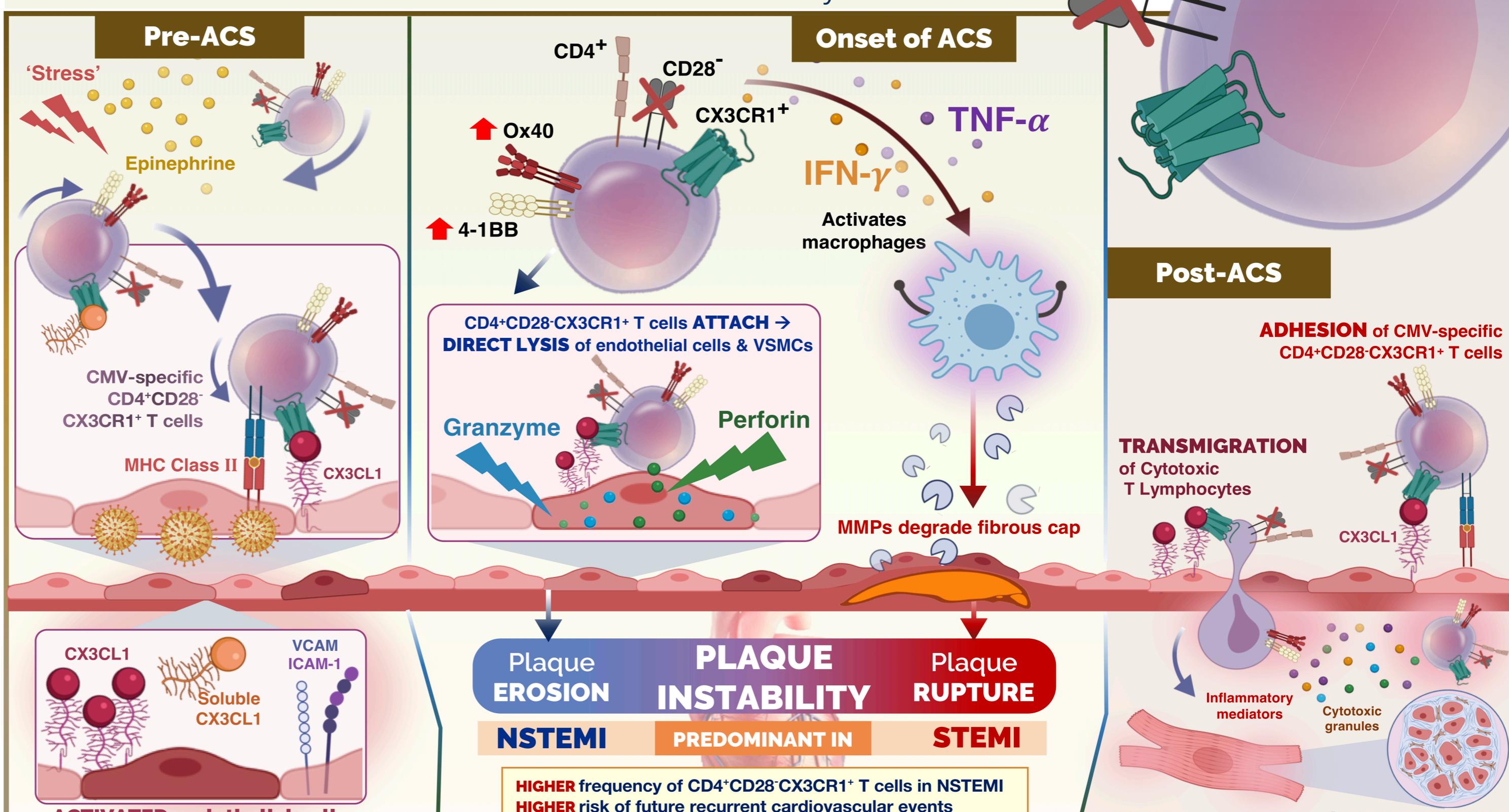


FIGURE 3. CMV-seropositive patients showed significantly higher absolute counts of CD4⁺CD28⁻CX3CR1⁺ (up to 30-fold), CD4⁺CD28⁻, and CD4⁺CX3CR1⁺ T cells compared with CMV-seronegative patients across all three time points.

DISCUSSION FIGURE. The role of CD4⁺CD28⁻CX3CR1⁺ T cells in myocardial infarction



5 CONCLUSIONS

- Monocytes and neutrophils decline beyond 6 months in patients with MI.
- CD4⁺CD28⁻CX3CR1⁺ T cells are exclusively found in CMV-seropositive patients with MI.
- NSTEMI patients seem to have a higher frequency of cytotoxic CD4⁺CD28⁻CX3CR1⁺ T cells which may account for a higher risk of recurrent cardiovascular events.

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6 FUTURE WORK

- In-depth characterisation of CD4⁺CD28⁻CX3CR1⁺ T cells through single-cell RNA sequencing (transcriptome) and spectral cytometry (surface proteome)
- Investigate the therapeutic potential of anti-CX3CL1 therapy or CX3CR1 antagonist in blocking the CX3CL1/CX3CR1 axis in clinical trials
- Analyse the role of cytotoxic T cells in post-MI complications (adverse ventricular remodelling and reinfarction) between STEMI vs NSTEMI patients