

# Coronary Allograft Vasculopathy is Associated With Decreased CD34<sup>+</sup> Peripheral Cell Count in Patients After Heart Transplantation

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## INTRODUCTION

- The underlying mechanisms of coronary allograft vasculopathy (CAV) after heart transplantation remain incompletely understood.
- CD34<sup>+</sup> cells represent one of the key determinants of coronary vascular homeostasis.

## AIM

- To investigate the potential association between CAV and CD34<sup>+</sup> cell count in heart transplant recipients.

## METHODS

- In a single-center prospective pilot cohort study we included 59 adult heart transplant recipients without history of congenital heart disease, multi-organ transplantation or oncologic therapy.
- All patients underwent coronary CT angiography, and the presence of CAV was defined in accordance with the ISHT criteria (Table 1).
- At the time of CT angiography, we collected blood samples and measured CD34<sup>+</sup> cell count using Beckman-Coulter Navios EX flow cytometry with standard antibodies according to ISAGE protocol as well as biomarkers of angiogenesis using Luminex assay kit.

## CONTACT INFORMATION

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Table 1: ISHLT criteria for CAV

Classification	Severity	Definition
CAV 0	Nonsignificant	No detectable angiographic lesion
CAV 1	Mild	• Angiographic LM < 50% or • Primary vessel maximum lesion < 70% or • Branch stenosis < 70%
CAV 2	Moderate	• Angiographic LM < 50%, • Single primary vessel ≥ 70% or • Branch stenosis in two systems ≥ 70%
CAV 3	Severe	• Angiographic LM ≥ 50%, • ≥ 2 primary vessels ≥ 70% or • Branch stenosis in all three systems ≥ 70% or CAV 1 or CAV 2 with allograft dysfunction (LVEF ≤ 45%) or evidence of significant restrictive physiology

Legend: CAV – coronary allograft vasculopathy; LM – left main coronary artery

Table 2: Patient clinical characteristics

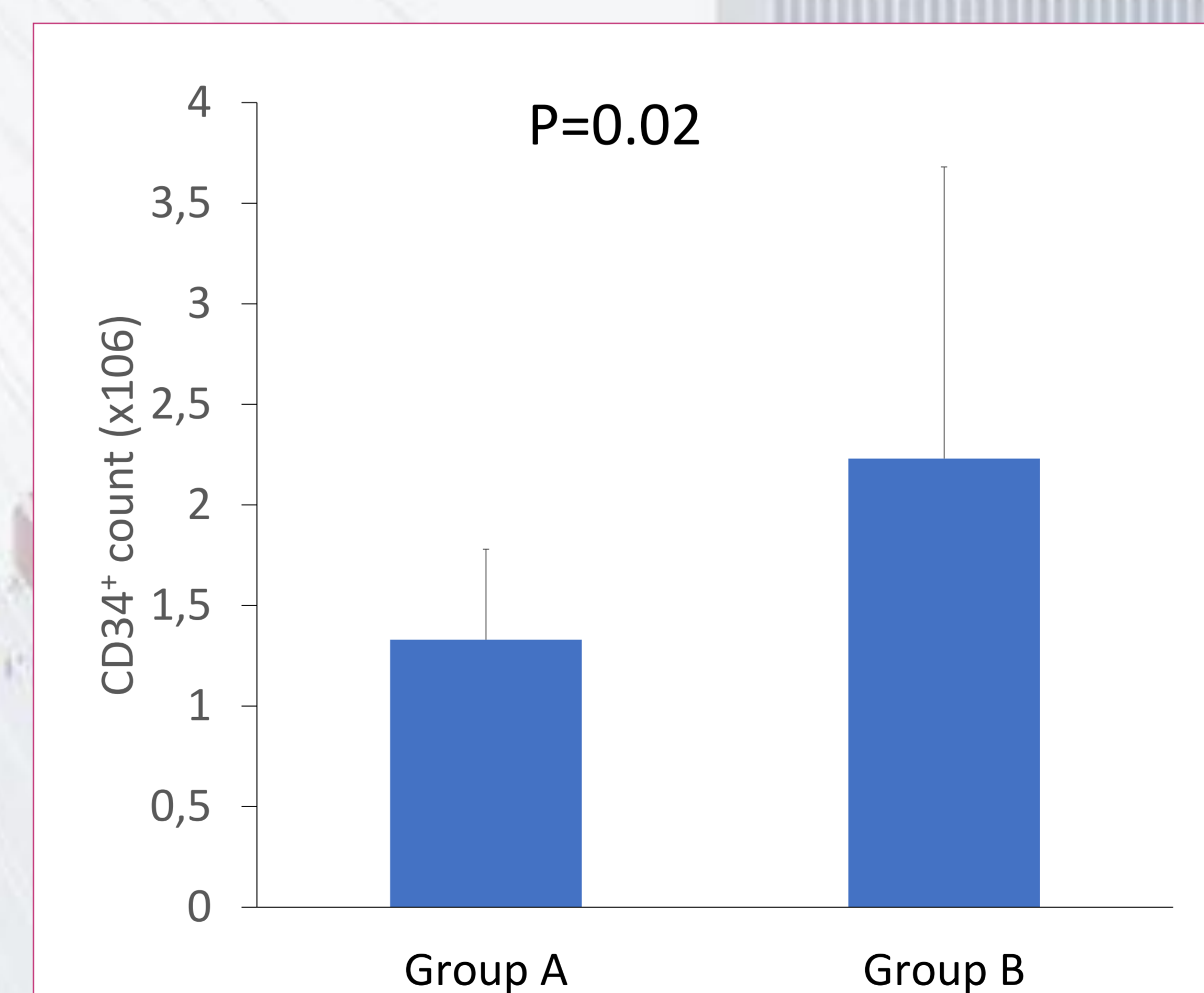
	All (N=59)	Group A (N=15)	Group B (N=44)	P
<b>Demographics</b>				
Age, y	60.3±11.2	61.7±11.0	59.8±11.3	0.56
Gender (male), %	85	100	79	0.06
HF etiology (ischemic), %	46	53	43	0.50
<b>Comorbidities</b>				
Hypertension, %	63	60	64	0.54
Diabetes, %	27	33	25	0.53
CKD, %	46	53	43	0.50
<b>Transplant data</b>				
Donor age, y	43.2±12.5	44.5±13.9	42.8±11.9	0.66
Donor COD (injury), %	69	67	70	0.79
Allograft ischemic time, min	192.9±68.9	202.6±71.8	189.7±67.7	0.66
<b>Pharmacological Therapy</b>				
Basiliximab induction, %	100	100	100	/
TAC therapy, %	95	87	97	0.10
TAC CO level, µg/L	7.74±2.6	8.8±3.8	7.4±1.9	0.14
MMF therapy, %	97	100	95	0.41
MMF, mg	2149.1±569.4	2066.7±442.2	2178.6±605.7	0.52
Methylprednisolone (1 <sup>st</sup> year), %	100	100	100	/
Statins, %	78	87	75	0.36
<b>Biochemistry</b>				
Sodium, mmol/L	140.1±2.4	140.5±1.9	139.9±2.5	0.37
Potassium, mmol/L	4.6±0.5	4.7±0.5	4.6±0.4	0.36
Creatinine, µmol/L	104.0±26.3	110.9±25.5	101.7±26.2	0.25
Bilirubin, µmol/L	13.6±7.9	13.4±8.4	16.7±7.8	0.91
NT-proBNP, pg/mL	904.7±2481.7	2032.8±4585.2	520.2±713.6	0.04
hs-Troponin, pg/mL	30.7±103.2	81.2±191.9	13.6±23.8	0.02
WBC, x10 <sup>6</sup> /L	6.9±2.2	7.7±2.1	6.8±2.2	0.17
Hemoglobin, g/L	144.9±118.2	146.2±16.5	144.5±18.8	0.76
Platelets, x10 <sup>9</sup> /L	210.9±88.4	229.3±56.3	204.7±96.1	0.36
<b>Echocardiography</b>				
LVEF, %	65.6±7.8	60.3±8.9	67.4±6.5	0.001
TAPSE, cm	1.7±0.4	1.7±0.3	1.8±0.4	0.94

Legend: HF – heart failure; CKD – chronic kidney disease; COD – cause of death; TAC – tacrolimus; MMF – mycophenolate mofetil; WBC – white blood cells; LVEF – left ventricular ejection fraction; TAPSE – tricuspid annular plane systolic excursion

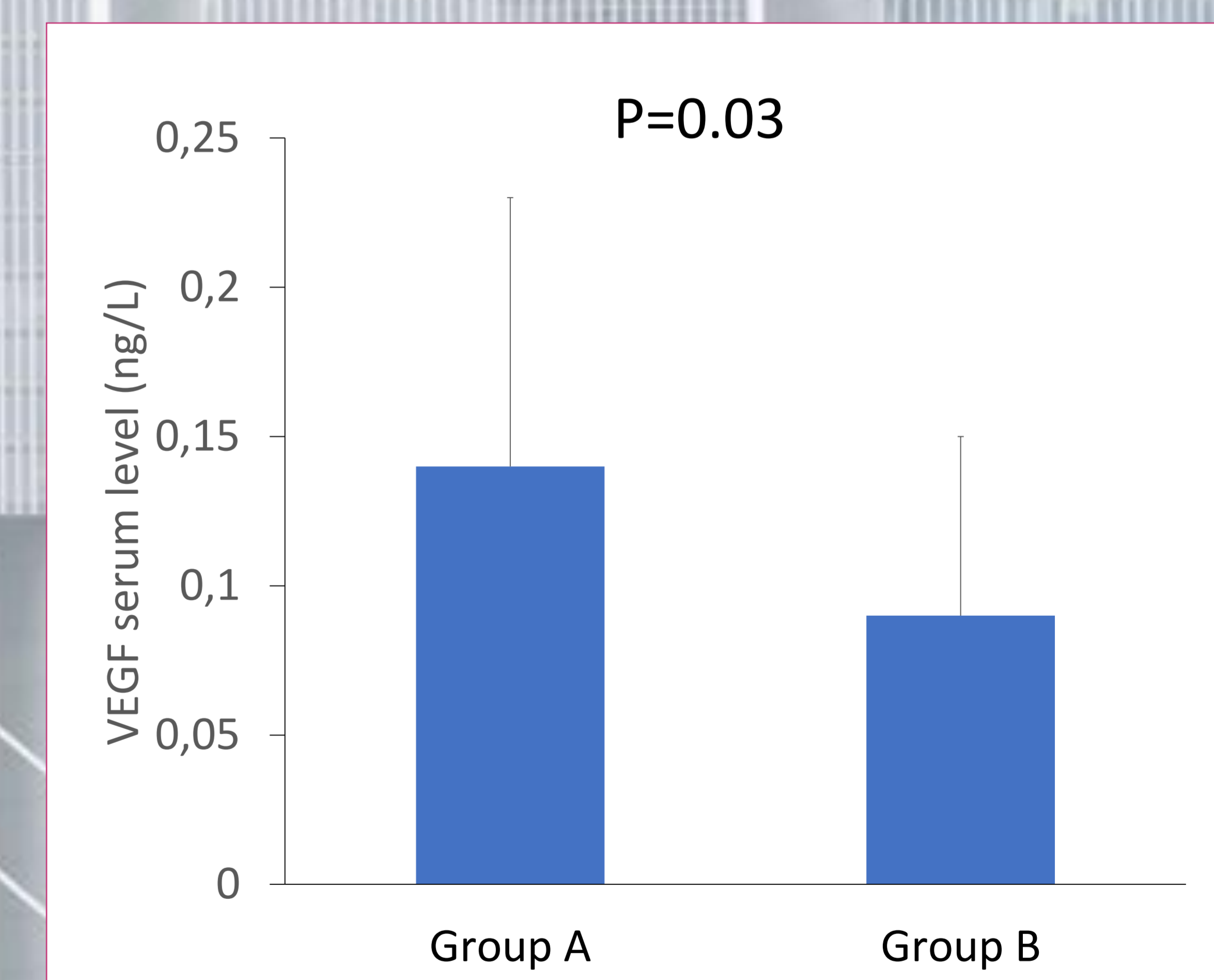
## RESULTS

- CAV was present in 15 patients (25%; Group A) and absent in 44 patients (75%; Group B).
- The patient clinical characteristics are presented in Table 2.
- Total leukocyte count was similar in both groups, we found significantly lower CD34<sup>+</sup> cell count in Group A compared to Group B (Figure 1).
- Compared to Group B VEGF serum levels were significantly increased in Group A (Figure 2).

**Figure 1:** CD34<sup>+</sup> peripheral cell count was significantly lower in heart transplant patients with CAV (Group A) than in patients without CAV (Group B).



**Figure 2:** VEGF serum levels were significantly higher in heart transplant patients with CAV (Group A) than in patients without CAV (Group B).



## CONCLUSIONS

- Decreased CD34<sup>+</sup> cell count and increased VEGF serum levels appear to be associated with CAV in heart transplant recipients.
- Further studies are warranted to investigate the potential of CD34<sup>+</sup> cells in prevention and treatment of CAV in this patient cohort.