Circulating CD14++CD16+ monocytes, NK cells and lymphocyte subsets correlate with conventional and novel deformation related indices of left ventricular function in kidney transplant recipients with no established cardiovascular disease.

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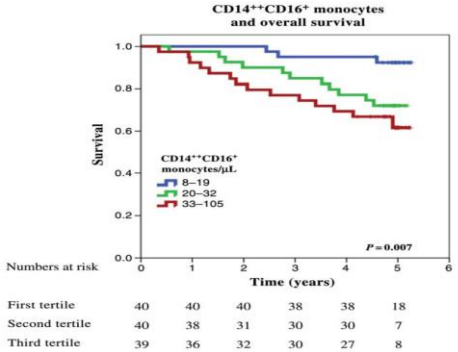
Introduction

- Kidney transplant recipients (KTRs) carry a great burden of cardiovascular disease (CVD) despite improved left ventricular (LV) remodeling after transplantation.
- Kidney allograft dysfunction and the immunosuppressed milieu play a major adverse role in myocardial structural changes in asymptomatic KTRs.
- There is an **intricate relationship between immune system responses with heart failure syndromes**, including aberrant activity and counts of proinflammatory **CD14++CD16+ monocytes, of natural killer (NK) cells and of T regulatory cells (Tregs).**
- The associations of immune cell subpopulations with subclinical markers of CVD remain to be determined in KTRs.

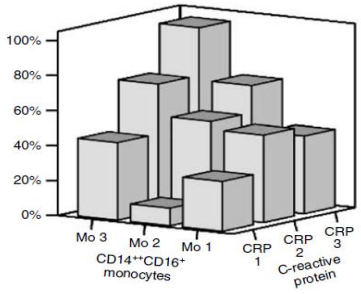
The aim of our study was to investigate potential correlations between blood levels of specific immune cells subsets with conventional and novel deformation related indices of LV function in KTRs.

CD14++CD16+ monocytes are independently associated with CV events in CKD



- *152 stable ambulatory patients with CKD*
- *5 year follow-up*

Rogacev et al, Eur Heart J 2011



94 dialysis patients
35 months FU

Heine et al, Kidney Int 2008

American Journal of Transplantation 2008; 8: 103–110
Blackwell Munksgaard

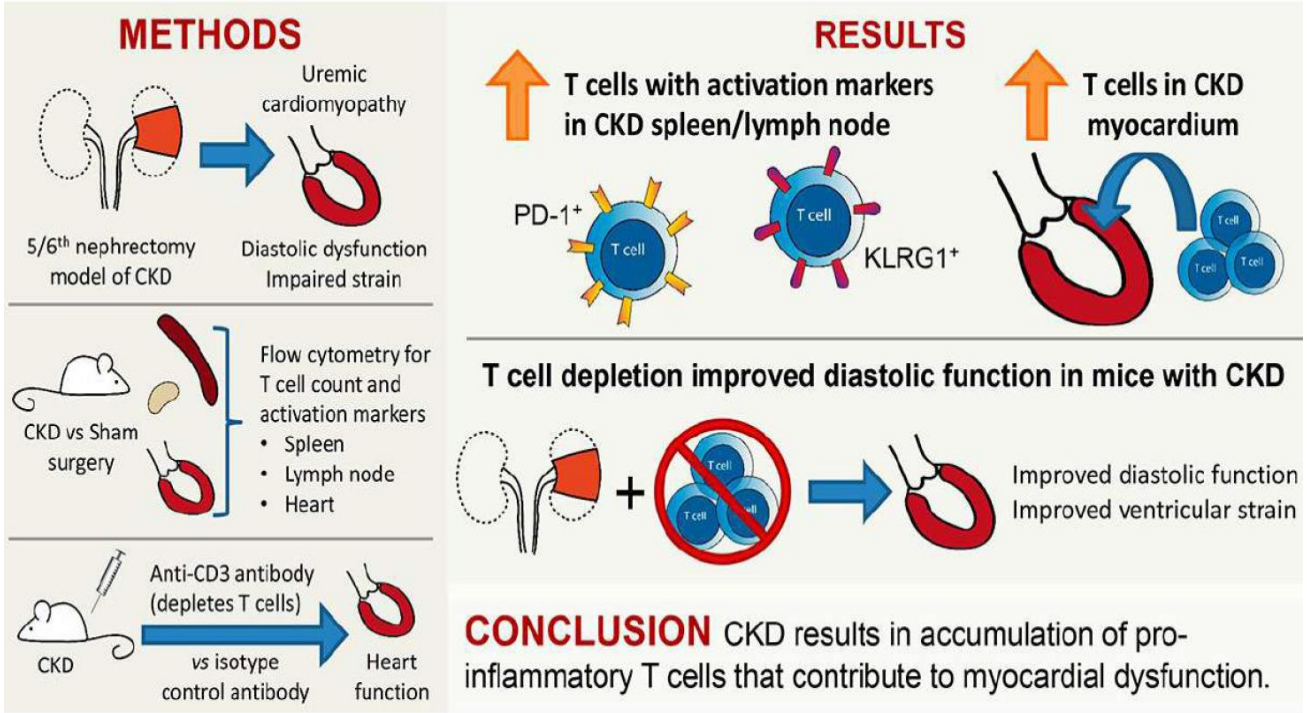
doi: 10.1111/j.1600-6143.2007.02035.x

Proinflammatory CD14+CD16+ Monocytes Are Associated With Subclinical Atherosclerosis in Renal Transplant Patients

C. Ulrich*, G. H. Heine, M. K. Gerhart, H. Köh and M. Girndt

- ***Proinflammatory monocyte subpopulations decrease after renal transplantation.***

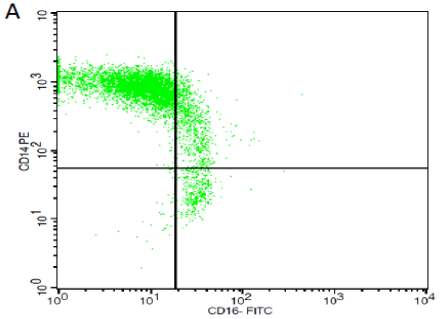
T cells play a causal role in diastolic dysfunction during uremic cardiomyopathy

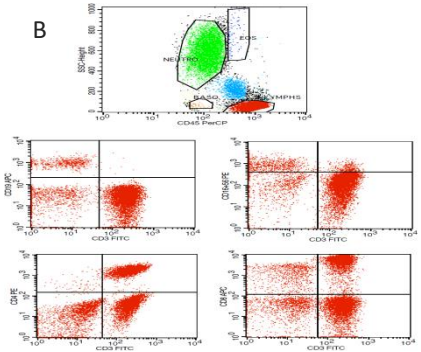


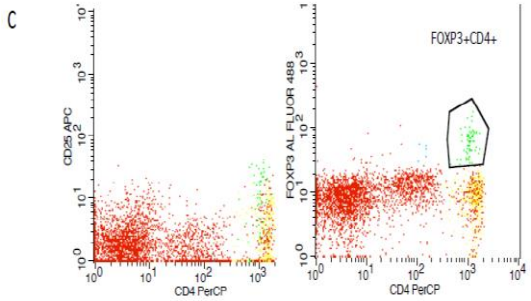
Winterberg, JASN 2019

Methods

- **31 stable KTRs** (mean age 58 +/-9.28 years, 67% males, 13% diabetics) **without established CVD were enrolled.**
- Control population included 17 patients with chronic kidney disease (CKD) stage G3 and without history of CVD, matched for age and eGFR.
- Additional exclusion criteria were history of malignancy, autoimmune disease and active or chronic infections.
- The **peripheral blood immune cell subsets** CD14++CD16-, CD14++CD16+ and CD14+CD16++ absolute values and percentages out of total monocytes, NK cells (CD3+CD16+56+), CD3-CD19+ B lymphocytes, CD3+ CD4+ T cells, CD3+CD8+ T cells and Tregs (CD4+CD25+ FoxP3+) absolute values and percentages out of total lymphocytes were measured by flow cytometry (FC).
- **Conventional** (left atrial volume index (LAVI), LV mass index (LVMI), E/E') **and novel 2D speckle tracking (2DST) echocardiographic indices of LV function** (global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), TWIST AND UNTWIST) were assessed simultaneously with FC.







Results

- KTRs had a mean eGFR of 58 +/-18 ml/min/1.73 m2 (CKD-EPI) and mean 24-hour proteinuria (PER) 707 +/-1185 mg/24h.
- Total lymphocytes, B-cells, T-cells and CD8+ T cells counts correlated positively with eGFR ($p<0.05$).
- Increased non-classical CD14+CD16++ monocytes were associated with PER ($p <0.01$).
- There was an inverse correlation between the percentage of classical CD14++CD16- monocytes with PER ($p <0.05$).

KTRs displayed higher CD14++CD16- *and* lower CD14+CD16++ monocytes, a lower percentage of NK cells and T cells and lower Tregs, compared to CKD patients.

	KTRs (No=31)	CKD (No=17)	*P value*
WBC (No/mm^3)	8675+/-2852	7060 +/-1671	*0.003*
Monocytes (No/mm^3)	629 +/-246	453 +/-144	*0.000*
CD14++ (No/mm^3)	517 +-/223	356 +/-137	*0.000*
CD14++ (%)	86 +/-8.3	79 +/-8.3	*0.001*
CD14+CD16++ (No/mm^3)	22 +/-14	31+/-16	*0.008*
CD14+CD16++ (%)	3.8+/-2.5	7.2+/-3.7	*0.000*
T lymphocytes (%)	81.4 +/-8.3	76.6 +/-8.4	*0.011*
NK cells (%)	13.4 +/-7.9	17.1 +/-7.8	*0.039*
Tregs (No/mm^3)	22 +/-13	38 +/-34	*0.006*
Tregs (%)	1.2 +/-0.75	2 +/-1.4	*0.002*

Correlation of immune cells subsets with classical and novel LV dysfunction indices

- Increased total monocytes were associated with elevated LAVI ($p<0.05$).
- An increased percentage of the intermediate pro-inflammatory CD14++CD16+ monocytes correlated positively with an increased E/E' value ($p<0.05$).
- Both CD4+ T cells number and Tregs percentage were inversely correlated with E/E' ($p<0.01$).
- Increased pro-inflammatory monocytes levels were directly associated with LV TWIST and inversely associated with LV UNTWIST values ($p<0.05$).
- Increased NK cells were associated with more negative GLS and GCS values ($p<0.05$).
- No significant correlations were observed between the rest immune cells with the classical or novel LV dysfunction indices.

Conclusion

- Alterations of immune cells subsets correlate with subclinical markers of LV dysfunction in KTRs with no established CVD.
- Future research is required to evaluate the role of immune subpopulations as tools to identify KTRs who are at the highest risk for complications and guide interventions.

Acknowledgments: None

References

Dounousi E , Duni A, Naka KK, Vartholomatos G, Zoccali C. The Innate Immune System and Cardiovascular Disease in ESKD: Monocytes and Natural Killer Cells. Curr Vasc Pharmacol 2021;19(1):63-76