INFLAMMATION AND MACROPHAGE INFILTRATION IN THE RENAL ALLOGRAFT

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INTRODUCTION

- In renal transplantation, allografts from living donors (LD) have superior graft function and survival compared with cadaver allografts.
- Studies have demonstrated that immediately following transplantation, cadaver renal allografts may experience an inflammatory response associated with prolonged cold ischemia and reperfusion injury.
- On the other hand, there are few studies conducted in humans comparing the inflammatory condition of the grafts at the time of the donation and influence in chronic graft dysfunction.

METHODS

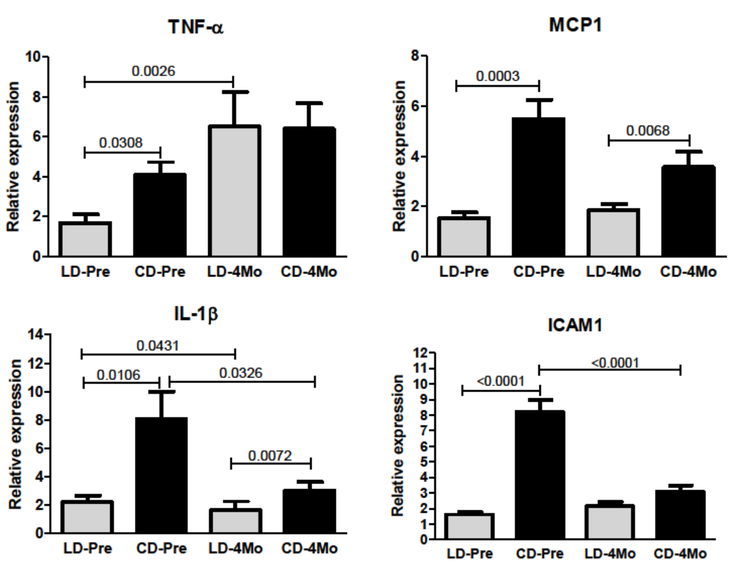
- Protocol biopsies were collected from kidney donors and recipients who underwent transplantation in our institution between 2008 and 2011.
- A total of 94 patients were enrolled. We aimed to take, from each transplanted kidney, two biopsy cores at the time of transplantation, just before implantation (baseline) and 4 months after surgery. One core was processed for mRNA analysis and the second was included in paraffin for CD68 immunohistochemistry.

OBJECTIVE

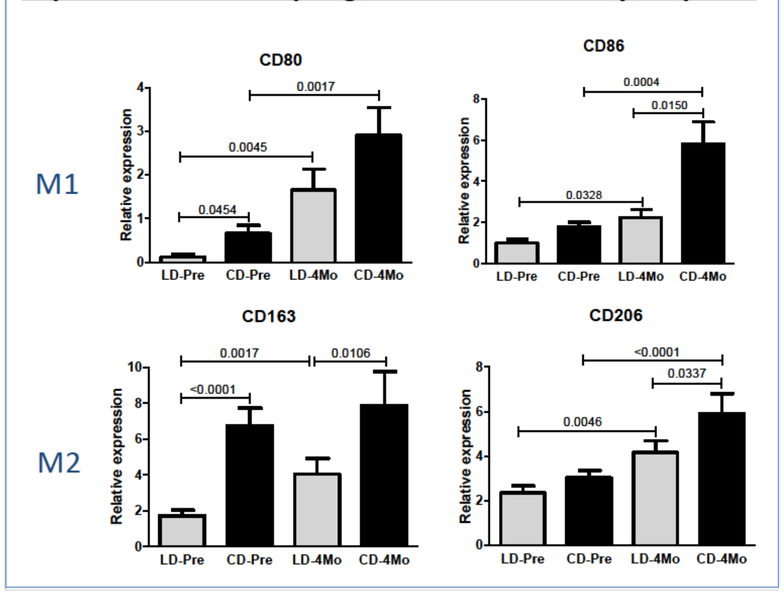
The aim of this study was to assess the inflammatory condition and expression of fibrotic factors of allografts from donors (DD and LD) and its relationship with long-term renal function (RF).

RESULTS

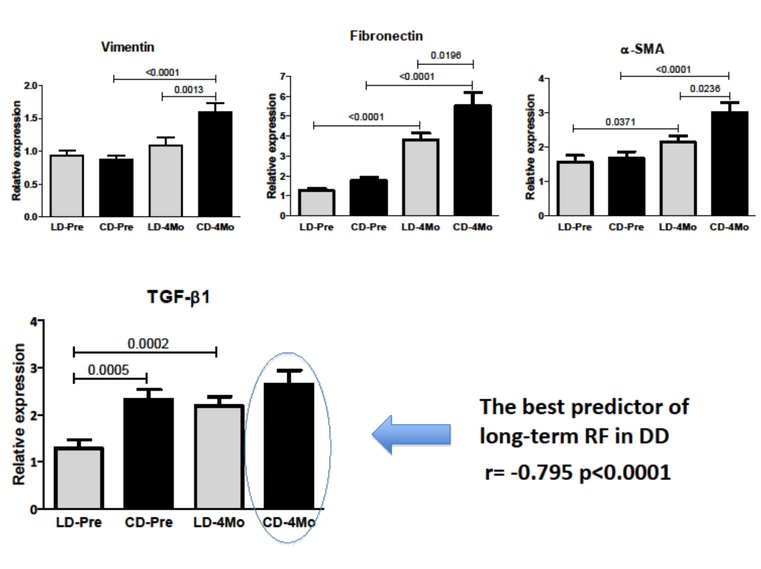
Inflammation in baseline kidney biopsies



Expression of macrophages markers in kidney biopsies



Expression of fibrotic markers in kidney biopsies

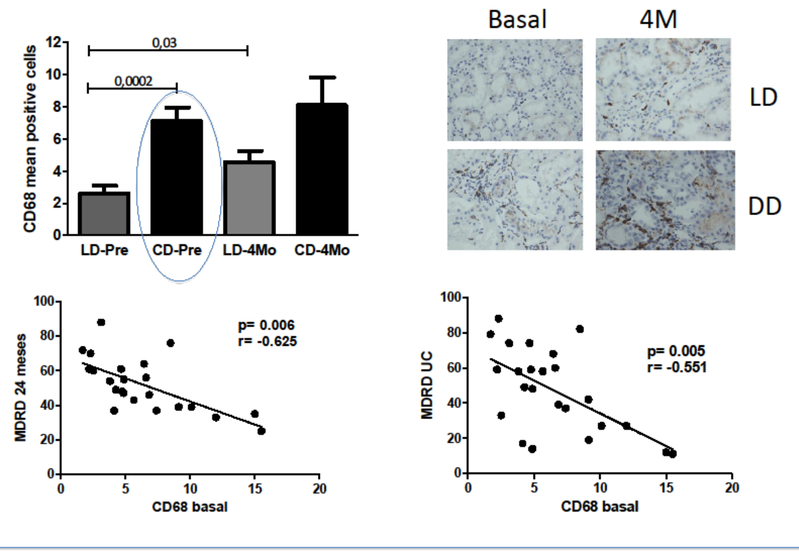


Correlations between gene expression and long-term renal function

4 MONTHS DD	MDRD (ml/min/1,73m²) 24M p value	24M rho Spearman	Last follow-up (±5 years) p value	Last follow-up (±5 years) rho Spearman
α-SMA	0,0426	-0,4171	0,0070	-0,5358
TGF-β	0,0026	-0,5860	0,0000	-0,8287
Fibronectin	0,1182	-0,3275	0,0007	-0,6437
CD16	0,0181	-0,4780	<0,0001	-0,7404
CD206	0,0035	-0,5725	0,0012	-0,6204
MCP1	0,0212	-0,4677	0,0011	-0,6239
CD163	0,0231	-0,4619	0,0010	-0,6281
Vimentin	0,1086	-0,3359	0,0233	-0,4613
TNF-α	0,0209	-0,4686	0,0202	-0,4709
IL-1β	0,0187	-0,4760	0,0003	-0,6739
CD14	0,0513	-0,4023	0,0003	-0,6790
ICAM1	0,0473	-0,4089	0,0007	-0,6429
IL-4R	0,0214	-0,4672	<0,0001	-0,7112
CD209	0,0323	-0,4380	0,0471	-0,4091
CD80	0,2065	-0,2674	0,0421	-0,4179
CD86	0,0357	-0,4306	0,0007	-0,6442

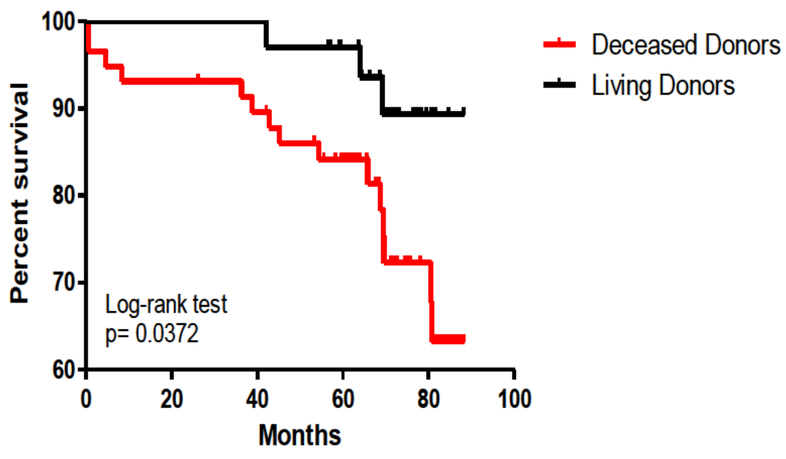
Δ4M-Baseline DD	MDRD (ml/min/1,73m²) 24M p value	24M rho Spearman	Last follow-up (±5 years) p value	Last follow-up (±5 years) rho Spearman
α-SMA	0,0958	-0,4814	0,1618	-0,4121
TGF-β	0,0210	-0,6300	0,0490	-0,5549
Fibronectin	0,0258	-0,6135	<0,0001	-0,9231
CD16	0,0398	-0,5750	0,0037	-0,7418
CD206	0,0500	-0,5530	0,1497	-0,4231
MCP1	0,0003	-0,8473	0,0024	-0,7637
CD163	0,0233	-0,6217	0,1744	-0,4011
Vimentin	0,0196	-0,6355	0,0367	-0,5824
TNF-α	0,0241	-0,6190	0,0346	-0,5879
IL-1β	0,0102	-0,6823	0,0007	-0,8132
CD14	0,1323	-0,4402	0,2309	-0,3571
ICAM1	0,0026	-0,7593	0,0673	-0,5220
IL-4R	0,0034	-0,7455	0,0112	-0,6758
CD209	0,0315	-0,6200	0,3541	-0,2937
CD80	0,1972	-0,3824	0,0252	-0,6154
CD86	0,8373	-0,0633	0,3344	-0,2912

Macrophage infiltration: CD 68



Kidney graft survival

(Mean follow-up = 88.2 months)



CONCLUSIONS

- We conclude that early macrophage infiltration, sustained inflammation and TGF-β1 expression, at least for the first 4 months, contribute significantly to the difference in DD and LD transplant outcome.
- The control of inflammation therefore offers great therapeutic potential in the prevention of progressive kidney fibrosis in recipients of transplants from deceased donors.

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53 ERA
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Renal transplantation. Experimental, immune-tolerance of allogenic and xenogenic transplants.
IARA DASILVA
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th, 2016
Held jointly with Österreichische Gesellschaft für Nephrologie
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