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# **The Role of Immune Reconstitution in the Onset of Subclinical Atheromasic Lesions**

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# Abstract

**Background:** In the present study we evaluated 263 patients starting antiretroviral therapy (ART) at baseline and after 12 months, with color Doppler ultrasonography of the epiaortic vessels, a well validated technique, considered the gold standard for the detection of premature vascular lesions .

**Methods:** The patients were submitted to color Doppler ultrasonography at baseline and after 12 months of therapy. An intima media thickness  $> 0,9$  mm and/or atherosclerotic plaques were considered pathologic findings. After 12 months of ART, patients with  $< 50$  CD4+ cell count/mm<sup>3</sup> at baseline were divided into three groups based on CD4+ at follow-up: group A) patients with  $< 100$  CD4+ (# 41); group B) patients with 100-199 CD4+ (# 50) and group C) patients with  $> 200$  CD4+ (# 62). The data were compared with those observed in 110 patients starting their ART with  $> 200$  CD4+ and remaining at follow up, over this value (group D). The four groups were comparable for gender, mean age and other risk factors for CVD. All patients were treated with a PI-based therapy. Backbone drugs were well balanced among the groups).

**Results:** Patients in group C showed a significant increase in the number of carotid lesions at follow-up. Moreover, comparing groups A+B+C with group D, the first group had a significant increase of lesions with respect to group D ( $p=0.00001$ ).

**Conclusions:** These data show that patients starting ARV with a high degree of immune depression tend to develop more subclinical carotid lesions with respect to patients starting ARV in a relatively better immunologic conditions. Moreover, patients experiencing a more rapid immune reconstitution develop a significantly higher number of subclinical vascular lesions.

# Objectives

In recent studies (SMART, MACS +WIHS) patients with low CD4+ cell count showed an increased risk for cardiovascular disease (CDV). An hyper production of proinflammatory cytokines (IL-6, hsPCR) have been hypothesized in these patients. No data exist regarding the role of immune reconstitution in the onset of CVD, another condition that could be related to an increase of circulating proinflammatory factors. In the present study we evaluated 263 patients starting antiretroviral therapy (ART) at baseline and after 12 months, with color Doppler ultrasonography of the epiaortic vessels, a well validated technique, considered the gold standard for the detection of premature vascular lesions .

# Patients and Methods

The patients were submitted to color Doppler ultrasonography at baseline and after 12 months of therapy. An intima media thickness  $> 0,9$  mm and/or atherosclerotic plaques were considered pathologic findings. After 12 months of ART, patients with  $<50$  CD4+ cell count/mm<sup>3</sup> at baseline were divided into three groups based on CD4+ at follow-up: group A) patients with  $<100$  CD4+ (# 41); group B) patients with 100-199 CD4+ (# 50) and group C) patients with  $> 200$  CD4+ (# 62). The data were compared with those observed in 110 patients starting their ART with  $> 200$  CD4+ and remaining at follow up, over this value (group D). The four groups were comparable for gender, mean age and other risk factors for CVD. All patients were treated with a PI-based therapy. Backbone drugs were well balanced among the groups (table 1). Statistical analysis was performed using chi square test.

# Results

As showed in table 2, patients with  $< 50$  CD4+ cell count at baseline that reached values  $>100$  (group C) showed a significant increase in the number of carotid lesions at follow-up. Moreover, comparing patients with  $<50$  cells at baseline (groups A+B+C) with patients with  $>200$  cells (group D), the first group had a significant increase of lesions with respect to group D ( $p=0.00001$ ).

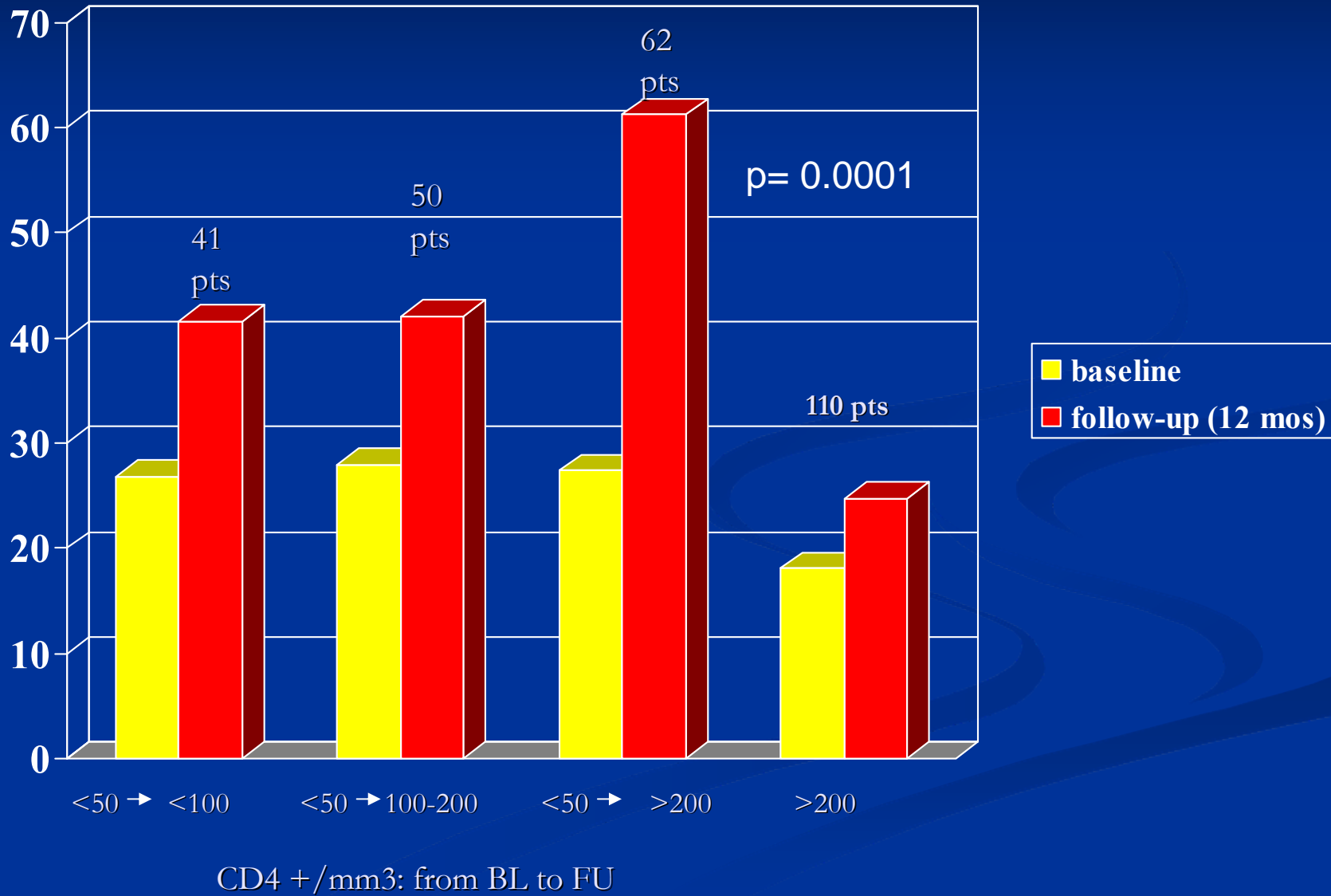
# Conclusions

These data show that patients starting ARV with a high degree of immune depression tend to develop more subclinical carotid lesions with respect to patients starting ARV in a relatively better immunologic conditions. Moreover, patients experiencing a more rapid immune reconstitution develop a significantly higher number of subclinical vascular lesions. This suggests that inflammatory events characterizing both immune deficiency and immune reconstitution could play a role in the onset of CVD.

<b>Group</b>	<b>A #41</b>	<b>B #50</b>	<b>C #62</b>	<b>D #110</b>
<b>Male (%)</b>	72	70	76	80
<b>Female (%)</b>	28	30	24	20
<b>age (median,range)</b>	40 (25-58)	38 (21-70)	37 (28-67)	36 (23-64)
<b>Hypercholesterolemia <math>\geq</math> 200 mg/dl (%)</b>	22	25	24	26
<b>Hypertriglyceridemia <math>\geq</math> 200 mg/dl (%)</b>	29	37	34	33
<b>Hyperglycemia <math>\geq</math> 110 mg/dl (%)</b>	3	4	4	2
<b>body mass index <math>\geq</math> 25 kg/m<sup>2</sup> (%)</b>	0	0	0	5
<b>high blood pressure &gt;140/90 mmHg (%)</b>	0	2	0	3
<b>PI-based therapy (%)</b>	100	100	100	100
<b>timidine-based backbone (%)</b>	16	12	17	18
<b>abacavir-based backbone (%)</b>	22	23	22	21
<b>tenofovir-based backbone (%)</b>	59	61	57	56
<b>ddx-based backbone (%)</b>	3	4	4	5

Group	patients with carotid lesions				
	baseline		follow up		
	%	#	%	#	
A	26.8	11	41.6	17	p= 0.27
B	28.0	14	42.0	21	p= 0.14
C	27.4	17	61,2	38	p= 0.0001
D	18.1	24	24.7	25	p= 0.71

%  
patients with  
carotid lesions



# References

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