

Lp (a) apheresis and CVD risk (modulation)

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Conflict of Interest Disclosure

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General Facts

- Apheresis is an extracorporeal procedure to remove lipoproteins from the plasma of patients
- Veno-venous
- 1,5-3h weekly or biweekly
- app 1000€/ apheresis
- There are different methods how lipoproteins can be removed

HELP: Heparin-induced extracorporeal precipitation

precipitation of a complex consisting of heparin, LDL, lipoprotein(a), fibrinogen and CRP at pH 5.12

Immuno-adsorption: Anti-apoB100 antibodies

plasma is passed through columns containing polyclonal anti-apoB100 antibodies

Dextransulfate: electrostatic binding

electrostatic interaction of negatively charged dextransulfate and positively charged apoB

Lipidfiltration/ membrane differential filtration

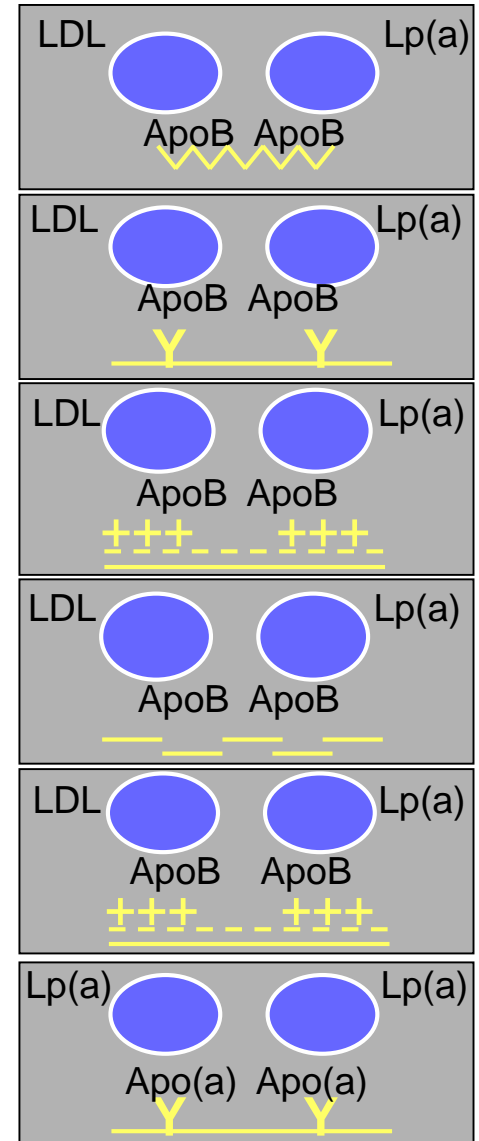
series of filters eliminate LDL and lipoprotein(a) from plasma based on size properties

DALI: direct adsorption of lipoproteins

electrostatic interaction of negatively charged polyacrylate anions with positively charged apoB

Lipopac: Anti-apoprotein(a) antibodies

plasma is passed through columns containing polyclonal anti-apo(a) antibodies



Effects on lipoproteins

Acute reductions in plasma lipoproteins in studies comparing different methods of LDL apheresis: immunoadsorption (IMA), dextran sulphate adsorption (DSA), HELP and DALI

Author (Ref.)	Patients (n)	Procedure (n)	Volume treated, l	LDL-C (%)	Δ% Lp(a)	HDL-C (%)
Knisel [27]	FH (5) (3)	IMA (690)	5.7	-60	-63	-22
		DSA (243)	4.8	-57	-	-8
Schaumann [28]	FH (7) ^a	IMA (14)	4.5	-69	-	-27
		DSA (14)	4.3	-75	-	-11
		HELP(14)	3.0	-60	-	-5
Richter [29]	FH (18) (8) (8)	IMA (3499)	-	-62	-51	-15
		DSA (579)	-	-65	-49	-17
		HELP (1497)	-	-59	-68	-17
Schmaldienst [30]	FH (8) ^a	IMA (32)	6.0	-82	-63	-23
		DSA (32)	5.1	-84	-63	-10
		DALI (32)	7.1 ^b	-77	-63	-13
Parhofer [31]	HC (10) ^c (8) (7)	IMA (100)	3.8	-64	-64	-14
		DSA (80)	3.1	-65	-61	-9
		HELP (70)	2.7	-67	-62	-15

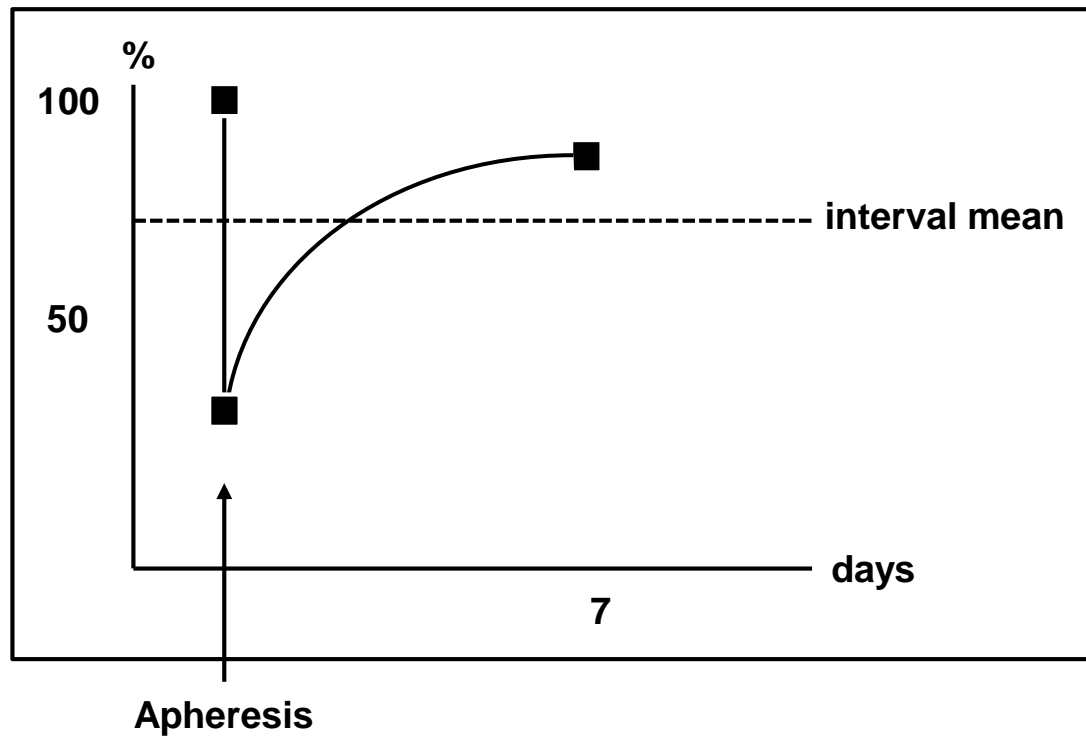
^a Crossover study.

^b Blood. All other volumes refer to plasma.

^c Refractory hypercholesterolaemia.

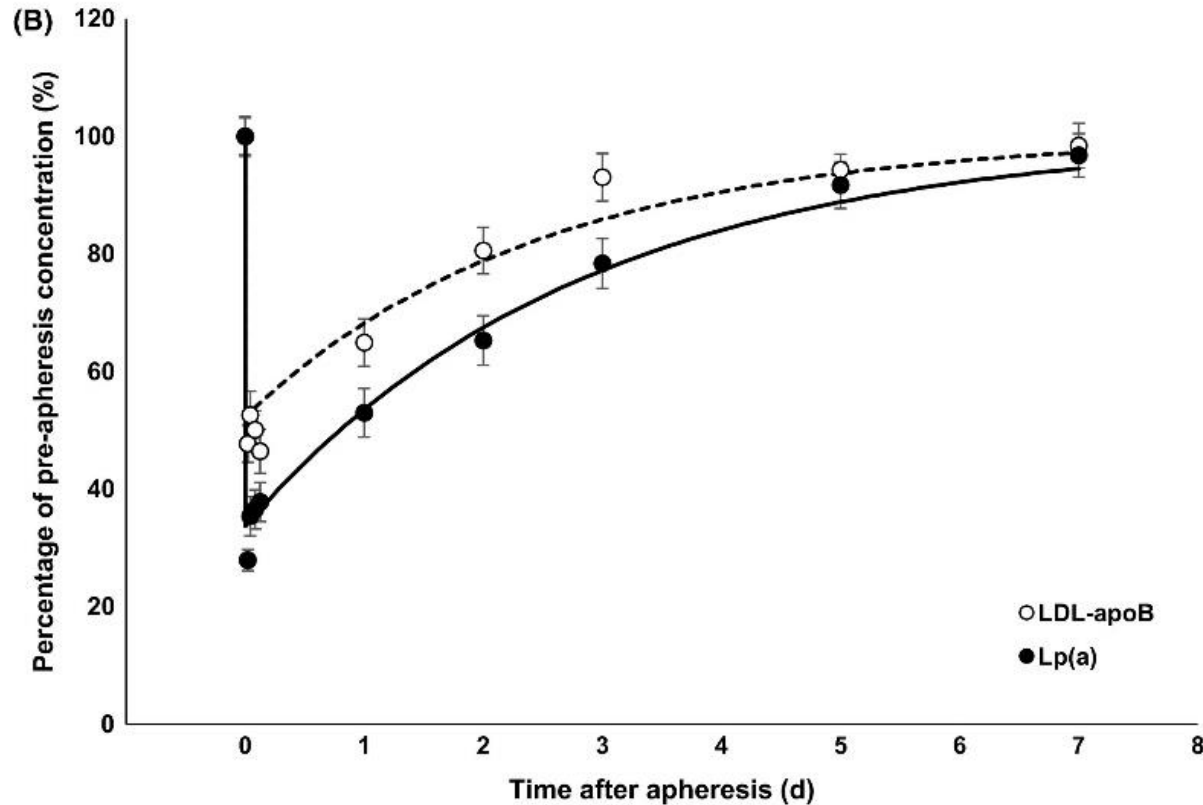


Rebound curve

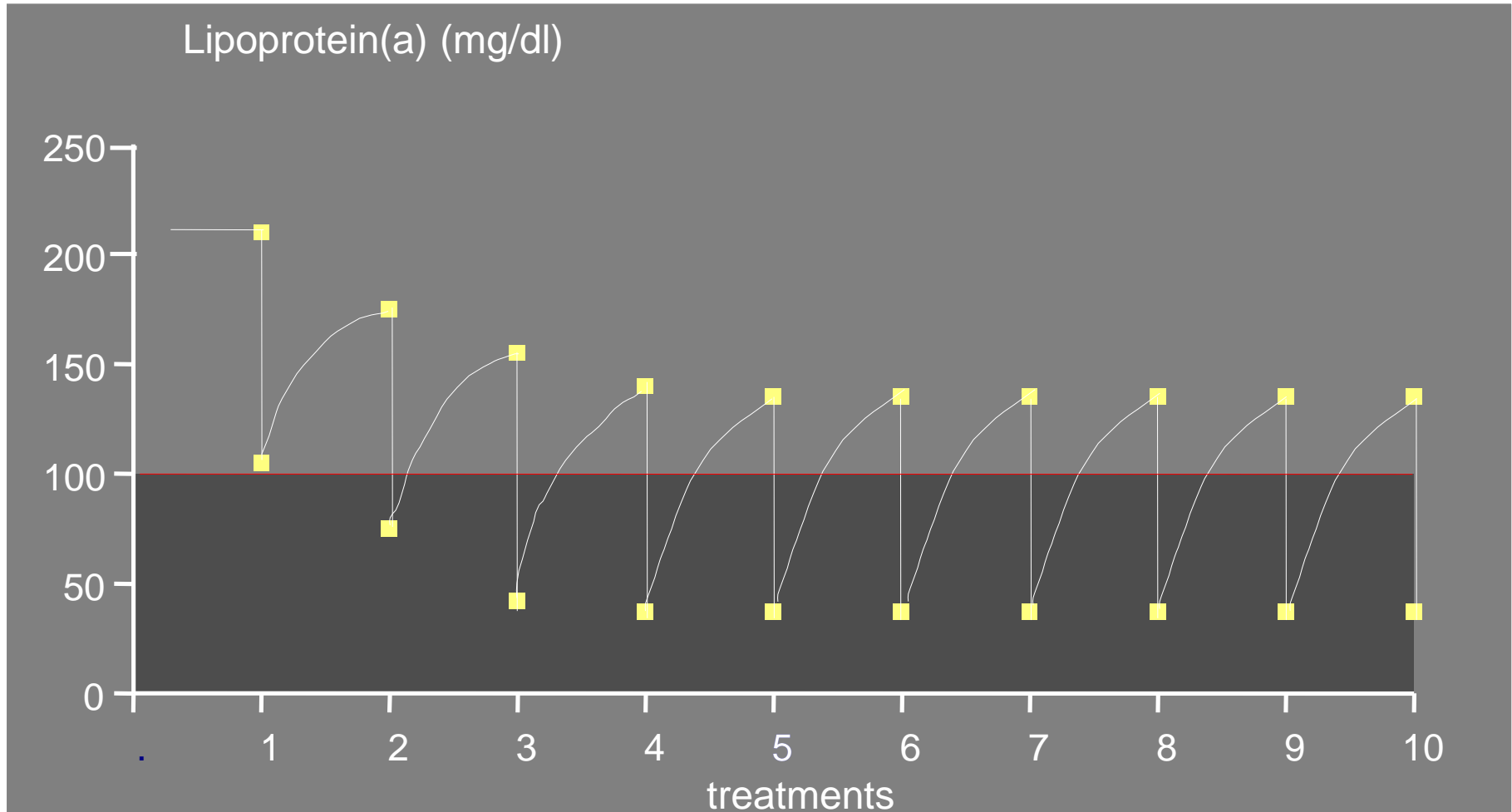




Rebound after apheresis

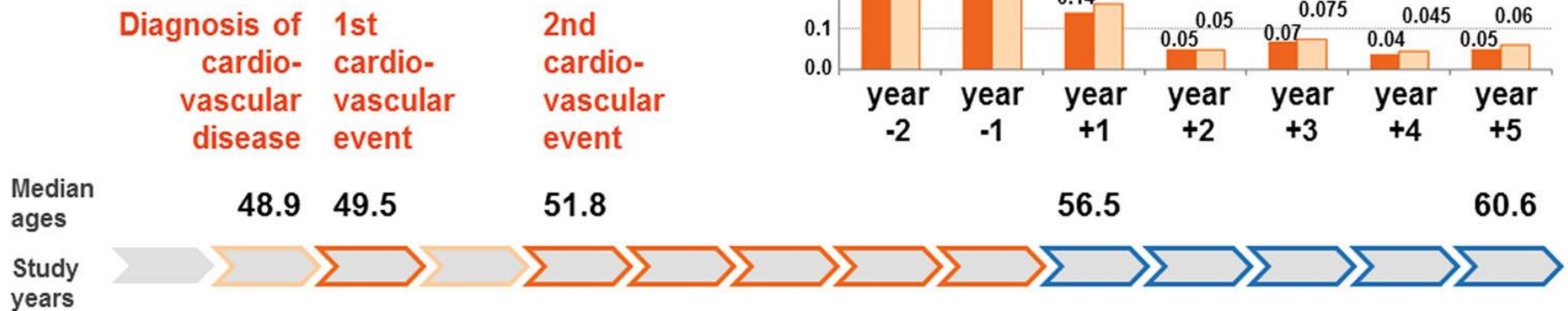


Elimination of ApoB Containing Lipoproteins



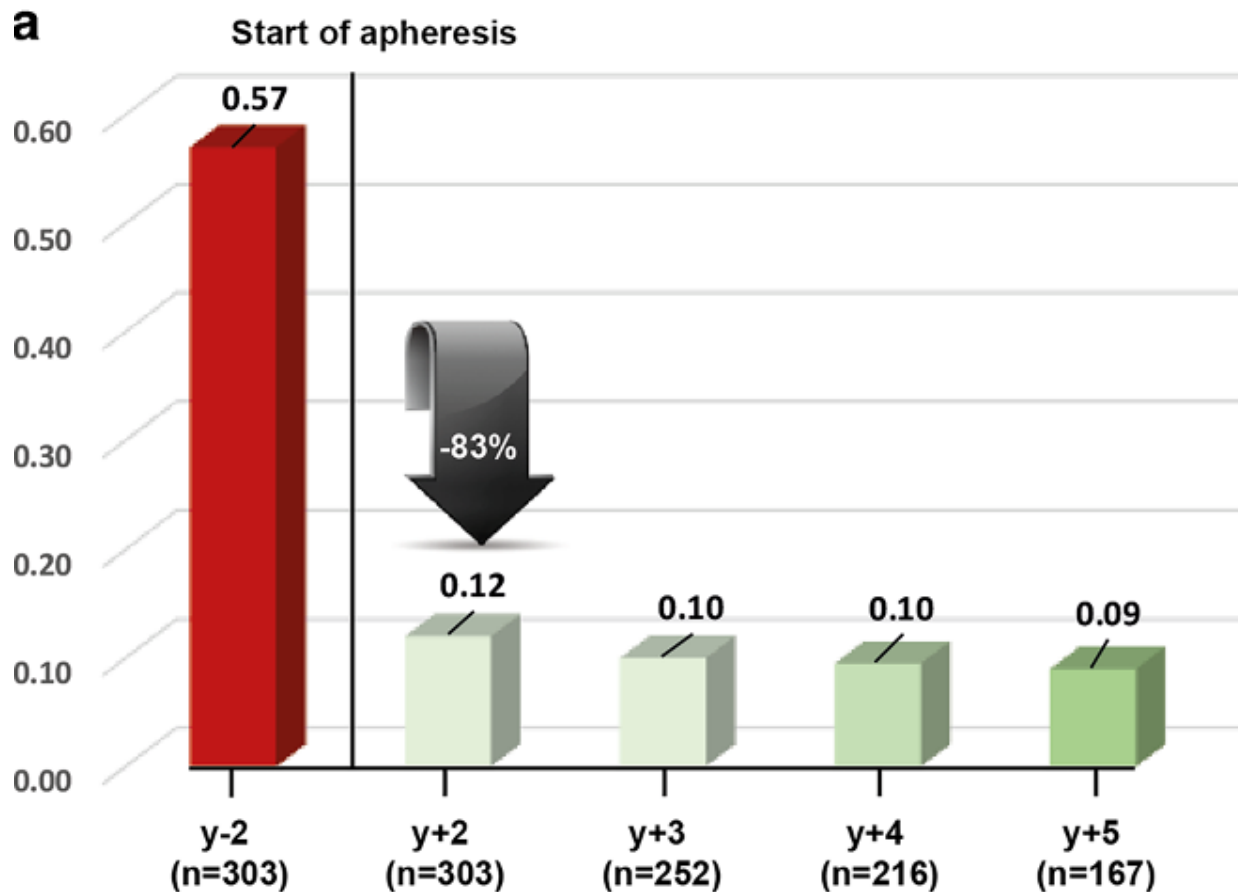


Pro (a) Life



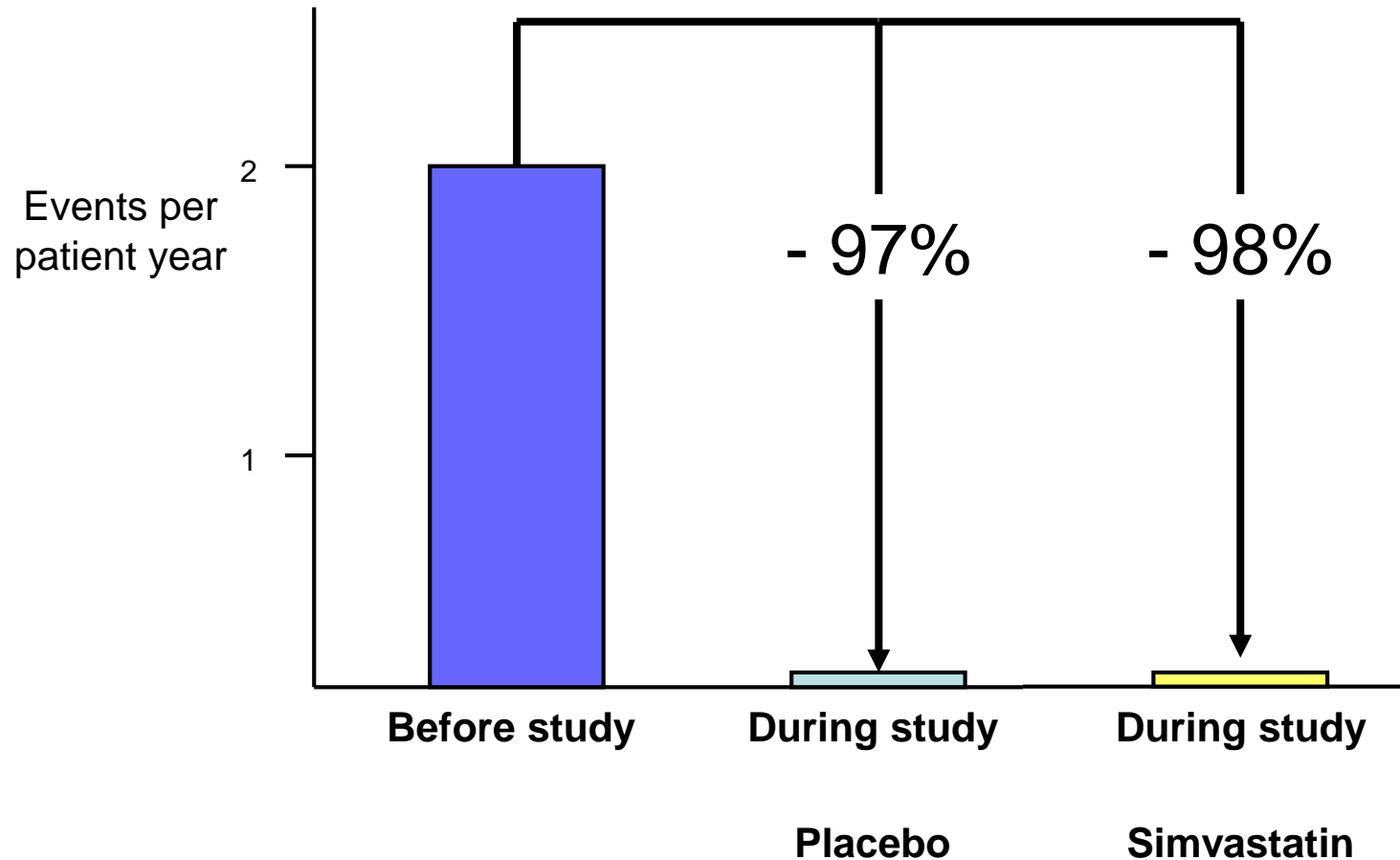


German lipoprotein apheresis registry (GLAR)



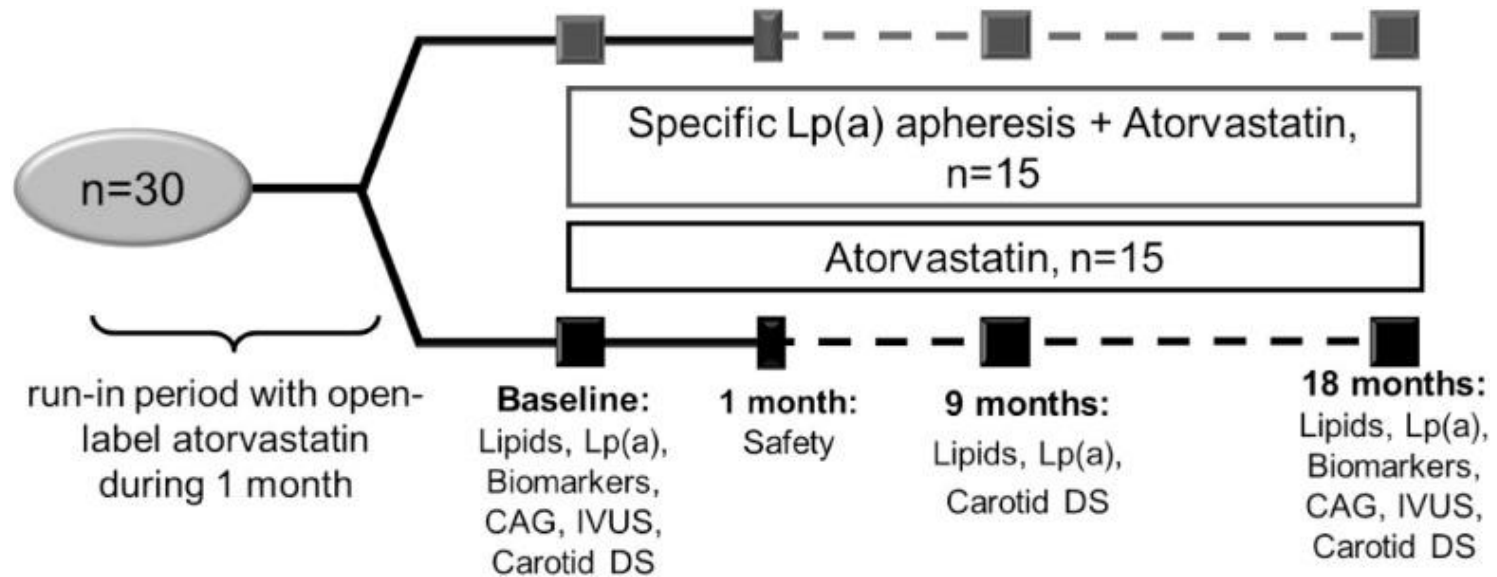
Similar Analysis with Data of “4S”

(n=4444; CAD; simvastatin vs. placebo; 5.4 years; event rates 22.6% (placebo) vs 15.9% (simvastatin))





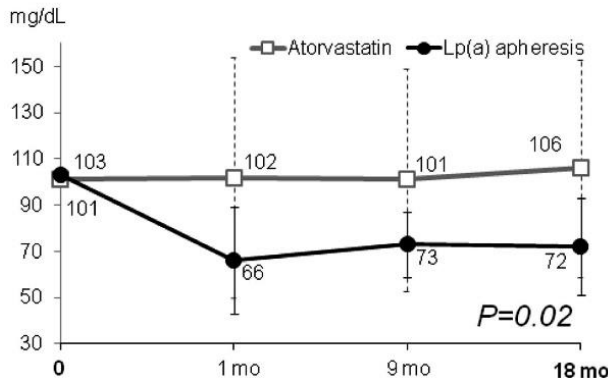
Effect of Lp(a) apheresis



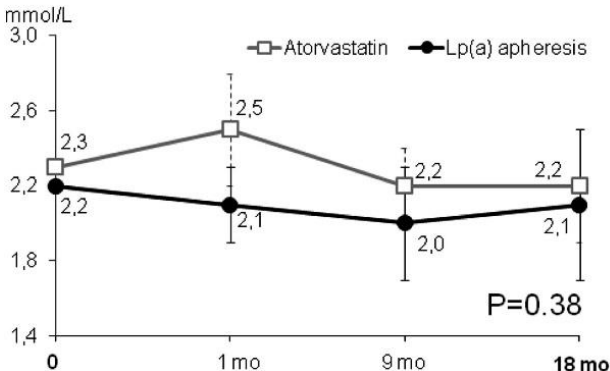


Effect of Lp(a) apheresis

Lipoprotein(a)



LDL-C

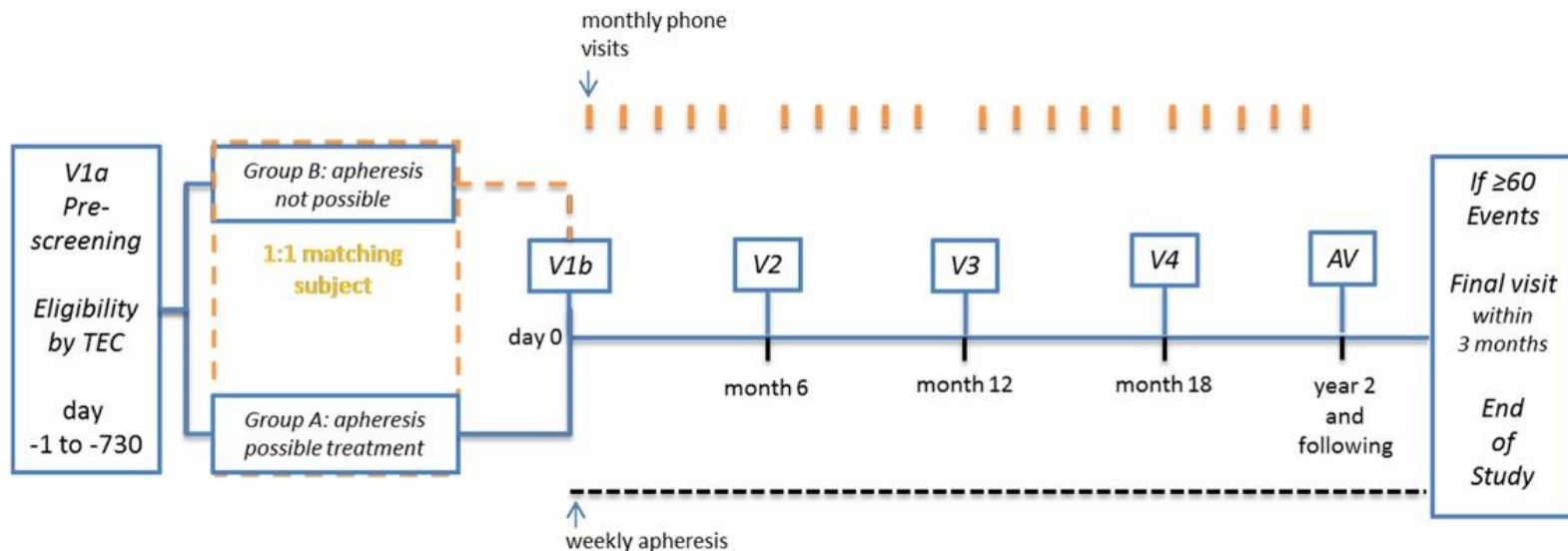


QCA parameters	Lp(a) apheresis	Atorvastatin	p Value
Number of coronary segments	42 segments	50 segments	
<i>Percent diameter stenosis, %</i>			
Baseline			
Mean	44.31 ± 15.95	43.68 ± 13.46	0.95
Median (95% CI)	40.00 (37.29–47.00)	43.50 (39.86–47.51)	
18-month			
Mean	<u>39.26 ± 13.61</u>	<u>48.72 ± 14.77</u>	0.001
Median (95% CI)	36.50 (32.00–43.35)	49.00 (40.07–52.93)	
Mean change from baseline	<u>-5.05 ± 12.38</u>	5.04 ± 11.43	0.0004
Median change from baseline	-2.00 (-5.00–0.00)	3.50 (0.00–6.93)	
Number with regression, n (%)	18 (43)	10 (20)	0.02*
<i>Minimal lumen diameter, mm</i>			
Baseline			
Mean	1.39 ± 0.63	1.44 ± 0.50	0.52
Median (95% CI)	1.30 (0.99–1.63)	1.40 (1.17–1.64)	
18-month			
Mean	1.59 ± 0.54	1.45 ± 0.65	0.08
Median (95% CI)	1.56 (1.34–1.73)	1.26 (1.16–1.58)	
Mean change from baseline	0.20 ± 0.39	0.01 ± 0.34	0.04
Median change from baseline	0.17 (0.03–0.36)	0.05 (-0.05–0.17)	

Multiselect trial

Matching criteria.

1. Identical sex
2. Age \pm 3 years
3. Identical ethnicity
4. Both subjects on or off PCSK9 inhibitor therapy
5. Both subjects with LDL-C in the same range of
 - Either between 2.6 mmol/L (100 mg/dL) and 3.39 mmol/L (129 mg/dL)
 - Or below 2.6 mmol/L (100 mg/dL)



Conclusion

- Lp(a) is a respected cardiovascular risk factor
- Lipoprotein apheresis reduces Lp(a) effectively
- Prospective, not controlled data shows positive effect of apheresis
- Plaqueregression through Lp(a) apheresis
- Matched (controlled) data is in progress ...