LDL-AFERESI

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LDL-aferesi

Rimozione selettiva da plasma o da sangue intero delle lipoproteine contenenti apoB100: LDL, VLDL, Lp(a), con metodiche chimico-fisiche o immunologiche

- Riduzione acuta delle lipoproteine aterogene
- Effetti pleiotropici: modulazione dei livelli circolanti di markers pro-infiammatori e pro-trombotici.

→ Rallentamento/regressione della malattia cardiovascolare del paziente con ipercolesterolemia familiare

→ miglioramento della perfusione nel miocardio

→ miglioramento delle patologie sostenute dalle alterazioni del microcircolo come la sordità improvvisa e la neuropatia ottica ischemica, piede diabetico ischemico

Effetto delle principali tecniche di LDL-aferesi sui lipidi plasmatici

Table 1
Mean percentage reduction of plasma lipoproteins and fibrinogen with different methods of LDL apheresis [8]

	DFPP (%)	Thermofiltration (%)	HELP (%)	DALI (%)	DSA (%)	IA (%)
LDL cholesterol	56–62	61	55–61	53–76	49–75	62–69
HDL cholesterol	25–42	6	5–17	5–29	4–17	9–27
Lp(a)	53–59	61	55–68	28–74	19–70	51–71
Triglycerides	37–49	56	20–53	29–40	26–60	34–49
Fibrinogen	52–59	42	51–58	13–16	17–40	15–21

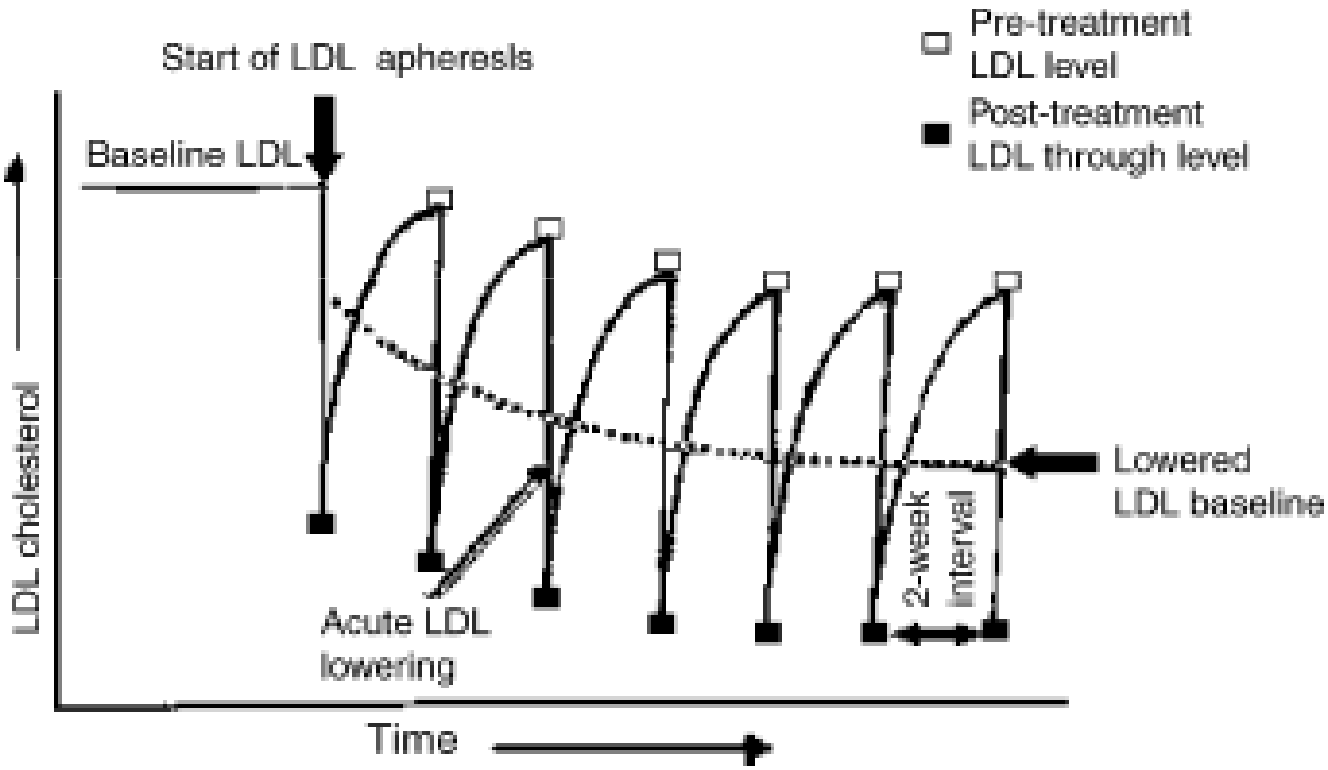
G.R. Thompson / Atherosclerosis 198 (2008) 247–255

Return to pretreatment LDL levels in approximately 13 days

(Kroon AA et al. Atherosclerosis 152, 519-526; 2000)

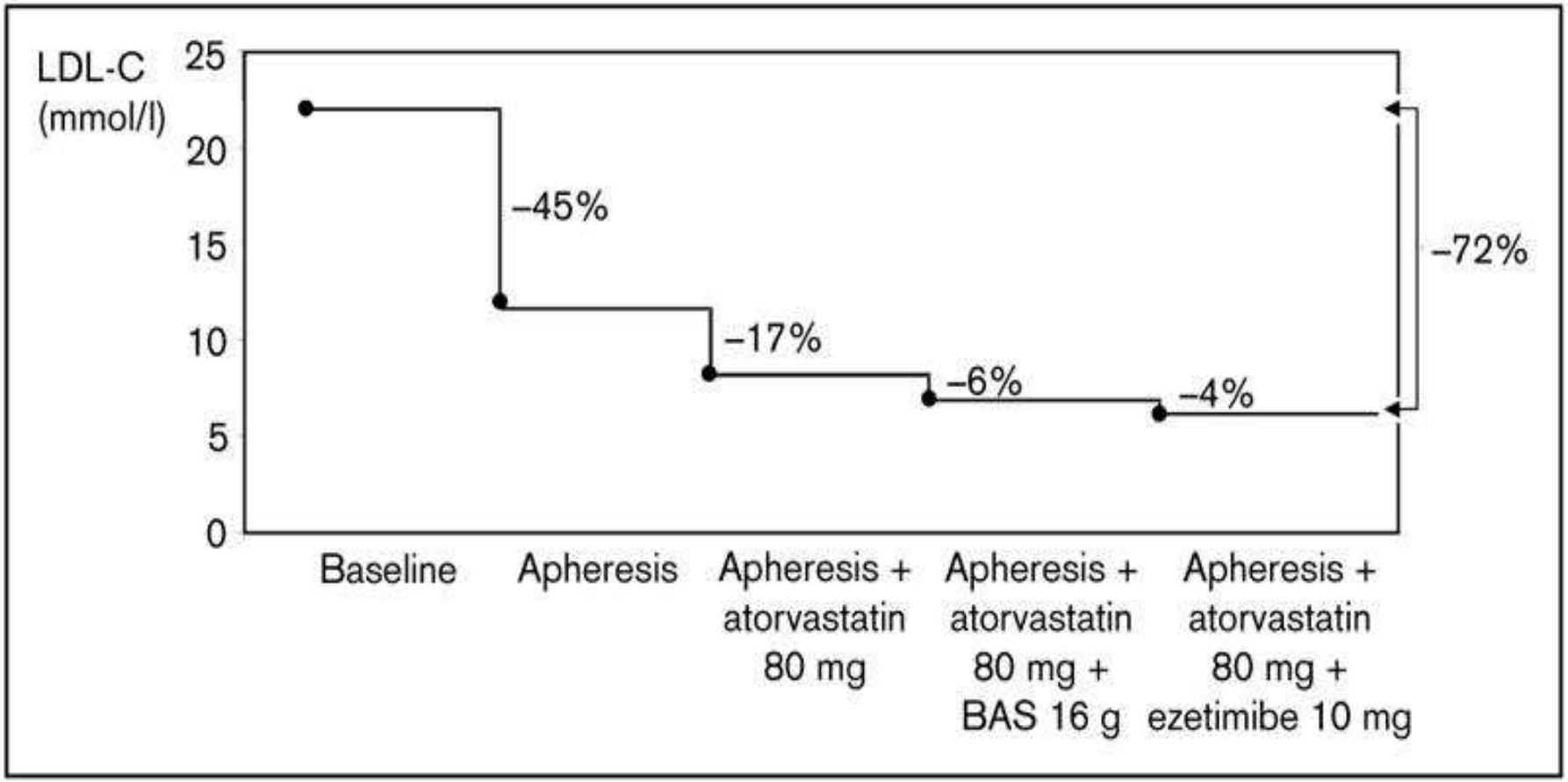
HDL may be reduced acutely but chronically it remains unchanged or slightly elevated from baseline

Variazioni del colesterolo LDL nel tempo in corso di trattamento con LDL AFERESI



J Thompsen, PDThompson. Atherosclerosis 2006

LDL-Aferesi e statine



Naoumova: Curr Opin Lipidol, Volume 15(4).August 2004.413-422

LDL-aferesi:
modificazioni delle dimensioni e densità delle LDL

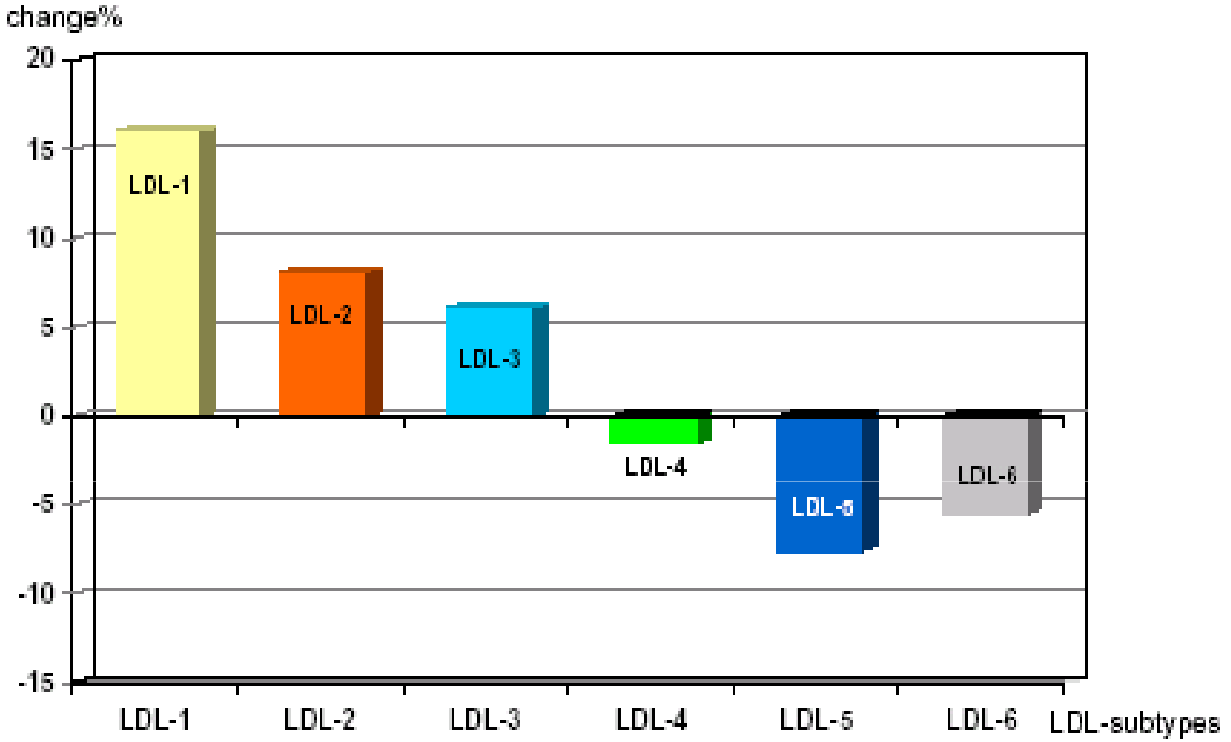


Fig. 3. Influence of LDL apheresis (different methods, including MDF) on LDL subtype distribution in patients with coronary heart disease and severe hyperlipoproteinemia. Mean values of 37 LDL apheresis treatments are presented (different methods, including MDF). LDL-cholesterol was separated into subtypes corresponding to size and density. Small, dense LDL particles (LDL-5 and LDL-6 subtypes) are more atherogenic than large, buoyant LDL particles (LDL-1 and LDL-2 subtypes). MDF and HELP lead to a shift of subfractions with a relative increase in large less atherogenic LDL-1 and LDL-2 subtypes and a relative decrease in small, dense LDL-subtypes [34].

(Schamberger BM et Al. *J.Lipid Res. 41:727-733, 2000)*

LDL-apheresis

vascular markers

Effects of heparin-mediated extracorporeal low-density lipoprotein precipitation beyond lowering proatherogenic lipoproteins—reduction of circulating proinflammatory and procoagulatory markers

Ying Wang [a], Frithjof Blessing [a], Autar K. Walli [a,*], Peter Überfuhr [b], Peter Fraunberger [a], Dietrich Seidel [a]

Table 3
Modulation of circulating proinflammatory markers by a single HELP-apheresis

Proinflammatory parameters	Pre-HELP	Post-HELP	Reduction (%)	*P*-value
sVCAM-1 (ng/ml)	674.8 ± 185.8	426.5 ± 151.5	37.0	<0.001
sICAM-1 (ng/ml)	148.1 ± 37.5	153.9 ± 40.9	−6.2	NS
sE-selectin (ng/ml)	31.1 ± 11.0	24.0 ± 9.8	23.6	<0.001
MCP-1 (pg/ml)	409.9 ± 124.2	346.9 ± 110.0	15.0	<0.001
ET-1 (pg/ml)	1.8 ± 0.5	1.3 ± 0.3	24.4	<0.001
LBP (μg/ml)	7.1 ± 3.8	4.7 ± 2.1	26.7	<0.01
Hs-CRP (mg/dl)	0.5 ± 1.24	0.17 ± 0.4	66.9	<0.001

NS: not significant.

Table 4
Reduction in procoagulatory factors by a single HELP-apheresis

Procoagulatory parameters	Pre-HELP	Post-HELP	Reduction (%)	*P*-value
Tissue factor (pg/ml)	280.0 ± 118.4	211.4 ± 113.8	26.5	<0.001
Fibrinogen (mg/dl)	339.3 ± 83.0	115.8 ± 43.7	66.1	<0.001
sCD40L (ng/ml)	5.25 ± 2.60	3.79 ± 2.39	16.0	<0.01
Homocysteine (μmol/l)	12.3 ± 4.4	9.6 ± 3.3	21.6	<0.001

Atherosclerosis 175 (2004) 145–150

C-reactive protein and other markers of inflammation among patients undergoing HELP LDL apheresis

Patrick M. Moriarty [a,*], Cheryl A. Gibson [b,1], Jessie Shih [c,2], Matthew S. Matias [c,2]

Changes in lipids, fibrinogen, and C-reactive protein across 6 months of treatment

Parameter (mg/dl)	Baseline	Mean decrease per treatment (%)	Change from baseline to 6 months (%)
Total cholesterol	359 ± 77	56	5% decrease
LDL-cholesterol	275 ± 69	64	9% decrease
HDL-cholesterol	46 ± 14	25	12% increase
Triglycerides	190 ± 64	34	8% increase
Fibrinogen	332 ± 46	65	25% decrease
C-reactive protein (mg/l)	9 ± 8	64	49% decrease

Baseline values are mean ± standard deviations.

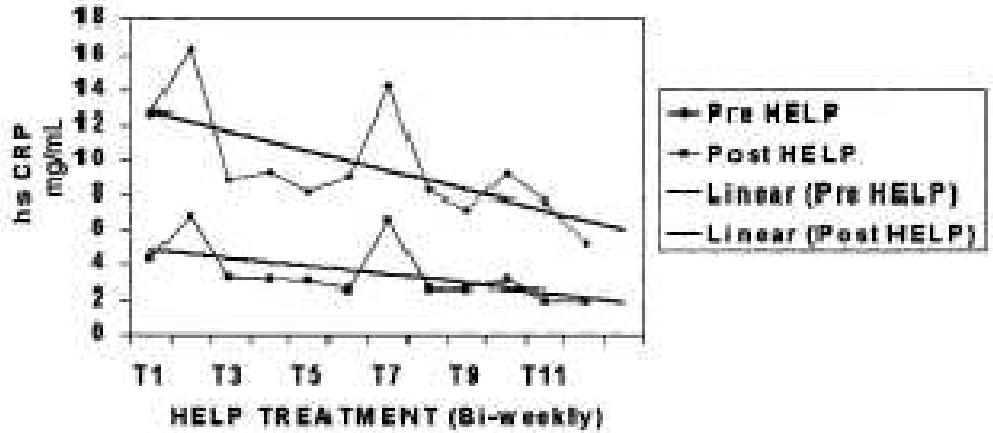


Fig. 1. Six-month trend analysis of pre- and post-treatment hsCRP levels for four patients on chronic LDL apheresis therapy.

(Atherosclerosis 2001)

Long-term reduction of C-reactive protein concentration by regular LDL apheresis☆

Carsten Otto [a,*], H. Christian Geiss [a], Klaus Empen [a,b], Klaus G. Parhofer [a]

Atherosclerosis 174 (2004) 151–156

IMA n=6

DSA n=13

HELP n=9

DALI n=6

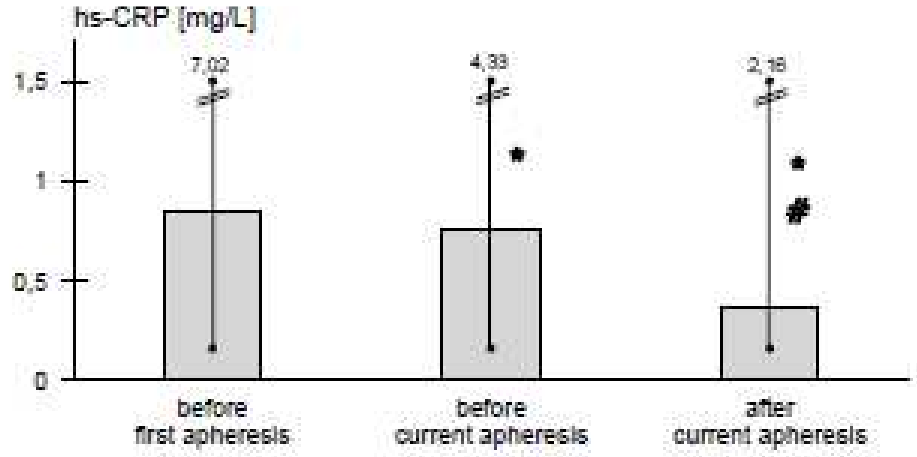


Fig. 1. CRP concentration (median and range) before the first and before as well as after a current LDL apheresis (* $P < 0.05$ compared to before first apheresis, # $P < 0.001$ compared to before current apheresis).

Over a period of more than 5 years LDL-apheresis slightly, but significantly reduced CRP concentration in patients with CHD on statin therapy

Acute affects of 4 LDL apheresis methods on the coagulation pathway (post-apheresis changes are shown as percentages of pre-apheresis values)

	IMA	DSA	HELP	DALI
Patients, n=	**5**	**4**	**6**	**6**
Volume treated	**6.2 l**	**4.9 l**	**3 l**	**6.8-9.4 l**
Anti-coagulant	**heparin/ACD**	**heparin**	**heparin**	**heparin/ACD**
Prothrombin time	**-17%**	**-62%**	**-53%**	**-28%**
aPTT	**+150%**	**+625%**	**+150%**	**+338%**
Fibrinogen	**-19%**	**-26%**	**-53%**	**-11%**
Factor V	**-28%**	**-74%**	**-63%**	**-68%**
Factor VII	**-28%**	**-30%**	**-36%**	**-4%**
Factor VIII	**-72%**	**-99%**	**-57%**	**-60%**
Factor XI	**-27%**	**-82%**	**-53%**	**-82%**
Factor XII	**-32%**	**-73%**	**-40%**	**-45%**
VW factor	**-29%**	**-48%**	**-56%**	**-49%**
Anti-thrombin III	**-22%**	**-24%**	**-22%**	**-7%**
Protein S	**-25%**	**-27%**	**-30%**	**-11%**

GR Thompson, Atherosclerosis 2003

Effects of a single HELP apheresis on vascular homeostasis

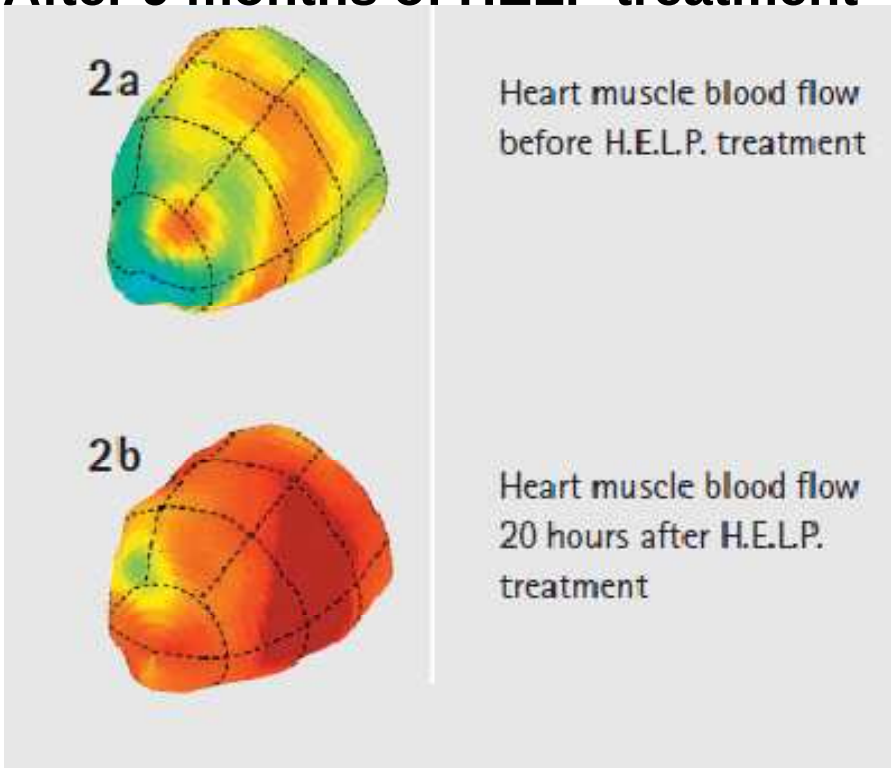
Lipid metabolism		Coagulation		Hemorheology	
Total cholesterol	–52%	Fibrinogen	–56%	Plasma viscosity	–14%
LDL cholesterol	–56%	Thrombin	–55%	Erythrocyte aggregability	–60%
HDL cholesterol	+14%	Factor V	-57%	Thrombocyte aggregability	–66%
VLDL cholesterol	–52%	Factor VII	-35%	Peripheral muscle oxygenation	+43%
Lp(a)	–52%	vWF	–56%	Coronary flow reserve	+14%
Triglycerides	–50%	AT III	–25%	Cerebral CO_2 reactivity	+14%

Da B. R. Jaeger Therapeutic Apheresis 2001.

LDL-apheresis (HELP) increases cardiac blood flow

Basal

After 9 months of HELP treatment



PET-coronary blood flow after adenosine infusion in 35 patients (11F, 24M)

Mellwig KP et al. Z Kardiol. 2003, 92 Suppl. 3:III30-III37

LDL-AFERESI:
Indicazioni al trattamento

Linee guida del Comitato Nazionale Interdisciplinare LDL-aferesi

Le indicazioni al trattamento con LDLa sono le seguenti:

- ipercolesterolemia familiare omozigote (e doppie eterozigosi): iniziare la terapia aferetica il più precocemente possibile in tutti i pazienti;
- ipercolesterolemie primitive: devono essere trattati i pazienti che rispondono ad almeno due dei seguenti requisiti:
  1) assenza di risposta alla terapia dietetica e plurifarmacologica;
  2) presenza di ateromasia grave (sintomatica o asintomatica; ivi compreso anche il pregresso Infarto Acuto del Miocardio);
  3) angioplastica coronarica, by-pass aorto-coronarico (o altra chirurgia maggiore vascolare), ove i presidi farmacologici non garantiscano, con ragionevole certezza, di mantenere la pervietà del/i by-pass;
  4) trapianto cardiaco.

LDL-apheresis

Side effects and
numbers of events

Italian Multicenter Study on Low-Density Lipoprotein Apheresis: Retrospective Analysis (2007)

Claudia Stefanutti and the Italian Multicenter Study on Low-density Lipoprotein Apheresis Working Group*

TABLE 4. *Italian Multicenter Study on Low-Density Lipoprotein Apheresis (IMS-LDLa): Side effects and number of evens*

IMS-LDLa Centers = 18 Side effects	No. of events
Symptomatic Hypocalcemia	8
Hematoma by venipuncture	230
Low outlet flow	125
Circuit coagulation	44
Allergic reaction	19
Gastrointestinal discomfort/vomiting	6
Fever and shivers	0
Hypotension/collapse	11
Vasovagal reaction	13
Hemolysis	6
Cardiac arrhythmias	0

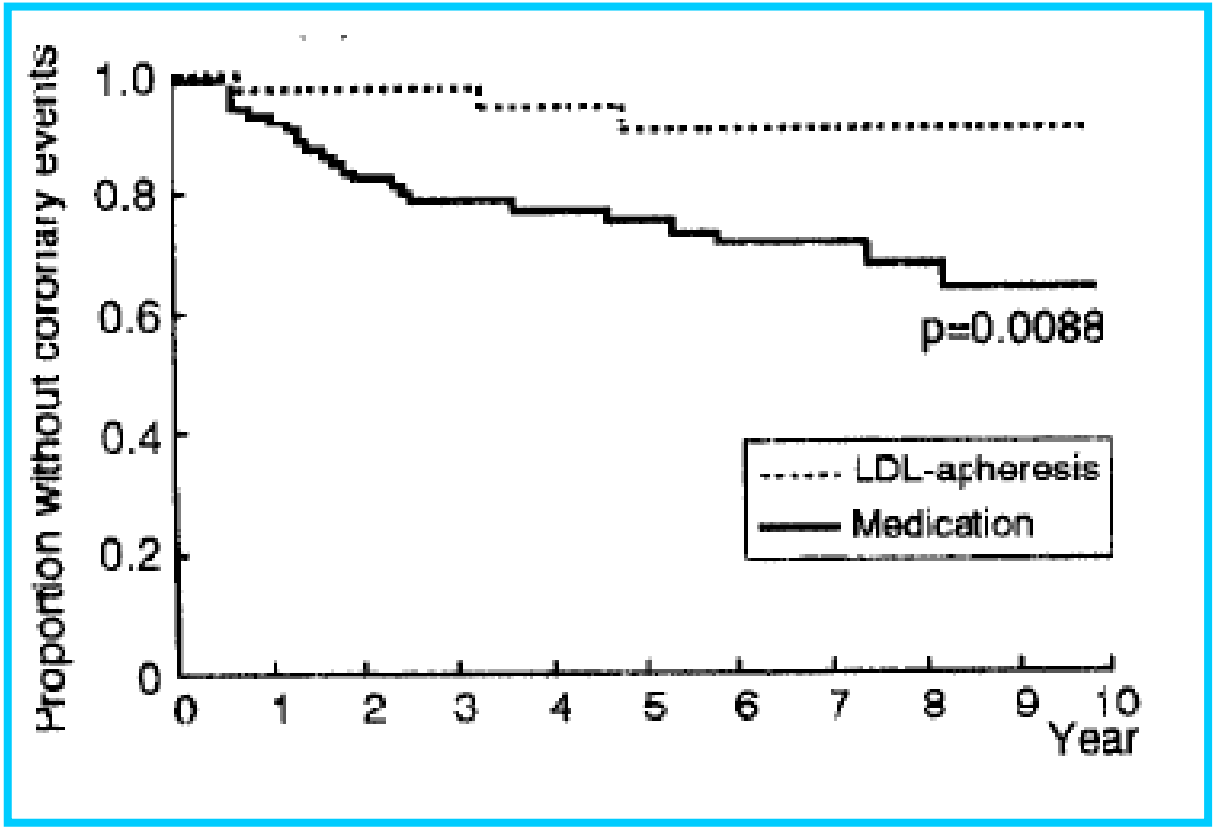
Total no. Sessions: **31012**; 74 M, 62F

LDL-apheresis

Clinical Trials

Long-Term Efficacy of Low-Density Lipoprotein Apheresis on Coronary Heart Disease in Familial Hypercholesterolemia

Hiroshi Mabuchi, MD, PhD, Junji Koizumi, MD, PhD, Masami Shimizu, MD, PhD, Kouji Kajinami, MD, PhD, Susumu Miyamoto, MD, PhD, Kousei Ueda, MD, PhD, and Tadayoshi Takegoshi, MD, PhD, for the Hokuriku-FH-LDL-Apheresis Study Group*



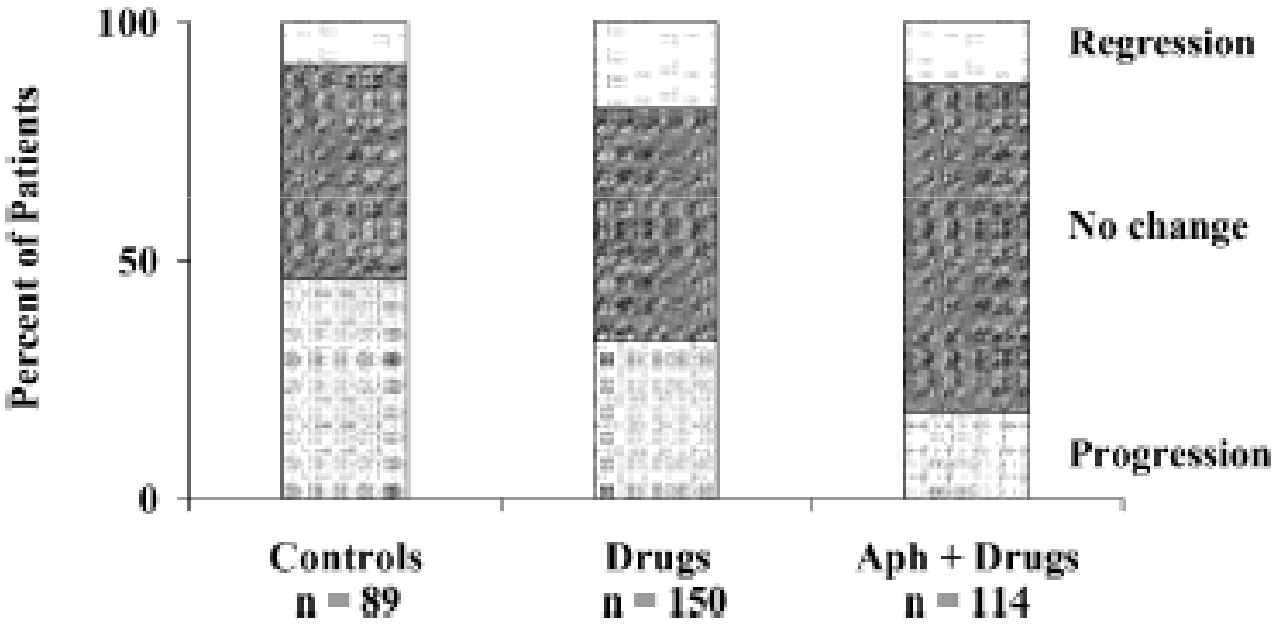
130 FH patients with CHD documented by coronary angiography

87 cholesterol-lowering drug therapy alone

43 LDL apheresis combined with cholesterol-lowering drug therapy

Am J Cardiol 1998, 82 1495-1498

Metanalisi dei trials con LDL aferesi : effetti sull'aterosclerosi coronarica documentata con angiografia (durata di almeno 2 anni)



G.R. Thompson, Atherosclerosis 2003

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PII S0735-1097(02)01955-1

CLINICAL STUDIES **Lipid Lowering**

Intravascular Ultrasound Evaluation of Coronary Plaque Regression by Low Density Lipoprotein-Apheresis in Familial Hypercholesterolemia

The Low Density Lipoprotein-Apheresis Coronary Morphology and Reserve Trial (LACMART)

Masunori Matsuzaki, MD, PHD, FACC,* Katsuhiko Hiramori, MD, PHD,† Tsutomu Imaizumi, MD, PHD, FACC,‡ Akira Kitabatake, MD, PHD, FACC,§ Hitoshi Hishida, MD, PHD,¶ Masanori Nomura, MD, PHD,‖ Takashi Fujii, MD, PHD,* Ichiro Sakuma, MD, PHD,§ Kenichi Fukami, MD, PHD,† Takashi Honda, MD, PHD,¶ Hiroshi Ogawa, MD,# Masakazu Yamagishi, MD, PHD, FACC**

Yamaguchi, Iwate, Fukuoka, Hokkaido, Nagoya, Kumamoto and Osaka, Japan

Gruppi di studio: 11 pz con FH trattati con LDL-aferesi e farmaci
7 pz con FH trattati solo con farmaci

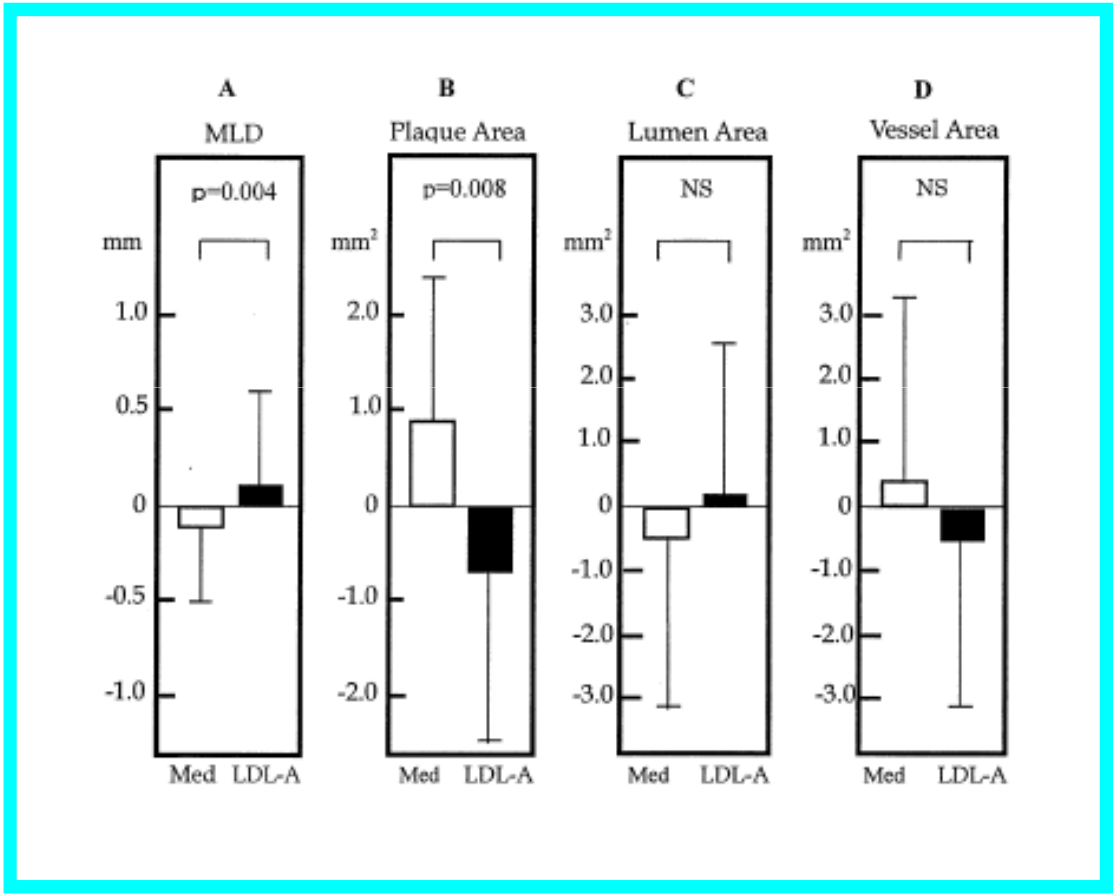
Follow-up: 1 anno

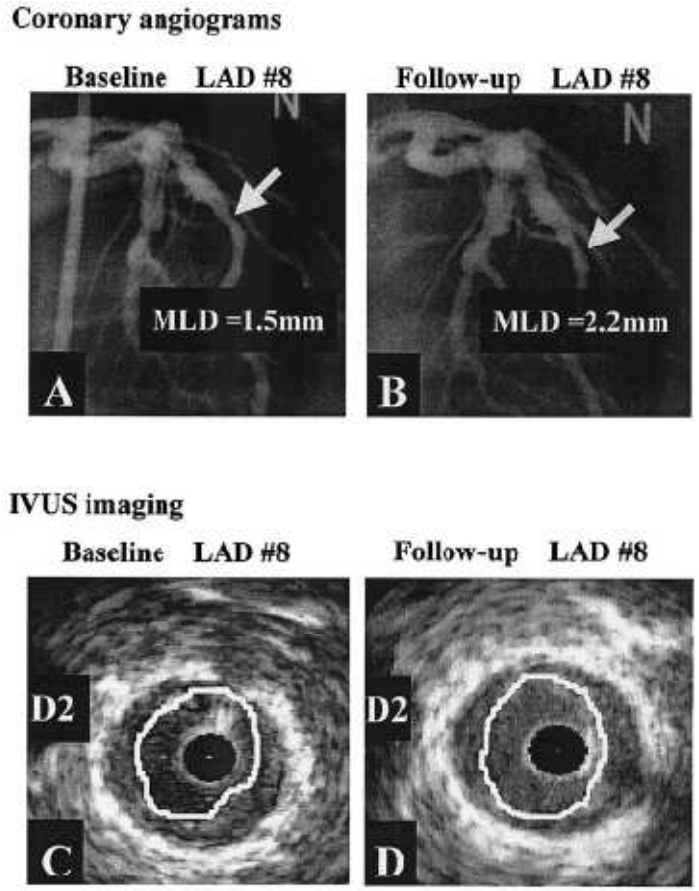
Table 2. Change in Serum Lipid Levels

	LDL-A Group (n = 11)			Medication Group (n = 7)			
	Baseline	Follow-Up	Reduction*	Baseline	Follow-Up	Reduction*	p Value**
TC (mg/dl)	275 ± 27	197 ± 19	28.4	251 ± 57	254 ± 38	−1.2	0.0001
TG (mg/dl)	143 ± 74	139 ± 93	2.8	163 ± 70	147 ± 41	9.8	0.65
HDL-C (mg/dl)	33 ± 20	36 ± 16	−9.1	44 ± 20	45 ± 22	−2.3	0.79
LDL-C (mg/dl)	213 ± 25	140 ± 27	34.3	174 ± 39	181 ± 53	−4	0.0001

Data presented are mean value ± SD. *(%). **Data obtained from two-way repeated-measures analysis of variance.
HDL-C = high density lipoprotein cholesterol; LDL-A = low density lipoprotein-apheresis; LDL-C = low density lipoprotein cholesterol; TC = total cholesterol; TG = triglycerides.

Net change in coronary angiogram and intravascular ultrasound parameters





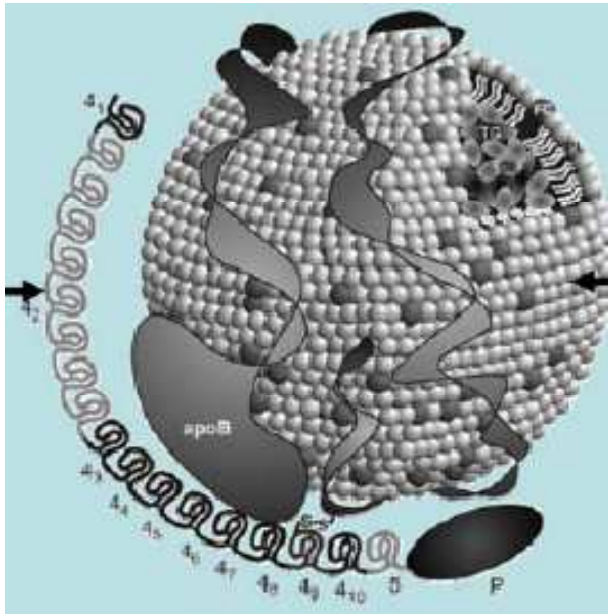
LACMART: ***LDL-Apheresis Coronary Morphology and Reserve Trial***

M. Matsuzaki et al., J. of the American College of Cardiology 40(2) 220-227, 2002

LDL-apheresis

CHD with elevated Lp(a) levels

Lipoprotein(a)



Lp(a) concentration is an independent predictor of vascular disease and CAD

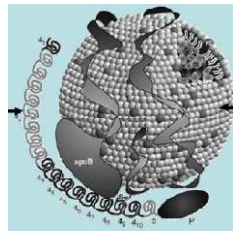
apo(a) shares a close structural homology with plasminogen and is similarly involved in the fibrinolytic system

Plasma **Lp(a)** and plasminogen levels are genetically controlled by gene loci located on chromosome 6

Lp(a) may be both involved in thrombogenesis and atherogenesis on the basis of its structure and properties

Bewu AD. Atherosclerosis 1990

Therapeutic Apheresis and Dialysis 11(1):2–8
doi:10.1111/j.1744-9987.2007.00449.x



Apheresis in Coronary Heart Disease With Elevated Lp (a): A Review of Lp (a) As a Risk Factor and Its Management

Christiane Keller

Reduction of Lp(a) by apheresis treatment is possible because Lp(a) contains one apoB100 which is specifically bound, precipitated or filtered, and eliminated from patients' plasma with the different procedures used

TABLE 1. *Reduction of plasma Lp (a) by different apheresis systems (in percent from the pre-treatment level)*

Author	HELP	DALI	LA-15	Immnuno-adsorption	Lipopak	Double filtration
Pokrovsky 1991	—	—	—	—	88	—
Ullrich 1996	—	—	—	—	76	—
Armstrong 1994	62 (in vitro)	—	—	—	—	—
Blessing 2004	45					
Gordon 1992	—	—	68	—	—	—
Bosch 2002	—	64	—	—	—	—
Bambauer 2001	—	29	25	25	59	—
Donner 1996	—	—	—	—	—	57.6

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ATHEROSCLEROSIS
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www.elsevier.com/locate/atherosclerosis

Treatment of symptomatic HyperLp(a)lipoproteinemia with LDL-apheresis: a multicentre study

C. Stefanutti[1,*], G. D'Alessandri[2], G. Russi[3], G. De Silvestro[4], M. G. Zenti[5], P. Marson[4], D. Belotherkovsky[1], A. Vivenzio[1], S. Di Giacomo[1]

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[2] *UOC Immunoematologia e Trasfusionale, ASL 3, Pistoia, Italy*
[3] *UOC Medicina Trasfusionale e Immunoematologia "Arcispedale S. Maria Nuova", Reggio Emilia, Italy*
[4] *UOC Immunotrasfusionale - Az. Ospedaliera di Padova - University of Padova, Italy*
[5] *Divisione di Endocrinologia e Malattie del Metabolismo, Azienda Ospedaliera-Universitaria di Verona*

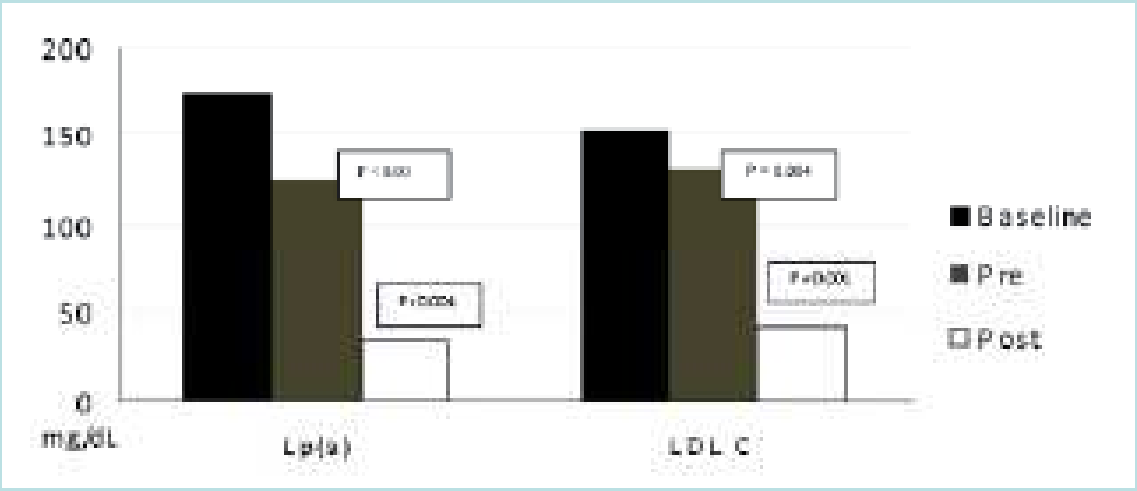
Inclusion criteria

- Lp(a) plasma levels > 60 mg/dL;
- LDLC levels < 160 mg/dL on lipid-lowering treatment with hypolipidemic drugs;
- CAD clinically documented (cardiac events and/or revascularization interventions)
- Evidence of absence of response to hypolipidemic drugs maximal for the reduction of Lp(a) concentration in plasma.

Mean plasma Lp(a) and LDL-C levels at baseline and before/after LDL-apheresis (3.1 years)

Mean plasma Lp(a) and LDLC levels at baseline, and before/after LDLa

Lp(a) mg/dL		
Baseline	172.3±153.8	
Pre	124.5 ± 107.2	p ≤ 0.001
Post	34.2± 40.6	p < 0.001
LDL C mg/dL		
Baseline	152.3±74.6	
Pre	130.4 ± 61.1	p = 0.004
Post	41.2 ± 25.1	p < 0.001



Atherosclerosis Supplements 10 (2009) 89–94

Frequency of CAD, revascularization interventions, and extracoronary artery disease

CAD documented by catheterization before LDLa	Revascularization interventions	Extracoronary artery disease
95%	79%	37%

CAD (# of vessels involved)	# Patients	Percentage
Monovasal	8	42.1
Bivasal	5	26.4
Trivasal	4	21
Plurivasal	2	10.5

CAD: Coronary Artery Disease; LDLa: LDL-apheresis

In 94.5% of the patients the lesions were stable (< 0% deviation) over 3.1±2.7 years. In 5.5% (#1 individual) CAD reccurred despite treatment with LDLa.

Atherosclerosis Supplements 10 (2009) 89–94

www.nature.com/clinicalpractice/cardio

Longitudinal cohort study on the effectiveness of lipid apheresis treatment to reduce high lipoprotein(a) levels and prevent major adverse coronary events

Beate R Jaeger[1]*, Yvonne Richter[2], Dorothea Nagel[2], Franz Heigl[3], Anja Vogt[4], Eberhard Roeseler[5], Klaus Parhofer[6], Wolfgang Ramlow[7], Michael Koch[8], Gerd Utermann[9], Carlos A Labarrere[10] and Dietrich Seidel[2], for the Group of Clinical Investigators[11]

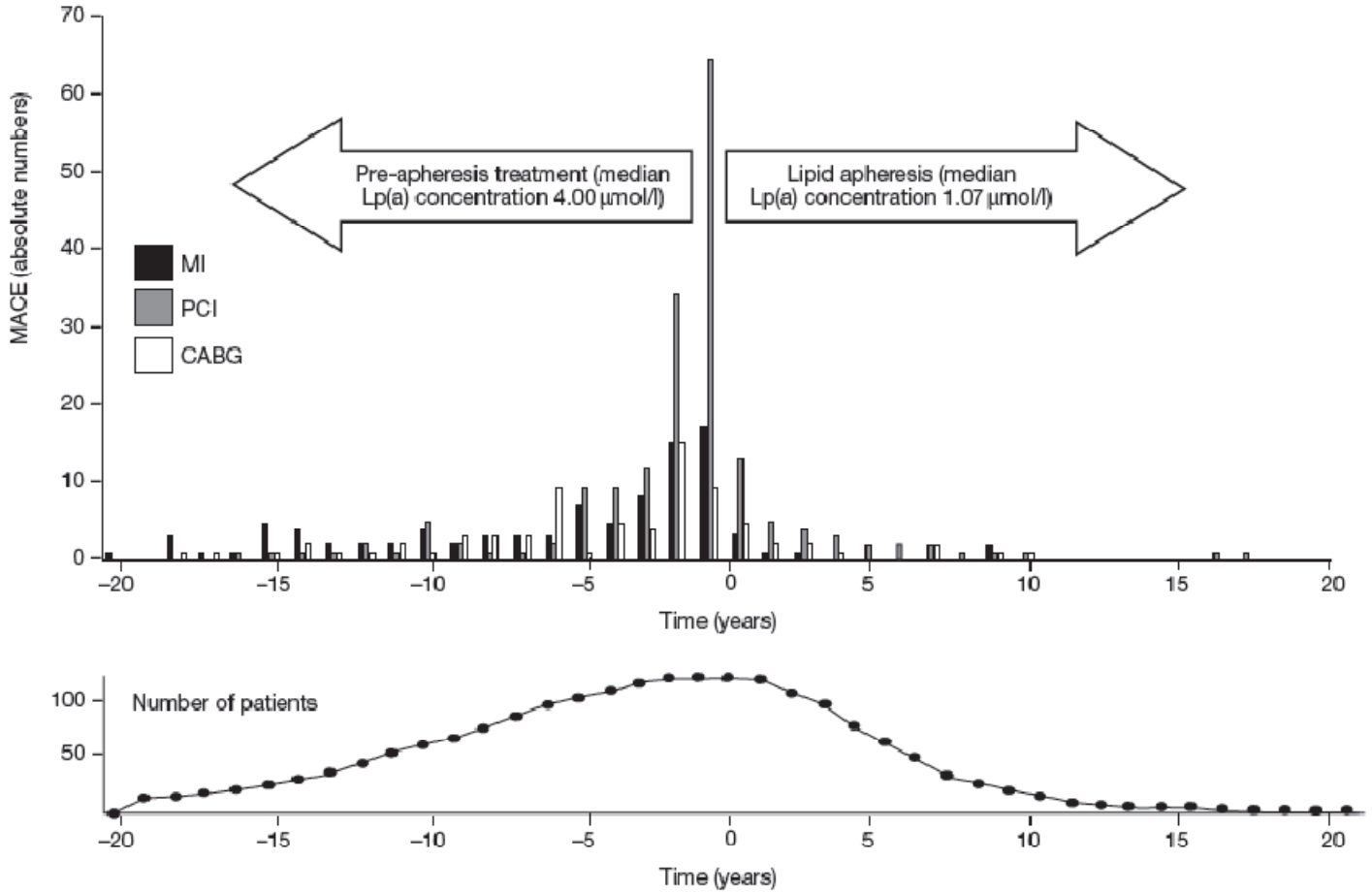
Background We investigated in a longitudinal, multicenter, cohort study whether combined lipid apheresis and lipid-lowering medication can reduce extremely high levels of lipoprotein(a) (Lp[a]) and thus prevent major adverse coronary events (MACE) more efficaciously than lipid-lowering medication alone.

Methods Eligible patients had coronary artery disease and Lp(a) levels ≥2.14 μmol/l (95th percentile). All patients received lipid-lowering medications alone until maximally tolerated doses were no longer effective, followed by combined lipid apheresis and lipid-lowering medication. The rates of the primary outcome, MACE, were recorded for both periods.

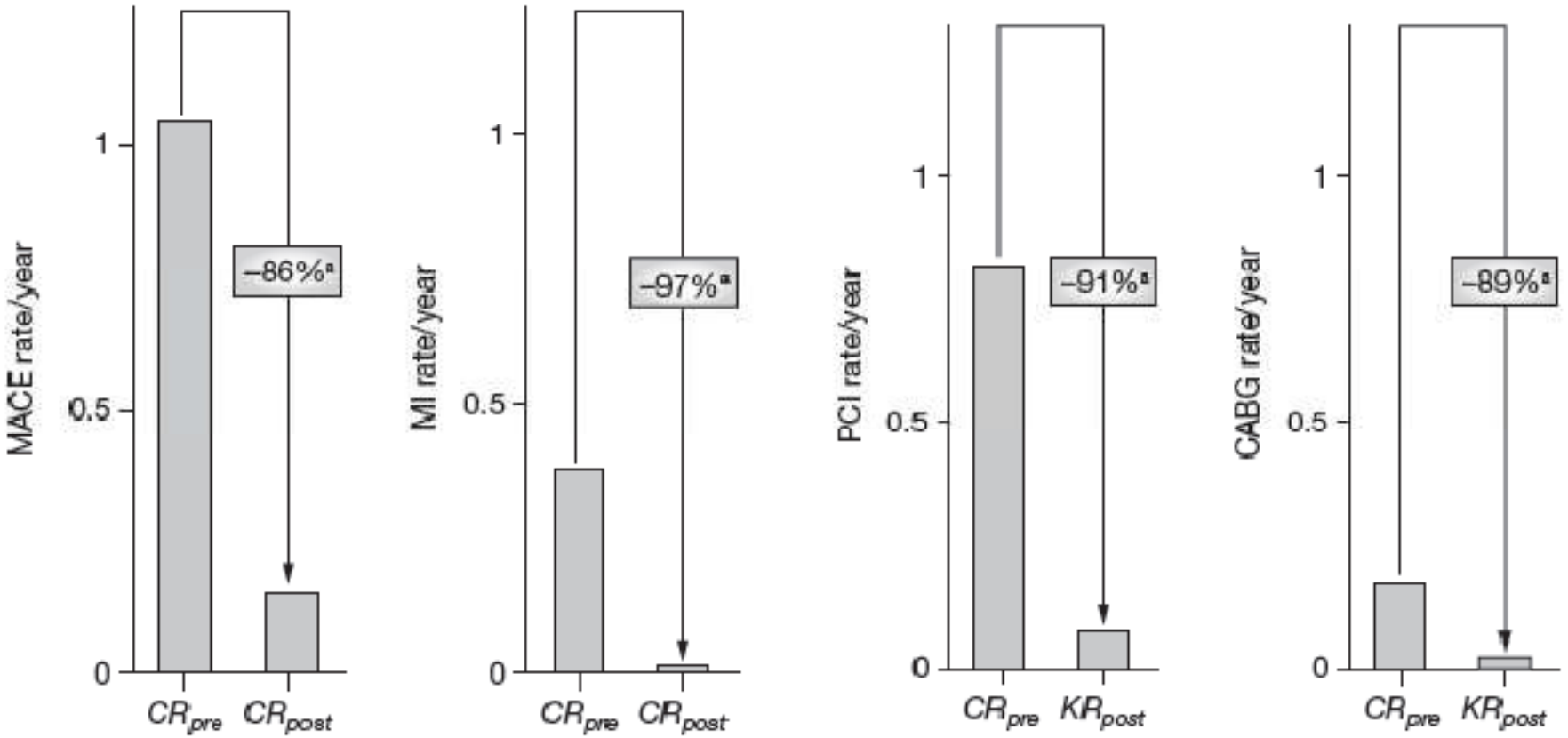
Median Lp(a) concentration 112 mg/dL

Median Lp(a) concentration 29,9 mg/dL

Mean annual MACE rate per patient was 1.056 vs 0.144 (p<0.0001)



Changes in annual nonfatal MACE rates before and after initiation of lipid apheresis



LDL-aferesi e iperLp(a)

. Occorre infine raccomandare il trattamento con LDL aferesi ai pazienti che presentano segni clinici di coronaropatia precoce e livelli di Lp(a) superiori a 60 mg%, in particolare se presentano livelli plasmatici di colesterolo LDL superiori a 130 mg%, nonostante terapia dietetica e farmacologica massimale (30).

La LDL-aferesi è stata sviluppata per il trattamento della malattia cardiovascolare nei pazienti FH

- Mancano studi clinici randomizzati controllati per valutare l'effetto del trattamento con LDL-aferesi su morbidità e/o mortalità CV
- Limitato numero di pazienti con indicazione al trattamento aferetico (in particolare "treatment-naive patients")
- Problema etico di **non** ridurre appropriatamente la colesterolemia in pazienti ad alto rischio (braccio controllo)

Atherosclerosis 217S (2011) S1–S44

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Review

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)☆,☆☆

7.6. *Low-density lipoprotein apheresis*

Rare patients with severe hyperlipidaemias, especially homozygous and severe heterozygous FH, require specialist evaluation and consideration of the need for LDL apheresis. By this expensive but effective technique, LDL and Lp(a) are removed from plasma during extracorporeal circulation weekly or every other week. Clearly this is a procedure that is only performed in highly specialized centres.

Conclusioni

- La LDL-aferesi trova indicazione nel trattamento cronico dei pazienti con ipercolesterolemia non controllata dalla terapia medica (FH o resistenza/intolleranza al trattamento con statine)
- La LDL-aferesi può ridurre oltre alla lipoproteine aterogene altri mediatori di malattia vascolare (infiammazione, emoreologia, trombosi, fibrinolisi).
- Gli effetti pleiotropici acuti e cronici della LDL-aferesi possono aprire il campo di utilizzo di questa metodica in diverse patologie vascolari

Coronary angiographic changes in trials of LDL apheresis

Date	Author or acronym (Ref)	Design	Subjects	Method	Drugs	Angiographic change
1992	LARS [76]	uc	FH hmz, 7; htz, 25; non-FH, 5	DSA, 1–4/m, 1 y	Probucol ± prava	P, 13%; NC, 49%; R, 38% (V or QCA)[a]
1994	Kitabatake [77]	uc	FH htz, 13	DSA 2/m, 1 y	Probucol ± prava, BAS	P, 13%; NC, 54%; R, 33% (QCA)[b]
1994	Waidner [78]	uc	FH hmz or htz, 25	IMA 1/w, 3 y	Not stated	P, 32%; NC, 68%; R, 0% (V)[a]
1994	HELP study [79]	uc	HC, 33	HELP 1/w, 2 y	BAS ± fib + NA	P, 15%; NC, 58%; R, 27% (QCA)[b]
1995	FHRS [80]	r, c	FH htz (a) 20 (b) 19	DSA, 2/m 2 y	Simva Simva + BAS	P, 10%; NC, 65%; R, 25% P, 21%; NC, 58%; R, 21% (QCA, $P = NS$)[a]
1996	LAARS [81]	r, c	HC or FH htz (a) 21 (b) 21	DSA, 2/m 2 y	 Simva Simva	 P, 43%; NC, 24%; R, 9% P, 52%; NC, 24%; R, 24% (QCA, $P = NS$)[a]
1998	Richter [82]	uc	FH htz, 23	IMA, HELP, DSA 1/w, 4.6 y	Simva	P, 0%; NC, 83%; R, 17% (V)[a]
1999	L-CAPS [83]	nr, c	FH htz (a) 25 (b) 11	DSA, 2/m 2 y	Probucol, prava, BAS	P, 8%; NC, 76%; R, 16% P 64%; NC, 36%; R, 0% (QCA, $P < 0.004$)[a]

Review Article

Lipid and low-density-lipoprotein apheresis. Effects on plasma inflammatory profile and on cytokine pattern in patients with severe dyslipidemia

Claudia Stefanutti [a,*], Claudia Morozzi [a], Andrea Petta [b]

Existing reported evidence of LDL-a effects on plasma cytokines and other mediators of inflammation.

Authors	Years	Cytokine/others mediators of inflammation	Apheresis type	Effects
Boos et al.	1995	CRP LPS TNF-α	H.E.L.P. (vitro)	↓CRP ↓LPS ↓TNF-α
Suzuki et al. [56]	1996	IL-1β TNF-α	Double filtration plasmapheresis thermofiltration low-density lipoprotein adsorptive methods	=IL-1β =TNF-α
Sampietro et al. [57]	1997	sICAM-1 sELAM TNF-α IL-6 acute-phase reactant proteins	Liposorber®	↓sICAM-1 ↓sELAM =TNF-α =IL-6 =acute-phase reactant proteins
Samtleben et al. [66]	1998	Endotoxin Fibrinogen TNF-α CRP	H.E.L.P.	↓Endotoxin ↓Fibrinogen ↓TNF-α ↓CRP
Rovers et al. [55]	1998	IL-1 TNF-α expression of CD11a, CD11b, CD11c and CD14 by the mononuclear cells	Liposorber®	↓IL-1 ↓TNF-α ↓expression of CD11a, CD11b, CD11c and CD14 by the mononuclear cells
Kojima et al. [79]	2001	HGF	Liposorber®	↑HGF
Kojima et al. [79]	2003	IL-6 CRP	Liposorber®	↑IL-6 ↓CRP
Nakamura et al. [60]	2003	IL-6 CRP	Liposorber®	↓IL-6 ↓CRP
Wang et al. [67]	2004	hsCRP svCAM sE-sel LPB ET-1 MCP-1 Fibrinogen TF scD40s	H.E.L.P.	↓hsCRP ↓svCAM ↓sE-sel ↓LPB ↓ET-1 ↓MCP-1 ↓Fibrinogen ↓TF ↓scD40s

Existing reported evidence of LDL-a effects on plasma cytokines and other mediators of inflammation (Stefanutti et al cytokine 2011)

Blaha et al. [46]	2004	P-sel E-sel MCP-1	Immunoadsorption columns	↑P-sel ↓E-sel ↓ MCP-1
Bengsch et al. [68]	2005	CRP IL-6	H.E.L.P.	↓CRP ↓IL-6
Kobayashi et al. [34]	2005	HsCPR MCP-1 Fibrinogen	Liposorber®	↓HsCPR ↓MCP-1 ↓Fibrinogen
Moriarty et al. [33]	2006	MCP-1 ET-1 LBP Lp-PLA2 VCAM-1 ICAM-1 E-sel Fibrinogen Ox-LDL CRP	H.E.L.P.	↓MCP-1 ↓ET-1 ↓LBP ↓Lp-PLA2 ↓VCAM-1 ↓ICAM-1 ↓E-sel ↓Fibrinogen ↓Ox-LDL ↓CRP
Otto et al. [62]	2007	CPR Fibrinogen IL-6 Myeloperoxidase Resistin	Liposorber D®	↓CPR ↓Fibrinogen ↓IL-6 ↓Myeloperoxidase ↓Resistin
Utsumi et al. [61]	2007	sICAM sVCAM P-sel ¬IL-1β ¬Il-6 ¬TNF-α	D.A.LI. Liposorber®	↓sICAM ↓Svcam ↓P-sel ¬IL-1β ¬Il-6 ¬TNF-α
Dihazi et al. [39]	2008	More than 70 functional proteins	D.A.LI followed by H.E.L.P. and DFPP	↓Kininogen1 ↓Fibronectin ↓Fibrinogen ↓Complement components
Hovland et al. [63]	2009	RANTES HsCPR INF-γ TNF-α PDGF	DL-75 (whole blood adsorption) LA-15 (plasma adsorption) EC-50 W (plasma filtration)	↓RANTES ↓HsCPR ↓INF-γ ↓TNF-α ↓PDGF