

Ipolipemizzanti nel diabete tipo 2: fra evidenze di efficacia e vincoli normativi

Quali esami, quando e quanto spesso

Francesco Logoluso

Medicina Interna, Endocrinologia, Andrologia e Malattie Metaboliche
Dipartimento dell'Emergenza e dei Trapianti di Organi
Direttore Prof. F. Giorgino
Università degli Studi di Bari

Premessa



Profilo lipidico

Età
Diabete Mellito
Ipertensione
Fumo
Familiarità CVD
Obesità
PCOS

Rischio CVS

$$\frac{\text{LDLc} - \text{LDLc Target}}{\text{LDLc}} \times 100$$

TARGET

A cosa serve il dosaggio dei lipidi ?

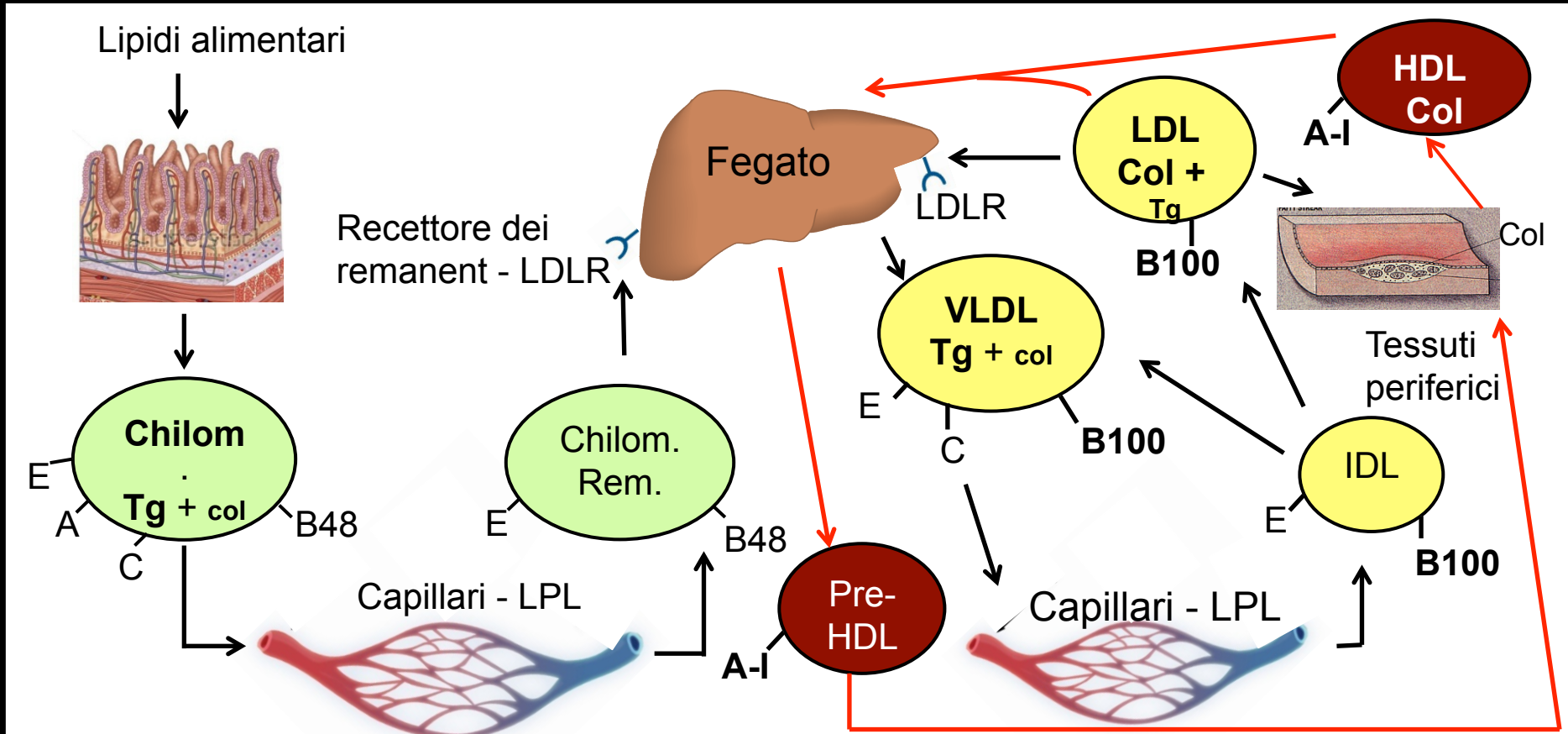


- **Determinare la condizione di base del paziente**
- **Stabilire la distanza dal target**
- **Scegliere il mezzo migliore per raggiungere il target**
- **Raggiunto il target, controllare che il risultato sia mantenuto nel tempo**

Quali lipidi ?

Lipidi esogeni

Lipidi endogeni



AAACE Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS' GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF ATHEROSCLEROSIS

Table 5

Major Coronary Artery Disease Risk Factors (10 [EL 4], 11 [EL 4],
12 [EL 4], 13 [EL 4], 14 [EL 2], 15 [EL 4], 16 [EL 2], 17 [EL 4],
18 [EL 2], 19 [EL 2], 20 [EL 4], 21 [EL 3])

Major risk factors	Additional risk factors	Nontraditional risk factors
Advancing age ^{a,d}	Obesity, abdominal obesity ^{c,d}	Elevated lipoprotein (a)
High total serum cholesterol level ^{a,b,d}	Family history of hyperlipidemia ^d	Elevated clotting factors
High non-HDL-C ^d	Small, dense LDL-C ^d	Inflammation markers (hsCRP; Lp-PLA ₂)
High LDL-C ^{a,d}	↑ Apo B ^d	Hyperhomocysteinemia
Low HDL-C ^{a,d,e}	↑ LDL particle number	Apo E4 isoform
Diabetes mellitus ^{a,b,c,d}	Fasting/postprandial hypertriglyceridemia ^d	Elevated uric acid
Hypertension ^{a,b,c,d}	PCOS ^d	
Cigarette smoking ^{a,b,c,d}	Dyslipidemic triad ^f	
Family history of CAD ^{a,d,g}		

Quando?

Adults With Diabetes

- **R8.** Annually screen all adult patients with diabetes mellitus for dyslipidemia (**Grade B; BEL 2**).

Older Adults (Older Than 65 Years)

- **R11.** Annually screen older adults with 0 to 1 CAD risk factor for dyslipidemia (**Grade C; BEL 1**). In addition, older patients should undergo lipid assessment if they have multiple CAD global risk factors (ie, risk factors other than age) (**Grade C; BEL 4**).
- **R12.** AACE believes that screening recommendations apply based on age and risk, not based on sex; therefore, women should be screened in the same way as men (**Grade A; BEL 1**).

Cosa dosare



- **Profilo lipidemico standard (a digiuno al mattino):**
 - Colesterolo totale
 - LDL
 - HDL
 - Trigliceridi
- **Indagini supplementari:**
 - Colesterolo non HDL
 - Apolipoproteina B
 - Apolipoproteina A-I
 - hsPCR, Lp-LPA₂

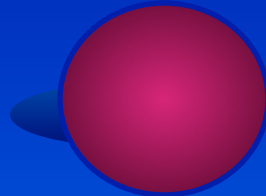
• **R15.** Use a fasting lipid profile to ensure the most precise lipid assessment. This should include total cholesterol, LDL-C, triglycerides, and HDL-C (Grade C; BEL 4).

Cosa dosare

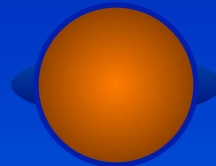
VLDL
Chilomicroni



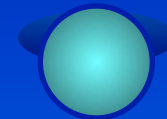
VLDL_R
Chilom._R



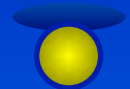
IDL



LDL



LDL
piccole
e dense



Lipoproteine ricche di Tg

**Lipoproteine ricche di
colesterolo**

LDLc

HDLc

Trigliceridi

Non-HDLc

Apolipoproteina B

Calcolato

Equazione di Friedwald

$$\text{LDLc} = \text{Col. Tot.} - \text{HDLc} - (1/5 \times \text{Tg})$$

Formula accurata se Tg < 200 mg/dl

Formula non valida se Tg > 400 mg/dl

Diretto

Tg > 250 mg/dl
Diabete Mellito
Paziente con CVS

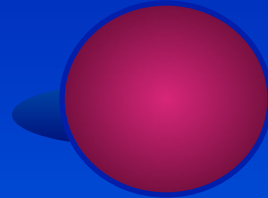
- **R17.** AACE recommends direct measurement of LDL-C in certain high-risk patients, such as those with fasting triglyceride levels greater than 250 mg/dL or those with diabetes mellitus or known vascular disease (**Grade C; BEL 3**).

Cosa dosare

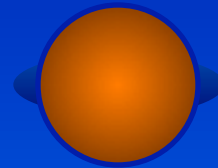
VLDL
Chilomicroni



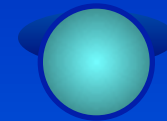
VLDL_R
Chilom._R



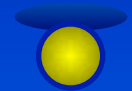
IDL



LDL



LDL
piccole
e dense



Lipoproteine ricche di Tg

**Lipoproteine ricche di
colesterolo**

LDLc

HDLc

Trigliceridi

Non-HDLc

Apolipoproteina B

Confronto tra Bassi livelli di HDL e altri fattori di rischio in maschi con premature CHD

Risk factor	Controls (n = 601)	Cases (n = 321)	
		Not adjusted	Adjusted
Cigarette smoking	29%	67%*	—
HDL-C < 35 mg/dL	19%	63%*	57%*
Hypertension (BP > 150/90)	21%	41%*	—
LDL-C ≥ 160 mg/dL	26%	26%	34%*
Diabetes mellitus	1%	12%*	—

*Significantly different from controls ($P < 0.001$)

Genest JJ et al. *Am J Cardiol* 1991;67:1185–1189

3Q2.3. High-Density Lipoprotein Cholesterol

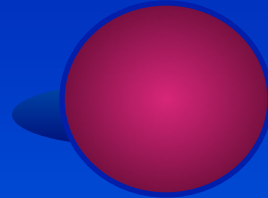
- **R18.** AACE recommends measurement of HDL-C as a screening test for dyslipidemia. Low HDL-C can act synergistically with other lipid risk factors to increase CAD risk. An HDL-C concentration greater than 60 mg/dL is an independent *negative* risk factor in both sexes.

Cosa dosare

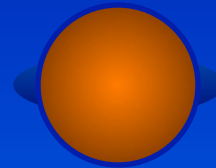
VLDL
Chilomicroni



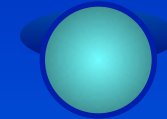
VLDL_R
Chilom._R



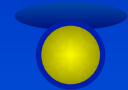
IDL



LDL



LDL
piccole
e dense



Lipoproteine ricche di Tg

**Lipoproteine ricche di
colesterolo**

LDLc

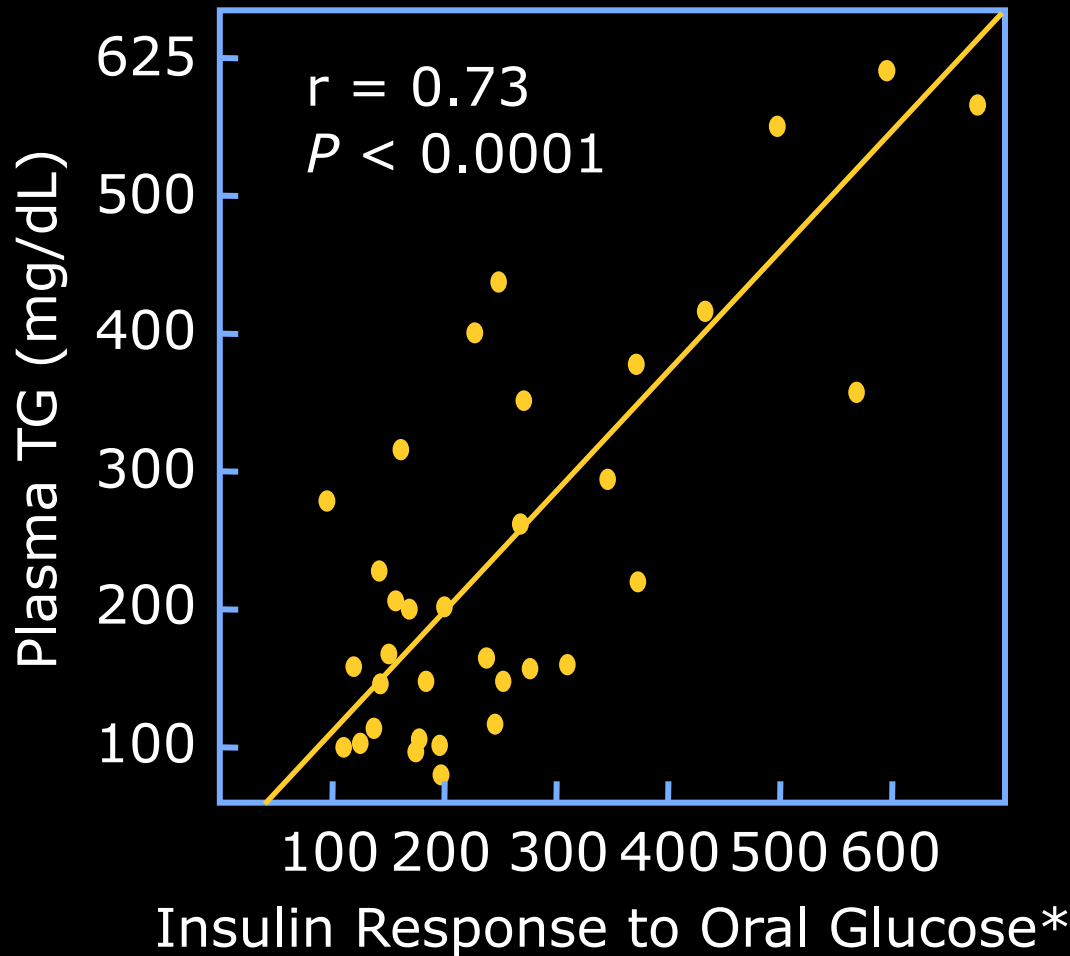
HDLc

Trigliceridi

Non-HDLc

Apolipoproteina B

Relazione tra insulino-resistenza e ipertrigliceridemia



* Total area under 3-hour response curve (mean of 2 tests).

Trigliceridi

3Q2.5. Triglycerides

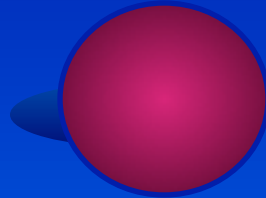
- **R21.** Increasing clinical evidence suggests that elevated triglycerides may be an independent risk factor for CAD; therefore, AACE recommends screening of triglycerides as a component of lipid screening. Triglycerides levels that are even moderately elevated (>150 mg/dL) may identify individuals at risk for the insulin resistance syndrome. Triglyceride levels 200 mg/dL or greater may indicate a substantial increase in CAD risk (**10 [EL 4]**).

Cosa dosare

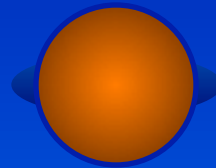
VLDL
Chilomicroni



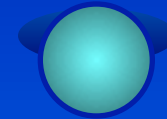
VLDL_R
Chilom._R



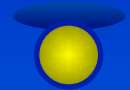
IDL



LDL



LDL
piccole
e dense



Lipoproteine ricche di Tg

**Lipoproteine ricche di
colesterolo**

LDLc

HDLc

Trigliceridi

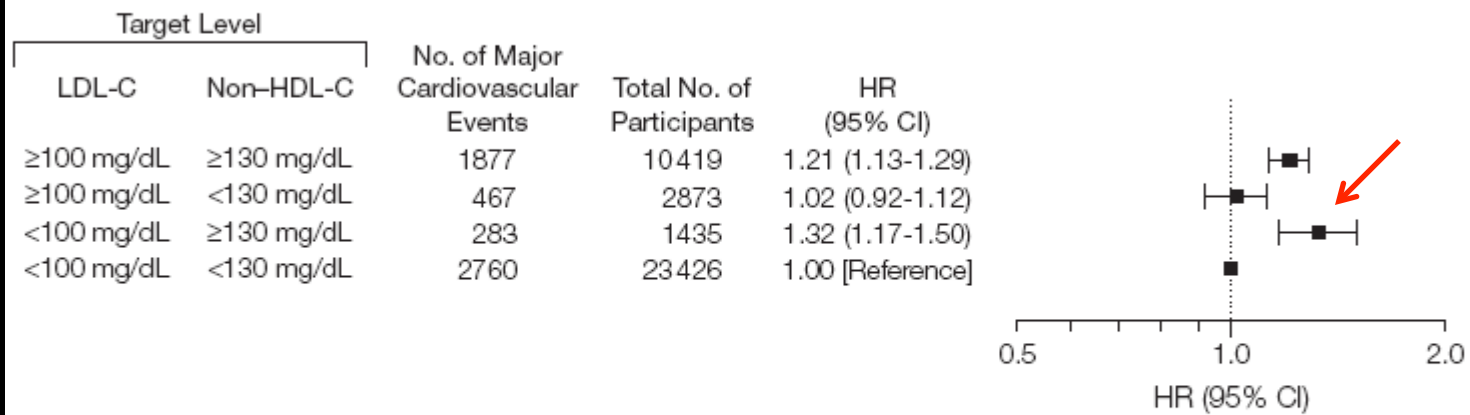
Non-HDLc

Apolipoproteina B

Association of LDL Cholesterol, Non-HDL Cholesterol, and Apolipoprotein B Levels With Risk of Cardiovascular Events Among Patients Treated With Statins

A Meta-analysis

Figure 3. Risk of Major Cardiovascular Events by LDL and non-HDL Cholesterol Categories



Data markers indicate hazard ratios (HRs) and 95% CIs for risk of major cardiovascular events. Results are shown for 4 categories of statin-treated patients based on whether or not they reached the low-density lipoprotein cholesterol (LDL-C) target of 100 mg/dL and the non-high-density lipoprotein cholesterol (non-HDL-C) target of 130 mg/dL. HRs were adjusted for sex, age, smoking, diabetes, systolic blood pressure, and trial.

Non-HDL-C

3Q2.4. Non-High-Density Lipoprotein Cholesterol

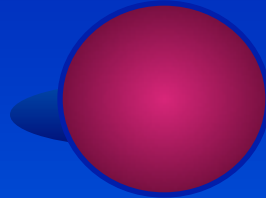
- **R19.** Calculate non-HDL-C (total cholesterol minus HDL-C) in patients with moderately elevated triglycerides (200 to 500 mg/dL), diabetes mellitus, and/or established CAD (Grade C; BEL 2).
- **R20.** If insulin resistance is suspected, AACE recommends evaluating non-HDL-C to gain useful information regarding the patient's total atherogenic lipoprotein burden. In addition, in any circumstance when triglycerides are 200 mg/dL or greater but less than 500 mg/dL, a non-HDL-C calculation will provide better risk assessment than LDL-C alone (**Grade C; BEL 4**). Non-HDL-C targets are 30 mg/dL higher than established LDL-C risk levels (Grade C; BEL 4).

Cosa dosare

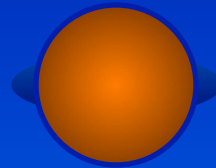
VLDL
Chilomicroni



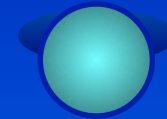
VLDL_R
Chilom._R



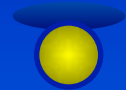
IDL



LDL



LDL
piccole
e dense



Lipoproteine ricche di Tg

**Lipoproteine ricche di
colesterolo**

LDLc

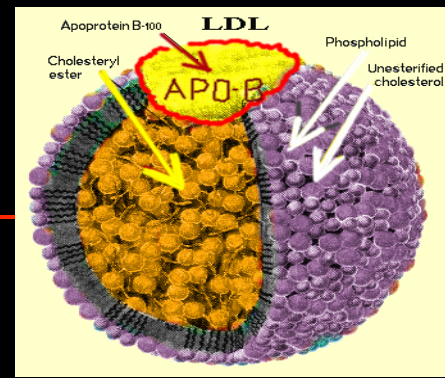
HDLc

Trigliceridi

Non-HDLc

Apolipoproteina B

apoB



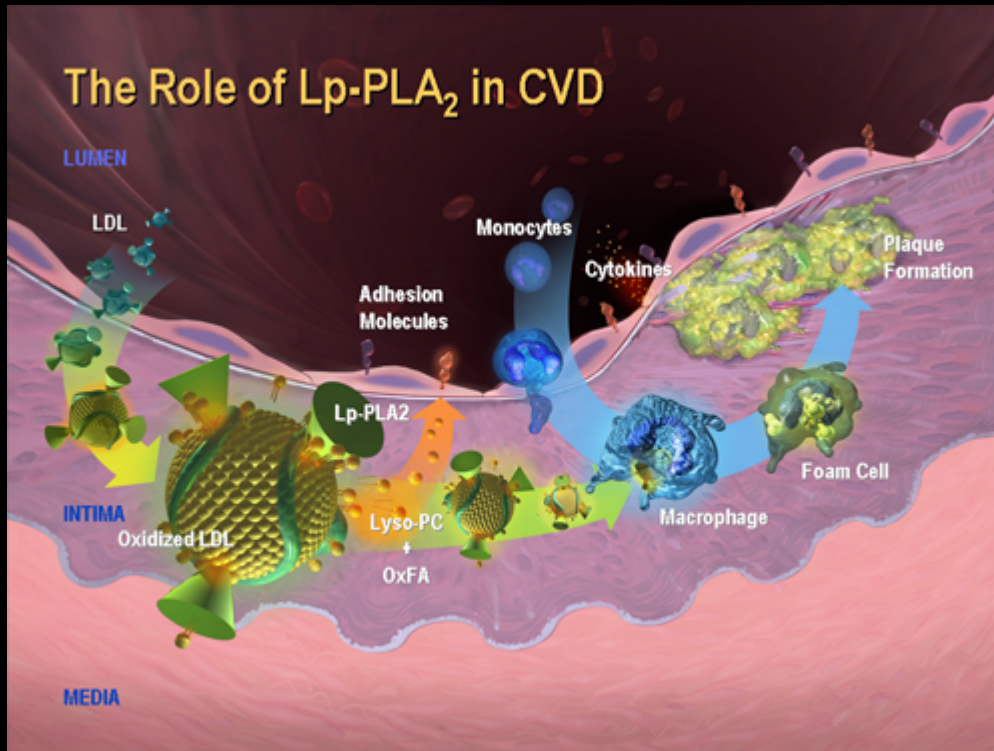
- **Principale apolipoproteina delle LDL**
- **Solo una molecola di apoB per particella di LDL, quindi rappresenta il numero di particelle LDL**
- **Esiste in due isoforme**
 - apoB100** espressa nel fegato e quindi presente sulle lipoproteine prodotte dal fegato
 - apoB48** forma troncata da un enzima espresso nell'uomo nell'intestino e quindi presente sulle lipoproteine derivate dall'intestino

Target

R22. AACE recommends that optimal apo B levels for patients at risk of CAD, including those with diabetes, are less than 90 mg/dL, while patients with established CAD or diabetes who have 1 or more additional risk factor(s) should have an apo B goal of less than 80 mg/dL (**Grade**

Quando

- ApoA1
- hsPCR
- Lp-PLA₂



apoAI

R24. AACE believes that assessment of apo AI may be useful in certain cases (**Grade B; BEL 2**). A normal apo AI level in a patient with low HDL-C suggests the existence of an adequate number of HDL-C particles that contain less cholesterol and may be an indication of less risk. The INTERHEART study found that the apo B to apo AI ratio was among the most significant risk factors for MI (**14 [EL 2]**).

hsCRP e Lp-PLA₂

R26. Assess markers of inflammation in patients where further stratification of risk is necessary. Highly sensitive CRP and Lp-PLA₂ provide useful additional information in these instances and appear to be synergistic in predicting risk of CVD and stroke (**Grade B; BEL 1**).

hsCRP

Lp-PLA₂

Quanto spesso

R54. AACE recommends reassessing patients' lipid status 6 weeks after therapy initiation and again at 6-week intervals until the treatment goal is achieved. Thereafter, AACE recommends that patients be tested at 6- to 12-month intervals. The specific interval should depend on patient adherence to therapy and lipid profile consistency. If adherence is a concern or the lipid profile is unstable, the patient will probably benefit from biannual assessment (**Grade C; BEL 4**).

Quanto spesso

R55. AACE recommends more frequent lipid status evaluation in the following *clinical* circumstances:

Peggioramento del controllo glicemico

Inizio terapia con un farmaco interferente con i livelli di lipidi

Progressione della malattia aterotrombotica

Aumento di peso significativo

Variazione inaspettata di un parametro lipidico

Sviluppo di un nuovo fattore di rischio CAD

Nuove evidenze o linee guida che suggeriscano nuovi target



European Heart Journal (2012) 33, 1635–1701
doi:10.1093/eurheartj/ehs092

JOINT ESC GUIDELINES



European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)

Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline

Lars Berglund, John D. Brunzell, Anne C. Goldberg, Ira J. Goldberg, Frank Sacks, Mohammad Hassan Murad, and Anton F. H. Stalenhoef

J Clin Endocrinol Metab, September 2012, 97(9):2969–2989