

Non-HDL cholesterol predicts coronary heart disease in primary prevention: findings from an Italian a 40-69 year-old cohort in general practice

Il colesterolo non-HDL predice la malattia coronarica in prevenzione primaria: risultati da una coorte italiana di 40-69 anni in medicina generale

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RIASSUNTO. *Il colesterolo non-HDL predice la malattia coronarica in prevenzione primaria: risultati da una coorte italiana di 40-69 anni in medicina generale.* A.V. Ciardullo L. Azzolini, M. Bevini, T. Cadioli, P. Malavasi, A. Morellini, M.M. Daghighio, P. Guidetti, M. Lorenzetti, C. Carapezzi.

Scopo. La frazione lipoproteica denominata “colesterolo non-HDL” viene raccomandata come un indice di rischio coronarico (RC) associata alla dislipidemia combinata ed è stata trovata un utile fattore predittivo del rischio coronarico nei pazienti diabetici. Abbiamo studiato l’associazione tra i fattori di RC noti, incluso la colesterolo non-HDL ed una “condizione di RC elevato”, cioè un “RC a 5-anni >15%” in medicina generale.

Metodi. Abbiamo studiato 4085 individui di età 40-69 anni, 489 diabetici e 3596 non-diabetici, appartenenti ad una coorte opportunistica. Sono state utilizzate le statistiche descrittive, e la regressione logistica multivariata aggiustata per età e sesso per i confronti tra i 2 gruppi.

Risultati. Circa il 12% dei partecipanti era diabetico.

I confronti aggiustati per età e sesso hanno mostrato che tutte le variabili erano significativamente peggiori nei diabetici rispetto ai non-diabetici (eccetto fumo, colesterolo totale e rapporto colesterolo totale/HDL). I diabetici avevano un “RC medio a 5-anni” più alto dei non-diabetici (18.8±11.9% vs 7.5±6.9%, P<0.01), e una prevalenza quattro volte maggiore di un “RC a 5-anni >15%” (55.4% vs 11.1%, P<0.01). Nei diabetici, le variabili associate ad una “condizione di RC elevato” sono: fumo, pressione arteriosa sistolica (PAS) e colesterolemia non-HDL; nei non-diabetici: fumo, PAS, colesterolemia non-HDL e HDL (inversamente).

Conclusioni. Il colesterolo non-HDL – oltre a fumo e PAS – è un forte predittore di una “condizione di RC elevato” sia negli individui diabetici che non-diabetici.

Parole chiave: Cardiopatia ischemica, diabete, lipidi plasmatici, medicina generale.

Monaldi Arch Chest Dis 2004; 62: 2, 69-72.

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Introduction

Existing guidelines do take advantage of non-HDL cholesterol as an index of risk associated with combined dyslipidemia, since it circumvents the potential limitation of triglycerides as a mere marker of coronary heart disease (CHD) risk [1].

Non-HDL cholesterol is defined as the difference between total and HDL cholesterol, and represents cholesterol carried on all of the potentially proatherogenic apoprotein B-containing particles (VLDL, IDL, and LDL as well as chylomicron remnants and lipoprotein[a]) [2].

The elevated CHD risk affecting patients with type 2 diabetes has been attributed to the combined dyslipidemia, which may confer a higher magnitude of risk than elevated LDL cholesterol alone [3-4].

Non-HDL cholesterol index has also been found useful in predicting CHD risk in people with diabetes [5].

The aim of the present work was to study the association between known CHD risk factors – enclosed non-HDL cholesterol – and a “high CHD risk condition” among 40- to 69-year-old diabetic and non-diabetic individuals from an opportunistic cohort cared by general practitioners (GPs).

Methods

We performed an observational study among 40- to 69-year-old individuals from an opportunistic cohort cared by GPs of an Italian health district adhering to a Local Health Plan for Cardiovascular Disease. In Italy, citizens pay the national health system for a doctor chosen from a list of available GPs, thus implying that everyone are in charge to a GP.

A “diabetic individual” was defined as an “individual treated for diabetes” and/or having a “blood glucose greater than 7.0 mmol/l (126 mg/dl)”.

A “high CHD risk condition” was defined as a “5-years CHD risk >15%”. We choose the New Zealand coronary risk function [6] – among the other charts available in literature – because of the demonstrated ability of GPs to interpret and applying it easily [7].

We collected data on the risk factors included in the CHD risk function, i.e. age, gender, cigarette smoking, systolic blood pressure (SBP), total and HDL cholesterol. Non-HDL cholesterol and the ratio of total to HDL cholesterol have been calculated.

Cross-sectional descriptive frequencies for *diabetic* and *non-diabetic* individuals have been calculated. Age- and gender- adjusted *diabetic* vs *non-diabetic* individuals comparison have also been computed by means of multivariate logistic regression.

Results

Twenty-three GPs (out of 76) enrolled over a 12 months period 4,085 (out of 37,054 inhabitants) 40-69-year-old individuals. None of them had already sustained a cardiovascular event and 12.0% had diabetes.

The participants’ characteristics and the “5-years CHD risk” findings are described in table 1.

All the study variables were significantly worse in *diabetic* than *non-diabetic* individuals with the exception of cigarette smoking, total blood cholesterol and the ratio of total to HDL cholesterol). They had a mean “5-year CHD-risk” significantly higher than *non-diabetic* individuals, and a four-folds prevalence of “5-years CHD risk >15%” (table 1).

About 60% of *diabetic* – vs 35% *non-diabetic* individuals – had a SBP greater than 140 mmHg, and 8% vs 2% a SBP greater than 160 mmHg, respectively (P<0.01). *Diabetic* patients had a twice “HDL lower than 1.0 mmol/l (40 mg/dl)” prevalence (20% vs 10%, P<0.01), but they showed a lower prevalence of “Total Cholesterol higher than 5.18 mmol/l (200 mg/dl)” (68% vs 74%, P<0.01). No difference was found in smoking habits between the two groups (23% vs 22%, P=0.89) (table 1). About 3% of *diabetic* patients had no CHD risk factors, vs 29% of *non-diabetic* individuals (P<0.01).

As to *diabetic* individuals, the study variables associated to a “high CHD risk condition” were

Table 1. - Patients’ characteristics and 5-years coronary heart disease (CHD) risk (mean±SD)

Variable	Diabetic Individuals No. 489	Non Diabetic Individuals No. 3596	P-value ^a
Age (years)	59.1±7.0	55.7±8.1	0.001
Male gender (%)	57.9	43.6	0.001
Cigarette smoking (%)	23.5	21.6	0.137
Systolic Blood Pressure [SBP] (mmHg)	143.5±12.5	136.1±12.5	0.001
Blood Total Cholesterol (mmol/l) [mg/dl]	5.77±1.11 [222.8±43.0]	5.82±0.93 [224.9±36.1]	0.891
Blood HDL Cholesterol (mmol/l) [mg/dl]	1.32±0.36 [51.1±14.0]	1.47±0.40 [56.8±15.4]	0.003
Blood Non-HDL Cholesterol (mmol/l) [mg/dl]	4.45±1.10 [171.7±42.3]	4.35±0.95 [168.1±36.9]	0.003
Ratio of Total to HDL Cholesterol	4.6±1.3	4.22±1.3	0.538
Prevalence of High Blood Cholesterol (%) [Total Cholesterol >5.18mmol/l]	68.4	74.5	0.003
Prevalence of Low HDL Cholesterol (%) [HDL Cholesterol <1.0mmol/l]	20.1	9.9	0.001
Prevalence of High SBP (%) [SBP >140 mmHg]	59.6	34.9	0.001
5-years CHD risk (%)	18.8±11.9	7.5±6.9	0.001
Prevalence of ‘high’ CHD risk (%) [5-years CHD risk >15%]	55.4	11.1	0.002

^a age- and gender-adjusted *diabetics* vs *non diabetics* comparison.

Table 2. - Predictors of a “5-year CHD-risk greater than 15%”

Variable	Diabetic Individuals No. 489 Exp beta ^a (95% CI)	Non Diabetic Individuals No. 3596 Exp beta ^a (95% CI)
Cigarette smoking	9.20 (4.63 to 18.26)	10.56 (7.73 to 14.43)
Systolic Blood Pressure	1.10 (1.07 to 1.12)	1.07 (1.06 to 1.08)
Blood Total Cholesterol	1.21 (0.68 to 2.15)	1.32 (0.96 to 1.82)
Blood HDL Cholesterol	0.13 (0.01 to 1.21)	0.11 (0.03 to 0.47)
Blood Non-HDL Cholesterol	1.63 (1.34 to 1.99)	1.89 (1.66 to 2.15)
Ratio of Total to HDL Cholesterol	1.39 (0.69 to 2.80)	1.31 (0.93 to 1.85)

^a age- and gender-adjusted.

cigarette smoking, systolic blood pressure, and non-HDL blood cholesterol levels, whereas total and HDL cholesterol, and the ratio of total to HDL cholesterol did not (table 2).

As to *non-diabetic* individuals, the study variables associated to a “high CHD risk condition” were cigarette smoking, systolic blood pressure, and HDL (inversely) and non-HDL blood cholesterol levels, whereas total and the ratio of total to HDL cholesterol did not (table 2).

Discussion

Cross-sectional and prospective studies have demonstrated the value of non-HDL cholesterol as an index of CHD risk across different populations, including Europeans [8-9].

Non-HDL cholesterol appears to track with multiple CHD risk factors in U.S. ethnic minorities that are disproportionately affected by diabetes [10].

Such use of non-HDL cholesterol has been proposed for diabetic patients as well as the general population. However, it has been pointed out that for non-HDL cholesterol to replace LDL cholesterol as the primary lipid target for the general population, strong evidence of its superiority will be needed [11].

At present, such evidence is not yet available. Nevertheless, the NCEP has clearly acknowledged the importance of non-HDL cholesterol for patients with hypertriglyceridemia, which may include those with type 2 diabetes [1].

Recent findings [5] have shifted the weight of evidence further in favour of the primacy of non-HDL cholesterol specifically for patients with type 2 diabetes. This study also report that the ratio of total to HDL cholesterol was a strong predictor of CHD, although the confidence intervals again overlapped significantly. Thus, in the search for the optimum index of risk, the ratio of total to HDL cholesterol should also be taken into account.

We are aware that our findings might be affected by a selection bias since – by indication – we did not use a random sample, but an opportunistic cohort of individuals assisted by GPs.

Nevertheless, we thought that our study might have provided some interesting information.

In particular, our findings seemed to confirm the primacy of non-HDL cholesterol for diabetic patients. In fact, in *diabetic* individuals we found that non-HDL blood cholesterol levels was associated to a “high CHD risk condition”, whereas total and HDL cholesterol, and the ratio of total to HDL cholesterol did not (table 2). Furthermore, the calculation of non-HDL cholesterol value is very simple and suitable to the busy GPs.

In conclusion, we found that cigarette smoking, systolic blood pressure, and non-HDL cholesterol levels strongly predicted a “high CHD risk condition” both in *diabetic* and *non-diabetic* individuals.

Abstract

Objects. *Non-HDL cholesterol is now recommended as an index of risk associated with combined dyslipidemia, and it has also been found useful in predicting coronary heart disease (CHD) risk in patients with diabetes. We studied the association between known CHD risk factors, enclosed non-HDL cholesterol, and a “high CHD risk condition”, i.e. a “5-years CHD risk >15%” in general practice.*

Methods. *We studied 4,085 40-69 year-old diabetic (no. 489) and non-diabetic (no. 3,596) individuals from an opportunistic cohort. Cross-sectional descriptive statistics, and age- and gender-adjusted multiple logistic exponential betas have been calculated.*

Results. *About 12% of the participants had diabetes. Age- and gender-adjusted comparison showed that all the study variables were significantly worse in diabetic vs. non-diabetic individuals (except cigarette smoking, total blood cholesterol and the ratio of total to HDL cholesterol). They had a mean “5-year CHD-risk” significantly higher than non-diabetic individuals ($18.8 \pm 11.9\%$ vs $7.5 \pm 6.9\%$, $P < 0.01$), and a four-folds prevalence of “5-years CHD risk >15%” (55.4% vs 11.1% , $P < 0.01$). As to diabetic individuals, the study variables associated to a “high CHD risk condition” were cigarette smoking, systolic blood*

pressure, and non-HDL blood cholesterol levels. As to non-diabetic individuals cigarette smoking, systolic blood pressure, and HDL (inversely) and non-HDL blood cholesterol levels were associated to a "high CHD risk condition".

Conclusions. Non-HDL cholesterol – and cigarette smoking and systolic blood pressure – strongly predicted a "high CHD risk condition" both in diabetic and non-diabetic individuals.

Keywords: Coronary heart disease, opportunistic cohort, diabetes, blood lipids, family medicine.

Addendum: We thanks the members of the "GPs' CV Risk Group" who should be considered co-authors: Bacchelli M, Bellodi C, Beltrami AC, Carretti G, Di Fiore A, Feltri G, Frignani A, Gagliano G, Gazzani G, Loscalzo G, Losi A, Mantovani L, Pavarotti V, Prandi B, Ribaldi A, Rosselli C, Tirelli G, Veratti M, Vincenzi A.

Acknowledgements: We are grateful to all the study participants. This work has been supported by the Carpi's Health District of Local Health Unit in Modena. No competing interests to declare.

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