COMPARISON OF C-REACTIVE PROTEIN AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN THE PREDICTION OF FIRST CARDIOVASCULAR EVENTS

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- De ce scriem?
- Ce este un articol stiintific?

Ce este un articol stiintific?

- De ce scriem?

-impartasirea informatiei (diseminare)

-prestigiu (recunoastere internationala-citari)

-avansare in cariera, atragere de fonduri (credibilitate)

- Document
- Contine informatii astfel incat altii
  - sa poata reproduce studiul/experimental realizat
  - sa poata verifica validitatea celor gasite

Clasificare articole stiintifice

- Articole tip review (reviews)
- Articole originale (original articles)
- Articole tip prezentari de caz (case reports)
- Articole tip scrisori catre editor (letter to editor), editorial (editorials)
- Articole tip erate, corrigendum (erratum, corrigendum)

Structura articol stiintific original

- Abstract (150-200 cuvinte)
- Articolul propriu-zis:
    - ACRONIM IMRaD
    - I:Introducere
    - M: Materiale si metode
    - R: Rezultate
    - D: Discutii

Plan pentru abordarea articolului stiintific

- Identificare tipul studiului
- Identificare obiectivele studiului
- Identificare populatie studiu
- Identificare end-points (efecte)
- Identificare variabilele studiului (expunerile, care sunt grupurile care se compara)
- Identificare metode statistice (metodele statistice au fost corect aplicate?)

Abstract

- Sumarizare a intregului articol
- De obieci numar limitat de cuvinte (150-200)
- Se prezinta pe scurt metodele folosite si principalele rezultate
- Trebuie sa fie independent de articol
- Acesta este de obicei cel mai citit (mai degraba decat articolul)

Introducere

- -date generale despre problema studiului
- -revizuirea (pe scurt) a literaturii de specialitate (“background”)
- -argumente care sa sustina studiul (inovatie, design superior altor studii din literatura ce ataca problematica similara,etc)
- -**obiectivul studiului-fraza de incheiere a introducerii**
- FRAZE SCURTE, CONCISE!

Introducere

data on other risk factors are urgently needed.[2,3]

Among the biologic markers considered by those panels, there was particular interest in C-reactive protein, a marker of inflammation that has been shown in several prospective, nested case–control studies to be associated with an increased risk of myocardial infarction,[4-9] stroke,[4,6,10,11] sudden death from cardiac causes,[12] and peripheral arterial disease.[13] Although the results of these studies are highly consistent, limitations inherent in the design of nested case–control studies make it difficult to assess the relative merit of C-reactive protein. In particular, population-based cut-off points for C-reactive protein remain uncertain, and reliable data describing receiver-operating-characteristic curves for C-reactive protein have not been available. Moreover, there are insufficient data from prospective cohort studies directly comparing the predictive value of C-reactive protein with that of LDL cholesterol.

Date generale?

Argumente care sa sustina prezentul studiu?

Obiective?

Introduere

Date generale?

Argumente care sa sustina prezentul studiu?

Obiective?

To overcome these limitations, we measured C-reactive protein and LDL cholesterol in all 27,939 participants in the Women's Health Study who provided usable base-line blood samples; these women had been followed for a mean of eight years. Using these data, we were able to calculate survival curves associated with C-reactive protein levels, to compare the predictive value of C-reactive protein and LDL cholesterol directly in a large, representative population sample, and to define the population distribution of C-reactive protein levels. We also determined the predictive value of each biologic marker among users and nonusers of hormone-replacement therapy; this is a clinically relevant issue, since hormone-replacement therapy affects levels of both C-reactive protein and LDL cholesterol.[14-16] Finally, we evaluated whether C-reactive protein provided prognostic information on risk after adjustment for all components of the Fra-

Obiectiv principal al studiului: Cercetarea capacitatii proteinei C reactive ca predictor pentru primul eveniment cardiovascular la femei

Materiale si metode

- Descriere amanuntita a **metodologiei (cum facem?)**:
  - **NU REZULTATELE (ce am gasit facand asa?)**
- tipul de studiu
- populatia studiului
- end-point-urile (efectele) si masurarea lor
- variabilele studiului si masurarea lor
- abordare statistica, inclusiv softul si versiunea folosita

Materiale si metode

- Tipul de studiu ????
- Populatia: 28.345 femei inrolate in studiul Women's Health Study in perioada XI '92-VII '95
- End-point (efect):

primul eveniment cardiovascular:

IMA

AVC ischemic

Moarte de origine cardiovasculara

between November 1992 and July 1995, at which time they provided information regarding demographic, behavioral, and lifestyle factors. All participants were followed for the occurrence of first cardiovascular events, including nonfatal myocardial infarction, nonfatal ischemic stroke, coronary revascularization procedures, and death from cardiovascular causes. The occurrence of myocardial infarction was considered confirmed if symptoms met the criteria of the World Health Organization and if the event was associated with abnormal levels of cardiac enzymes or diagnostic electrocardiographic criteria. Stroke was confirmed if the participant had new neurologic deficits that persisted for more than 24 hours. Computed tomographic scans or magnetic resonance images were available for the great majority of events and were used to distinguish hemorrhagic from ischemic events. The performance of either percutaneous coronary revascularization or coronary-artery bypass surgery was confirmed by a review of hospital records. Deaths from cardiovascular causes were confirmed by review of autopsy reports, death certificates, medical records, and information obtained from family members.

IMA

AVC ISCHEMIC

MOARTE SUBITA C-V

Before randomization, blood samples were collected in tubes con-

Cum au fost definite end-point-urile (efectele)?

Materiale si metode

- Variabilele studiului:
- -nivelul proteinei C reactive la inrolare in studiu
- -nivelul LDL colesterolului la inrolare in studiu

Before randomization, blood samples were collected in tubes containing EDTA from 28,345 study participants and stored in liquid nitrogen until the time of analysis. Samples were then transferred to a core laboratory facility, where they were assayed for C-reactive protein with a validated, high-sensitivity assay (Denka Seiken) and for LDL cholesterol with a direct-measurement assay (Roche Diagnostics). This laboratory is certified for the measurement of lipids and is a core facility for ongoing standardization programs regarding the measurement of C-reactive protein. Of the samples received, 27,939 could be evaluated and were assayed for C-reactive protein and LDL cholesterol.

Rezultate

- Se trec rezultatele obtinute, fara comentarii asupra lor

-date descriptive despre cohorta/loturi : gen, varsta, diagnostic pozitiv, alte date relevante

-rezultatele testelor statistice aplicate (grafice tip placinta- de evitat!, bare, histograme, box plot, tabele..)

-NU prezentati doar valoarea p ci includeti si 95% interval incredere

-sunt de preferat TABELE (mai putin spatiu si mai multa informatie)

-prezentare modele predictive, etc

-timpul trecut, prezentare CONCISA!

- **Se face referire la grafice si tabele incluse in text**

Rezultate

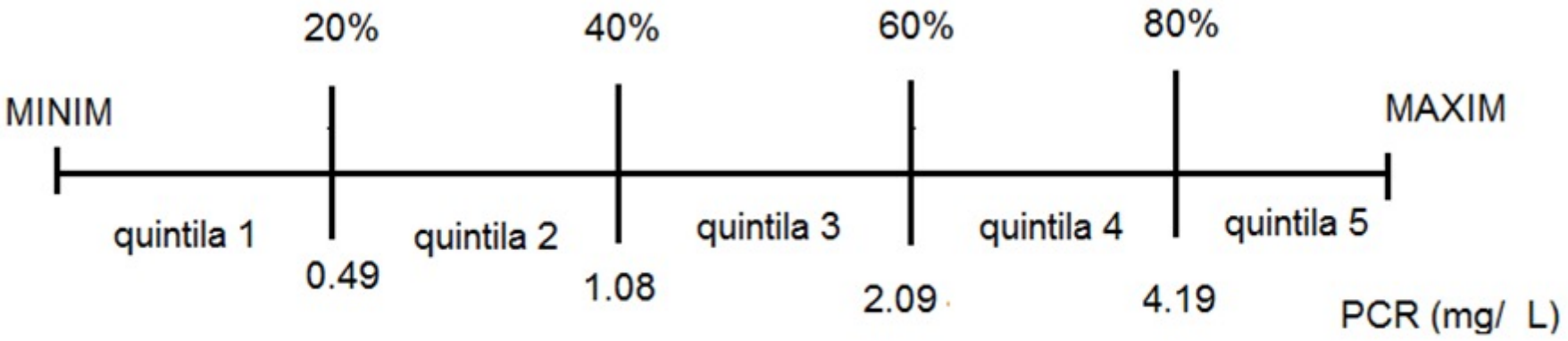
- Tabelele si figurile trebuie sa fie cat mai clare
- Trebuie sa aiba legenda
- Trebuie explicate prescurtarile folosite

- O figura/tabel bine prezentat trebuie sa transmita mesajul independent de articol!

Rezultate

Populatia studiului:

- 27.939 femei (au fost exclusi participantii la care nu s-a putut doza PCR, LDL) -15.745 fara terapie hh substitutie
- Impartire intreaga cohorta in quintile (20%) ale nivelurilor PCR => 5 grupuri
- Impartire cohorta in quintile ale nivelurilor LDL cho =>5 grupuri


20%
40%
60%
80%
MINIM
MAXIM
quintila 1
quintila 2
quintila 3
quintila 4
quintila 5
0.49
1.08
2.09
4.19
PCR (mg/ L)

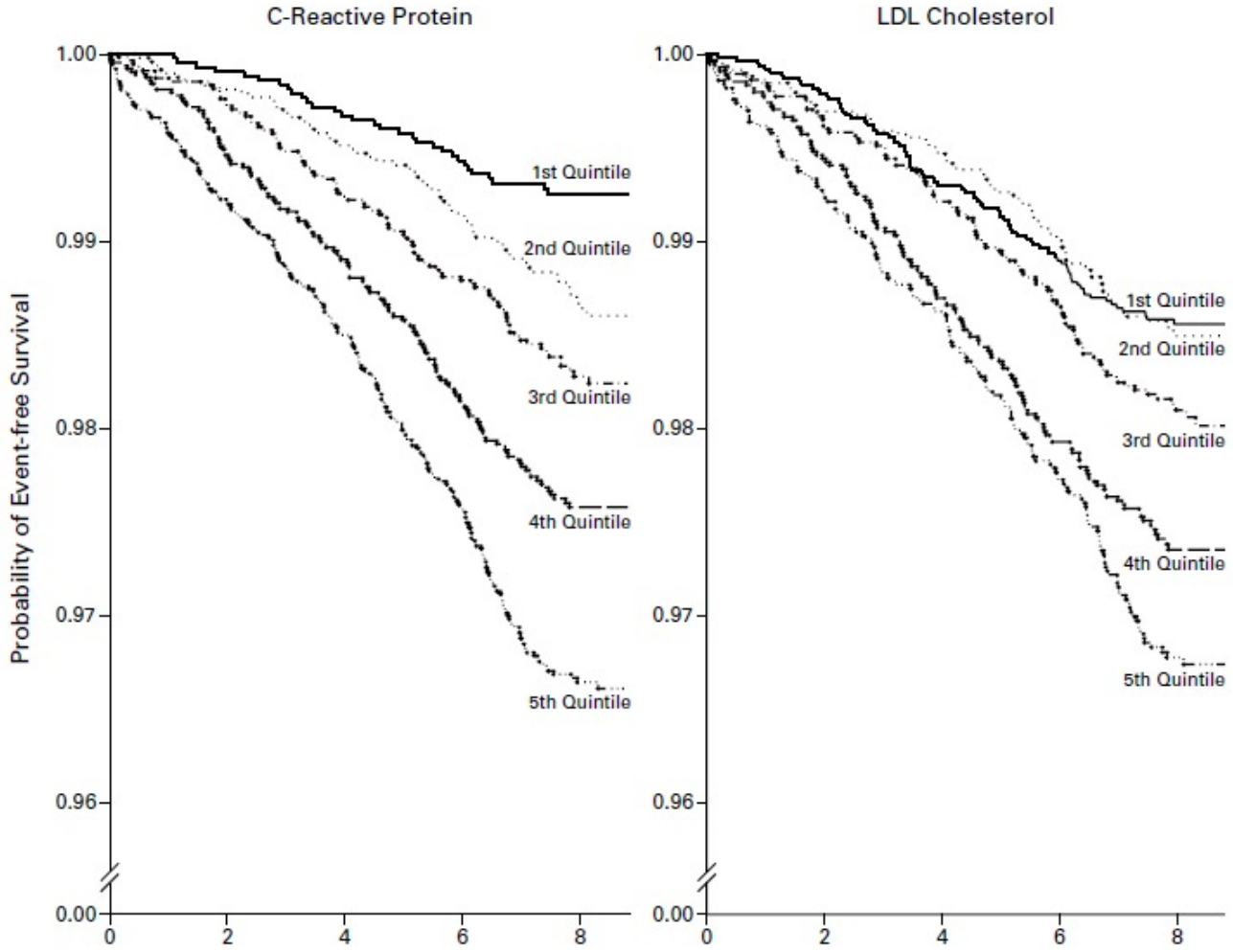


Figure 1. Event-free Survival According to Base-Line Quintiles of C-Reactive Protein and LDL Cholesterol.

The range of values for C-reactive protein was as follows: first quintile, ≤0.49 mg per liter; second quintile, >0.49 to 1.08 mg per liter; third quintile, >1.08 to 2.09 mg per liter; fourth quintile, >2.09 to 4.19 mg per liter; fifth quintile, >4.19 mg per liter. For LDL cholesterol, the values were as follows: first quintile, ≤97.6 mg per deciliter; second quintile, >97.6 to 115.4 mg per deciliter; third quintile, >115.4 to 132.2 mg per deciliter; fourth quintile, >132.2 to 153.9 mg per deciliter; fifth quintile, >153.9 mg per deciliter. To convert values for LDL cholesterol to millimoles per liter, multiply by 0.02586. Note the expanded scale on the ordinate.

- Evaluarea riscului pe care il are “expunerea” la concentratii mai mari ale PCR si ale LDL cho
- RISC RELATIV (studiu tip cohorta)

TABLE 2. CRUDE, AGE-ADJUSTED, AND RISK-FACTOR–ADJUSTED RELATIVE RISK OF A FIRST CARDIOVASCULAR EVENT ACCORDING TO THE QUINTILE OF C-REACTIVE PROTEIN AND LDL CHOLESTEROL AT BASE LINE.*

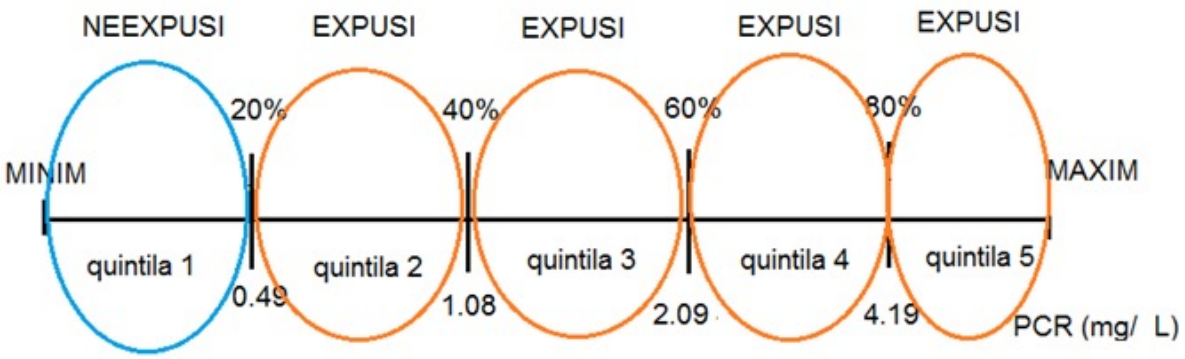
VARIABLE	QUINTILE OF C-REACTIVE PROTEIN						
	1 (≤0.49 mg/liter)	2 (>0.49–1.08 mg/liter)	3 (>1.08–2.09 mg/liter)	4 (>2.09–4.19 mg/liter)	5 (>4.19 mg/liter)	P VALUE	AREA UNDER ROC CURVE
Crude relative risk (95% CI)	1.0	1.8 (1.1–2.7)	2.3 (1.5–3.4)	3.2 (2.2–4.8)	4.5 (3.1–6.6)	<0.001	0.64
Age-adjusted relative risk (95% CI)	1.0	1.5 (1.0–2.4)	1.8 (1.2–2.8)	2.5 (1.7–3.7)	3.6 (2.5–5.2)	<0.001	0.74
Risk-factor–adjusted relative risk (95% CI)	1.0	1.4 (0.9–2.2)	1.6 (1.1–2.4)	2.0 (1.3–3.0)	2.3 (1.6–3.4)	<0.001	0.81
	QUINTILE OF LDL CHOLESTEROL						
	1 (≤97.6 mg/dl)	2 (>97.6–115.4 mg/dl)	3 (>115.4–132.2 mg/dl)	4 (>132.2–153.9 mg/dl)	5 (>153.9 mg/dl)	P VALUE	AREA UNDER ROC CURVE
Crude relative risk (95% CI)	1.0	1.0 (0.8–1.4)	1.3 (1.0–1.8)	1.8 (1.4–2.4)	2.2 (1.7–2.9)	<0.001	0.60
Age-adjusted relative risk (95% CI)	1.0	0.9 (0.7–1.3)	1.1 (0.9–1.5)	1.5 (1.1–1.9)	1.7 (1.3–2.2)	<0.001	0.73
Risk-factor–adjusted relative risk (95% CI)	1.0	0.9 (0.7–1.2)	1.1 (0.8–1.4)	1.3 (1.0–1.7)	1.5 (1.1–2.0)	<0.001	0.81

*P values are for tests of trend across quintiles. ROC denotes receiver operating characteristic, and CI confidence interval. Risk-factor–adjusted relative risks have been adjusted for age, smoking status, the presence or absence of diabetes mellitus, blood pressure, and use or nonuse of hormone-replacement therapy. All models have been adjusted for treatment assignment. For all relative risks, the reference category is the first quintile. To convert values for LDL cholesterol to millimoles per liter, multiply by 0.02586.

- Pentru calcularea riscului relativ este necesar realizarea unui tabel de contingenta 2X2
- RR= RISCUL EXPUSI/RISCUL NEEXPUSI

		EFECT		
		DA	NU	
FACTOR RISC	DA (EXPUSI)	a	b	a+b
	NU (NEEXPUSI)	c	d	c+d
		a+c	b+d	

		EFECT- primul eveniment cardiovascular in perioada de follow-up		
		DA	NU	
FACTOR RISC	DA (EXPUSI) Quintile (2/3/4/5)	a	b	a+b
	NU (NEEXPUSI) Prima quintila PCR	c	d	c+d
		a+c	b+d	



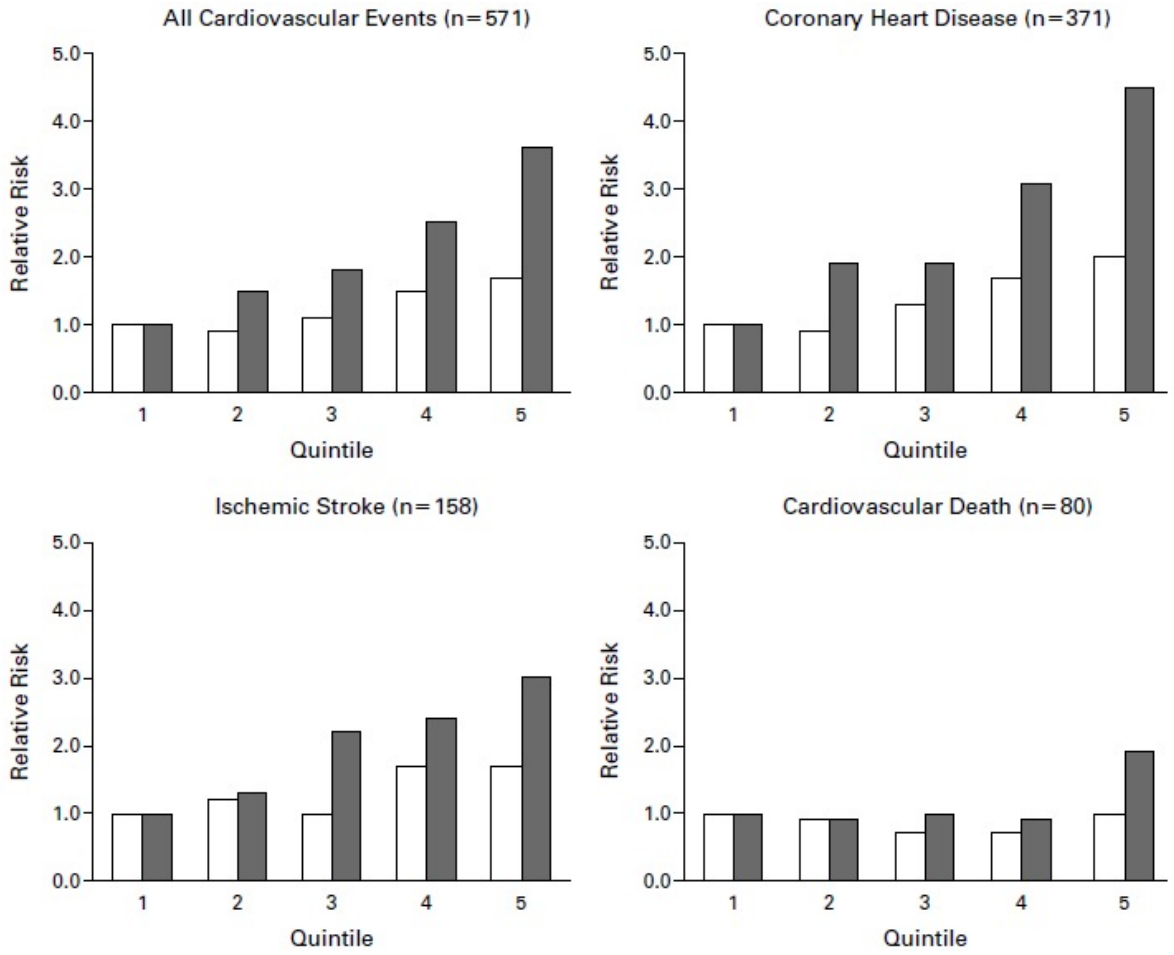
-
- Riscul neexpusi=c/c+d
- Riscul relativ= {[a/(a+b)/[c/(c+d)]}

TABLE 2. CRUDE, AGE-ADJUSTED, AND RISK-FACTOR–ADJUSTED RELATIVE RISK OF A FIRST CARDIOVASCULAR EVENT ACCORDING TO THE QUINTILE OF C-REACTIVE PROTEIN AND LDL CHOLESTEROL AT BASE LINE.*

VARIABLE	QUINTILE OF C-REACTIVE PROTEIN						
	1 (≤0.49 mg/liter)	2 (>0.49–1.08 mg/liter)	3 (>1.08–2.09 mg/liter)	4 (>2.09–4.19 mg/liter)	5 (>4.19 mg/liter)	P VALUE	AREA UNDER ROC CURVE
Crude relative risk (95% CI)	1.0	1.8 (1.1–2.7)	2.3 (1.5–3.4)	3.2 (2.2–4.8)	4.5 (3.1–6.6)	<0.001	0.64
Age-adjusted relative risk (95% CI)	1.0	1.5 (1.0–2.4)	1.8 (1.2–2.8)	2.5 (1.7–3.7)	3.6 (2.5–5.2)	<0.001	0.74
Risk-factor–adjusted relative risk (95% CI)	1.0	1.4 (0.9–2.2)	1.6 (1.1–2.4)	2.0 (1.3–3.0)	2.3 (1.6–3.4)	<0.001	0.81
	QUINTILE OF LDL CHOLESTEROL						
	1 (≤97.6 mg/dl)	2 (>97.6–115.4 mg/dl)	3 (>115.4–132.2 mg/dl)	4 (>132.2–153.9 mg/dl)	5 (>153.9 mg/dl)	P VALUE	AREA UNDER ROC CURVE
Crude relative risk (95% CI)	1.0	1.0 (0.8–1.4)	1.3 (1.0–1.8)	1.8 (1.4–2.4)	2.2 (1.7–2.9)	<0.001	0.60
Age-adjusted relative risk (95% CI)	1.0	0.9 (0.7–1.3)	1.1 (0.9–1.5)	1.5 (1.1–1.9)	1.7 (1.3–2.2)	<0.001	0.73
Risk-factor–adjusted relative risk (95% CI)	1.0	0.9 (0.7–1.2)	1.1 (0.8–1.4)	1.3 (1.0–1.7)	1.5 (1.1–2.0)	<0.001	0.81

*P values are for tests of trend across quintiles. ROC denotes receiver operating characteristic, and CI confidence interval. Risk-factor–adjusted relative risks have been adjusted for age, smoking status, the presence or absence of diabetes mellitus, blood pressure, and use or nonuse of hormone-replacement therapy. All models have been adjusted for treatment assignment. For all relative risks, the reference category is the first quintile. To convert values for LDL cholesterol to millimoles per liter, multiply by 0.02586.

- Riscurile relative defalcate pe evenimente cardiovasculare (end-pointurile secundare: IMA, AVC ischemic, moarte cardiovasculara)



Riscurile relative defalcate la pacientele cu si fara terapie de substitutie hormonala

VARIABLE	QUINTILE OF C-REACTIVE PROTEIN						
	1	2	3	4	5	P VALUE	AREA UNDER ROC CURVE
Nonusers of HRT							
Crude relative risk	1.0	2.3	2.8	4.3	6.9	<0.001	0.67
Age-adjusted relative risk	1.0	1.9	2.2	3.2	5.4	<0.001	0.78
Risk-factor–adjusted relative risk	1.0	1.8	1.8	2.4	3.0	<0.001	0.84
Users of HRT							
Crude relative risk	1.0	1.0	1.5	1.9	2.4	<0.001	0.60
Age-adjusted relative risk	1.0	0.9	1.3	1.6	2.1	<0.001	0.69
Risk-factor–adjusted relative risk	1.0	0.9	1.1	1.3	1.3	0.08	0.77

	QUINTILE OF LDL CHOLESTEROL						
	1	2	3	4	5	P VALUE	AREA UNDER ROC CURVE
Nonusers of HRT							
Crude relative risk	1.0	1.0	1.2	1.8	2.6	<0.001	0.61
Age-adjusted relative risk	1.0	0.8	1.0	1.3	1.6	<0.001	0.75
Risk-factor–adjusted relative risk	1.0	0.8	0.9	1.1	1.4	0.002	0.84
Users of HRT							
Crude relative risk	1.0	1.1	1.5	1.8	1.7	0.001	0.58
Age-adjusted relative risk	1.0	1.1	1.3	1.7	1.5	0.005	0.68
Risk-factor–adjusted relative risk	1.0	1.0	1.3	1.5	1.5	0.02	0.77

*ROC denotes receiver operating characteristic, and HRT hormone-

Discutii

- Comentarii despre rezultate, comparatii cu alte rezultate din literatura de specialitate
- Subliniati ce ADUCE NOU STUDIUL!
- Viitoare implicatii ale descoperirilor studiului
- Limitarile studiului, viitoare directii de cercetare
- La final, concluziile!!

The current study suggests that C-reactive protein, a marker of systemic inflammation, is a stronger predictor of future cardiovascular events than LDL cholesterol. In this study, C-reactive protein was superior to LDL cholesterol in predicting the risk of all study end points; this advantage persisted in multivariable analyses in which we adjusted for all traditional cardiovascular risk factors and was cle
well as nonusers of hormone-repla
base line. However, C-reactive prot
lesterol levels were minimally corr
combined evaluation of both C-re
LDL cholesterol proved to be super

Our data also help establish the population distribution of C-reactive protein. That the cutoff points for the quintiles in the current population are very close to those previously described in smaller studies from the United States and Europe is reassuring and consistent with evidence describing the stability and reproducibility of values obtained for C-reactive protein with new, high-sensitivity assays.[24] These data also demonstrate that a single set of cutoff points for C-reactive protein in women can be used regardless of their status with regard to hormone-replacement therapy — an issue that has been of concern in previous work.[14-16]

The current data also have implications for the targeting of preventive therapies. We previously demonstrated in a randomized trial that statin therapy may have clinical value for primary prevention among persons with elevated C-reactive protein but low LDL

Comentariu, comparatii cu alte studii din literatura?

Limitari ale studiului?

Concluzii?

cholesterol but high levels of C-reactive protein.[2]

Unlike other markers of inflammation, C-reactive protein levels are stable over long periods, have no diurnal variation, can be measured inexpensively with available high-sensitivity assays, and have shown specificity in terms of predicting the risk of cardiovascular disease.[24,28-30] However, despite the consistency of prospective data in diverse cohorts,[4-13,16,25,31] decisions regarding the clinical use of C-reactive protein remain complex. To evaluate fully the clinical usefulness of any new biologic marker requires more than a direct comparison with LDL cholesterol or the Framingham risk score; other factors, such as lipid subfractions, triglycerides, Lp(a) lipoprotein, homocysteine, insulin resistance, and hypofibrinolysis, either in combination with

Comentariu, comparatii cu alte studii din literatura?

Limitari ale studiului?

Viitoare directii de cercetare?

Concluzii?

factors, such as high blood pressure, smoking, obesity, diabetes, low levels of physical activity, and use of hormone-replacement therapy, may be more or less important for individual patients. Thus, as our findings indicate, new biologic and statistical approaches will be needed as information from basic vascular biology begins the transition into clinical practice.

Referinte

- Atentie la stilul bibliografic!
- Din Instructiuni pentru autori luati forma bibliografiei
- Stilul Vancouver
- “Previous review [12] presented relevant data about H1 blockers and cardiac output”

12. Leurs R, Church MK, Taglialatela M. H_1-antihistamines: inverse agonism, anti-inflammatory actions and cardiac effects. Clin Exp Allergy. 2002 32(4):489-498.

- Stilul Harvard

Leurs, R, Church,M,K, Taglialatela,M, 2002, “H_1-antihistamines: inverse agonism, anti-inflammatory actions and cardiac effects”. *Clin Exp Allergy*, vol.32, no4, pp.489-498.

Cum imi fac strategia de scriere articol?

- Trebuie scris, scris, scris (cat mai des!)
- STRATEGIE (idee)
  - Incepeti cu MATERIAL SI METODE
  - Continuati cu REZULTATELE (decideti ce informatie prezentati, cum prezentati-tabele, figuri)
  - INTRODUCERE, DISCUTII
  - La final: titlu si abstract

EVITATI prea multe abrevieri sau jargon!

Cum ati continua studiul?

- Putem realiza un studiu clinic randomizat?
- Putem realiza o sinteza sistematica si o meta-analiza?

Concluzii (plus de RETINUT)

»**IMRaD**

- Identificare tipul studiului
- Identificare obiectivele studiului
- Identificare populatie studiu
- Identificare end-points (efecte)
- Identificare variabilele studiului (expunerile, care sunt grupurile care se compara)
- Identificare metode statistice (metodele statistice au fost corect aplicate?)

Reminder cu ce am discutat azi

- https://prezi.com/view/QSBWSVkXn89DTWoksBZx/
- https://www.facebook.com/RomJInternMed/