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Research Article

Aggregation of Cardiovascular Risk in First-Degree Relatives of Patients with Acute Myocardial Infarction: Famiam Study

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Abstract

Objectives: To examine whether the distribution of traditional cardiovascular risk factors, or biochemical markers of subclinical damage differs among first-degree relatives of patients who have suffered an acute myocardial infarction and the population without such a history.

Methods: A cross sectional study compared 99 first-degree relatives of patients with myocardial infarction to a control group of 81 individuals. Anthropometric variables were recorded, habits, history and blood tests including glucose, lipid profile, high-sensitivity C reactive protein (hs-CRP), interleukin-6 (IL-6), homocysteine, myeloperoxidase, fibrinogen and von Willebrand factor (vWF). The cardiovascular risk will be determined by the Framingham, Score and Regicor schemes.

Results: Biochemical values in relatives vs controls were significantly different for total cholesterol (205,4±42,4 mg/dL vs 185,2±34,5 mg/dL; p<0,05), low density lipoprotein cholesterol (129,9±36,1 mg/dL vs 108,6±29,3 mg/dL; p<0,05), triglycerides (139,8±83,2 mg/dL vs 110,9±63,2 mg/dL; p<0,05) and IL-6 (5,6±7,2 pg/dL vs 3,9±4,1 pg/dL; p<0,05). Followed biochemical parameters were comparable in both groups: glucose (114,7±365,9 mg/dL vs 122,7±40,4 mg/dL; ns), hs-CRP (1,99±1,7 mg/dL vs 1,8 ±1,6 mg/dL; ns), mieloperoxidase (1,17±0.9 IU/L vs 1,18±0.9 IU/L; ns) and homocysteine (15,6±7,7 µmol/dl vs 15,5±8.1 µmol/L; ns). The cardiovascular risk measured by the Framingham scheme in relatives was 14,9±10,1% and 13,5±10,2% in control group (ns) whilst measured by the Score scheme was 2,4±2,6% and 2,6±2,3%, respectively (ns).

Conclusions: The present study highlights a worse lipid profile and proinflammatory markers among first-degree relatives of patients with myocardial infarction in the control group.

INTRODUCTION

Cardiovascular disease (CVD) is the main cause of death and morbidity in most industrialized countries, representing 17.1 millions of deaths/year and thus high costs to public health systems [1]. Despite the advances in the diagnosis and prevention, the incidence is still growing and CVD is yet one of the dominant causes of mortality and disability in Spain, counting around 35% deaths each year [2,3]. Of note, individuals with a first-degree relative with coronary artery disease, especially of early clinical presentation (before the age of 55 for male or before the age of 65 for female relative) present greater risk of developing ischemic heart disease. The chance of developing CVD increases with the number of relatives and with the early presentation, [4] which leads to assume a genetic predisposition. The main difference between polygenic and monogenic mendelian inheritance

consists in that polygenetic disease is under the influence of multiple genes and environmental factors, but not a single gene [5-11]. Now on, mendelian inheritance is thought to explain a relatively minor fraction of familial coronary artery disease (CAD). It is irrefutably required to know whether or not first-degree relative of patients suffering from an acute myocardial infarction (AMI) present a comparable cardiovascular risk distribution, in order to prevent possible cardiovascular events in those relatives. The purpose of the current study is to determine the cardiovascular risk distribution and biochemical variables of subclinical damage between first-degree relatives of patients with AMI in respect to similar population without such familial history. Thus, in this investigation, we aim to provide potential parameters for future research in the primary prevention of CVD.

MATERIAL AND METHODS

Study populations

We recruited 99 first-degree relatives of patients having suffered an AMI [FAMIG] and a control group [CG] (n=81). Age range for both groups was comprised between 50 and 75 years old. The studied populations were obtained through non probability sampling (consecutive sampling), that consists on selecting each of the individuals that fulfil the inclusion and exclusion criteria [12].

Inclusion criteria for FAMIG: cohort data and blood for the present study were obtained contacting first-degree relatives of patients admitted with an AMI at the hospital (parents or brothers and sisters), only healthy individuals were recruited. CG group was defined as healthy individuals without cardiovascular history or any first-degree relatives with an AMI. Patients do not come alone to the hospital but are usually accompanied by an immediate family member (for instance children and other first-degree relatives). At that point, we checked if the family members fulfill our recruitment strategy and asked them to be included as the FAMIG group (1st degree relatives).

Both groups were recruited when arriving at the centre (Hospital Rafael Méndez, Lorca, Murcia, Spain); all participants provided written informed consent. For both study groups, exclusion criteria included previous cardiovascular pathology factors or treatment that could affect biochemical variables (infectious and inflammatory disorders, cancer, creatinine >200 µmol/L, steroids and hormone replacement therapy). After applying those criteria, two different first-degree relative groups were selected, with and without history of AMI. Both groups were sex and gender matched. Individuals included in the present study display all a good health-related quality of life, largely influenced by social and economic conditions of the cohort.

Analysed variables were age (years), gender, weight, height, body mass index (BMI, kg/m^2), abdominal perimeter (cm), blood pressure (mmHg), history of hypertension, dyslipidemia, diabetes, smoking, exercise habits and alcohol consumption (regular alcohol intake is estimated about > 30 gr/day in man and > 15 gr/day in woman).

Blood collection

For laboratory analysis, non-fasting peripheral venous blood samples were collected from all participants for routine blood test. Levels of glucose (mg/dL), lipids such as cholesterol (mg/dL), HDL cholesterol (mg/dL), LDL cholesterol (mg/dL) and triglycerides (mg/dL) were analysed. Biochemical markers of oxidation: mieloperoxidase (IU/L) and anti-oxidized LDL autoantibodies (ox-LDL, IU/mL) were also performed. Two inflammatory markers were measured: high sensitivity C reactive protein (hs-CRP, mg/L) and interleukin 6 (IL-6, pg/mL) together with thrombotic markers such as fibrinogen (mg/dL), von Willebrand factor (vWF, IU/mL) and homocysteine (µmol/L).

Cardiovascular risk was determined following the FRAMINGHAM, SCORE and REGICOR schemes [13-15]. Individuals recognizing to smoke daily at the recruitment and occasionally were considered smokers. Habitual alcohol intake is considered when it happens regularly (daily or weekly). Exercise habits are positive at least 30 min and three times per week. Abdominal perimeter was used to determine abdominal obesity (females>88 cm and males>102 cm), according to the ATPIII criteria [16]. Dyslipidemia was defined as total cholesterol ≥200 mg/dL or LDL≥130 mg/dL or HDL≥40 mg/dL in males (≥46 mg/dL in females), or triglycerides≥150 mg/dL or lower values under hypolipidemic treatment.

Statistical analysis

Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Data are expressed as mean ± standard deviation (SD) and confidence interval [CI 95%] for normally distributed data. Each categorical variable is expressed as frequency (percentage) of patients. Differences between groups were assessed by the unpaired t test for independent samples. A p-value of <0.05 was considered statistically significant. SPSS 15.0 software was used for statistical analyses (SPSS, Inc, Chicago, Illinois, USA).

RESULTS

Concerning the gender, FAMIG presented 39.0% males whist CG had a 43.2%; those data were not significantly different. Similarly, age was also comparable for both groups: 66.2±13.2 years old in FAMIG compared to 62±14.1 years old in CG (non significant).

Cardiovascular risk factors distribution

The different clinical features and biomarkers were compared in the two groups and summarized in Table 1 and 2. There were not significant differences in functional groups regarding baseline characteristics such as age, male sex, hypertension, dyslipidemia or diabetes. Smoking habits were shown higher in FAMIG, 34.3% [27.3-41.3] compared to 21% [14.0-28.0.8] in CG individuals (p<0.05). Similarly, overweight was notoriously raised in FAMIG compared to the other group (48,5% *vs* 37%, p<0.05). Individuals of both groups did not differed in alcohol intake, obesity, abdominal obesity or exercise practise (Table 1).

Blood pressure, anthropometric and biochemical variables

Body mass index, blood pressure (systolic and diastolic), total cholesterol, HDL, glucose and creatinine clearance were not found different between the two studied groups (Table 2). Levels of triglycerides in FAMIG were found significantly raised (139.8±83.2 mg/dL) when compared to CG (110.9±63.2 mg/dL) ($p<0.05$). Besides, cholesterol LDL was also higher in the FAMIG group, 129.9±36.1 mg/dL compared to 108.6±29.3 mg/dL in the CG ($p<0.05$) (Table 3).

Biochemical parameters of subclinical damage

Levels of antibodies against oxidized LDL were significantly increased in FAMIG individuals (30.9± 12.2 IU/mL) compared to controls (27±10.5 IU/mL) ($p<0.05$). Concerning inflammatory markers, interleukin 6 was also shown raised in FAMIG (5.6±7.2 pg/mL) towards CG (3.9±4.1 pg/mL) ($p<0.05$). Analysed markers such as mieloperoxidase, homocysteine, hs-CRP, fibrinogen and vWF were not found altered in both groups (Table 4).

Cardiovascular risk through risk schemes

Both, the FAMIG and CG groups display a similar FRAMINGHAM coronary heart disease score (14.9± 10.1% vs 13.5±10.2%, ns). Besides, SCORE risk scheme found also comparable risk for both groups (2.4 ±2.6% vs. 2.6±2.3% ns). Finally, REGICOR scheme concludes that the cardiovascular risk for the FAMIG was 6.1±4.1% and 5.1±3.8% ns).

DISCUSSION

As people grow older they are increasingly at risk of CVD. Knowing the main risk factors together with the analysis of biomarkers of subclinical damage (inflammation, thrombogenic and oxidation...) are well-recognised tools in the prevention of CVD. Although several authors insist on 50% of CAD incurs in the

Table 1: Clinical characteristics of the cross-sectional study (n, % and confidence interval).

	FAMIG (n=99)	GC (n=81)	p value
Hypertension, n (%)	48 (48,5) 39,4%-57,6%	35 (43,2) 36%-50,4%	ns
***Diabetes,* n (%)**	28 (28,3) 20,3%-36,3%	24 (29,6) 22%-37,2%	ns
Dyslipidemia, n (%)	57 (57,6) 50%-65,2%	46 (56,8) 48,8%-64,8%	**ns**
Smoking, n (%)	34 (34,3) 27,3%-41,3%	17 (21) 14%-28%	**p<0,05**
Regular Alcohol intake, n (%)	21 (21,2) 13,5%-28,9%	14 (17,3) 10,1%-24,5%	Ns
Obesity (BMI ≥30 kg/m^2), n (%)	28 (28,3) 19,3%-37,3%	22 (27,2) 19,8%-34,6%	ns
Abdominal obesity, n (%)	61 (61,6) 53,9%-69,3%	46 (56,8) 49%-64,6%	ns
Overweight (BMI 25-29,99 kg/m2), n (%)	48 (48,5) 38,4%-58,6%	30 (37) 27%-47%	**p<0,05**
Regular Exercise, n (%)	43 (43,4) 35%-51,8%	38 (46,9) 39,1%-54,7%	ns

Abbreviations: FAMIG: First-Degree Relative of Patients with AMI; GC: Individuals without AMI First-Degree Relative; ns: non significant, BMI: Body Mass Index.

Table 2: Anthropometric characteristics of the studied populations.

	FAMIG (n=99)	GC (n=81)	p value
Body mass index (Kg/m^2)	28,1±5,2	29,1±4,8	ns
BP systolic (mm Hg)	130,8±17,0	128,4±14,8	ns
BP diastolic (mm Hg)	72,4±11,4	70,5±8,9	ns
Total cholesterol (mg/dL)	205,4±42,4	185,2±34,5	**p<0,05**
Triglycerides (mg/dL)	139,8±83,2	110,9±63,2	**p<0,05**
HDL cholesterol (mg/dL)	46,3±15,8	47,9±16,8	ns
LDL cholesterol (mg/dL)	129,9±36,1	108,6±29,3	**p<0,05**
Glucose (mg/dL)	114,7±35,9	122,7±40,4	ns
Creatinine clearance (mL/min)	83,7±25,8	84±26,9	ns

Data are presented as mean [SD] for normally distributed variables.
Abbreviations: FAMIG: First-Degree Relative of Patients with AMI; GC: Individuals without AMI First-Degree Relative; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; NS: Non Significant.

Table 3: Analysed biochemical parameters of subclinical damage.

	FAMIG (n=99)	GC (n=81)	p value
Myeloperoxidase (UI/L)	1,17±0,9	1,18±0,9	ns
Autoantibodies anti ox-LDL (UI/mL)	30,9±12,2	27±10,5	**p<0,05**
Interleukin 6 (pg/mL)	5,6±7,2	3,9±4,1	**p<0,05**
High-sensitivity CRP (mg/L)	1,99±1,7	1,8±1,6	ns
Fibrinogen (mg/dL)	375,3±99,1	390,5±97,9	ns
von Willebrand factor (UI/ml)	123,9±91,3	114,2±73,1	ns

Data are presented as mean ±SD for normally distributed variables.
Abbreviations: FAMIG: First-Degree Relative of Patients with AMI; GC: Individuals without AMI First-Degree Relative; Ox-LDL: Oxidized Low Density Lipoprotein; CRP: C Reactive Protein; NS: Non Significant.

Table 4: Cardiovascular Risk analysis through different schemes: Framingham, SCORE and REGICOR.

	FAMIG (n=99)	GC (n=81)	p value
Framingham, (%)	14,9±10,1	13,5±10,2	ns
SCORE, (%)	2,4±2,6	2,6±2,3	ns
REGICOR, (%)	6,1±4,1	5,1±3,8	ns

Data are presented as mean ± SD for normally distributed variables.
Abbreviations: FAMIG: First-Degree Relative of Patients with AMI; GC: Individuals without AMI First-Degree Relative; SCORE: Systematic Coronary Risk Evaluation; REGICOR: Registre Gironí Del Cor; NS: Non Significant.

absence of those risk factors, [17] most of clinical studies confirm they are still of major importance [18-21]. Among leading CVD risk factors and classical biomarkers in different parental groups (with and without first-degree blood relative AMI); it is important to notice that diabetes prevalence did not show remarkable differences. In fact, in the present study diabetes was higher than in other Spanish studies for the general population (10-12%) [19,22-24]and increases with the age [18,23]. According to the current literature, [17-25] the ERICE study revealed distinct risk factors prevalence depending on the geographic area distribution. Interestingly, the Mediterranean area counts of higher diabetes prevalence supported with raised glucose blood levels. Taking together diabetes becomes increasingly common with advancing age (>65 years old) [18] and in the current geographic area, which could explain these findings. The present study also has identified hypercholesterolemia as a possible factor of stronger risk. Accordingly, those frequency data were similar to other previous studies counting with 50-69% of dyslipidemia prevalence [27].

On the other hand, the present study provides additional evidence with respect to biochemical markers. High-sensitivity CRP and IL-6 have been traditionally considered as mediators of the inflammatory response with a similar behaviour in pathological conditions [28,29]. In this context, although not statistically significant hs-CRP was slightly increased in FAMIG, being those values lower when compared to values from published AMI patients [30,31]. The current data are in agreement with the absence of an acute inflammatory status and cohort of similar characteristics. Intriguingly, it should be mentioned that IL-6 values were significantly raised in individuals with a first-degree relative compared to the CG. Although the clinical importance of these changes is still unknown, an increase in IL-6 cytokine expression in FAMIG could reflect the switch to a pro-inflammatory condition, may play a role in the pathogenesis of CVD and potentially influencing worse outcomes. In fact, it is possible and indeed likely that proinflammatory cytokines may be useful markers for predicting vascular risk among apparently healthy individuals [32].

Clinical research has identified the common factors contributing to CVD resulting in the recommendation of risk schemes as FRAMINGHAM, SCORE and REGICOR. Those guidelines already considered the family history in the chance of developing CVD in the next 10 years (double the CVD risk percentage if any CVD present in a first degree relative before age 60). However, the above risk schemes did not found differences between FAMIG and CG, representing thus the absence of real CV risk or the presence of a hidden and silent risk. From our general population with no history of CVD, concentrations of IL-6 alone identified a group with first-degree relatives, whereas classic risk factors included in the traditional risk scores did not. These preliminary findings point out that new biomarkers might display an effective predictive value, not only when added to classic risk factors, but also alone. It is also important to notice that the antibodies anti-LDLox were significantly higher in the first degree relatives compared to the control group, which would undoubtedly support an increased risk of cardiovascular events in such group too.

LIMITATIONS

Our study is limited by the relatively small numbers of patients. A higher number of relatives and controls could have been stratified by age and/or gender with statistical potential. The study is descriptive in its nature and the pathophysiological nature of a worse lipid profile and an inflammatory pattern would need to be fully established. Notwithstanding interpretative limitations of plasma biomarkers, the present study has found associations between relatives and various inflammation and repair biomarkers as well as association with factor risks.

In summary, up to date biochemical markers are used as complementary information of the pathophysiological status added to the list of traditional risk factors. However, the current results account for the importance of using biomarkers in the primary prevention of CV events, alone or in combination with classic risk schemes.

CONCLUSIONS

In conclusion, we have observed that individuals with a first-degree relative AMI patient present a worse lipid profile and higher pro-inflammatory status compared to controls. Despite that, the classic risk schemes did not define a different CV risk for both groups. A long-term study of such individuals would further assess whether IL-6 is a reliable prevention marker either alone or in combination with other risk factors and biomarkers. Moreover, whether presenting a first-degree relative AMI contributes to the causal progression of the disease remains to be established with further future studies.

REFERENCES

1. Conthe P, Lobos JM. Definition and current situation of cardiometabolic risk. Rev Clin Esp. 2008; 208: 63-65.
2. Dégano IR, Elosua R, Kaski JC, Fernández-Bergés DJ, Grau M, Marrugat J. Plaque stability and the southern European paradox. Rev Esp Cardiol (Engl Ed). 2013; 66: 56-62.
3. Dégano IR, Elosua R, Marrugat J. Epidemiology of acute coronary syndromes in Spain: estimation of the number of cases and trends from 2005 to 2049. Rev Esp Cardiol (Engl Ed). 2013; 66: 472-481.
4. Jousilahti P, Puska P, Vartiainen E, Pekkanen J, Tuomilehto J. Parental history of premature coronary heart disease: an independent risk factor of myocardial infarction. J Clin Epidemiol. 1996; 49: 497-503.
5. Wang L, Fan C, Topol SE, Topol EJ, Wang Q. Mutation of MEF2A in an inherited disorder with features of coronary artery disease. Science. 2003; 302: 1578-1581.
6. Helgadottir A, Manolescu A, Thorleifsson G, Gretarsdottir S, Jonsdottir H, Thorsteinsdottir U, et al. The gene encoding 5-lipoxygenase activating protein confers risk of myocardial infarction and stroke. Nat Genet. 2004; 36: 233-239.
7. Wang X, Ria M, Kelmenson PM, Eriksson P, Higgins DC, Samnegård A, et al. Positional identification of TNFSF4, encoding OX40 ligand, as a gene that influences atherosclerosis susceptibility. Nat Genet. 2005; 37: 365-372.
8. Girelli D, Martinelli N, Peyvandi F, Olivieri O. Genetic architecture of coronary artery disease in the genome-wide era: implications for the emerging "golden dozen" loci. Semin Thromb Hemost. 2009; 35: 671-682.
9. Pamies Andreu E, Palmero Palmero C, García Lozano R, Stiefel García-Junco P, Miranda Guisado ML, Martín Sanz V, et al. [The effect of the angiotensinogen M235T and the angiotensin-converting enzyme I/D polymorphisms on arterial hypertension and other cardiovascular risk factors]. Med Clin (Barc). 1999; 113: 164-168.
10. Yoshikazu M, Uichi I, Hitoshi E, Yukihiro H, Yoshitane S, Hironori N, et al. Angiotensin Converting Enzyme Gene Polymorphism in Essential Hypertension Based on Ambulatory Blood Pressure Monitoring. Am J Hypert. 1997; 10:786-789.
11. Sentí M, Fernández-Fernández JM, Tomás M, Vázquez E, Elosua R, Marrugat J, et al. Protective effect of the KCNMB1 E65K genetic polymorphism against diastolic hypertension in aging women and its relevance to cardiovascular risk. Circ Res. 2005; 97: 1360-1365.
12. Berg, Sven."Snowball Sampling–I" Encyclopedia of Statistical Sciences, John Wiley and Sons, Inc. 2006; 7817-7821.
13. Tabla de riesgo cardiovascular del estudio Framingham, por categorías. Medifam. 2001; 11:122-39.
14. Marrugat J, Solanas P, D'Agostino R, Sullivan L, Ordovas J, Cordón F, Ramos R. [Coronary risk estimation in Spain using a calibrated Framingham function]. Rev Esp Cardiol. 2003; 56: 253-261.
15. Marrugat J, D'Agostino R, Sullivan L, Elosua R, Wilson P, Ordovas J, Solanas P. An adaptation of the Framingham coronary heart disease risk function to European Mediterranean areas. J Epidemiol Community Health. 2003; 57: 634-638.
16. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific tissues related to definition. Arterioscler Thromb Vasc Biol. 2004; 24:13-18.
17. Lobos JM, Royo-Bordonada MA, Brotons C, Alvarez-Sala L, Armario P, Maiques A, et al. [European Guidelines on Cardiovascular Disease Prevention in Clinical Practice. CEIPC 2008 Spanish adaptation]. Rev Clin Esp. 2009; 209: 279-302.
18. Canto JG, Iskandrian AE. Major risk factors for cardiovascular disease: debunking the "only 50%" myth. JAMA. 2003; 290: 947-949.
19. Gabriel R, Alonso M, Segura A, Tormo MJ, Artigao LM, Banegas JR et al. Prevalencia, distribución y variabilidad geográfica de los principales factores de riesgo cardiovascular en España. Análisis agrupado de datos individuales de estudios epidemiológicos poblacionales: estudio ERICE. Rev Esp Cardiol. 2008; 61:1030-1040.
20. Masia R, Pena A, Marrugat J, Sala J, Villa J, Pavesa M, et al. High prevalence of cardiovascular risk factors in Gerona, Spain, a province with low myocardial infarction incidence. REGICOR Investigations. J Epidemiol Community Health. 1998; 52:707-715.
21. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005; 352: 1685-1695.
22. Medrano MJ, Cerrato E, Boix R, Delgado-Rodríguez M. Cardiovascular risk factors in Spanish population: metaanalysis of cross-sectional studies. Med Clin (Barc). 2005; 124: 606-612.
23. Gil Montalbán E, Zorrilla Torras B, Ortiz Marrón H, Martínez Cortés M, Donoso Navarro E, Nogales Aguado P, et al. [Prevalence of diabetes mellitus and cardiovascular risk factors in the adult population of the autonomous region of Madrid (Spain): the PREDIMERC study]. Gac Sanit. 2010; 24: 233-240.
24. Bertomeu V, Castillo-Castillo Y. Situación de la enfermedad cardiovascular en España. Del riesgo a la enfermedad. Rev Esp Cardiol Supl. 2008; 8: 2E-9E.
25. Plan Integral de Cardiopatía Isquémica 2010-2012. MurciA: Ministerio de Sanidad y Consumo; 2010.
26. Alvarez Sabín J, Alonso de Leciñana M, Gállego J, Gil-Peralta A, Casado I, Castillo J, et al. [Plan for stroke healthcare delivery]. Neurologia. 2006; 21: 717-726.
27. Cordero A, Fácila L, Galve E, Mazón P. [Progress in hypertension and diabetes mellitus]. Rev Esp Cardiol. 2010; 63 Suppl 1: 101-115.
28. Smith PL, Lombardi G, Foster GR. Type I interferons and the innate immune response--more than just antiviral cytokines. Mol Immunol. 2005; 42: 869-877.

29. Falk E. Pathogenesis of atherosclerosis. J Am Coll Cardiol. 2006; 47: C7-12.

30. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med. 1997; 336: 973-979.

31. Thompson SG, Kienast J, Pyke SD, Haverkate F, Van de Loo JC. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. N Engl J Med. 1995; 332: 635-641.

32. Ridker PM, Rifai N, Stampfer MJ, Hennekens CH. Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. Circulation. 2000; 101: 1767-1772.

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