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ORIGINAL ARTICLE

High-density lipoprotein cholesterol, C-reactive protein, and prevalence and severity of coronary artery disease in 5641 consecutive patients undergoing coronary angiography

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ABSTRACT

Background Although high-density lipoprotein cholesterol (HDL-C) and C-reactive protein (CRP) are well-established predictors for future cardiovascular events, little information is available regarding their correlation with the prevalence and severity of angiographically evaluated coronary artery disease (CAD).

Material and methods Five thousand six hundred forty-one consecutive patients undergoing coronary angiography for the evaluation of CAD were analysed. Cardiovascular risk factors were assessed by routine blood chemistry and questionnaire. CAD severity was graded by visual estimation of lumen diameter stenosis with significant stenoses defined as lumen diameter reduction of ≥ 70%. Coronary angiograms were graded as one-, two- or three-vessel disease, as nonsignificant CAD (lumen irregularities < 70%) or non-CAD.

Results HDL-C (60·3 ± 18·5 vs. 51·9 ± 15·3 mg dL^{-1}; $P < 0·001$) was higher and CRP was lower (0·65 ± 1·68 vs. 1·02 ± 2·38 mg dL^{-1}; $P < 0·001$) in non-CAD ($n = 1517$) compared to overall CAD patients ($n = 4124$). CAD patients were older (65·2 ± 10·5 years vs. 59·9 ± 11·4 years), more often diabetics (19·2% vs. 10·6%) and hypertensives (79·2% vs. 66·0%) and included more smokers (18·8% vs. 16·5%) (all $P < 0·005$). Low-density lipoprotein cholesterol (124·5 ± 38·3 vs. 126·0 ± 36·3 mg dL^{-1}; P = NS) was similar in overall CAD and non-CAD patients with more statin users (43·4% vs. 27·9%; $P < 0·001$) among CAD patients. Comparing non-CAD with different CAD severities using analysis of variance, results did not change substantially. In a multivariate analysis, HDL-C and CRP remained independently associated with the prevalence of CAD. In addition, HDL-C is also a potent predictor for the severity of CAD.

Conclusions In this large consecutive patient cohort, HDL-C and CRP are independently associated with the prevalence of CAD. In this analysis, HDL-C is an even stronger predictor for CAD than some other major classical risk factors.

Keywords Angiography, coronary artery disease, C-reactive protein, high-density lipoprotein cholesterol, prevalence, severity.

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Introduction

Cardiovascular events will be the leading cause of death worldwide by the year 2020 [1]. Hence, the relation of risk factors with future events has been established [2,3]. Among those risk factors, high-density lipoprotein cholesterol (HDL-C) and C-reactive protein (CRP) were shown to independently predict future cardiovascular events [4,5]. Despite this clear association with the *incidence* of coronary artery disease (CAD), much less information is available regarding the relationship of HDL-C and CRP with the *prevalence* and *severity* of CAD [6]. As risk factors of the incidence are also commonly, but not necessarily, associated with the prevalence of disease, we aimed to assess the independent association of HDL-C and CRP with the angiographically evaluated presence and severity of CAD in a large cohort of consecutive, nonselected patients within a quality improvement initiative.

Materials and methods

The study was performed in accordance with the Declaration of Helsinki. Within a period of 28 months, data from 5641 consecutive patients referred for elective coronary angiography for the evaluation of CAD were collected. Data were assembled within a prospective quality improvement initiative including a cardiovascular risk factor screening database. All patients routinely gave written informed consent for the coronary angiography, which was performed according to standard Judkins technique [7]. Patients referred for acute, non-elective angiography (i.e. primary or rescue percutaneous coronary intervention for ST elevation acute coronary syndromes and patients with an early invasive strategy for non-ST elevation acute coronary syndromes), patients who will undergo organ transplantation (liver, kidney or lung) or valve repair/replacement, and those who underwent heart transplantation were excluded in this study.

Risk factor assessment

Cardiovascular risk factors were assessed by questionnaire and blood chemistry. Hypertension was defined as suggested by the Seventh Report of the Joint National Committee [8] and diabetes mellitus was defined according to the criteria of the American Diabetes Association [9]. Positive family history for premature CAD was present when a first-degree relative suffered a myocardial infarction before the age of 55 years (male) or 65 years (female) [10]. Smokers were defined as subjects who had smoked regularly within the previous 12 months [11]. Former smokers were those who stopped smoking more than 12 months ago. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), HDL-C and triglycerides were directly determined by enzymatical colour assay from Roche Diagnostics (HDL-C plus 2nd generation/LDL-C plus 2nd generation, Roche Diagnostics, Mannheim, Germany) as well as CRP by immunoturbidimetric assay (Tina-quant® CRPLX, Roche Diagnostics) within 36 h prior to angiography. As statins are known to influence CRP, LDL-C and HDL-C, we recorded prior statin use (> 4 weeks of therapy) in our patients.

Medical history

In addition, symptoms (typical angina pectoris according to the Canadian Cardiovascular Society, angina class [12], atypical or no chest pain); medical history, including recent (within 6 months) or prior (more than 6 months ago) myocardial infarctions, any revascularization (percutaneous coronary intervention or coronary artery bypass grafting) and prior valve repair/replacement; and therapeutic decisions (medical therapy, coronary artery bypass grafting, percutaneous coronary intervention, ad hoc undetermined and others) according to angiographic results were recorded.

Scoring of coronary angiograms

Significant CAD was defined as at least 70% lumen diameter reduction of major epicardial coronary arteries at visual estimation. Coronary angiograms were interpreted by an experienced interventional cardiologist as it is done in routine practice. Patients were classified as having one-vessel, two-vessel or multi-vessel disease, and as having nonsignificant CAD (defined as lumen irregularities < 70% lumen diameter reduction) or no CAD (no lumen irregularities).

Statistical analysis

According to Kolmogorov–Smirnov test, all continuous variables had normal distribution except CRP and triglycerides, for which a natural log transformation was applied to normalize the data for analysis. Results are expressed as mean ± standard deviation.

For univariate analysis, *t*-test and analysis of variance (ANOVA) with post-hoc Scheffé's test were used. Multivariate analysis, including variables significantly different at univariate tests as covariates, was performed with multinomial logistic regression analyses predicting the different levels of CAD. In addition, in multivariate analyses, Wald statistics were determined to give a measure for the individual impact of a given single risk factor. Both univariate and multivariate analyses were performed using SPSS for Windows, version 14·0.1 (SPSS Inc., Chicago, IL, USA).

Results

Overall CAD versus non-CAD patients

Of 5641 consecutive patients undergoing coronary angiography, 4124 (3019 men; 73·2%) had some angiographic evidence of CAD. Hence, the non-CAD group (no lumen irregularities) included 1517 patients (n = 753 men; 49·6%). Baseline characteristics of CAD versus non-CAD patients as well as of men versus women are presented in Table 1. The mean age of the study population is 63·9 ± 10·9 years; patients with any degree of CAD were significantly older and were more often men than patients without CAD ($P < 0·001$). HDL-C levels were lower (51·9 ± 15·3 vs. 60·3 ± 18·5 mg dL^{-1}; $P < 0·001$) and CRP levels were higher (1·02 ± 2·38 vs. 0·65 ± 1·68 mg dL^{-1}; $P < 0·001$) in overall CAD patients. In addition, diabetes, smoking and hypertension were more prevalent in overall CAD versus non-CAD patients. Levels of LDL-C were not significantly different between non-CAD and overall CAD patients, with more frequent statin users among the latter. As ongoing statin therapy may influence LDL-C, HDL-C and CRP, we compared patients without statin treatment (n = 3427) with patients on statin therapy (i.e. prior statin users > 4 weeks) (n = 2214). Prior statin users more often had CAD (80·8% vs. 68·1%, $P < 0·001$), and were more often diabetics (20·5% vs. 14·5%, $P < 0·001$) and hypertensives

Table 1 Baseline characteristics and risk factors in CAD versus non-CAD patients and in men versus women

	CAD patients	Non-CAD patients	*P*-value (CAD vs. non-CAD)	Men	Women	*P*-value (men vs. women)
n	4124	1517		3772	1869	
Age (years)	65·2 ± 10·5	59·8 ± 11·4	< 0·001	63·1 ± 10·9	65·2 ± 10·9	< 0·001
Male gender (%)	73·2	49·6	< 0·001			
Hypertension (%)	79·2	66·0	< 0·001	75·0	76·8	NS
Diabetes (%)	19·2	10·6	< 0·001	16·8	16·9	NS
Smokers (%)	18·8	16·5	< 0·05	20·4	13·6	< 0·001
Prior statin use (%)	43·4	27·9	< 0·001	40·9	36·0	< 0·001
Total cholesterol (mg dL^{-1})	191·6 ± 45·1	199·3 ± 45·3	< 0·001	189·7 ± 44·3	201·6 ± 46·1	< 0·001
LDL-C (mg dL^{-1})	124·5 ± 38·3	126·0 ± 36·3	NS	123·7 ± 37·2	127·4 ± 38·8	< 0·003
HDL-C (mg dL^{-1})	51·9 ± 15·3	60·3 ± 18·5	< 0·001	50·4 ± 14·3	61·9 ± 18·3	< 0·001
Triglycerides (mg dL^{-1})	157·7 ± 116·4	143·2 ± 153·1	< 0·001	162·2 ± 143·9	136·8 ± 81·9	< 0·001
CRP (mg dL^{-1})	1·02 ± 2·38	0·65 ± 1·68	< 0·001	0·97 ± 2·35	0·82 ± 1·92	< 0·02
Body mass index (kg m^{-2})	26·9 ± 4·0	26·8 ± 4·5	NS	27·2 ± 3·8	26·5 ± 4·7	< 0·001

CAD, coronary artery disease; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 2 Baseline characteristics and risk factors according to angiographic results

	Non-CAD	Nonsignificant CAD	1-VD	2-VD	3-VD
n	1517	920	1336	924	944
Age (years)	59·9 ± 11·44	66·1 ± 9·7*	63·2 ± 11·1*§¶	65·1 ± 10·1*†	67·4 ± 10·1*†¶
Male gender	49·6	62·0*	72·2*§¶	78·7*§	80·3*§†
Hypertension (%)	66·0	86·5*	82·1*	85·4*	89·5*†
Diabetes (%)	10·6	18·6*	16·4*	19·0*	27·2*§†¶
Smokers (%)	16·5	22·0	25·0*	22·7	19·7
Prior statin use (%)	27·9	40·0*	41·4*	44·6*	48·4*§†
Total cholesterol (mg dL^{-1})	199·3 ± 45·3	195·9 ± 44·0	191·1 ± 43·9*	192·2 ± 46·5*	187·0 ± 46·0*§
LDL-C (mg dL^{-1})	126·0 ± 36·3	126·4 ± 36·7	124·7 ± 36·6	124·6 ± 39·4	122·2 ± 38·5
HDL-C (mg dL^{-1})	60·3 ± 18·5	55·5 ± 17·2*	52·3 ± 15·3*§	50·4 ± 14·0*§	49·4 ± 13·6*§†
Triglycerides (mg dL^{-1})	143·2 ± 153·1	158·9 ± 128·2*	151·7 ± 98·2	167·3 ± 141·7*	155·7 ± 98·8
CRP (mg dL^{-1})	0·65 ± 1·68	0·76 ± 1·76	1·04 ± 2·63*§	1·15 ± 2·68*§	1·12 ± 2·20*§
Body mass index (kg m^{-2})	26·8 ± 4·5	27·0 ± 4·2	26·9 ± 4·1	26·9 ± 3·9	27·0 ± 3·8

*P < 0·001 vs. non-CAD. §P < 0·01 vs. nonsignificant CAD. †P < 0·001 vs. 1-VD. ¶P < 0·001 vs. 2-VD.
CAD, coronary artery disease; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VD, vessel disease.

(84·7% vs. 69·8%, P < 0·001). In addition, LDL-C (118·9 ± 38·7 vs. 128·8 ± 36·7 mg dL^{-1}; P < 0·001) and HDL-C (53·6 ± 15·9 vs. 54·6 ± 17·0 mg dL^{-1}; P < 0·001) were lower in patients on prior statin therapy. Body mass index (27·2 ± 4·0 vs. 26·8 ± 4·2 kg m^{-2}; P < 0·001) and triglycerides (162·4 ± 137·9 vs. 148·2 ± 119·7 mg dL^{-1}; P < 0·001) were higher in prior statin users, whereas CRP (0·87 ± 2·0 vs. 0·97 ± 2·3 mg dL^{-1}) and incidence of smoking (17·8% vs. 18·4%) were not different.

Different severity of CAD according to angiographic results

Furthermore, patients were grouped based on angiographic results into those with non-CAD (n = 1517; 26·9%), those with nonsignificant CAD (n = 920; 16·3%), and those with one-vessel disease (n = 1336; 23·7%), two-vessel disease (n = 924; 16·4%) or three-vessel disease (n = 944; 16·7%). Characteristics and cardiovascular risk factors for each group are shown in Table 2.

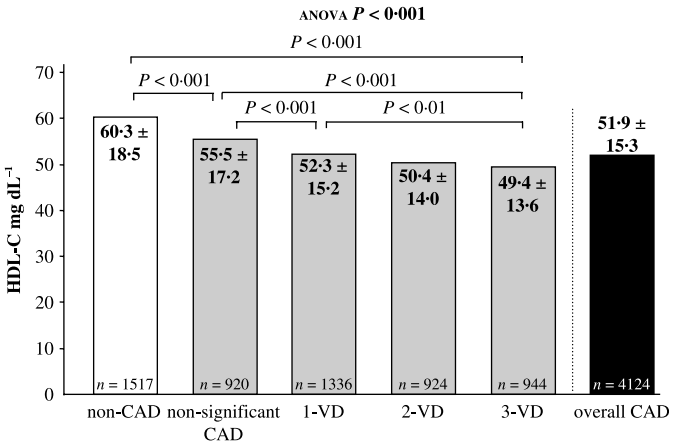

Figure 1 Bar graphs of high-density lipoprotein cholesterol (HDL-C) levels (mg dL^{-1}) in non-coronary artery disease (CAD) patients (white), overall CAD patients (black) and in CAD patient groups (grey) with different severity scores according to angiographic results. VD, vessel disease.

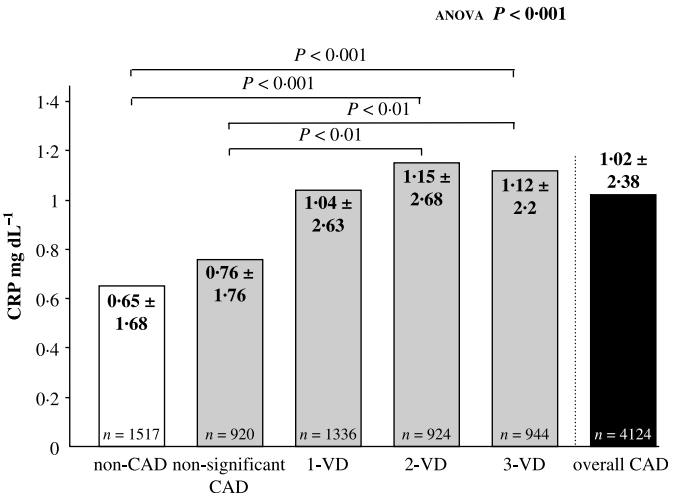

Figure 2 Bar graphs of C-reactive protein (CRP) levels (mg dL^{-1}) in non-coronary artery disease (CAD) patients (white), overall CAD patients (black) and in CAD patient groups (grey) with different severity scores according to angiographic results. VD, vessel disease.

Generally, with increasing severity of CAD, each traditional risk factor except body mass index increased in prevalence or severity. LDL-C remained similar in all groups, with more prior statin users in more advanced CAD. ANOVA with post-hoc analyses revealed that HDL-C and CRP were significantly different between groups (Figs 1 and 2).

Multivariate analyses

As HDL-C decreased and CRP increased with an increasing number of risk factors ($P < 0{\cdot}001$; Fig. 3a,b), the independent association of both variables with the prevalence and severity of CAD was determined in multinomial logistic regression analyses adjusted for variables significantly different at univariate statistics. Concerning the prevalence of disease (overall CAD versus non-CAD patients), all of the variables significant at univariate analyses retained their association in the multivariate model (Table 3), except triglyceride levels. As HDL-C and CRP levels are different in men and women, we additionally performed multivariate analysis according to gender (Table 3). In men, overall results did not change substantially. In women, HDL-C remained significantly associated with the prevalence of CAD, whereas CRP and total cholesterol lost their significant association with the prevalence of angiographic disease.

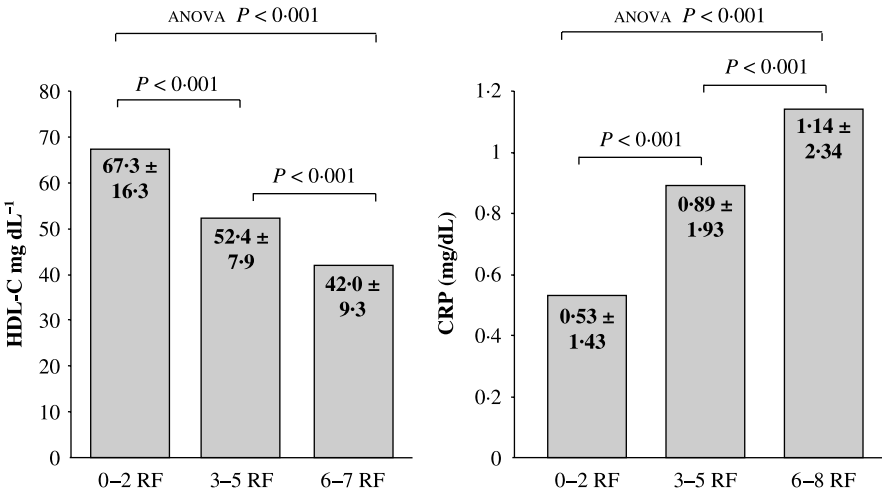

Figure 3 High-density lipoprotein cholesterol (HDL-C) levels (a) and C-reactive protein (CRP) levels (b) in relation to the number of risk factors (RF).

Table 3 Multivariate analyses evaluating the associations of baseline characteristics and risk factors with the presence of CAD (nonsignificant CAD, 1-VD, 2-VD and 3-VD patients together) in overall patients, in men and in women

	CAD vs. non-CAD			
Overall patients	**OR**	**95% CI**	***P*-value**	**Wald statistics**
Age (per year)	1·058	(1·051–1·066)	< 0·001	247·7
Male gender	2·753	(2·371–3·197)	< 0·001	175·9
HDL cholesterol (per mg dL^{-1})	0·976	(0·971–0·982)	< 0·001	77·3
Prior statin use	1·751	(1·511–2·029)	< 0·001	55·3
Smokers	1·720	(1·396–2·118)	< 0·001	25·9
Hypertension	1·494	(1·244–1·793)	< 0·001	18·5
Diabetes	1·539	(1·250–1·894)	< 0·001	16·5
CRP (per log unit)	1·343	(1·158–1·558)	< 0·001	15·1
Total cholesterol (per mg dL^{-1})	1·003	(1·001–1·005)	< 0·02	9·2
Triglycerides (per log unit)	0·917	(0·621–1·355)	NS	0·2
Men				
Age (per year)	1·058	(1·048–1·067)	< 0·001	150·3
HDL-C (per mg dL^{-1})	0·974	(0·967–0·981)	< 0·001	48·1
Prior statin use	1·919	(1·576–2·337)	< 0·001	42·2
Smokers	1·520	(1·170–1·975)	< 0·002	9·8
Hypertension	1·359	(1·077–1·715)	< 0·01	6·7
Diabetes	1·448	(1·097–1·911)	< 0·01	6·8
CRP (per log unit)	1·444	(1·192–1·749)	< 0·001	14·1
Total cholesterol (per mg dL^{-1})	1·004	(1·002–1·007)	< 0·003	10·1
Triglycerides (per log unit)	0·853	(0·523–1·392)	NS	0·4
Women				
Age (per year)	1·061	(1·049–1·074)	< 0·001	99·3
HDL-C (per mg dL^{-1})	0·978	(0·971–0·986)	< 0·001	29·5
Prior statin use	1·565	(1·249–1·962)	< 0·001	15·1
Smokers	2·045	(1·437–2·910)	< 0·001	15·8
Hypertension	1·722	(1·271–2·333)	< 0·001	12·3
Diabetes	1·665	(1·217–2·276)	< 0·001	10·2
CRP (per log unit)	1·193	(0·939–1·516)	NS	2·1
Total cholesterol (per mg dL^{-1})	1·002	(0·999–1·004)	NS	1.1
Triglycerides (per log unit)	1·001	(0·516–1·942)	NS	0

CAD, coronary artery disease; CI, confidence interval; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; OR, odds ratio; VD, vessel disease.

In regard to the angiographic severity scoring, HDL-C commonly remained independently associated with the severity of CAD in overall patients, and CRP lost its independent relation (Table 4). Again, gender-specific multinomial regression analyses revealed similar results for men, whereas in women HDL-C was only independently associated with three-vessel disease when comparing the latter with nonsignificant CAD or one-vessel disease (Table 4).

In addition, the Wald statistics at multivariate analyses revealed that HDL-C, compared to other cardiovascular risk factors including CRP, functions as a potent predictor of both prevalence and severity of CAD (Table 3).

Discussion

Our study shows an independent association of HDL-C and CRP with the prevalence of CAD. In addition, HDL-C but not

Table 4 Multivariate analyses evaluating the association of HDL-C and CRP with different severity scores of angiographic results in overall patients, in men and in women

		Overall		Men		Women	
		HDL- C (per mg dL^{-1})	CRP (per log unit)	HDL-C (per mg dL^{-1})	CRP (per log unit)	HDL-C (per mg dL^{-1})	CRP (per log unit)
Nonsignificant CAD vs. 1-VD	OR	0·99	1·14	0·98	1·12	1·00	1·20
	95% CI	(0·98–0·99)	(0·95–1·38)	(0·97–0·99)	(0·89–1·41)	(0·99–1·01)	(0·85–1·68)
	P-value	< 0·03	NS	0·003	NS	NS	NS
Nonsignificant CAD vs. 2-VD	OR	0·99	1·23	0·98	1·18	0·98	1·44
	95% CI	(0·98–0·99)	(1·01–1·51)	(0·97–0·99)	(0·99–1·49)	(0·97–1·00)	(0·97–2·15)
	P-value	< 0·001	< 0·04	0·003	NS	NS	NS
Nonsignificant CAD vs. 3-VD	OR	0·98	1·18	0·97	1·17	0·98	0·93
	95% CI	(0·97–0·99)	(0·96–1·44)	(0·96–0·98)	(0·92–1·48)	(0·96–0·99)	(0·61–1·43)
	P-value	< 0·001	NS	< 0·001	NS	< 0·003	NS
1-VD vs. 2-VD	OR	0·99	1·06	1·00	1·05	0·99	1·21
	95% CI	(0·99–1·00)	(0·89–1·27)	(0·99–1·01)	(0·86–1·29)	(0·97–1·00)	(0·82–1·77)
	P-value	NS	NS	NS	NS	NS	NS
1-VD vs. 3-VD	OR	0·99	1·00	0·99	1·04	0·97	0·78
	95% CI	(0·98–0·99)	(0·83–1·19)	(0·98–0·99)	(0·85–1·28)	(0·96–0·99)	(0·51–1·18)
	P-value	< 0·001	NS	< 0·03	NS	< 0·02	NS
2-VD vs. 3-VD	OR	0·99	0·92	0·99	0·99	0·99	0·65
	95% CI	(0·98–0·99)	(0·77–1·11)	(1·98–1·00)	(0·80–1·22)	(0·97–1·01)	(0·41–1·02)
	P-value	< 0·03	NS	NS	NS	NS	NS

CAD, coronary artery disease; CI, confidence interval; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; NS, not significant; OR, odds ratio; VD, vessel disease.

CRP levels generally correlate with the severity of CAD. Despite a large body of evidence for the prognostic value of HDL-C [4,13–21] and CRP [22] for future cardiovascular events, to our knowledge this is the largest study investigating their independent association with the prevalence and severity of *angiographically* evaluated CAD.

HDL-C

It is well known that higher HDL-C levels protect from future cardiovascular events [23–25] and its therapeutic elevation is associated with plaque regression on intravascular ultrasound studies [26]. Data are less conclusive concerning its interrelationship with CAD prevalence or even severity, with some studies reporting a significant association [27–35] and others not [36–38]. Altogether, the number of patients with angiographic evaluation of CAD in these reports was much lower than in our study. In addition, most of these reports are 10–30 years old and, therefore, cannot account for well-known secular trends in cardiovascular risk factors [39].

The strength of our study is the large number of consecutive, nonselected patients undergoing angiographic evaluation of suspected CAD. In a similar-sized investigation, Wilson *et al*. did not find a significant correlation of HDL-C with CAD prevalence on a multivariate analysis in 2608 patients, which might be due to methodological differences. In contrast to our study, CAD was not defined by angiography but by clinical criteria. Hence, the number of CAD patients included was rather small (n = 54), which were compared with a rather large number of patients without CAD (n = 2554). On the other hand, studies defining CAD by angiographic results reported significant inverse correlations of HDL-C with CAD presence (and severity) [27,29,30,38,40–42]. However, these studies commonly included approximately 100 [29] to 500 [40] selected patients, whereas our sample size is at least 10 times more and includes consecutive, nonselected patients. In our opinion, the present data therefore may more closely reflect the situation in daily clinical practice. Furthermore, as most former studies primarily focused on lipid subfractions, we tried to include all classic risk factors and CRP as newer cardiovascular risk factors in our multivariate model. Given the still highly significant association of HDL-C on multinomial regression analyses especially in men, our data emphasize the importance of HDL-C as a risk factor for both the prevalence and severity of CAD beyond its well-known prognostic function for the incidence of events. However, its use in individual patients for the evaluation of CAD presence and/or severity might be limited by the broad standard deviation. A further limitation of its daily clinical use include gender-specific differences of reference intervals [43], which additionally complicate its routine application in the evaluation of CAD presence and/or severity particularly in women. Finally, results on HDL-C might have been influenced by triglyceride levels, which were increased in CAD patients at univariate tests. However, we tried to control for this possible confounding factor by including triglyceride levels in the multivariate analyses.

CRP

Inflammation is an inherent process of atherosclerosis [44]. Among a myriad of circulating parameters, CRP has been extensively studied and is associated with unstable CAD and acute coronary syndromes. Furthermore, its predictive role for future cardiovascular events (incidence) is widely accepted [22]. Hence, CRP has become a therapeutic target within the risk factor management. Beside its correlation with the incidence, much less information is available concerning its association with the prevalence of CAD [45–52].

Among those studies, the largest (Intermountain study) [46] found a strong univariate association of CRP with the prevalence of angiographically assessed CAD in 2554 patients. We confirmed this observation in an even larger patient cohort and included a multivariate analysis. The latter approved the association of CRP with the prevalence but not with the severity of CAD independently of established cardiovascular risk factors (smoking, hyperlipidaemia, hypertension, family history of premature CAD, diabetes, age, gender). Interestingly, although different assays were used (fluorescence polarization versus immunoturbidimetric assay), CRP levels were comparable in CAD patients in both investigations. In gender-specific multinomial regression analyses, the independent association of CRP with CAD prevalence was only present in men, but not in women (Table 3). This might be due to the overall lower number of women in our study, the higher prevalence of non-CAD among women or an influence of hormonal status [53], which was not recorded in our database.

The lack of multivariate correlation of CRP with CAD severity as demonstrated in our study is in accordance with a recent report by Sukhija *et al*. in 249 patients [48]. The discrepancy between univariate and multivariate analysis in our study and the work from Sukhija *et al*. is probably related to fact that conventional risk factors correlate with CRP levels. Hence, CRP loses its independent association with the severity of CAD when these are included in the analyses. Nevertheless, beside its role as predictive marker for incident events, CRP might be useful as a 'rule out' tool when evaluating CAD prevalence with the limitation of its broad standard deviation.

Study limitations

Certain limitations in the present study are worth mentioning. Quantification of coronary angiographic findings is limited to the visual interpretation of the attending cardiologist. Three vessel intravascular ultrasound would reveal better information about the atherosclerotic burden, but is impossible to be applied routinely in consecutive patients. Therefore, some of the patients without angiographic evidence of CAD have

atherosclerotic plaques within the vessel wall. This may cause higher levels of CRP in our non-CAD patients in comparison to 'real' non-CAD patients, which we believe would not substantially change results. Despite these shortcomings of coronary angiography as a 'lumenography', it is still the method of choice in everyday practice driving clinical decisions.

Measuring HDL-C and CRP only once may have also influenced results, despite their known stability over time. On the other hand, especially for CRP, patients with known and clinically relevant infections are not referred for elective coronary angiography. Thus, our study should reflect the real world in our opinion.

Conclusions

Our study shows an independent association of HDL-C and CRP with the prevalence of CAD. In addition, HDL-C but not CRP levels generally correlate with the severity of CAD. Therefore, we suggest HDL-C and CRP, with its limitation of a broad standard deviation, as predictive risk factors for future cardiovascular events but also consider them when evaluating the prevalence of CAD before invasive diagnosis takes place. In addition, HDL-C may probably help in identifying the severity of CAD.

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