ARTICLE

Pathobiological Determinants of Atherosclerosis in Youth Risk Scores Are Associated With Early and Advanced Atherosclerosis

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ABSTRACT

OBJECTIVES. Atherosclerosis begins in childhood and progresses during adolescence and young adulthood. The Pathobiological Determinants of Atherosclerosis in Youth Study previously reported risk scores to estimate the probability of advanced atherosclerotic lesions in young individuals aged 15 to 34 years using the coronary heart disease risk factors (gender, age, serum lipoprotein concentrations, smoking, hypertension, obesity, and hyperglycemia). In this study we investigated the relation of these risk scores to the early atherosclerotic lesions.

METHODS. We measured atherosclerotic lesions in the left anterior descending coronary artery, right coronary artery, and abdominal aorta and the coronary heart disease risk factors in persons 15 to 34 years of age who died as a result of external causes and were autopsied in forensic laboratories.

RESULTS. Risk scores computed from the modifiable risk factors were associated with prevalence of microscopically demonstrable lesions of atherosclerosis (American Heart Association grade 1) in the left anterior descending coronary artery and with the extent of the earliest detectable gross lesion (fatty streaks) in the right coronary artery and abdominal aorta. Risk scores computed from the modifiable risk factors also were associated with prevalence of lesions of higher degrees of microscopic severity (intermediate as well as advanced) in the left anterior descending coronary artery and with extent of lesions of higher degrees of severity (intermediate and raised lesions) in the right coronary artery and abdominal aorta.

CONCLUSIONS. Risk scores calculated from traditional coronary heart disease risk factors to identify individual young persons with high probability of having advanced atherosclerotic lesions also are associated with earlier atherosclerotic lesions, including the earliest anatomically demonstrable atherosclerotic lesion. These results support lifestyle modification in youth to prevent development of the initial lesions and the subsequent progression to advanced lesions and, thereafter, to prevent or delay coronary heart disease.

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Key Words
prevention, atherosclerosis, risk factors, coronary heart disease, aorta, adolescence, youth

Abbreviations
CHD— coronary heart disease
AHA—American Heart Association
PDAY—Pathobiological Determinants of Atherosclerosis in Youth
LAD—left anterior descending coronary artery
RCA—right coronary artery
AA—abdominal aorta
HDL— high-density lipoprotein
OR— odds ratio
CI— confidence interval

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ATHEROSCLEROSIS BEGINS IN childhood and progresses during adolescence and young adulthood[1] to result in lesions that cause clinically manifest coronary heart disease (CHD) in middle-aged and older individuals.[2,3] The present consensus regarding the pathogenesis of atherosclerosis, expressed in reports of the American Heart Association (AHA) Committee on Vascular Lesions, is that a seamless process begins with intimal lipid accumulation and culminates in ruptured and thrombosed fibrous plaques.[4,5] The Bogalusa Heart Study and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study showed that the CHD risk factors (gender, age, serum lipoprotein concentrations, smoking, hypertension, obesity, and hyperglycemia) were associated with both the early and advanced lesions of atherosclerosis in adolescence and young adulthood, decades before the occurrence of CHD.[6–14]

The PDAY Study also developed risk scores, which provided weighted summaries of the effects of the individual risk factors, to predict the presence of advanced lesions in the coronary arteries and abdominal aortas of adolescents and young adults.[15] These risk scores had discrimination similar to that obtained for prediction of CHD events in the Framingham study.[16] Although these and similar results[17–19] were based on observational data and have not been verified by controlled clinical trials, they provided strong justification for efforts to control CHD risk factors in youth.[20]

But how early in youth is risk-factor control useful? Intervention to control risk factors potentially will have more benefit on the progression of atherosclerosis if begun in time to affect the earlier and more readily reversible lesions. Here we show that the PDAY risk scores based on only the modifiable risk factors (ie, not including age and gender) are associated with early and intermediate lesions of atherosclerosis as well as advanced lesions in the PDAY sample.

METHODS

Study Design and Subjects

Fifteen cooperating centers followed standardized procedures to collect specimens and data and to submit them to central laboratories. The subjects and methods are described in previous publications[1,8–10] and are summarized briefly here.

Study subjects were persons 15 through 34 years of age who died of external causes (accidents, homicides, or suicides) within 72 hours after injury and were autopsied within 48 hours after death in a cooperating forensic laboratory. Approximately 25% of subjects were women, and ~54% of subjects were black. The institutional review board of each participating center approved this study.

Arteries and Lesions

PDAY investigators prepared microscopic sections of a standard site in the left anterior descending coronary artery (LAD) known to be highly susceptible to advanced atherosclerosis.[12] Two pathologists evaluated LAD sections according to the AHA grading system.[5] Grade 0 designated a normal artery with no intimal lipid and with or without adaptive intimal thickening. Grade 1 lesions contained isolated macrophage foam cells, and grade 2 lesions contained numerous macrophage foam cells and fine particles of extracellular lipid but no pools of extracellular lipid; grade 1 and 2 lesions corresponded with gross fatty streaks. Grade 3 lesions contained numerous macrophage foam cells and $\geq$1 pool of extracellular lipid but no well-defined core of lipid and represented the intermediate or transitional lesion. Grade 4 lesions contained numerous macrophage foam cells plus a well-defined core of extracellular lipid covered by normal intima. Grade 5 lesions showed $\geq$1 core of extracellular lipid plus a fibrous cap, vascularization, or calcification. Grade 4 and 5 lesions corresponded with gross raised lesions and are susceptible to rupture and thrombosis.[5] Grade 6 lesions were not encountered in the PDAY sample. A diagram and photomicrographs of the lesion grades are given by Stary et al.[5] It is assumed that lesions of a given severity have passed through all of the lower levels of the lesion at an earlier age. AHA grades in the LAD and all of the risk factors were available for 1127 cases.

PDAY investigators also prepared gross specimens of the right coronary artery (RCA) and the abdominal aorta (AA).[9] Three pathologists blindly and independently estimated the extent of fatty streaks and raised lesions (fibrous plaques and complicated plaques) in the RCA and the AA. The average of the 3 independent grades was the consensus grade of fatty streaks and raised lesions. Assessment of atherosclerotic lesions and all of the risks factor measurements were available for 1427 RCAs and 1458 AAs.

Four graders, different from the foregoing 3 pathologists, independently estimated the fraction of fatty streaks that were classified as raised fatty streaks, also known as intermediate lesions, in each RCA and in each AA with the consensus (3 pathologists) extent of fatty streaks >2%.[21] If the consensus extent of fatty streaks was $\leq$2%, the 4 graders independently scored the specimen as negative or positive for the presence of intermediate lesions. These intermediate lesions are interpreted as lesions in transition between fatty streaks and fibrous plaques.

Risk-Factor Measurements

The methods for measuring the risk factors are described in previous publications.[8–10] Briefly, we measured total serum cholesterol and high-density lipoprotein (HDL) cholesterol (after precipitation of other lipoproteins) by a

cholesterol oxidase method and calculated non-HDL cholesterol by subtraction. We constructed categories of non-HDL cholesterol by adding 30 mg/dL (0.78 mmol/L)[22] to the cut points for low-density lipoprotein cholesterol recommended by the National Cholesterol Education Program[23] and used the HDL cholesterol categories as recommended by the same group. A serum thiocyanate level ≥90 μmol/L defined a smoker. Hypertension was identified when the intimal thickness of small renal arteries indicated a mean blood pressure ≥110 mm Hg.[10] BMI >30 kg/m² indicated obesity, and red blood cell glycohemoglobin ≥8% indicated hyperglycemia.[24]

PDAY Risk Scores

The PDAY risk scores[15] were developed originally to estimate the probability of advanced atherosclerotic lesions. We defined advanced lesions as present in the coronary arteries if there was an AHA grade 4 or 5 lesion in the LAD or if raised lesions covered ≥9% of the intimal surface of the RCA. We defined advanced lesions as present in the AA if raised lesions covered ≥15% of the intimal surface.

The risk scores are calculated by adding the points for each risk factor given in Table 1. These points are then related to the probability of advanced lesions using the graphs given by McMahan et al.[15] Coefficients for the risk factors were normalized so that each increase of 1 unit in the risk score was equivalent to the multiplicative change in the odds (additive change in the logarithm of the odds) because of a 1-year increase in age.

Statistical Analysis

To examine the association of AHA grade and risk score using the ordered nature of the AHA grade,[25] the AHA grades were partitioned over a series of incremental cut points with the level of lesions for categorization as lesion positive rather than lesion negative becoming increasingly severe. These dichotomizations form the cumulative odds model. We report odds ratios (ORs) appropriate for each cut point. The association of AHA grade and risk score computed from the modifiable risk factors with adjustment for gender and age was analyzed using multivariable logistic regression analysis for the cumulative odds model.[25,26]

The extent of intermediate lesions in cases for which the consensus grade of fatty streaks was >0 and ≤2% and the consensus of the 4 graders was that intermediate lesions were present were regarded as censored observations.[21] The mean extent of intermediate lesions, after transformation with a logit transformation, was assumed to be a linear function of the predictor variables. The likelihood function was constructed for a combination of censored and uncensored observations.[27] Estimates of the parameters were obtained using the method of maximum likelihood. The extent of intermediate lesions in censored observations was estimated and the combined extent of intermediate lesions and raised lesions calculated.

We classified the gross lesions into 3 categories of increasing severity: all lesions, intermediate and raised lesions, and raised lesions. The relation of extent of lesions (percentage of intimal surface involved) and risk score computed from only the modifiable risks factors with adjustment for age and gender was analyzed by multiple regression analysis.[28] A logit transformation, with a small constant added to avoid the logarithm of 0, was applied to the percentage of surface area involved. Ratios of involvement between 2 risk score categories were estimated using Fieller's theorem.[29]

TABLE 1 PDAY Risk Scores for Predicting Advanced Atherosclerotic Lesions

Risk Factor	Risk Score	
	Coronary Arteries	AA
Immutable risk factors		
Age, y		
15–19[a]	0	0
20–24	5	5
25–29	10	10
30–34	15	15
Gender		
Male[a]	0	0
Female	−1	1
Modifiable risk factors		
Non-HDL cholesterol, mg/dL[b]		
<130[a]	0	0
130–159	2	1
160–189	4	2
190–219	6	3
≥220	8	4
HDL cholesterol, mg/dL[b]		
< 40	1	0
40–59[a]	0	0
≥60	−1	0
Smoking		
Nonsmoker[a]	0	0
Smoker	1	4
Blood pressure		
Normotensive[a]	0	0
Hypertensive	4	3
Obesity (BMI), kg/m²		
Men		
≤30[a]	0	0
>30	6	0
Women		
≤30	0	0
>30	0	0
Hyperglycemia (glycohemoglobin), %		
<8[a,b]	0	0
≥8	5	3

[a] Reference category.

[b] To convert mg/dL to mmol/L, multiply values for non-HDL and HDL cholesterol by 0.0259.

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RESULTS

LAD Lesions

Figure 1 shows the prevalence of atherosclerosis at varying levels of microscopic severity by the PDAY coronary artery risk score computed from the modifiable risk factors, gender, and 10-year age group. Severity was defined by a series of incremental cut points with increasing AHA grade, which dichotomized PDAY cases into lesion-positive and lesion-negative classifications. The bottom line shows the prevalence of only grade 5 lesions, and each superior line adds an additional grade so that the top line includes all of the lesions (grades 1–5). With few exceptions, the prevalence increased with increasing risk score. Because the numbers of women with risk score ≥11 was small (2 for 15–24 years and 5 for 25–34 years), we combined the ≥11 category with the 6 to 10 category in women. Not only is the prevalence of high-risk scores lower in women than in men, but Fig 1 shows the well-known lag in lesion development in women compared with men.[1] Although the prevalence of intermediate (grade 3) and advanced lesions (grades 4 and 5) was low for risk scores 6 to 10 and ≥11 in persons 15 to 24 years of age, the prevalence of earlier lesions (grades 1 and 2) was substantial.

Table 2 provides ORs for LAD lesions by risk score computed from the modifiable risk factors, adjusted for gender and age, separately for each lesion dichotomization. All of the ORs for risk scores computed from the modifiable risk factors were >1. ORs for risk scores computed from the modifiable risk factors of 6 to 10 were statistically significant (95% confidence interval [CI] does not include 1.00) for grades 1 through 5 versus grade 0 and grades 2 through 5 versus grades 0 and 1. ORs for risk scores computed from the modifiable risk factors of ≥11 were statistically significant except for grade 5 versus grades 0 through 4. This OR for grade 5 versus grades 0 through 4 was substantial but was not statistically significant, because the prevalence of the grade 5 lesions was low (Fig 1).

Regardless of the cut point used to dichotomize the AHA grades, the odds of being in the worse category increased with increasing risk score (ie, the risk score was associated with prevalence of all degrees of severity of lesions). Because a grade 2, 3, 4, or 5 lesion had passed through the grade 1 lesion stage at a younger age, this finding includes the association of the risk score with accelerated transition from grade 0 (normal tissue) to the grade 1 lesion.

RCA Lesions

Figure 2 shows the percentage of intimal surface area involved with gross lesions in the RCA by the PDAY coronary artery risk score computed from the modifiable risk factors, gender, and 10-year age group. The bottom line shows the involvement with raised lesions, the middle line shows the involvement with intermediate lesions and raised lesions, and the top line shows involvement with all of the lesions. Table 3 gives the ratios of surface area involved with lesions in the RCA by risk score categories computed from only the modifiable risk factors to the surface area involved with lesions in individuals having low (≤0) risk because of the absence of modifiable risk factors. The ratios for risk scores 6 to 10 and ≥11 were significant for total lesions, intermediate plus raised lesions, and raised lesions. The ratios for risk score 1 to 5 were >1, but only the ratio for intermediate plus raised lesions was statistically significant. These results indicate that the risk score computed from the modifiable risk factors was associated with the extent of lesions of all degrees of severity in the RCA and with accelerated transition from normal tissue to fatty streaks.

AA Lesions

Figure 3 shows the percentage of intimal surface area involved with gross lesions in the AA by the PDAY AA risk

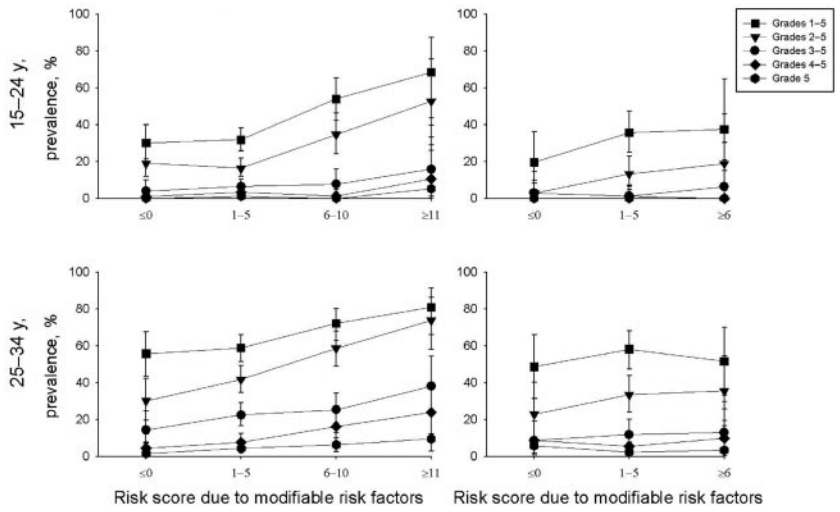

FIGURE 1
Prevalence of AHA lesion grades by category of PDAY coronary artery risk score computed from the modifiable risk factors for men (left) and women (right) and 10-year age group. ■, any lesion (ie, initial fatty streaks and more severe lesions [AHA grades 1–5]); ▼, advanced fatty streaks and more severe lesions (AHA grades 2–5); ●, intermediate (transitional) lesions and more severe lesions (AHA grades 3–5); ◆, initial fibrous plaques and more severe lesions (AHA grades 4–5); ⬣, advanced fibrous plaques (AHA grade 5). Bars, 95% CIs.

TABLE 2 **ORs for LAD Lesions According to Risk Score Computed From Modifiable Risk Factors, Adjusted for Gender and Age**

Lesion Comparison	Risk Score Computed From Modifiable Risk Factors			
	−1 to 0 (n = 241), OR	1 to 5 (n = 589), OR (95% CI)	6 to 10 (n = 232), OR (95% CI)	≥11 (n = 65), OR (95% CI)
AHA grades 1–5 vs 0	1[a]	1.26 (0.91–1.73)	2.12 (1.44–3.12)[b]	3.77 (1.98–7.20)[b]
AHA grades 2–5 vs 0 and 1	1[a]	1.37 (0.94–1.99)	2.62 (1.72–4.00)[b]	5.65 (3.01–10.60)[b]
AHA grades 3–5 vs 0–2	1[a]	1.56 (0.89–2.73)	1.77 (0.96–3.28)	3.79 (1.81–7.97)[b]
AHA grades 4 and 5 vs 0–3	1[a]	1.35 (0.60–3.03)	2.28 (0.97–5.35)	4.98 (1.89–13.09)[b]
AHA grade 5 vs 0–4	1[a]	1.64 (0.46–5.86)	2.08 (0.54–8.09)	3.94 (0.88–17.60)

[a] Reference.
[b] Significantly ($P \leq .05$) different from 1.00.

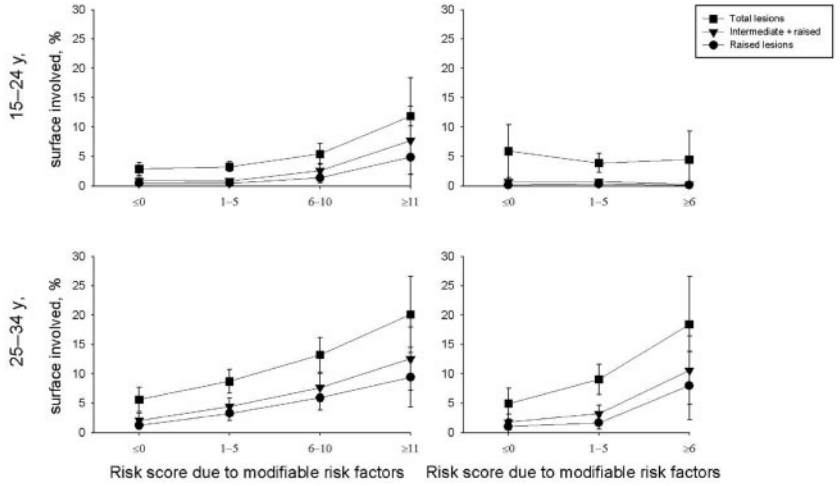

FIGURE 2
Extent of lesions in the RCA by PDAY coronary artery risk score computed from the modifiable risk factors for men (left) and women (right) and 10-year age group. ■, any lesion (ie, fatty streaks, intermediate lesions, and raised lesions); ▼, intermediate lesions and raised lesions; ●, raised lesions. Bars, 95% CIs.

score computed from the modifiable risk factors, gender, and 10-year age group. Only 3 categories of AA risk score were used because of the small number (n = 7) with AA risk score ≥11. Table 4 gives the ratios of surface area involved with lesions in the AA in risk score categories computed from only the modifiable risk factors to the surface area involved with lesions in individuals having 0 risk score based on the modifiable risk factors. The ratios for risk scores 1 to 5 and for ≥6 were significant for all of the lesions, intermediate plus raised lesions, and raised lesions. As with the coronary artery lesions, the AA risk score based on modifiable risk factors was associated with the extent of lesions of all degrees of severity in the AA.

Risk Levels

Slightly >20% of PDAY subjects had low (−1 or 0) coronary artery risk scores (Tables 2 and 3), and ~5% had high risk scores (≥11). Approximately 25% of the subjects had low (0) AA risk scores (Table 4).

DISCUSSION

Summary of Results

PDAY risk scores computed from only the modifiable risk factors (serum lipoprotein concentrations, smoking, hypertension, obesity, and hyperglycemia) were associated with the earliest microscopically demonstrable lesion of atherosclerosis (AHA grade 1) in the LAD and with the extent of the earliest detectable gross lesion (fatty streaks) in the RCA and AA. The risk scores computed from the modifiable risk factors also were associated with prevalence of higher degrees of microscopic severity in the LAD and with extent of lesions of higher degrees of lesion severity in the RCA and AA. Slightly >20% of the subjects were low risk (coronary artery risk score of −1 or 0), and ~5% could be considered high risk (coronary artery risk score ≥11). Thus, ~75% had slight or moderate risk (coronary artery risk score 1–5 or 6–10).

Comparison With Other Studies

In 93 autopsied young people, the Bogalusa Heart Study[11] found associations of risk factors measured antemortem with coronary and aortic fatty streaks and fibrous plaques. The findings reported here also are consistent with the idea that atherosclerosis progresses in an uninterrupted fashion from adolescence and youth into adulthood.[30] Furthermore, the rate of progression is influenced by the CHD risk factors.[17–19,31,32] Even functional changes, which are believed to accompany or possibly

TABLE 3 **Ratios of Surface Area Involved With Lesions in the RCA According to Risk Score Computed From Modifiable Risk Factors to Surface Area Involved in Individuals Having Low Risk, Adjusted for Gender and Age**

Lesion	Risk Score Computed From Modifiable Risk Factors			
	−1 to 0 (n = 309), Ratio	1 to 5 (n = 740), Ratio (95% CI)	6 to 10 (n = 294), Ratio (95% CI)	≥11 (n = 84), Ratio (95% CI)
All lesions	1[a]	1.21 (0.97–1.55)	2.00 (1.55–2.60)[b]	3.67 (2.64–4.98)[b]
Intermediate + raised	1[a]	1.33 (1.03–1.77)[b]	2.27 (1.69–3.08)[b]	5.28 (3.53–7.55)[b]
Raised	1[a]	1.22 (0.95–1.60)	1.82 (1.37–2.44)[b]	3.97 (2.62–5.68)[b]

[a] Reference.
[b] Significantly ($P \leq .05$) different from 1.00.

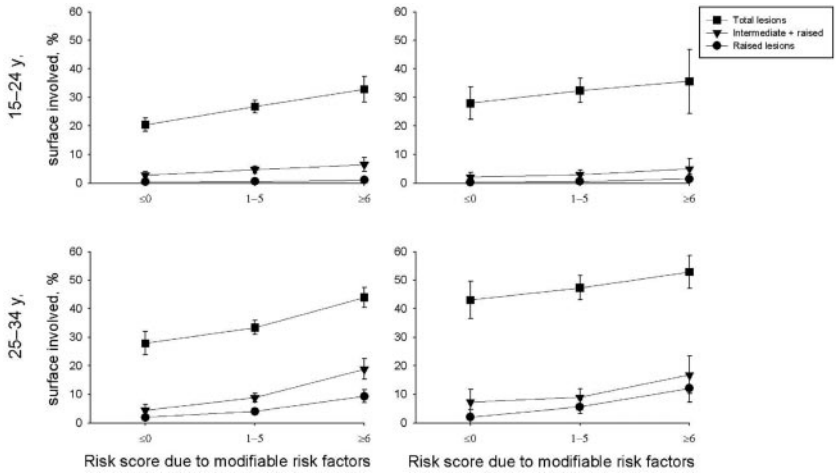

FIGURE 3
Extent of lesions in the AA by PDAY AA risk score computed from the modifiable risk factors for men (left) and women (right) and 10-year age group. ■, any lesion (ie, fatty streaks, intermediate lesions, and raised lesions); ▼, intermediate lesions and raised lesions; ●, raised lesions. Bars, 95% CIs.

TABLE 4 **Ratios of Surface Area Involved With Lesions in the AA According to Risk Score Computed From Modifiable Risk Factors to Surface Area Involved in Individuals Having Low Risk, Adjusted for Gender and Age**

Lesion	Risk Score Computed From Modifiable Risk Factors		
	0 (n = 362), Ratio	1 to 5 (n = 792), Ratio (95% CI)	≥6 (n = 304), Ratio (95% CI)
All lesions	1[a]	1.18 (1.09–1.29)[b]	1.43 (1.30–1.57)[b]
Intermediate + raised	1[a]	1.69 (1.33–2.19)[b]	3.16 (2.42–4.16)[b]
Raised	1[a]	1.32 (1.03–1.72)[b]	2.70 (2.03–3.60)[b]

[a] Reference.
[b] Significantly ($P \leq .05$) different from 1.00.

precede the fatty streak, are associated with serum cholesterol levels.[33]

Among PDAY cases, the prevalence of advanced atherosclerosis in low-risk 30- to 34-year-old persons is about the same as in high-risk 15- to 19-year-old persons. Among Framingham subjects, coronary event rates in high-risk young individuals are roughly equivalent to those in low-risk individuals 25 years later.[16]

Early Control of Modifiable Risk Factors

Risk reduction in younger individuals should retard the progression of atherosclerosis in its early stages, just as risk-factor reduction lowers rates of adult events.[34–38] An example will illustrate the importance of risk-factor control at an early age. A 16-year-old male with a non-HDL cholesterol 160–189 mg/dL (4 points), smoker (1 point), obesity (6 points), and no other risk factors has 11 points in the coronary artery risk score because of modifiable risk factors. Figure 4 (redrawn from Fig 1 in McMahan et al[15]) indicates that a man of age 15 to 19 years with these risk factors has only a 6% chance of having an advanced coronary artery lesion, but he has an ~70% chance of having any (grades 1–5) lesion in the LAD (Fig 1) and has ~12% surface area involvement with any lesion in the RCA (Fig 2). These results indicate that atherogenesis is well underway in this individual's late teenage years. Tables 2 and 3 show that for all levels of lesion severity and not just the earliest lesion, this young man is at high risk relative to an individual with no points because of the modifiable risk factors.

High relative risk at young ages likely will be transformed into high absolute risk of advanced coronary artery lesions later in life, because the modifiable risk factors not only persist over time (ie, track[39,40]) but typically worsen with age.[41] When the age component is included in the risk score for the example individual, high relative risk because of the modifiable risk factors results in the chance of an advanced coronary artery lesion being ~13% at age 20 to 24 years, ~25% at age 25 to 29 years, and ~43% at age 30 to 34 years (Fig 4).

The original presentation of the PDAY risk score[15] was focused on the prediction of advanced lesions. The

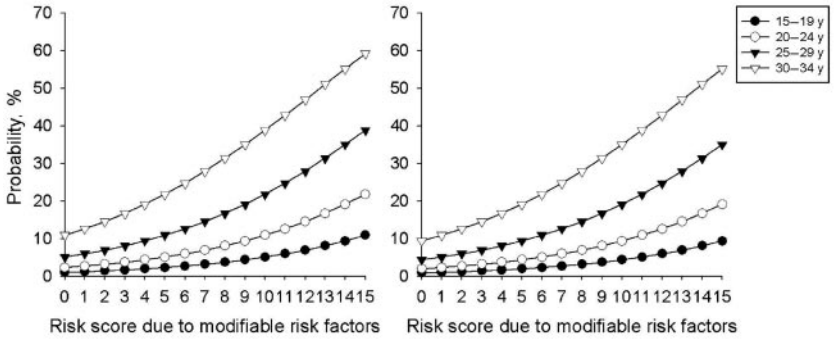

FIGURE 4
Estimated probability of advanced atherosclerotic lesions in the coronary arteries by the part of the PDAY risk score because of the modifiable risk factors and 5-year age group for men (left) and women (right). (Redrawn from McMahan CA, Gidding SS, Fayad ZA, et al. *Arch Intern Med*. 2005;165:883–890; copyright © 2005 American Medical Association, all rights reserved.)

present article shows that the same risk score predicts the presence of the earlier lesions as well: in microscopic terms, grades 1, 2, and 3; in gross terms, fatty streaks and intermediate lesions. This result reinforces the conclusion that the risk factors accelerate the process of atherosclerosis beginning with the earliest lesion and its transition to advanced lesions. Individuals with high relative risk (ie, individuals with high scores from the modifiable risk factors even at young ages) are at high risk for progressing atherosclerosis. Such individuals are candidates for intervention using lifestyle modification, and it seems likely that such intervention may be particularly effective when only the early lesions are present.

Risk-factor control in youth is feasible. Both the Dietary Intervention Study in Children[42] and the Special Turku Coronary Risk Factor Intervention Project for Children[43] showed reductions in serum lipids by dietary modification in children. Lifestyle modification, including diet, exercise, smoking avoidance or cessation, and weight management, reduces risk factors.[44,45] The observation that only ~20% of the PDAY subjects have a PDAY coronary artery risk score of 0 or −1 suggests that the majority of young people could benefit from lifestyle improvement to prevent progression of atherosclerosis to advanced lesions.

There is emerging evidence that risk-factor control in children also affects noninvasive and functional markers associated with atherosclerosis. Pravastatin treatment to lower low-density lipoprotein cholesterol in a cohort with familial hypercholesterolemia retarded the progression of carotid artery intima-media thickness.[46] Limitation of saturated fat intake from 7 months of age not only reduced serum cholesterol levels but also improved endothelial function in boys at 11 years of age.[33]

Limitations

Hemodilution and hemoconcentration introduce variation into the measurements made in serum and are expected to attenuate the associations of these risk factors with lesions. Therefore, the associations reported here likely are underestimated.

Figure 4 suggests an increased prevalence of advanced lesions with increasing age, even for those with little or no risk because of the modifiable risk factors. Risk factors such as family history (not available in the PDAY study) may be present. Alternatively, current risk-factor criteria may not represent ideal levels, and, thus, we may be observing a moderate-risk group rather than a low-risk group.

CONCLUSIONS

These results support the public health strategy of beginning risk-factor control in youth through improved cardiovascular health behaviors. They also support the use of risk scores as tools to identify young persons most likely to have atherosclerotic lesions, including the earliest anatomically demonstrable lesions, or young persons likely to develop advanced atherosclerosis as they grow older. Even in 15- to 19-year-olds, atherosclerosis has begun in a substantial number of individuals, and this observation suggests beginning primary prevention at least by the late teenage years to ameliorate every stage of atherosclerosis and to prevent or retard progression to more advanced lesions.

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