cholesterol ≥190 mg/dl, 45% had LDL cholesterol 130 to 189 mg/dl, 32% had diminished HDL cholesterol, and 39% had elevated TG (Table 1). Patients with LDL cholesterol ≥190 mg/dl tended to be younger, to be less obese, and to have lower blood pressure than the other groups. The most common dietary recommendations were to decrease trans fat and saturated fat intake (63%), to increase fruit and vegetable intake (62%), to decrease the glycemic index (30%), to decrease portion size (15%), or to decrease sugar-sweetened beverage consumption (14%). A recommendation to increase exercise was given to 55% and to continue current exercise to 35%.

The mean value of each abnormal lipid fraction improved and a proportion within each category normalized, while BMI decreased very modestly (BMI z-score = −0.05; interquartile range: −0.22 to 0.05; $p < 0.0001$; proportion obese 39% vs. 36%, $p = 0.03$). BMI decrease appeared to modify the slope of change in moderate LDL cholesterol elevation (no BMI decrease −2.6 ± 1.8, $p = 0.14$; BMI decrease −9.6 ± 2.3, $p < 0.0001$) and TG elevation (no BMI decrease −18.3 ± 11.5, $p = 0.11$; BMI decrease −54.69 ± 13.9, $p = 0.0001$), while HDL cholesterol and LDL cholesterol ≥190 mg/dl were not modified by BMI decrease.

The presented data represent a feasible, short-term, clinical practice benchmark for pediatric lipid management. Previous studies offering dietary advice successfully lowered LDL cholesterol by roughly 10% and sustained improvement for 3 years, with no growth or safety concerns (3). Our data suggest that comparable improvements may be achieved in less resourced real-world practice. High TG and low HDL cholesterol dyslipidemia studies note relations between weight loss and modest lipid improvements that may persist for nearly 5 years (4). Other studies suggest that lowering carbohydrate intake alone may improve TG and HDL cholesterol (5). Our results suggest that lifestyle modification to improve moderate LDL cholesterol elevation or TG may covary with weight loss. Generalizability of the present findings may be limited by the tertiary care structure, inadequate power for subset analyses, limited comparison of specific lifestyle recommendations (as providers coalesced around only a few), unmeasured medical history confounders, and local laboratory variation. Although we accounted for baseline lipid level, residual regression to the mean cannot be excluded. Overall, our data suggest that real-world clinical practice can approximate trial data in addressing the 1 in 5 youth with abnormal lipid levels.

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Statin Medication Enhances Progression of Coronary Artery Calcification

The Heinz Nixdorf Recall Study

Statins are suggested to stabilize plaque by decreasing lipid-rich and necrotic plaque components and increasing plaque calcification (1,2). However, to date the relationship between statin administration and progression of coronary artery calcification (CAC) is poorly understood, and existing data are

limited to patient cohorts and relatively short follow-up times. Therefore, in this study, we aimed to investigate whether the use of statins influences the progression of CAC during >5 years of follow-up in an observational study based on participants from the general population cohort of the Heinz Nixdorf Recall Study, free from clinical cardiovascular disease at baseline (3). CAC score was assessed using electron-beam computed tomography at baseline and after 5 years using an identical scanning protocol and quantified by the Agatston score. Regression analysis was used to determine the association of CAC progression with statin intake, with log transformation of CAC to normalize for its distribution.

We included 3,483 participants (mean age 59 ± 8 years, 47% men) in this analysis. Overall, 230 subjects received statin medications at baseline. Median CAC scores at baseline were 58.8 (interquartile range [IQR]: 2.6 to 273.3) for subjects with statin intake and 5.9 (IQR: 0 to 80.2) for subjects without. Median follow-up CAC scores were 141.3 (IQR: 19.6 to 554.7) for subjects with statin intake and 21.2 (IQR: 0.0 to 174.6) for those without.

In unadjusted regression analysis, taking a statin was associated with 39% higher progression in CAC+1 (Table 1). This relationship was slightly attenuated after adjustment for cardiovascular risk factors but remained statistically significant, with approximately 31% higher progression of CAC+1, attributable to statin intake. Likewise, subjects with statin intake had almost 2-fold odds for CAC progression greater than the expected range compared with subjects without statin medication in unadjusted and adjusted regression analyses.

When stratifying by low-density lipoprotein (LDL) level at baseline, in unadjusted analysis we found that statin intake in subjects with LDL cholesterol ≥115 mg/dl was associated with lower CAC progression than statin intake in subjects with LDL cholesterol levels <115 mg/dl (LDL <115 mg/dl: 56% [IQR: 17% to 109%], p = 0.003; LDL ≥115 mg/dl: 36% [IQR: 13% to 63%], p = 0.001). When adjusting for cardiovascular risk factors, this difference was attenuated (31% [IQR: −3% to 77%], p = 0.07, and 25% [IQR: 5% to 50%], p = 0.01, respectively).

To rule out that the association of statins with higher CAC progression was caused by higher CAC score at baseline in subjects with statin medication, additionally the association of statin with CAC progression was determined in a subanalysis, matching 202 subjects with statin intake at baseline 1:2 with control subjects without statin medication by age group, sex, presence of hypertension and diabetes, smoking status, and CAC category at baseline (n = 404). In regression analysis based on the case-control subgroup, statin intake again was associated with higher CAC progression (Table 1). When stratifying by CAC score at baseline (≥100 vs. <100), a relevant association of statin intake with CAC progression was confirmed for subjects with low CAC scores, whereas for subjects with higher CAC at baseline, the effect estimate of statin intake on CAC progression was considerably lower. Looking at subjects with CAC progression greater than the expected range, we observed 2-fold odds for subjects receiving statin medication with baseline CAC scores <100, which decreased to 1.5 when CAC was ≥100 at baseline.

In a further analysis, we investigated the association of statin intake with coronary events. Participants with statin intake showed a tendency toward a lower coronary event rate (4 of 205 [1.9%]) compared with matched subjects (11 of 410 [2.7%]), which converted into a hazard ratio of 0.74 (95% confidence interval: 0.24 to 2.33; p = 0.60).

In this population, statin intake enhanced CAC progression, mostly in the less advanced stage of atherosclerosis. However, on statin, CAC progression did not lead to increased risk for coronary events. Although the present study design could not rule out bias by statin indication, our results may support the hypothesis of a plaque-stabilizing effect of statins, which might be reflected by an increase in CAC. Our results may influence expectations of clinicians

TABLE 1 Association of Coronary Artery Calcification Progression With Statin Intake in the Overall Study Cohort in Unadjusted and Adjusted Models as Well as for Case-Control Subgroup Analysis

	% Progression in CAC+1* (95% CI)	p Value	OR for CAC Progression Higher Than Expected Range (95% CI)	p Value
Overall cohort (n = 3,483)				
Unadjusted	39 (20–62)	<0.0001	1.93 (1.47–2.54)	<0.0001
Model 1	31 (13–52)	0.0005	1.95 (1.48–2.57)	<0.0001
Model 2	27 (9–48)	0.002	1.82 (1.37–2.40)	<0.0001
Model 3	31 (12–52)	0.0006	1.93 (1.45–2.57)	<0.0001
Case-control subgroup analysis (n = 606)				
All	43 (19–72)	0.0002	1.82 (1.28–2.58)	0.0008
CAC <100 (n = 363)	67 (23–125)	0.0009	2.01 (1.28–3.16)	0.002
CAC ≥100 (n = 243)	13 (0.05–28)	0.04	1.50 (0.86–2.64)	0.15

Depiction of the association of statin intake with percentage progression of CAC+1 as well as odds ratio for CAC progression higher than expected range. Model 1 adjusted for age and sex. Model 2 adjusted for age, sex, systolic blood pressure, BMI, antihypertensive medication, diabetes, and smoking status. Model 3 adjusted for age, sex, systolic blood pressure, BMI, antihypertensive medication, diabetes, smoking status, LDL cholesterol, and HDL cholesterol. *CAC score was log-transformed to adjust for its skewed distribution, and CAC progression was calculated as [log(CAC+1) at follow-up] − [log(CAC+1) at baseline], which was then retransformed to depict the percentage change in CAC+1.

BMI = body size index; CAC = coronary artery calcification; CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein; OR = odds ratio.

and patients when monitoring statin therapy by repetitive CAC scorings. Further studies using computed tomographic angiography including lesion-specific information over time and larger numbers of subjects taking statins are needed to confirm our results.

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How Often Does Athlete Sudden Cardiac Death Occur Outside the Context of Exertion?

We read with great interest the paper by Finocchiaro et al. regarding the causes of sudden cardiac death (SCD) in athletes and its precipitating factors (1).

The authors observed that SCD in athletes occurred at rest in almost 40% of the cases, a third of which occurred during sleep. This is substantially higher (more than 2-fold) than in the large cohorts published so far among athletes who had SCD (2,3). The authors specified that since 40% of SCDs occurred outside the context of exertion, it is highly unlikely that the provision of automated external defibrillators (AEDs) in public venues would have prevented SCDs among these athletes.

An important limitation has to be acknowledged before describing the circumstances of SCD occurrence. This study was based on autopsy series, and therefore, it only included patients who did not survive, which creates a potential bias. This is important to consider because SCDs that occur during sports are known to have a dramatically higher survival rate than those occurring outside the context of exercise (4). In addition, SCDs that occur during sleep are most likely to occur at home, where the survival rate is much lower than in public places (5).

Therefore, both SCDs occurring during sleep and those occurring outside the context of sport were probably overrepresented in this study, and a real estimation of the incidence of SCDs at rest cannot be accurately performed. In addition, cases of SCDs that were prevented by the use of AEDs on the field were not considered in this pathology study, and any conclusion regarding the impact of AEDs should be drawn with particular caution.

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