Prevalence of Subclinical Coronary Artery Disease in Middle-Aged, Male Marathon Runners Detected by Cardiac CT

Prävalenz subklinischer koronarer Herzkrankheit bei männlichen Marathonläufern mittleren Alters: Detektion mittels koronarer CT-Angiografie

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Zusammenfassung

Ziel: Ziel der Studie war die Evaluierung der Prävalenz der KHK bei männlichen Marathonläufern mittleren Alters mittels Dual Source cCTA (DSCTA). **Material und Methoden:** 50 Marathonläufer (52,7 ± 5,9 Jahre) wurden zusätzlich zur sportmedizinischen Routinediagnostik mittels DSCTA einschließlich Calcium-Scoring (CS) untersucht. Das CS wurde bei allen Personen im high-pitch-Modus (hpDSCTA), die CTA bei 21 Personen im hpDSCTA und 29 Personen im sequentiellen „step-and-shot"-Modus (sDSCTA) durchgeführt. Die effektive Dosis (ED) wurde für beide Scanverfahren bestimmt. Der Risikofaktor für koronare Ereignisse wurde basierend auf Standardrisikofaktoren mittels des PROCAM-Scores berechnet. Der Koronarstatus wurde wie folgt klassifiziert: 1. keine KHK (CS = 0, keine Koronarplaques), 2. milde Koronarsklerose (CS> 0, Stenose < 50 %), 3. moderate Koronarsklerose (CS > 0, Stenose > 50 %) 4. signifikante KHK (CS > 0, Stenose > 75 %). **Ergebnisse:** Der mediane PROCAM-Score betrug 1,85 ± 1,56 %. 26 von 50 Marathonläufern hatten keine KHK. 1 Person hatte eine signifikante KHK, 3 Personen eine moderate sowie 20 eine milde Koronarsklerose. Die Laufband-Ergometrie konnte bei keinem Sportler Koronarischämien nachweisen. Als Faktoren für ein erhöhtes KHK-Risiko konnten Alter, Blutdruck, persönliche Mindestzeit, familiäre Anamnese und der PROCAM-Score identifiziert werden. Die mediane ED für die DSCTA lag bei 1,259 ± 0,542 mSv. Bei der hpDSCTA war die ED im Vergleich zur sDSCTA signifikant niedriger (0,762 vs. 1,618 mSv, p < 0,0001). **Schlussfolgerung:** Bei fast 50 % der asymptomatischen Marathonläufer über 45 Jahren kann mittels cCTA eine Koronarsklerose nachgewiesen werden. Bei 24 % dieser Probanden waren die Plaques in den proximalen Abschnitten der Koronararterien lokalisiert. Tatsächlich leidet jedoch nur ein kleiner Anteil dieser Personen an einer obstruktiven KHK.

Abstract

Purpose: To evaluate the prevalence of coronary artery disease (CAD) in middle-aged, male marathon runners using coronary dual source CT angiography (DSCTA). **Materials and Methods:** 50 male marathon runners older than 45 years (mean age: 52.7, standard deviation: 5.9 years, range: 45 to 67 years) received DSCTA including calcium scoring (CS) in addition to standard pre-participation screening. Based on standard risk factors, the risk for coronary events was calculated using the PROCAM score. Coronary status was defined using the following system: 1. absence of CAD (CS zero, no coronary plaques) 2. mild coronary atherosclerosis (CS > 0, coronary plaques with luminal narrowing < 50 %), 3. moderate coronary atherosclerosis (CS > 0, luminal narrowing > 50 %), 4. significant CAD (CS > 0, luminal narrowing > 75 %). **Results:** The mean PROCAM score was 1.85 % (standard deviation = 1.56, range 0.39 to 8.47 %). 26/50 marathon runners had no atherosclerosis. 1 of the remaining 24 participants had significant CAD, 3 had moderate coronary atherosclerosis and 20 had mild coronary atherosclerosis. Treadmill exercise testing was unremarkable in terms of myocardial ischemia in all participants. Age, systolic blood pressure, personal minimum time, family history of cardiovascular disease and PROCAM score were factors associated with an increased risk for coronary atherosclerosis. **Conclusion:** Coronary atherosclerosis can be detected in almost 50 % of male marathon runners aged older than 45 years. In 24 % of the participants plaques were located in the proximal coronary system. However, only a minority of these persons have obstructive CAD. As expected, treadmill exercise testing failed to detect these persons that possibly have a higher risk for coronary events.

Die Laufband-Ergometrie kann wie erwartet diese Risikopersonen für koronare Ereignisse nicht erkennen.

Kernaussagen:
- Koronarsklerose bei ~50 % männlicher Marathonläufer > 45 Jahre
- Nur ein kleiner Teil dieser Personen leidet an einer obstruktiven KHK
- Auf dem Laufbandergometer können diese Risikopersonen nicht erkannt werden
- Kardio-CT mögliche Hilfe bei der Detektion der Athleten mit erhöhtem koronaren Risiko, insbesondere bei familiärem Risikoprofil

Key points:
- Coronary atherosclerosis can be detected in ~50 % of male marathon runners > 45 years
- Only a minority of these persons have obstructive CAD
- Treadmill exercise testing failed to detect these persons
- Cardiac CT might help to identify athletes with elevated risk for coronary events, especially in persons with a family history of coronary artery disease

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Introduction

Regular physical exercise is an inherent part of the prevention of cardiovascular disease [1]. On the other hand, intensive physical exertion raises the risk for fatal cardiac events in persons with underlying cardiovascular diseases [2]. To reduce the risk for (fatal) cardiovascular events, pre-participation screening is recommended before starting physical activity or performing competitive sports. However, the concept of pre-participation screening differs between the American Heart Association (AHA) and the European Society of Cardiology (ESC). While the AHA only recommends standard history and physical examination in younger athletes [3], the ESC guidelines consider the evaluation of a resting ECG to be an integral part in terms of pre-participation screening [4]. According to the AHA, medically supervised exercise testing should be performed only in competitive male athletes older than 40 years (or women older than 55 years) and with at least two additional cardiovascular risk factors or in persons with a markedly abnormal single risk factor [3]. A comparable approach has been published by the sections of exercise physiology and sports cardiology of the European Association of Cardiovascular Prevention and Rehabilitation. Maximal exercise testing is restricted to high-risk persons with at least moderate intensity activity [5]. While hypertrophic cardiomyopathy is the most common cause for sudden cardiac death in younger athletes [6], fatal cardiovascular events in athletes older than 35 years are typically the result of coronary artery disease (CAD) [7] in accordance with the general population, since atherosclerosis is a disease of aging beginning in the youth [8, 9]. Unfortunately the diagnostic accuracy of exercise testing to predict coronary events is low [10] as it depends on the pre-test probability with a high rate of false-negative tests in patients with a high pre-test probability and a high rate of false-positive tests in patients with a low pre-test probability [11]. In contrast, cardiac computed tomography angiography (CTA) is characterized by high diagnostic accuracy to detect or rule out coronary artery disease noninvasively [12, 13]. Based on these assumptions, there might be the need for extended cardiovascular pre-participation screening using CTA.

Materials and methods

Marathon runners

The local ethics committee and the federal authority for radiation protection agreed to this study. 50 male marathon runners recruited by an advertisement in local newspapers and aged > 45 years were included in the study. They received CTA in addition to standard pre-participation screening. All participants gave their informed consent to take part in this study. The investigation was conducted in accordance with the Declaration of Helsinki.

Pre-participation screening

To exclude cardiovascular and other relevant diseases, each participant underwent a physical examination, rest ECG and color Doppler echocardiography. The resting heart rate and blood pressure at rest were determined. In addition, all athletes underwent treadmill stress tests to evaluate maximal oxygen uptake (VO2 max). Training experience, weekly training volume averaged over the preceding 6 months, number of completed marathons and personal minimum time were recorded in each participant.
Exclusion criteria were known CAD, allergic reaction to iodinated contrast media, renal insufficiency (glomerular filtration rate < 60 ml/min), hyperthyroidism (basal TSH < 0.03 mU/L in combination with elevation of the peripheral thyroid hormones).

Cardiovascular risk factors

To assess the cardiovascular risk profile, standard blood parameters (total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride levels, fasting glucose) were determined in each participant after a fasting period of at least 8 h. Additional risk factors like family history of cardiovascular disease (defined as confirmed coronary artery disease or peripheral artery disease in a first degree relative), diabetes mellitus, smoking or hypertension were evaluated on the basis of the medical history. The PROCAM (Prospective Cardiovascular Munster study) score [14] was calculated to characterize the individual's global cardiovascular risk more accurately.

Dual source computed tomography

All examinations were performed with a second-generation dual source CT system (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). The participants were placed on the examination table in a supine position. After planning the scan range, an initial prospective ECG-triggered, high-pitch non-contrast DSCT scan was performed for the assessment of coronary calcium using the following parameters: Collimation 2 × 64 × 0.6 mm with a z-flying focal spot, gantry rotation time 280 ms, pitch 3.4, tube current 70 mA per rotation with automatic tube current modulation, and tube voltage 120 kV.
Afterwards, the circulation time was determined using a test bolus with 10 ml of iodinated contrast media (370 mg iodine/ml, Ultravist 370, Bayer Healthcare, Germany) at a flow setting of 6.0 ml/s and a 20 ml saline chaser with a dual-head injector (CT Stellant, Medrad, Indianola, Pennsylvania).

Depending on heart rate, participants were scanned with one of the following scan protocols: In participants with a heart rate < 60/min a prospective triggered, high-pitch DSCTA, and in participants with a heart rate > 60/min a prospective triggered, sequential DSCTA ("step-and-shoot") was performed. In high-pitch DSCTA the tube current was set to 350 mA/rotation as a reference setting for automated tube current modulation, tube voltage 100 kV, collimation 2 × 64 × 0.6 mm with a z-flying focal spot, gantry rotation time 280 ms, pitch 3.4. In prospective triggered, sequential DSCTA the following parameters were used: tube current 350 mAs, tube voltage 100 kV, collimation 2 × 64 × 0.6 mm with a z-flying focal spot, gantry rotation time 280 ms, scan range of 13.5 cm (four blocks of sequential detector coverage).

In both scan techniques 60 % of the RR-interval was set to trigger the scan.

70 ml of contrast media and a saline chaser were applied at a flow setting of 6.0 ml/s.

For calcium scoring (CS) overlapping images with 3-mm effective slice thickness and a medium sharp non-edge-enhancing convolution kernel (B35f) were reconstructed. CTA images were reconstructed using a soft B26 f kernel at a slice thickness of 0.75 mm and an increment of 0.4 mm.

Evaluation of the coronary artery angiography was performed in consensus by two experienced radiologists. Thin slab maximum-intensity projections and curved multiplanar reformations were used. For rating of image quality and stenosis detection, a modified 15-segment model of the American Heart Association was used: right coronary artery (RCA): 1: proximal, 2: middle, 3: distal, and 4: combined posterior descending and posterolateral branches; left main stem (LM): 5; left anterior descending artery (LAD): 6: proximal, 7: middle, 8: distal, 9: first diagonal, and 10: second diagonal; left circumflex artery (LCX): 11: proximal, 12: first marginal branch, and 13: distal, 14: left posterolateral branch, and 15: left posterior descending.

Extent of coronary artery disease

The total calcium burden was graded according to Rumberger et al. [15] in the following categories: Agatston score 0 (no evidence of coronary calcium), 1 – 10 (minimal evidence of coronary calcium), 10 – 100 (mild evidence of coronary calcium), 100 – 400 (moderate evidence of coronary calcium) and > 400 (extensive evidence of coronary calcium).

Furthermore, we defined CAD adapted to this score using the following system including calcium score and evaluation of coronary stenosis by CTA: 1. absence of CAD (CS zero, no coronary plaques), 2. mild CAD (CS > 0, coronary plaques with luminal narrowing < 50 %), 3. moderate CAD (CS > 0, luminal narrowing > 50 %), 4. significant CAD (CS > 0, luminal narrowing > 75 %).

Statistical analysis

Statistical analysis was performed with computer software (JMP version 10, SAS Institute, Cary, NC). Continuous, normally distributed variables are summarized as the mean (standard deviation SD) [range], and, if necessary, the median was added. Differences between the two groups were tested by student's t-test in case of normal distribution (t-statistic). Otherwise, the Wilcoxon test was performed (Chi^2-statistic).

Differences between two or more than two groups were performed by Pearson's chi^2-test. Odds ratios were calculated from contingency tables. A p-value of less than 0.05 was regarded as statistically significant.

Results

Patient characteristics

The mean age of the participants was 52.7 years (SD 5.9), ranging from 45 to 67 years. The mean PROCAM score was 1.9 % (range 0.39 % to 8.47 %, SD 1.6 %). The number of completed marathons ranged from 1 to 72 (median 7, mean 13.8, SD 16.2) with a personal minimum time between 2:33 h and 4:30 h (median 3:28 h, mean 3:28 h, SD 0:27 h). 43 of the participants were active marathon runners with the last completed marathon within the last 12 months. From the remaining 7 participants, 3 had finished their last marathon in the last 24 months, 2 in the last 36 months and only 2 participants were sedentary with the last marathon having been run more than 5 years ago. No athlete was suffering from diabetes. Hypercholesterolemia (defined as > 160 mg/dl or present medication with lipid lowering drugs) was present in 3 athletes. 4 participants had a history of hypertension (defined as the presence of antihypertensive medication). 17 (34 %) athletes were ex-smokers, 24 (48 %) had a family predisposition of CAD, 1 athlete was obese. Detailed data are given in **Table 1**.

Beside one marathon runner that reported atypical chest discomfort during physical activity, all other persons were free of cardiovascular symptoms suspicious of coronary artery disease. Treadmill exercise testing was unremarkable in terms of myocardial ischemia in all participants.

Coronary computed tomography and extent of coronary artery disease

All coronary scans were of diagnostic quality. 26/50 (52 %) marathon runners had no atherosclerosis. 1 of the remaining 24 participants had significant CAD, 3 had moderate CAD and 20 had mild coronary artery disease. The distribution of CAD within the athletes according to the time since the last finished marathon was as follows: 23 of 43 athletes who had finished their last marathon within the last 12 months had no evidence of CAD, 18 athletes had mild CAD and 2 athletes had moderate CAD. The athlete with significant CAD had finished his last marathon within the last 24 months, one of the other two athletes from this group had no evidence of CAD and the other one had mild CAD. In the group of athletes who had finished their last marathon within the last 36 months, one of two had no evidence of CAD and the other one had moderate CAD. Among the sedentary athletes, one had no CAD and one had mild CAD. Age, systolic blood pressure, personal minimum time and PROCAM score differed between athletes with and without coronary atherosclerosis (**Table 1**).

The mean calcium score was 43.5 (range 0 – 745.8, median 0, SD 121.0). 26/50 athletes had no coronary calcium, 9 athletes had a calcium score up to 10, 9 athletes had a calcium score between 10 and 100, and 4 athletes had a calcium score between 100 and 400 and 1 athlete had a calcium score > 400 (**Fig. 1**). The correlation between age and calcium score ($r^2 = 0.18$, $p = 0.002$) as well as PROCAM score and calcium score ($r^2 = 0.22$, $p = 0.0005$) was only moderate (**Fig. 2, 3**). The oldest athlete without coronary lesions was 67 years old, and the youngest athlete with coronary atherosclerosis was 45 years old.

In total 34 coronary lesions were detected (9 non-calcified, 8 mixed, 17 calcified). In one person an additional stress MRI was recommended to exclude myocardial ischemia due to moderate coronary stenosis. The person with atypical chest pain showed high-grade stenosis in the left anterior descending artery (**Fig. 4**). Invasive angiography could confirm high-grade steno-

Table 1 Patient characteristics, mean (SD), [range].

Tab. 1 Patientencharakteristika, Mittelwert (SD), [Spannbreite].

	study population (n = 50)	no CAD (n = 26)	CAD (n = 24)	difference	t-value or Chi²	p-value group 1 vs. group 2
age [years]	52.6 (5.9) [45 – 67]	50.9 (5.7) [45 – 67]	54.5 (5.5) [45 – 67]	3.62 [0.42 – 6.81]	6.409#[1]	p = 0.01
weight [kg]	76.6 (9.59) [54 – 105]	75.4 (10.2) [54 – 101]	77.8 (8.8) [64 – 105]	2.3 [–3.03 – 7.80]	0.88	p = 0.38
height [cm]	180 (6) [170 – 195]	180 (7) [170 – 195]	180 (4) [171 – 186]	–0.27 [–3.4 – 2.87]	–0.17	p = 0.87
systolic blood pressure [mmHg]	131 (15) [105 – 165]	125 (13) [105 – 150]	137 (15) [105 – 165]	12.28 [4.31 – 20.25]	3.10	p = 0.003
diastolic blood pressure [mmHg]	83 (8) [65 – 100]	81 (7) [65 – 90]	85 (8) [70 – 100]	3.64 [–0.71 – 7.98]	1.69	p = 0.01
BMI [kg/m²]	23.5 (2.5) [18.7 – 33.1]	23.1 (2.5) [18.7 – 26.6]	24.0 (2.7) [20.4 – 33.1]	0.96 [–0.47 – 2.40]	1.35	p = 0.19
VO_2 max [mL/kg/min]	48.7 (6.6) [37 – 63]	49.8 (6.8) [37 – 63]	47.3 (6.3) [38 – 59]	–2.54 [–6.31 – 1.23]	–1.36	p = 0.1813
number of completed marathons	13.8 (16.2) [1 – 72]	12.0 (13.3) [1 – 55]	15.6 (18.9) [1 – 72]	3.57 [–6.10 – 13.23]	0.75	p = 0.46
training volume [h/week]	5.0 (1.8) [2 – 12]	5.0 (2.1) [2 – 12]	4.9 (1.4) [2 – 8]	–0.04 [–1.07 – 0.98]	–0.08	p = 0.93
training experience [years]	16.3 (9.8) [3 – 50]	16.6 (11.0) [3 – 50]	15.9 8.6) [4 – 41]	–0.74 [–6.33 – 4.85]	–0.27	p = 0.79
personal minimum time [h:min]	3:28 (0:27) [2:33 – 4:30]	3:21 (0:26) [2:33 – 4:14]	3:34 (0:27) [2:50 – 4:30]	0:13 [0:00:07 – 0:30:03]	2.09	p = 0.048
total cholesterol [mg/dl]	195 (34) [122 – 271]	197 (34) [152 – 271]	195 (34) [122 – 260]	–2.15 [–21.55 – 17.25]	–0.22	p = 0.82
LDL cholesterol [mg/dl]	104 (29) [47 – 166]	104 (29) [47 – 166]	104 (30) [66 – 148]	–0.46 [–17.34 – 16.45]	–0.06	p = 0.96
HDL cholesterol [mg/dl]	62 (13) [34 – 91]	63 (9) [42 – 78]	61 (16) [34 – 91]	–1.79 [–9.28 – 5.70]	–0.48	p = 0.63
triglyceride [mg/dl]	87 (55) [31 – 359]	84 (43) [41 – 359]	90 (66) [31 – 160]	5.78 [–26.30 – 37.85)	0.36	p = 0.72
fasting glucose [mg/dl]	93 (7) [73 – 107]	92 (6) [73 – 102]	95 (8) [79 – 107]	2.46 [–1.57 – 6.50]	1.23	p = 0.2258
high sensitive C-reactive protein [mg/dl]	0.16 (0.57) [0.01 – 4.02]	0.09 (0.12) [0.01 – 0.46]	0.25 (0.81) [0.01 – 4.02]	0.16 [–0.18 – 0.51]	0.96	p = 0.35
PROCAM score [%]	1.9 (1.6) [0.39 – 8.47]	1.3 (1.0) [0.39 – 5.01]	2.4 (1.8) [0.46 – 8.47]	1.11 [0.24 – 1.97]	2.60	**p = 0.01**
Relative PROCAM score [%]	16.8 (10.4) [5.5 – 44.3]	14.8 (10.2) [6.0 – 44.3]	18.9 (10.5) [5.5 – 44.3]	0.04 [–0.02 – 0.10]	1.37	p = 0.18

[1] Chi²

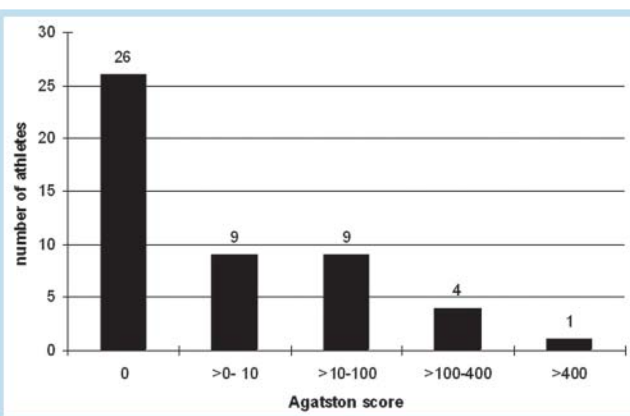

Fig. 1 Distribution of Agatston score within the study population.

Abb. 1 Verteilung des Agatston Score innerhalb der Studienpopulation.

sis and percutaneous transluminal angioplasty and stent implantation were performed.

Plaque location

A total of 16 proximal plaques (segments 1, 6 or 11) were detected (8 calcified plaques, 4 mixed plaques, 4 non-calcified plaques) in 12 (24 %) athletes. 4 participants had two proximal segments with atherosclerotic lesions. From the 4 proximal non-calcified plaques 2 were classified as moderate, the other 2 as mildly stenotic. **Fig. 5** shows a mixed plaque located in the proximal left anterior descending artery.

Impact of traditional risk factors

Besides age, systolic blood pressure and PROCAM score, only a family history of cardiovascular disease was associated with an increased risk for coronary atherosclerosis (**Table 2**). The distribution of former smoking, hypertension or hypercholesterolemia was not different between persons with or without coronary cal-

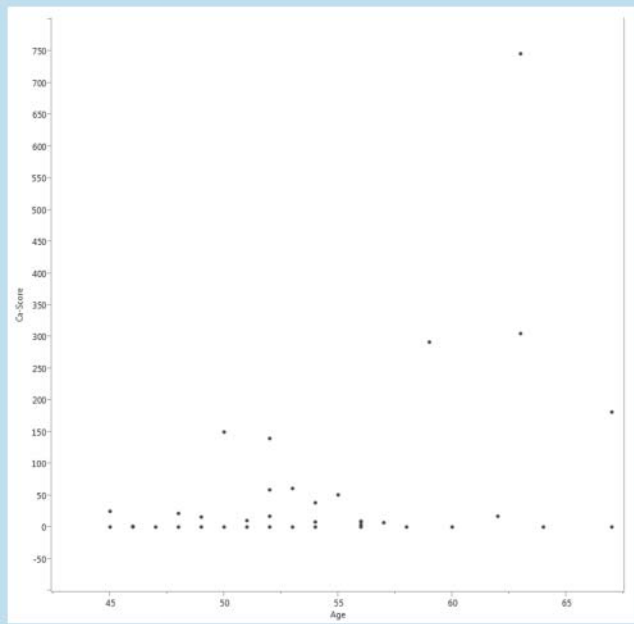

Fig. 2 Correlation between calcium score and age.

Abb. 2 Korrelation zwischen Calcium-Score und Alter.

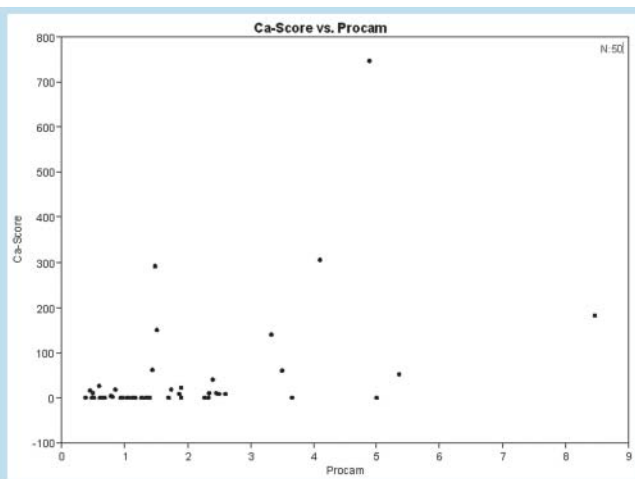

Fig. 3 Correlation between calcium score and PROCAM score.

Abb. 3 Korrelation zwischen Calcium-Score und PROCAM Score.

cifications or the four groups according to the degree of CAD (no vs. mild vs. moderate vs. significant CAD).

Scan mode and radiation exposure

Calcium scoring was performed using the high pitch mode in all participants. The mean effective radiation dose for calcium scoring was 0.30 mSv (range 0.18 – 0.46, SD 0.05). For CTA the high pitch mode was used in 21 (42 %) athletes, while the remaining athletes were scanned using the step-and-shot technique. The mean effective dose for CTA was 1.26 mSv (range 0.64 – 2.74, median 1.20, SD 0.54). The effective dose was statistically significantly lower in persons scanned in high pitch mode (0.76 vs. 1.62 mSv, $p < 0.0001$).

Fig. 4 Curved multiplanar reconstruction of the left anterior descending artery with high-grade stenosis (arrow).

Abb. 4 Gekrümmte multiplanare Rekonstruktion des Ramus interventrikularis anterior mit einer hochgradigen Stenose (Pfeil).

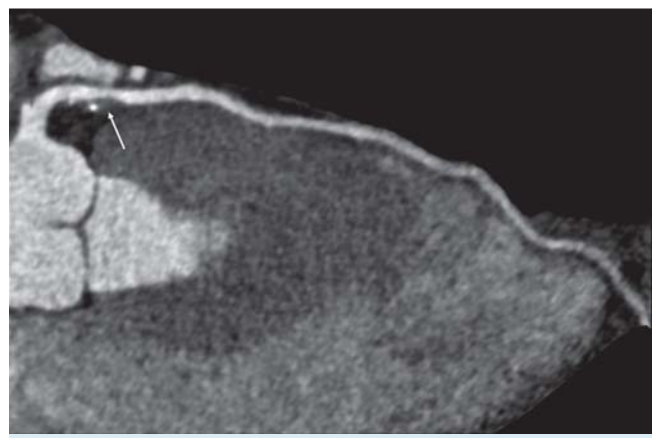

Fig. 5 Moderate stenosis of the proximal left anterior descending artery caused by mixed plaque formation. Curved multiplanar reconstruction.

Abb. 5 Moderate Stenose des Ramus interventrikularis anterior durch eine gemischte Plaque (Pfeil). Gekrümmte multiplanare Rekonstruktion.

Table 2 Risk factors and their association between coronary calcification and the degree of coronary artery disease (CAD).

Tab. 2 Risikofaktoren und ihre Assoziation zwischen koronaren Kalzifikationen und dem Schweregrad der Koronaren Herzkrankheit (KHK).

risk factor	coronary atherosclerosis Pearson's Chi²	odds ratio [95 % CI]	degree of CAD - Pearson's Chi²
family risk	**0.0019**	**6.60 [1.92 – 22.62]**	**0.02**
hypertension	0.5713	1.71 [0.26 – 11.26]	0.55
former smoking	0.2715	1.94 [0.60 – 6.34]	0.46
hypercholesterolemia	0.0861	–	0.44

Discussion

According to our data, male marathon runners have a low risk of having obstructive coronary artery disease, as only one participant in our study had high-grade stenosis leading to revascularization.
On the other hand, coronary atherosclerosis was seen in almost 50 % of our participants. This is of major importance, as a high percentage of coronary events is caused by non-obstructive coronary alterations [16]. Identifying individuals with coronary atherosclerosis (non-obstructive as well as obstructive) might therefore help to calculate the risk for cardiovascular events more precisely.

Study population

In contrast to other studies, athletes with only one finished marathon were not excluded. Thus, our results might be more transferable to real life as persons with no or minimal long-distance running experience constitute a relevant group of marathon participants today. Additionally, the participants were characterized very well in terms of their sports activity and cardiovascular fitness. Thus, the influence of training volume, training experience, number of completed marathons, VO2 max. or personal minimum time on our results could be evaluated.

Traditional risk factors and PROCAM score

Interestingly, beside age and a family history of cardiovascular disease, traditional cardiovascular risk factors did not differ between athletes with and without coronary artery disease. Both groups had very favorable cardiovascular risk profiles, which is underlined by a mean PROCAM score of only 1.9 % with a maximum of 8.47 %. Compared to the PROCAM score of an age-matched group, the relative risk was only 16.8 %. The highest relative PROCAM score was 44.3 %. The observed difference between participants with and without coronary artery disease in terms of the PROCAM score might be driven by the fact that persons with coronary atherosclerosis were older. Probably some of the participants had a higher PROCAM score before starting regular physical activity which might explain at least in part the mismatch between PROCAM score and calcium score in some athletes (**Fig. 3**).
Although there was a significant difference in terms of systolic blood pressure between athletes with and without coronary calcifications, this observation has no clinical consequence as blood pressure might be subject to short-term changes, e. g. due to mental stress. Nevertheless, there could be other reasons for high blood pressure in these persons like unrecognized hypertension. Since we only had a measurement of blood pressure at one time point, further examination of these participants with e. g. 24h-blood pressure monitoring would be necessary for evaluating this fact.
On the other hand, a family history of cardiovascular disease was associated with an odds ratio of 6.6 for having coronary artery disease. As a consequence, more detailed risk stratification in athletes with a family history of cardiovascular disease should be taken into account.

Coronary artery disease in marathon runners

The association between premature coronary artery disease and marathon running is discussed controversially. Large prospective epidemiologic studies have shown reduced rates of coronary heart disease with regular exercise [1, 17]. However, in their study including 108 marathon runners, Mohlenkamp et al. reported higher calcium scores in athletes compared to age- and risk-factor-matched controls. This observation is of major importance as coronary calcification is an independent risk factor for all-cause mortality and cardiovascular events [18].
In contrast to the study published by Mohlenkamp, the median CS in our cohort was lower (0 vs. 36) which might be explained by different factors: Firstly, our collective was younger (53 years vs. 57 years). Secondly, lipid values (104 vs. 121 mg/dL) and the percentage of ex-smokers (34 % vs. 51.9 %) were lower. And thirdly, our marathon runners were probably fitter with a median personal minimum time of less than 3:30 h. Taken together, the comparison between the two studies is doubtful.
Data about contrast-enhanced CTA are rare. Just recently a paper from Karlstedt et al. reported about CTA results in 25 marathon runners (21 male, mean age 55 years) [19]. Coronary atherosclerosis was only detected in 2 athletes. However, the low prevalence of CAD might be explained by the very strict exclusion criteria as athletes with a history of smoking, hypertension, hypercholesterolemia or diabetes were not enrolled. Additionally, data about coronary calcium score are missing.

Prognostic value of CTA

The prognostic value of CTA in persons without known CAD has been demonstrated in a cohort of more than 24 000 individuals [20] although screening examinations with CTA are not recommended [13]. According to the CONFIRM registry, the absence of CAD is associated with an excellent outcome, whereas the risk for death increases by the extent of CAD. These data were confirmed by a study from Hou et al. [21]. In 5007 persons they were able to demonstrate that CTA was superior to CS in terms of predicting cardiovascular events. Remarkably, not only the extent of CAD - but also the plaque characteristics were predictive for major events with an unfavorable outcome for mixed plaques. Newest data from the CONFIRM registry showed that mixed or calcified plaques in the proximal coronary system or a proximal stenosis of more than 50 % is equivalent to an increase in age of 5 years or the risk caused by smoking [22]. Applying this system, 10 (20 %) of our athletes fulfil one of these criteria and might be at higher risk than expected by traditional risk markers.
However, as recently shown, the prognosis of persons with a comparable extent of disease – as assessed by CTA – depends on additional parameters like diabetes mellitus [23]. Thus, marathon runners might have a favorable prognosis compared to sedentary persons with a similar coronary status. The prognostic value of our data will be evaluated during a five-year follow-up period and thus remains unclear at present. Nevertheless, all athletes with coronary artery disease were advised to take ASA. Although there is no evidence of such an approach reducing the cardiovascular risk, vigorous exercise is associated with a transient higher risk for acute coronary events [24].

Limitations

Our study had limitations. First, the number of participants was quite low. Additionally we only enrolled male marathon runners. This was driven by two considerations: Firstly, the risk to suffer from sudden cardiac death due to coronary artery disease is lower in women [25], and secondly radiation exposure applied for chest CT is higher in female persons [26]. Furthermore, the study protocol did not provide for scanning a control group due to ethical reasons.

Conclusion

In conclusion, we could demonstrate that the prevalence of high-grade coronary stenosis in asymptomatic male marathon runners is low. However, almost 50 % of our study population had coronary atherosclerosis despite a very favorable cardiovascular risk profile. A proximal plaque location was found in 24 % of our marathon runners. Thus, standard risk factors as well as the PROCAM score obviously underestimate the cardiovascular risk of male marathon runners, which must be however evaluated by outcome studies. Cardiac CT might help to determine the cardiovascular risk in marathon runners although a routine examination cannot be recommended at present.

Clinical relevance

- Coronary atherosclerosis can be detected in almost 50 % of male marathon runners aged older than 45 years.
- Only a minority of these persons have obstructive CAD. Treadmill exercise testing failed to detect these persons.
- Cardiac computed tomography might help to identify athletes with an elevated risk for coronary events, especially in persons with a family history of coronary artery disease.

Abbreviations

CAD	Coronary artery disease
CTA	CT angiography
CS	Calcium scoring
SD	Standard deviation

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