

Diagnostik von Fettstoffwechselstörungen / Primärprävention



Axel Schmermund

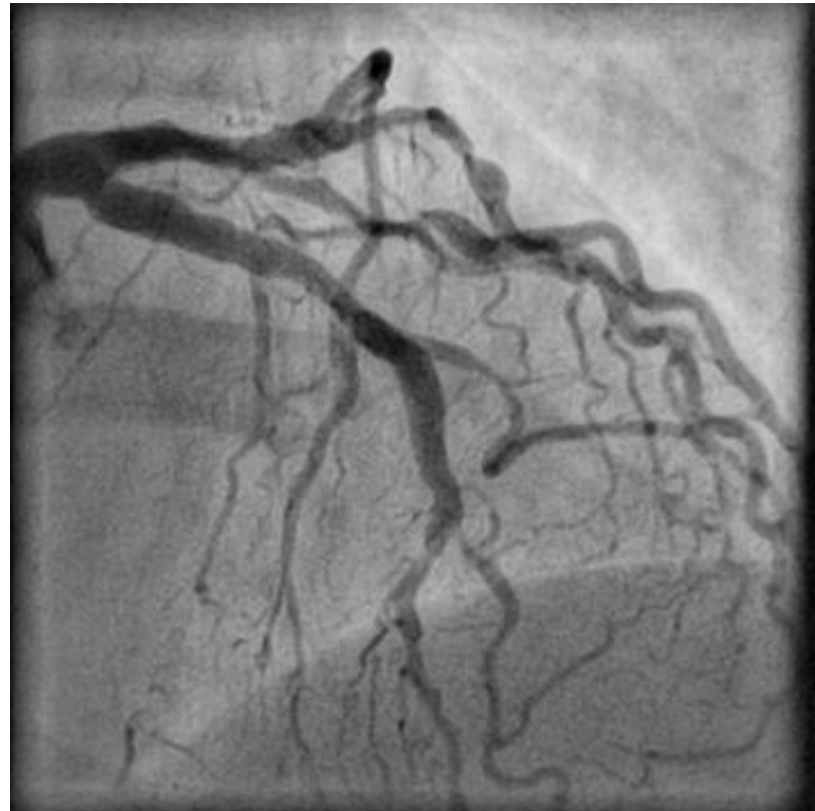
CCB, Cardioangiologisches Centrum Bethanien

Frankfurt a.M.

www.ccb.de

Patientin, 54 Jahre, inst. Angina

Koronarangiografie



Patientin, 54 Jahre, inst. Angina

Risikoanalyse:

- LDL-Cholesterin 205 mg/dl (Ges. 302, HDL 70, Trgl. 117)
- Keine weiteren bekannten RF
- Familie gesund
- Früher aktiv im Reitsport
- Viel Bewegung, schlank
- Mitinhaberin eines erfolgreichen Rennstall-Gestüts

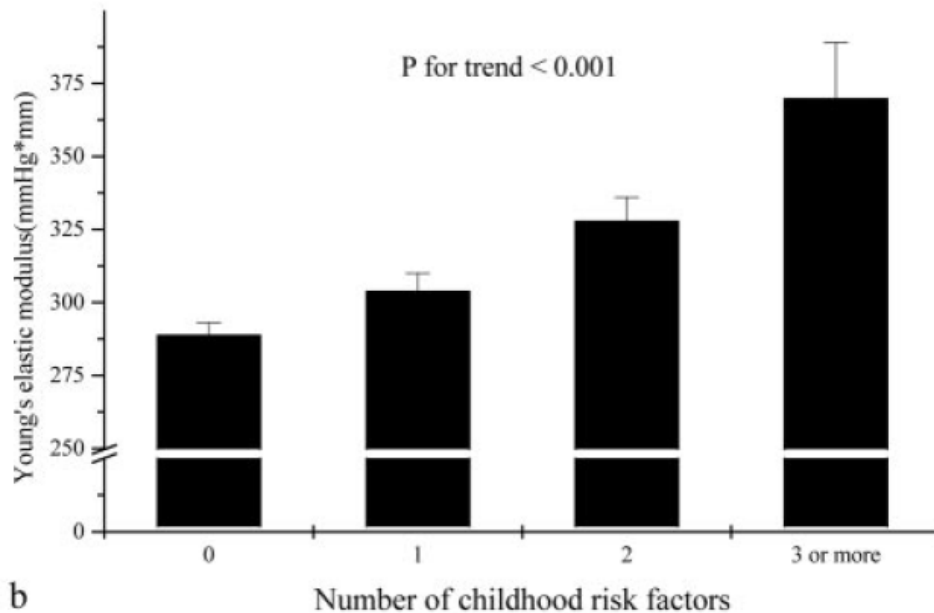
Risikoprädiktion

- Risiko entsteht im Verlauf des Lebens (lifetime risk)
- Kombination aus genetischen Faktoren, Umweltfaktoren und Lebensstil
- Klinischen Ereignissen geht eine Risikoexposition voraus (Exposition gegenüber mind. 1 Risikofaktor)

Risikoprädiktion

CV Risk in Young Finns Study - 20 Jahre später...

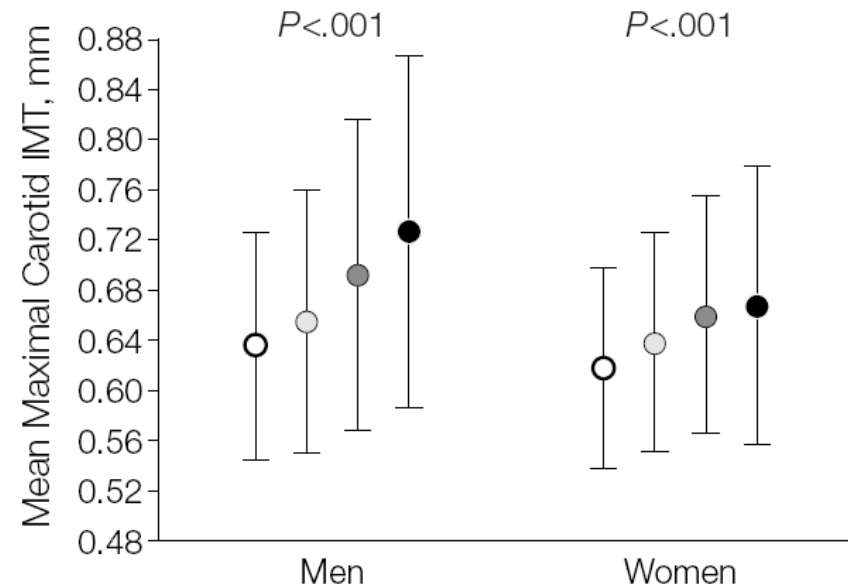
„arterial stiffness“



Juonala et al. Circulation 2005;112:1486-1493

A Risk Factors Measured at Ages 12-18 y

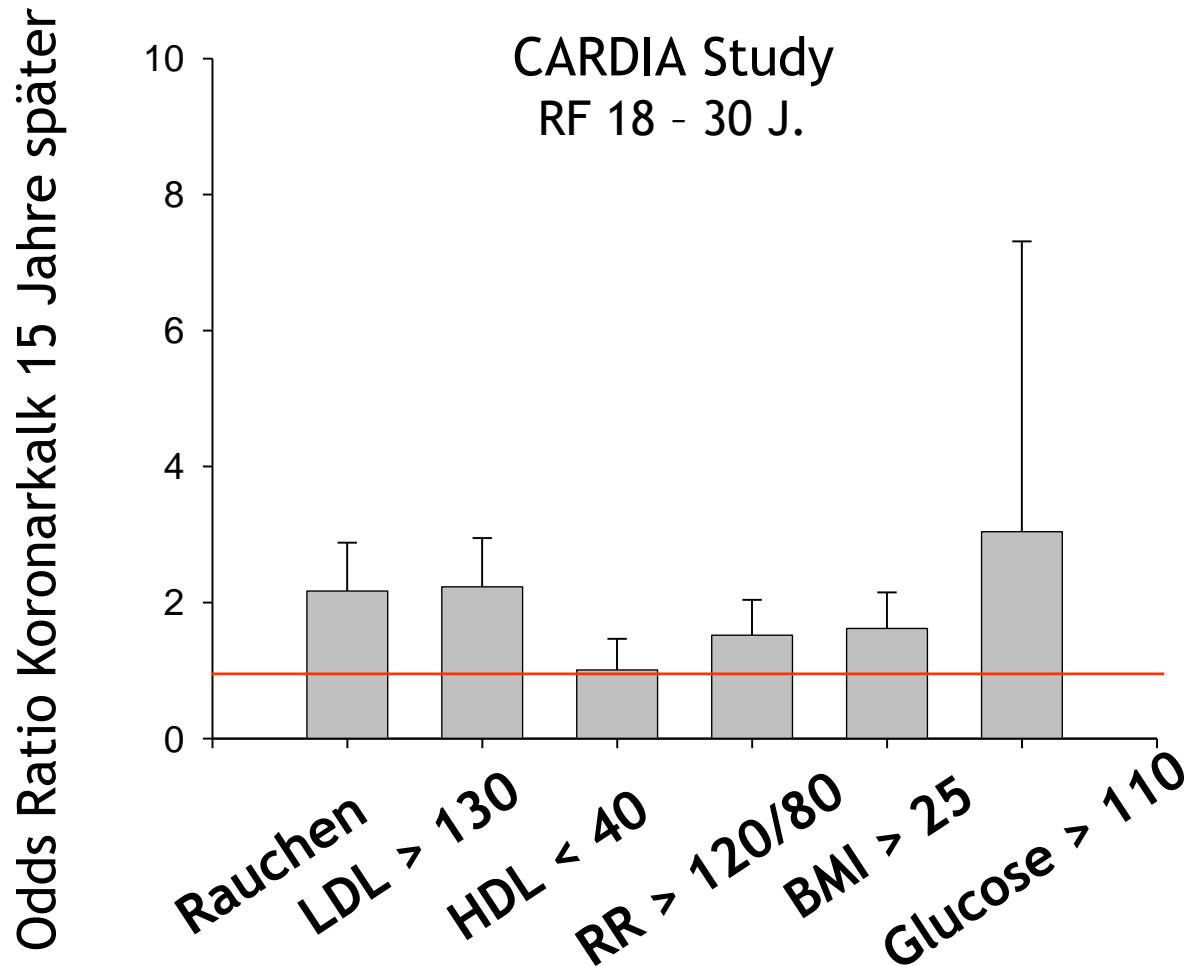
IMT



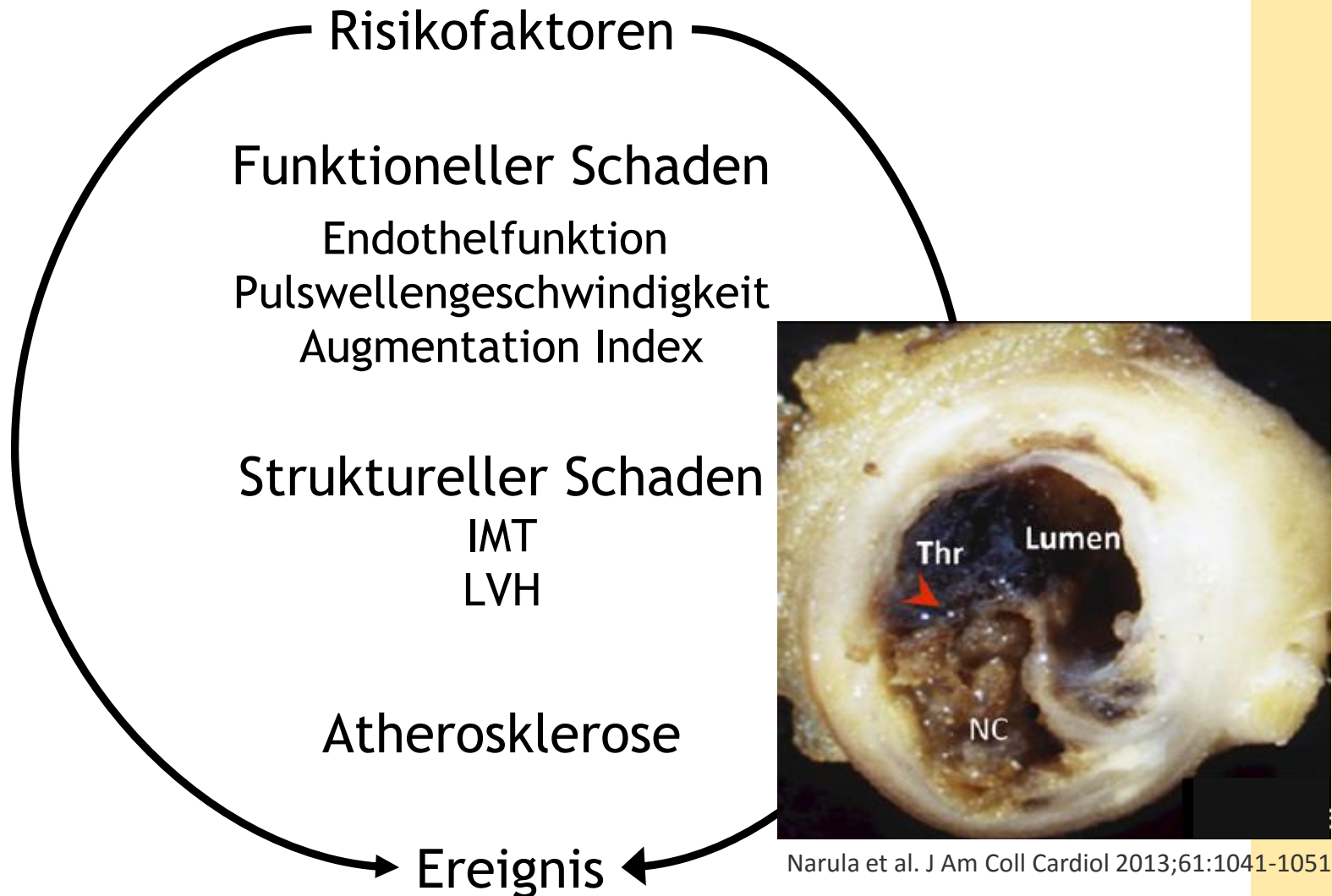
Raitakari et al. JAMA 2003;290:2277-2283

Risikoprädiktion

CARDIA - 15 Jahre später...



Risikoprädiktion



Hohes Risiko - Therapie

Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis

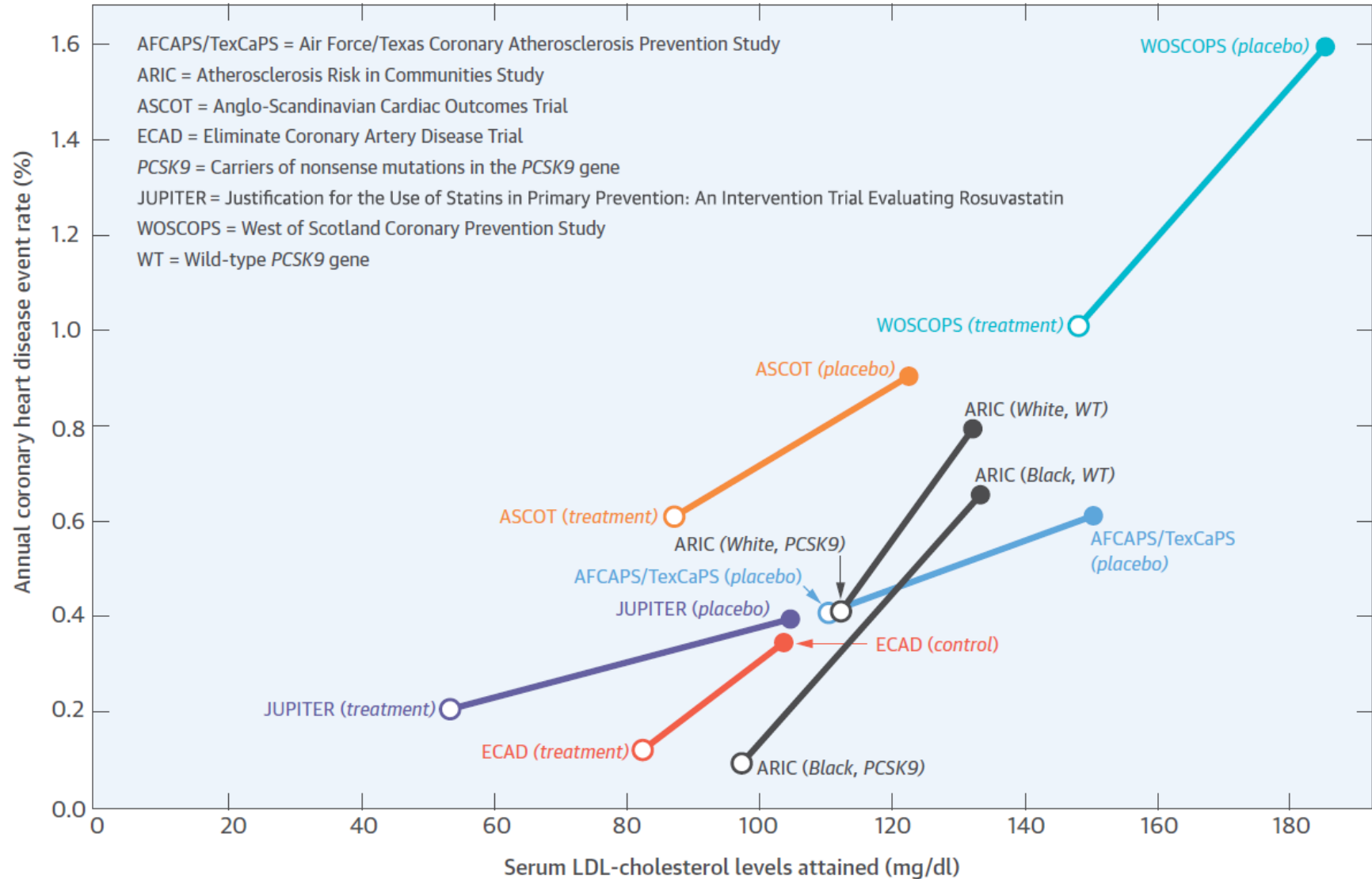
M R Law, N J Wald, A R Rudnicka

Table 7 Expected % decrease in incidence of ischaemic heart disease events for specified decreases in serum cholesterol according to age at event, based on 10 largest cohort studies of serum cholesterol and ischaemic heart disease⁶

Age (years)	LDL cholesterol reduction (mmol/l)*						
	0.6	1.0	1.4	1.8	2.2	2.6	3.0
50	39	56	68	77	84	88	91
60	27	41	52	61	68	74	79
70	20	31	41	49	56	62	67

*Decreases in incidence follow from linear dose-response relation indicating constant proportional change in risk for specified change in cholesterol. Thus at age 60 years relative risk for decrease of 1.0 mmol/l is 0.59 (41% decrease), therefore $0.59^{1.4} = 0.48$ (52% decrease) for 1.4 mmol/l decrease.

Hohes Risiko - Therapie



Risikoprädiktion

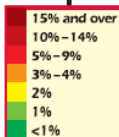
- Risiko entsteht im Lauf des Lebens (lifetime risk)
- Kombination aus genetischen Faktoren, Umweltfaktoren und Lebensstil
- Klinischen Ereignissen geht eine Risikoexposition voraus (Exposition gegenüber mind. 1 Risikofaktor)
- Die Bedeutung einzelner RF bemisst sich am Gesamtrisiko - „don't treat a risk factor, treat a person“

Risikoprädiktion

Table 3 Intervention strategies as a function of total CV risk and LDL-C level

Total CV risk (SCORE) %	LDL-C levels				
	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.5 mmol/L	100 to <155 mg/dL 2.5 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	>190 mg/dL >4.9 mmol/L
<1	No lipid intervention	No lipid intervention	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled
Class ^a /Level ^b	I/C	I/C	I/C	I/C	IIa/A
≥1 to <5	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled
Class ^a /Level ^b	I/C	I/C	IIa/A	IIa/A	I/A
>5 to <10, or high risk	Lifestyle intervention, consider drug*	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class ^a /Level ^b	IIa/A	IIa/A	IIa/A	I/A	I/A
≥10 or very high risk	Lifestyle intervention, consider drug*	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class ^a /Level ^b	IIa/A	IIa/A	I/A	I/A	I/A

SCORE

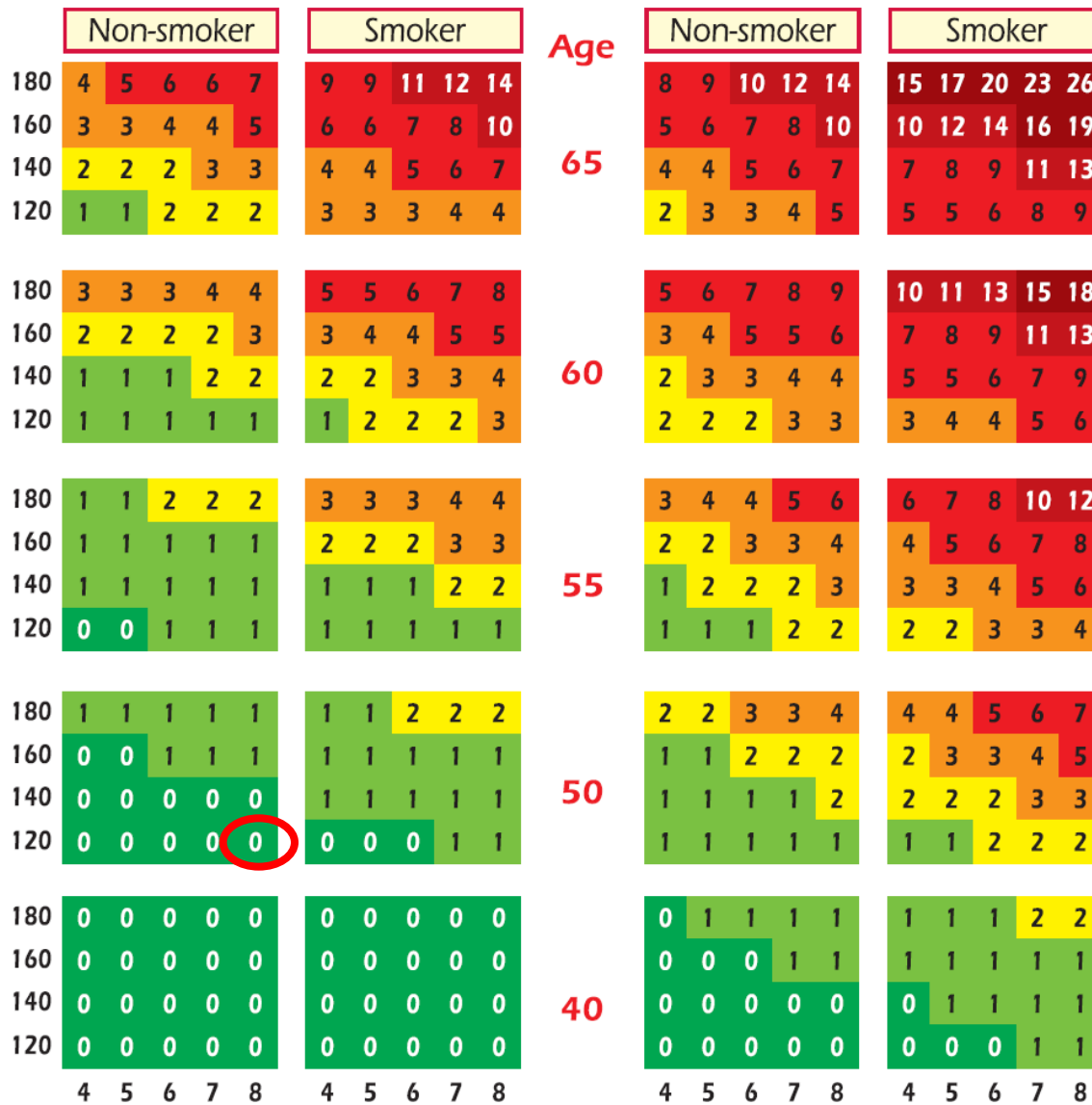


10-year risk of fatal CVD in populations at low CVD risk

WOMEN

MEN

Systolic blood pressure (mmHg)



Total cholesterol (mmol/L)

150 200 250 300 mg/dL

Risikoprädiktion

Risikoabschätzung modifiziert:

- Diabetes
- Familiäre Prädisposition bzgl. (Herz-)Gefäßkrankheiten
- Einzelne stark ausgeprägte RF
- Vielzahl wenig ausgeprägte RF, z.B. Lp(a), Homozystein, Fibrinogen
- Sozioökonomischer Status
- Psychosoziale Risikofaktoren

Risikoprädiktion

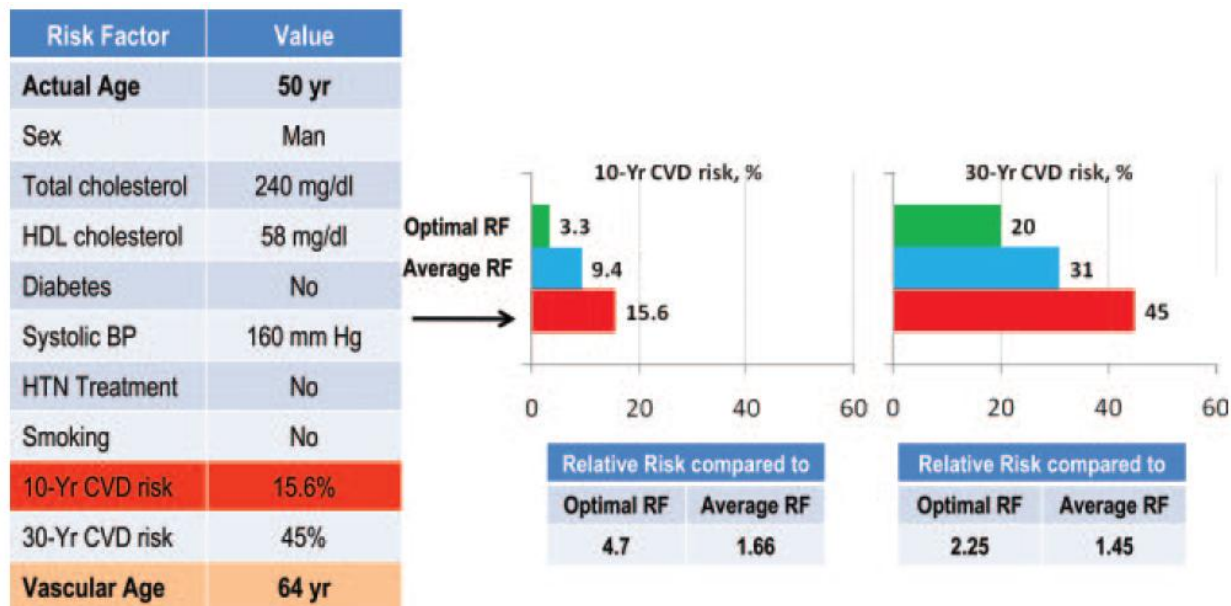
Risikostratifizierung wann?

- Männer > 40, Frauen > 50 Jahre
- Wunsch des Patienten
- einzelne RF bekannt
- positive Familienanamnese
- unklare Beschwerden

Gesamtrisiko

Risikoprädiktion

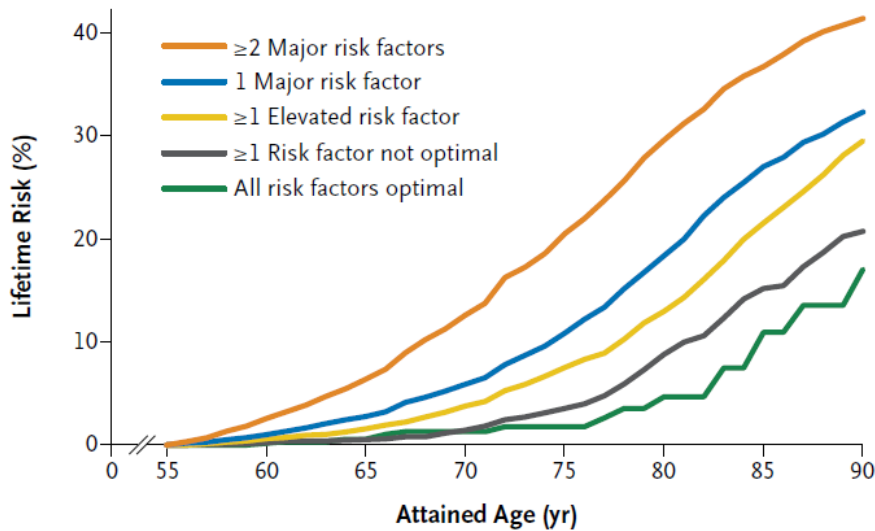
- Lebenszeitrisiko
- Relatives Risiko verglichen mit
 - a) Durchschnitt
 - b) Optimalem Risiko (Fehlen jeglicher RF)



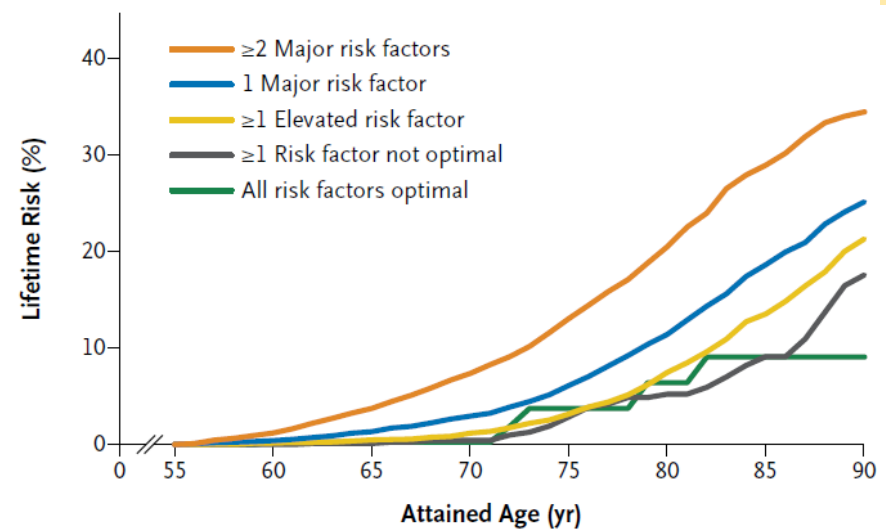
Risikoprädiktion

Framingham: „Optimal“ Chol < 180 mg/dl, RR < 120/80 mmHg,
Nichtraucher, kein Diabetes

Männer



Frauen



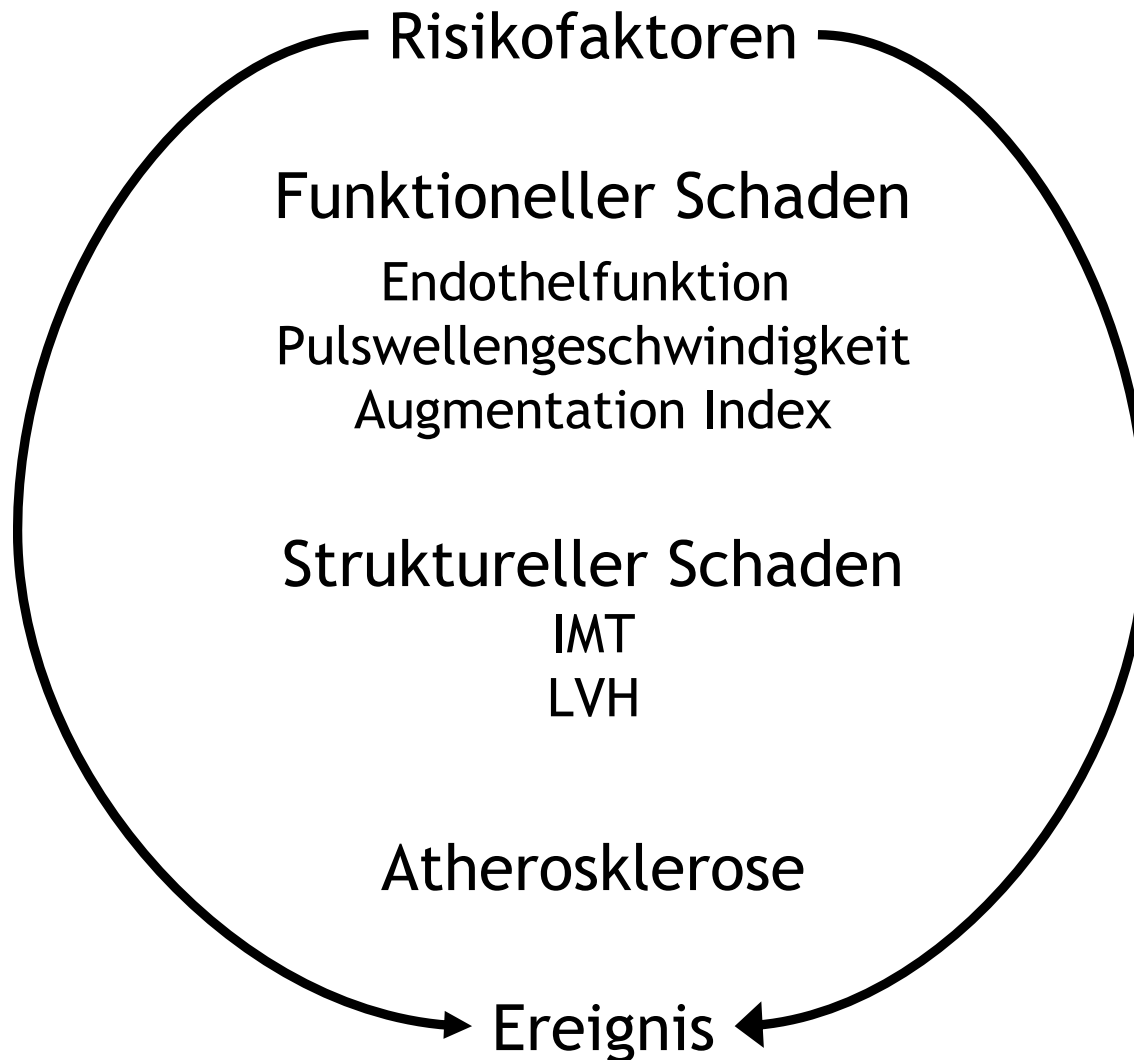
Risikoprädiktion

Framingham: „Optimal“ Chol < 180 mg/dl, RR < 120/80 mmHg,
Nichtraucher. kein Diabetes

TABLE 1. Characteristics of Study Participants at 50 Years of Age

Characteristic	Men (n=3564)	Women (n=4362)
Total cholesterol, mean±SD, mmol/L (mg/dL)	5.66±1.03 (219±40)	5.72±1.14 (221±44)
HDL cholesterol, mean±SD, mmol/L (mg/dL)	1.14±0.31 (44±12)	1.47±0.41 (57±16)
Systolic blood pressure, mean±SD, mm Hg	130±17	127±19
Diastolic blood pressure, mean±SD, mm Hg	82±10	79±11
Diabetes, n (%)	103 (2.9)	61 (1.4)
Current smoker, n (%)	1679 (47.1)	1649 (37.8)
BMI, mean±SD, kg/m ²	27.1±3.8	25.4±4.6
All optimal risk factors,* n (%)	114 (3.2)	196 (4.5)
≥1 Not optimal risk factor,† n (%)	392 (11.0)	602 (13.8)
≥1 Elevated risk factor,‡ n (%)	827 (23.2)	1051 (24.1)
1 Major risk factor,§ n (%)	1508 (42.3)	1767 (40.5)
≥2 Major risk factors,§ n (%)	723 (20.3)	746 (17.1)

Risikoprädiktion



Bildgebung

Insulinresistenz

Adipositas

Homozystein

Lipoprotein(a)

Diabetes

Hypertonie

Fibrinogen

Sozioökonomische
Faktoren

Männl. Geschlecht

Genetische Faktoren

Alter

Psychosoziale
Faktoren

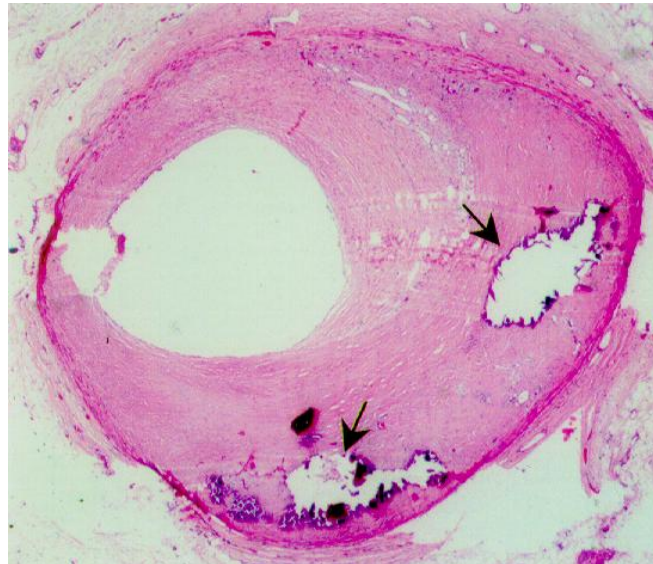
Nikotin

Cholesterin

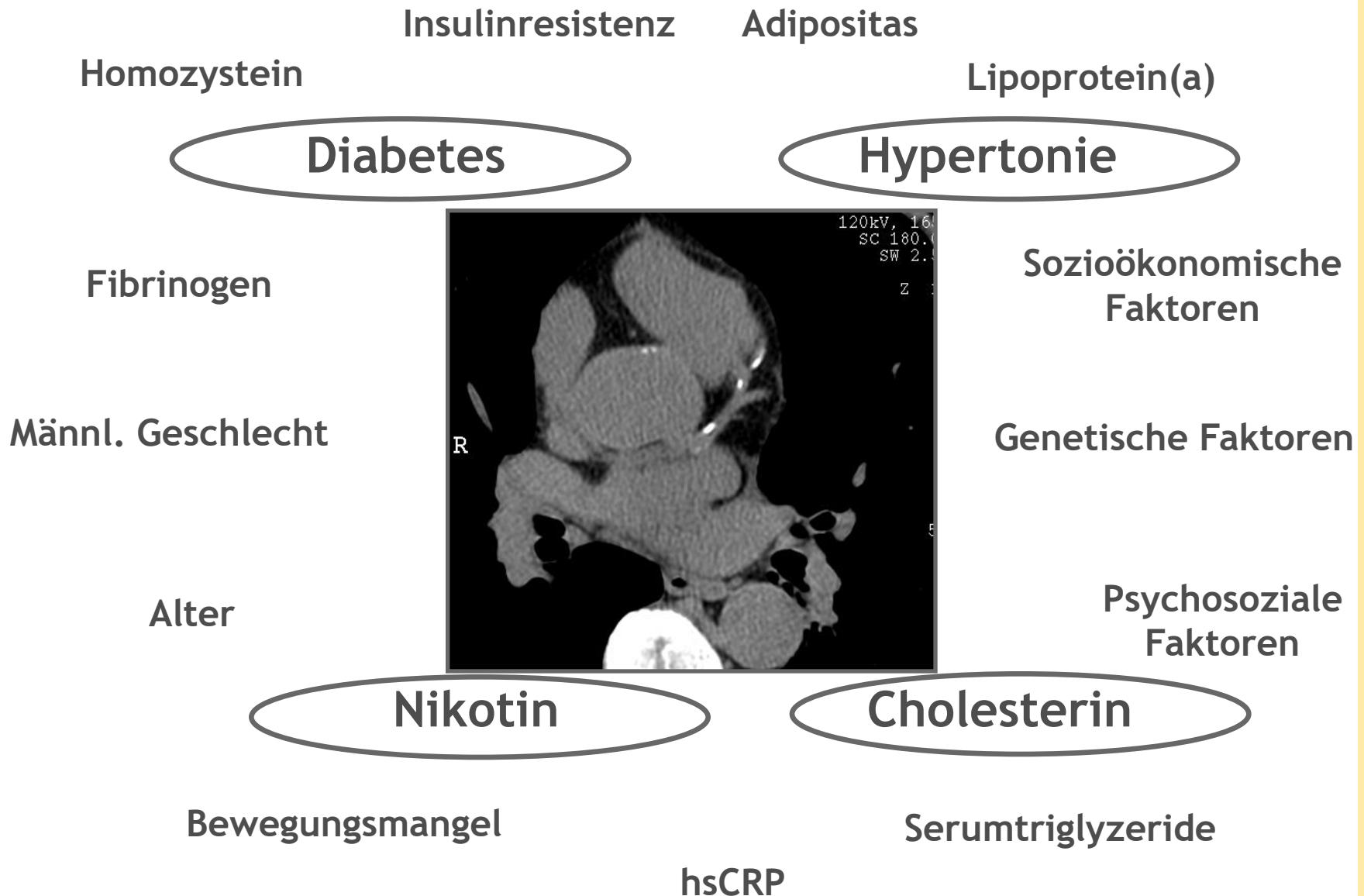
Bewegungsmangel

Serumtriglyzeride

hsCRP



Bildgebung





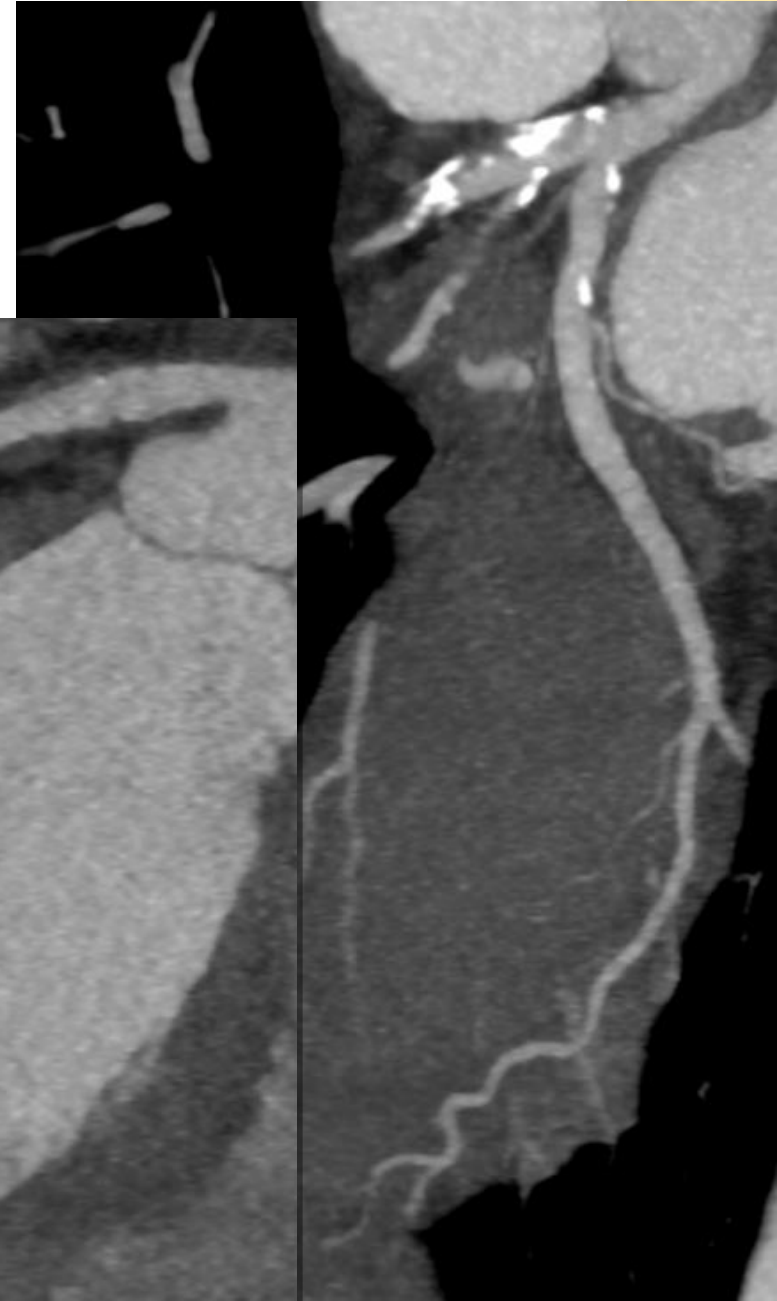
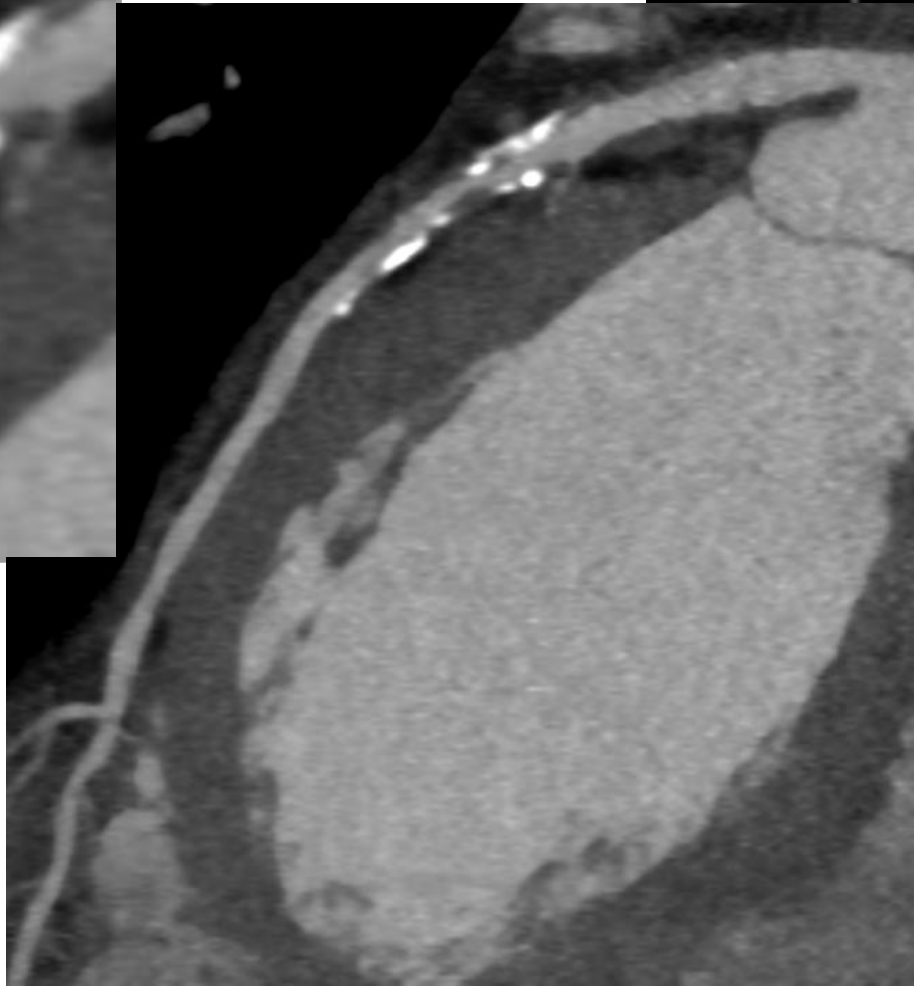
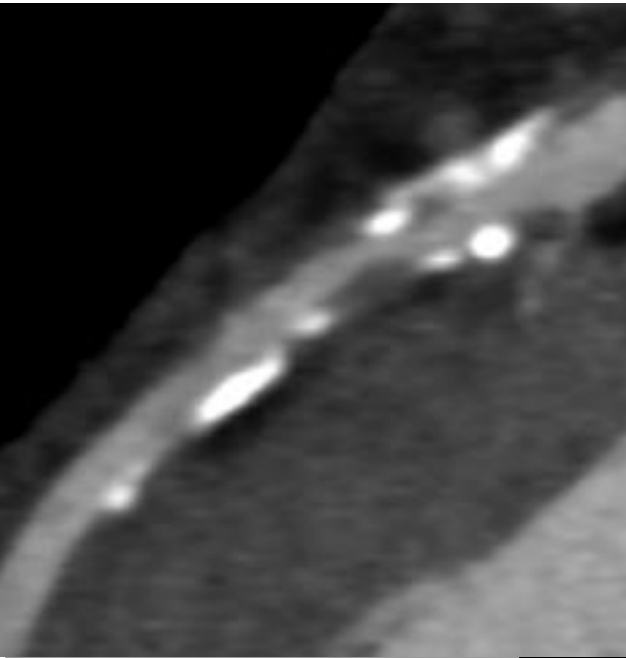
Kardio-CT - Force

Nichtinvasive Koronarangiografie



Kardio-CT - Force

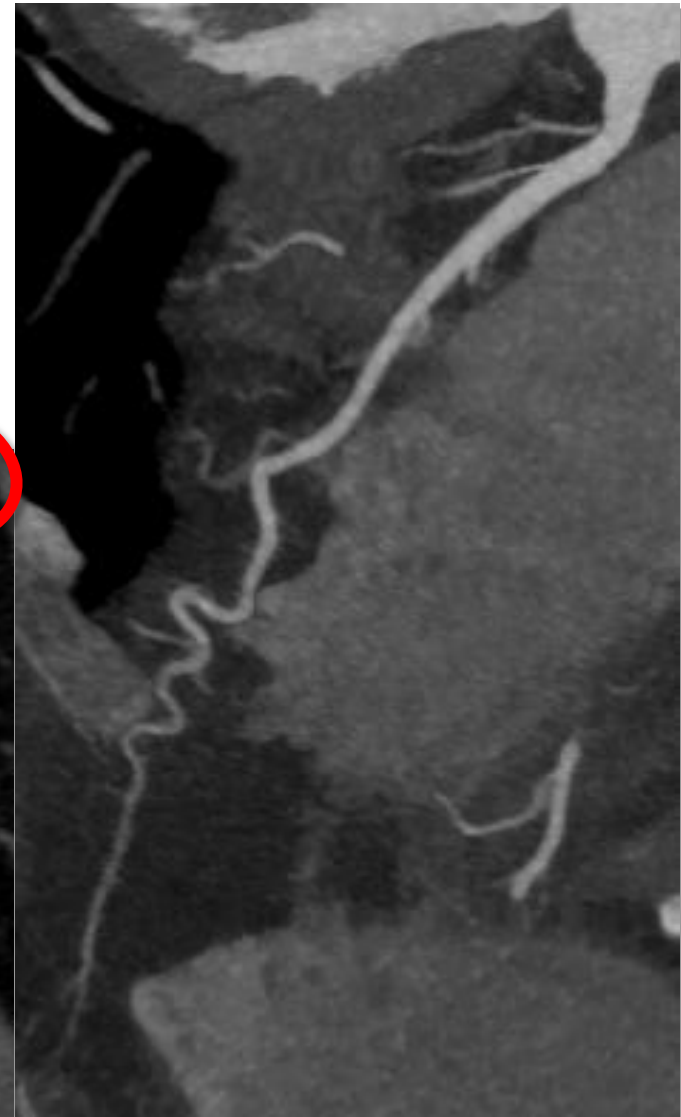
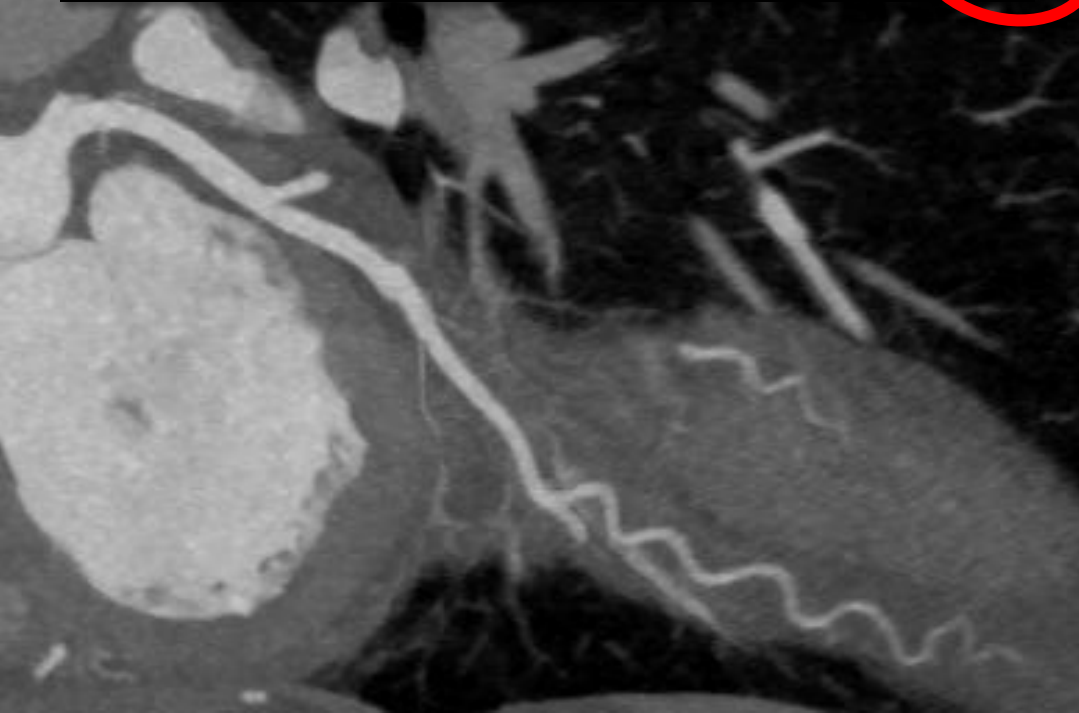
Nichtinvasive Koronarangiografie



Kardio-CT - Force

Nichtinvasive Koronarangiografie

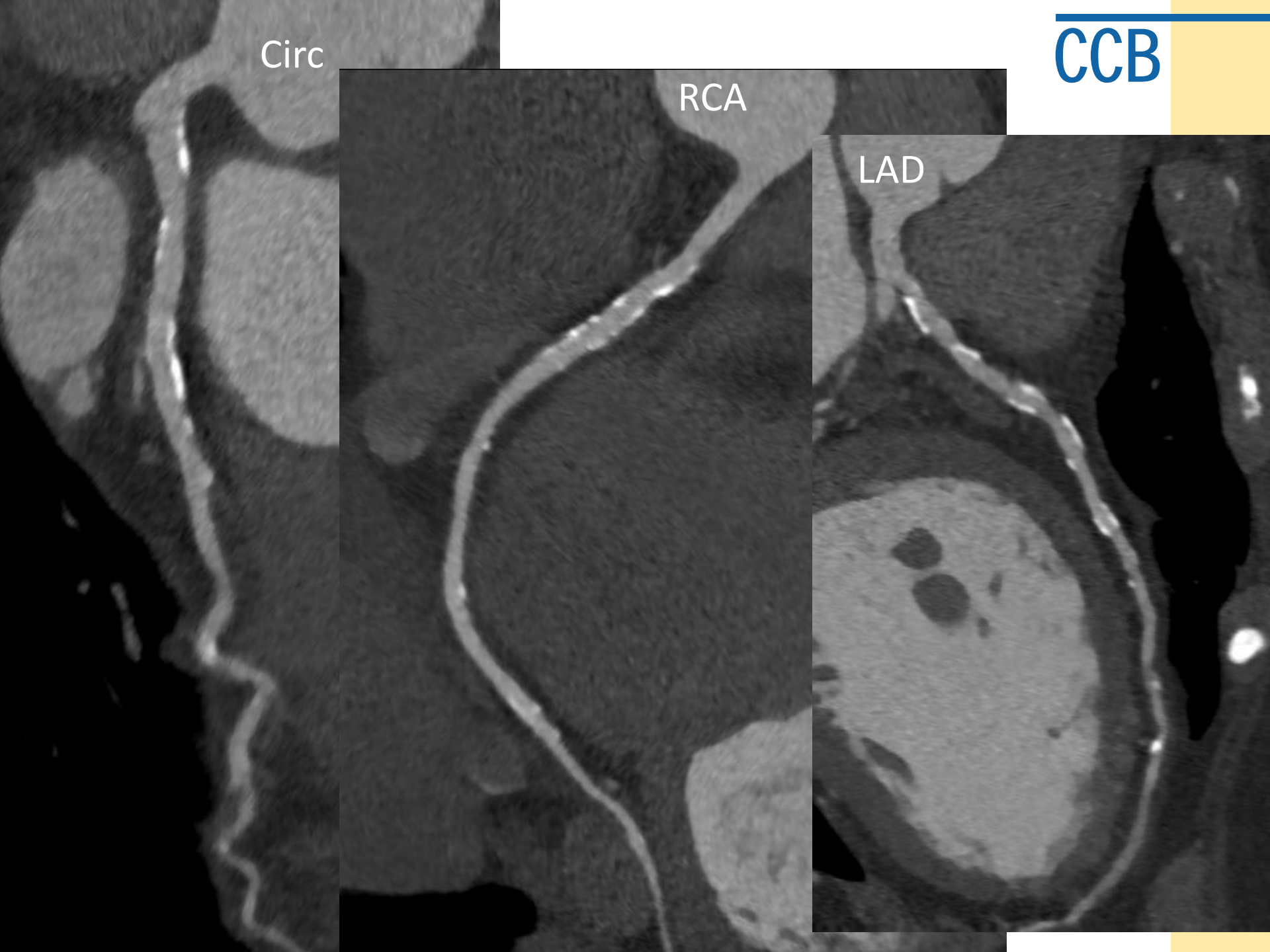
	Scan	kV	mAs / ref.	CTDIvol* mGy	DLP mGycm
Patientenposition H-SP					
Topogramm	1	100	34 mA	0.08 L	1.9
Fl_CaSc	2D	120	80	1.33 L	20.4
Kontrast					
TestBolus	3	80	30	1.02 L	1.0
Last scan no.	4				
Kontrast					
Fl_CorCTA	5D	70	450	1.26 L	19.4



Circ

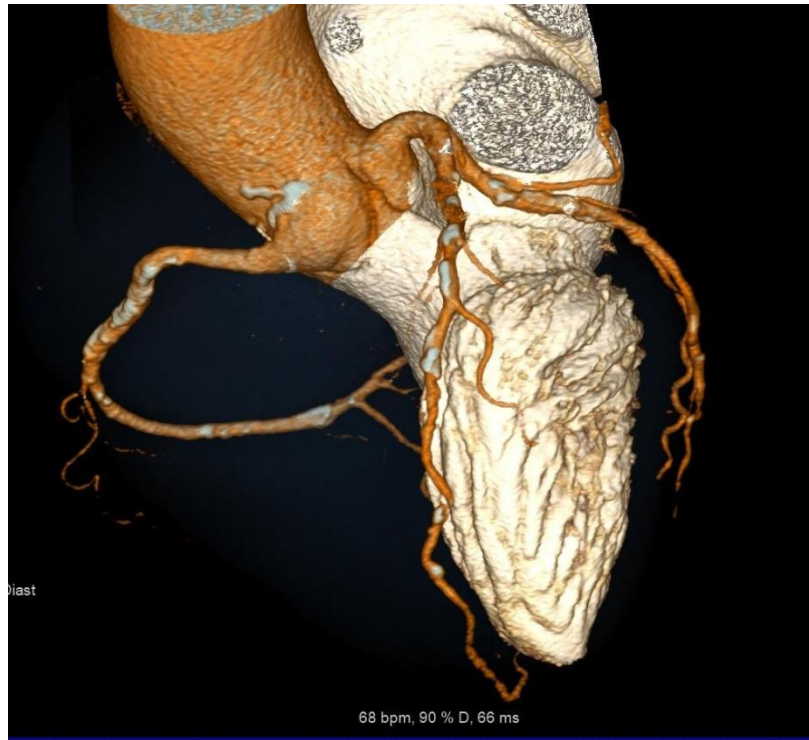
RCA

LAD



Kardio-CT - Force

Nichtinvasive Koronarangiografie



82-jährige Patientin, VHF, HF ca. 70/min
Agatston Kalkscore > 1600

Spiral mode, 90 kV

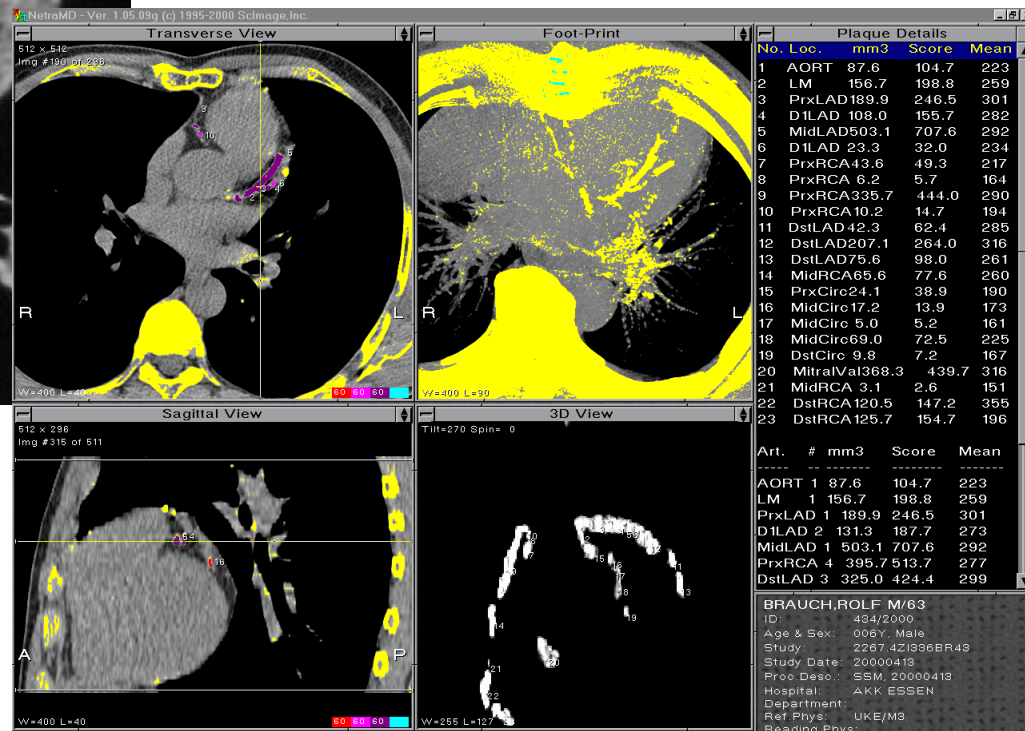
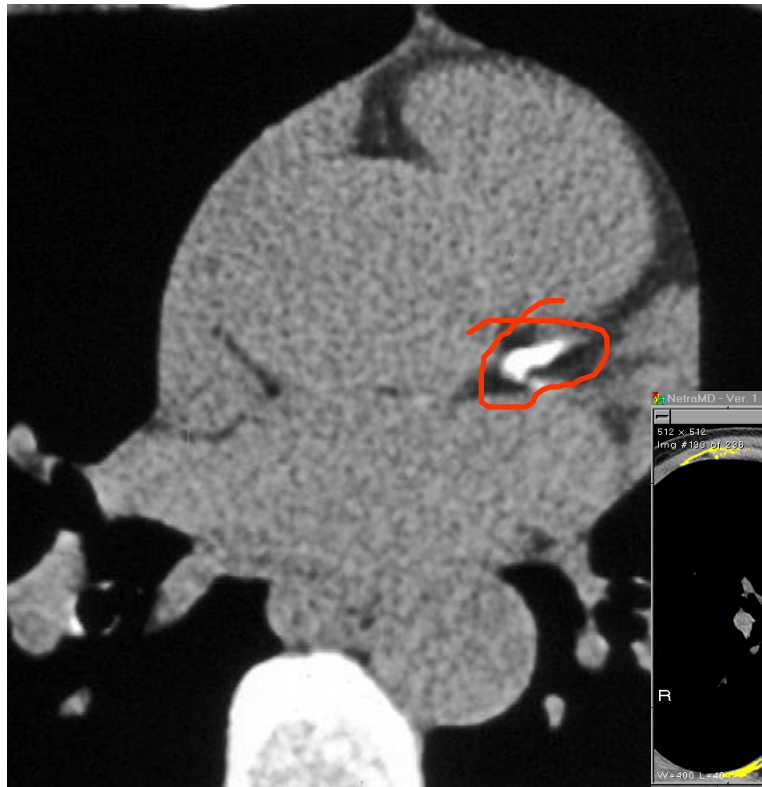
Kardio-CT - Force

Rolle in der Risikostratifizierung (Primärprävention)?

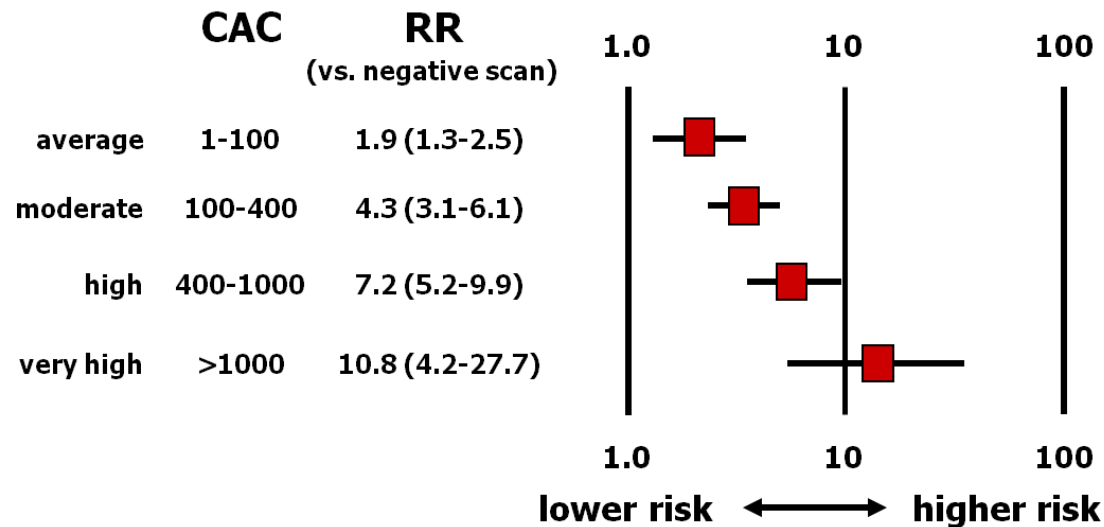
Tab. 1 Empfehlungen

Fragestellung	Bewertung MR	Bewertung CT
1 Koronare Herzerkrankung		
<i>1.1 Risikoabschätzung asymptomatischer Individuen</i>		
1.1.1 Screening	K Keine Indikation zur MRT	K Keine Indikation zur CT
1.1.2 Stratifizierung nach Bestimmung der Risikofaktoren	K Keine Indikation zur MRT	I3 Indikation zum koronaren Kalknachweis mittels CT als mögliche weitere Risikostratifizierung bei Patienten mit einem intermediären KHK-Risiko (10–20% Ereignisrisiko in den nächsten 10 Jahren gemäß Framingham). Zahlreiche Studien zur prognostischen Bedeutung des Koronarkalknachweises mittels CT und zur Überlegenheit im Vergleich zu traditionellen Risikofaktoren [1, 2, 3, 4, 5, 6, 7] K Keine Indikation zum Kalknachweis bei hohem oder niedrigem KHK-Risiko K Keine Indikation zur CT-Angiographie der Koronararterien

Kardio-CT - Koronarkalk



Kardio-CT - Koronarkalk



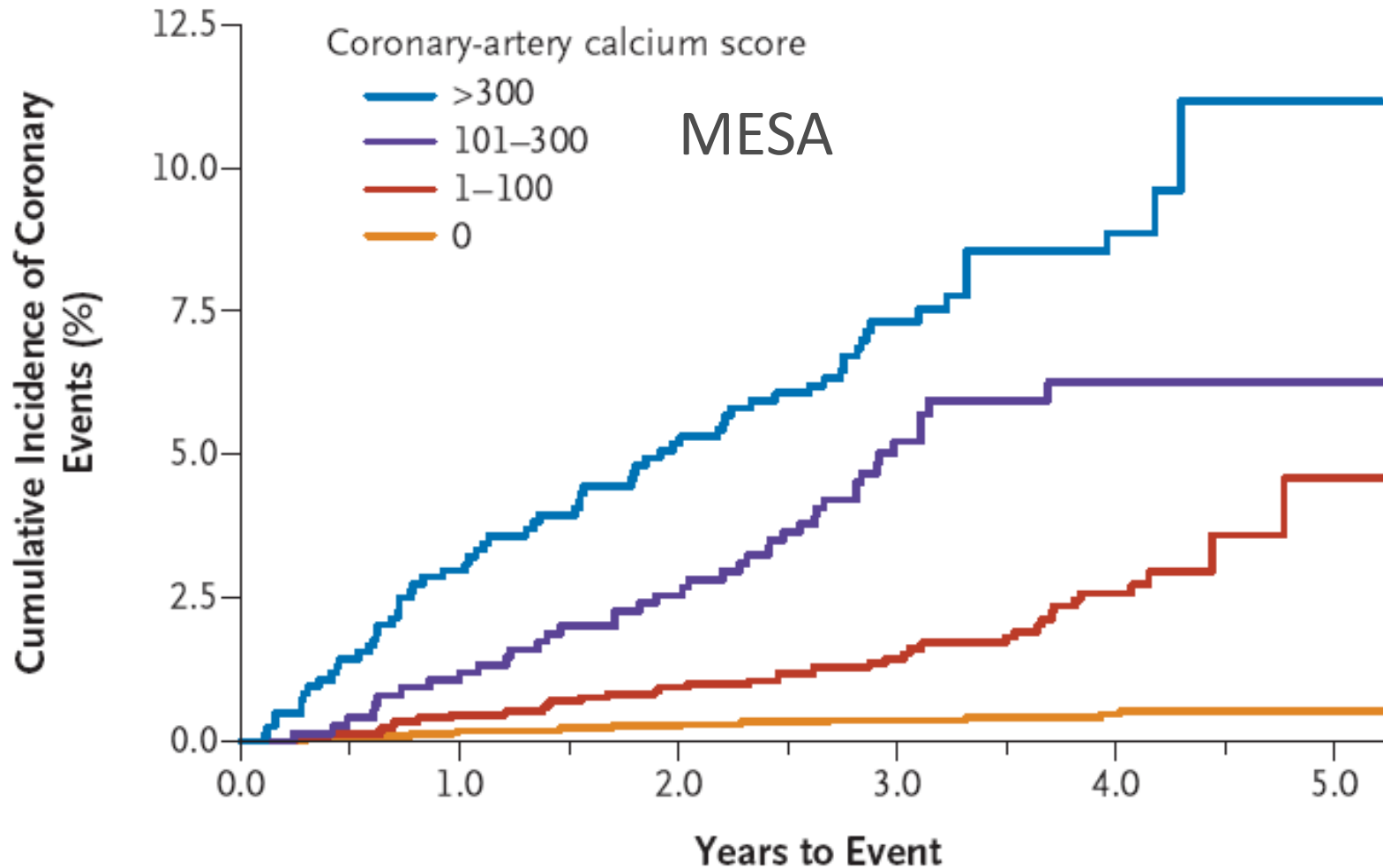
Studies included (n=25.789):

Kondos et al.	Chicago	Circ '03
Greenland et al.	South Bay	JAMA '04
Arad et al.	St. Francis	JACC '05
La Monte et al.	Cooper Clinic	AmJEpi '05
Taylor et al.	PACC-Project	JACC '05
Vliegenthardt et al.	Rotterdam	Circ '05

Inclusion criteria:

- data not published in the 2000 ACC document
- data on prognostic value of CAC in **asymptomatic cohorts since 2002**
- outcome reported on **CHD death or MI** during follow-up
- must allow for **calculation of RRR**
- must include **risk-adjustment** for established RF / Framingham Score

Kardio-CT - Koronarkalk



- ♥ 4.814 Männer/Frauen, 45 - 75 Jahre, unselektiert (Bochum, Essen, Mülheim/Ruhr)
- ♥ Messung von
 - Risikofaktoren (a) klassisch, (b) neu („mögliche“), c) psychosozial
 - Ruhe-EKG, Bel.-EKG
 - Karotis Intima-Media Dicke
 - Knöchel-Arm Index
 - Koronarkalk (EBT)
- ♥ Beobachtung initial über 5 Jahre, aktuell ~ 15 Jahre
- ♥ Primäre Endpunkte: Herztod, Myokardinfarkt
- ♥ Ziel: *Zusätzliche Wertigkeit der Methoden im Vergleich mit den kausalen (klassischen) Risikofaktoren*

Universitätsklinik Essen: Kardiologie, Epidemiologie & Biometrie, Labormedizin, Endokrinologie

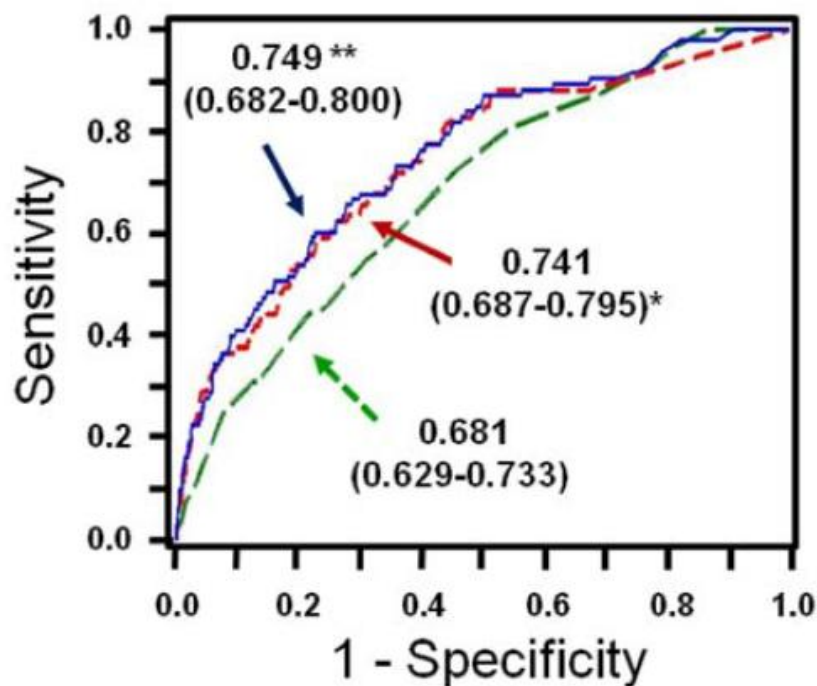
Universität Witten/Herdecke: Radiologie

Universität Düsseldorf: Sozialmedizin

Kardio-CT - Koronarkalk

A

--- FRS (continuous)
--- log(CAC+1)
--- FRS + log(CAC+1)

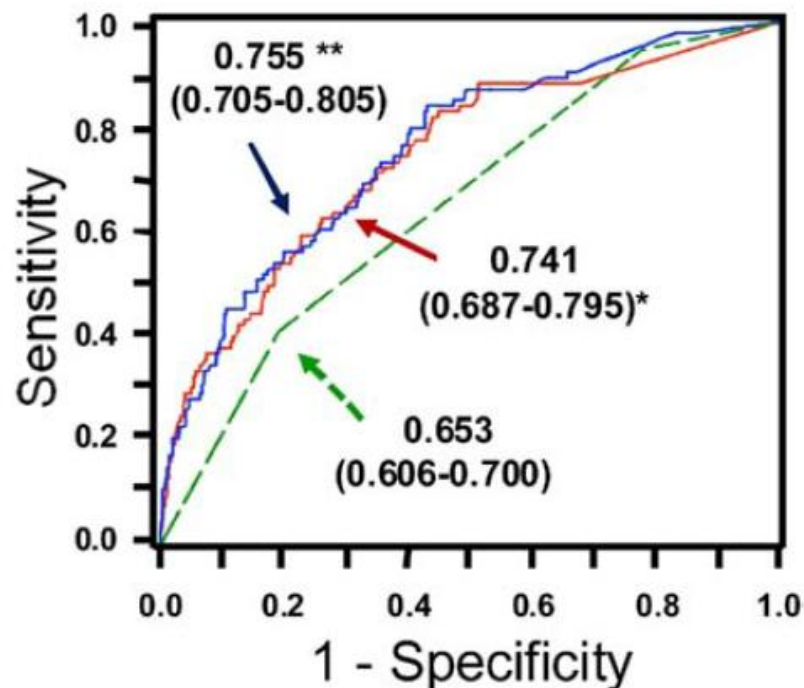


** : $p=0.003$ versus FRS

* : $p=0.046$ versus FRS

B

--- ATPIII categories
--- log(CAC+1)
--- ATPIII cat. + log(CAC+1)



** : $p=0.0001$ versus ATPIII categories

* : $p=0.003$ versus ATPIII categories

61-jähriger Mann, Teilnehmer *Heinz Nixdorf Recall Studie*

Vorstellung in Studie wegen Köln-Marathon (4:28h, 6. Wettkampflauf) verschoben

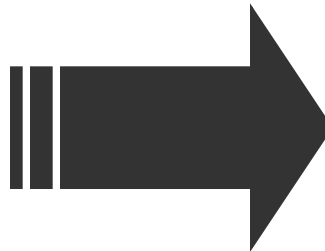
3 Tage nach dem Lauf:

- BMI 23 kg/m²
- Bekannte art. Hypertonie (Rx mit HCT & Losartan)
- LDL-Cholesterin 82 mg/dl, HDL 51 mg/dl
- Familienamnese leer
- Lipoprotein(a) 14,2 mg/dl

TABLE 3. Coefficients of PROCAM Scoring Scheme

Age, y	
35-39	0
40-44	6
45-49	11
50-54	16
55-59	21
60-65	26
LDL cholesterol, mg/dL	
<100	0
100-129	5
130-159	10
160-189	14
≥190	20
HDL cholesterol, mg/dL	
<35	11
35-44	8
45-54	5
≥55	0
Triglycerides, mg/dL	
<100	0
100-149	2
150-199	3
≥200	4
Smoker	
No	0
Yes	8
Diabetes mellitus	
No	0
Yes	6
MI in family history	
No	0
Yes	4
Systolic blood pressure, mm Hg	
<120	0
120-129	2
130-139	3
140-159	5
≥160	8

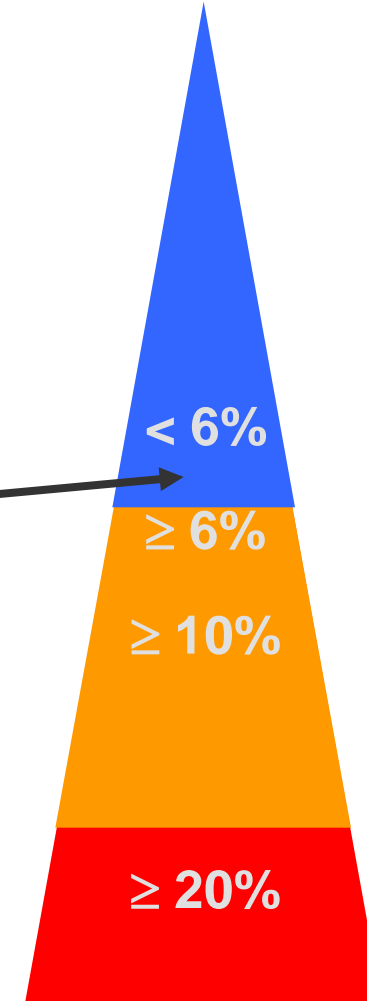
Procam (Münster Heart Study)

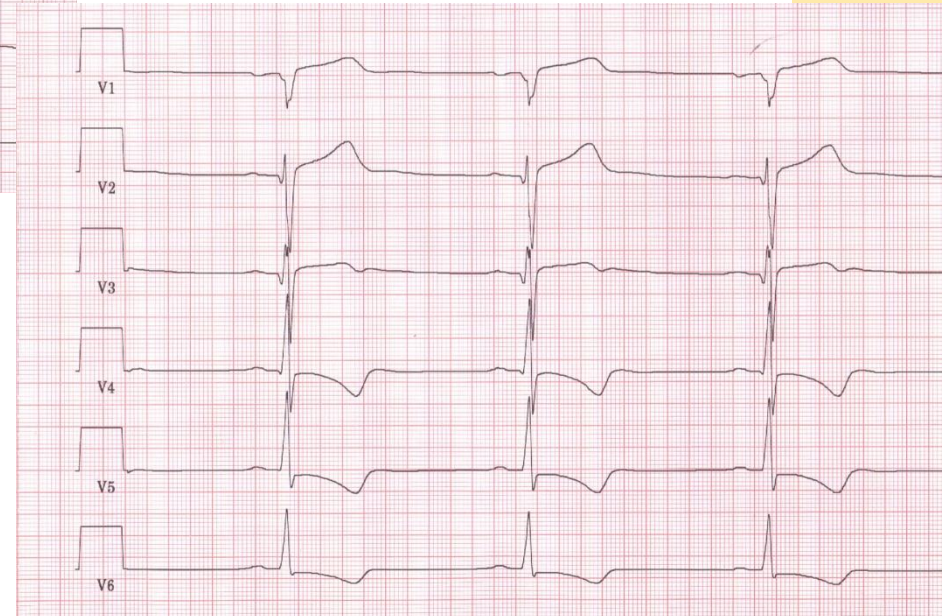
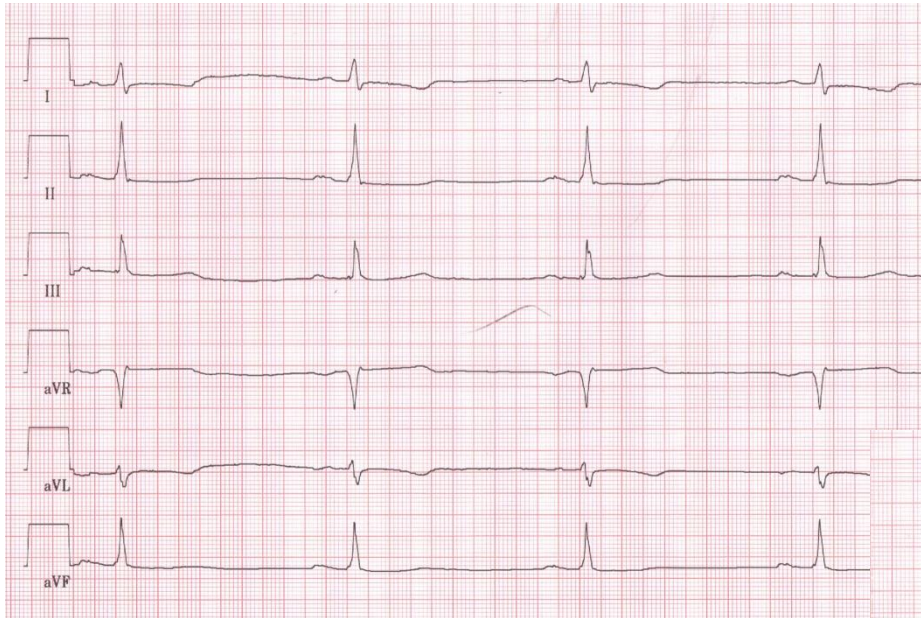


- 5.389 Männer
- 35 - 65 Jahre
- 10 Jahre F/U
- 325 "harte" Ereignisse

5,7%

10-J. Risiko



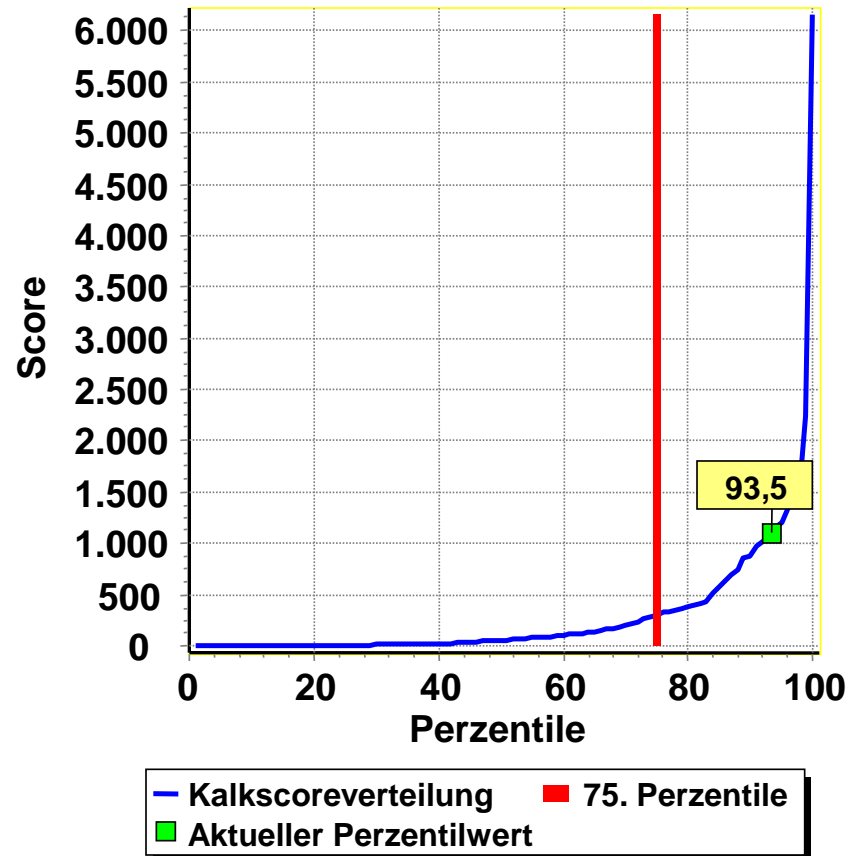


CK: 64 U/l

Trop I: 3,7 ng/ml



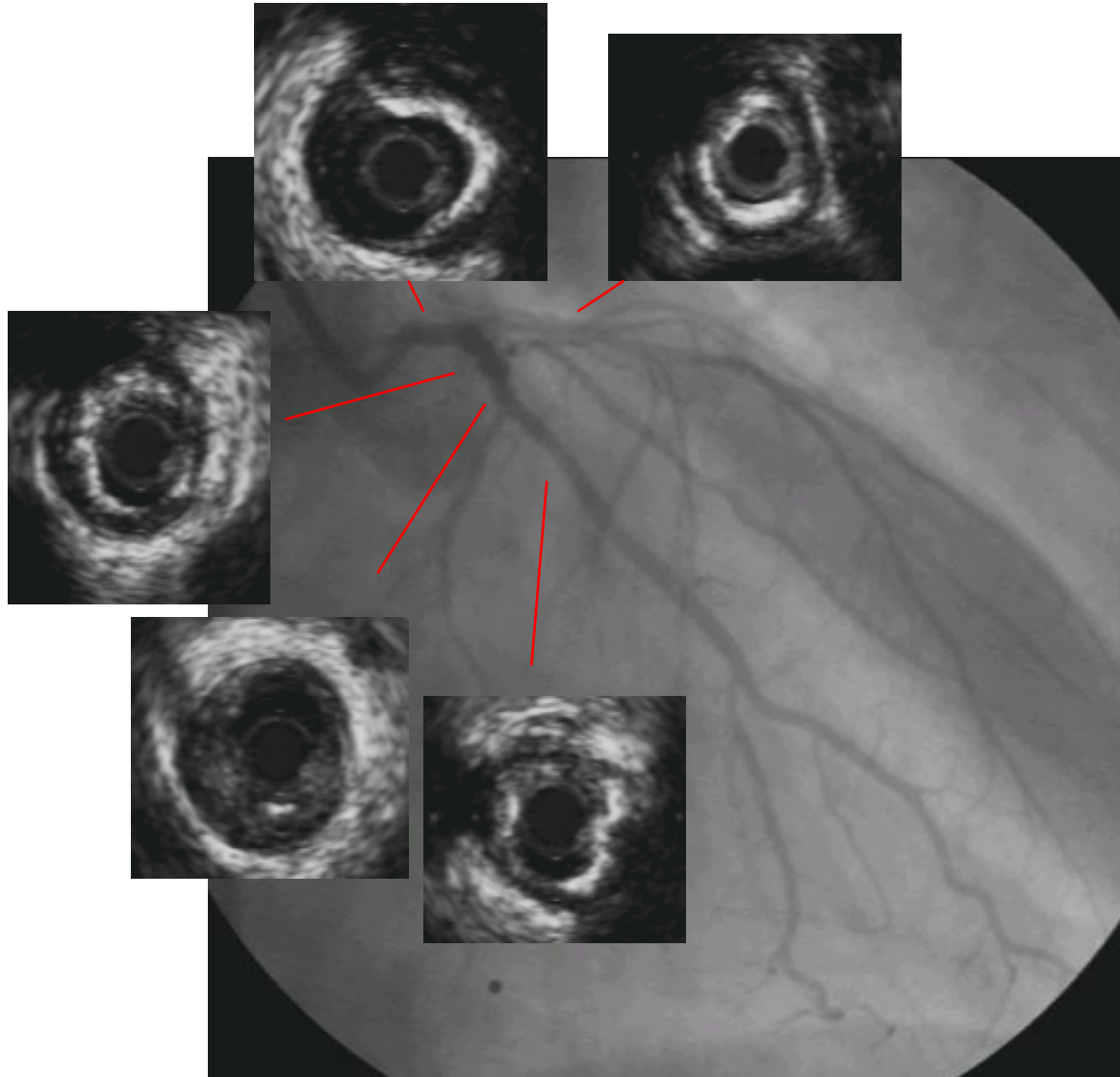
Kalkscoreverteilung - (61 Jahre, Männer)



Gesamtscore: 1105

Perzentile: 93,5

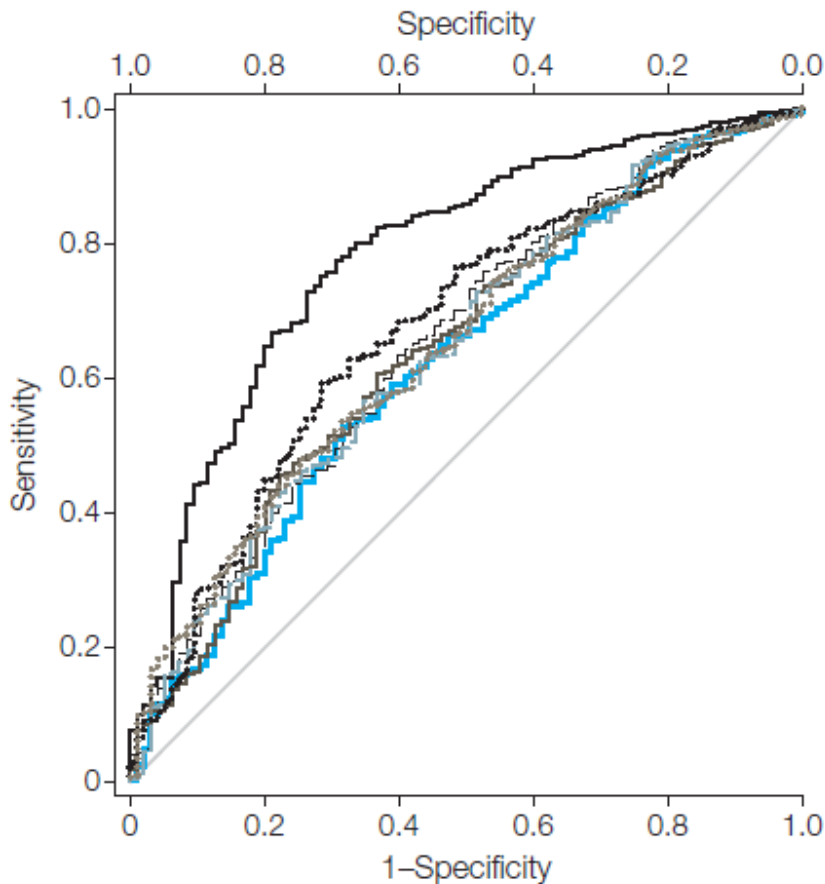
Heinz Nixdorf Recall Studie



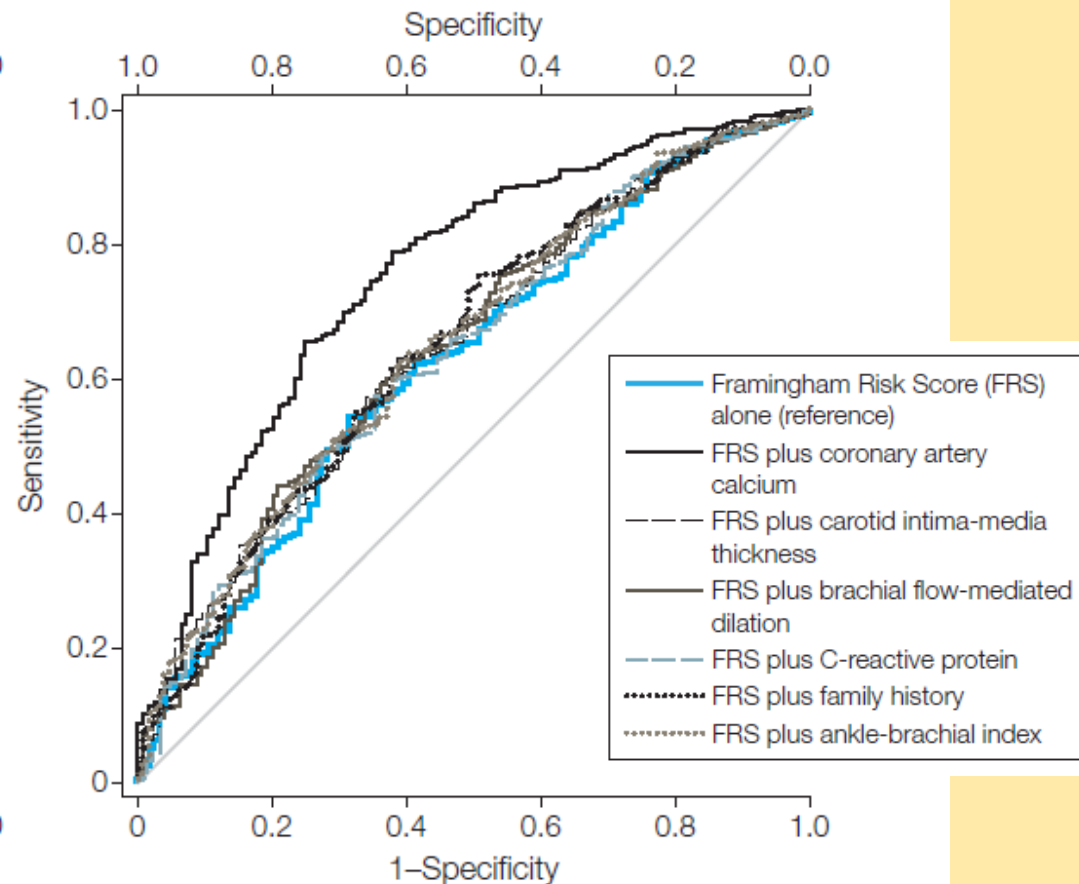
Koronarkalkbestimmung

MESA Studie, 1330 Pers. / intermed. Risiko, FRS < 5% bis <20%

A Incident coronary heart disease

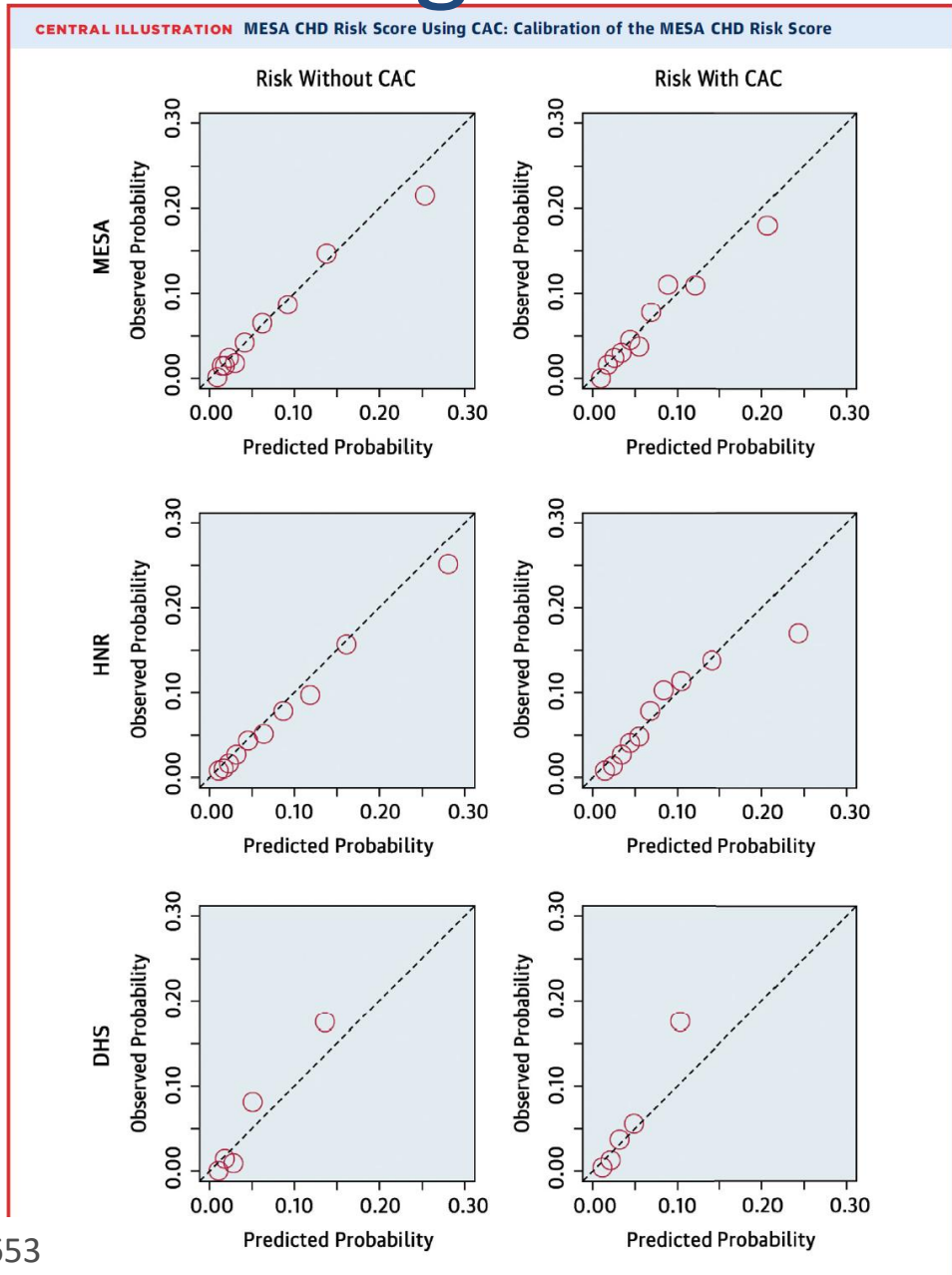


B Incident cardiovascular disease



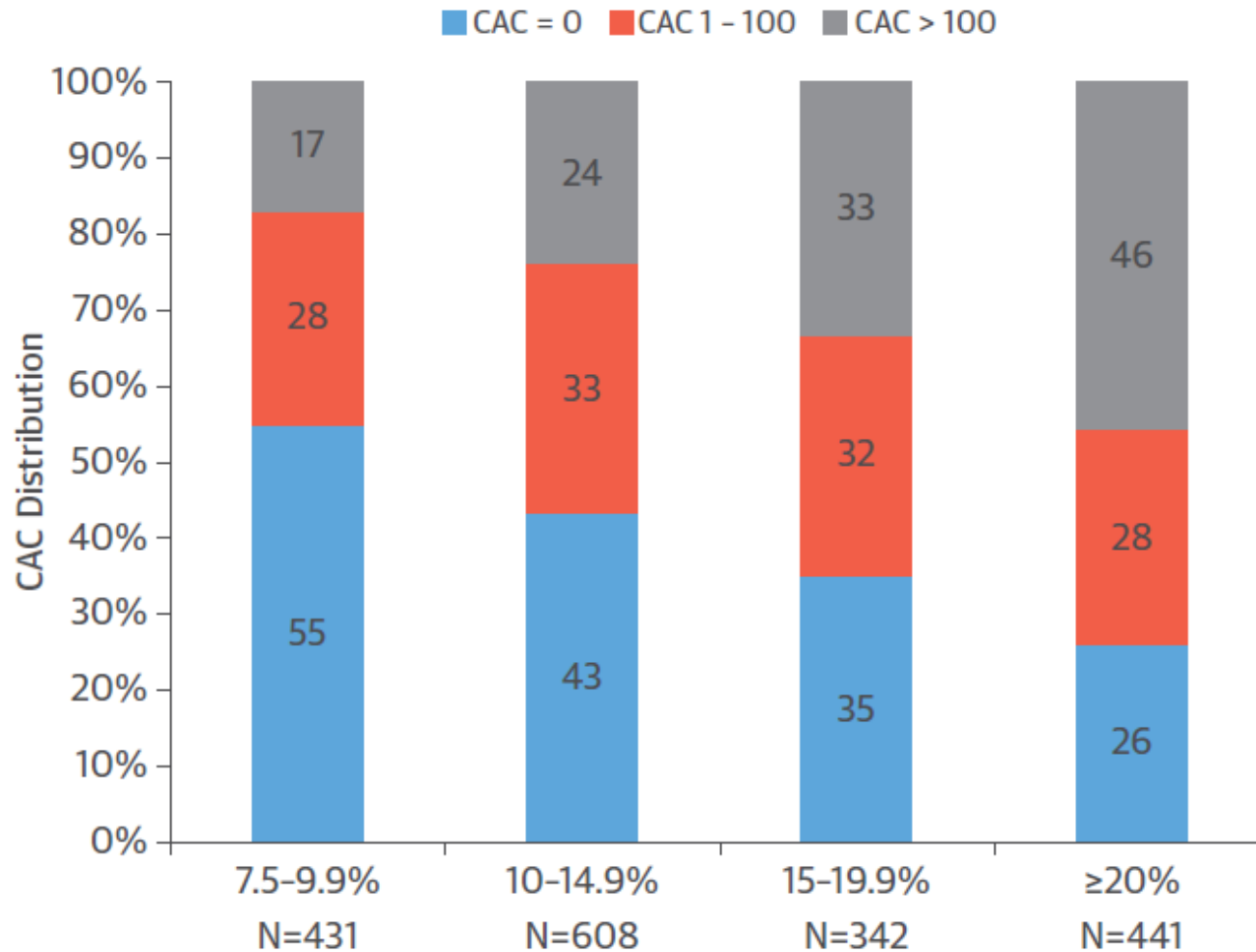
Koronarkalkbestimmung

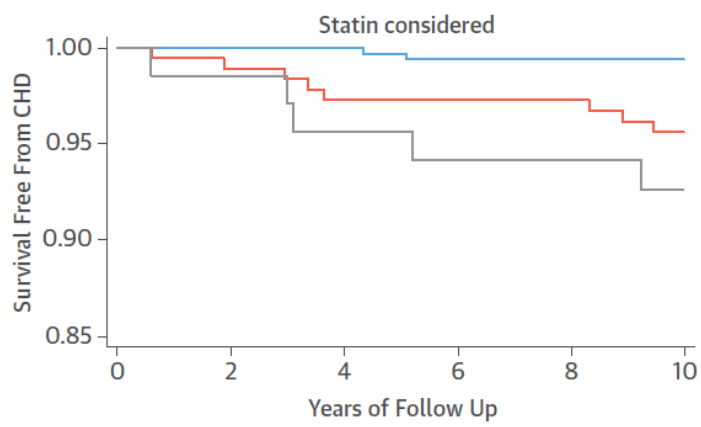
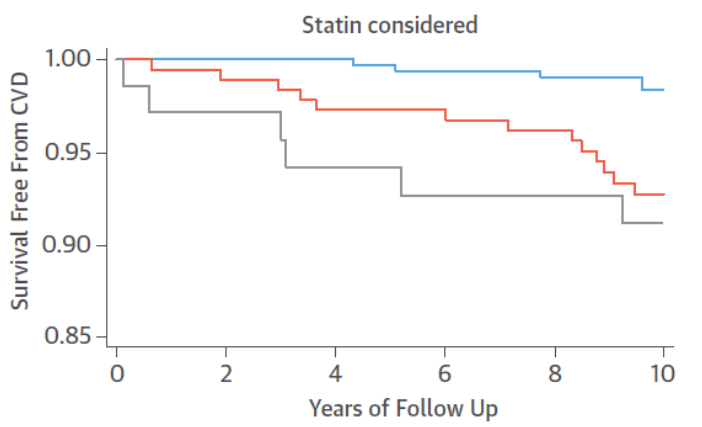
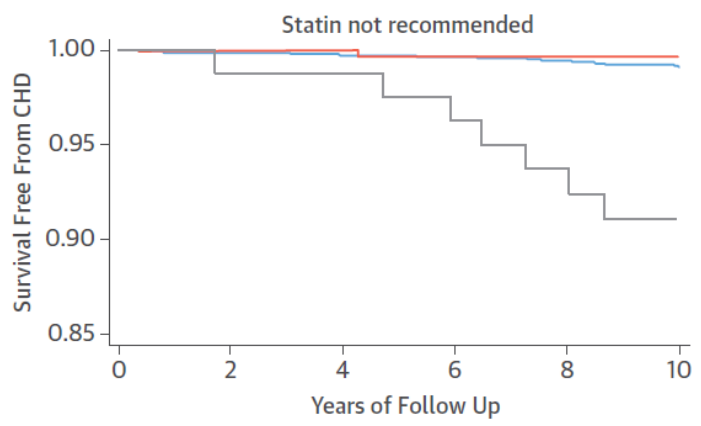
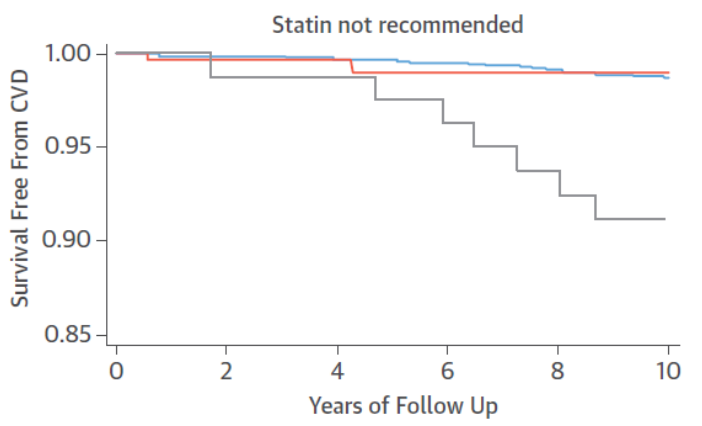
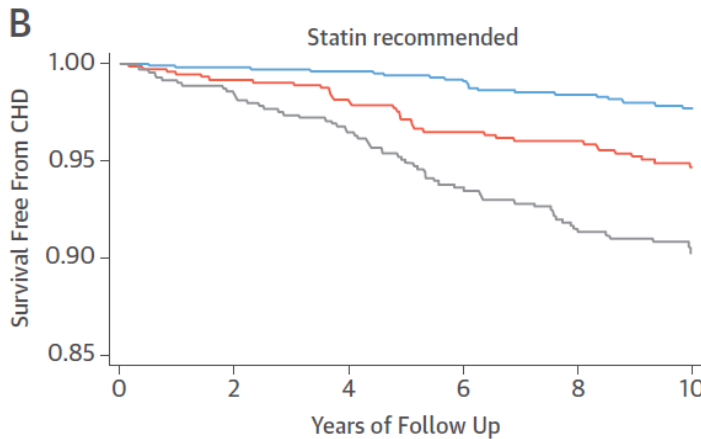
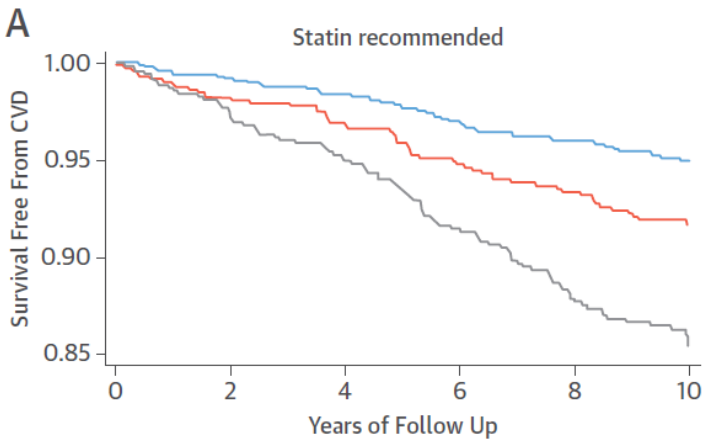
„proof of principle“



Koronarkalkbestimmung

„proof of principle“





— CAC = 0 — CAC 1 - 100 — CAC > 100

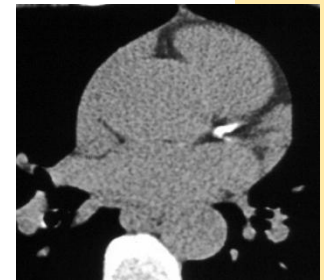
Risikoprädiktion



- Anamnese, Untersuchung
- Gesamtrisiko (*ESC Score, FRS*) – ASCVD
- Zusätzliche RF (Diabetes, Fam-anamnese)

a) Risikokonstellation klar
(hoch - niedrig):
Therapieentscheidung

b) Risiko unklar: Bildgebung
(Kardio-CT Kor.kalk)



Wunsch des Patienten, Umfeld, Möglichkeiten

Patientin, 54 Jahre, inst. Angina

