Low coronary risk calculator based detection rates of old arteries in middle-aged women at recommended decision thresholds

From the Arteris database of the Vascular Risk Foundation

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www.varifo.ch
www.arteris.ch

Background

Absence of major cardiovascular risk factors at age 40

delays the first occurrence of morbidity and decreases the risk for multi-morbidity.

Favorable Cardiovascular Health, Compression of Morbidity, and Healthcare Costs Forty-Year Follow-Up of the CHA Study (Chicago Heart Association Detection Project in Industry)

1. **Do we detect elevated risk early enough?**
2. **Is there a gender discrimination?**
3. **Should we use AGLA or SCORE risk estimates?**
4. **Do we have a problem with diagnostic discrimination?**
5. **Are risk cutoffs appropriately calibrated?**

Background

A clinician's **preventive efficacy** is dependent on **meaningful sensitivity** and specificity thresholds of cardiovascular risk equations in order to **identify subjects at increased risk** for cardiovascular events.

A **"present time" assessment of the accuracy** of coronary risk calculators has been derived from patients admitted for a first myocardial infarction.

A **low sensitivity** for cardiovascular events was found in the **Copenhagen General Population** Study (Mortensen, EHJ 2015), where 767 fatal and non-fatal cardiovascular events occurred over an observation time of 7 years. Sensitivity at the 5% SCORE level was 26%.

Similarly (Selby, Preventive Medicine, 2015), **AGLA** at the 20% level was found to have a **sensitivity of 24%** to detect subjects with a hospitalisation due to an acute coronary syndrome.

Background

Advanced carotid **atherosclerosis** has a **relevant prevalence** across age groups in women.

CH women aged 40-65: number needed to image 1:11 for arterial age > 70

Extensive carotid atherosclerosis and the diagnostic accuracy of coronary risk calculators

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TPA80	Age Group	CH		DE	
		N	%	N	%
Women	40-55	18	4.5	27	4.4
	56-65	60	14.0	45	25.7
	66-75	78	36.3		

Methods

We assessed the **prevalence of old arteries (70 years or more**, AA70) in 3'248 healthy subjects in Switzerland and in Germany aged **between 40 and 65** years.

We **compared sensitivity** and specificity of **PROCAM / AGLA and SCORE** coronary risk calculators **to detect AA70** for two decision thresholds.

Subjects were assessed at the practice based level as described elsewhere (1). In the Swiss Imaging Center in Olten, subjects were **referred by their primary care physician** (58%) or **self-referred** to the vascular risk foundation (42%). In the German Center in Koblenz, all subjects were referred within a **working medicine** setting.

(1) Romanens M, Ackermann F, Sudano I, Szucs T, Spence JD. Arterial age as a substitute for chronological age in the AGLA risk function could improve coronary risk prediction. Swiss Med Wkly. 2014;1–7.

Methods

Subjects had to be **free of cardiovascular symptoms or disease** and not currently being treated for high blood pressure or cholesterol. Laboratory values, blood pressure and medical history were assessed locally.

Burden of **longitudinal carotid plaque surface** was imaged with a high resolution ultrasound linear transducer probe (7.5–12.0 MHz), which identified plaques with intimal thickening ≥1.0 mm

Large carotid Plaque

Plaque surface is 23 mm²
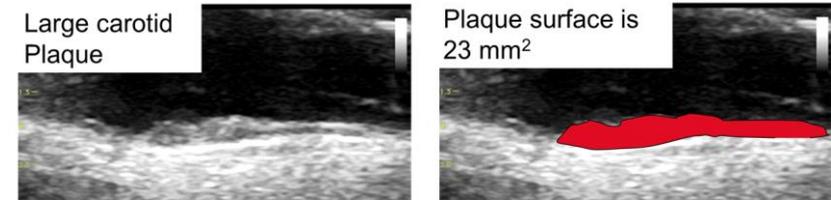
Total Plaque Area is the sum of all plaques from both sides

Methods

Figure 1: Measurement of TPA by surface, for this plaque 23 mm^2

Large carotid Plaque

Plaque surface is 23 mm^2
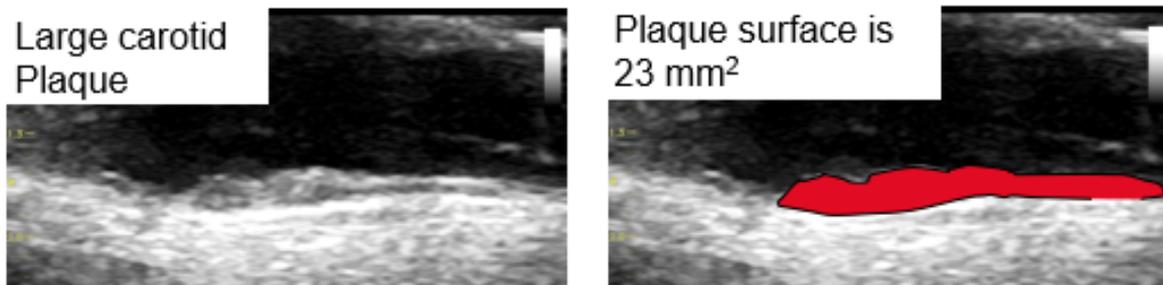
Plaque area of 23 mm^2 corresponds to an arterial age of 34 years in men and 43 years in women. AA70 corresponds to a total plaque area of 108 mm^2 in men and 66 mm^2 in women. This represents high risk atherosclerosis: AA70 = 96th percentile for men (SENS 9%, SPEC 97%) and 95th percentile for women (SENS 18%, SPEC 95%) in the Tromso study (N=6'226, FU 6 years, 297 myocardial infarctions during FU (2). Bayes posttest risk for 4% AGLA: 11% in men, 13% in women, for 10% AGLA: 25% in men and 29% in women.

Results

Table 1: Group 1 (AA ≥ 70) compared with group 2 (AA <70)

	Group 1	Group 2	p=
Number of subjects (N)	394	2854	
Female, N, %	144, 37%	1175, 41%	0.0800
Age women (mean ± SD)	57.0 ± 5.8	51.6 ± 6.7	< 0.0001
Age men (mean ± SD)	55.5 ± 5.6	50.5 ± 6.4	< 0.0001
Arterial age women (mean ± SD)	79.2 ± 7.9	35.8 ± 16.4	< 0.0001
Arterial age men (mean ± SD)	76.9 ± 6.4	39.5 ± 16.6	< 0.0001
Family history for CAD (N, %)	93, 24%	588, 21%	< 0.0001
Current smoker (N, %)	153, 39%	614, 22%	< 0.0001
Blood pressure, mm Hg mean ± SD	132 ± 18	124 ± 15	< 0.0001
TPA mm2 mean ± SD	131 ± 51	28 ± 26	< 0.0001
Cholesterol, mmol/l, mean ± SD	6.4 ± 1.6	6.0 ± 1.1	< 0.0001
HDL, mmol/l, mean ± SD	1.4 ± 0.4	1.5 ± 0.4	= 0.0001
LDL, mmol/l, mean ± SD	4.2 ± 1.1	3.8 ± 0.9	< 0.0001
Triglycerides, mmol/l, mean ± SD	1.7 ± 1.1	1.6 ± 1.1	= 0.0043
PROCAM (% ± SD)	9.9 ± 9.6	4.4 ± 5.5	< 0.0001
SCORE (% ± SD)	2.6 ± 2.1	1.2 ± 1.3	< 0.0001

Legend: AA= arterial age, CAD = coronary artery disease, TPA = total carotid plaque area

Results

Table 2: Sensitivity and Specificity for AA70 („old arteries") according to PROCAM, AGLA, and SCORE, by sex

Switzerland

AGLA 10%

	Female	Male
SENS	**6** (2 - 14)	30 (21 - 41)
SPEC	99 (97 - 99)	87 (84 - 89)

SCORE 5%

	Female	Male
SENS	**5** (1 - 12)	18 (11 - 28)
SPEC	99 (98 - 100)	94 (92 - 96)

Germany

PROCAM 10%

	Female	Male
SENS	**8** (3 - 18)	56 (48 - 64)
SPEC	99 (98 - 100)	83 (81 - 86)

SCORE 5%

	Female	Male
SENS	**0** (0 - 6)	16 (10 - 22)
SPEC	100 (99 - 100)	98 (97 - 99)

Results

**Table 2: Sensitivity and Specificity for AA70 („old arteries")
according to PROCAM, AGLA, and SCORE, by sex**

Switzerland

	AGLA 4%	
	Female	**Male**
SENS	33 (23 - 44)	72 (61 - 82)
SPEC	92 (90 - 94)	57 (53 - 61)
	SCORE 2%	
SENS	33 (23 - 44)	76 (65 - 85)
SPEC	89 (86 - 92)	59 (56 - 63)

Germany — **PROCAM 4%**

	Female	**Male**
SENS	21 (12 - 33)	86 (80 - 91)
SPEC	94 (92 - 96)	50 (47 - 53)
	SCORE 2%	
SENS	10 (4 - 20)	65 (58 - 73)
SPEC	97 (95 - 98)	79 (77 - 82)

Discussion

According to AGLA (www.agla.ch), the **presence of atherosclerotic plaques in the carotid artery is a very high risk finding (≥40% 10 year risk for myocardial infarction)** and should be treated accordingly.

We present a **well validated way to quantify carotid plaques** using longitudinal surfaces of all plaques found in both carotid arteries.

Based upon previous work, quantified plaques can be translated into arterial age.

Romanens M, Ackermann F, Sudano I, Szucs T, Spence JD. Arterial age as a substitute for chronological age in the AGLA risk function could improve coronary risk prediction. Swiss Med Wkly. 2014;1–7.

A **reduction of AGLA/PROCAM to an intermediate risk threshold of 4%** instead of 10% (SCORE to 2% instead of 5%) yielded acceptable sensitivity with acceptable specificity in women (**Number needed to image 1:11**, women 40-65, CH).

Lower risk thresholds identify especially more women with high risk atherosclerosis aged 40-65 years.

Using **Bayes theorem** for a prior of 4%, AA70 results in 11% AGLA risk in men and 13% in women, therefore **shifting patients from very low to intermediate risk.**

Low Cost Imaging
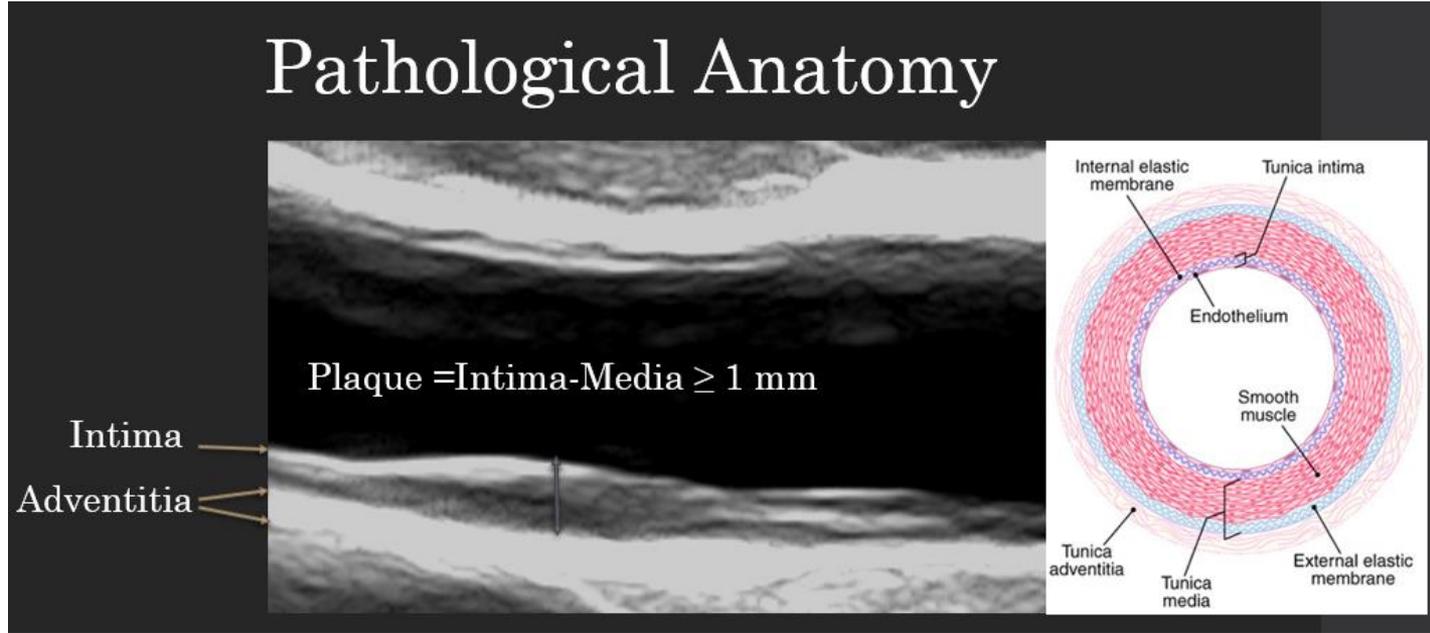
Transducer CHF 4'000, free software, immediate diagnosis

Conclusion

Lower decision thresholds for **women** to detect increased cardiovascular risk appears appropriate.
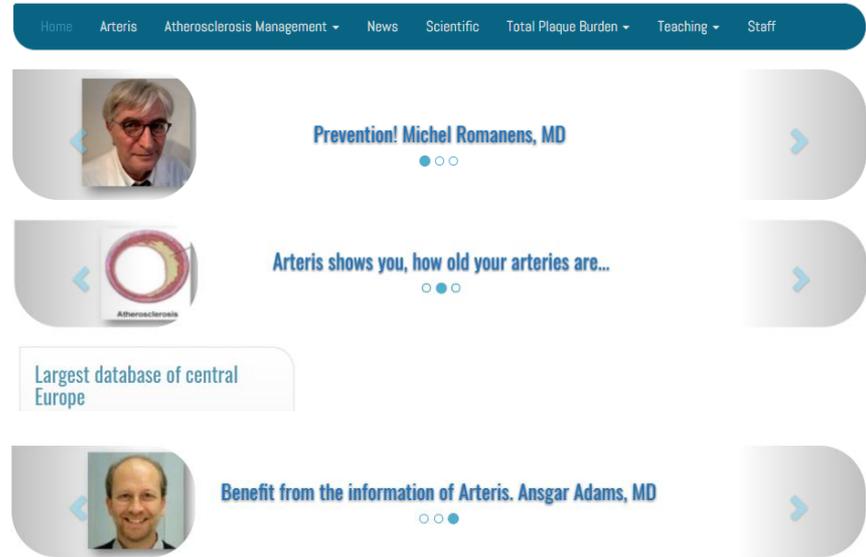
Women aged 40-65 years with AGLA of ≥ 4% may be adequate candidates for **lipid lowering interventions.**

Early detection of atherosclerosis can be achieved with a **low cost** and highly reproducible ultrasound machine.

Today, such technology is widely available and **may be used more frequently** in the future to **evidence and track** atherosclerosis.