Emerging Risk Modifiers Based on Atherosclerosis Imaging: Fancy Radiology or Simple Bedside Ultrasound?

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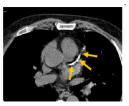
Introduction

Because of a relatively low sensitivity of coronary risk charts, such as PROCAM or SCORE, to detect subjects with future myocardial infarction, many new emerging risk factors are proposed to improve vascular risk prediction. However, little is known on the relative performance of different emerging risk factors. In this work we have the opportunity to present comparative data on atherosclerosis imaging in 430 consecutive practice based subjects having undergone a coronary calcium scan (CAC) and a quantification of carotid atherosclerosis (total plaque area of carotid arteries, TPA, www.tpainfo.ch). In order to achieve comparability of global risk calculators, e.g. PROCAM, and atherosclerosis imaging, risk estimates are calculated for 10 year coronary risk.

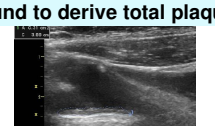
Methods

In 430 practice based subjects (211 with data on PROCAM and posttest risk based on atherosclerosis imaging; 350 subjects with CAC and TPA, 80 subjects with known vascular disease) we used a) sex matched sensitivities for TPA (Stroke 2007;38:2873) and CAC (J Am Coll Cardiol 2009;53:354) for further calculation of coronary risk, b) posttest risk (TPA-PTP and CAC-PTP, Kardiovaskuläre Medizin 2007;10:139 based on the Bayes formula) and c) diagnostic performance of TPA and CAC to detect subjects with known vascular disease, measured by the area under the curve (AUC).

Atherosclerosis imaging With Computed Tomography to detect coronary calcium



Atherosclerosis Imaging of Carotid Artery with www.tpainfo.ch Ultrasound to derive total plaque area



Calculator for posttest risk using the MESA Cohort (Budoff, JACC 2009)
These results are derived from the MESA study, with 3231 men and 3601 women
Mean observation time 3.8 years, incident myocardial infarctions: N=163
Posttest Risk Calculations are exemplified for a AGLA risk of 10%

CAC MEN			CAC WOMEN		
0	PRETEST PROBABILITY	0.100	0	PRETEST PROBABILITY	0.100
	SENSITIVITY	0.930		SENSITIVITY	0.830
	SPECIFICITY	0.400		SPECIFICITY	0.610
	RESULT	0.019		RESULT	0.030
1-100	PRETEST PROBABILITY	0.100	1-100	PRETEST PROBABILITY	0.100
	SENSITIVITY	0.930		SENSITIVITY	0.830
	SPECIFICITY	0.400		SPECIFICITY	0.610
	RESULT	0.147		RESULT	0.191
101-400	PRETEST PROBABILITY	0.100	101-400	PRETEST PROBABILITY	0.100
	SENSITIVITY	0.740		SENSITIVITY	0.480
	SPECIFICITY	0.700		SPECIFICITY	0.850
	RESULT	0.215		RESULT	0.262
>400	PRETEST PROBABILITY	0.100	>400	PRETEST PROBABILITY	0.100
	SENSITIVITY	0.380		SENSITIVITY	0.250
	SPECIFICITY	0.860		SPECIFICITY	0.950
	RESULT	0.232		RESULT	0.357

Results

350 asymptomatic practice based subjects aged 59±10 years (women: 31%) had a mean TPA of 57±55 mm2 and a mean CAC of 132±346. The percentile in quartiles distribution for TPA and CAC is presented in Table 1:

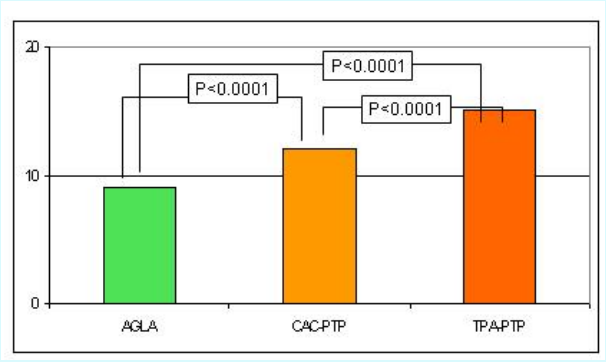
TPA Men		CAC Men	
Percentile		Percentile	
0th	0.000 (minimum)	0th	0.00 (minimum)
25th	18.000 (1st quartile)	25th	0.00 (1st quartile)
50th	42.800 (median)	50th	14.00 (median)
75th	83.708 (3rd quartile)	75th	127.00 (3rd quartile)
100th	383.000 (maximum)	100th	3057.00 (maximum)

TPA Women		CAC Women	
Percentile		Percentile	
0th	0.00 (minimum)	0th	0.0 (minimum)
25th	17.00 (1st quartile)	25th	0.0 (1st quartile)
50th	37.55 (median)	50th	0.5 (median)
75th	75.90 (3rd quartile)	75th	84.2 (3rd quartile)
100th	261.60 (maximum)	100th	3211.0 (maximum)

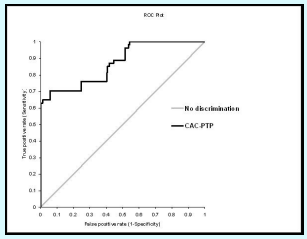
Kappa agreement was 0.23 (p<0.0001) for quartiles of TPA and CAC, with 49 (14%) of subjects exhibiting the 3. or 4. quartile of TPA, but having the 1. quartile CAC and 29 (9%) of subjects exhibiting the 3. or 4. quartile of CAC but the first quartile of TPA (Pearson's X2 statistic 5.8, p=0.016, Table 2).

	CAC quartiles				
TPA quartiles	1	2	3	4	Total
1	40	13	18	11	82
2	48	11	21	12	92
3	29	10	27	22	88
4	20	9	15	44	88
Total	137	43	01	09	350

In 211 subjects aged 58±10 years (women: 27%), 10 year coronary risk was assessed with AGLA and posttest risk calculations based on CAC (CAC-PTP) and TPA (TPA-PTP). Mean (+1SD) of 10 year risk estimates were 9%±8% for AGLA, 12%±15% for CAC-PTP, 15%±15% for TPA-PTP and are presented in Figure 1:



Using TPA-PTP, 54 subjects were classified as having a high coronary risk > 20% in 10 years. On ROC analysis, CAC-PTP showed an area under the curve of 87% (95% CI 81-93, p<0.0001, Figure 2). Sensitivity and specificity of CAC-PTP was 65% and 94% respectively, to detect 10 year risk≥20% as defined by TPA-PTP.



AUC of TPA and CAC to detect 80 subjects with known vascular disease (76 CAD, 4 TIA or Stroke, 18 women) was 63% and 70% respectively, p=0.058.

Discussion

The principle finding of this study is the potential of CAC-PTP to underestimate true coronary risk when compared to TPA-PTP: more subjects had significant amounts of atherosclerosis in carotid arteries, which were underestimated by coronary calcium scores. Further, the increase of posttest risk when compared to AGLA was statistically significant both for CAC-PTP and TPA-PTP, but also statistically higher for TPA-PTP (15% 10 year risk) when compared to CAC-PTP (12% 10 year coronary risk). As can be expected from the literature, both CAC and TPA increase 10 year risk estimates in a significant portion of subjects. In our practice based group of subjects without known vascular disease, the pretest 10 year risk for myocardial infarction was low (9%), but intermediate for TPA-PTP (15%) and CAC-PTP (12%). Moreover, both CAC and TPA were able to identify 80 of 430 subjects with known vascular disease, with a non-significant trend to better performance for CAC (p=0.058).
All subjects were imaged in a primary care setting, therefore our results, which were assessed on a sex specific risk algorithm, appear to be valid both for men and women and in the setting of primary care.
Since a significant proportion of subjects with high TPA values but low CAC values were found, it appears prudent to first use TPA as a risk stratifier, before more costly and irradiating methods are used.

Conclusions

In our practice based sample with a high prevalence of subclinical atherosclerosis, CAC significantly underestimates cardiovascular risk and has no higher diagnostic ability to detect subjects with known vascular events when compared to TPA. Our simple bed side test outperformed CAC measurements in a primary care setting and should be used at the first place, if atherosclerosis imaging should be applied in a subset of subjects, in whom referring doctors feel the need for an additional coronary risk assessment. Using TPA first, it is likely, that risk is detected early and can be managed with more accuracy.