Progression of Coronary Artery Calcification is Associated with Long Term Cardiovascular in Hypertensive Patients

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Clinical use of serial assessment

- Serial assessment of CAC scores has been proposed as a simple non invasive method to track the progression of coronary artery disease
- Progression of CAC was suggested as:
  - A surrogate endpoint in interventional studies
  - A prognostic tool for future CV events

Soft (vulnerable) AS plaques can not be assessed!!

AIM

- Coronary artery calcification (CAC) is an independent predictor of cardiovascular (CV) events in hypertensive adults.
- The additive clinical value of serial CAC measurements over the baseline CAC score for risk stratification is not clear.
- We aimed to find whether CAC progression predicts long term CV events in hypertensive patients.

Methods

•The study group was a subgroup of 544 high-risk hypertensive patients who enrolled in 1995 to the calcification side arm study of the International Nifedipine Study Intervention as Goal for Hypertension Therapy (INSIGHT) that aimed to compare the effect of the calcium antagonist, nifedipine gastrointestinal therapeutic system, versus a diuretic on the progression of coronary calcification

•210 Mean age 64±5.6 years, 54% male

all were free of symptoms or known CV disease, had at least two CT scans one year apart and had available long-term follow-up .

Methods

- Progression of CAC was defined as the absolute change in CAC score between maximal score during follow-up and baseline score.
- Three categories of CAC progression were defined: Zero progression – was defined as "non-progressors", and progression below and above the median of maximal progression were defined as "slow progressors" and "rapid progressors" respectively.

	Non prog	Slow prog	Rapid prog	P value
Male gender n(%)	31 (43)	43(55)	40(68)	0.014
Age (years)	62 ±5.0	64 ±5.4	65± 6.2	0.002
Body Mass Index (kg/m2)	29 ±4.7	29 ±4.2	29 ±5.1	0.861
Smokers n(%)	13 (18)	16 (21)	15 (25)	0.561
Diabetes n(%)	25 (34)	28 (36)	18 (31)	0.800
Hypercholesterolemia n(%)	38 (52)	37 (47)	19 (32)	0.062
Proteinuria n(%)	0	6 (8)	7 (12)	0.015
LVH n(%)	41 (56)	48 (61.5)	39 (66)	0.504
SBP (mm/Hg)	164 ±16	164± 18	168 ±17	0.304
Diastolic blood pressure (mm/Hg)	94 ±8.1	93 ±8.1	94± 8.3	0.729
Heart rate (beats/min)	73 ±10	73 ±9	74 ±9	0.602
Total Cholesterol (mg/dl)	234 ±43	235± 37	237 ±49	0.914
Serum Glucose (mg/dl)	122 ±42	120 ±43	123 ±44	0.923
Triglycerides (mg/dl)	170 ±82	152 ±61	185 ±124	0.111
Creatinine (mg/dl)	0.97 ±0.16	1.00 ±0.23	1.00 ±0.25	0.275
EGFR (mi/min)	73 ±16	73 ±17	75 ±21	0.784

	Non	Slow	Rapid	P
CAC prevalence n (%)	23 (31.5)	64 (82)	59 (100)	<0.001
Total calcium score (mean ±SD)	79 ±360	77 ±194	299 ±401	<0.001
Maximal increase in total calcium score	79 ±358	111 ±201	589 ±459	<0.001
Annual increase in total calcium score	0	14 ±14	154 ±124	<0.001

64 patients had no CAC at baseline , among them:

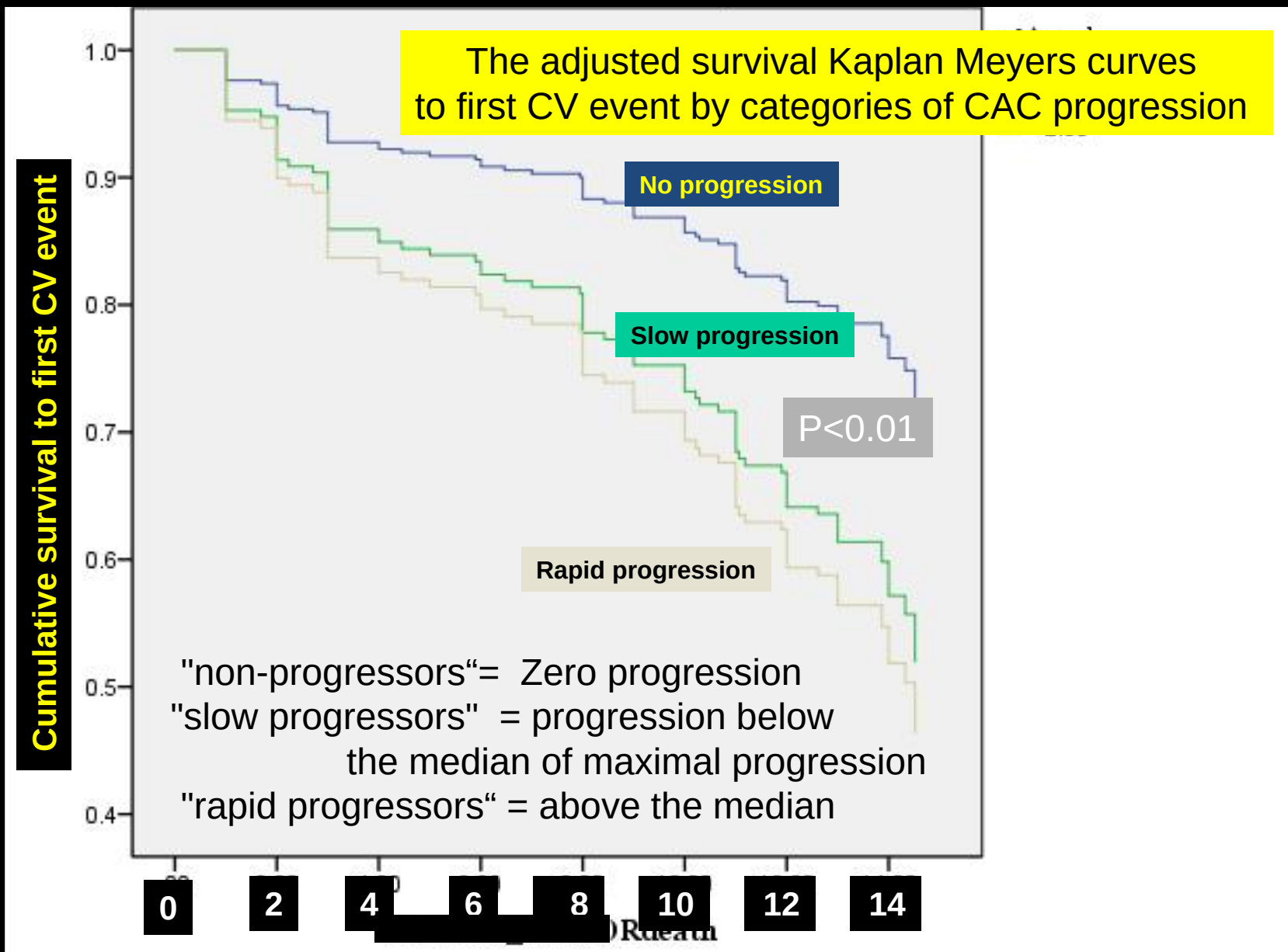
50 (78%) did not developed new calcifications on repeated CT scan after 3 years

12 (19%) developed only minimal spotty lesions with TCS<10

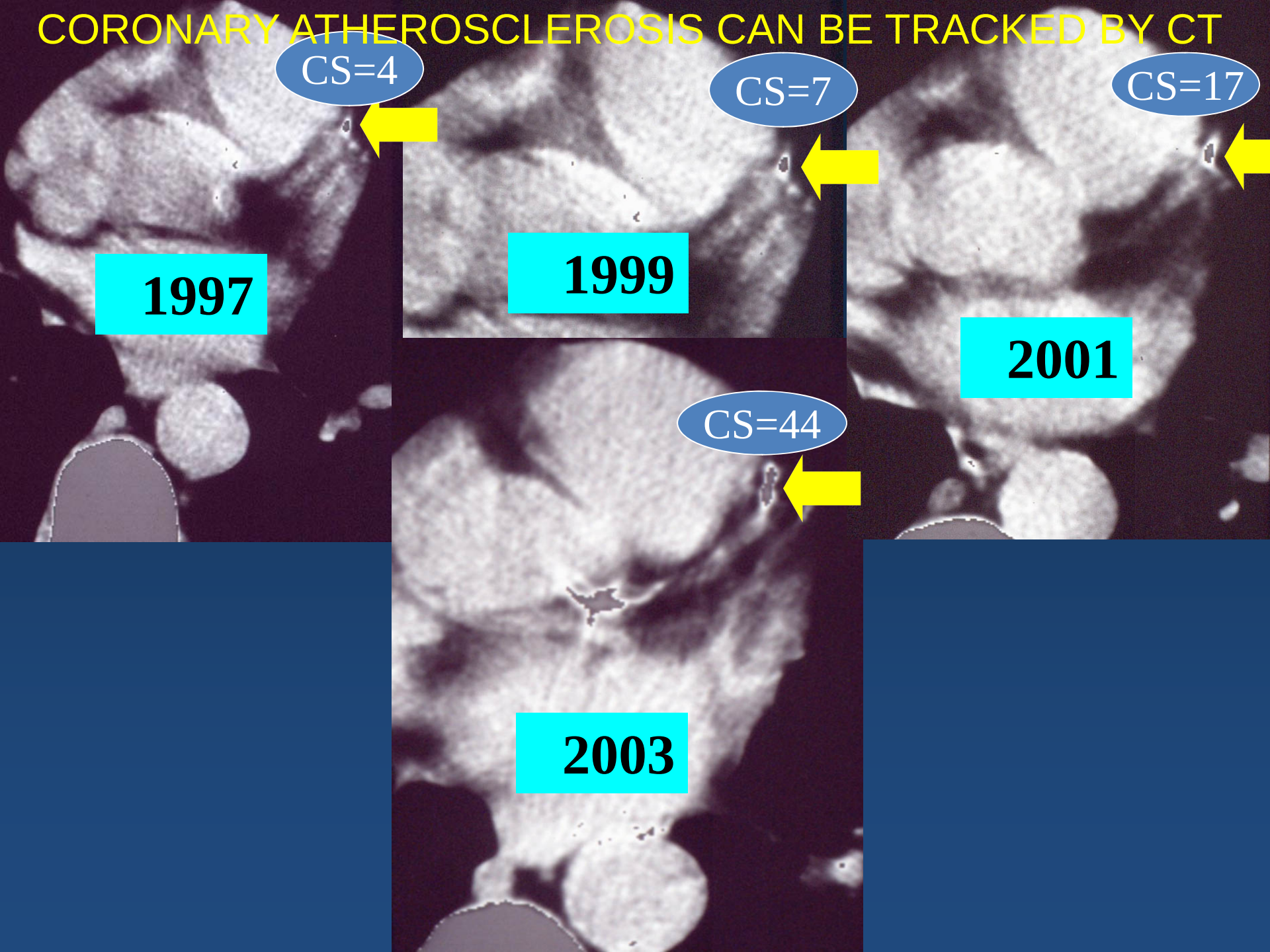
2 (3%) patients had TCS<30 score units.

Hazard Ratio for cardiovascular events by Annual progression

	No prog N=73	Slow prog N=78	Rapid prog N=59	P
Total event rate	18 (25%)	36 (46%)	29 (49%)	0.005
Unadjusted HR	1.0	2.18 (1.24-3.84)	2.66 (1.47-4.80)	<0.001
Age, gender and total calcium score adjusted	1.0	2.08 (1.17-3.71)	2.19 (1.17-4.12)	0.024
Multivariate adjusted*	1.0	1.91 (1.05-3.47)	2.13 (1.12-4.03)	0.047


The adjusted survival Kaplan Meyers curves to first CV event by categories of CAC progression
Cumulative survival to first CV event
1.0
0.9
0.8
0.7
0.6
0.5
0.4
No progression
Slow progression
P<0.01
Rapid progression
"non-progressors"= Zero progression
"slow progressors" = progression below the median of maximal progression
"rapid progressors" = above the median
0
2
4
6
8
10
12
14

CORONARY ATHEROSCLEROSIS CAN BE TRACKED BY CT



Conclusions

- Progression of CAC can be assessed by ungated CT.
- Rapid progression of CAC is associated with long term increased risk of CV events, in hypertensive patients.

CAC PROGRESSION: what we have learned

- CAC progression is faster in patients with CAD.
- "Calcium Begates Calcium": Baseline CAC is the most powerful predictor of CAC progression
  (Hyo-Chun Yoon et al Radiology 2002)
- **Calcific plaques are not the main target of treatment** (*Nicholls SJ et al J Am Coll Cardiol 2007)*
- Annual progression of CAC does not appear to be a suitable surrogate end point for treatment trials in patients with CVD and CKD.

  (McCullough PA et al Arch Intern Med 2009)

Does serial measurements of CAC contributes to CV risk assessment?

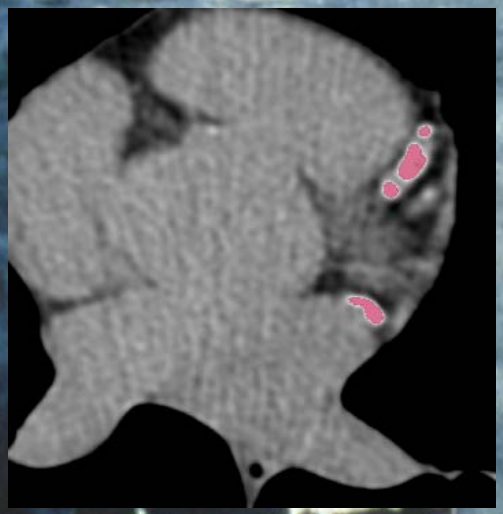
- The additive clinical value of serial CAC measurements for risk stratification should be further studied and several main questions have not been resolved:
  - Who can benefit?
  - When to repeat ?
    - 3 years when TCS>0 ?
    - 5 years in the absence of CAC
  - Incremental prognostic value over baseline TCS? – Yes m/p
  - The accuracy of low dose scan for tracking CAC ?

CAC PROGRESSION and all cause mortality

Progression of CAC predicts all cause mortality:

- 4,609 consecutive asymptomatic individuals
- Average inter-scan time 3.1 years.
- Conclusion: "The CAC progression added incremental value in predicting all-cause mortality over baseline score, time between scans, demographics, and CV risk factors."

(Budoff MJ et al JACC Cardiovascular Imaging 2010)



Coronary Calcium
for Sub-clinical CAD

THANK YOU

Coronary Artery Calcification and Change in Atheroma Burden in Response to Established Medical Therapy

Nicholls SJ et al J Am Coll Cardiol 2007:49:263-70

- Retrospective analysis of 776 pts, participants in the REVERSAL and CAMELOT studies Investigates the relationship between the degree of plaque calcification and both atheroma burden and its rate to progression in response to use of systemic interventions to target established risk factors.
  - ***More calcified atheromas were resistant to change, either progression or regression.***
  - ***Conversely, less calcification was a sign of potential for significant changes over time, either progression or regression.***

Calcific plaques are not the most biologic active component of AS!