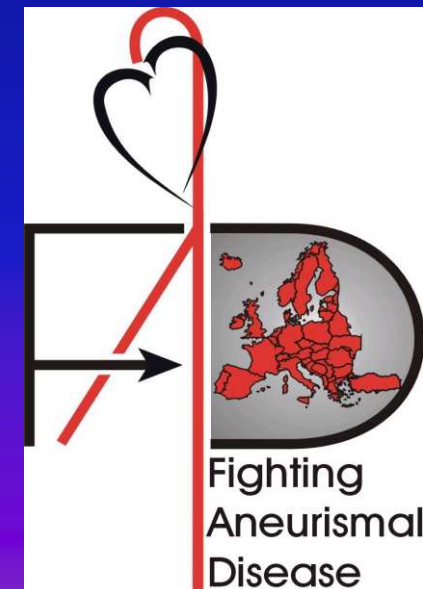


2nd International Meeting on Aortic Diseases: New insights into an old problem
Palais des Congrès, Liège, Belgium

Antiplatelet therapy to inhibit AAA growth rate

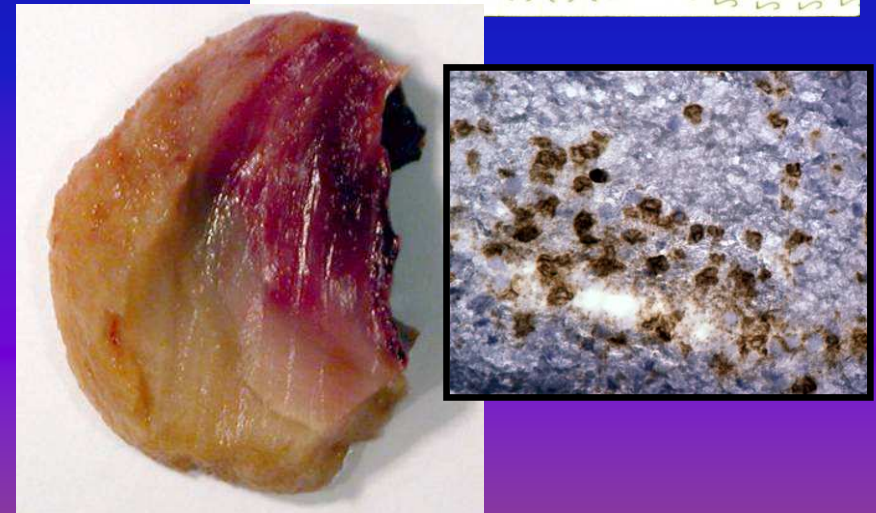


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The potential role of the intraluminal mural thrombus (ILT) by centrifugal convection

- The physiological mass transport in the aortic wall is mainly centrifugal filtration from lumen to adventitia
- Probably enhanced in AAA
 - high porosity of ILT
 - missing endothelium
 - elastin degradation
- The thrombus may thus have pathogenic effects through the interface between circulating blood and thrombus.
- If so, can it be inhibited by antiplatelets ?



Questions

- When does the ILT develop?
– a cause or caused by AAA?

VIVA trial (2008-)

- Does the ILT size depend upon low dose aspirin use?

VIVA trial (2008-)

- Does AAA growth rate and need for later repair depend upon use of low dose aspirin?

Viborg study (1994-05)

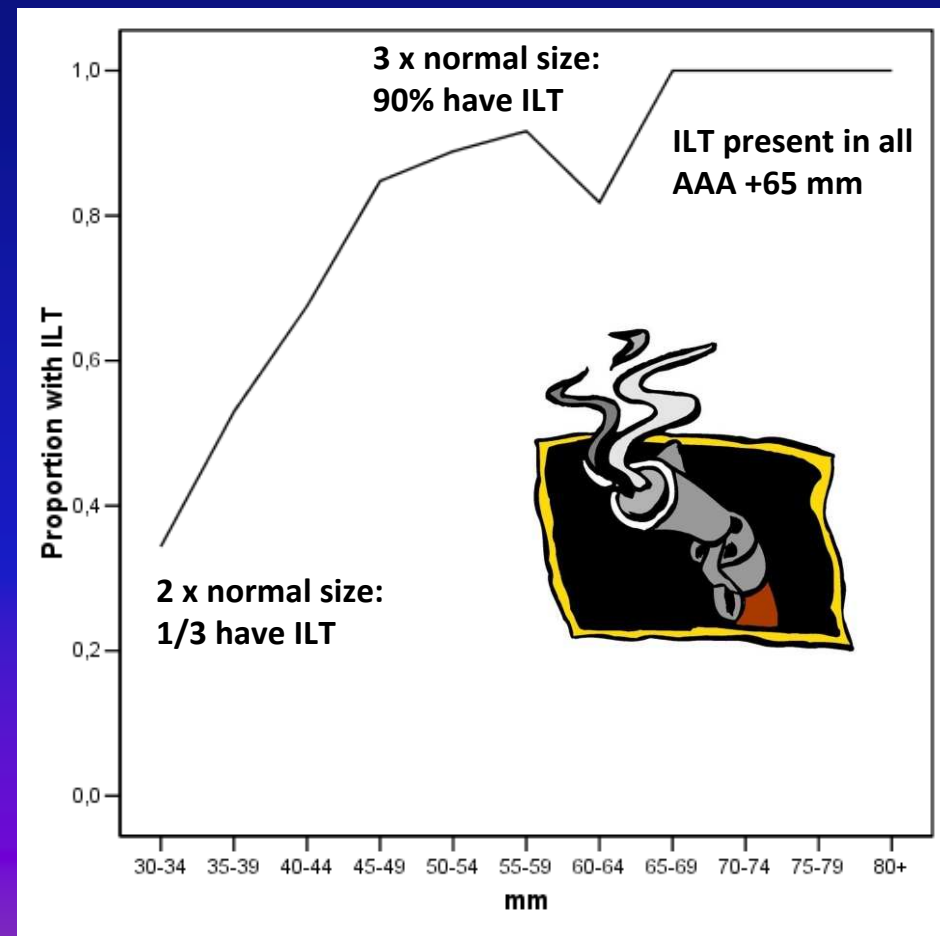
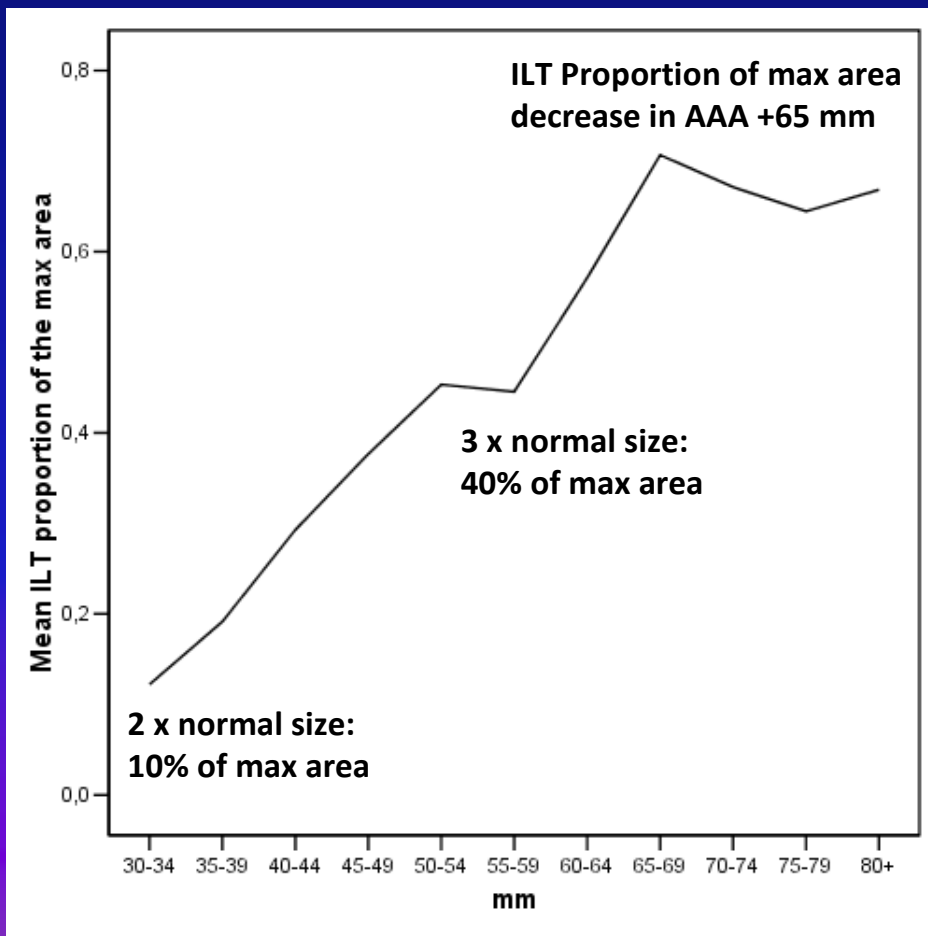
VIVA - Methods and preliminary results

- 51.330 65-74 yr men randomised 1:1 to vascular screening incl. AAA or being controls
- 25.665 to be invited
- 22.502 have been invited
- 16.928 attended (75%)
- 552 out of 16.887 had AAA (3.3%)
 - ≥ 3 cm in AP aortic diameter
 - ILT measurement at the max. AAA diameter:
 - Transverse view: Inner area/outer area by semi-automated technique

VIVA trial
AAA, PAD and hypertension



When does the mural thrombus develop ?



Does the size of the ILT depend upon low dose aspirin – use ?

	Use of Anti-platelets (n=220)	Mean	Std. Deviation	P-value
Maximal AAA diameter	No	38.77	7.19	0.54
	Yes	39.18	6.90	

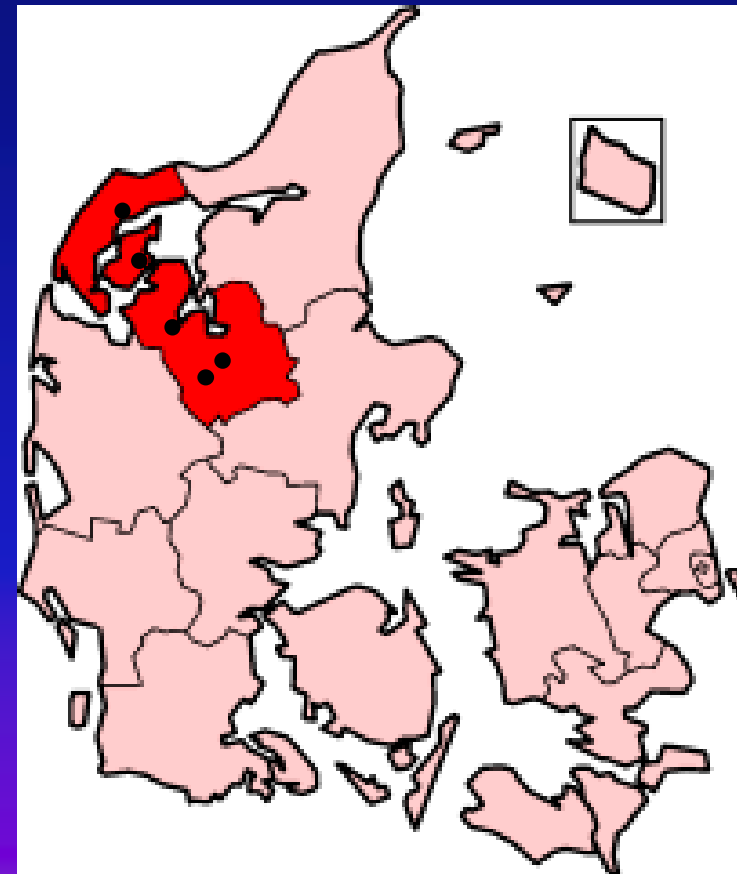
Does the size of the ILT depend upon low dose aspirin – use ?

	Use of Anti-platelets (n=220)	Mean	Std. Deviation	P-value
Maximal AAA diameter	No	38.77	7.19	0.54
	Yes	39.18	6.90	
ILT proportion of max. area	No	.24	.27	0.45
	Yes	.22	.28	

	Use of warfarin (n=41)	Mean	Std. Deviation	P-value
Maximal AAA diameter	No	38,88	7,00	0.63
	Yes	39,43	7,29	
ILT proportion of max. area	No	,23	,27	0.42
	Yes	,26	,30	

Does the AAA growth rate and need for later repair depend upon use of low dose aspirin ?

- Observational cohort study within a randomized screening trial.
- 1994-98: All 12,639 men aged 64-73 yr.
- Randomised 1:1
- 6,306 controls
- 6,333 invited to hospitalbased US screening (5 locations)
- April 1994 to March 2005 followed by
 - annual control scans (3-5 cm)
 - referred to surgical evaluation (+5 cm)



Does the AAA growth rate and need for later repair depend upon use of low dose aspirin ?

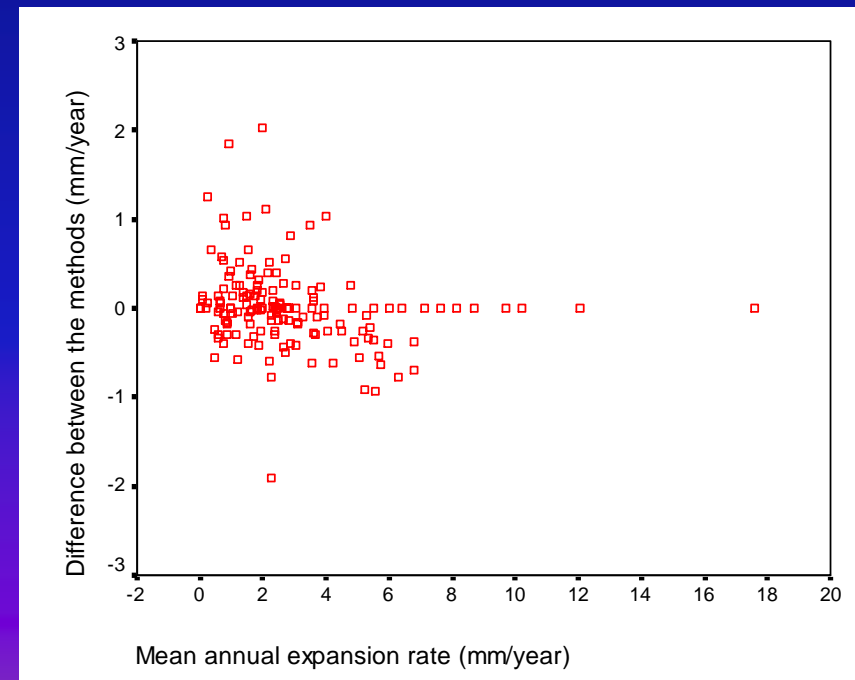
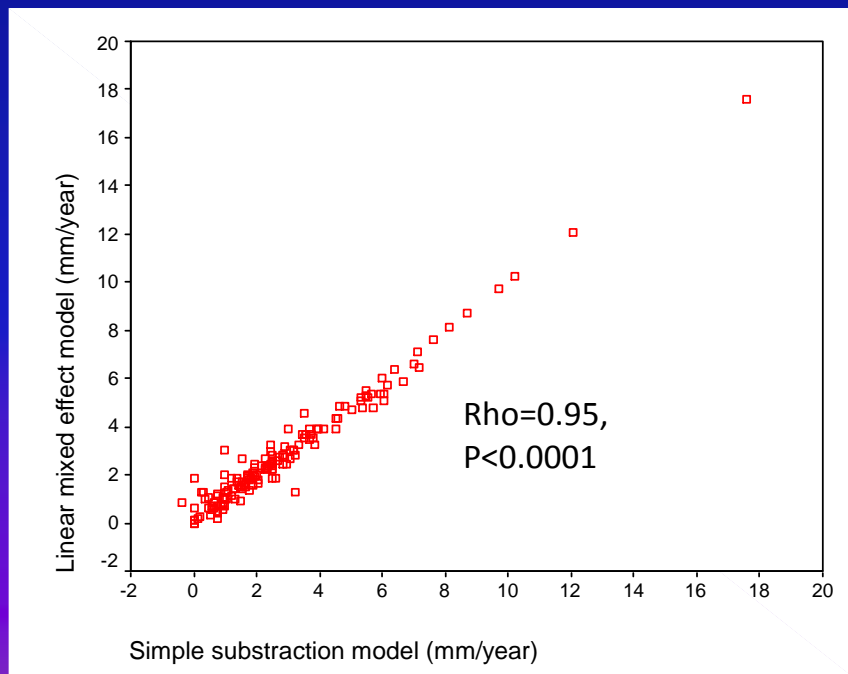


” They must want cash. They’re registered at three banks and two credit unions!”

- AAA repairs: *The Danish nationwide vascular registry*
- Deaths: *The Danish Civil Registration System.*
- Charlson Comorbidity Index to classify comorbidity: Nation wide *registry of Hospital discharge diagnoses*
- Socioeconomic conditions as educational level, occupation and income: *The social national registries*

Does the AAA growth rate and need for later repair depend upon use of low dose aspirin ?

- At diagnosis, smoking habits, and use of medications was recorded
- Expansion rate: a **linear mixed effect model** using anterior-posterior measurements (N=148).



Does the AAA growth rate and need for later repair depend upon use of low dose aspirin ?

- **Statistical analysis**
- A novel hypothesis. The presence of the mural thrombus was not specifically assessed in 1994-1998 when the cohort was formed.
- Cases were stratified by the initial AAA diameter:
 - 40-49 mm (+ILT) and below 40 mm (-ILT)
- For both the linear mixed effect model (Growth rate), and the Cox proportional hazard regression (Need for later repair), Wald tests with at significance level of 5% was used.

Baseline characteristics

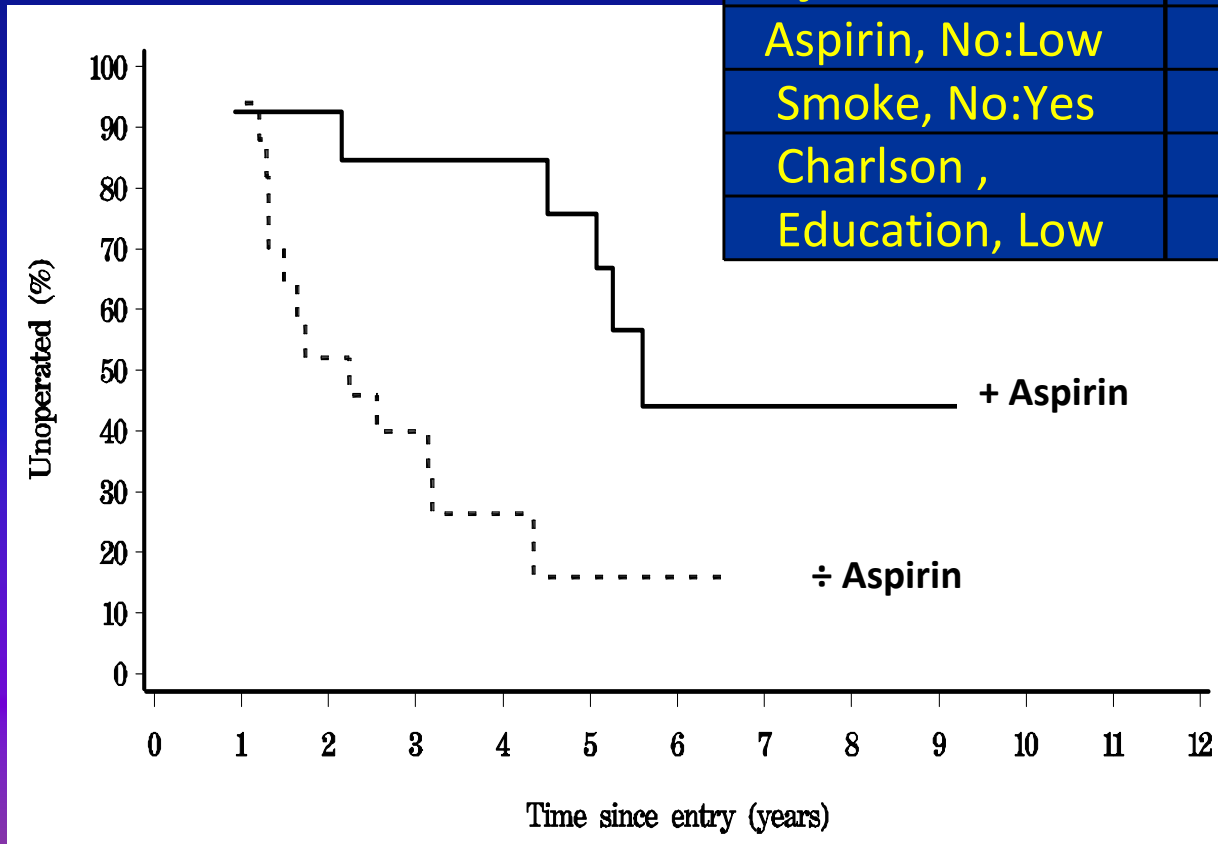
	< 40 mm		40-49 mm	
	No Aspirin	Aspirin	No Aspirin	Aspirin
Numbers	69	48	17	14
Observation time (median years)	7.3	7.6	2.2	5.1
Age (median years)	67.2	67.0	67.5	68.4
Initial AAA diameter (mm)	32	32	42	42
Median Charlsons Comorb. Index	0.0	1.0	0.0	0.0
Current smoking, n (%)	47 (68 %)	25 (52 %)	11 (65 %)	8 (57 %)
Higher educational level	25 (36 %)	16 (33 %)	10 (59 %)	12 (86%)
Operations	14 (20 %)	9 (19 %)	13 (76 %)	7 (50 %)

Use of low dose aspirin was associated with reduced AAA growth rate

	< 40 mm		40-49mm	
Parameter	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Crude				
Aspirin	-0.30 (-0.91; 0.32)	0.3447	2.27 (0.42; 4.11)	0.0173
Adjusted				
Aspirin	-0.44 (-1.06; 0.17)	0.1563	2.13 (0.58; 3.68)	0.0082
No Smoke	-0.85 (-1.47; -0.24)	0.0066	-3.52 (-5.23; -1.80)	0.0002
Charlson = 0	-0.17 (-0.53; 0.19)	0.3513	1.13 (0.01; 2.25)	0.0475
Low Education	0.07 (-0.55; 0.69)	0.8256	1.27 (-0.42; 2.95)	0.1363

Use of low dose aspirin was associated with reduced need for later elective repair ?

	< 40 mm	40-49mm
	HR (95% CI)	HR (95% CI)
Crude		
No:Low dose	1.02 (0.44; 2.35)	2.74 (1.06; 7.07)
Adjusted		
Aspirin, No:Low	0.91 (0.38; 2.13)	2.75 (0.86; 8.77)
Smoke, No:Yes	0.89 (0.37; 2.14)	0.24 (0.08; 0.76)
Charlson ,	0.51 (0.24; 1.09)	0.97 (0.46; 2.03)
Education, Low	0.98 (0.41; 2.31)	1.97 (0.73; 5.37)



Conclusions

- ILT is not frequently present in very small AAA (33%)
- ILT is frequently present in middle-sized AAA (90%)
- BUT present in all AAA above 65 mm
- Use of Low dose aspirin doesn't influence the size of ILT
- However, in middle sized AAA, use of low dose aspirin is associated with 50% significant reduction in growth rate
- The need for later repair was 2.75 times higher among none aspirin users, unchanged after adjustment but lost statistical significance
- Needs to be confirmed in larger cohortes