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The role of perivascular inflammation and COVID-19 and aortic inflammation

M.J. Graumans, H.R. Zandbergen, K.B. Rombouts, L.J. Meijboom, R.H.H. Wellenberg, S. van Bergen, E. Roos, M. Bugiani, Y. Appelman, C.M. van Tiel, E. Lutgens, R. A. Boon, H.W.M. Niessen, J.P. Meekel, E.C. Eringa, K.K. Yeung

Associate Prof. Dr. Kak Khee Yeung, MD, PhD, FEBVS
Vascular Surgeon and Principal investigator Translational Vascular Surgery
Amsterdam Cardiovascular Sciences
Department of Surgery, Amsterdam UMC, the Netherlands

Disclosures

Speaker name: Kak Khee Yeung

I have the following potential conflicts of interest to report:

- Dekkerbeurs Senior Clinical Scientist, Dutch Heart Foundation

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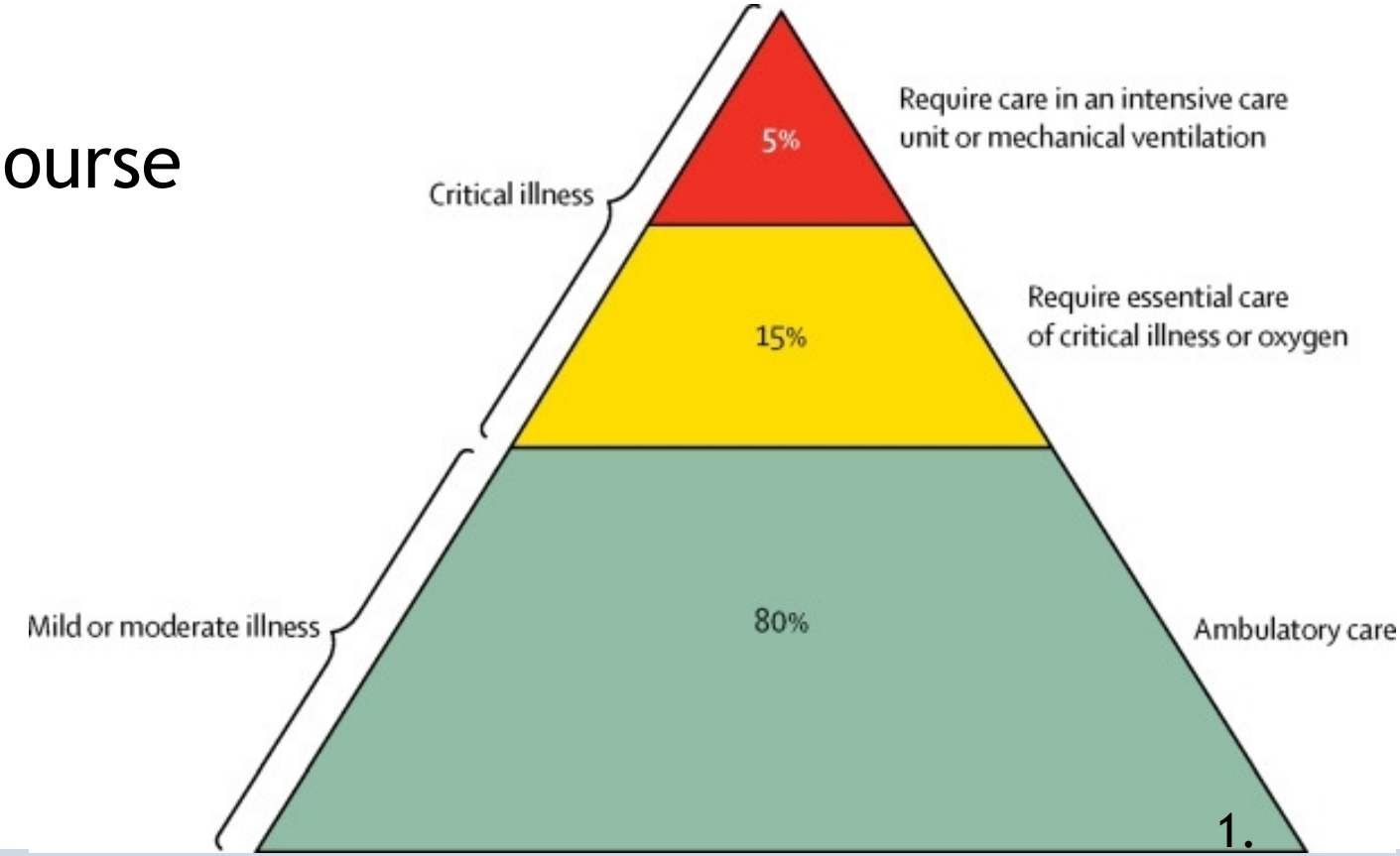
- Unrestricted research grants: W. L Gore & Associates

COVID-19

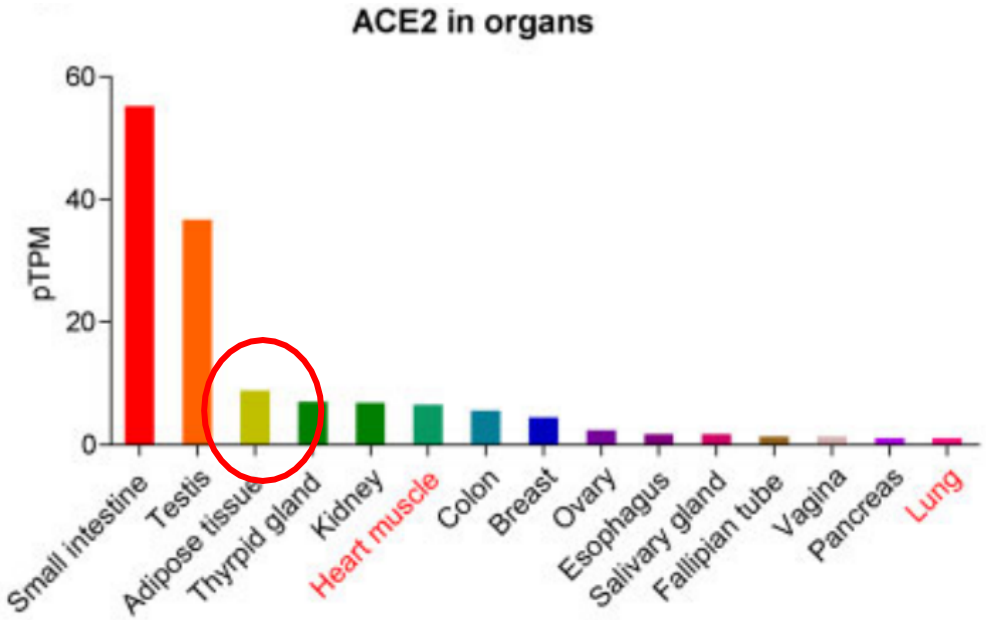
- Risk factors (obesity, CVD, age, diabetes)
- Difficult to predict the clinical course

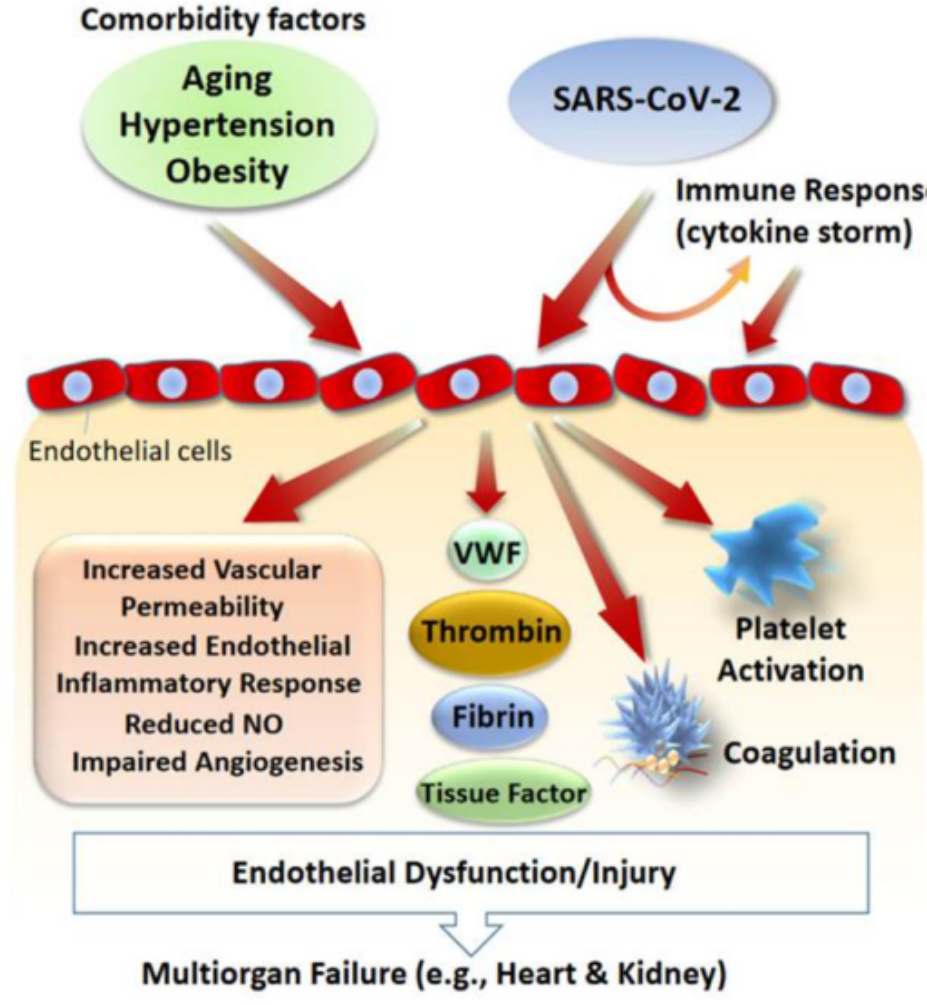


1. Wu et al (2020)

Endothelial dysfunction & COVID-19

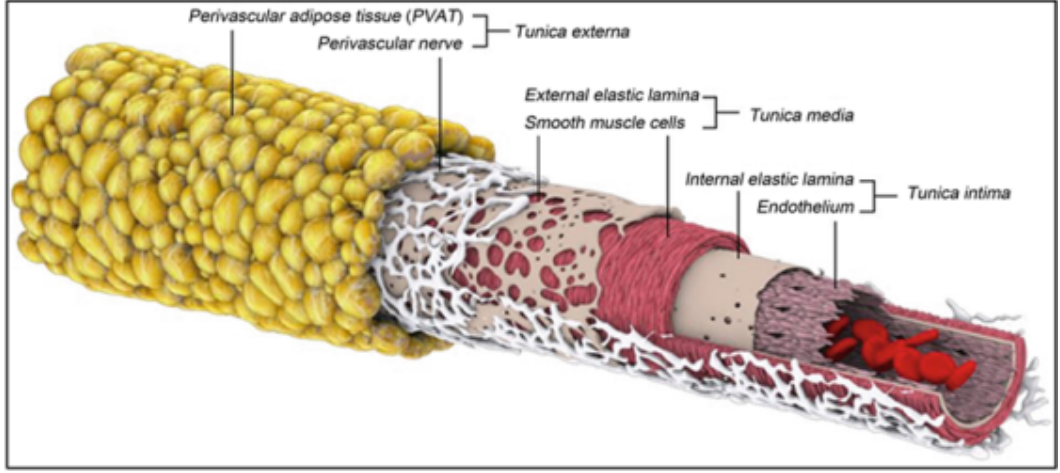
- ACE-2 is primarily located in endothelial cells
- Patients with CVD / Diabetes / Obesity have upregulated levels of ACE-2 receptors





2. R. Amraei et al, (2020). COVID-19, Renin-Angiotensin System and Endothelial Dysfunction. Cells, July (2020)

Perivascular fat tissue (PVAT)

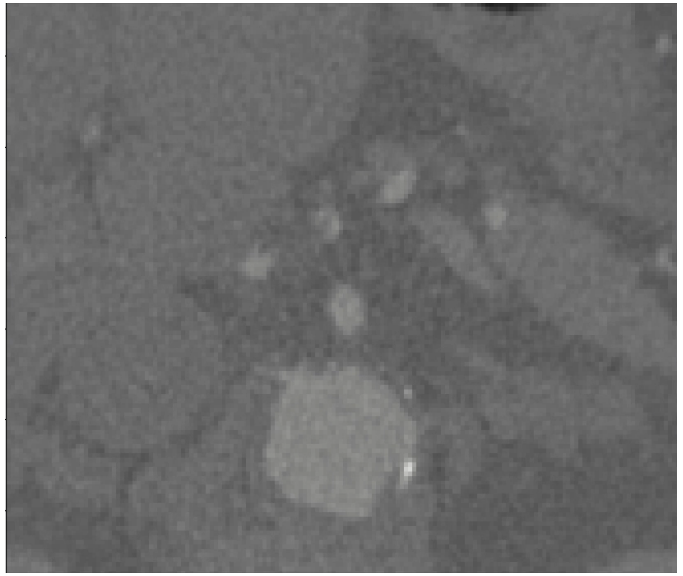


- Perivascular adipose tissue (PVAT) deposits correlate positively with cardiovascular diseases
- Supportive tissue → paracrine & autocrine organ
- Effects on the cardiovascular system mediated by adipokines
- In homeostasis → anti-inflammatory function
- PVAT-inflammation results in a pro-inflammatory switch in secretome
  - Virus infections are a known cause of PVAT inflammation

1. Wu et al (2020)

PVAT & COVID-19

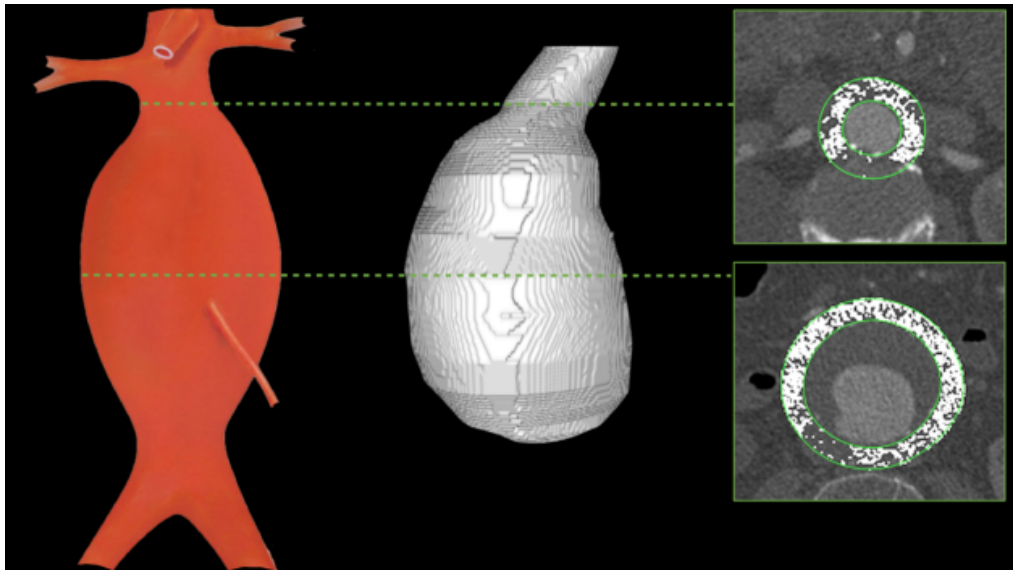
- Severe COVID-19 is characterized by vascular dysfunction and systemic vascular inflammation
- PVAT deposits correlate positively with cardiovascular diseases[1,2]
- PVAT inflammation can be detected using CTA (previously in AAA)



High Density of Periaortic Adipose Tissue in Abdominal Aortic Aneurysm

Marina Dias-Neto [a,b,†], Jorn P. Meekel [c,d,†], Theodorus G. van Schaik [c,d], Jacqueline Hoozemans [d], Fábio Sousa-Nunes [b], Tiago Henriques-Coelho [b], Rutger J. Lely [e], Willem Wisselink [c], Jan D. Blankensteijn [c], Kak K. Yeung [c,d,*]

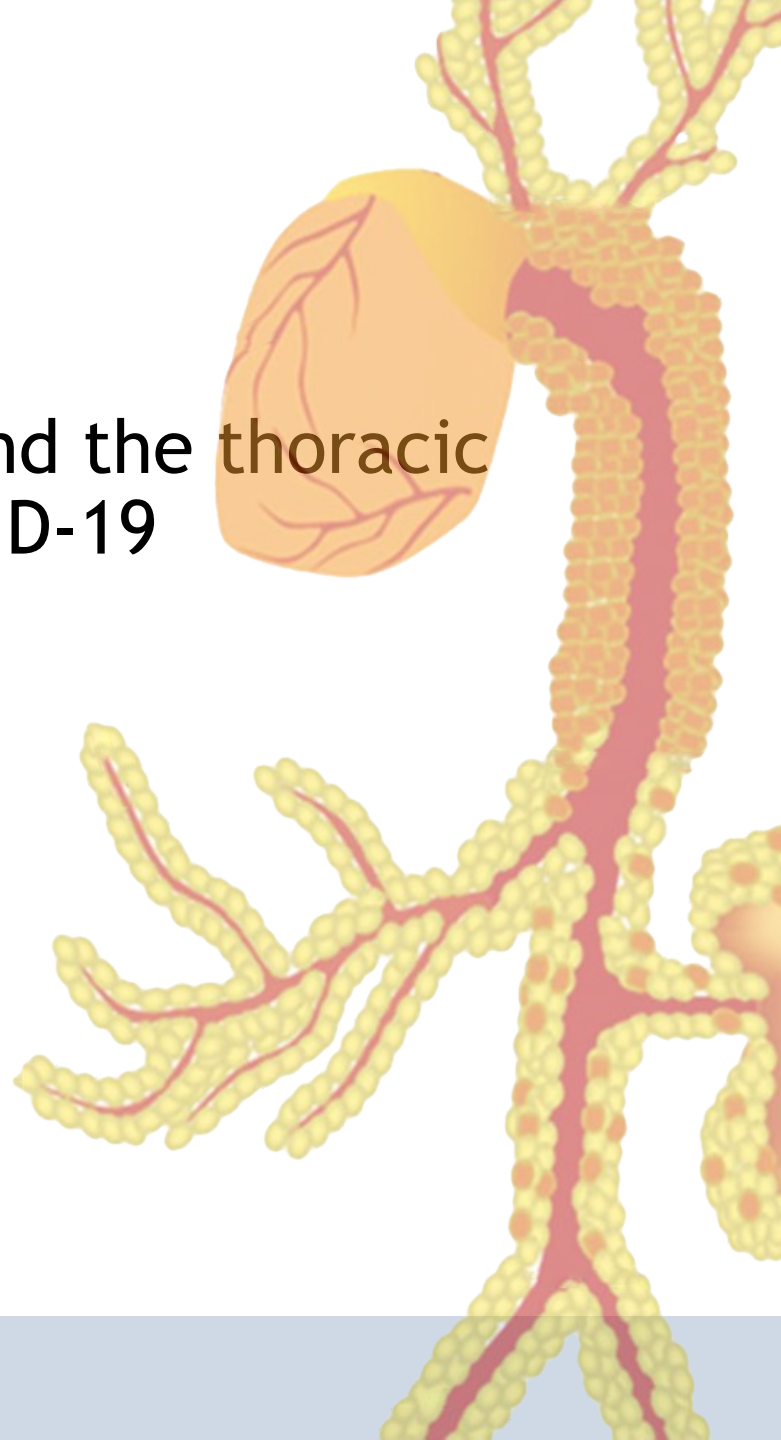
[a] Department of Angiology and Vascular Surgery, São João Hospital Centre, Porto, Portugal
[b] Cardiovascular Research Unit, Faculty of Medicine, University of Porto, Portugal
[c] Department of Vascular Surgery, VU University Medical Centre, Amsterdam, The Netherlands
[d] Department of Physiology (Amsterdam Cardiovascular Sciences) VU University Medical Centre, Amsterdam, The Netherlands
[e] Department of Interventional Radiology, VU University Medical Centre, Amsterdam, The Netherlands



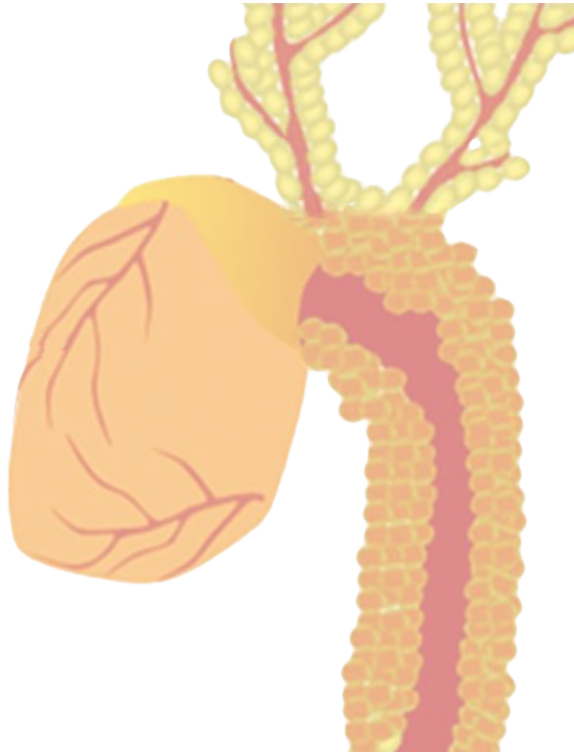
1 Brinkley TE et al. Periaortic fat and cardiovascular risk: a comparison of high-risk older adults and age-matched healthy controls. Int J Obes (Lond), 2014.
2 Talman AH et al. Epicardial adipose tissue: far more than a fat depot. Cardiovasc Diagn Ther, 2014.

Aim

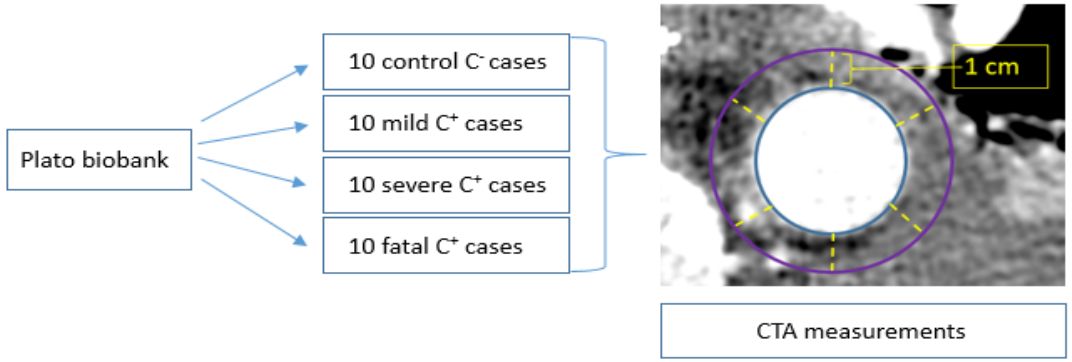
- To determine whether PVAT inflammation around the thoracic aorta is related to the clinical outcome of COVID-19



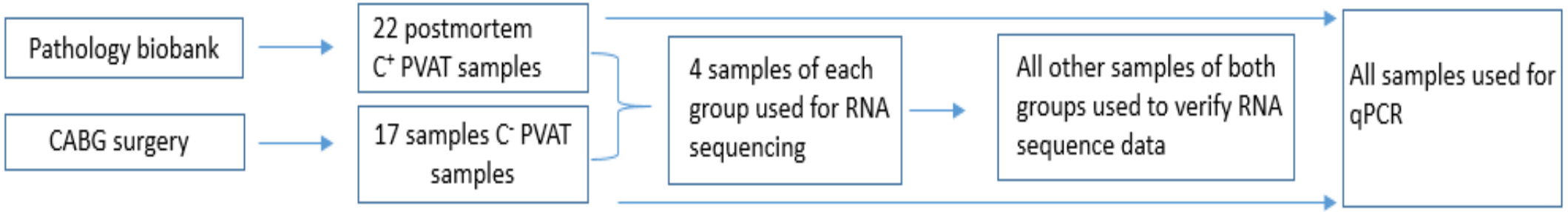
Method



- Retrospective translational study (n=10 per group)

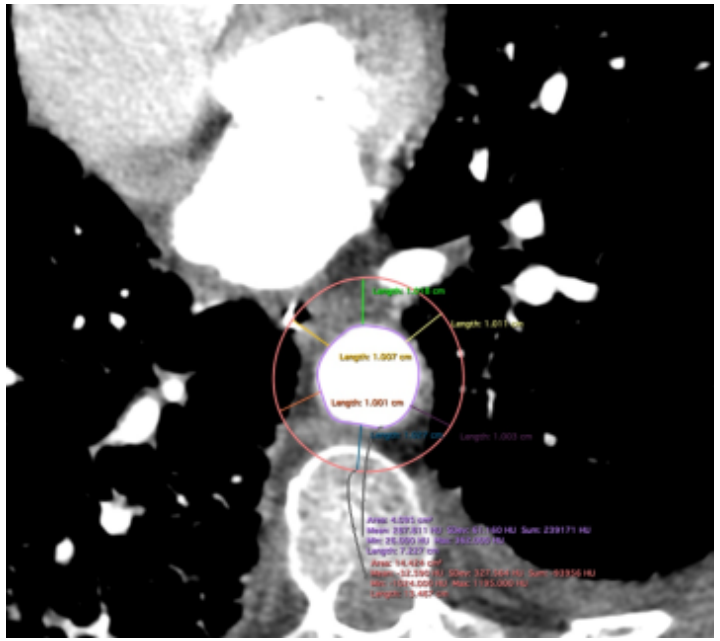


- PVAT tissue analysis (n=22 post-mortem COVID-19 vs controls):

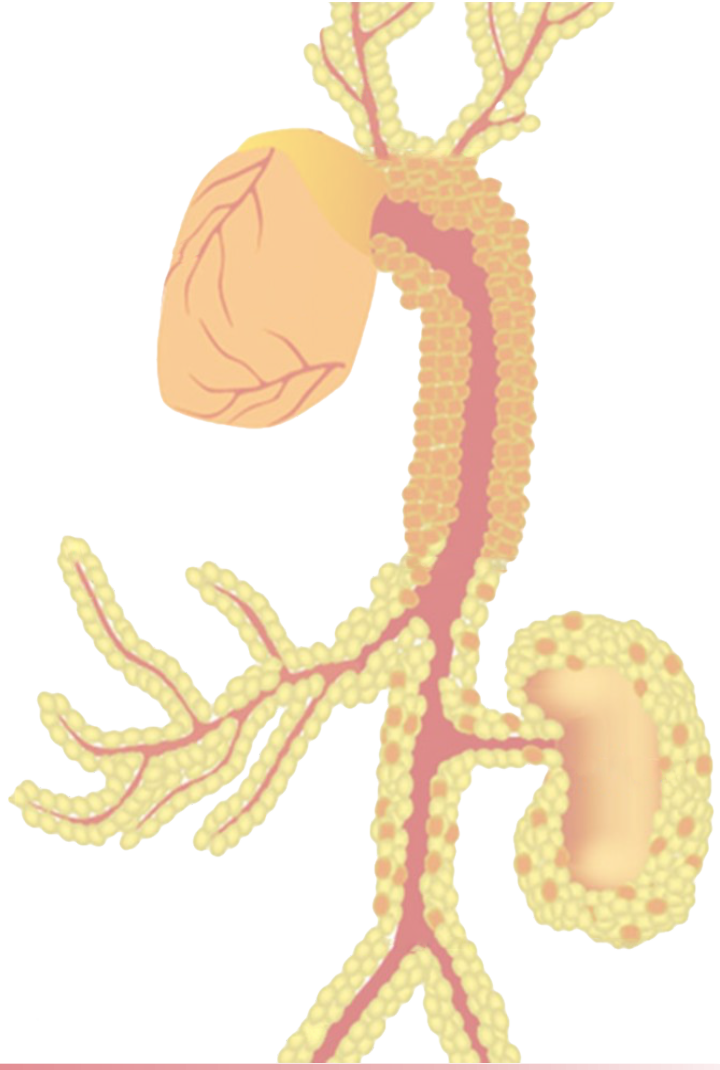


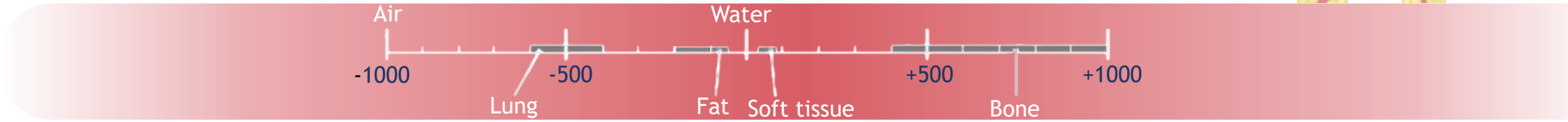
Method

- PVAT: HU-value between -45 & -195



Descending aorta





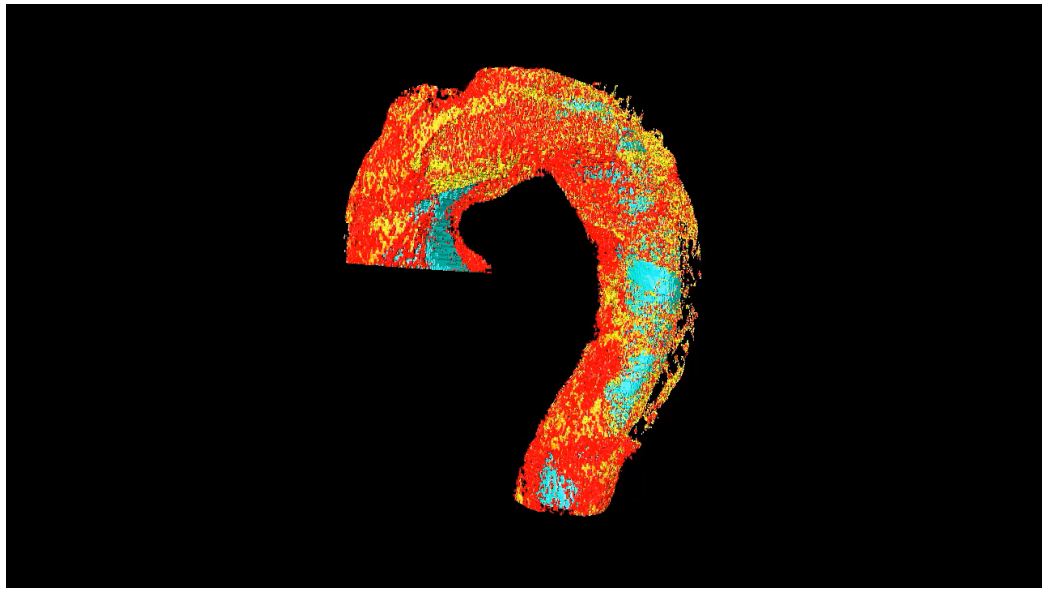
Figures: Meekel JP et al. High density of peri-aortic adipose tissue in abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2018.

Demographics

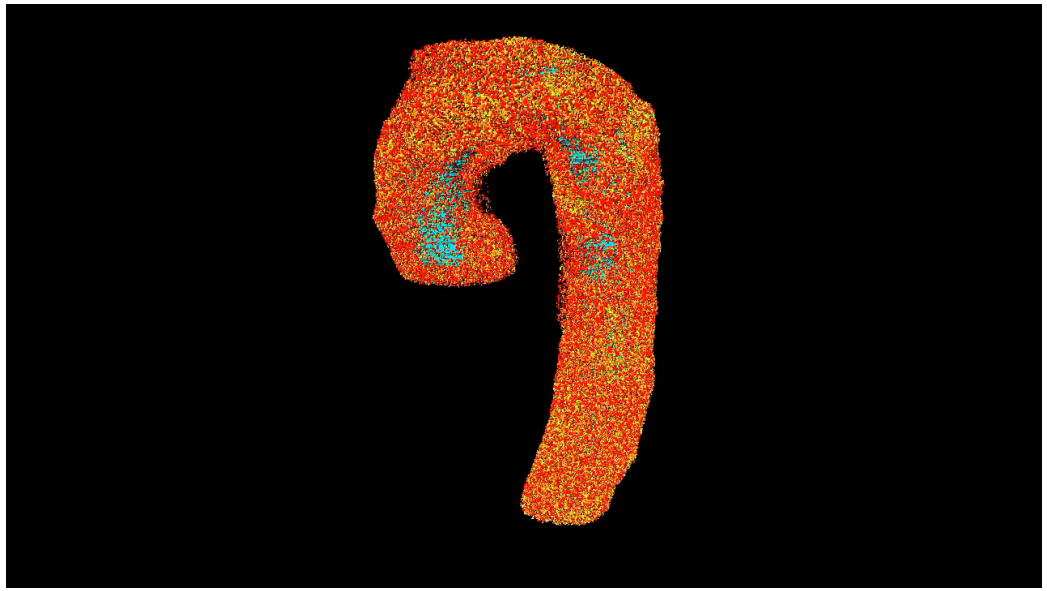
Table 1. Demographics						
		Control	**Mild**	**Severe**	**Fatal**	**P-value**
Sex	Female / Male	8/2	3/7	0/10	2/8	0,001
Age, years	Mean ± sd	50 ± 18	63 ± 10	61 ± 10	61 ± 12	0,13
BMI, kg/m²	Mean ± sd	29,7 ± 1	28,8 ± 5	30,5 ± 5	27,7 ± 4	0,59
Smoking	Yes	2/10	3/10	4/10	5/10	0,07
	Missing	0/10	1/10	3/10	4/10	
Comorbidities	Diabetes mellitus	0/10	2/10	2/10	3/10	0,35
	Hypertension	3/10	4/10	1/10	3/10	0,50
	CAD / M.I.	1/10	2/10	1/10	2/10	0,85
	Asthma	0/10	3/10	0/10	0/10	0,02
	COPD	0/10	2/10	0/10	2/10	0,31
At the Emergency Department						
Complaints prior to admission (days)	Mean ± sd	4,1 ± 5	9,8 ± 4	8,5 ± 5	8,4 ± 6	0,15
Heart rate (beats per minute)	Mean ± sd	98 ± 15	96 ± 16	112 ± 35	94 ±20	0,46
Saturation (%)	Mean ± sd	95 ± 4	96 ± 2	72 ± 13	92 ± 9	0,26
Systolic bloodpressure (mm Hg)	Mean ± sd	143 ± 14	136 ± 19	135 ± 10	131 ± 31	0,77
Diastolic bloodpressure (mm Hg)	Mean ± sd	86 ± 10	80 ± 11	90 ± 11	74 ± 15	0,15
Temperature (°C)	Mean ± sd	37 ± 0,7	37,7 ± 0,9	38,3 ± 1,0	37,4 ±0,8	0,09

Results in 3D PVAT models: initial CT-scan

Mild COVID-19 case



Fatal COVID-19 case



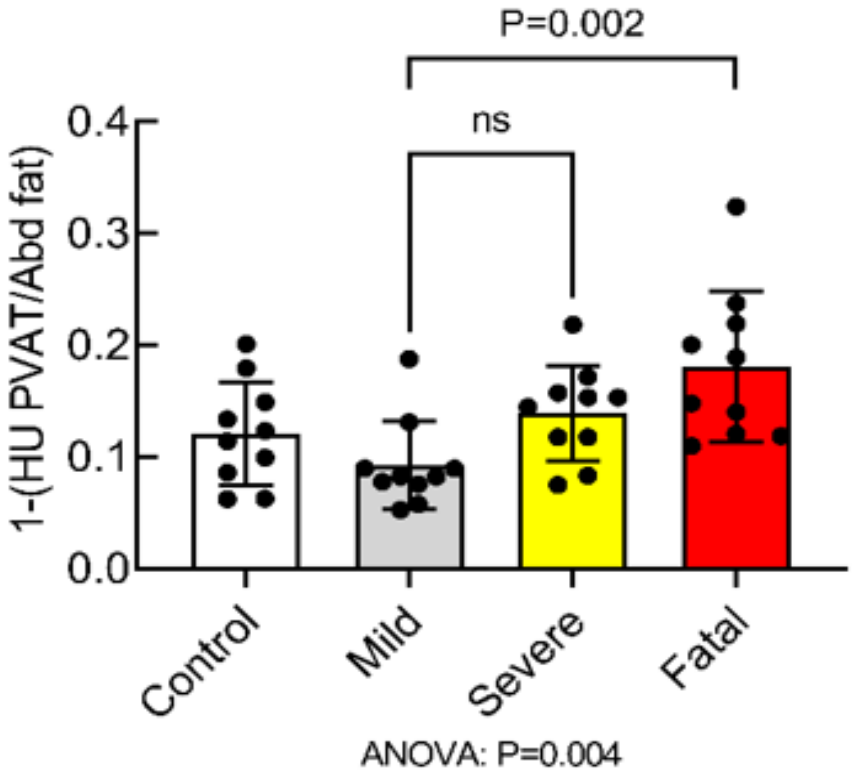
Lumen

Inflammation

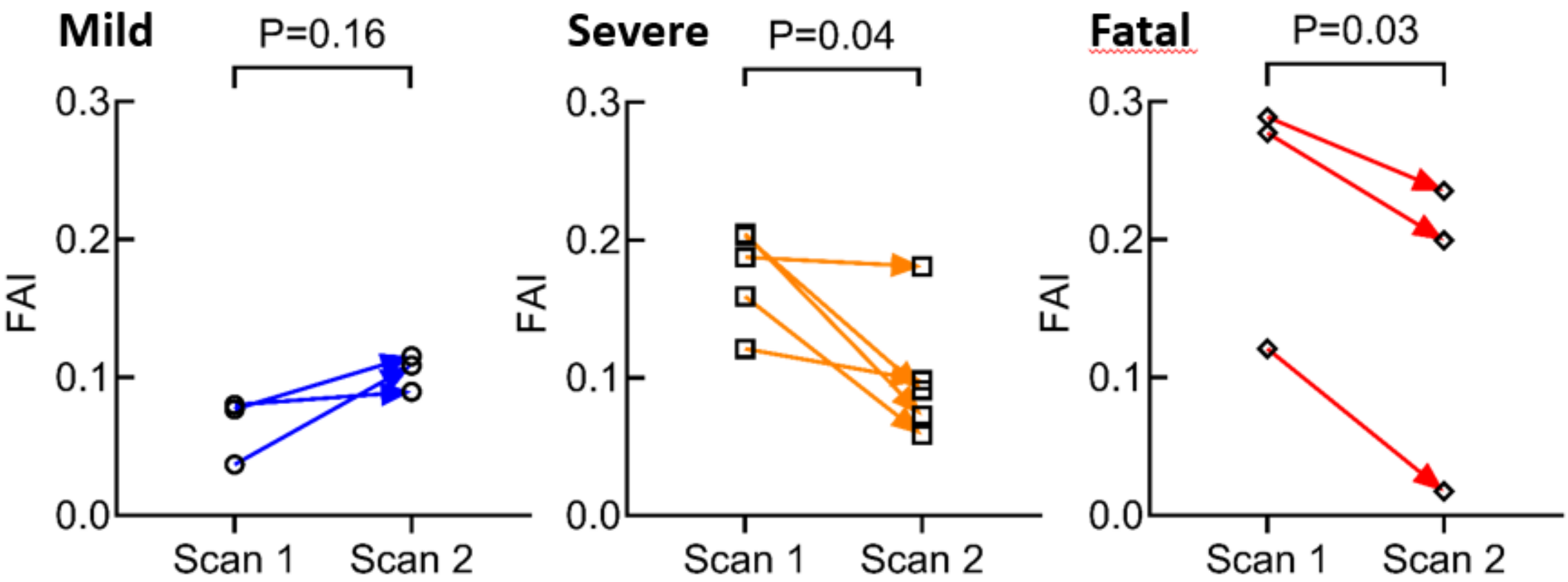
Results

- Significant difference mild and fatal group

- CRP levels similar between COVID-19 groups (P=0.45 & P=1.0)
- No relation between mean inflammation and thromboembolic events (P=0.31)
- Association inflammation and superinfections (P=0.03)

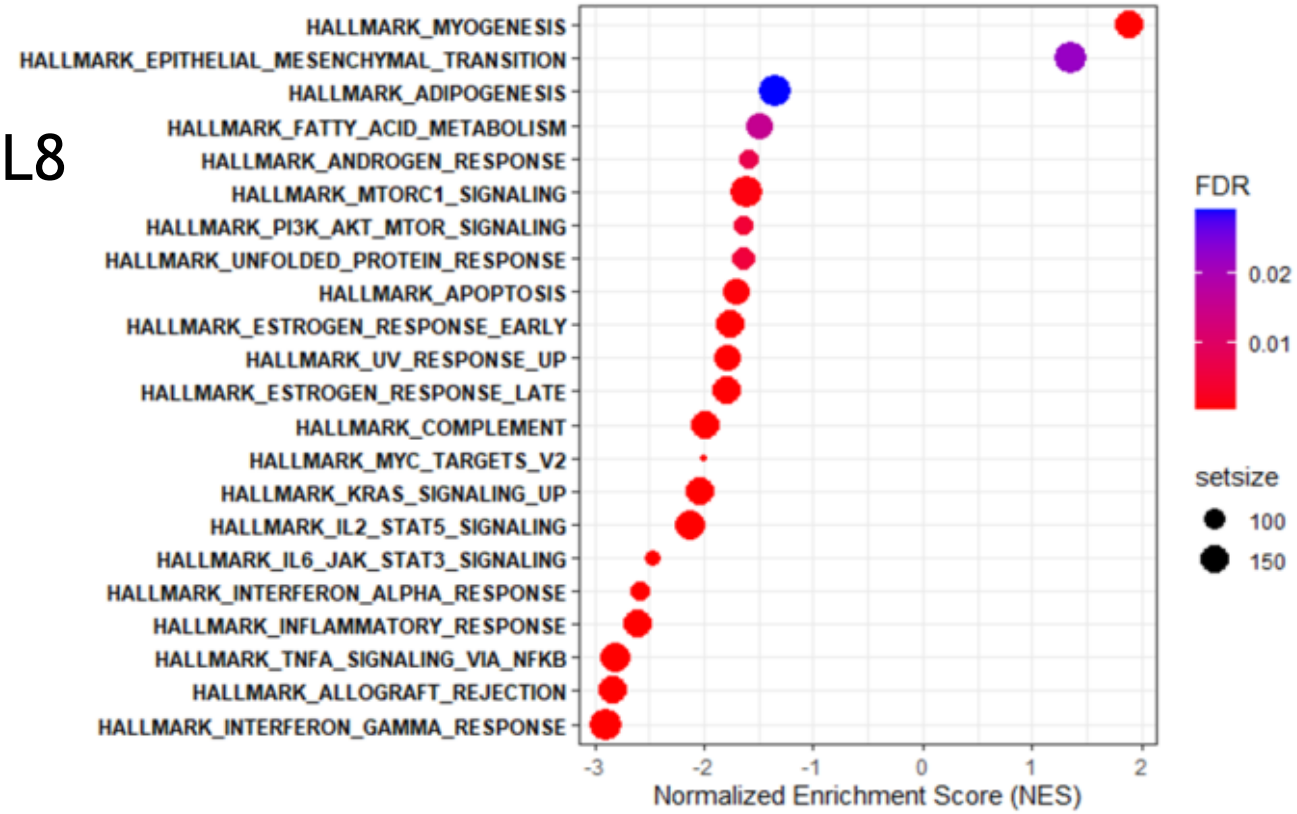


PVAT inflammation in sequential CT-scans



Hypoinflammation of postmortem C+ samples

- Hypoinflammation: CCL2, CCL8
- Myogenesis: fibrosis

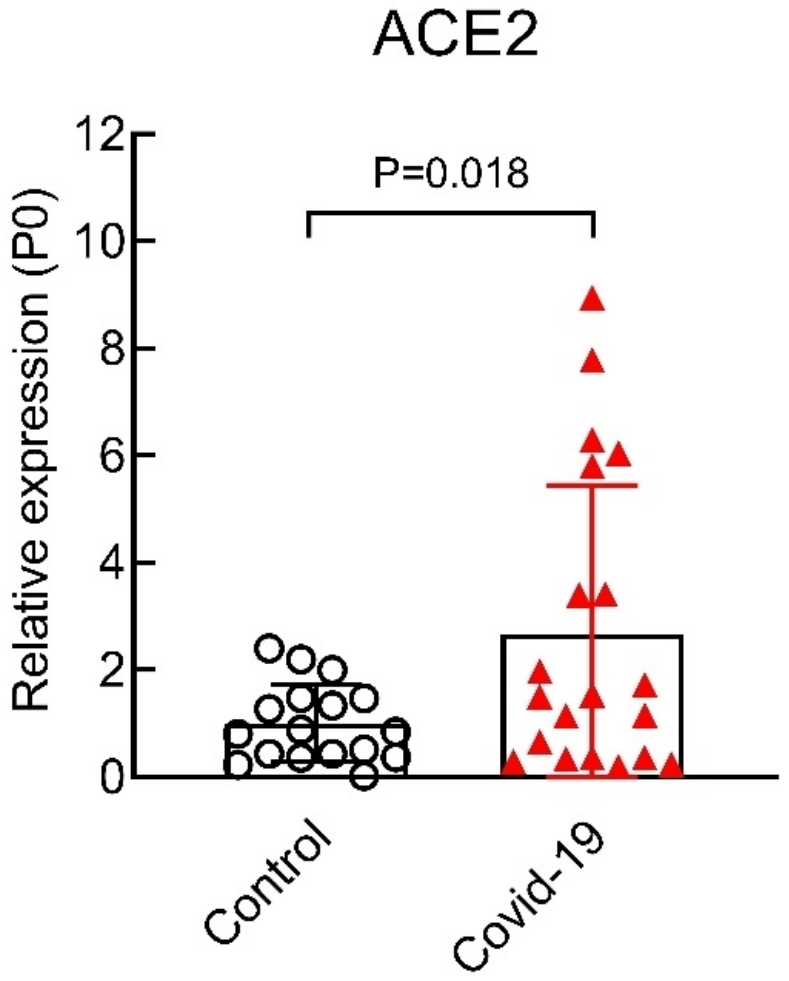


Gene Set Enrichment analysis (GSEA)

SARS-COV-2 capable of infecting PVAT

- 349% more ACE2 expression in the COVID-19 samples compared to CABG controls

- SARS-CoV-2 detected in 2/22 postmortem samples



Limitations

- Retrospective study
  - Different CT-settings
  - Postmortem samples ≠ fatal COVID-19 group
- Postmortem vs peroperative CABG samples
  - No difference in hypoxic transcriptomes in RNA sequencing

Conclusion

- Early vascular hyperinflammation is related to fatal COVID-19 (could be a biomarker)
- SARS-CoV-2 is capable of infecting PVAT
- Fatal COVID-19 compensatory anti-inflammatory response state
- Non-invasive diagnostic tool for vascular inflammation
- Ongoing:
  - prospective study
  - vascular complications study group

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Associate prof. Dr. Kak Khee Yeung

Maarten Graumans

Dr. Jorn Meekel

E-mail: K.yeung@amsterdamumc.nl