



70TH ESCVS CONGRESS & 7TH IMAD MEETING

20 | 23 JUNE 2022

Liège | Théâtre de Liège | Belgium

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70th ESCVS
International congress of the European Society
for Cardiovascular and Endovascular Surgery



7th IMAD meeting



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IgG4-Related Disease and evolution of the Aortic Stenosis

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IgG4-Related Disease (RD)

- Rare relapsing-remitting systemic inflammatory condition
- Multiorgan Disease
- Associated to tumor-like lesions
- Umbrella Disease of several conditions



- | | |
|--|---|
| <ul style="list-style-type: none">• Pancreas• Bile ducts• Thyroid gland• Lacrimal glands• Orbita• Salivary glands• Aorta | <ul style="list-style-type: none">• Kidney• Skin• Breast• Prostate• Lung• Aortic Valve |
|--|---|

- | | | |
|---|---|---|
| <ul style="list-style-type: none">• Autoimmune Pancreatitis• Sclerosing Cholangitis• Riedel's Thyroiditis• Mikulicz's Syndrome | <ul style="list-style-type: none">• Küttner's tumor• Inflammatory pseudotumor• Chronic Sclerosing Aortitis• Periarteritis• Ormond's Disease | <ul style="list-style-type: none">• Multifocal fibrosclerosis• Mastitis• Prostatitis• Sjogren's syndrome |
|---|---|---|



IgG4-RD

- Diagnostic Criteria
 - > Clinical data
 - > Radiological data
 - > Pathological data →
 - > IgG4 serum levels (cut off levels > 1.35g/l)
 - > Response to treatment

- Treatment
 - > Prednisone (40mg/day)
 - > Rituximab (anti-CD20 Ab)

Histology

- > Lymphoplasmacytic infiltrations
- > Storiform fibrosis
- > Obliterative Phlebitis

Immunohistochemistry (IHC)

- > IgG4 / IgG positive plasma cells > 0.4
- > IgG4+ plasma cells /high-powered field (HPF) > 10



Case Report

IgG4-Related Disease Causing Rapid Evolution of a Severe Aortic Valvular Stenosis



Samuel Bruls, MD, Audrey Courtois, MS, PhD,
Philippe Delvenne, MD, PhD,
Roland Hustinx, MD, PhD,
Michel Moutschen, MD, PhD,
Laurence De Leval, MD, PhD,
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Mean Gradient: 35mmHg
AV Area: 0.9cm²

Rapid evolution
1 year

Echocardiography
Mean Gradient: 46mmHg
AV Area: 0.7cm²

Patient 82-year old male admitted for
suspicion for lymphoma

CT -> retroperitoneal infiltration

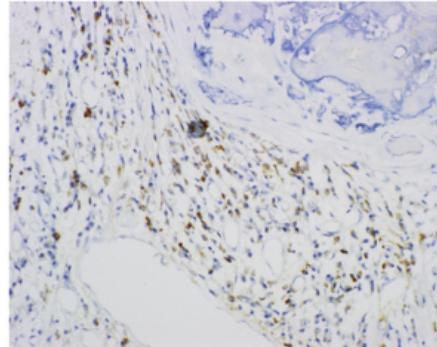
FDG-PET-CT -> FDG uptake lymph node sites

IHC -> IgG4+ infiltrate

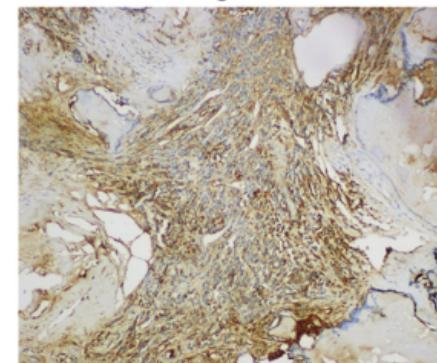
dyspnea

Aortic Valve (AV) IHC

IgG4



IgG



AV Replacement Surgery -> Treatment with corticosteroids -> one year follow up -> Patient ok



Case Report

RHEUMATOLOGY

Letter to the Editor (Case report)

IgG4-related disease of the mitral and aortic valves presenting as rapid, recurrent prosthetic valve failure

Guy Katz¹, Brett Victor², Adam Binder³,
Siddharth Bhattacharya⁴ and John H. Stone⁵

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⁴Department of Pathology & Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA and ⁵Division of Rheumatology, Allergy, & Immunology, Massachusetts General Hospital, Boston, MA, USA

Patient 78-year-old male admitted for mitral and aortic valve replacement

dyspnea ↓ 2 years

Echo: Prolapse of mitral leaflet of bioprosthetic valve resulting in paravalvular leak and severe stenosis

IHC: IgG4+/IgG+ plasma cell ratio > 0.5
IgG4+ plasma cells / HPF > 50

- IgG4-RD involving the heart valves can lead to premature prosthetic valve failures
- Inflammation in the tissue is driven by circulating cells or antigens



Hypotheses

- IgG4-RD could play a role in rapid progression of AV stenosis
- IgG4-RD could lead to adverse events post aortic valve replacement (paravalvular leak) (especially if not treated with corticosteroids)

Prospective Study – Single Center (CHU Liège)

- Enrolment of AV Stenosis Patients that underwent valve replacement surgery between Jan 20 – Jan 21
- Collection of 108 aortic valve cusps in paraffin
- Collection of plasma/serum and DNA
- Progression of their disease before surgery
- Follow-up post-surgery up to 3 years to detect adverse events



Early Preliminary Results : Cohort Demographic Characteristics

Characteristics of AS Patients	n=107
Mean Age \pm SD, y	72.5 \pm 9.6
Female, n (%)	48 (44.9)
Mean BMI \pm SD, Kg/m ²	28.0 \pm 5.2
Mean BSA \pm SD, m ²	1.9 \pm 0.2
Risk Factors	
Diabetes, n (%)	64 (60.9)
Smokers (Active/Former), n (%)	63 (60.0)
Hyperlipidaemia, n (%)	76 (72.4)
Hypertension, n (%)	81 (77.1)
Renal Insufficiency, n (%)	20 (19.8)
COPD, n (%)	18 (17.3)
Mean CRP \pm SD, mg/l	7.6 \pm 16.1
Mean NLR \pm SD	3.2 \pm 2.7
Mean Serum IgG4 \pm SD, g/l	0.33 \pm 0.2

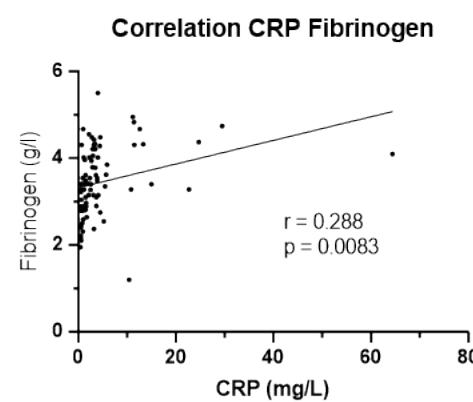
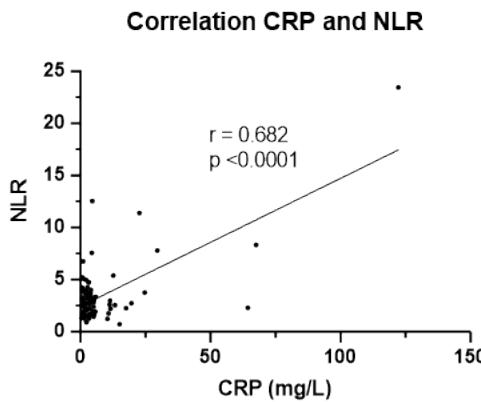
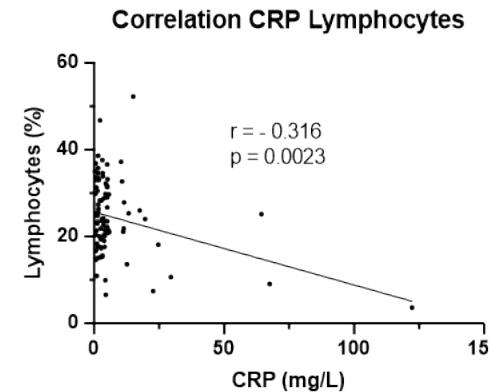
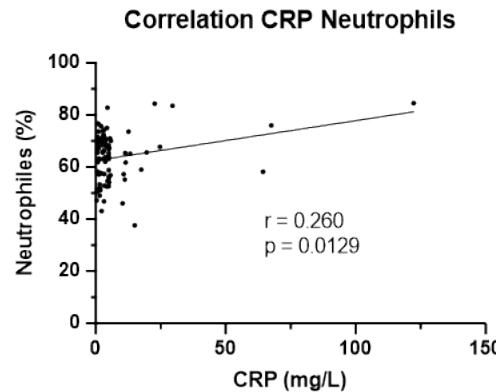
Characteristics of Aortic Valve	n=107
Bicuspid Aortic Valve, n (%)	23 (21.9)
Aortic Valve Area \pm SD, cm ²	0.83 \pm 0.2

Characteristics of AS	n < 107
Evolution AS (Rapid), n/tot (%)	8/44 (18.2)
Score NYHA (III+IV), n/tot (%)	24/61 (39.3)

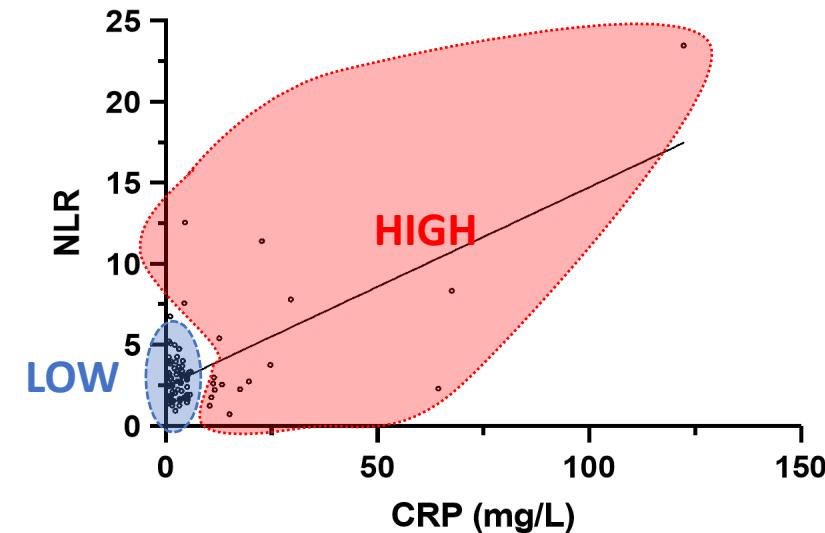
Post Surgery	n=107
Paravalvular Leak, n (%)	26 (24.3)



Inflammatory Markers in Cohort



Correlation CRP and NLR

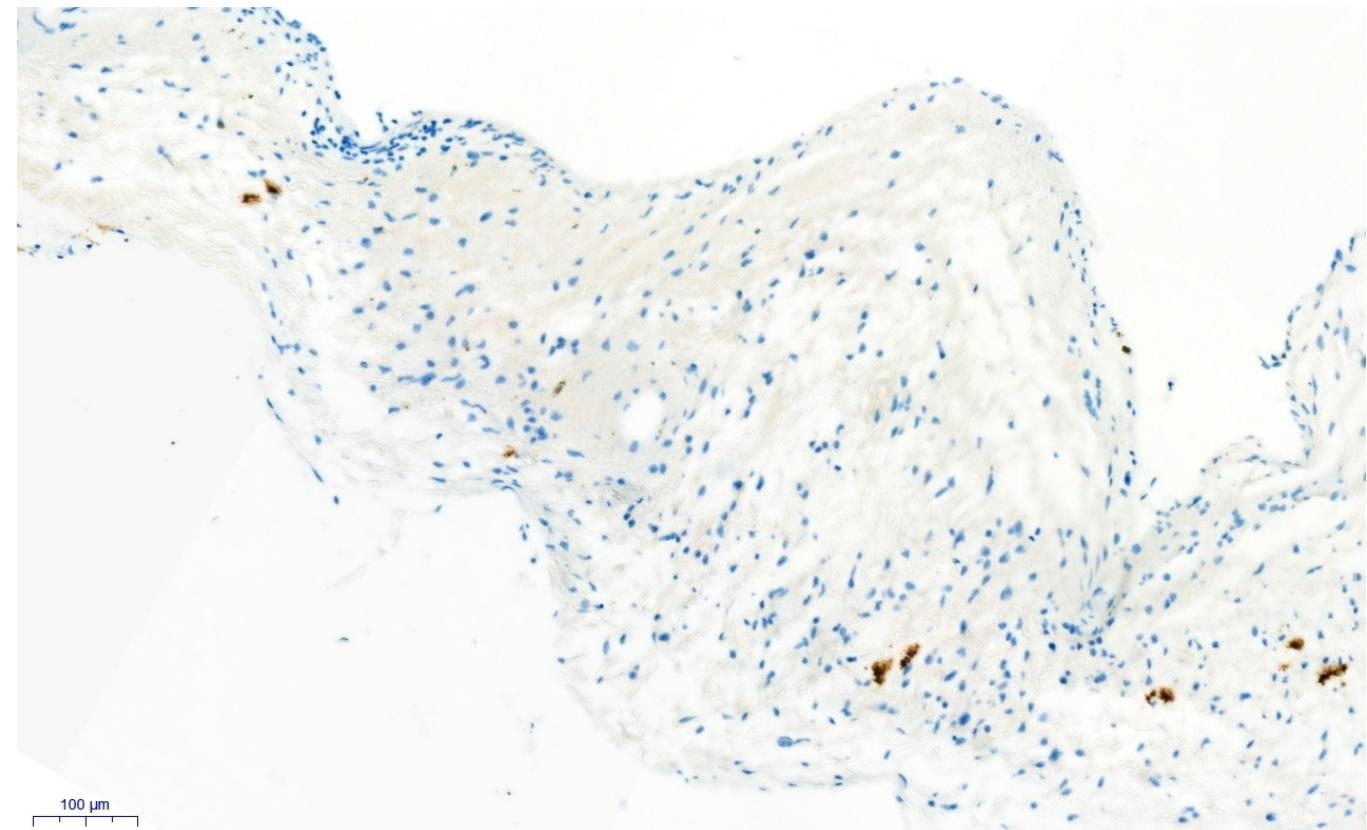
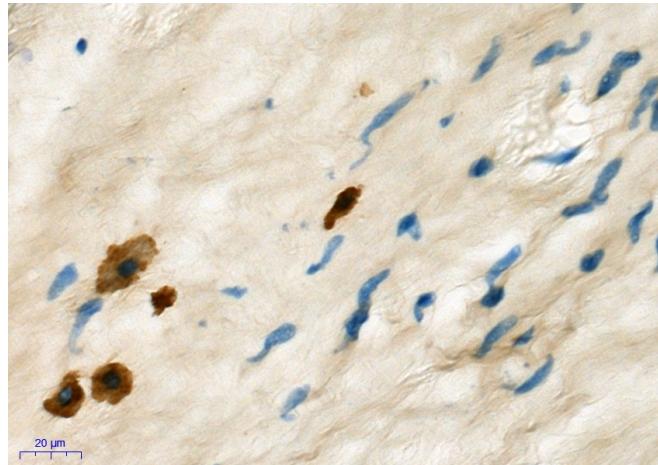


Data analyzed	Low CRP/NLR	High CRP/NLR	p-value
<i>Smoking n/tot (%)</i>	47/85 (55.3)	15/19 (78.9)	0.057
<i>Diabetes n/tot (%)</i>	52/86 (39.5)	7/19 (36.8)	0.828
<i>Hypertension n/tot (%)</i>	64/86 (74.4)	17/19 (89.5)	0.157
<i>Hyperlipidaemia n/tot (%)</i>	64/86 (74.4)	12/19 (63.2)	0.320
COPD n/tot (%)	11/85 (12.9)	7/19 (36.8)	0.013
Renal Insufficiency n/tot (%)	15/86 (17.4)	9/19 (47.4)	0.005
<i>Paravalvular Leak n/tot (%)</i>	24/88 (27.3)	17/2 (10.5)	0.123
<i>Adverse Events n/tot (%)</i>	47/87 (54.0)	14/19 (73.7)	0.116
<i>Rapid Evolution n/tot (%)</i>	5/32 (15.6)	3/12 (25.0)	0.473



Early Preliminary Results from the AV Stenosis Liege Cohort

- IgG4 serum levels in normal range
- Number of IgG4 + plasma cells /HPF < 10
- Ratio IgG4+/ IgG+ plasma cells < 10 %





Early Preliminary Results from the AV Stenosis Liege Cohort

Characteristics	<u>Low AV IgG4+cells</u> n=75	<u>High AV IgG4+cells</u> n=27	p-value
<i>Mean Age ± SD, y</i>	73.6 ± 8.6	69.6 ± 11.9	0.12
<i>Female, n (%)</i>	34 (45.3)	11 (40.7)	0.68
<i>Mean Weight ± SD, Kg</i>	78.5 ± 16.6	79 ± 13.9	0.68
<i>Mean BMI ± SD, Kg/m²</i>	28.2 ± 5.4	27.9 ± 4.6	0.92
<i>Mean BSA ± SD, m²</i>	1.9 ± 0.2	1.9 ± 0.2	0.56
<i>Bicuspid AV, n (%)</i>	13 (17.3)	10 (37.0)	0.036
<i>Diabetes, n (%)</i>	31 (42.5)	8 (29.6)	0.24
<i>Smokers (Active/Former), n (%)</i>	20 (39.2)	17 (63)	0.046
<i>Hyperlipidaemia, n (%)</i>	55 (75.3)	18 (66.7)	0.39
<i>Hypertension, n (%)</i>	57 (78.1)	20 (74.1)	0.67
<i>Renal Insufficiency, n (%)</i>	18 (24.6)	6 (22.2)	0.80
<i>BPCO, n (%)</i>	14 (19.4)	4 (14.8)	0.59
<i>Mean CRP ± SD, mg/l</i>	6.2 ± 15.9	9.0 ± 18.2	0.86
<i>Mean NLR ± SD</i>	3.1 ± 2.9	3.6 ± 2.3	0.15
<i>Mean Serum IgG4 ± SD, g/l</i>	0.33 ± 0.2	0.33 ± 0.2	0.84
<i>Evolution AS (Rapid), n/tot (%)</i>	5/29 (17.2)	3/13 (23.1)	0.66
<i>Aortic Valve Area ± SD, cm²</i>	0.83 ± 0.2	0.82 ± 0.2	0.90
<i>Paravalvular Leak, n (%)</i>	15 (20.0)	10 (37.0)	0.078
<i>Score NYHA (III+IV), n/tot (%)</i>	14/42 (33.3)	7/15 (46.7)	0.36



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