VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Prevalence of transthyretin amyloidosis in patients undergoing TAVR for severe aortic stenosis – preliminary results of prospective study

Zemková M.[1], Hlubocká Z.[1], Paleček T.[1], Habásko J.[1], Zogala D.[2], Linhart A.[1]

[1] 2nd internal department of Cardiology and Angiology, General University Hospital in Prague
[2] Department of nuclear medicine, General University Hospital in Prague

KOMPLEXNÍ KARDIO VASKULÁRNÍ CENTRUM VFN Praha

Transthyretin amyloidosis (ATTR)

- Buildup of abnormal protein deposits (amyloids)
- Wild-type (wtTTR) a hereditary type (hTTR)
- The most common type of cardiac amyloidosis (concerns myocardium in up t 100 % cases)
- Diagnosis: echocardiography, MRI, DPD scintigraphy, endomyocardial biopsy or biopsy of other tissues

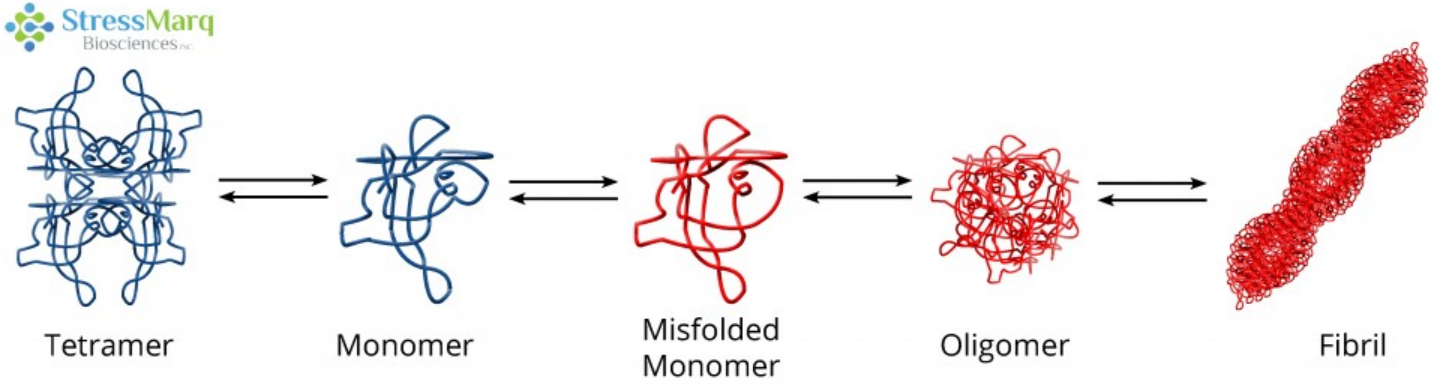
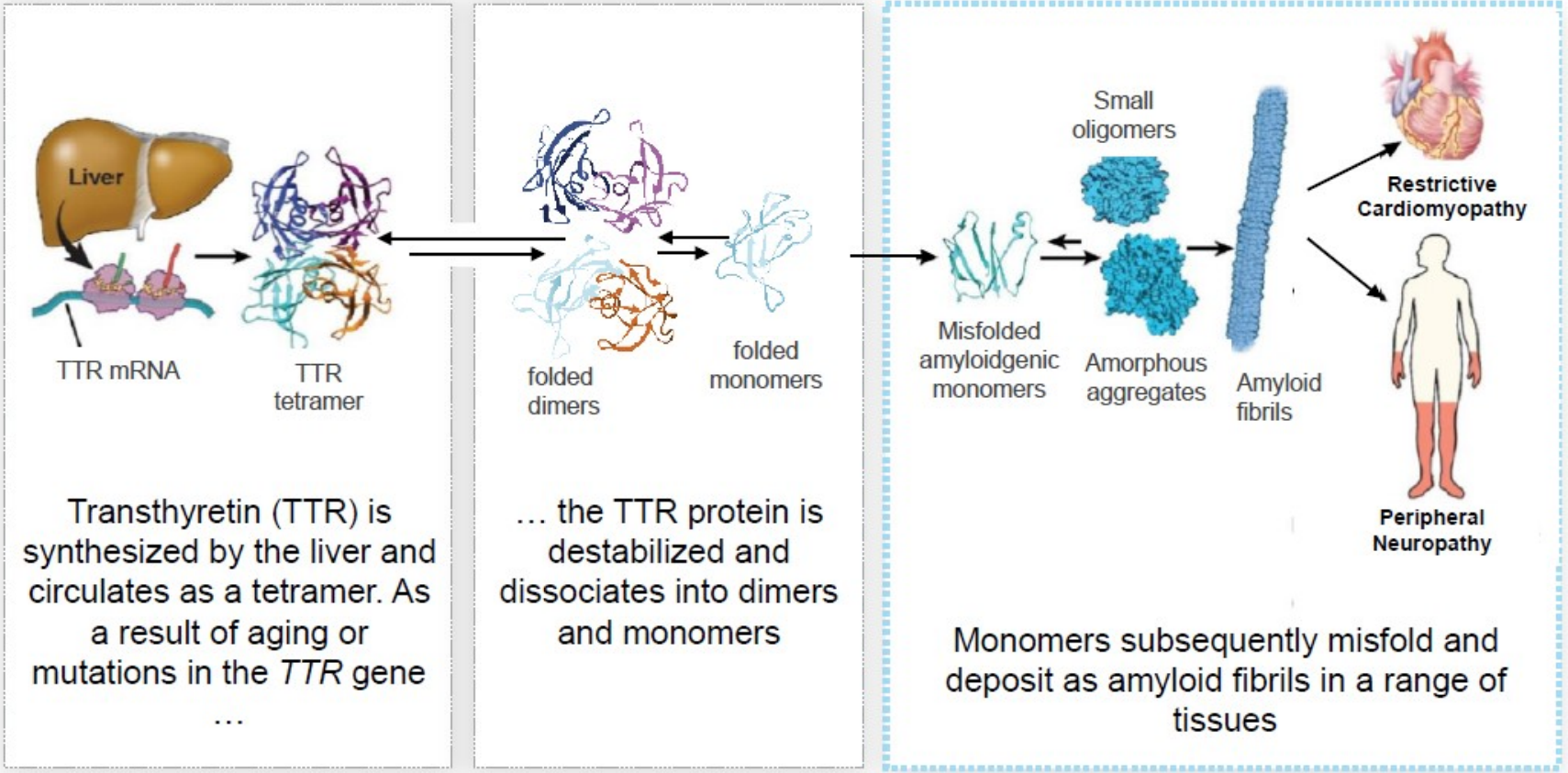


Figure from: www.stressmarq.com/transthyretin-ttr-in-amyloid-di

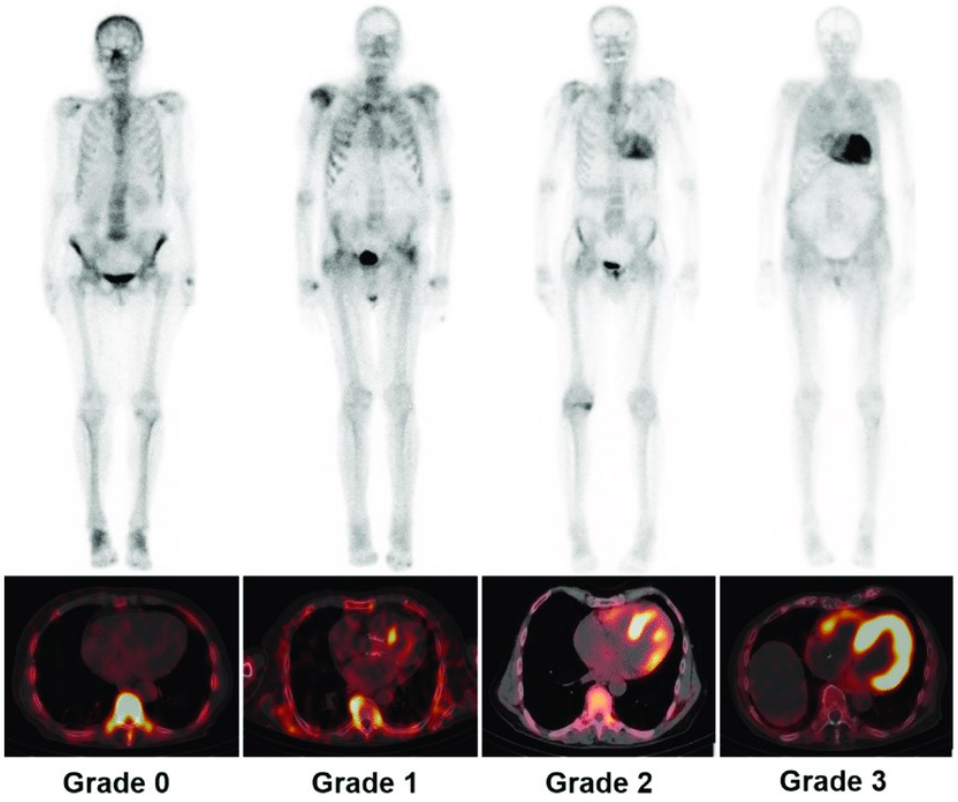
Pathophysiology of ATTR

TTR, is an abundant protein **T**ransporting **T**hyroxine (T4) and **R**etinol in plasma and CSF



F. L. Ruberg et al, JACC 2019, https://doi.org/10.1016/j.jacc.2019

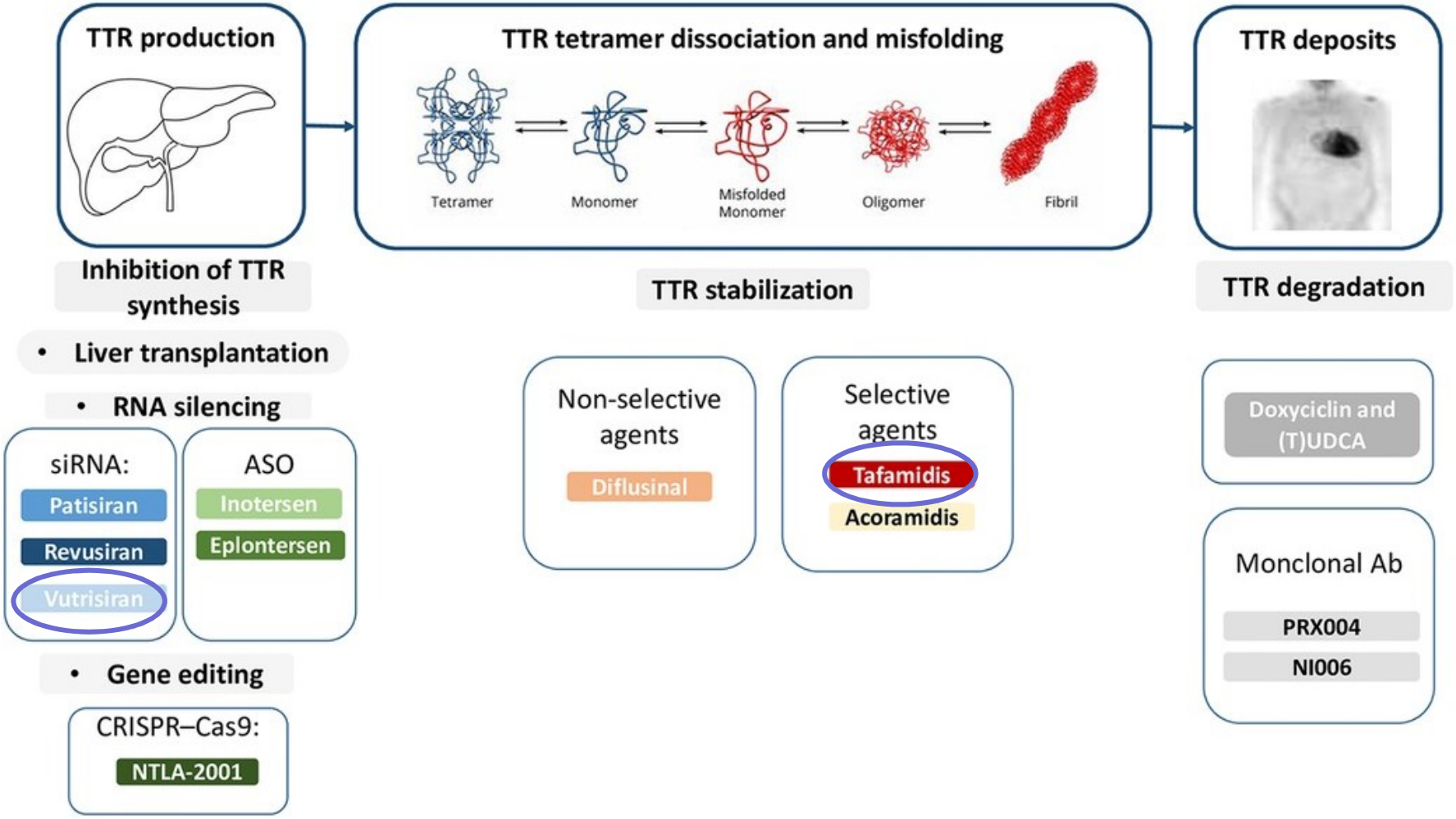
DPD scintigraphy



- Cardiac uptake of the radiopharmaceutical (myokardium vs skeleton)
- Perugini grade 0-3
- Very high sensitivity (92 %) and specificity (95 %)
- Positive DPD ≠ ATTR (always exclude AL amyloidosis)

https://doi.org/10.1016/j.jacc.2005

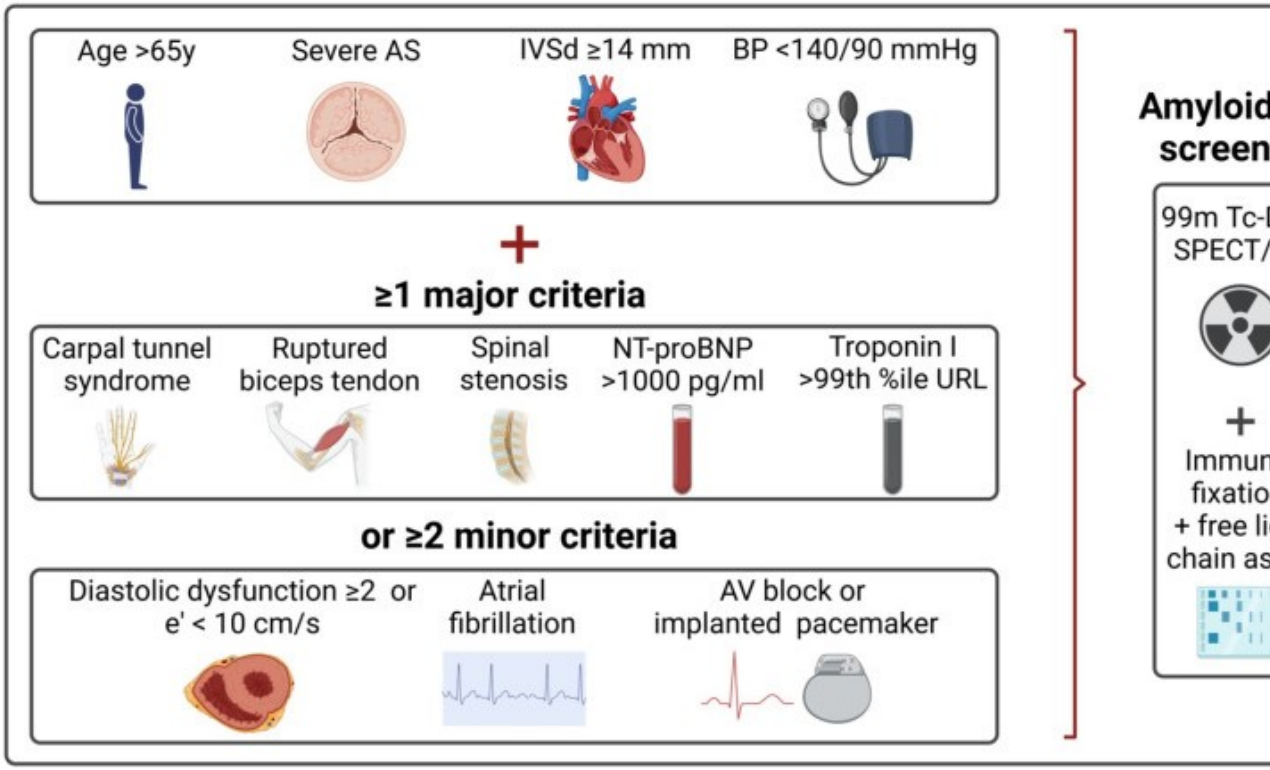
Specific treatment options



Tomasoni et al., Frontiers in Cardiovascular Me
2023, DOI=10.3389/fcvm.2023.1154594

ATTR and aortic stenosis

- Amyloid deposition in heart valves is associated with accelerated progression of aortic stenosis
- Diagnosis is challenging due to similarities in symptoms
- Prognosis is generally poorer for patients with both conditions



Jakstaite AM et al. Screening for Occult Transthyretin Amyloidosis in Patients with Severe A
Stenosis and Amyloid Red Flags. J Clin Med. 2024 Jan 24;13(3):671. doi: 10.3390/jcm1303

The importance of early diagnosis

Main therapy approaches are derived from the observation:

More amyloid
=
Worse outcomes

Less amyloid
=
Better outcomes

Diagnosis & initiation of therapy at an earlier stage of disease & shorter duration of symptoms

=

associated with better preserved cardiac structure, function and long-term survival

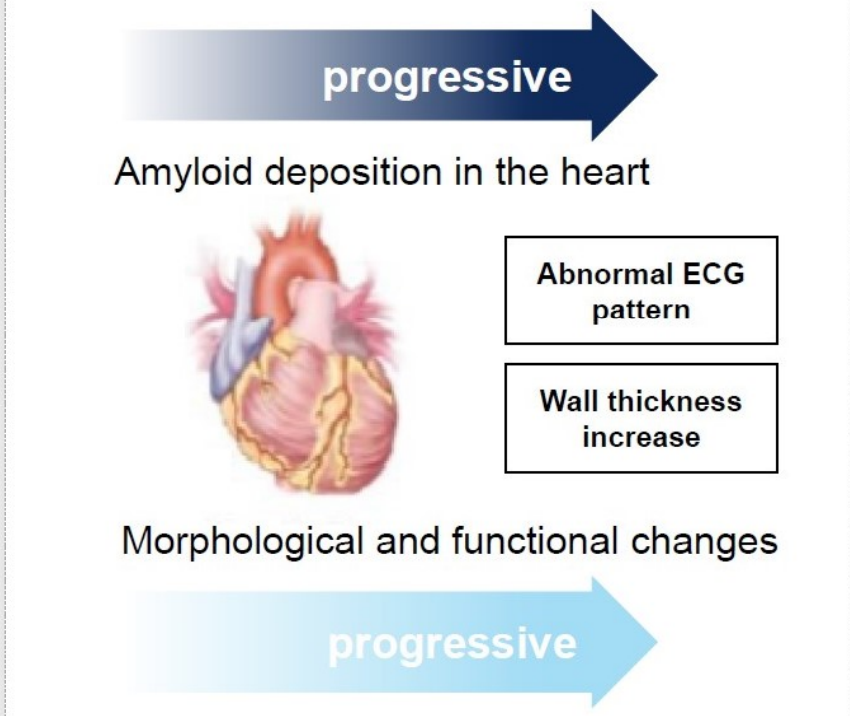


Figure adapted from lecture of prof. Julian Gillmore, ESC Congre

Prevalence of ATTR in patients with severe aortic stenosis undergoing TAVR – postdoctoral research

Aims:

- To determine the prevalence of ATTR in patients with severe aortic stenosis undergoing TAVR
- To identify echocardiographic signs and phenotypic manifestations typical of ATTR in context of severe aortic stenosis

Methods

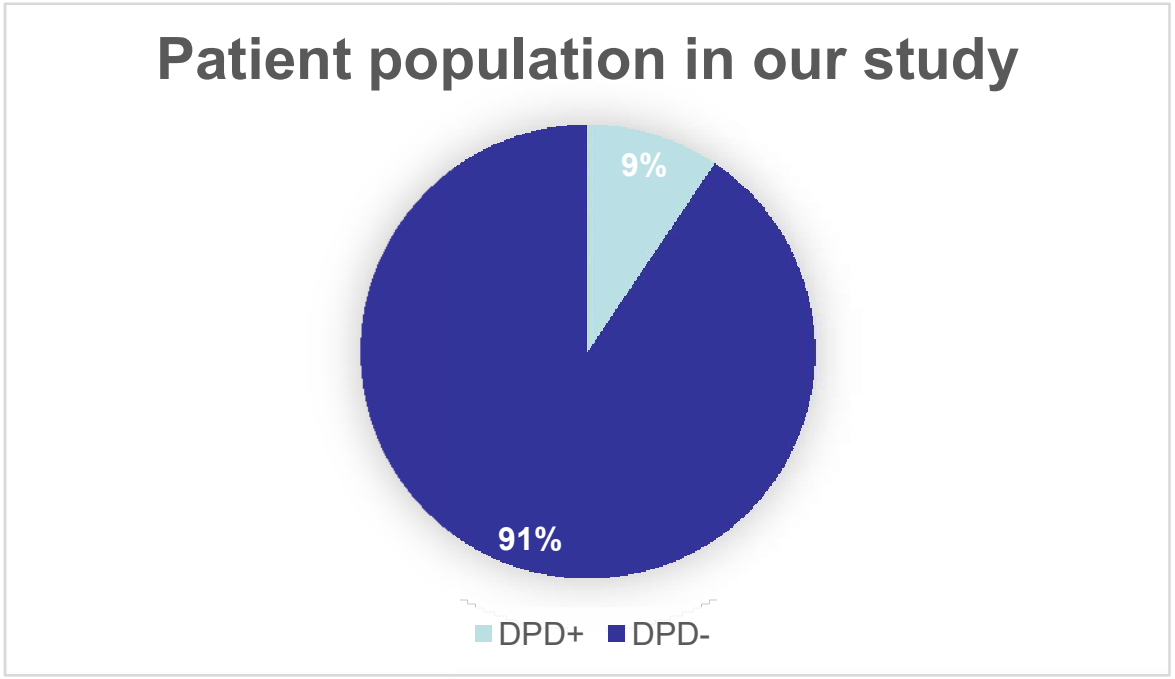
- Prospective, single-center study
- A total of 106 patients with severe aortic stenosis undergoing TAVR included
- As of November 2024, total of 55 patients analysed
- Each patient undergoes:
  - Clinical examination, laboratory tests including NT-proBNP, ECG
  - Complex echocardiographic exam before and after TAVR
  - DPD scintigraphy (±free light chains, immunoelectrophoresis)

Baseline clinical characteristics

	DPD+ N=10	DPD- N=45	p value
Age (y)	80,5±4,8	78,3±5,9	0.25
Sex (male)	7 (70 %)	29 (64 %)	0.89
Body surface area (m^2)	1,92±0,15	1.94±0,21	0.72
NT-proBNP (ng/l)	1755 (1506; 8976)	1345 (507; 2234)	0.12
Carpal tunnel syndrome (y)	5 (50 %)	0 (0 %)	<0.001

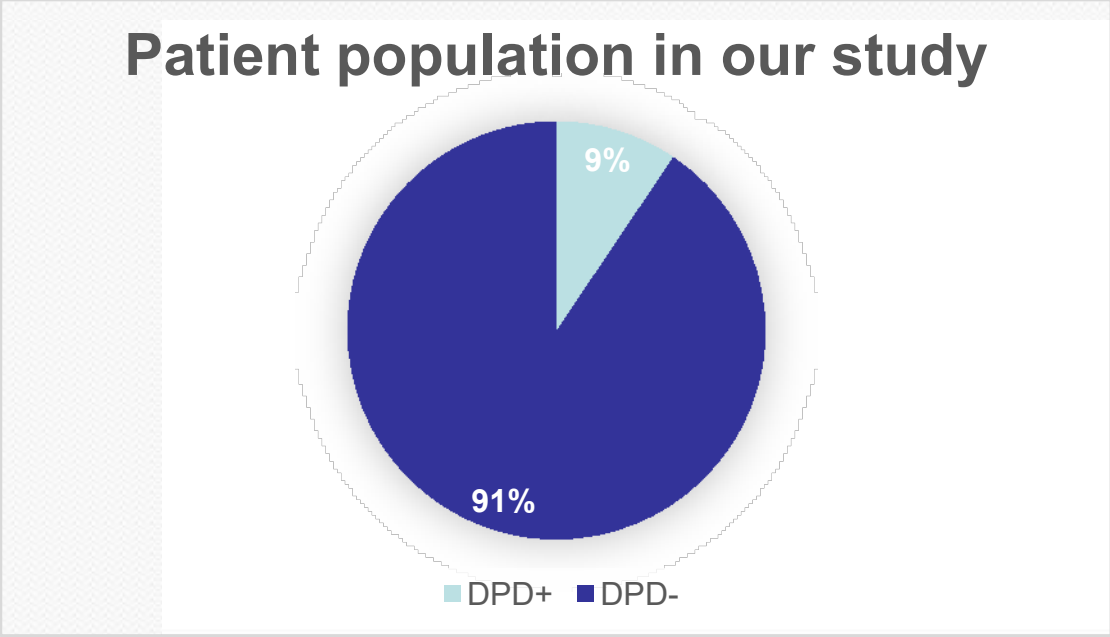
Results – ATTR prevalence

- A total of 106 patients were included
- Positive cases: 10, which is 9.43 %

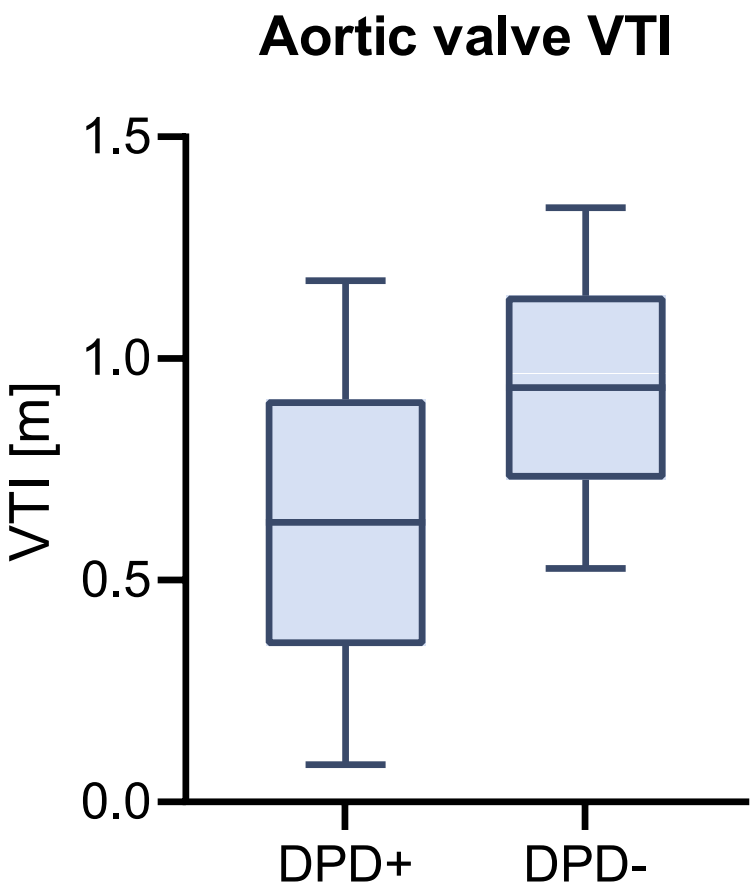


Interim analysis

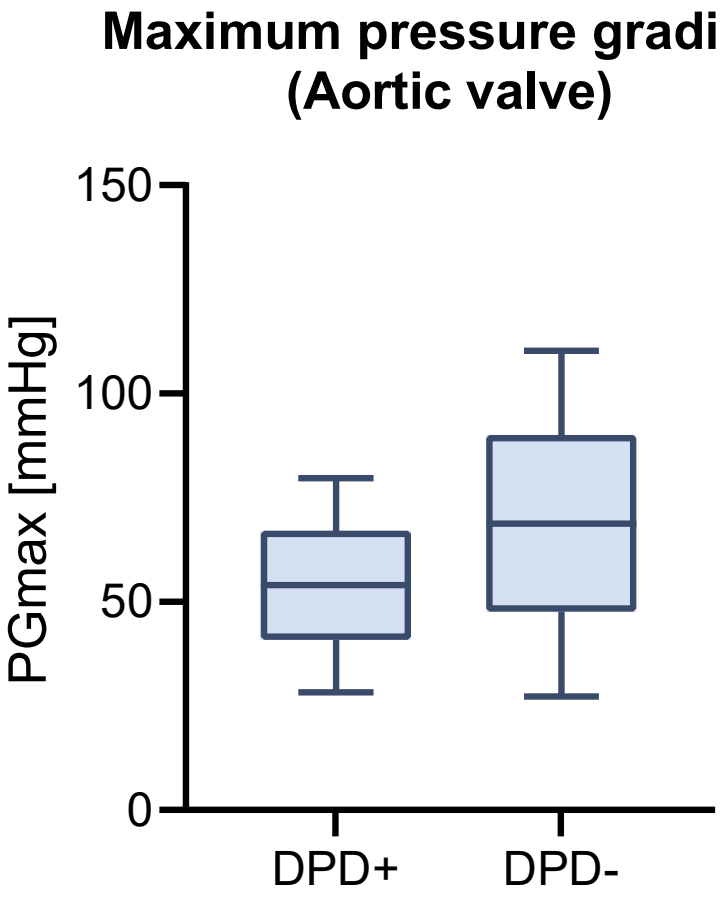
- A total of 106 patients were included
- Positive cases: 10, which is 9.43%
- As of November 2024, total of 55 patients analyzed



Results – aortic valve data



p<0.001

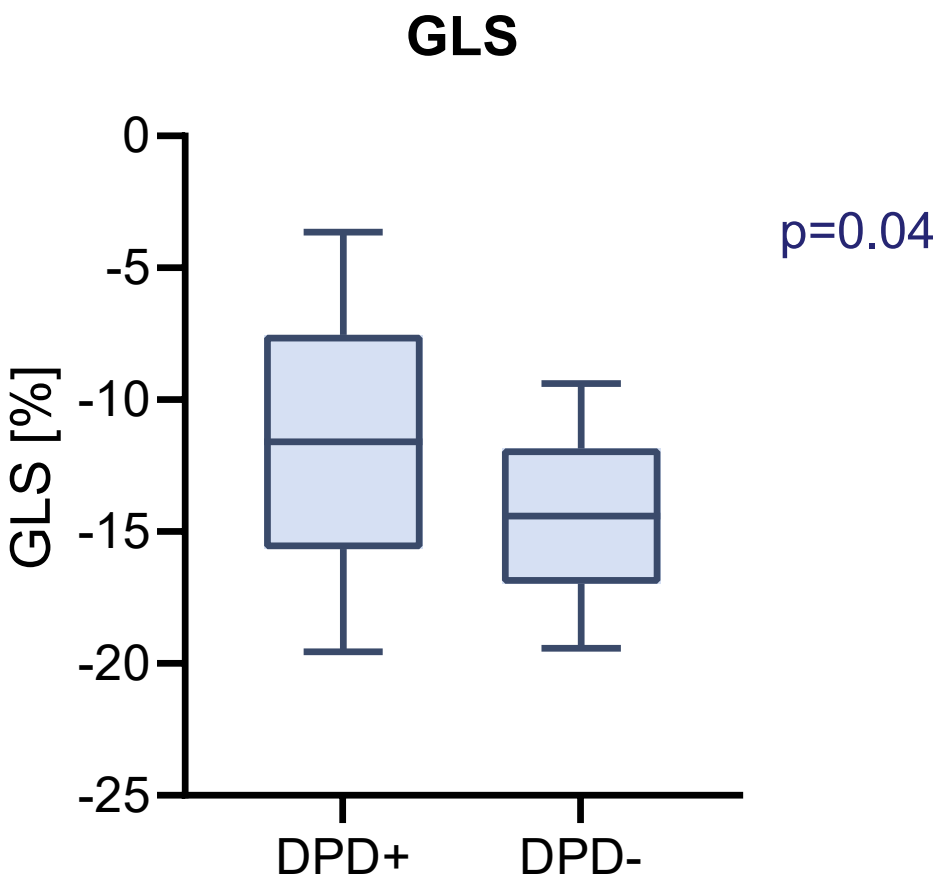


p<0.05

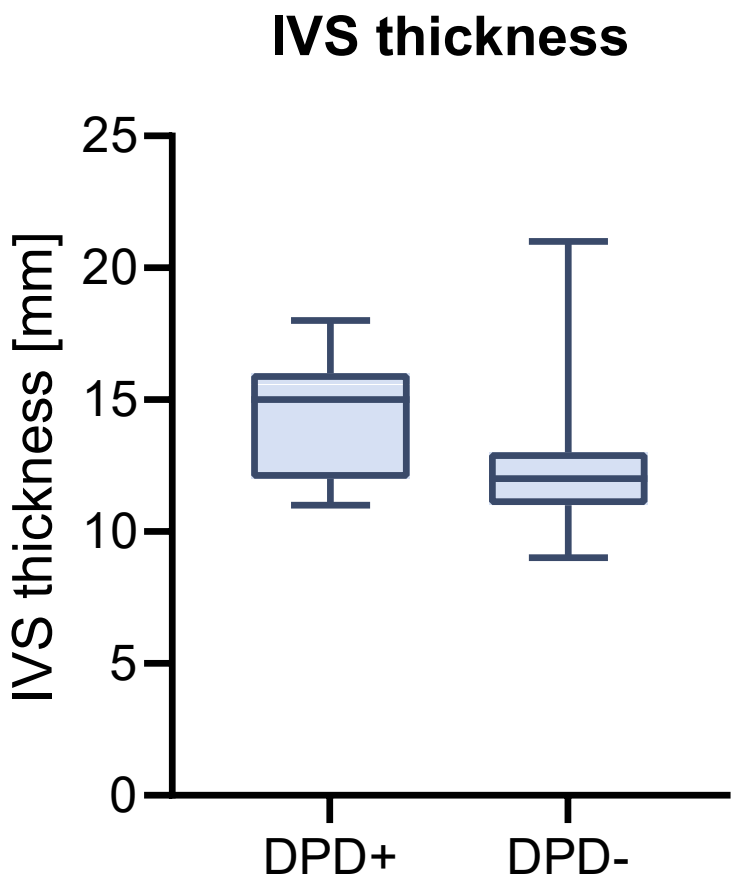
Results - Echocardiography

	DPD+ N=10	DPD- N=45	p value
VS thickness (mm)	**15 (12; 16)**	**12 (11; 13)**	**0.04**
LVMi (g/m^2)	123 (111; 155)	111 (102; 144)	0.09
EF (%)	57 (48; 66)	61 (55; 67)	0.30
GLS (%)	**-11,6±4,1**	**-14,4±2,6**	**0,04**
VTI AV (m)	**0,63±0,3**	**0,93±0,2**	**<0.001**
PG max (mmHg)	**54,00±13,1**	**68,8±21,2**	**0.049**
PG mean (mmHg)	34,6±8,7	43,3±13,6	0.09
AVAi (cm^2/m^2)	0,51±0,08	0,45±0,1	0,06
e' septálně (m/s)	0,04 (0,03; 0,06)	0,06 (0,05; 0,07)	0.06
e' laterálně (m/s)	**0,05 (0,04; 0,07)**	**0,08 (0,06; 0,10)**	**0.045**
LAVi (ml/m^2)	57 (46; 61)	46 (38,5; 63)	0.21
PASP (mmHg)	**46±15,7**	**36±9,8**	**0,03**

Preliminary results – left ventricle

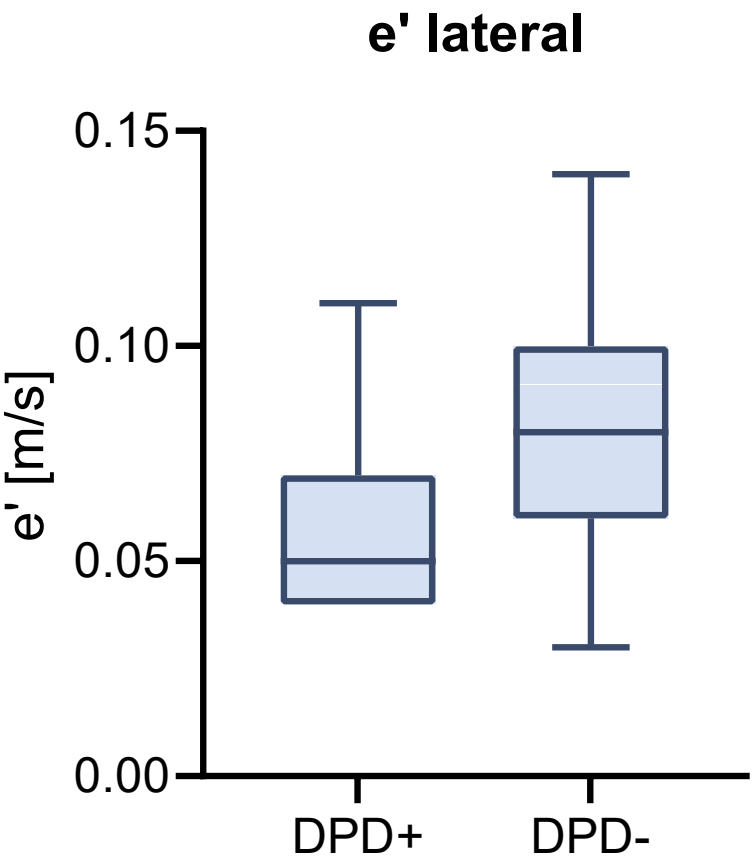


p=0.04

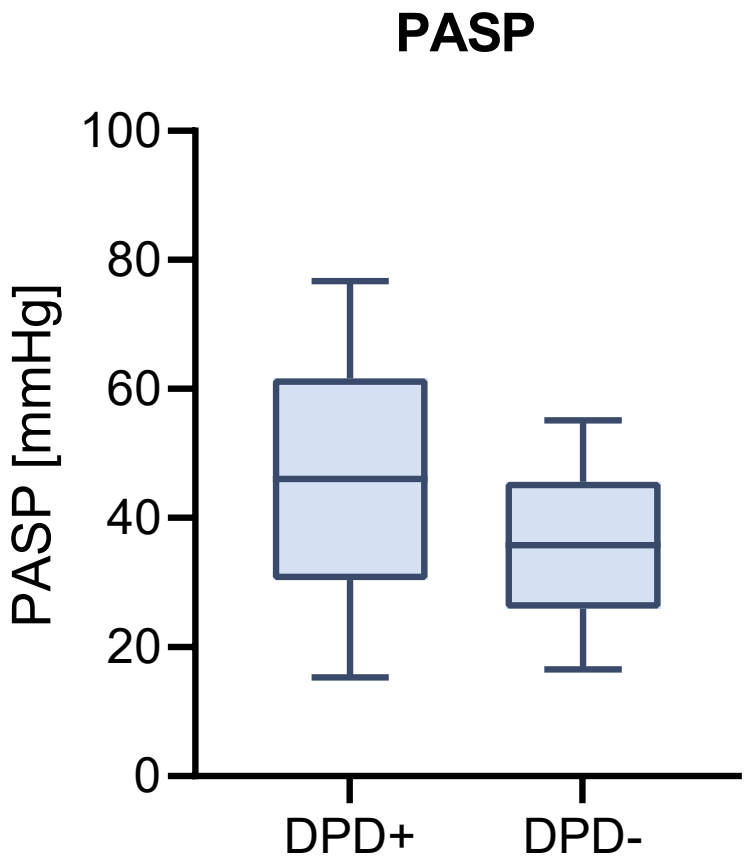


p=0.04

Preliminary results – diastolic function

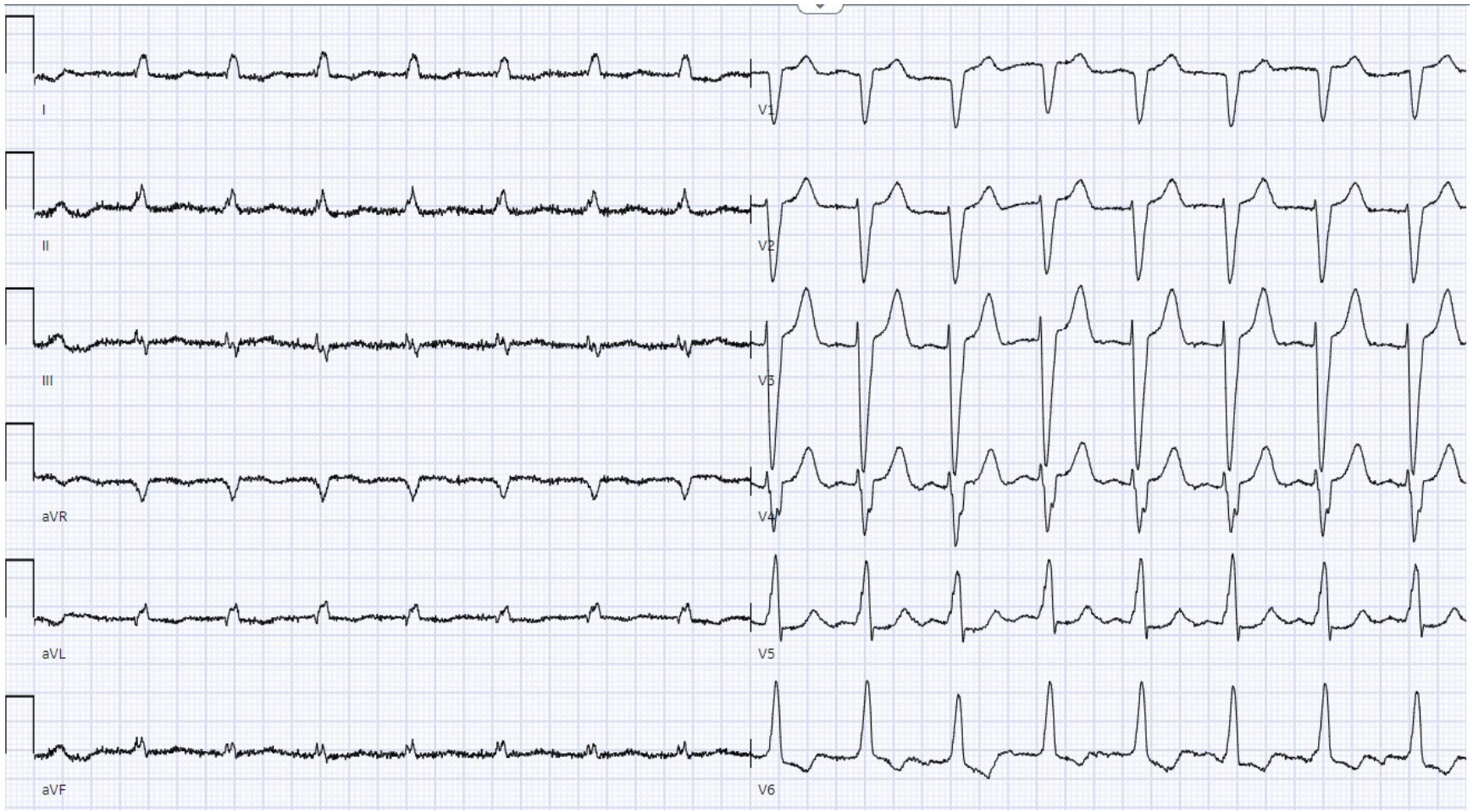


p=0.045

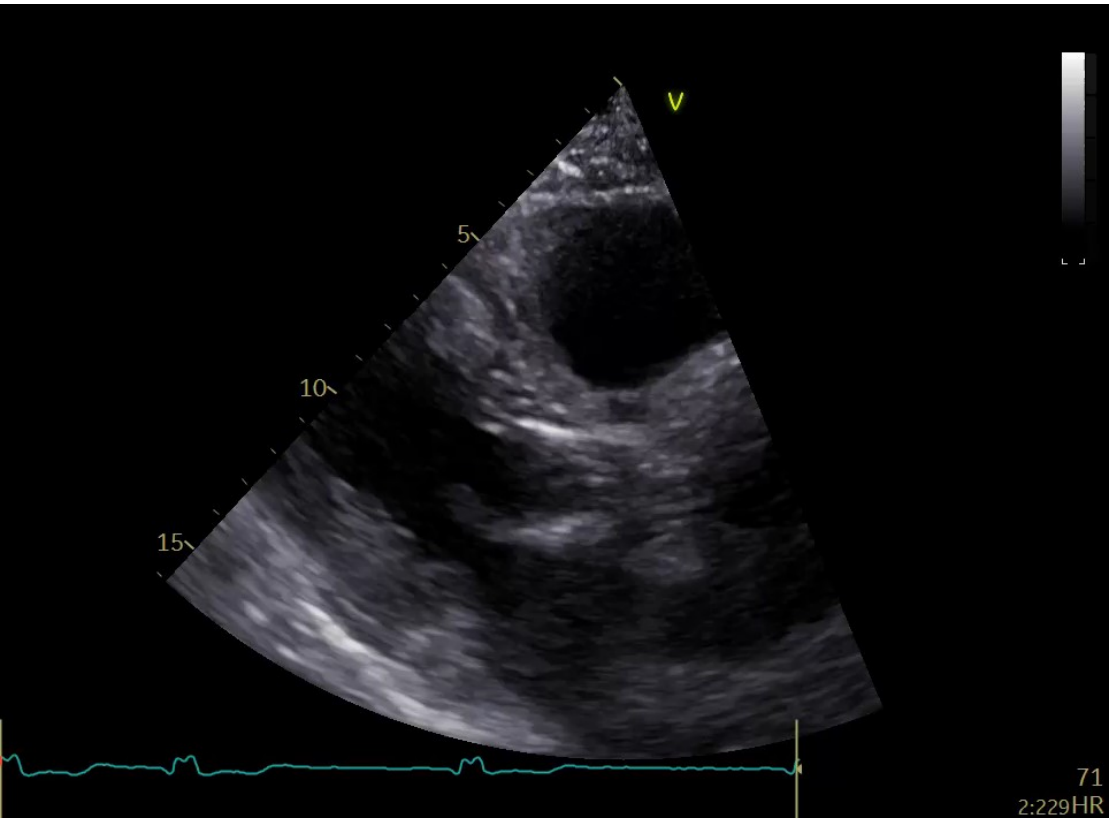


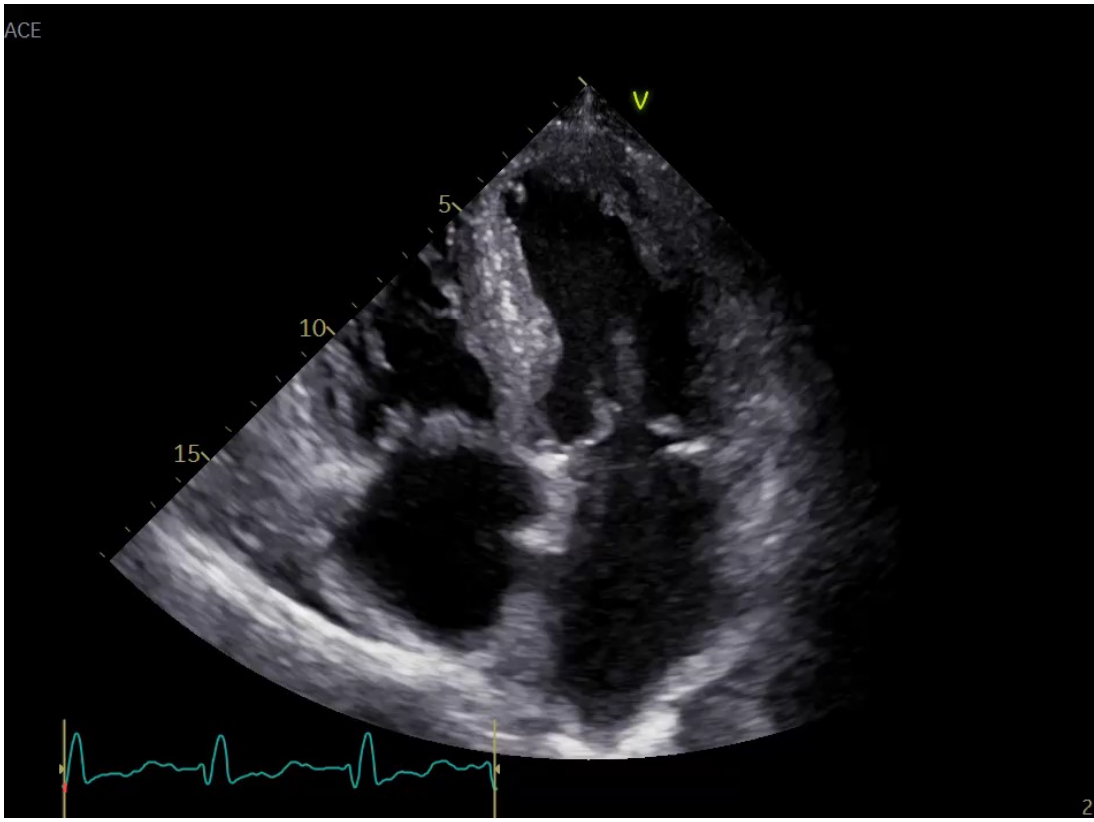
p=0.03

J.L. - ECG

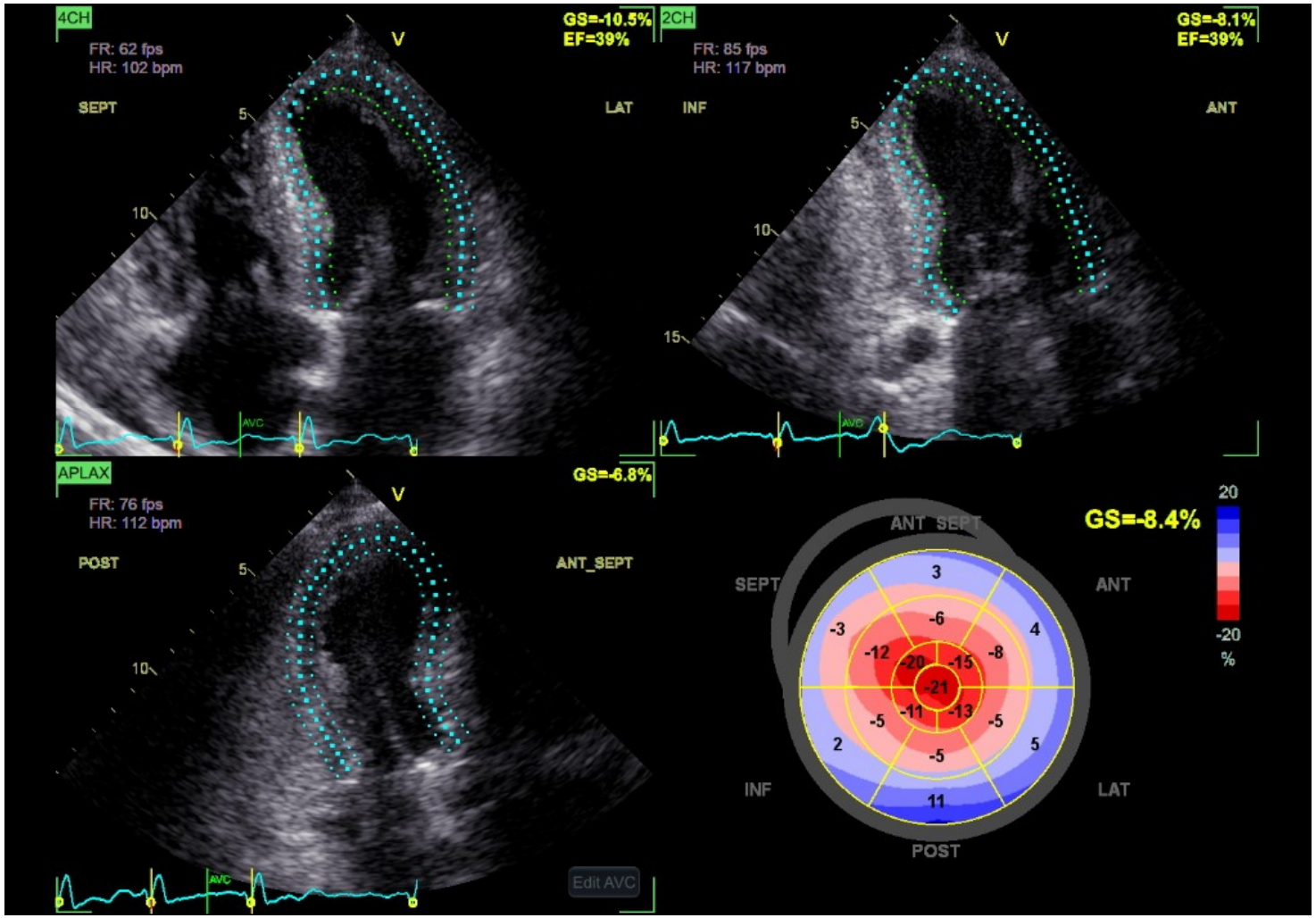


J.L. – echocardiograpgy





J.L. – global longitudinal strain



J.L. – DPD scintigraphy

- **On scintigraphy, we register significantly increased accumulation of the radiopharmaceutical in the myocardium, visually scored as 3 according to Perugini.**
- **Higher accumulation of the radiopharmaceutical in the left sternoclavicular joint - degenerative changes suspected.**
- **CONCLUSION:** Increased accumulation of DPD in the myocardium corresponds to the considered diagnosis of cardiac amyloidosis (suspected transthyretin type, if paraprotein is excluded).

Conclusions

- Prevalence of ATTR in our population was 9 %
- ATTR is associated with increased IVS thickness and decreas GLS
- ATTR patients had signs of more advanced diastolic dysfuncti
- Aortic stenosis in ATTR patients presented with lower pressur gradient and VTI, suggesting low-flow state

Conclusions

- Diagnosis of ATTR is crucial for early therapy to improve patients prognosis (specific treatment)
- Identifying cardiac amyloidosis in aortic stenosis is complex
- Further search for biomarkers indicating presence of amyloidosis in patients with aortic stenosis is needed

Conclusions

- Cardiac amyloidosis is a disease that worsens patient prognosis
- Early therapy is crucial for improving overall prognosis (options for specific treatment)
- In the context of aortic stenosis, diagnosing cardiac amyloidosis is not straightforward; there are red flags that could indicate the presence of TTR amyloidosis
- There is a need to continue the search for biomarkers that would indicate the presence of amyloidosis in patients with aortic stenosis

VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Thank you for your attention!