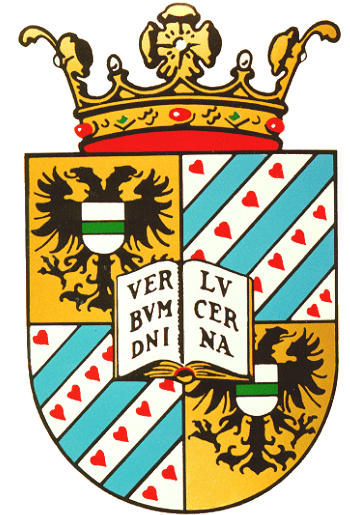


Cardiologische aspecten van amyloïdose

Ontmoetingsdag 1 februari 2020
Amyloïdose Nederland

Prof. Maarten van den Berg, cardioloog
Universitair Medisch Centrum Groningen

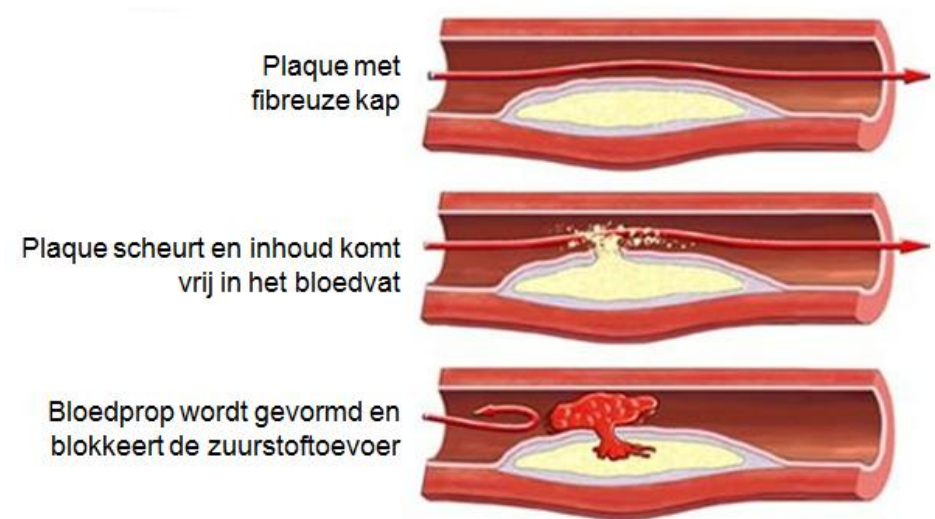
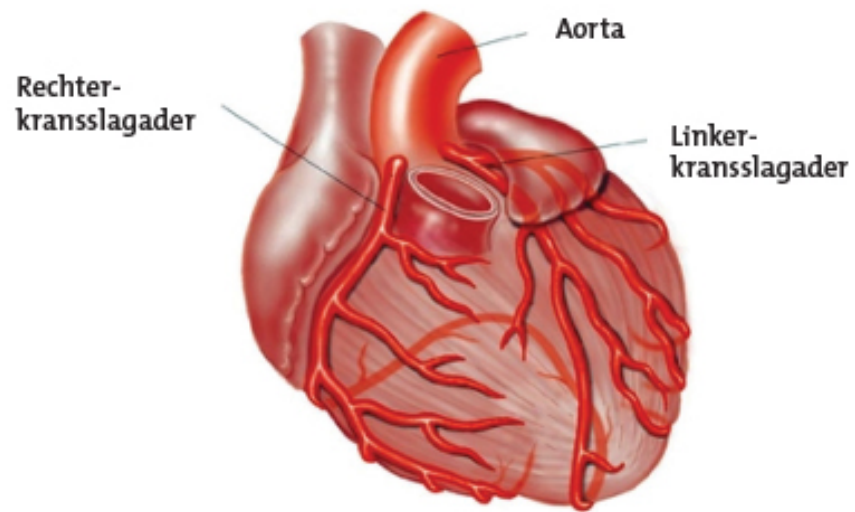


Ziektebeelden in de cardiologie

- Coronairlijden
- Ritme- en geleidingsstoornissen
- Hartfalen



Coronairlijden (“aderverkalking”)



Coronairlijden

Manifestaties:

- Angina pectoris
- Acuut hartinfarct
- Hartstilstand

Onderzoeken:

- Klachten, risicofactoren
- Inspanningstest
- Myocardscan
- CT-scan
- Hartcatheterisatie



Coronairlijden

Oorzaken:

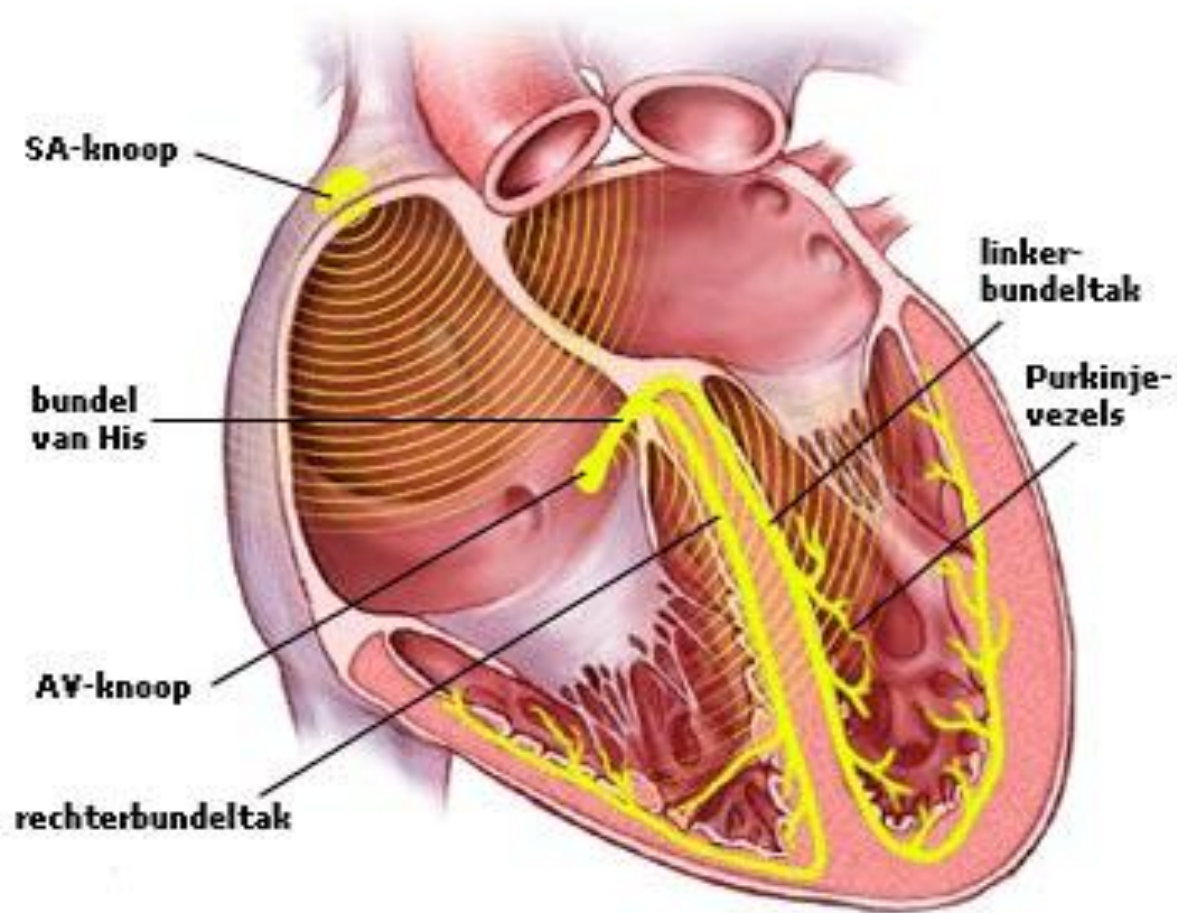
- Risicofactoren: roken, hypertensie, cholesterol, familie
- NB Amyloïdose

Behandeling:

- Risicofactoren: o.a. statine
- Aspirine
- Beta-blokker
- Dotteren
- Bypassoperatie



Ritme- en geleidingsstoornissen

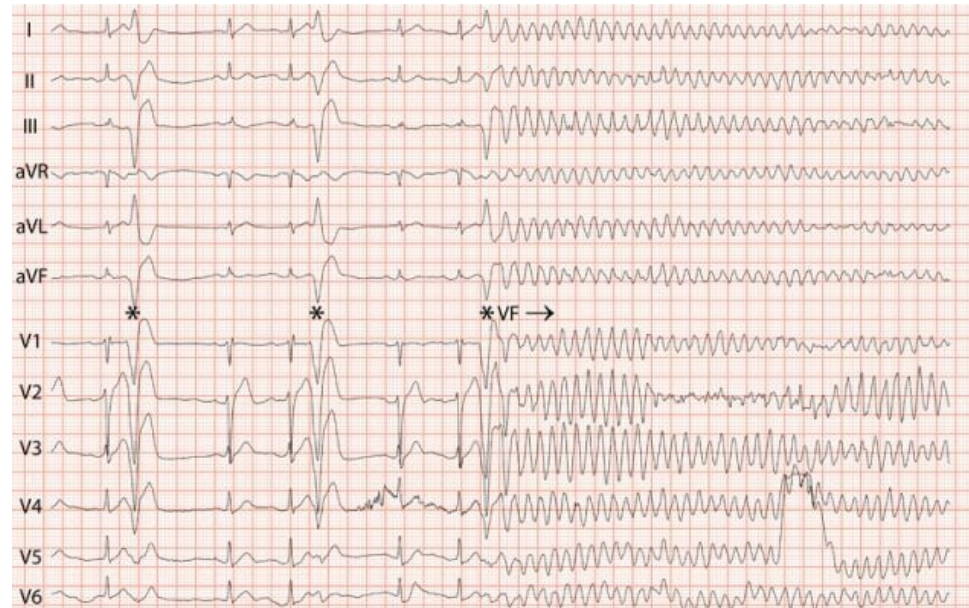


“Te snel”

boezemfibrilleren

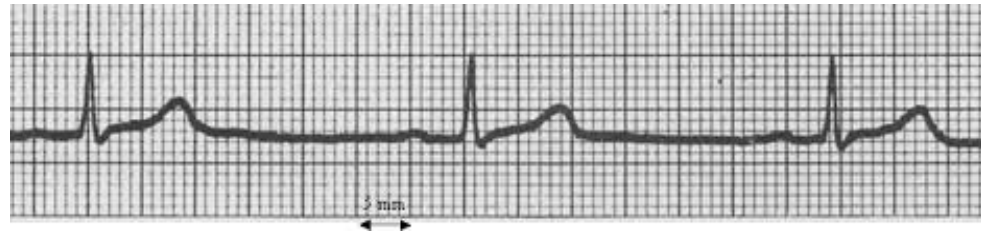
ventrikelfibrilleren

Ventricular Extrasystole



“Te langzaam”

sinusbradycardie



AV blok



AV blok



Ritme- en geleidingsstoornissen

Klachten:

- hartkloppingen, overslagen, hart op hol, wegrakingen, hartstilstand

Onderzoeken:

- ECG
- 24-uurs ECG (Holter)
- Inspanningstest
- Echocardiogram



Ritme- en geleidingsstoornissen

Oorzaken:

- Coronairlijden
- Kleplijden
- Cardiomyopathie, bv amyloïdose

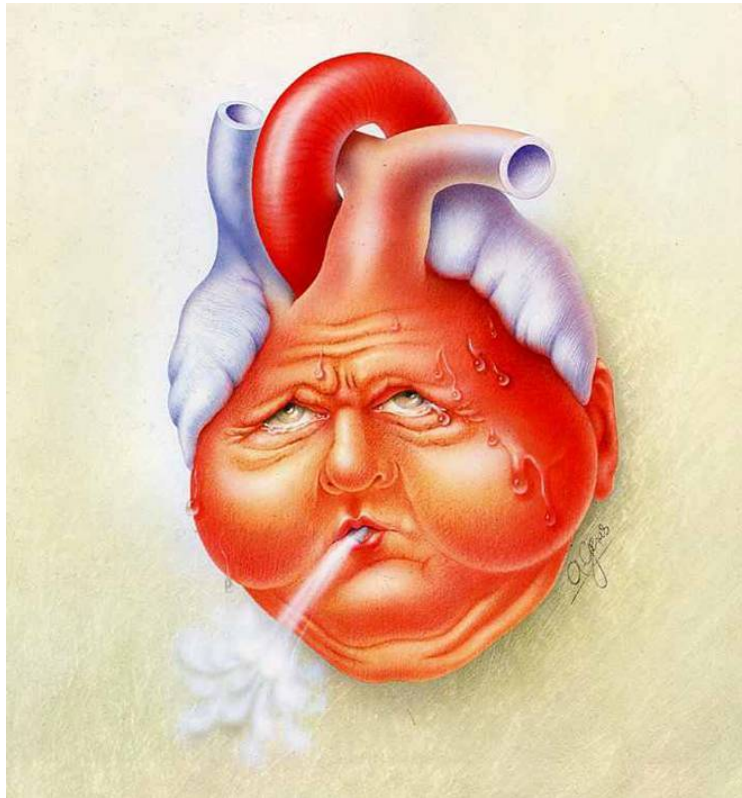
Behandeling:

- Oorzaak behandelen
- Medicatie, bv beta-blokker
- Pacemaker
- ICD



Hartfalen

Klachten: vermoeidheid, kortademigheid, vocht vasthouden



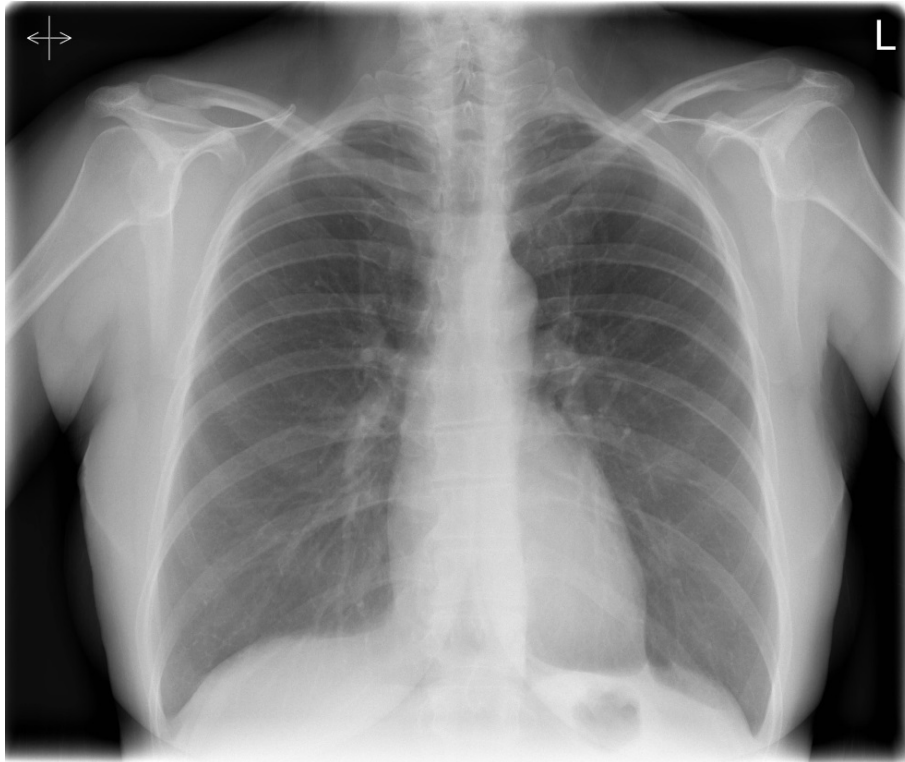
Hartfalen

Onderzoeken:

- ECG
- Bloedonderzoek: BNP
- X-thorax
- Inspanningstest
- Echocardiogram
- 24-uurs ECG (Holter)
- Hartcatheterisatie
- MRI



Thorax foto



Hartfalen

Hart te wijd, slap; heart failure reduced ejection fraction (“HFrEF”)

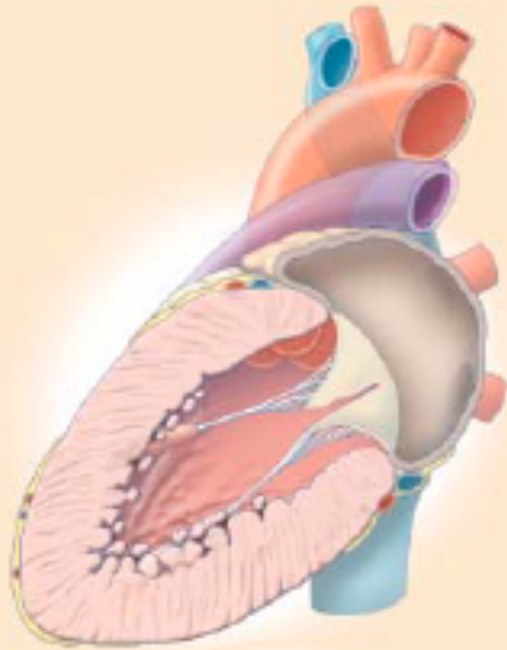
- Doorgemaakt hartinfarct
- Langdurige lekkage hartkleppen
- Cardiomyopathie

Hart te dik, stijf; heart failure preserved ejection fraction (“HFpEF”)

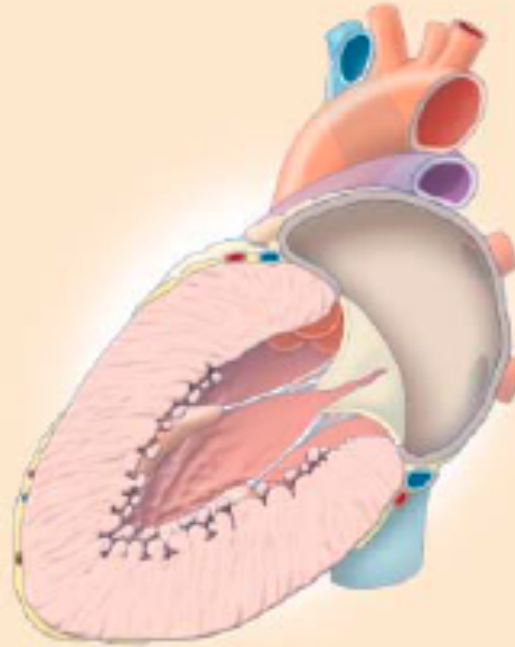
- Hoge bloeddruk
- Cardiomyopathie, bv amyloïdose



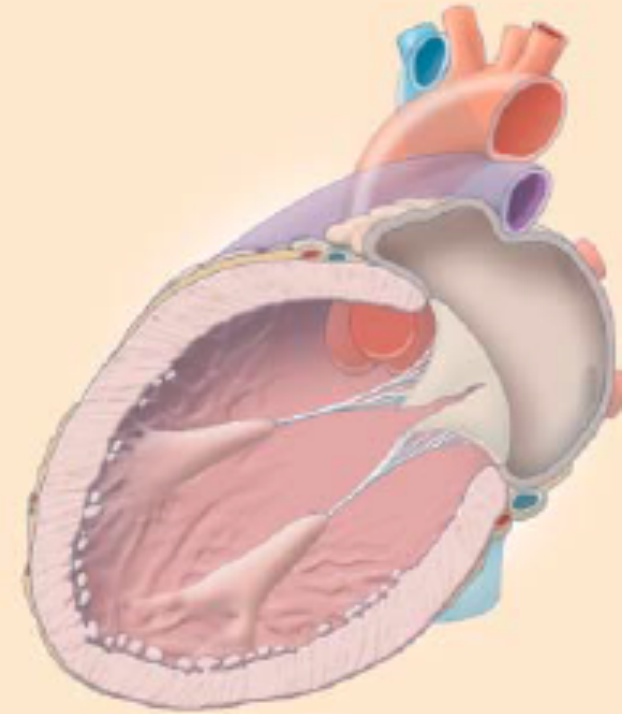
Ventricular remodeling in diastolic and systolic heart failure



Normal heart



Hypertrophied heart
(diastolic heart failure)



Dilated heart
(systolic heart failure)

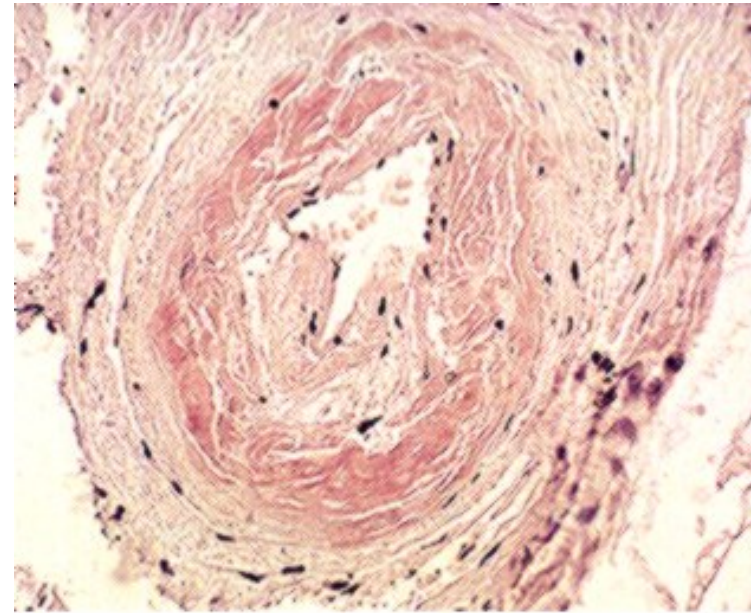
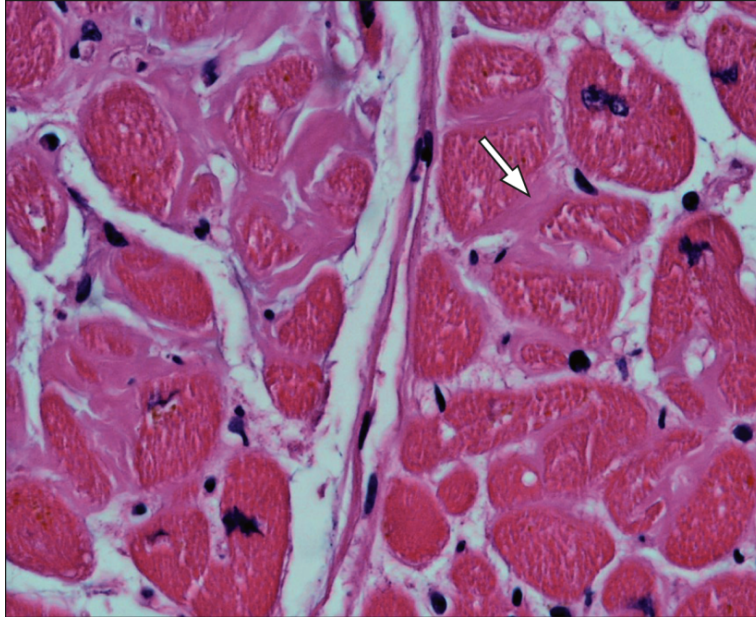
Cardiale amyloidose

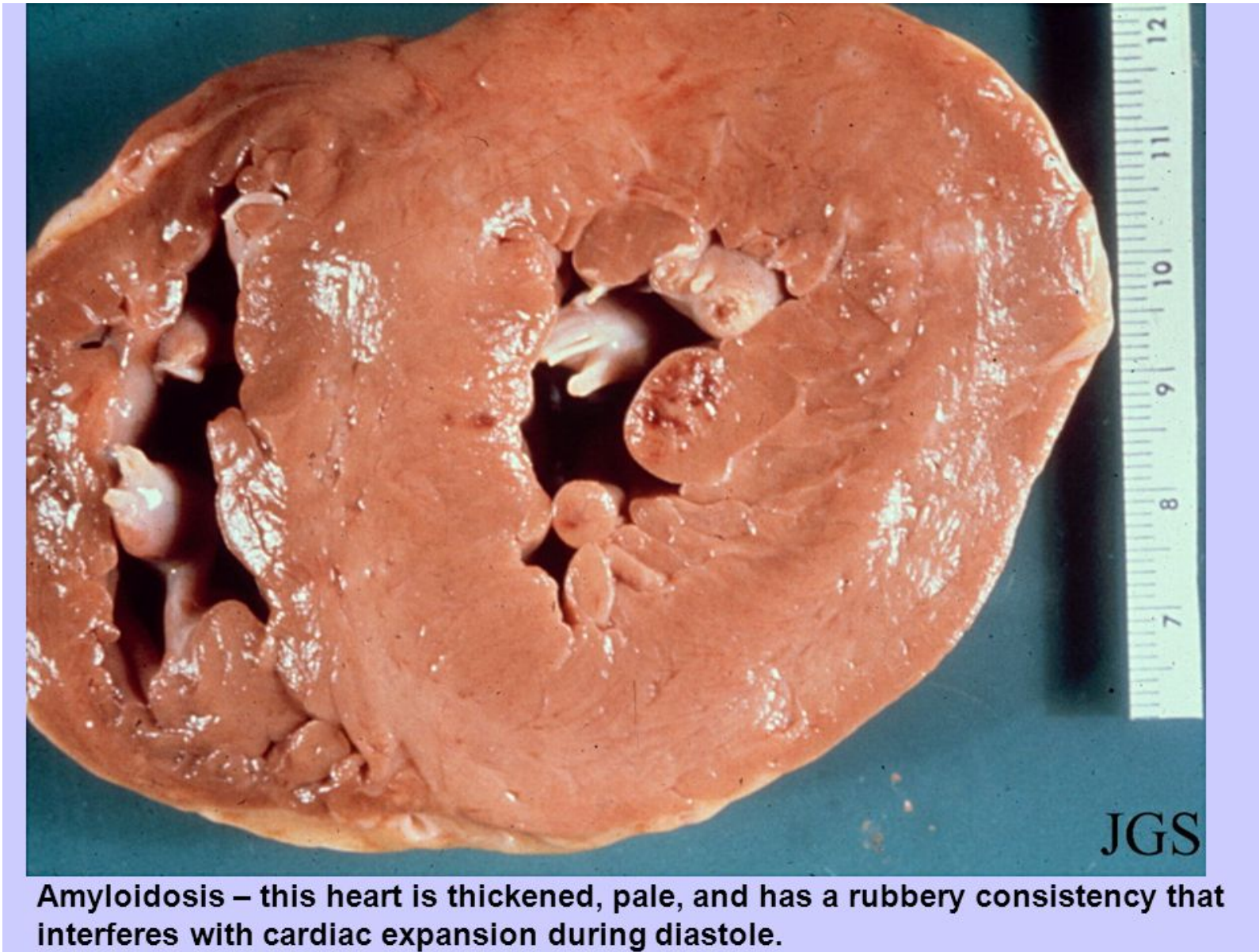
Stapeling van amyloïd in het hart:

- AL amyloïdose
- transthyretine amyloïdose:

erfelijk (ATTRv)

wild type (ATTRwt)





Amyloidosis – this heart is thickened, pale, and has a rubbery consistency that interferes with cardiac expansion during diastole.

Cardiale amyloïdose: Klachten

- Hartfalen: vermoeidheid, kortademigheid, vocht vasthouden
- Ritmestoornissen: hartkloppingen etc.
- Geleidingsstoornissen: wegrakingen etc.
- Angina pectoris

NB -Progressieve aandoening
 -Hart doet uiteindelijk meestal mee

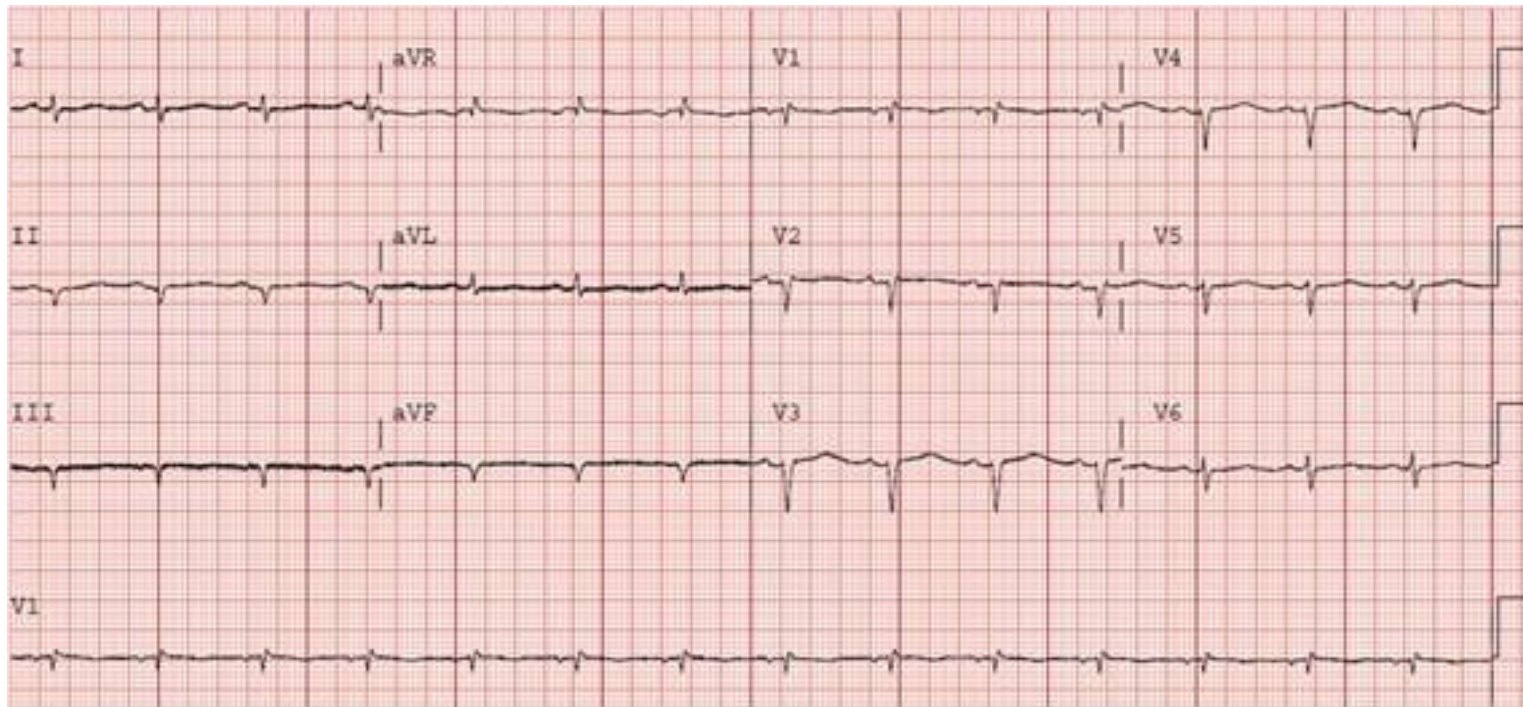
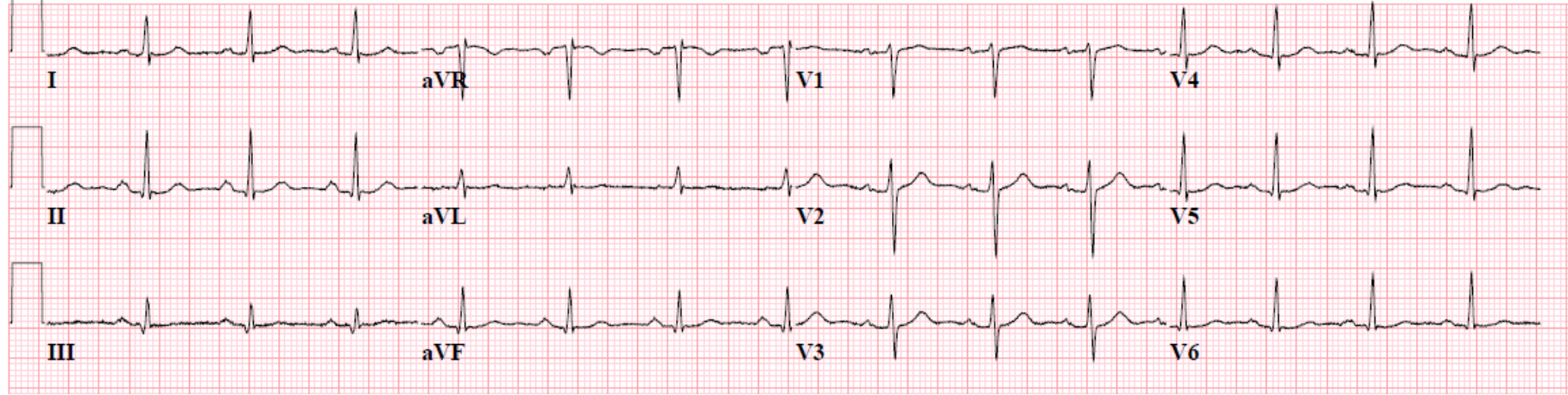


Onderzoeken

- ECG
- Echocardiogram
- 24-uurs ECG
- Bloedonderzoek
- MRI
- Myocard-biopsie
- Bot-scan



STUDIE:

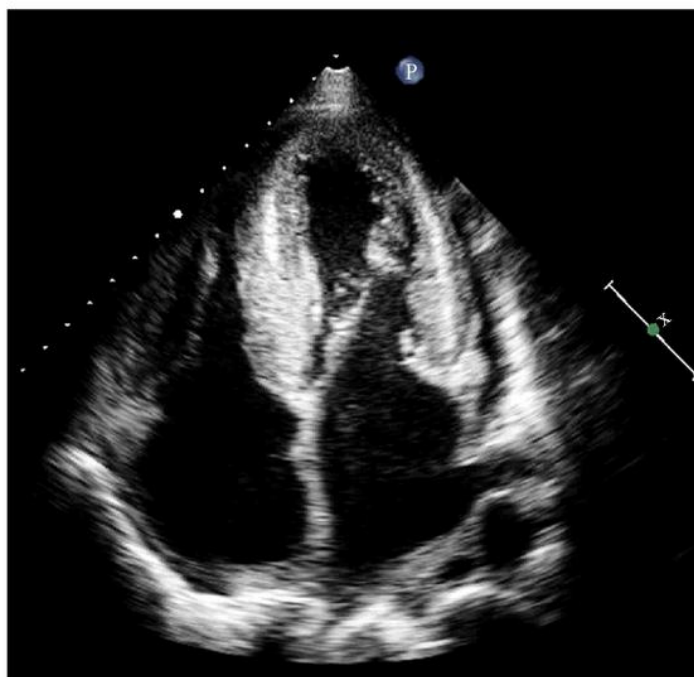
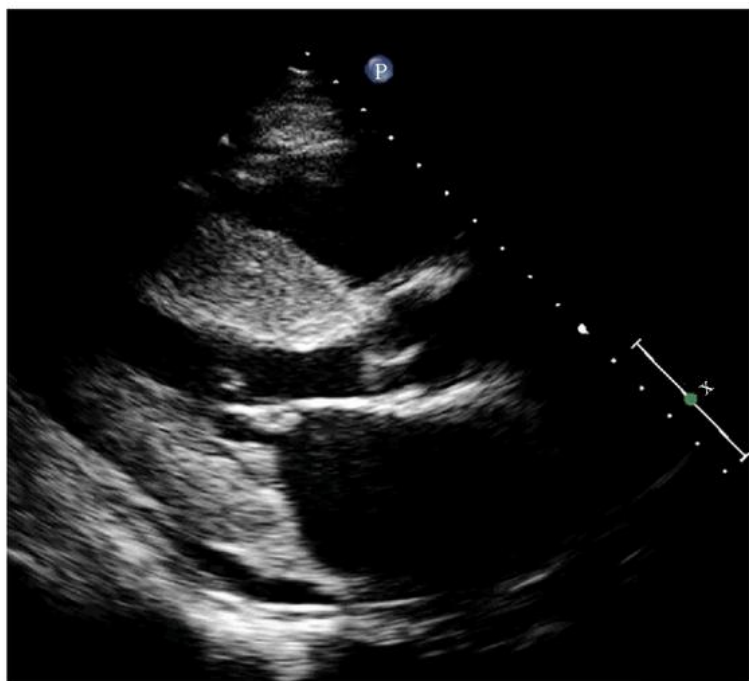
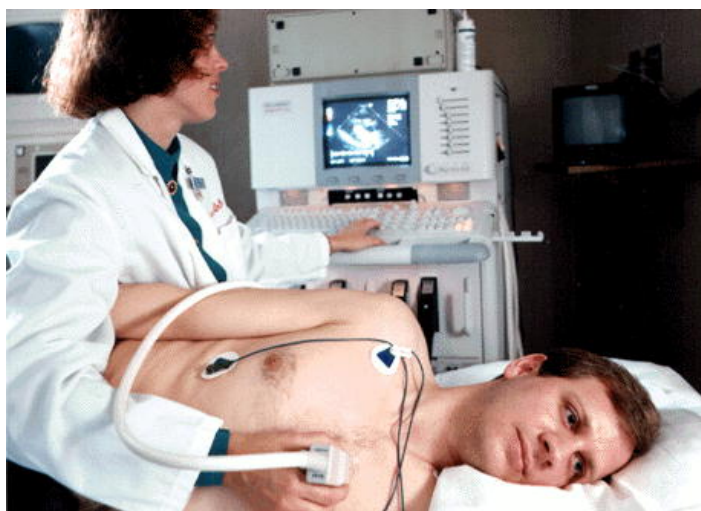


Echocardiogram

- Verdikte wanden (hypertrofie):
 - Li-kamer >10 mm, Re-kamer >5 mm
 - Geen andere verklaring (bv aortaklepvernauwing)
- Geen verwijding (dilatatatie)
- Goede (systolische) pompfunctie;
 - ejectie fractie $>60\%$
- Gestoorde vulling (diastolische dysfunctie)
- Verwijding boezems
- Pericardvocht



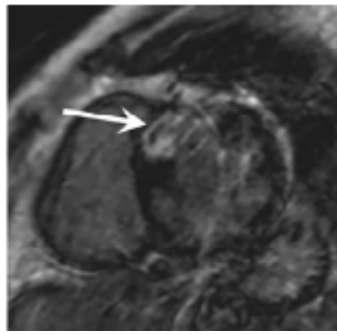
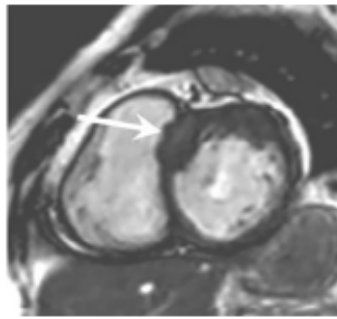
Cardiologische aspecten van amyloïdose



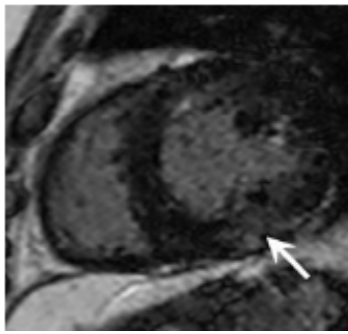
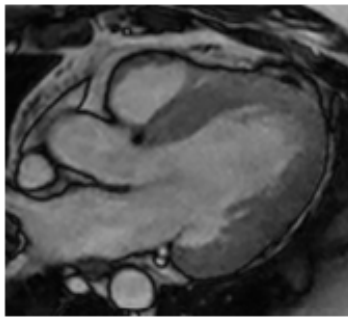
MRI/CMR



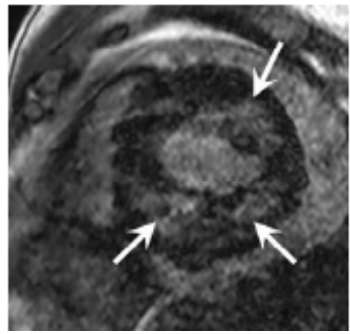
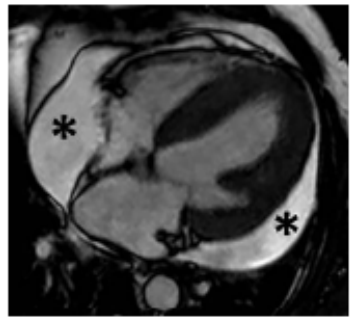
Hypertrophic
Cardiomyopathy



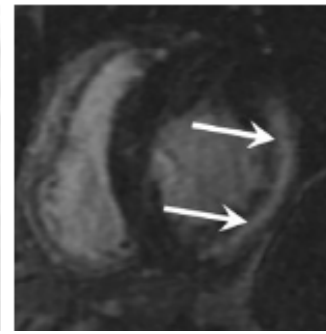
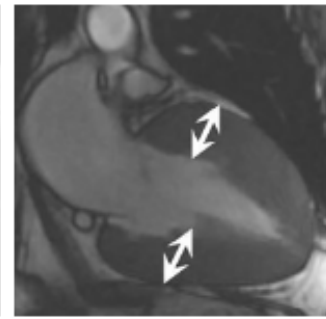
Hypertensive
Heart disease



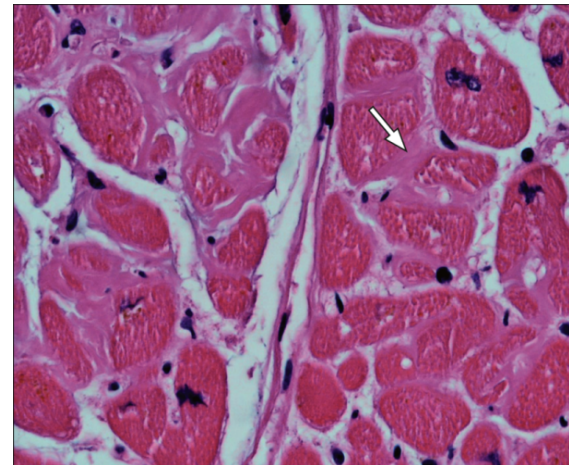
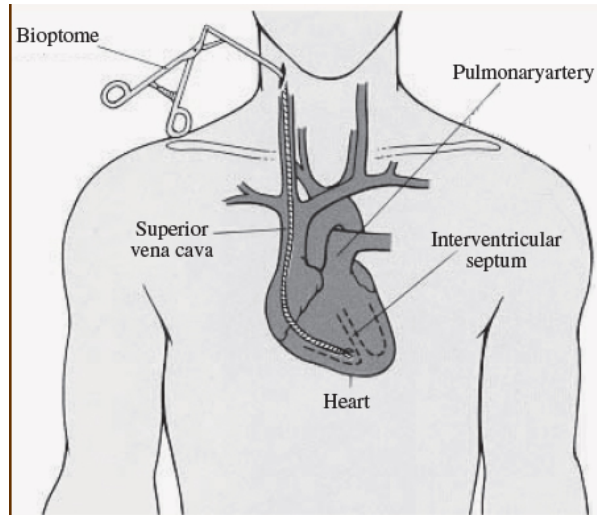
Amyloidosis



Fabry's disease



Myocardiopsie

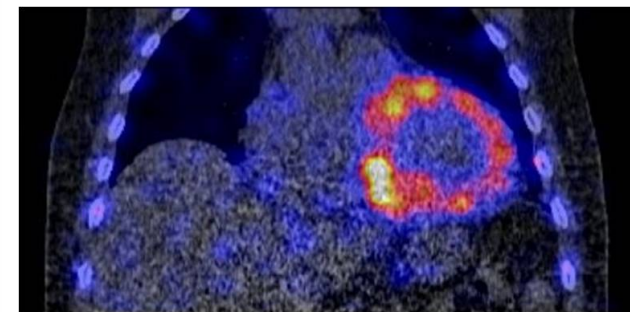
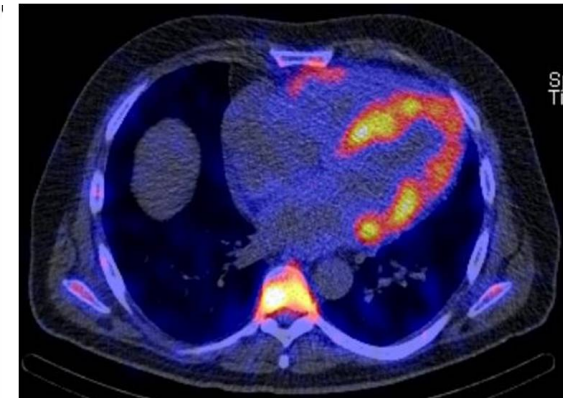
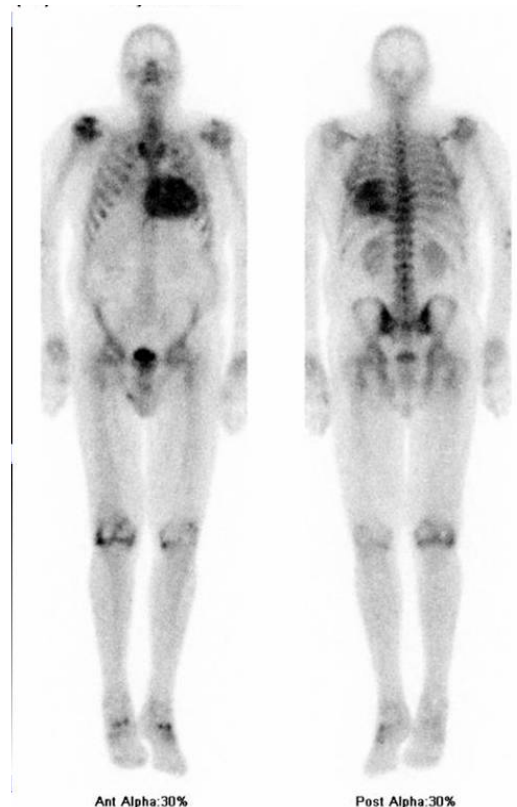


Myocardiopathie: belastend, complicaties

Alternatieven:

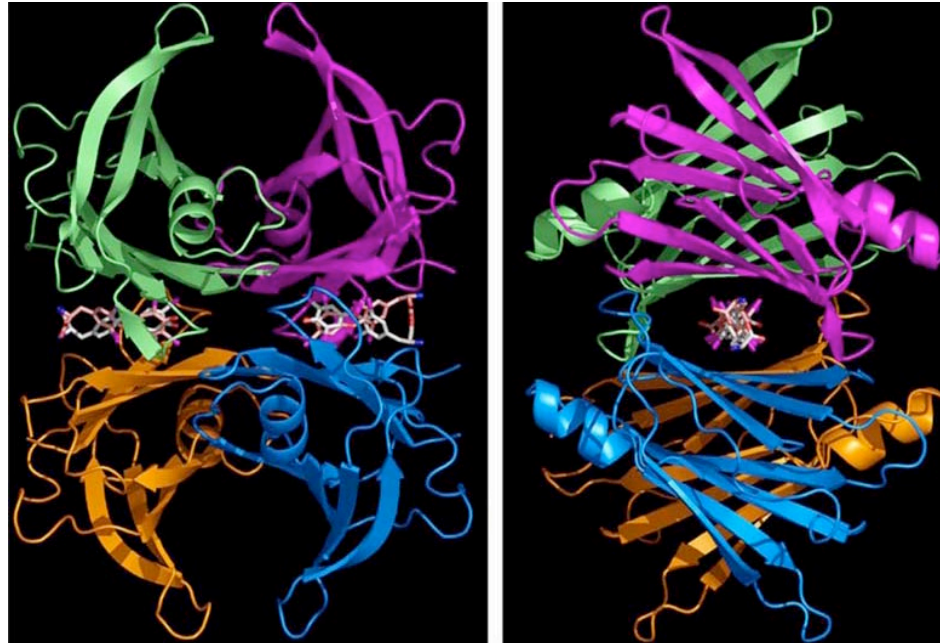
- Amyloïdose: reeds aangetoond?
- Vetbiopsie
- Bot-scan

NB alleen transthyretine



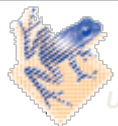
Transthyretine amyloïdose - ATTR

Transthyretine:
transporteiwit,
productie in lever



2 vormen:

- Erfelijk, familiair: mutatie in coderende gen
>10 families, >100 patienten
UMCG - expertisecentrum
- Verworven (wild type)

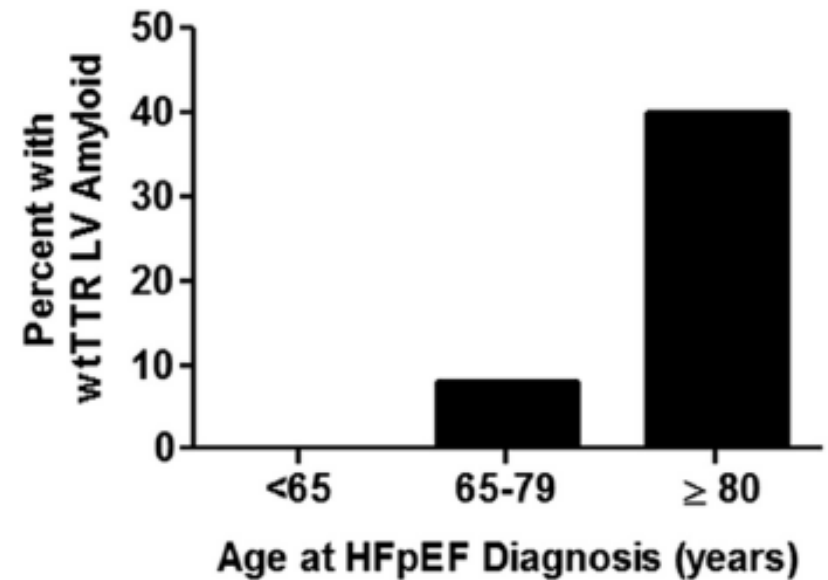
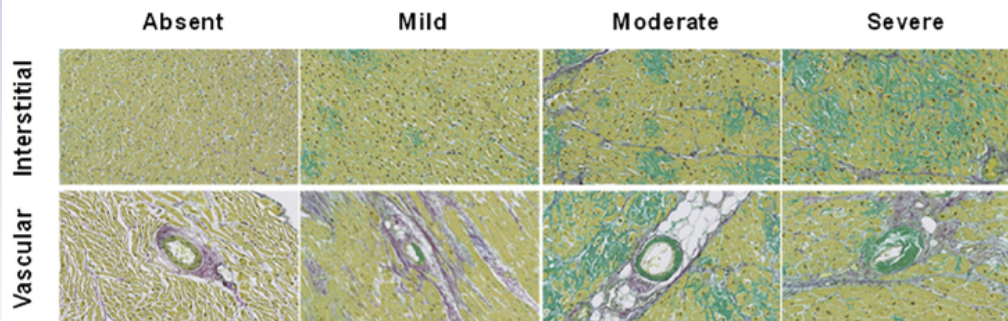


Transthyretine amyloidose – wild type

Seniele amyloidose

Oorzaak van hartfalen (HFpEF)

Autopsie-studie:



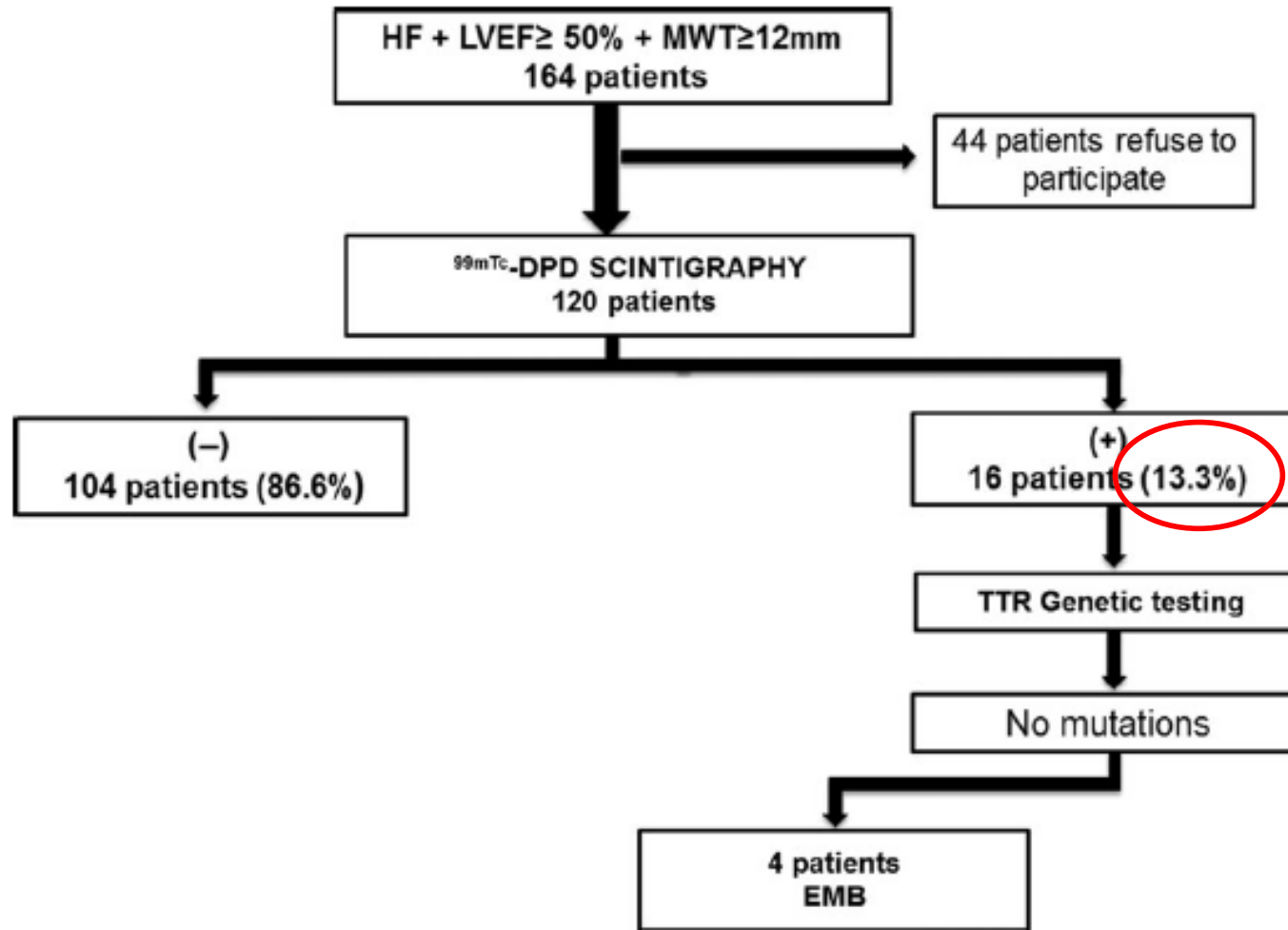


Figure 3 Assembly of the cohort and participant flow. LVEF, left ventricular ejection fraction; MWT, maximal wall thickness; EMB, endomyocardial biopsy; HF, heart failure; TTR, transthyretin.

Conclusion:

ATTRwt is an underdiagnosed disease that accounts for a significant number (13%) of HFpEF cases. The effect of emerging TTR-modifying drugs should be evaluated in these patients.

Prevalentie HFpEF obv ATTRwt in NL

- Hartfalen: ≈ 200.000 patiënten
 - >60 jaar: 98%
 - HFpEF: 50%
 - Mannen: 30%
- > ≈ 30.000 oudere mannen met HFpEF
- Oudere mannen met HFpEF: 5-10% obv ATTRwt
- > ≈ 2000 pt in NL met HFpEF obv ATTRwt



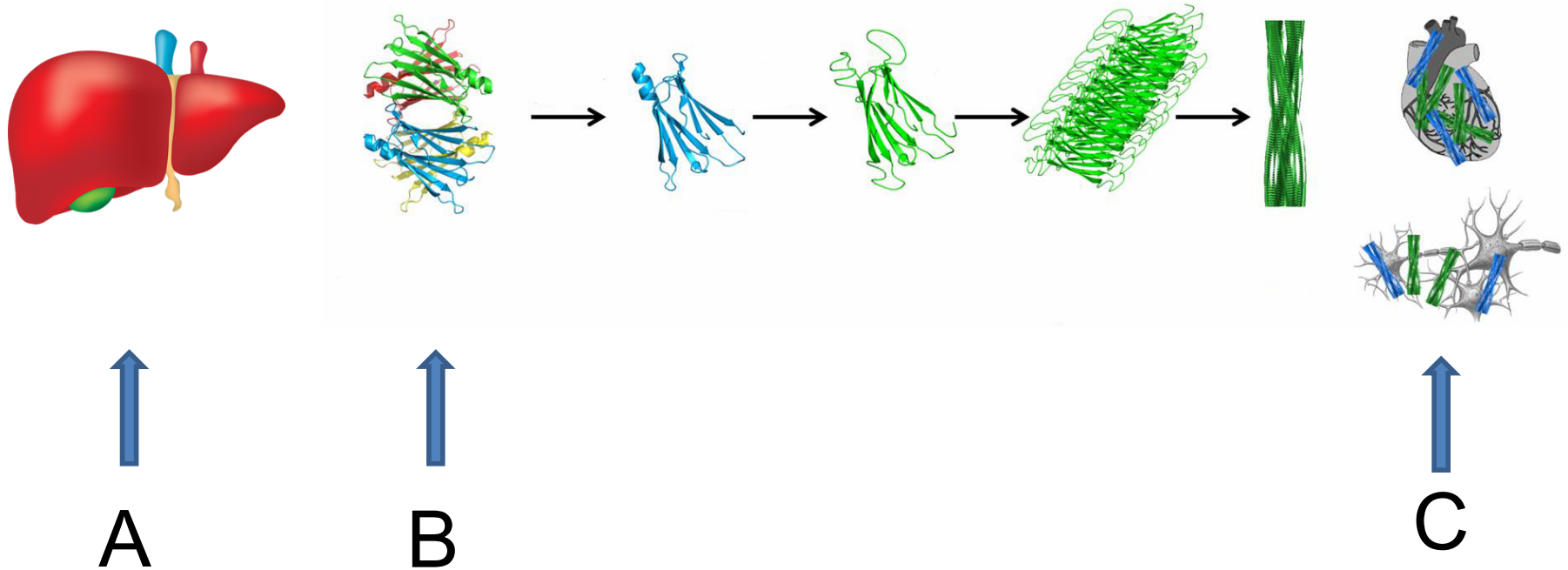
Cardiale amyloidose - behandeling

- Matige - slechte prognose!
NB mede afhankelijke van oorzaak (AL vs ATTR)
- Hartfalen: HFpEF
 - zoutbeperking
 - geen goede opties
 - symptomatisch: diuretica
 - geen digoxine, calcium-blokkers
 - igv HFrEF: ACE-remmers, beta-blokker
 - ev. pacemaker
 - ev. ICD



Behandelprincipes ATTR:

- A Productie transthyretine verminderen
- B Transthyretine stabiliseren
- C Amyloïd opruimen



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Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

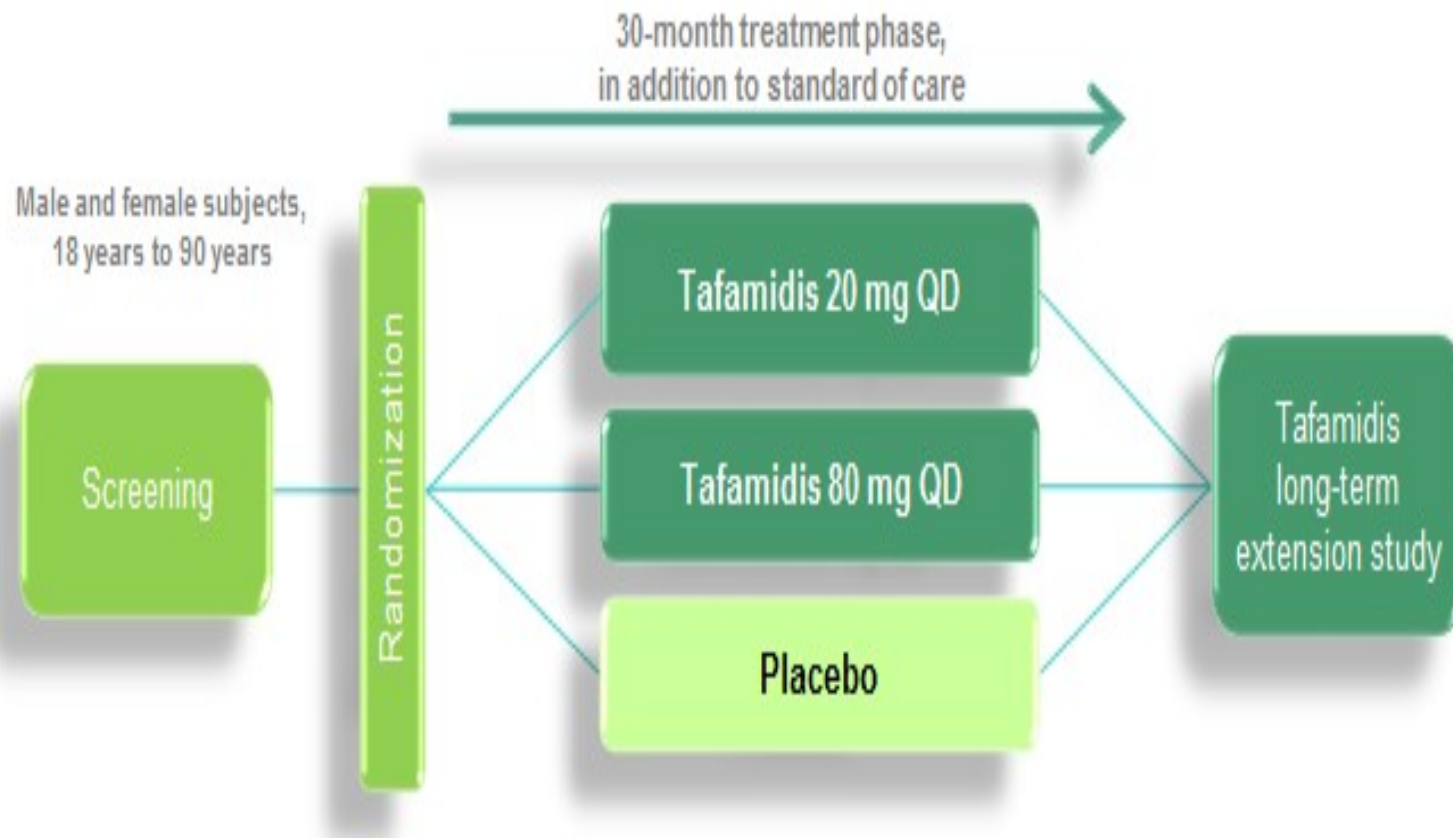
ATTR-ACT study

Tafamidis: stabiliseert transthyretine



ATTR-ACT Study Design

Tafamidis: transthyretine stabiliser



Inclusion/Exclusion Criteria¹

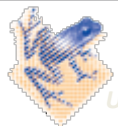
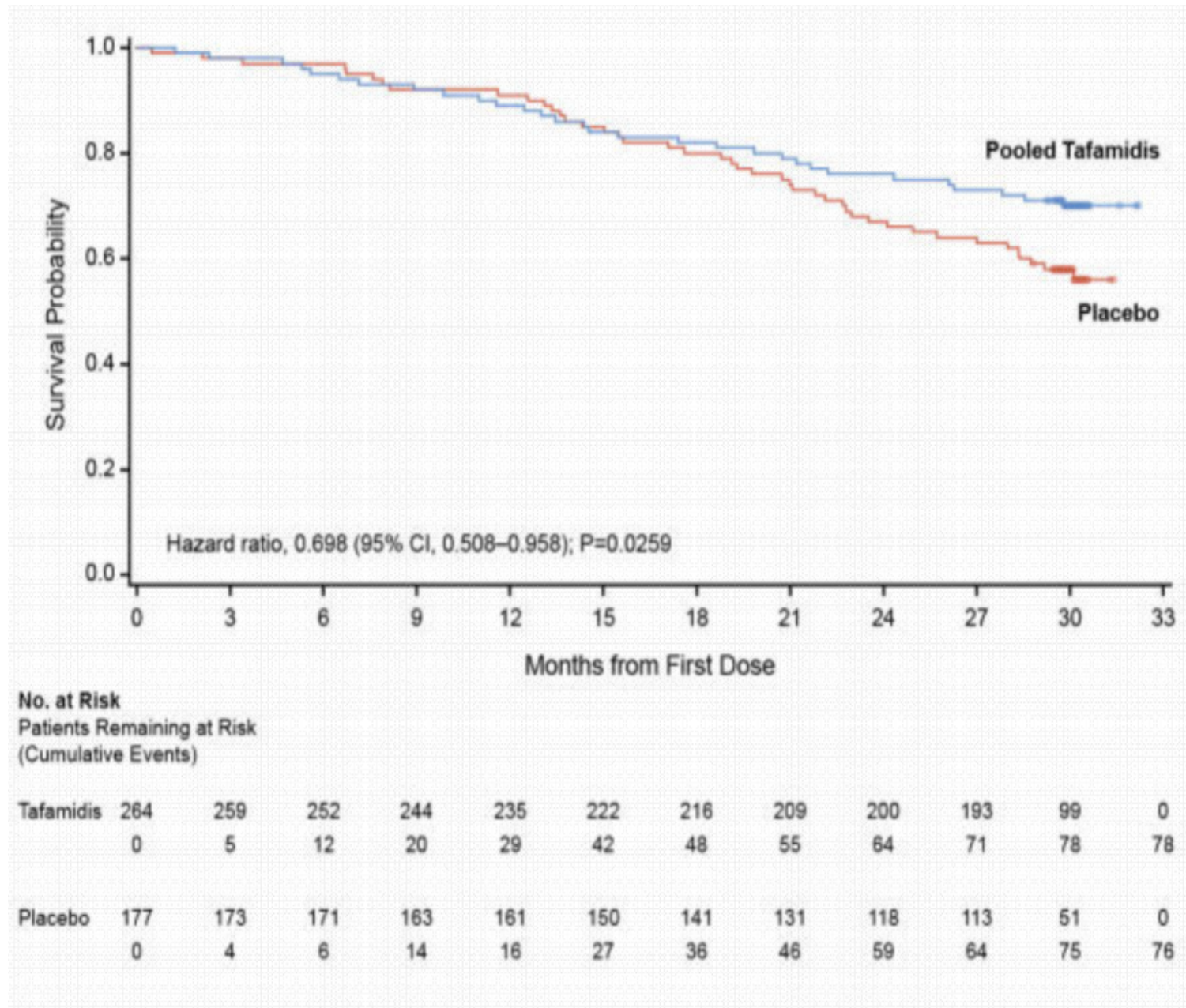
- **Key Inclusion Criteria**
 - Presence of amyloid deposits in biopsy tissue (cardiac or non-cardiac) and TTR precursor protein identification by mass spectrometry, immunohistochemistry or scintigraphy
 - Evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness >12 mm
 - A medical history of heart failure (HF) with at least 1 prior hospitalization for HF signs or symptoms of congestive HF requiring treatment with a diuretic for improvement
 - NT-proBNP ≥ 600 pg/mL
 - 6-Minute Walk Test distance >100 meters
- **Key Exclusion Criteria**
 - New York Heart Association (NYHA) class IV
 - Glomerular filtration rate (eGFR) of <25 mL/min/1.73 m²

¹Maurer MS, et al. Circ Heart Fail 2017;10.

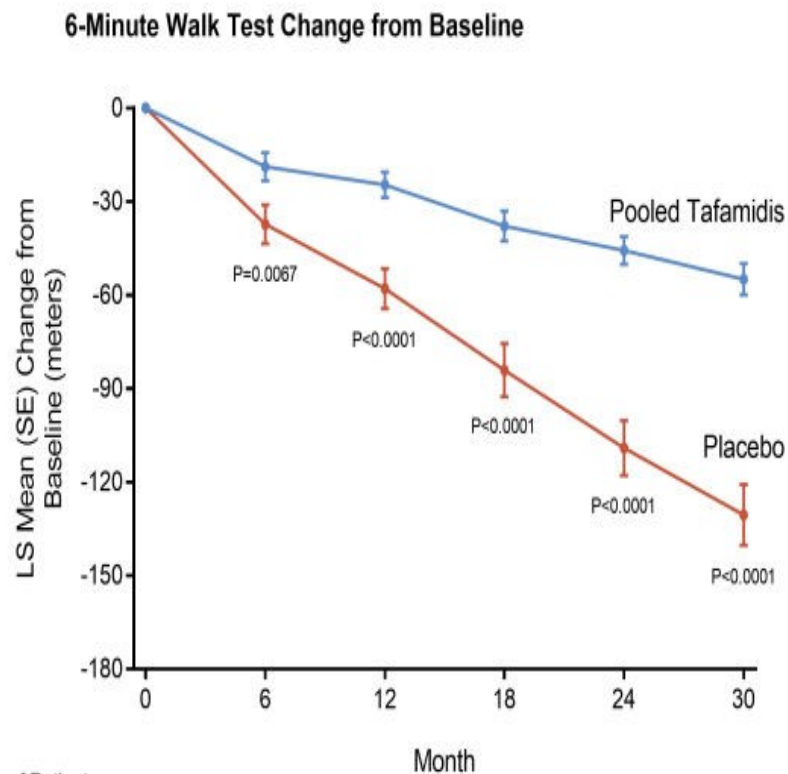
“Bewezen HFpEF obv ATTR – amyloidose”



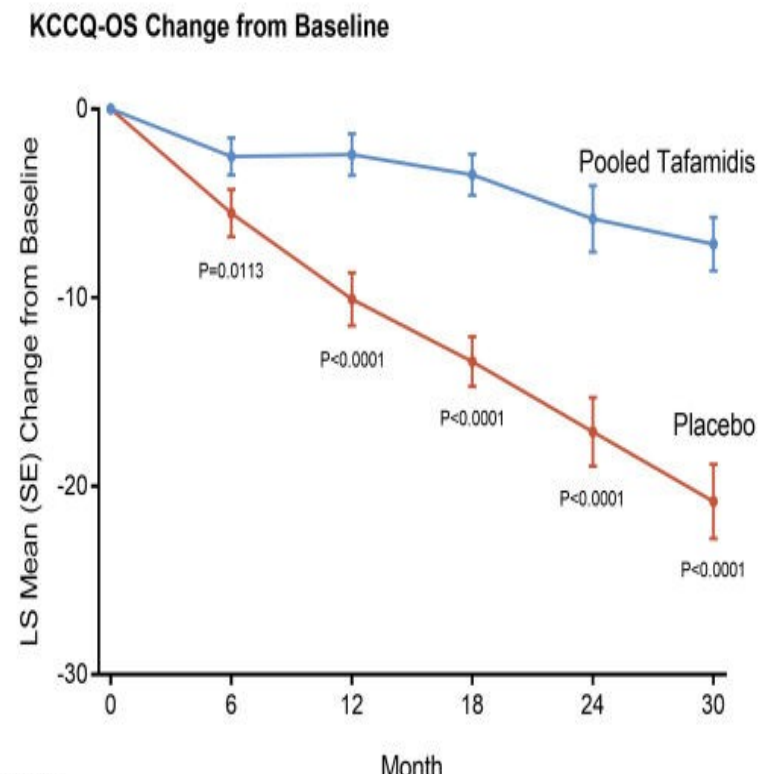
All-Cause Mortality



Key Secondary Endpoints: 6-minute Walk Test and KCCQ-OS



No. of Patients	Month	0	6	12	18	24	30
Tafamidis		264	233	216	193	163	155
Placebo		177	147	136	111	85	70



No. of Patients	Month	0	6	12	18	24	30
Tafamidis		264	241	221	201	181	170
Placebo		177	159	145	123	96	84



Cardiale amyloïdose - Conclusies

- Denk er aan!
- Komt relatief vaak voor
- Diagnose goed te stellen
- Matige - slechte prognose
- Algemeen: lastig te behandelen
- ATTR; nieuwe behandelingen

