Kardiale Amyloidose: nur wer sucht, der findet

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Disclosures

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Alnylam, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius, Imedos, Medtronic, Mepha, MSD, Mundipharma, Novartis, Orion Pharma, Pierre Fabre, Pfizer, Roche, Schwabe Pharma, Vifor, Zoll

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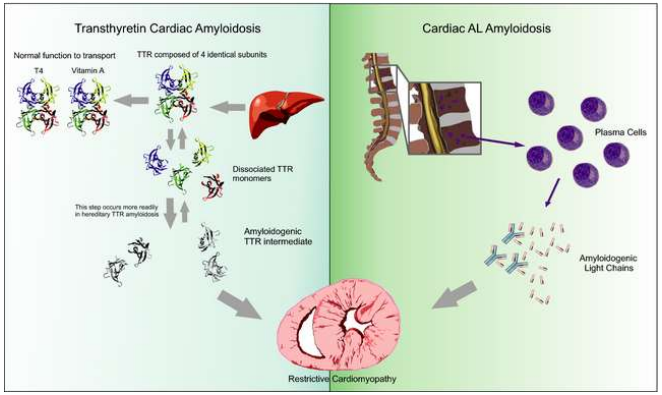
Kardiale TTR und AL-Amyloidose



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Patel KS, Hawkins PN, J Internal Med 2015

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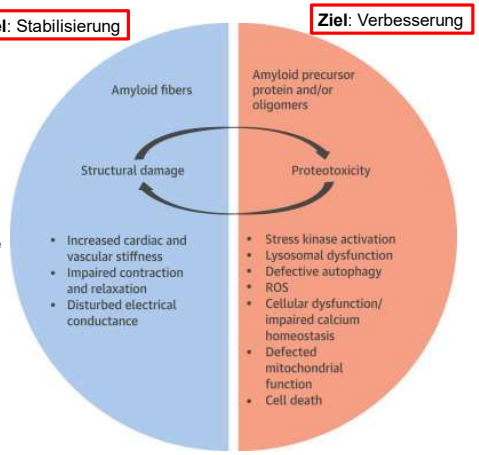
Kardiale Amyloidose ist vor allem: HERZINSUFFIZIENZ

- **Dyspnoe, periphere Ödeme**
- **Palpitationen (insbesondere atriale Arrhythmien)**
- **Müdigkeit, Schwäche**
- **Leistungsintoleranz**
- **Thrombembolische Komplikationen**
- **Niereninsuffizienz (erhöhte Füllungsdrücke und reduziertes Herzminutenvolumen)**
- **Erhöhter ZVD führt zu Hepatomegalie, Aszites, Anasarka)**



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Rodney H. Falk et al, JACC 2016

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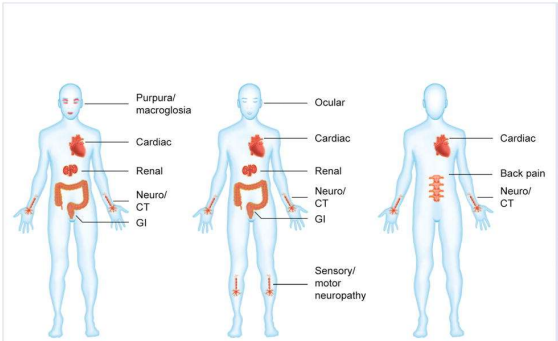
Beide, AL and TTR-Amyloidose können das Herz befallen



Skin/soft tissue
- Purpura
- Macroglosia
- Back pain

Cardiac
- Fatigue
- Shortness of breath
- Edema
- Arrhythmias

Renal
- Renal insufficiency
- Proteinuria
- Edema

GI
- Diarrhea
- Constipation
- Nausea
- Early satiety

Neuro
- Carpal tunnel (CT)
- Peripheral neuropathy
- Orthostasis
- Weakness

Ocular
- Vitreous opacification
- Glaucoma
- Papillary abnormalities

Nativi-Nicolau J et Maurer M Curr Opin Card 2018

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Diagnostic Work-up

An eine kardiale Amyloidose sollte gedacht werden bei jedem **Patienten mit einer unklaren Herzinsuffizienz und einem Echo/MRI, welches für eine Amyloidose typisch** ist

Left Ventricular Wall Thickness ≥ 12 mm

+ ≥1 of

- Heart failure in ≥ 65 years
- Aortic stenosis in ≥ 65 years
- Hypotension or normotensive if previously hypertensive
- Sensory involvement, autonomic dysfunction
- Peripheral polyneuropathy
- Proteinuria
- Skin bruising
- Bilateral carpal tunnel syndrome
- Ruptured biceps tendon
- Subendocardial/transmural LGE or increased ECV
- Reduced longitudinal strain with apical sparing
- Decreased QRS voltage to mass ratio
- Pseudo Q waves on ECG
- AV conduction disease
- Possible family history

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ESC Myocardial WG position paper, EHJ 2021

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Diagnostischer Work-up

An eine kardiale Amyloidose sollte gedacht werden bei jedem **Patienten mit einer unklaren Herzinsuffizienz und einem Echo/MRI, welches für eine Amyloidose typisch** ist

Was ist typisch für eine Amyloidose?

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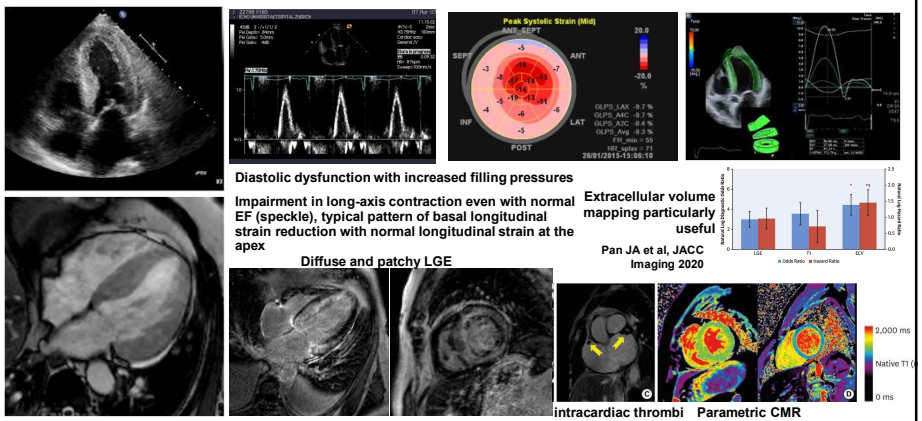
Echocardiography and MRI are the cornerstone of diagnosis



Diastolic dysfunction with increased filling pressures

Impairment in long-axis contraction even with normal EF (speckle), typical pattern of basal longitudinal strain reduction with normal longitudinal strain at the apex

Diffuse and patchy LGE

Extracellular volume mapping particularly useful

Pan JA et al, JACC Imaging 2020

intracardiac thrombi

Parametric CMR elevated septal native T1 up to 1,550 msec

Images courtesy of Robert Manka, USZ

Lee SP et al, JCVI 2019

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Diagnosis of Cardiac Amyloidosis

Invasive
(all types)

Cardiac Biopsy positive for amyloid

or

Extracardiac Biopsy positive for amyloid
+
Echocardiographic/CMR criteria

Non-Invasive
(only for ATTR)

Grade 2 or 3 cardiac uptake at diphosponate Scintigraphy
+
Negative serum free light chains & negative serum and urine immunofixation (SPIE & UPIE)
+
Echocardiographic/CMR criteria

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ESC Myocardial WG position paper, EHJ 2021

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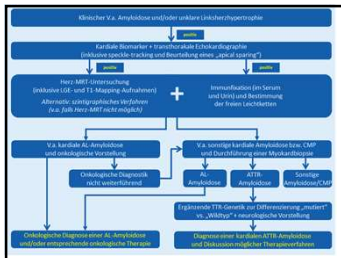
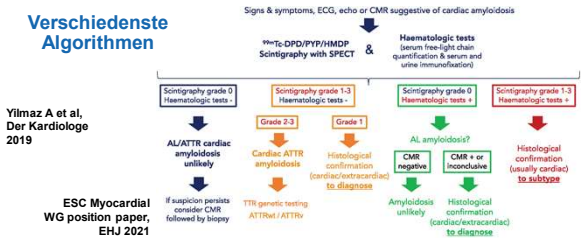
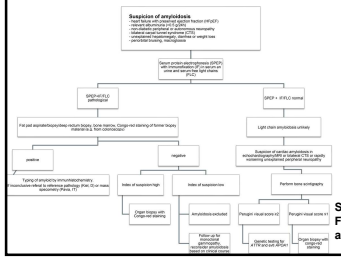
Verschiedenste Algorithmen



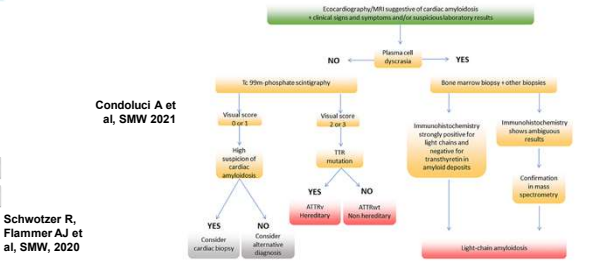
Yilmaz A et al, Der Kardiologe 2019



ESC Myocardial WG position paper, EHJ 2021



Schwotzer R, Flammer AJ et al, SMW, 2020



Condoluci A et al, SMW 2021

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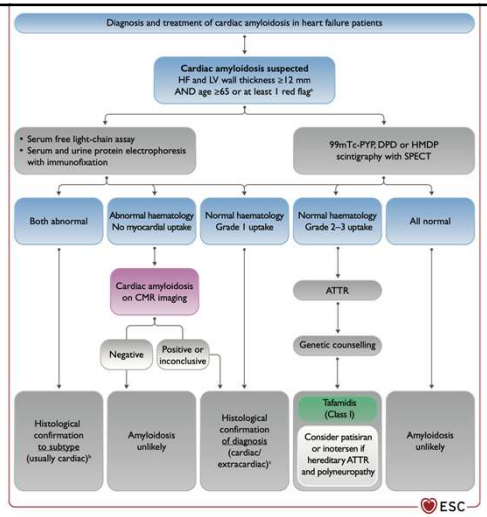
ESC 2021 Guidelines

Diagnose Algorithmus



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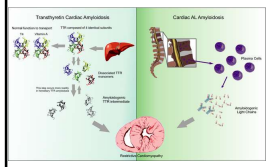
Unser Algorithmus bei Patienten mit vermuteter Amyloidose



Patel KS, Hawkins PN, J Internal Med 2015

Laptseva N et al, Cardiovasc 19

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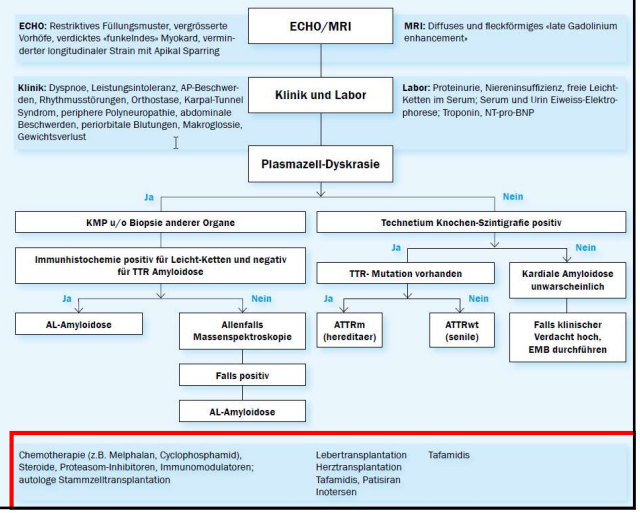

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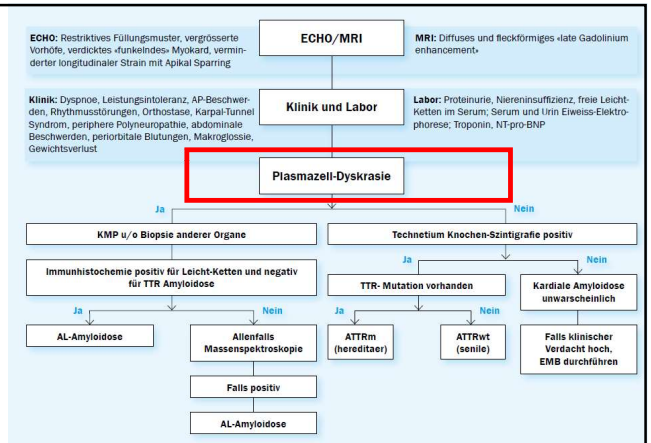
Unklare Herzinsuffizienz und ein typisches Echo/MRI?

Jetzt muss die Amyloidose bewiesen und der Typ bestimmt werden!

Wichtigste Frage: Gibt es eine Plassmazell-Dyskrasie?

Protein-Elektrophorese und Immunfixation im Serum UND Urin!



Laptseva N et al, Cardiovasc 19

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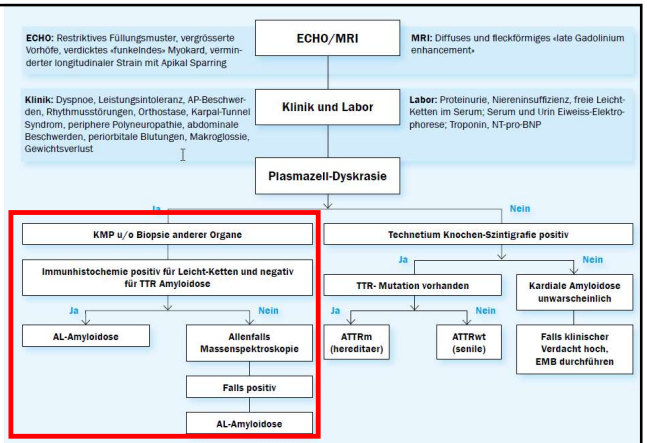
Wichtigste Frage: Gibt es eine Plassmazell-Dyskrasie?

Protein-Elektrophorese und Immunfixation im Serum UND Urin!

Wenn Ja – Diagnose geht immer über eine Biopsie



Laptseva N et al, Cardiovasc 19

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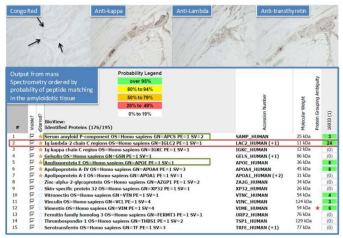
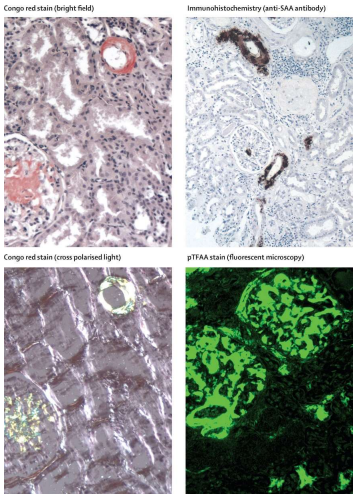
Biopsies

- **Diagnosis is confirmed if amyloid deposits are found in endomyocardial biopsies or other tissues in patients with suspected amyloidosis**
- Immunohistochemistry
- EMB is very sensitive
- Mass spectrometry is the gold standard



Wechalekar AD et al, Lancet 2016



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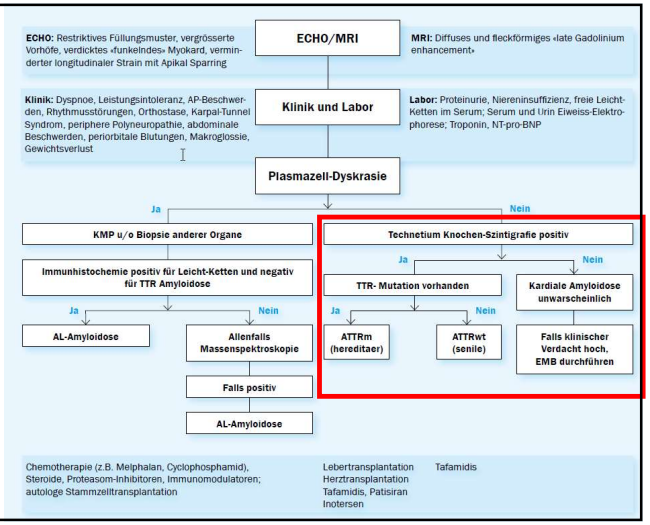
Wichtigste Frage: Gibt es eine Plassmazell-Dyskrasie?

Protein-Elektrophorese und Immunfixation im Serum UND Urin!

Wenn Nein – Diagnose kann auch über Tc-Szintigraphie gehen



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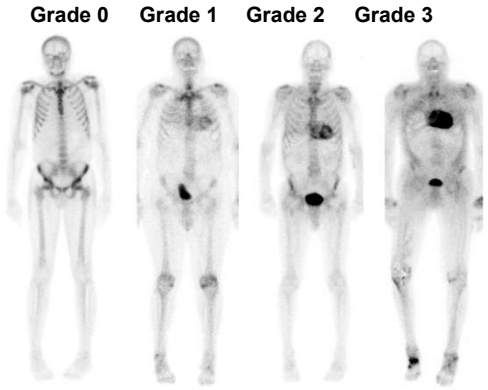
Technetium Szintigraphie
Semiquantitative Analyse der Tracer Aufnahme (Perrugini Grade)



Condoluci A et al. SMW 2021

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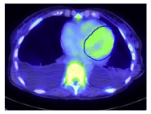
Akkurater Gebrauch der Szintigraphie wichtig!

Achtung:

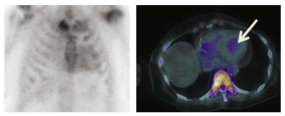
- Die Daten für die Szintigraphie sind verzerrt (hochselektionierte Patienten in Amyloidose-Zentren)
- Die Richtigkeit / Treffsicherheit ist vermindert mit der grossflächigen Einsatz der Szintigraphie
- Umso wichtiger sind die Befolgung der Konsensus-Empfehlungen

Hanna M et al JACC 2020



Positive PYP ≠ ATTR; Diagnosis = AL

❖ Always screen for AL



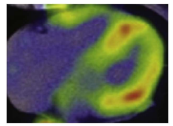
Positive PYP = blood pool uptake, no amyloid

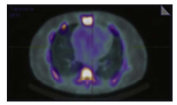
❖ Always perform SPECT

✓ Heart Failure with typical echo and/or CMR
✓ Negative sFLC, serum/urine IFE
✓ Positive PYP with SPECT

Accurate Diagnosis = ATTR-CM

Perform TTR DNA sequence





Negative PYP, Clinical suspicion persists

Cardiac biopsy: Diagnosis = ATTRv

❖ Perform biopsy if strong clinical suspicion

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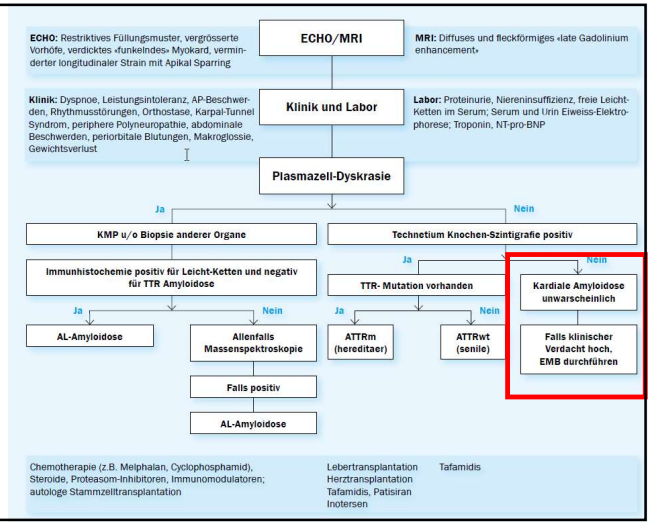
Unklare Herzinsuffizienz und ein typisches Echo/MRI?

Bei Verdacht auf kardiale TTR Amyloidose trotz Plasmazell-Dyskrasie oder bei negativer Szintigraphie: EMB durchführen



Laptseva N et al, Cardiovasc 19

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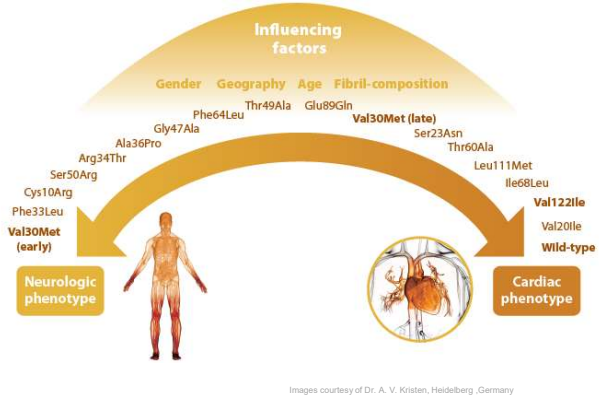
Association of genotypes and phenotypes

- Some *TTR* mutations present with **predominantly neurological symptoms (TTR-PN)**, some with a combination of neurologic and cardiac symptoms (mixed type), **while others are predominantly cardiac (TTR-CM)**
- Wild-type transthyretin amyloidosis presents with almost exclusively cardiac phenotype.



Images courtesy of Dr. A. V. Kristen, Heidelberg ,Germany

1. Ando Y, et al. *Orphanet Rare Diseases* 2013;8:31. 2. Benson MD et al. *Muscle Nerve* 2007;36:411–23. 3. Planté-Bordeneuve V et al. *Lancet Neurol.* 2011;10(12):1086–97. 4. Falk RH et al. *Prog. Cardiovasc. Dise.* 2010; 52:347–361. 5. Schmidt HHJ. *Expert Opin. on Orph. Drugs* 2013; 1 (10) 837-845.

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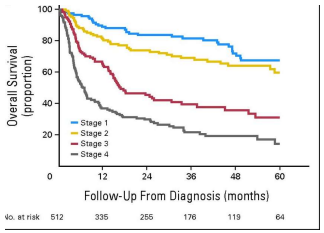
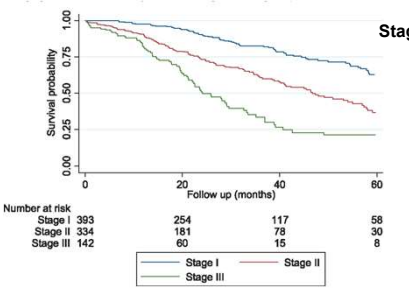
Revised Mayo Stage for AL



Shaji Kumar et al.
JCO 2012

Staging for ATTR



Stage I: NT-proBNP < 3000ng/l and eGFR > 45ml/min

Stage II: in-between

Stage III: NT-proBNP > 3000ng/l and eGFR < 45ml/min

Gilmore JD et al, EHJ 2017

Staging – Je tiefer die kardialen Biomarker, desto besser die Prognose

Tab. 1 Risikostratifikation mittels Biomarker bei (kardialer) Amyloidose

	NT-proBNP	Troponin T	Differenz aus den freien Leichtketten kappa und lambda (= FLC-diff)	eGFR	Erläuterung des Scores
Mayo Clinic Staging System-Staging	≥1800 pg/ml	≥0,025 ng/ml	≥18 mg/dl	–	Jeweils 1 Punkt pro Biomarker und somit insgesamt Score von 0 bis 3 Punkten, der die Einteilung in das Stadium I–IV ermöglicht. Das mittlere Überleben liegt entsprechend in Abhängigkeit vom Stadium bei 94, 40, 14 und 6 Monaten
Staging nach Grogan et al.	>3000 pg/ml	>0,05 ng/l	–	–	Einteilung in 3 Stadien mit 4-Jahres-Überlebensraten von 57, 42 und 18 % in Abhängigkeit davon, ob keiner, einer oder beide Biomarker die angegebenen Konzentrationen überschreiten
Staging nach Gillmore et al.	>3000 ng/l	–	–	<45 ml/min	Einteilung in 3 Stadien nach eGFR und NT-proBNP mit mittleren Lebenserwartungen von 69 (beide Marker normal), 47 (ein Marker pathologisch), und 24 Monaten (beide Marker pathologisch) in den 3 Gruppen

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Yilmaz A et al, Der Kardiologe 2019

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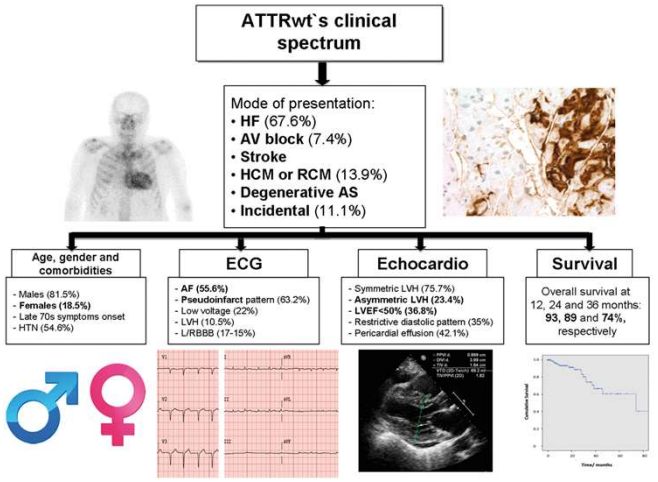
Summary of findings in ATTRwt



Goncales et al. EHJ 2017

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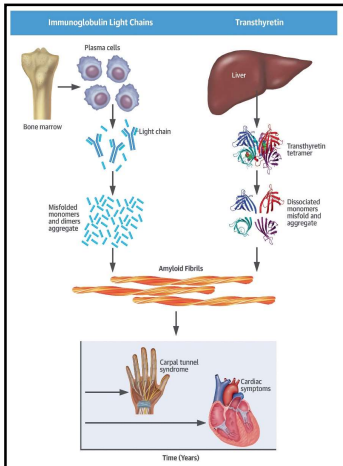

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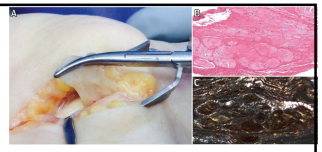
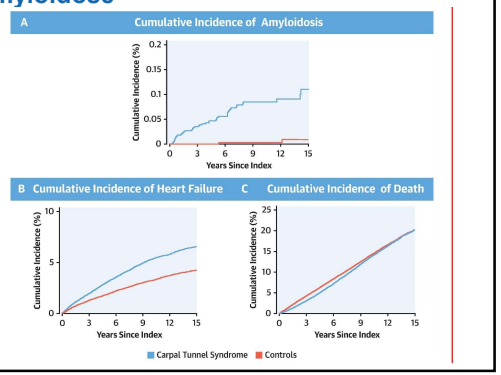
Sperry BW et al, JACC 2018

Geläufige Assoziation: Karpaltunnel-Syndrom und Amyloidose





Fosbol EL et al, JACC 19

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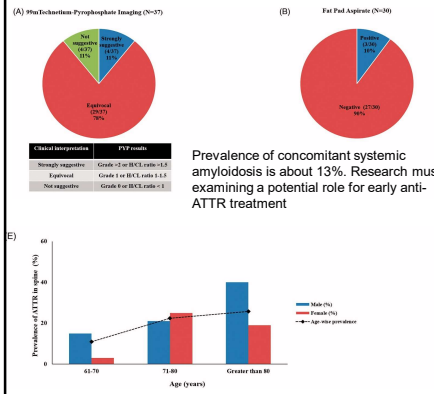
Spinalkanalstenose und Bizepssehnen Ruptur



Prevalence of concomitant systemic amyloidosis is about 13%. Research must examining a potential role for early anti-ATTR treatment

Table. Frequency of Ruptured Distal Biceps Tendon Among Patients in the Biopsy-Proven ATTRwt vs Heart Failure (Control) Groups

Ruptured Distal Biceps Tendon Status	ATTRwt Group, No. of Events (n = 111)	Heart Failure Group, No. of Events (n = 40)
Present	37 33%	1 2.4%
Absent	74	39

Abbreviation: ATTRwt, wild-type transthyretin amyloidosis.

Fisher exact test comparing ruptured biceps tendon prevalence in ATTRwt and heart failure group, $P < .001$.

Mean 5 years before cardiac diagnosis

Geller HI et al, JAMA 2017

Image courtesy of Otmar Pfister

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Godara A et al, Amyloid 2021

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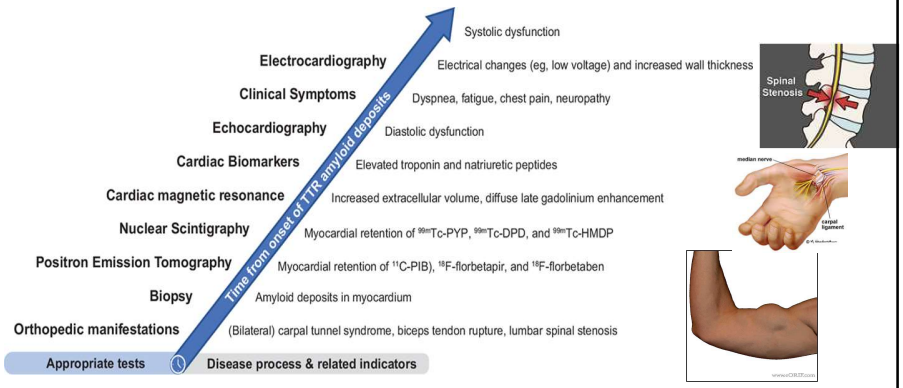
Timeline der angebrachten diagnostischen Tests (TTR) – Therapie am besten so früh wie möglich?



Maurer MS et al, Circulation HF Expert Consensus 2019

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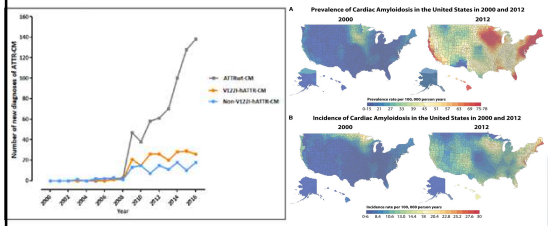
ATTR-CM is diagnosed much more often

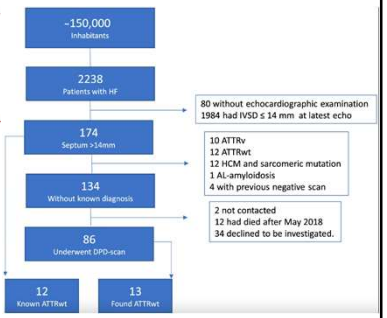
ICD Code for heart failure within Umeå University (S) area.

Estimated prevalence of TTR Amyloidosis: 1:6000



Lane T et al, Circulation 2019

Gilstrap LG et al, Circ HF 2019



Lindmark K et al, ESC Heart Failure 2020

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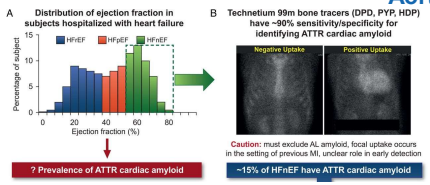
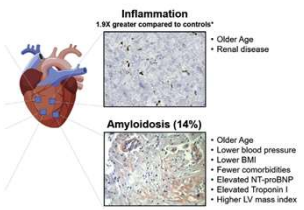
Transthyretin amyloid (ATTR) ist häufig bei Patienten mit HFpEF und Aortenstenose

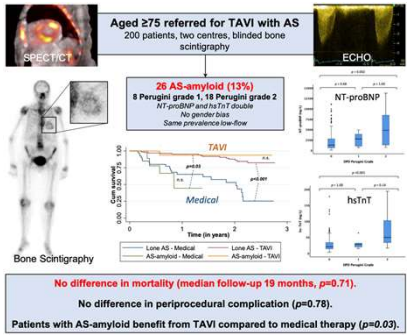


Adam Castaño et al. Eur Heart J 2015

HFpEF myocardial Tissue Findings



Hahn VS et al, JACC Heart Failure 2020



Scully PR et al, EHJ 2020

27

Kardiale Amyloidose – 5 wichtigste klinische Aspekte

1. **SYMPTOME UND KLINIK DER HERZINSUFFIZIENZ**
2. **SYNKOPE UND PLÖTZLICHE HERZTODE**. Synkope bei körperlicher Anstrengung (schlechte Prognose) durch Unvermögen den Cardiac Output zu erhöhen und durch Hypotonie aufgrund einer autonomen Dysfunktion
3. **ABNORMITÄTEN IM REIZLEITUNGSSYSTEM:** insbesondere bei ATTR Amyloidose mit konsekutiver PM-Abhängigkeit
4. **THROMBEMBOLIEN UND HIRNINFARKTE:** insbesondere bei AL und in jenen mit VHF: sehr hohes Stroke-Risiko
5. **MITBETEILIGUNG DER KLEINEN GEFÄSSE:** Angina pectoris trotz normaler Koronarangiographie

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Therapie der kardialen Amyloidose

SYMPTOMATISCHE THERAPIE DER HERZINSUFFIZIENZ

- **Diuretika: Eckpfeiler der Therapie (CAVE Überdiurese)**

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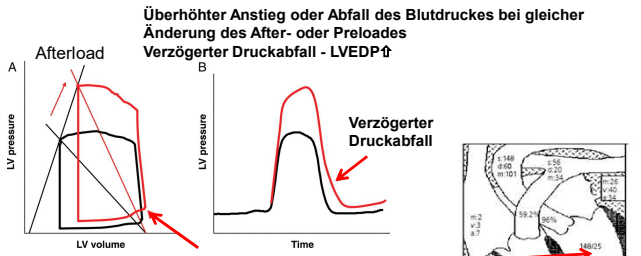
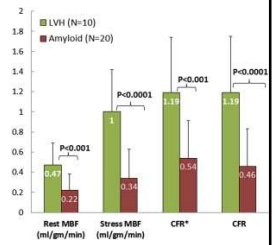
Dyspnoe und thorakale Beschwerden
Häufig durch erhöhte Füllungsdrücke und Mikrozirkulationsstörung bedingt

Überhöhter Anstieg oder Abfall des Blutdruckes bei gleicher Änderung des After- oder Preloades
Verzögerter Druckabfall - LVEDP⇧

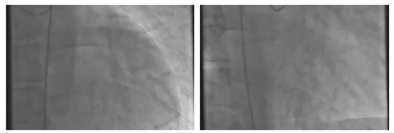




Eingeschränkte koronare Vasodilatation und erhöhte Widerstände bei kardialer Amyloidose

Borlaug B A , and Paulus W J Eur Heart J 2011

Dorbala S et al, JACC: Heart Failure 2014



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Therapie der kardialen Amyloidose

SYMPTOMATISCHE THERAPIE

- **Diuretika: Eckpfeiler der Therapie (CAVE Überdiurese)**

- Beta-Blocker und Ca-Channel Blocker sind ev. sogar gefährlich (CO abhängig von der Herzfrequenz – Schlagvolumen kann nicht angepasst werden)
- Keine klinischen Studien mit ACEI oder ARB. Haben das Potential schwere Hypotonien auszulösen, insbesondere bei der AL Amyloidose
- Antikoagulation bei VHF
- ICD in ausgewählten Patienten

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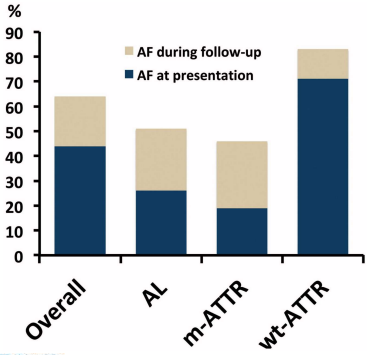
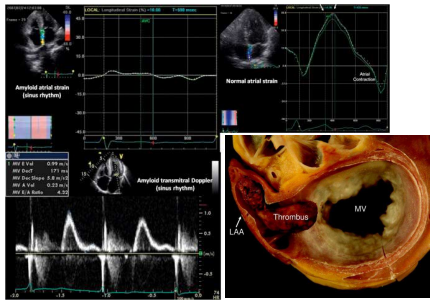
Achtung: Vorhofflimmern!

Prevalence at presentation and incidence of atrial fibrillation during the follow-up





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Sanchis K et al, Amyloid 2019

Rodney H. Falk, et al, JACC 2016

Feng D et al. Circulation. 2007

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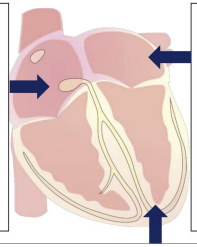
Arrhythmien bei kardialer Amyloidose

Wichtigste Punkte:

- **Antikoagulation bei VHF**
- **Vermeiden strikter Frequenz-Kontrolle bei VHF**
- **Keine Daten für VHF-Ablation. Amiodarone kann gebraucht werden**
- **IDC und CRT nur in vereinzelten Fällen (Multidisziplinärer Team-Approach)**

CARDIAC AMYLOIDOSIS
- Prevalence of 18 to 55 cases per 100,000 person-years.
- May account for more than 13% of heart failure hospitalizations.
- May be present in up to 3% of individuals ≥75 years of age.

Bradyarrhythmias
- High rates of sinoatrial and atrioventricular conduction disease (i.e. prolonged HV).
- Conduction disease associated with advanced disease, and associated with worsen outcomes/death.
- Despite this, there are no specific recommendations to guide pacemaker implantation (apart from conventional indications).
- Decisions in pacing and cardiac resynchronization are best made with a multidisciplinary team.



Atrial Fibrillation
- Atrial fibrillation can occur in up to 44-70% of patients.
- **Rate control:** Most agents should be avoided: beta-blockers and calcium-channel blockers poorly tolerated, and calcium-channel blockers and digoxin bind to myofibrils causing toxicity.
- **Rhythm control:** Cardioversion is frequently attempted. Amiodarone is frequently used. Limited experience with catheter ablation.
- High rates of intracardiac thrombus-anticoagulation irrespective of $CHADS_2$ score.

Ventricular Arrhythmias
- Contrasting studies reporting variable rates of ICD therapies in patients with cardiac amyloidosis.
- A substantial proportion may die from electromechanical dissociation rather than ventricular arrhythmias.
- Decisions surrounding ICD implantation should be patient-centered and made in collaboration with relevant expertise.

USZ Universitäts Spital Zürich **Cheung CC et al, Can J Card 2020**

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Therapie der kardialen Amyloidose

SYMPTOMATISCHE THERAPIE

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- Antikoagulation bei VHF
- ICD in ausgewählten Patienten
- **Allenfalls TAVI bei Patienten mit TTR-Amyloidose und schwerer Aortenstenose**
- **Transplantation**

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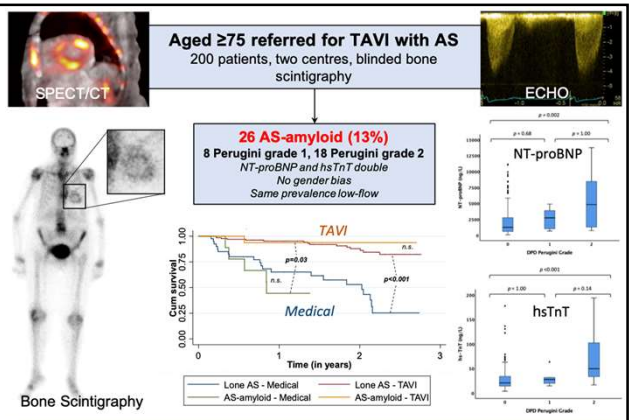
TTR-Patienten mit schwerer Aortenstenose können von einer Transkatheter Aortenklappe profitieren



Scully PR et al, EHJ 2020

No difference in mortality (median follow-up 19 months, *p*=0.71).

No difference in periprocedural complication (*p*=0.78).

Patients with AS-amyloid benefit from TAVI compared to medical therapy (*p=0.03*).

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Herztransplantation bei Amyloidose

Majority of patients (particularly AL) have significant non-cardiac amyloidosis

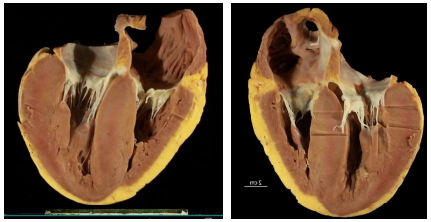
Only 4% isolated cardiac AL amyloidosis

but

Majority of patients with TTR amyloidosis have the disease clinically isolated to the heart, but most of the patients are beyond the age for transplantation

Transplantation possible if

clinically isolated to the heart and too great risk for intensive chemotherapy required for hematopoietic cell transplantation. TPL followed by such a therapy



Courtesy of 'Kardiopathologische Sammlung USZ' (PD Dr. A. Pazhenkottil / Dr. P. Bode)

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Therapie der kardialen Amyloidose

THERAPIE DER ZUGRUNDELIEGENDEN ERKRANKUNG

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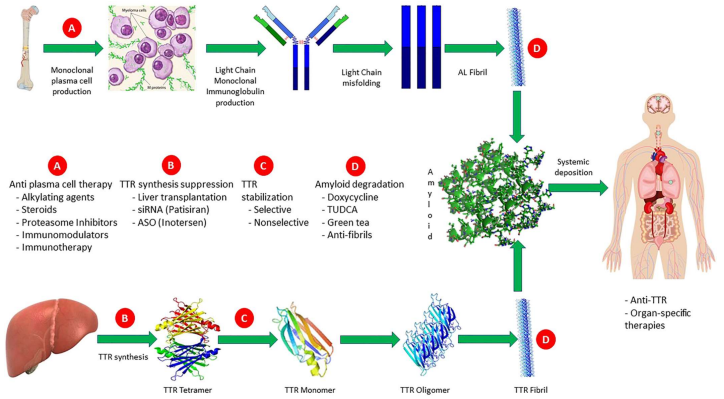
Therapeutische Möglichkeiten der kardialen Amyloidose



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Adam RD et al. ESC Heart Failure 2021

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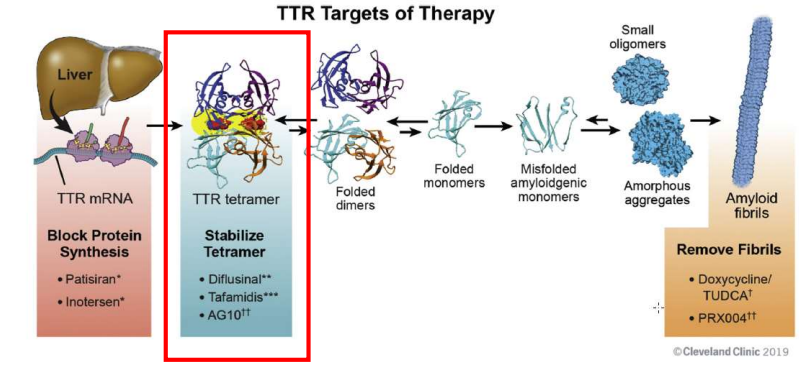
Neue Strategien zur Behandlung von Transthyretin (ATTR) Amyloidose



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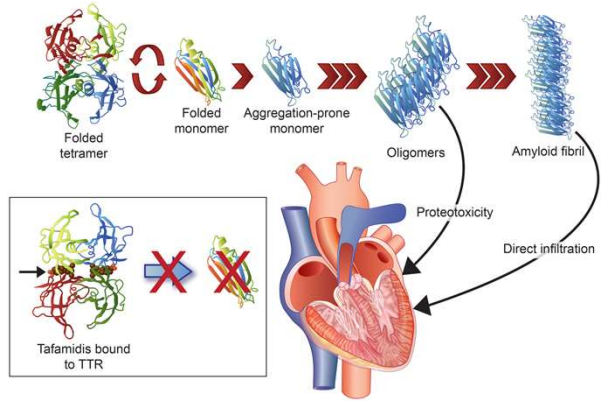
Ruberg FL et al, JACC 2019

39

Effect of tafamidis on the transthyretin (TTR) tetramer



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Falk RH et al, EHJ 2019

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ATTR-ACT Study

Primary Endpoint:

All-cause mortality hierarchically assessed, followed by frequency of CV-related hospitalizations over the course of 30-months. Analysis compared the results of the pooled tafamidis (80 mg and 20 mg) treatment group with the placebo group.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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., Maria B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

Characteristic	Pooled Tafamidis (N=264)	Placebo (N=177)
Age, mean (SD)	74.5 (7.2)	74.1 (6.7)
Male, n (%)	241 (91.3)	157 (88.7)
ATTRm, n (%)	63 (23.9)	43 (24.3)
ATTRwt, n (%)	201 (76.1)	134 (75.7)

Characteristic	Pooled Tafamidis (N=264)	Placebo (N=177)
LV ejection fraction, mean (SD)	48.4 (10.3)	48.6 (9.5)
Interventricular wall thickness, mean (SD)	16.7 (3.8)	16.2 (3.5)
LV posterior wall thickness, mean (SD)	17.0 (3.9)	16.7 (4.1)
LA anterior-posterior diameter size, mean (SD)	43.8 (7.0)	43.7 (6.1)
LV stroke volume mean (SD)	45.8 (16.1)	45.1 (16.9)
Global longitudinal strain, mean (SD)	-9.3 (3.5)	-9.4 (3.6)
NYHA Class, n (%)		
NYHA Class I	24 (9.1)	13 (7.3)
NYHA Class II	162 (61.4)	101 (57.1)
NYHA Class III	78 (29.5)	63 (35.6)
NT-proBNP, median (Q1, Q3)	2995.9 (1751.5, 4861.5)	3161.0 (1864.4, 4825.0)
Troponin I, median (Q1, Q3)	0.14 (0.09, 0.20)	0.14 (0.08, 0.19)

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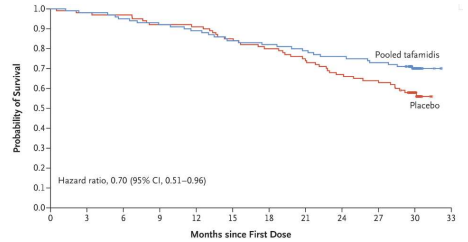
Reduktion der Mortalität und der Hospitalisationen

	No. of Patients	P Value from Finkelstein–Schoenfeld Method	Win Ratio (95% CI)	Patients Alive at Mo 30 *no. (%)*	Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30 *per patient per yr*
Pooled Tafamidis	264	<0.001	1.70 (1.26–2.29)	186 (70.5)	0.30
Placebo	177			101 (57.1)	0.46

«Win Ratio»: pairs of patients with treatment who win, divided with pairs of patients with placebo who win

30% Reduktion der Mortalität mit Tafamidis (HR=0.70; 95% CI, 0.51 to 0.96) – Cox Proportional Hazard Model

32% Reduktion der Hospitalisationen mit Tafamidis



Maurer SM et al NEJM 2018

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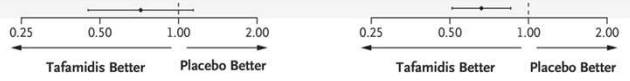
Primärer Endpunkt nach Subgruppen

Subgroup	P Value from Finkelstein–Schoenfeld Method	Survival Analysis Hazard Ratio (95% CI)	P Value for Interaction	Cardiovascular Hospitalization Relative Risk Ratio (95% CI)	P Value for Interaction
Overall — pooled tafamidis vs. placebo	<0.001				
TTR genotype			0.79		0.11
ATTRm	0.30				
ATTRwt	<0.001				
NYHA baseline			0.22		<0.001
Class I or II	<0.001				
Class III	0.78				
Dose					
80 mg vs. placebo	0.003				
20 mg vs. placebo	0.005				



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Maurer SM et al NEJM 2018

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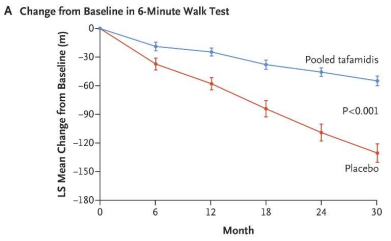
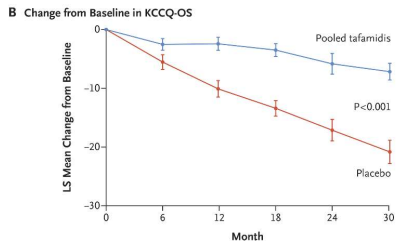
Wichtige sekundäre Endpunkte 6-Minuten Gehtest und Lebensqualität (KCCQ-OS)

Abnahme der Gehstrecke unter Tafamidis und Placebo



Abnahme der Lebensqualität unter Tafamidis und Placebo



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Maurer SM et al NEJM 2018

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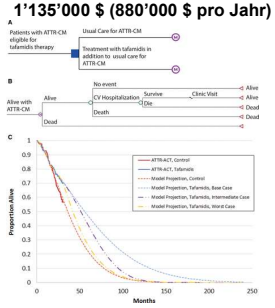
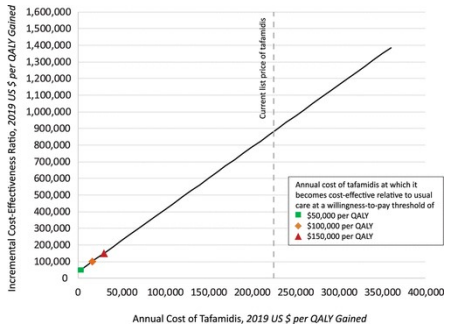
Kosten/Nutzen ist ein viel diskutiertes Thema
Substantieller klinischer Benefit zum Preis von deutlich überschrittenen konventionellen Kosten-/Nutzen Berechnungen

Projezierte zusätzliche 1.29 "quality adjusted life-years" zu eine Preis von 1'135'000 $ (880'000 $ pro Jahr)





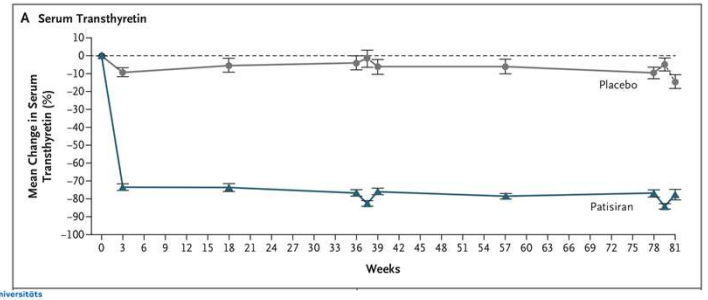
Dhruv S. Kazi. Circulation. 2020

Generally accepted threshold: $100 000 per quality-adjusted life-year gained

45

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

RNA interference (RNAi) resulting in the cleavage of target messenger RNA (mRNA) by small interfering RNAs bound to the RNA-induced silencing complex



Adams D et al, NEJM 2018

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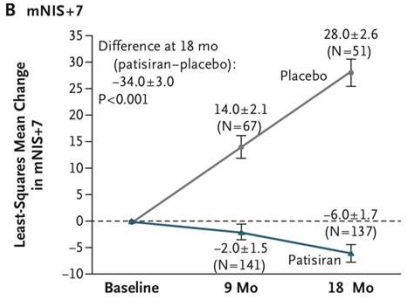
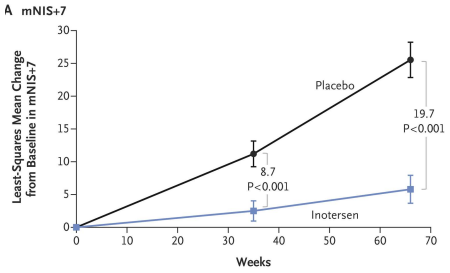
PATISIRAN (RNAi Therapeutic) und INOTERSEN (antisense oligonucleotide inhibitor) verhindern die Produktion von TTR und verlangsamen oder stoppen die neurologischen Symptome bei der hereditären TTR-Amyloidose





Adams D et al, NEJM 2018

Benson MD et al NEJM 2018

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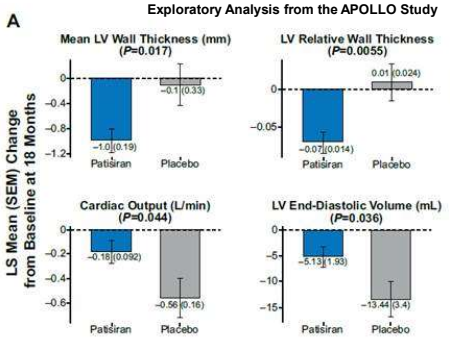
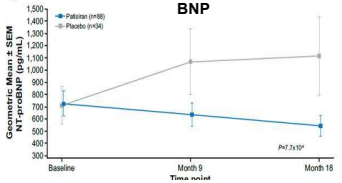
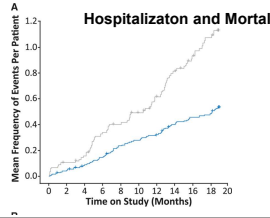
Patisiran hat wahrscheinlich auch einen günstigen Effekt auf die kardiale ATTRm Amyloidose



Solomon SD et al, Circulation 2019





This compound is not approved for the treatment of ATTR-CM.

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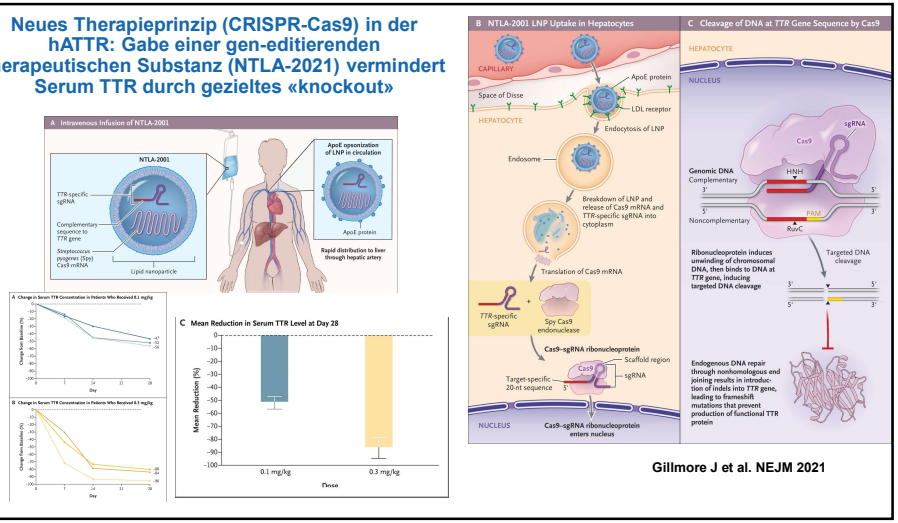
Neues Therapieprinzip (CRISPR-Cas9) in der hATTR: Gabe einer gen-editierenden therapeutischen Substanz (NTLA-2021) vermindert Serum TTR durch gezieltes «knockout»



Gillmore J et al. NEJM 2021

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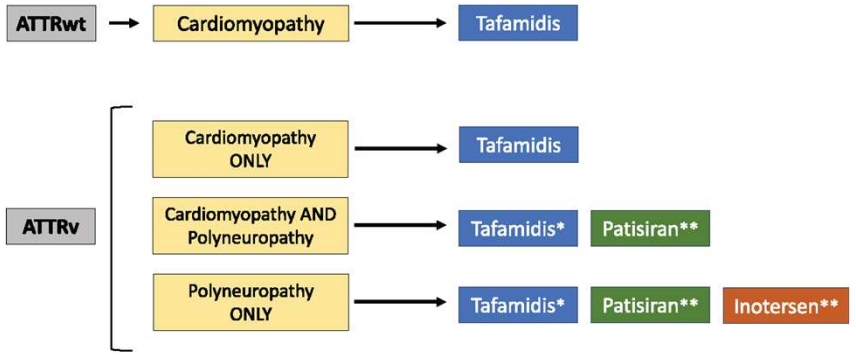
Position Statement HFA 2021



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* Polyneuropathy Stage 1
** Polyneuropathy Stage 1 & 2

Garcia-Pavia P et al, EHJ 2021

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ESC 2021 Guidelines-Empfehlungen für die Behandlung der TTR Kardiomyopathie

Recommendations for the treatment of transthyretin amyloidosis-cardiac amyloidosis

Recommendations	Class[a]	Level[b]
Tafamidis is recommended in patients with genetic testing proven hereditary hTTR-CMP and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[979]	I	B
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[979]	I	B

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CA = cardiac amyloidosis; CMP = cardiomyopathy; CV = cardiovascular; hTTR = hereditary transthyretin; NYHA = New York Heart Association; wtTTR = wild-type transthyretin.
[a]Class of recommendation.
[b]Level of evidence.

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Conclusions

- **Die Therapie der kardialen Amyloidose beinhaltet einerseits die symptomatische Therapie der Herzinsuffizienz und andererseits die Therapie der zugrundeliegenden Erkrankung**
- **Diuretika sind der Eckpfeiler der symptomatischen Therapie**
- **Mit Tafamidis steht erstmals eine Therapie zur Verfügung, welche die Erkrankung selbst beeinflusst und die Mortalität und Hospitalisations-Häufigkeit reduziert und die Lebensqualität verbessert**
- **Weitere vielversprechende Therapien zur Behandlung der Amyloidose sind in Entwicklung**

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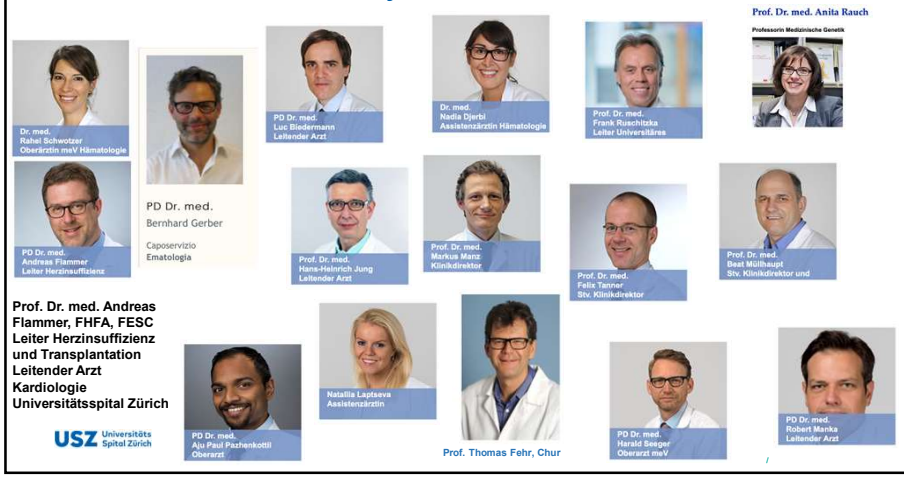
Team Amyloidose Netzwerk



Prof. Dr. med. Andreas Flammer, FHFA, FESC
Leiter Herzinsuffizienz und Transplantation
Leitender Arzt
Kardiologie
Universitätsspital Zürich

USZ Universitäts Spital Zürich

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Established in 1871
Swiss Medical Weekly
Formerly: Schweizerische Medizinische Wochenschrift
An open access, online journal • www.smw.ch
Review article: Medical guidelines | Published 20 October 2021 | doi:10.4414/SMW.2021.w30053
Cite this as: Swiss Med Wkly. 2021;151:w30053

Management of transthyretin amyloidosis

Guidelines from the 1st Swiss Amyloidosis Network (SAN) Consensus conference

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