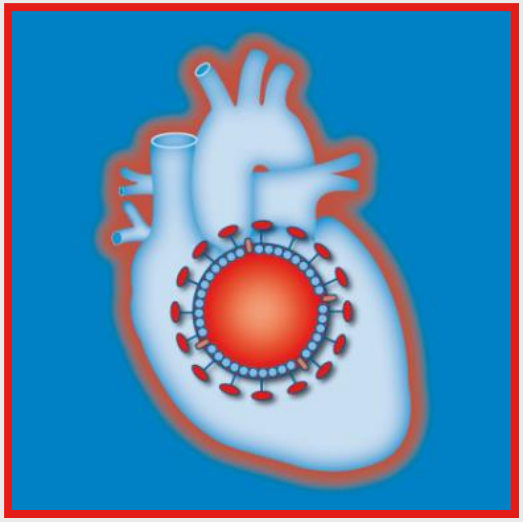
Stellenwert der Biopsie



Carsten Tschöpe

Empfehlungen zur Diagnostik bei Kardiomyopathien

McMurray et al, Eur Heart J 2012; 14: 803-869

Aetiology		Echo	CMR	Cath	SPECT	MDCT	PET
Myocarditis		+	+++	+++[c]	-	-	-
Sarcoidosis		+	+++	++[c]	-	-	++
Hypertrophic CMP:	HCM	+++	++	++	-	-	-
	Amyloidosis	++	+++	+++[c]	-	-	-
Dilated CMP:	Myocarditis	+	+++	+++[c]	-	-	-
	Eosinophilic syndromes	+	+++	+++[c]	-	-	-
	Iron: haemochromatosis	+	+++	-	-	-	-
	Iron: thalassaemia	+	+++	-	-	-	-
ARVC		++	+++	+++[c]	-	+	-
Restrictive CMP:	Pericarditis	++[a]	++[b]	++[a]	-	++[d]	-
	Amyloidosis	++	+++	+++[c]	-	-	-
	Endomyocardial fibrosis	+	+++	+++[c]	-	-	-
	Anderson-Fabry	+	+	-	-	-	-
Unclassified CMP	Takotsubo-CMB	++	++	+++	-	-	-

Empfehlungen zur Diagnostik bei Kardiomyopathien

McMurray et al, Eur Heart J 2012; 14: 803-869

Aetiology		Echo	CMR	Cath	SPECT	MDCT	PET
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	Iron: haemochromatosis	+	+++	-	-	-	-
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ARVC		++	+++	+++[c]	-	+	-
Restrictive CMP:	Pericarditis	++[a]	++[b]	++[a]	-	++[d]	-
	Amyloidosis	++	+++	+++[c]	-	-	-
	Endomyocardial fibrosis	+	+++	+++[c]	-	-	-
	Anderson-Fabry	+	+	-	-	-	-
Unclassified CMP	Takotsubo-CMB	++	++	+++	-	-	-

Europäische Leitlinie zur inflammatorischen Kardiomyopathie

Caforio et al, Eur Heart J 2013

European Heart Journal (2013) **34**, 2636–2648
doi:10.1093/eurheartj/eht210

ESC REPORT

Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Alida L. P. Caforio[1†*], Sabine Pankuweit[2†], Eloisa Arbustini[3], Cristina Basso[4], Juan Gimeno-Blanes[5], Stephan B. Felix[6], Michael Fu[7], Tiina Heliö[8], Stephane Heymans[9], Roland Jahns[10], Karin Klingel[11], Ales Linhart[12], Bernhard Maisch[2], William McKenna[13], Jens Mogensen[14], Yigal M. Pinto[15], Arsen Ristic[16], Heinz-Peter Schultheiss[17], Hubert Seggewiss[18], Luigi Tavazzi[19], Gaetano Thiene[4], Ali Yilmaz[20], Philippe Charron[21], and Perry M. Elliott[13]

Empfehlungen zur Diagnostik

Caforio et al, Eur Heart J 2013 34: 2636-2648

- **EKG durchführen**
- **Troponin, CRP bestimmen**
- **Keine Viusserologie bestimmen**
- **Keine nuklearmedizinische Techniken: Ausnahme bei V.a Sarkoidose**
- **Echokardiographie**
- **MRT nach den Lake-Loise Kriterien**
- **Myokardbiopsie**

Europäische Leitlinie der ESC zur Myokardbiopsie

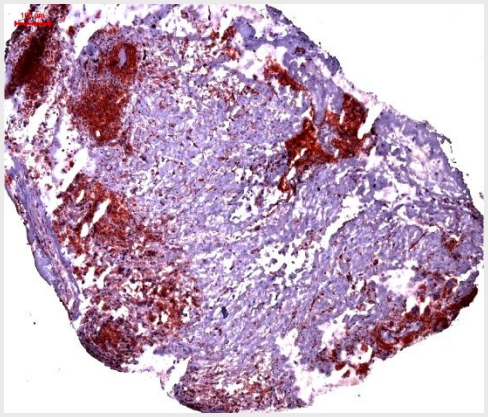
Ponikowski et al Eur Heart J 2016

Chest radiography (X-ray) is recommended in patients with HF to detect/exclude alternative pulmonary or other diseases, which may contribute to dyspnoea. It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting.	I	C
Right heart catheterization with a pul - is recommended in patients with s - should be considered in patients w pulmonary hypertension and its re - may be considered in order to adj standard therapies and whose haer	 I IIa IIb	 C C C
EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis which can be confirmed only in myocardial samples and specific therapy is available and effective.	IIa	C
Thoracic ultrasound may be considered for the confirmation of pulmonary congestion and pleural effusion in patients with AHF.	IIb	C
Ultrasound measurement of inferior vena cava diameter may be considered for the assessment of volaemia status in patients with HF.	IIb	C

Myokardbiopsie bei unklaren Fällen

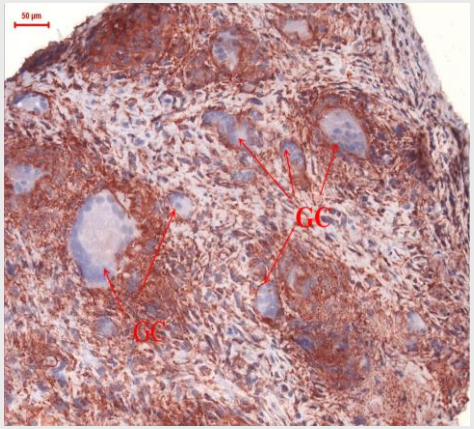
Schwere akute ungeklärte Herzinsuffizienz

Fulminante Myokarditis



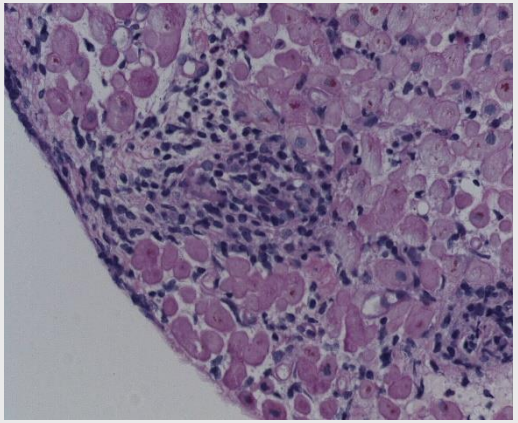
(EF: 32%)

Riesenzell-myokarditis



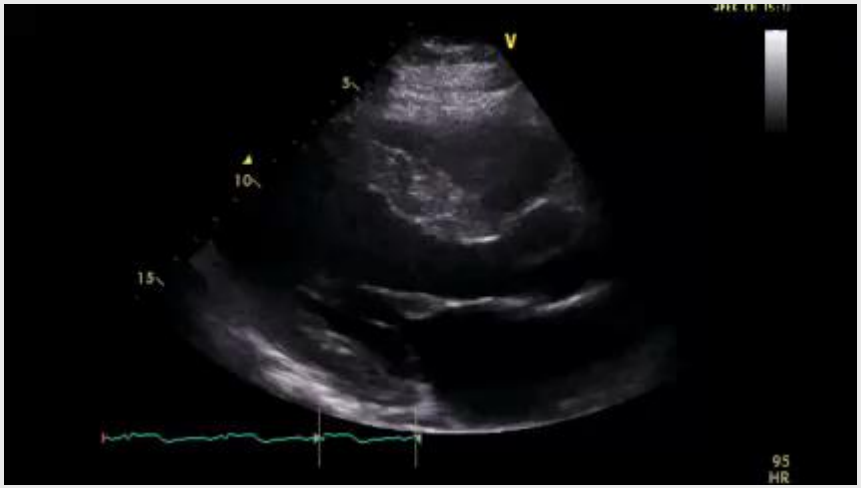
(EF: 32%)

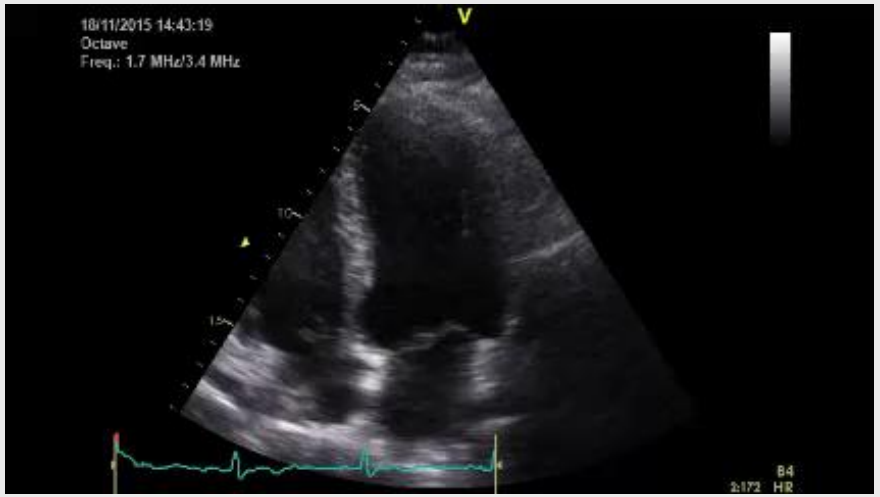
Eosinophilie Myokarditis

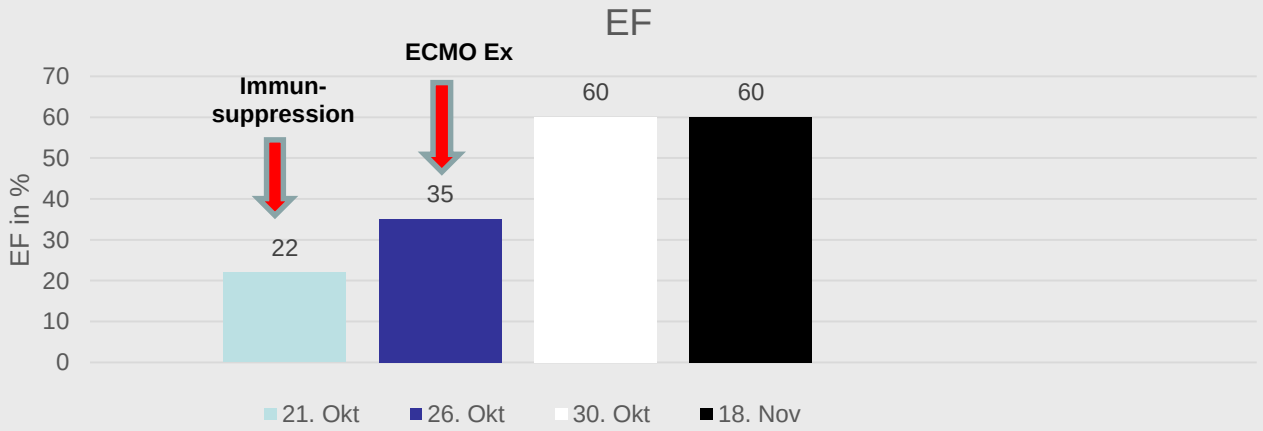


(EF: 30%,)

Verlauf einer Riesenzellmyokarditis







Tschöpe et al

AHA SCIENTIFIC STATEMENT

Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies

A Scientific Statement From the American Heart Association

Circulation December 2016

The intent of this American Heart Association (AHA) scientific statement is to summarize our current understanding of dilated cardiomyopathies. There is special emphasis on recent developments in diagnostic approaches and therapies for specific cardiomyopathies. Recommendations in this document are based on published studies, published practice guidelines from the American College of Cardiology (ACC)/AHA[1] and other organizations,[2,3] and the multidisciplinary expertise of the writing group. Existing evidence in epidemiology, classification, diagnosis, and management of specific cardiomyopathies is usually derived from nonrandomized observational studies, registries, case reports, or expert opinion based on clinical experience, not large-scale randomized clinical trials or systematic reviews. Therefore, in this document, rather than using the standard ACC/AHA classification schema of recommendations and level of evidence,[4] we have included key management strategies at the end of each section and categorized our recommendations according to the level of consensus. Although the format of our recommendations might resemble the ACC/AHA classification of recommendations used in the ACC/AHA practice guidelines, because of the preponderance of expert opinion or level of evidence C evidence in our document, we elected to use different terminology to provide a distinction from the practice guidelines, in which stronger levels and quality of evidence with randomized clinical trials or meta-analyses are usually present.[4] The levels of evidence follow the AHA and ACC methods of classifying the level of certainty of the treatment effect.[4]

Biykem Bozkurt, MD, PhD, FAHA, Chair
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Leslie T. Cooper, MD, FAHA
Anita Deswal, MD, MPH, FAHA
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Kumudha Ramasubbu, MD
Kismet Rasmusson, DNP, FAHA
Jeffrey A. Towbin, MD, FAHA
Clyde Yancy, MD, FAHA
On behalf of the American Heart Association Committee on Heart Failure

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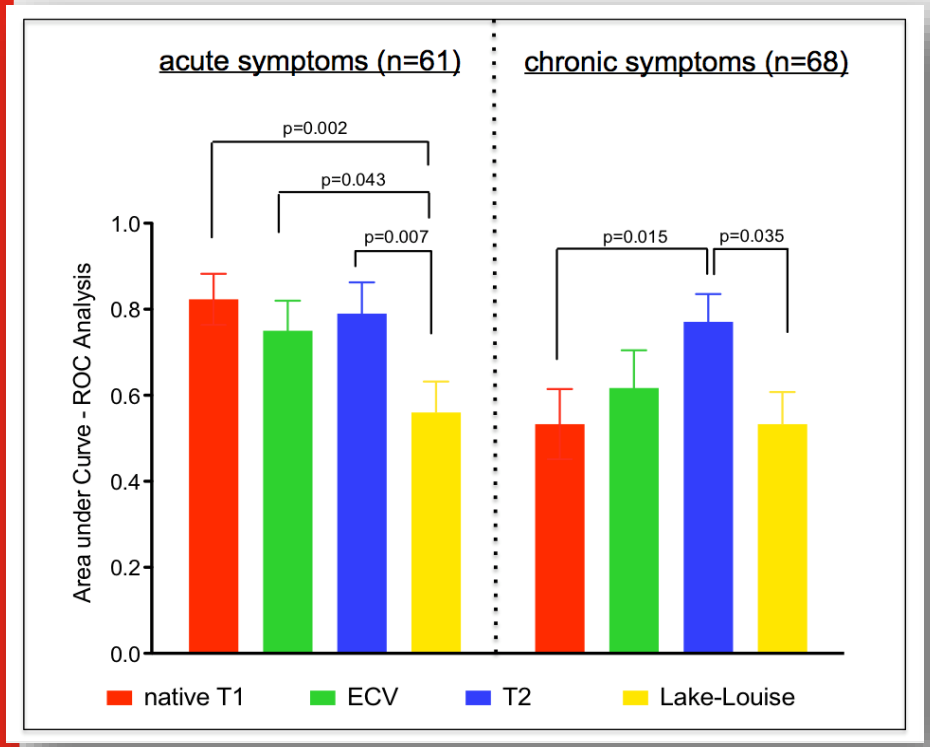
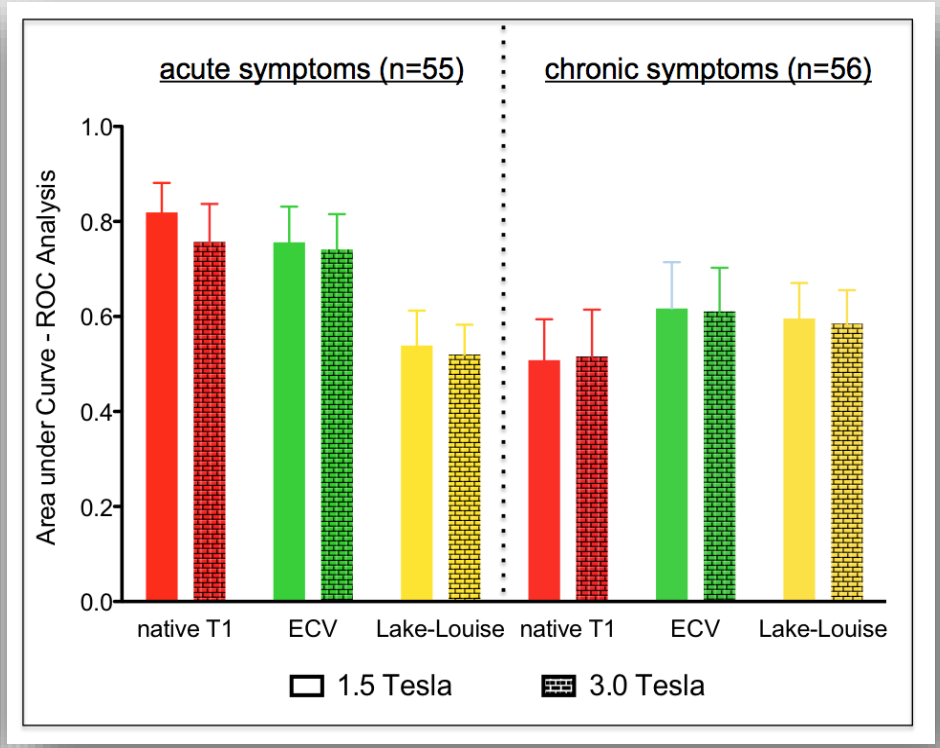
4. Symptomatische Tachykardien

(Level of Evidence C)

MRT – bei der Myokarditis:T1-, T_2- Mapping bei kardialer Inflammation

Lurz P et al JACC 2016

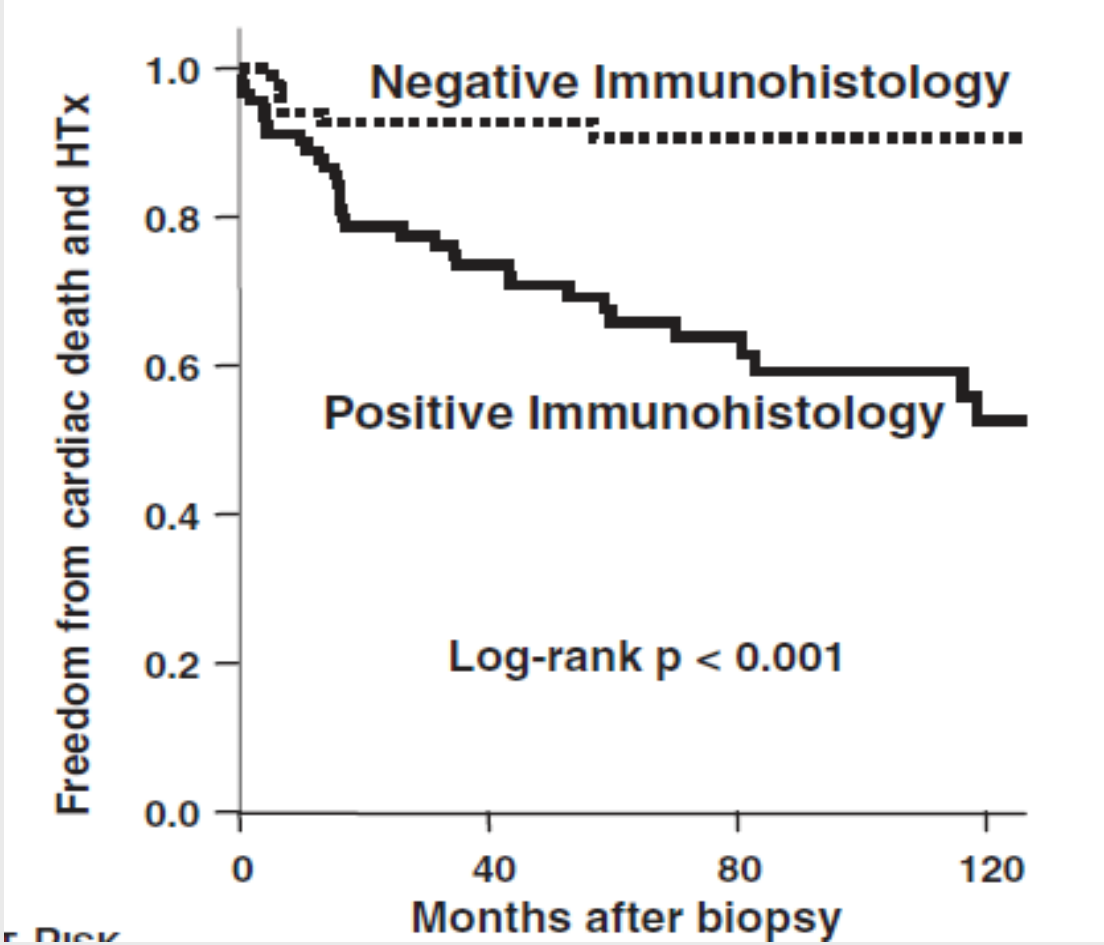




Examination in 129/111 Patients with Suspected Myocarditis

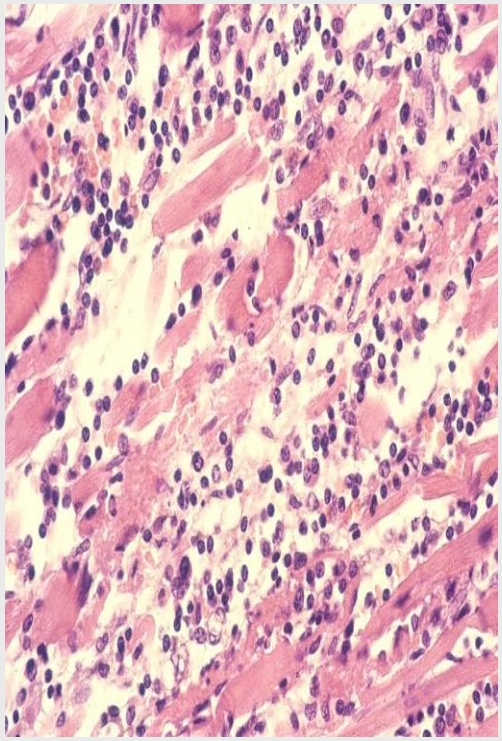
Immunhistologischer Nachweis einer Entzündungsreaktion ist für die Myokarditis Prognose entscheidend

(Kindermann Iet al Circulation. 2008 Aug 5;118(6):639-48)

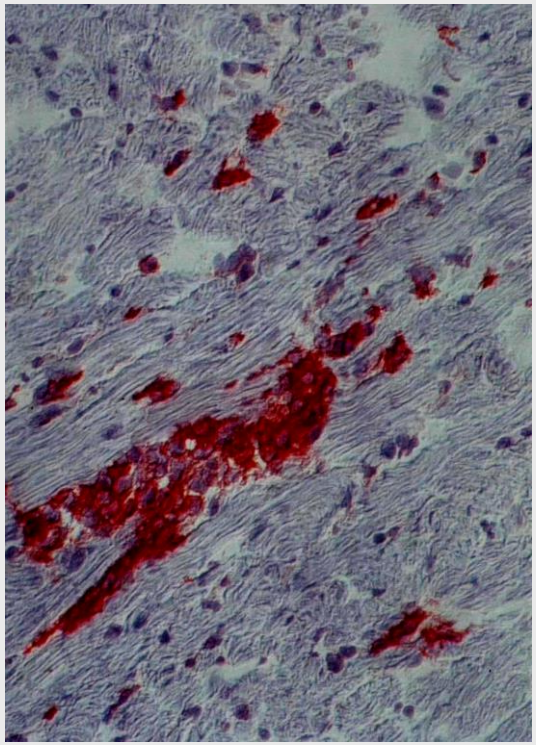


Vorraussetzung: Adäquate Diagnostik

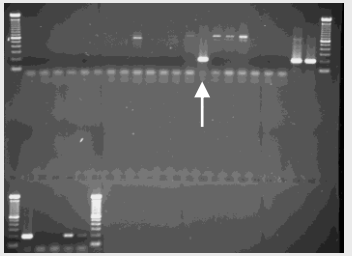
Histologie



Immuno-Histologie



Molecular-biologie

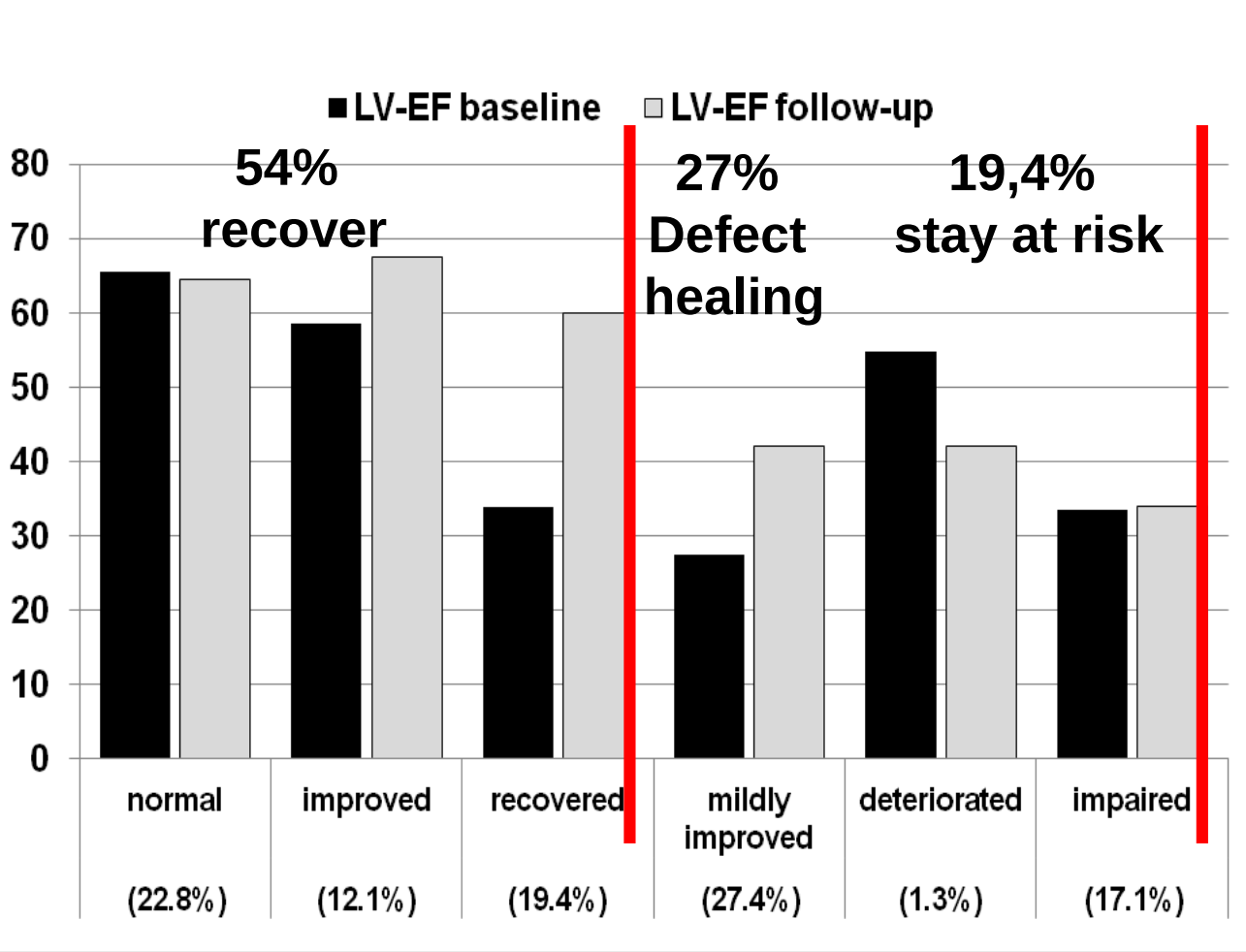


Coxsackie

Caforio et al, Eur Heart J 2013

45% der Patienten mit V.a. kardiale Inflammation werden sich nicht erholen trotz Standardtherapie

Spontaneous Course of biopsy proven MC/DCMi *
(clinical mean follow-up: 30 months, n=922)



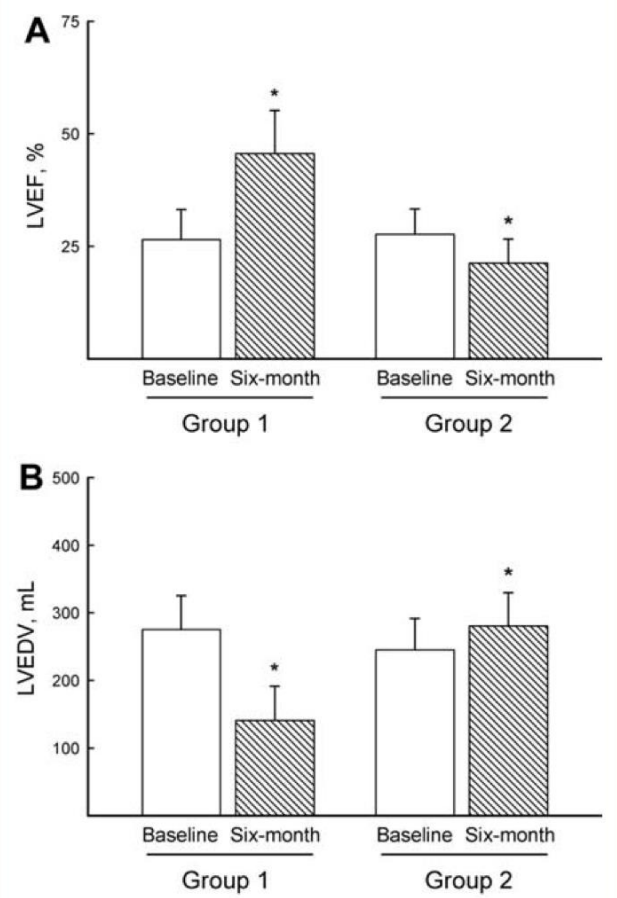
* No specific treatment due to viral persistence

Kühl et al

Immunosuppression in virus-negativer DCMi:

6 Wochen

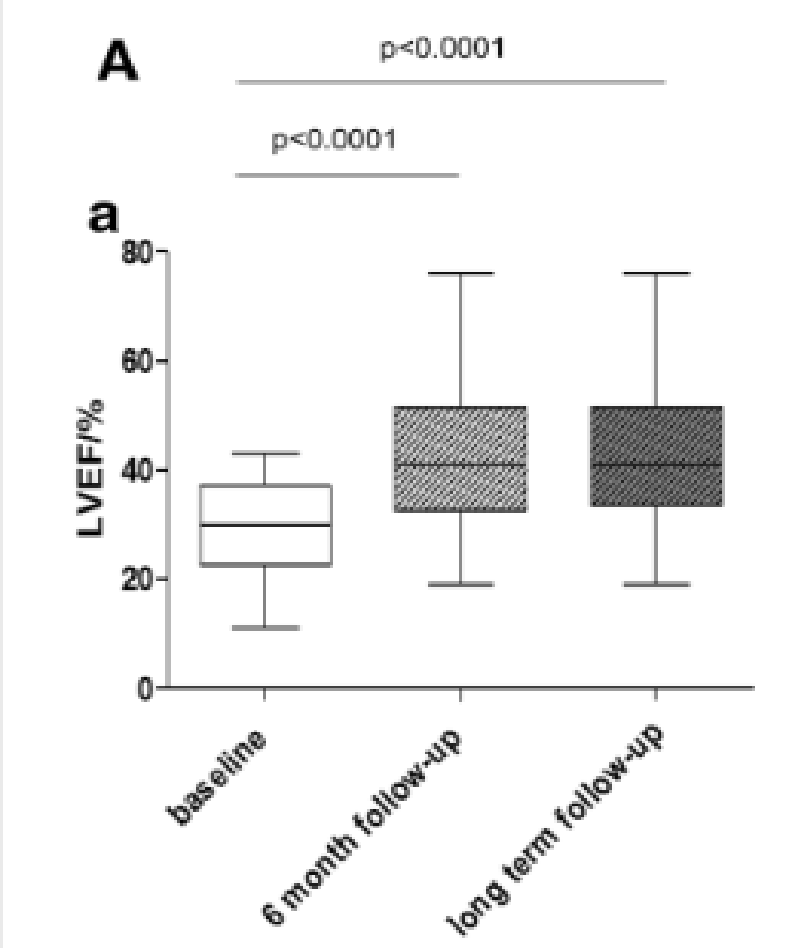
Frustaci et al. Eur Heart J 2009



Immunosuppres. placebo

6 Jahren

Escher et al. CRC 2016



ESC Empfehlungen

Caforio et al, Eur Heart J 2013

European Heart Journal (2013) **34**, 2636–2648
doi:10.1093/eurheartj/eht210

ESC REPORT

Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis:

Immunsuppression nach Ausschluss einer Entero/Adenovirus Persistenz

Roland Jahns[16], Karin Klingel[17], Ales Linhart[12], Bernhard Maisch[2], William McKenna[13], Jens Mogensen[14], Yigal M. Pinto[15], Arsen Ristic[16], Heinz-Peter Schultheiss[17], Hubert Seggewiss[18], Luigi Tavazzi[19], Gaetano Thiene[4], Ali Yilmaz[20], Philippe Charron[21], and Perry M. Elliott[13]

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A Scientific Statement From the American Heart Association

Circulation December 2016

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3. Symptomatische Tachykardien
4. Herzinsuffizinez, die nicht adäquat auf die Standardtherpaie reagiert

(Level of Evidence C)

Moykarditis

Zusammenfassung:

- Meist gute Prognose unter Schonung und Standard-HF Therapie

- Biopsie: Schock (IIa)
- ca. 2- Wochen - 3 Monaten ohne Besserung (IIb)

- Biopsie-gesteuerte Immunsuppressive Therapie

- Kontroll-Biopsie bei Therapieversager

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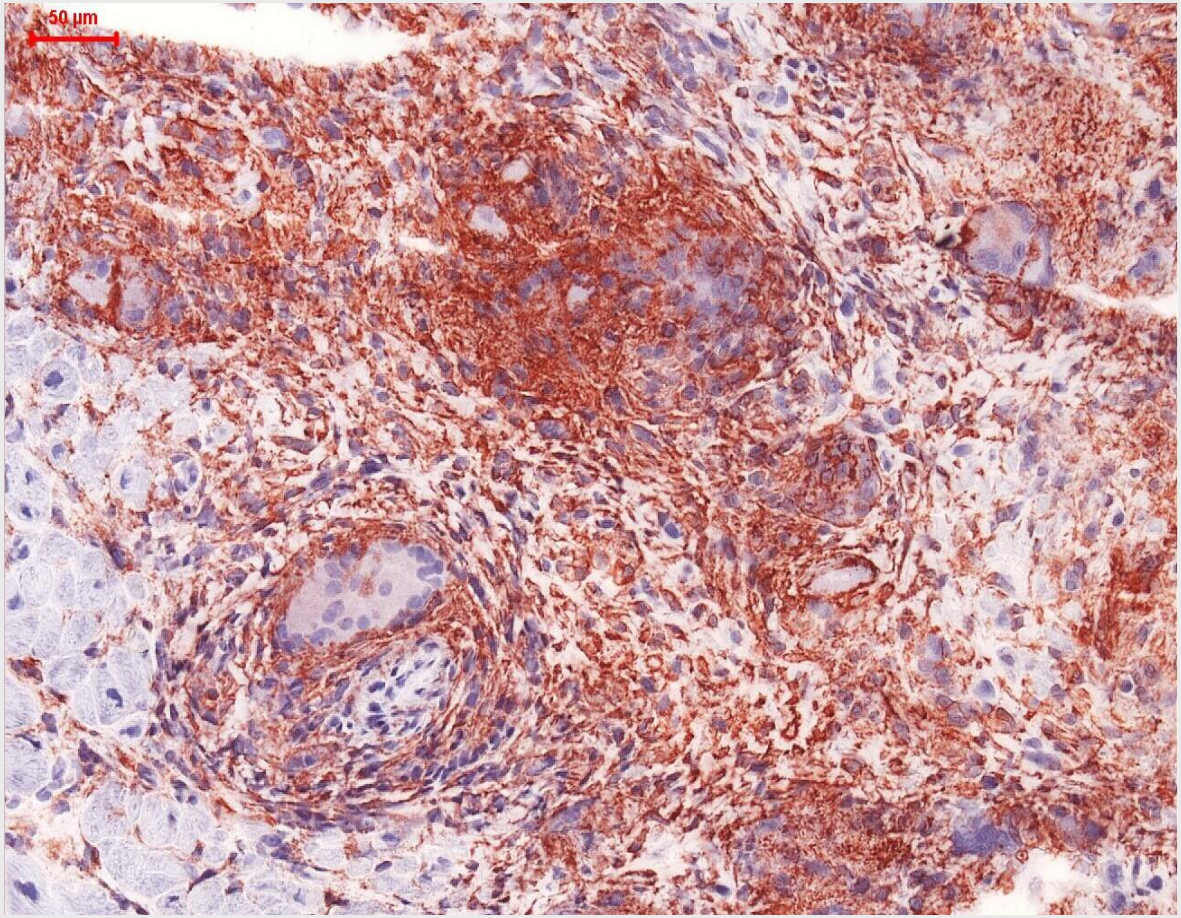
(Level of Evidence C)

Kardiale Sarkoidose



Klinische Manifestationen bei kardialer Sarkoidose und ihre Prävalenz

Costabel et al, Pneumologie 2014; 68: 124-132

- **10% der Sarkoidose Patienten erleiden eine kardiale Beteiligung**
- **Meist ist dabei der linke Ventrikel und das Reizleitungssystem von der Granulombildung betroffen**

Klinische Manifestation	Prävalenz in Studien (in %)
AV-Block	26–62
Schenkelblock	12–61
supraventrikuläre Tachykardie	0–15
ventrikuläre Tachykardie	2–42
Herzinsuffizienz	10–30
plötzlicher Herztod	12–65

Diagnostisches Vorgehen zur Evaluierung einer kardialen Sarkoidose bei unklaren Herzrhythmusstörungen und/oder reduzierter LV-Funktion

Costabel et al, Pneumologie 2014; 68: 124-132

1. EKG : gehört zum Screening

2. Echo : gehört zum Screening

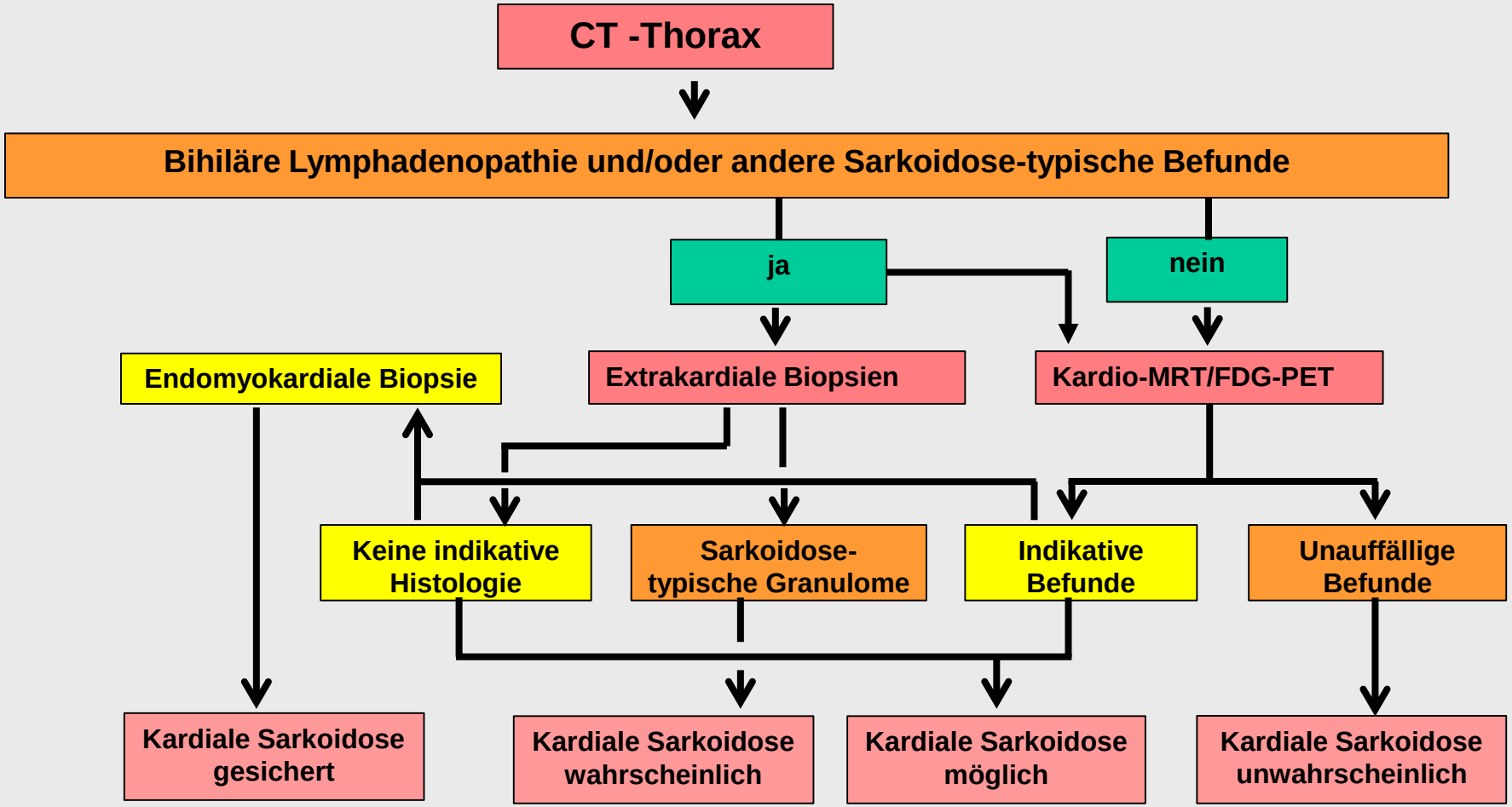
3. 18 FDG-PET/MRT : spezifisch

4. Extrakardiale Biopsie : spezifisch für die Grunderkrankung

5. Myokardbiopsie : sehr spezifisch

Diagnostisches Vorgehen zur Evaluierung einer kardialen Sarkoidose bei unklaren Herzrhythmusstörungen und/oder reduzierter LV-Funktion

Costabel et al, Pneumologie 2014; 68: 124-132



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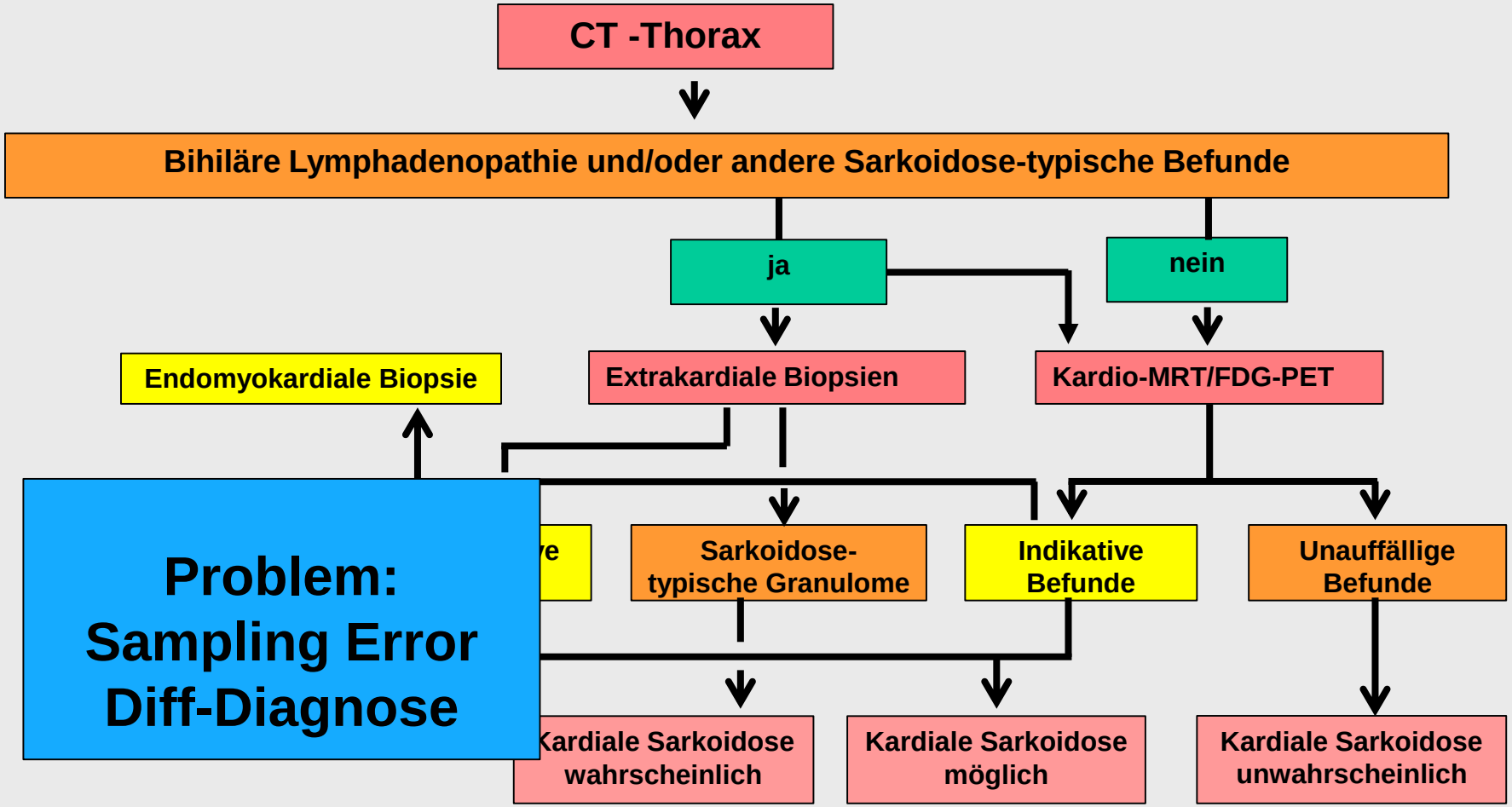
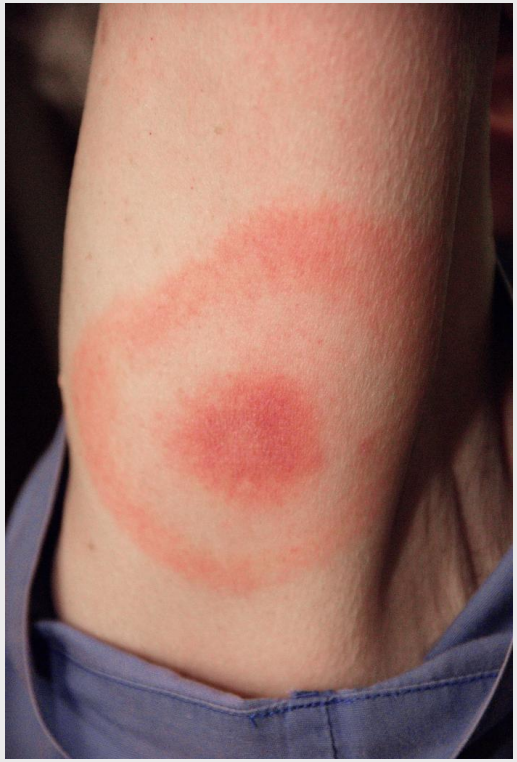
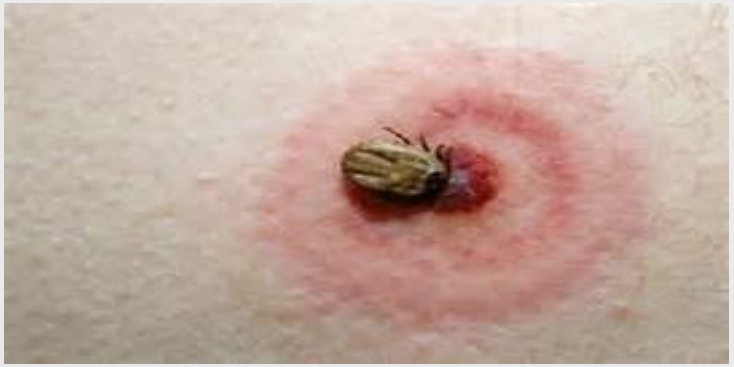
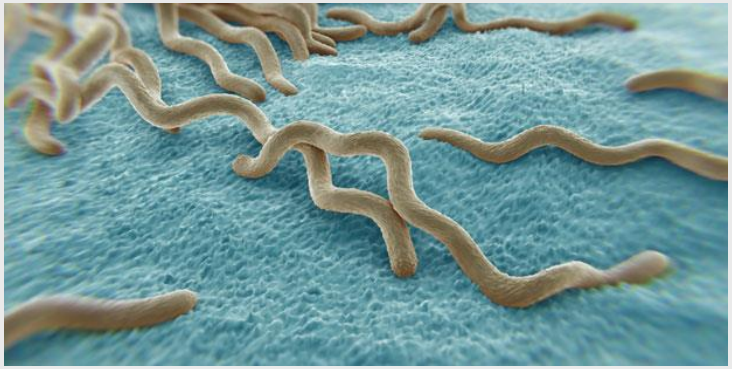


Myokarditiden

Borreliose







Manifestation der Borreliose

Stadium 1: Lokalinfektion (2 Wochen)

- “Wanderröte”; verschwindet nach Tagen ohne Heilung
- Grippe (nach 2 Wochen)

Stadium 2: Systemische Infektion (3 Monate)

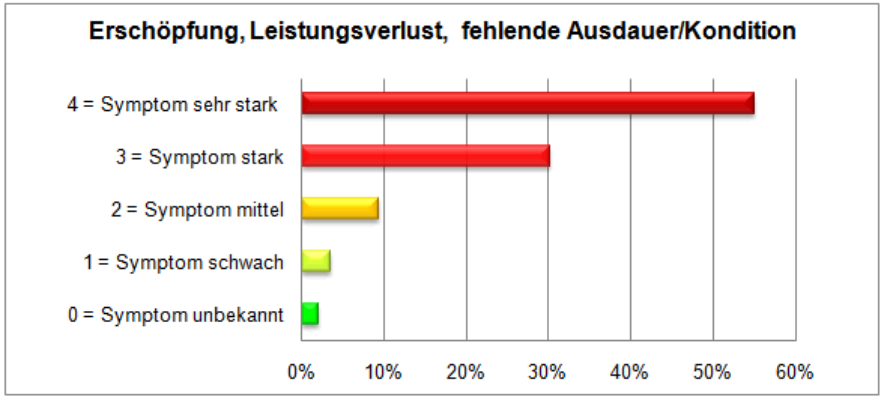
- Grippe
- Kopf/Nervenschmerzen/Tastsinnstörungen
- Gelenkentzündungen
- “Herzprobleme”

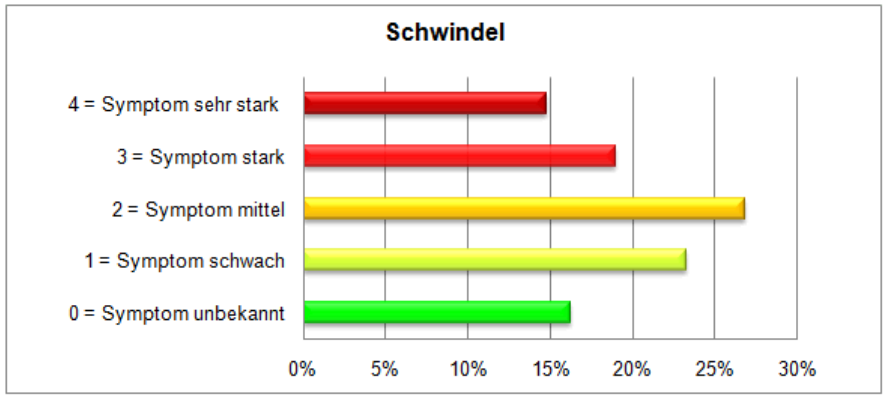
Stadium 3: Chronische Infektion (über Jahre)

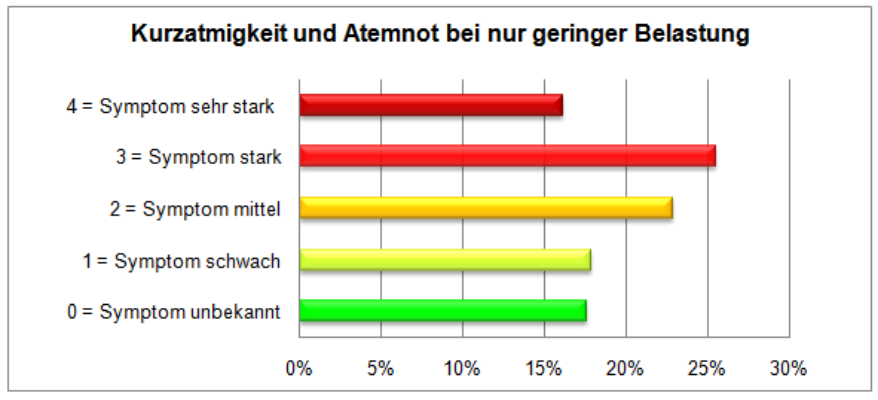
- Immer wieder aufflammende Symptome aus 1 und 2 (Fatique-ähnlich)

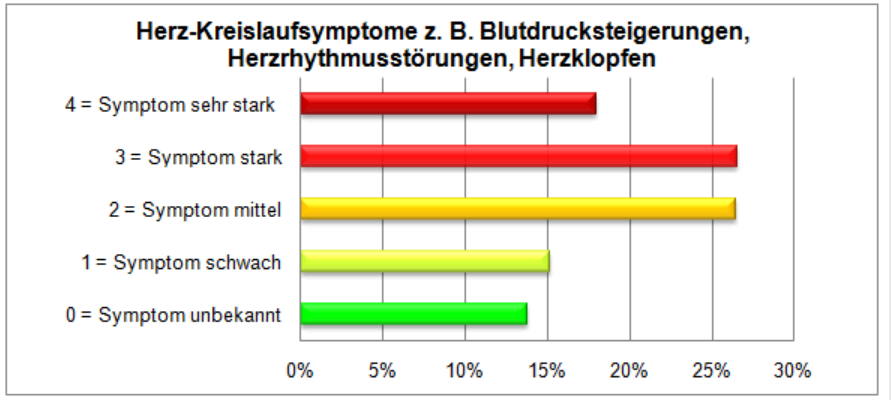
Leitfragen bei Verdacht auf eine Borreliose

www.borreliose-nachrichten.de.



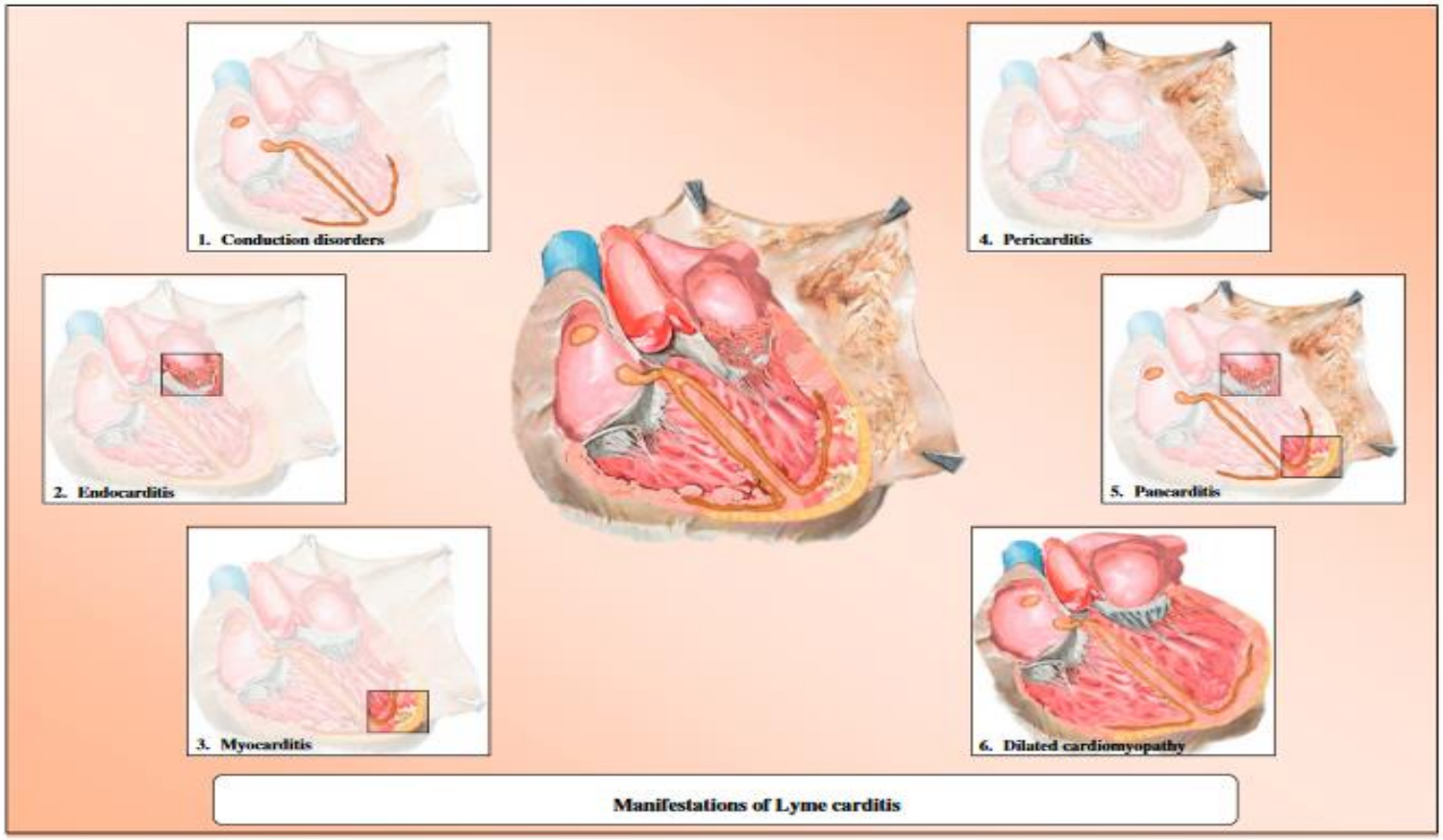






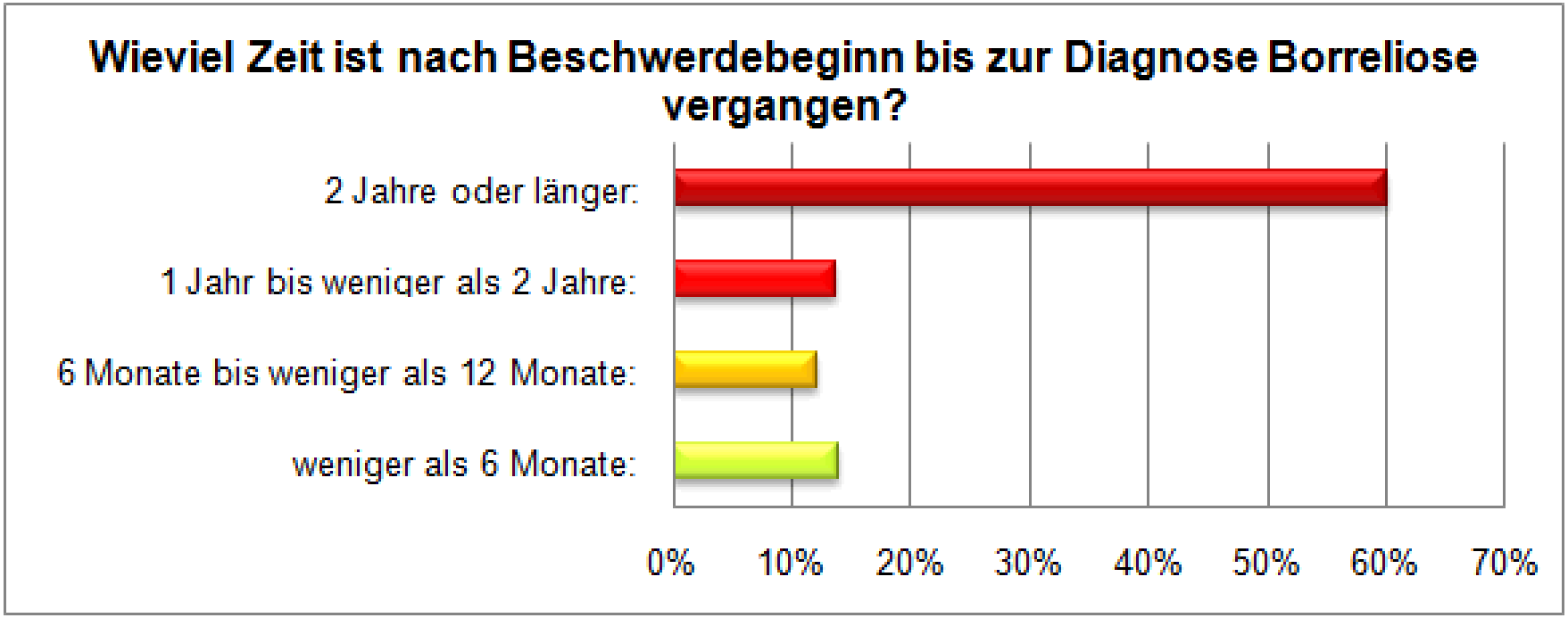
Manifestation der kardialen Borreliose

(Kostić T, et al Int J Cardiol. 2016 Dec 27. pii: S0167-5273(16)34820-3)



Leitfragen bei Verdacht auf eine Borreliose

www.borreliose-nachrichten.de.



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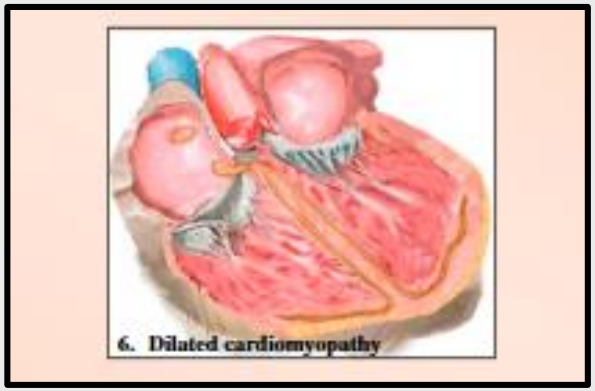


- selten

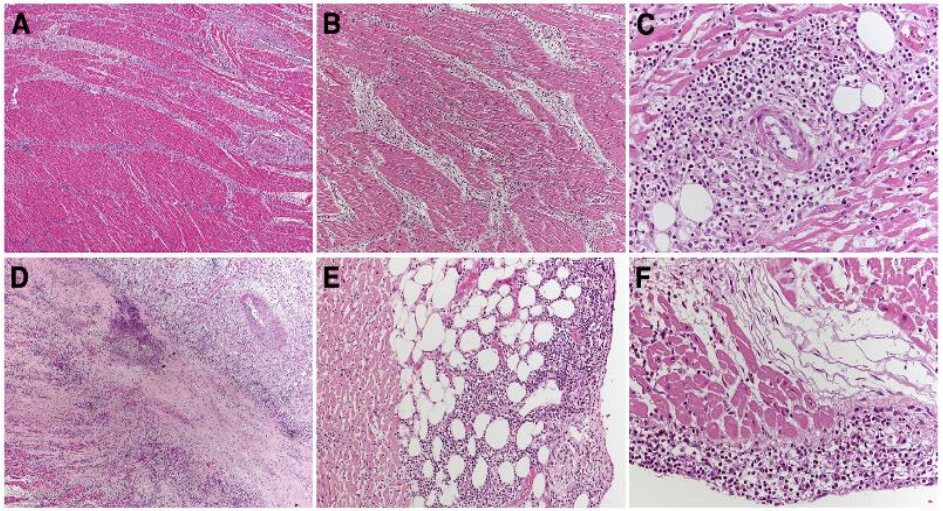
- Kann sich akut wie eine ACS

- **MRT: akut / Ödem**
- **Biopsie (?)**

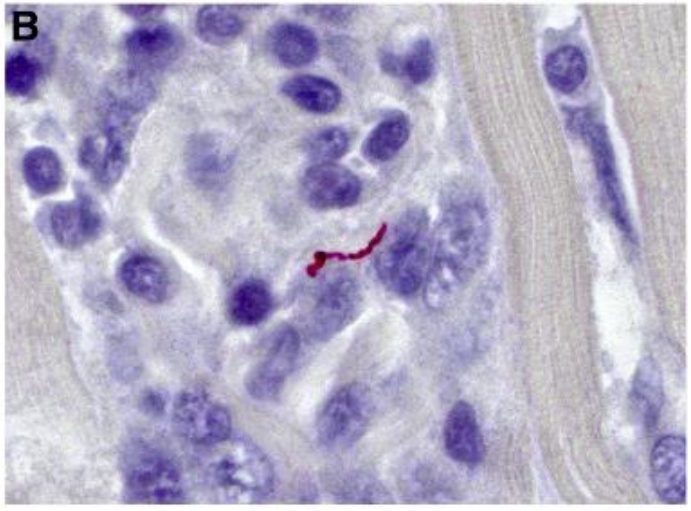
Rolle der Endomyokardbiopsie bei V.a. kardiale Borreliose

(Muehlenbachs Aet al Am J Pathol. 2016 May;186(5):1195-205)

Eosinophile Infiltrate



Spirochäten

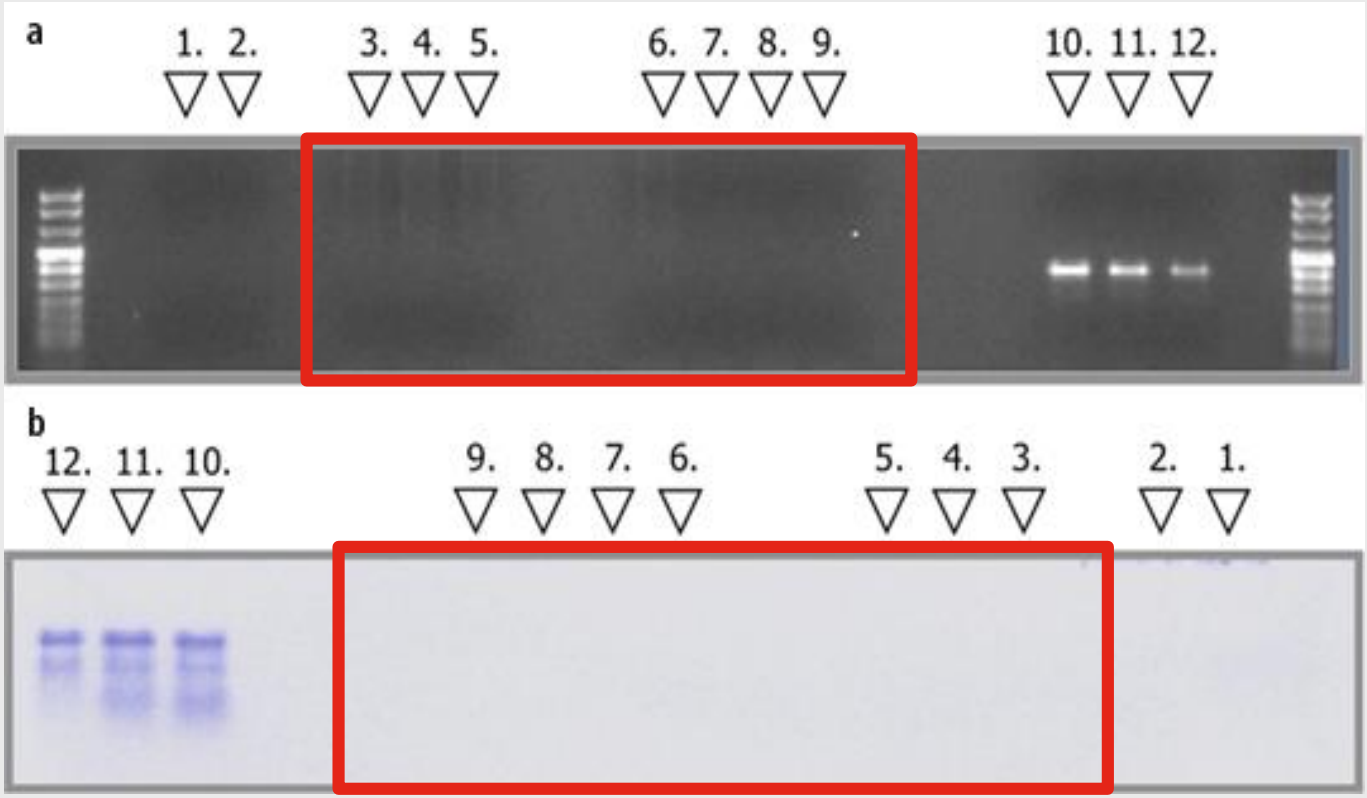


Kein Nachweiss in der PCR oder beim Proteinnachweis von Borrelien in Endomyokardbiopsien bei seropositiver Borreliose und kardialer Manifestation

(Karatolios K, et al Herz. 2015 Mar;40 Suppl 1:91-5)

PCR

Southern-blot



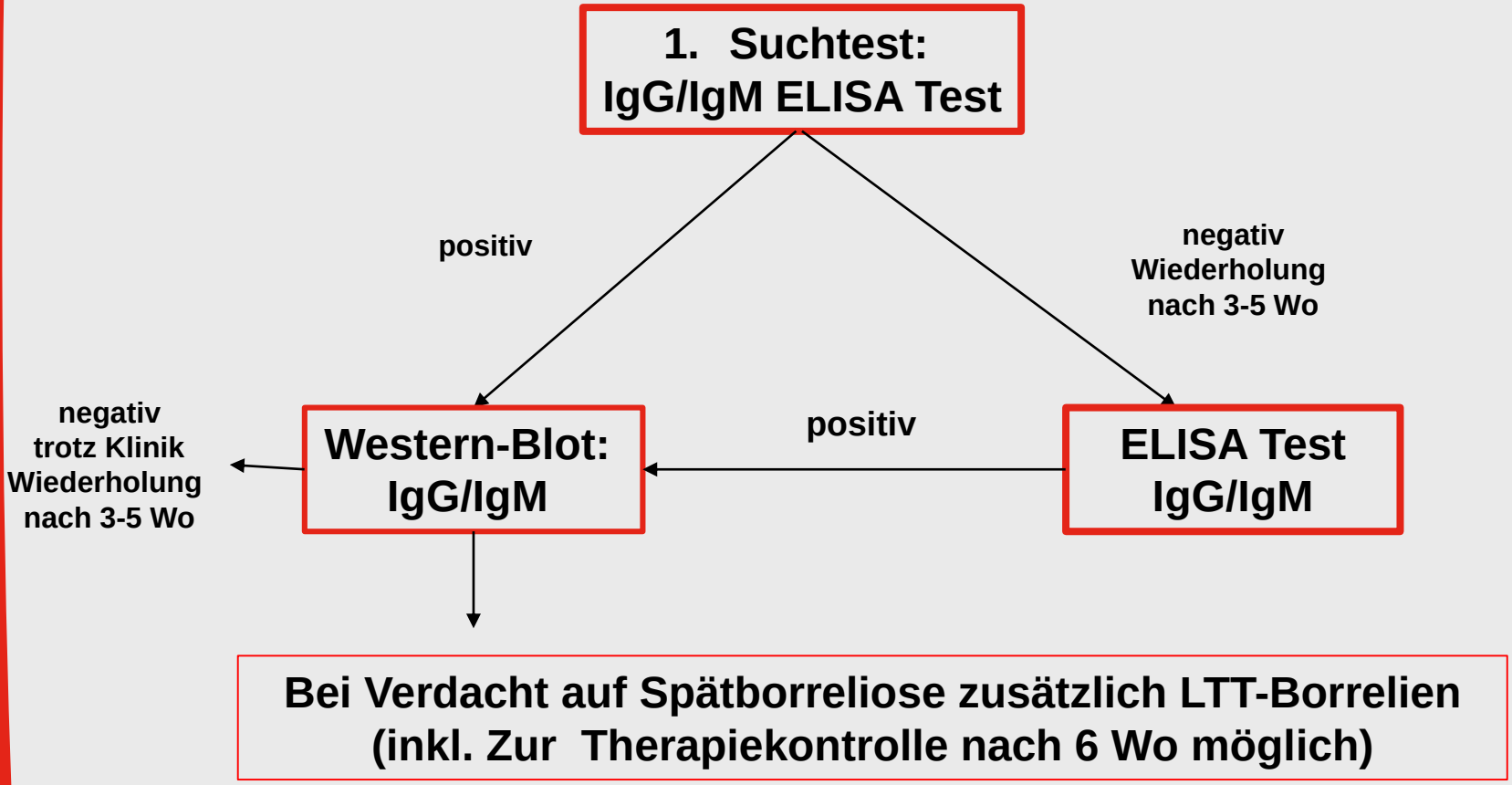
77 von 77 Endomyokardbiopsien von Seropositven Patienten waren negativ

Borreliose

Diagnostik

Algorithmus zur Borreliose Diagnostik

(Kostić T, et al Int J Cardiol. 2016 Dec 27. pii: S0167-5273(16)34820-3)



Sarkoidose / Borreliose

Zusammenfassung:

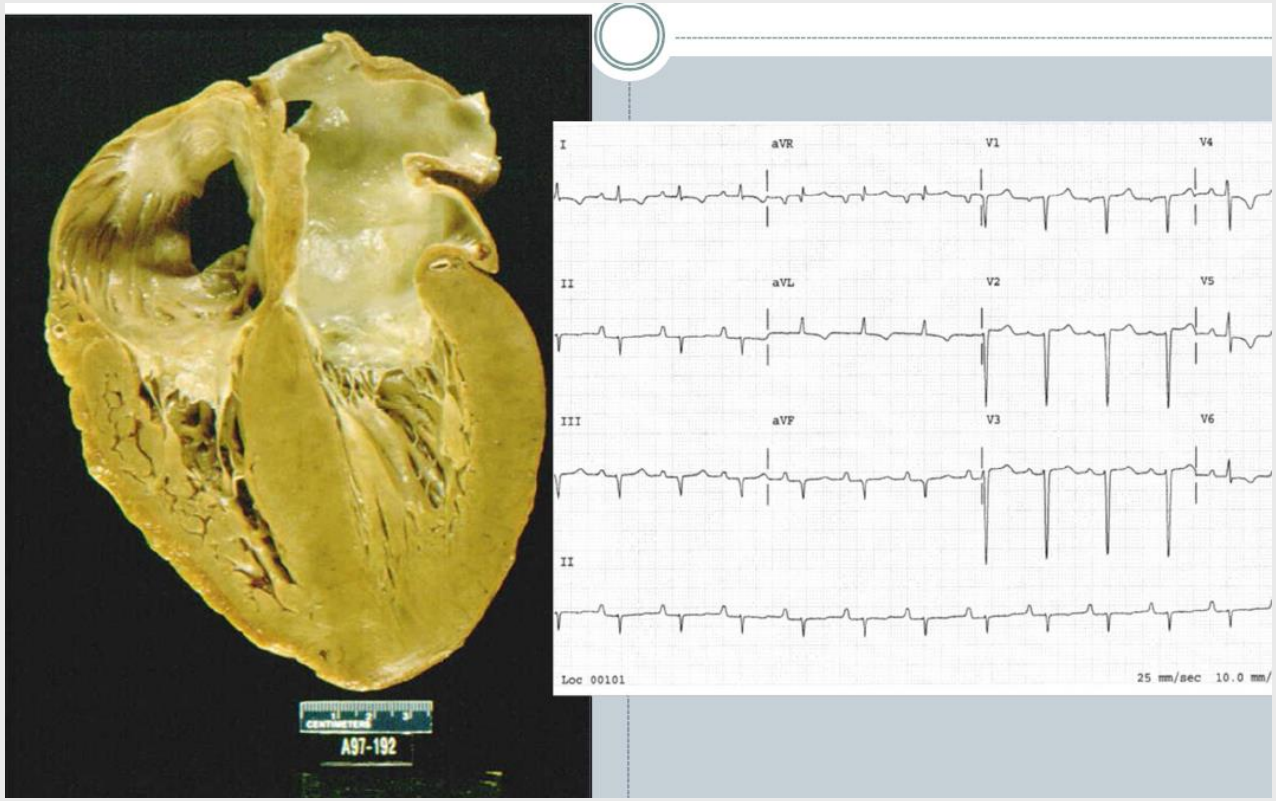
- Keine Primäre Biopsie Indikation
- Hohe Sampling error rate
- Jedoch zum Ausschluss von Differentialdiagnosen wichtig

Empfehlungen zur Diagnostik bei Kardiomyopathien

McMurray et al, Eur Heart J 2012; 14: 803-869

Aetiology		Echo	CMR	Cath	SPECT	MDCT	PET
Myocarditis		+	+++	+++[c]	-	-	-
Sarcoidosis		+	+++	++[c]	-	-	++
Hypertrophic CMP:	HCM	+++	++	++	-	-	-
	Amyloidosis	++	+++	+++[c]	-	-	-
Dilated CMP:	Myocarditis	+	+++	+++[c]	-	-	-
	Eosinophilic syndromes	+	+++	+++[c]	-	-	-
	Iron: haemochromatosis	+	+++	-	-	-	-
	Iron: thalassaemia	+	+++	-	-	-	-
ARVC		++	+++	+++[c]	-	+	-
Restrictive CMP:	Pericarditis	++[a]	++[b]	++[a]	-	++[d]	-
	Amyloidosis	++	+++	+++[c]	-	-	-
	Endomyocardial fibrosis	+	+++	+++[c]	-	-	-
	Anderson-Fabry	+	+	-	-	-	-
Unclassified CMP	Takotsubo-CMB	++	++	+++	-	-	-

Hereditäre Transthyretin-Amyloidose



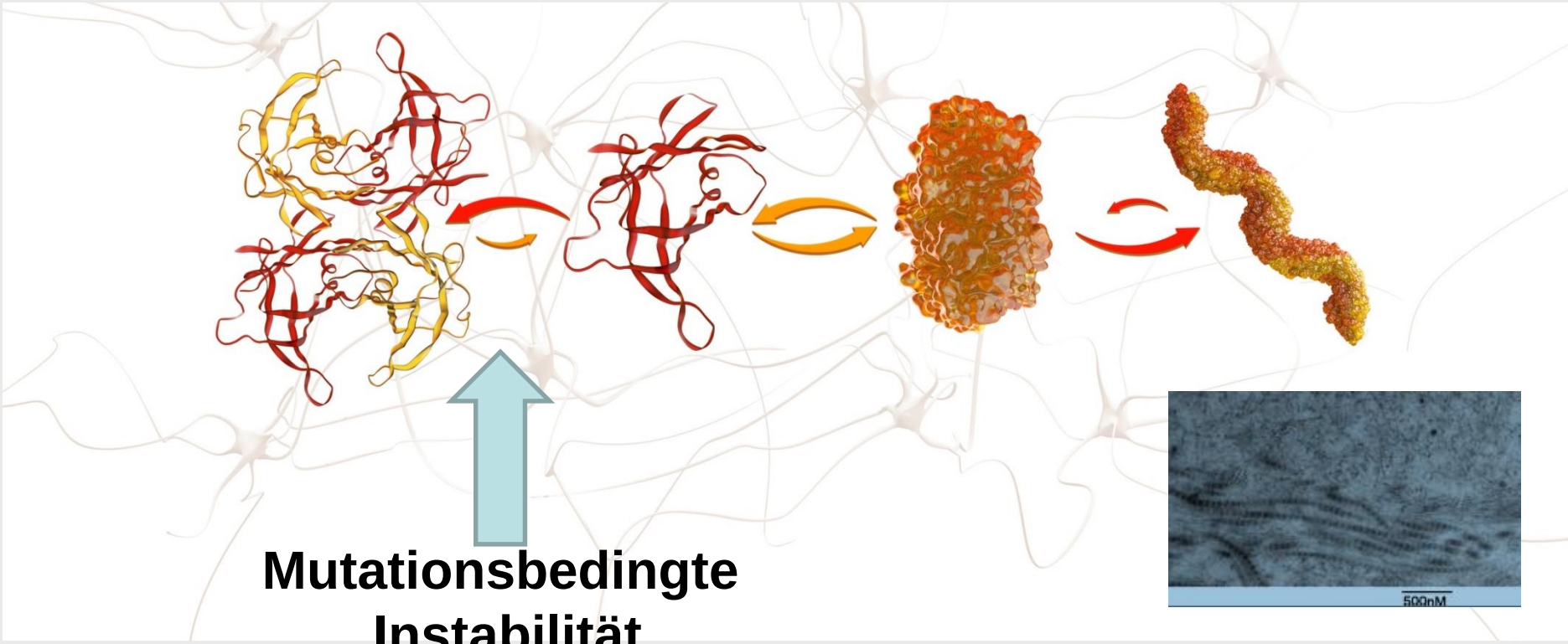
Klassifizierung der Amyloidosen

1. Ando Y et al., *Arch Neurol* 2005;62:1057–1062. 2. Merlini G et al., *J Intern Med* 2004;255:159–178.
3. Falk R et al., *N Engl J Med* 1997;337:898–909. 4. Sekijima Y et al. *Curr Pharm Des* 2008;14:3219–3230.

TYPE OF AMYLOID	PRECURSOR PROTEIN	MAJOR ORGANS INVOLVED	COMMENT
AL	Immunoglobulin light chain	Heart, kidney, liver, nerves, skin, bowel	Rapidly Progressive. Related to multiple myeloma
TTRm	Variant transthyretin	Nerve Heart	Autosomal dominant with variable penetrance. High gene prevalence in African Americans
TTRwt	Wild-type TTR	**Heart**	Slowly progressive. Rapidly increasing prevalence. Disease of men.
Isolated atrial amyloidosis	ANP	Atrium	Little clinical significance

Mutationsbedingte Instabilität lässt das Transthyretin Tetramer zerfallen und führt zu unlöslichen Amyloidfibrillen

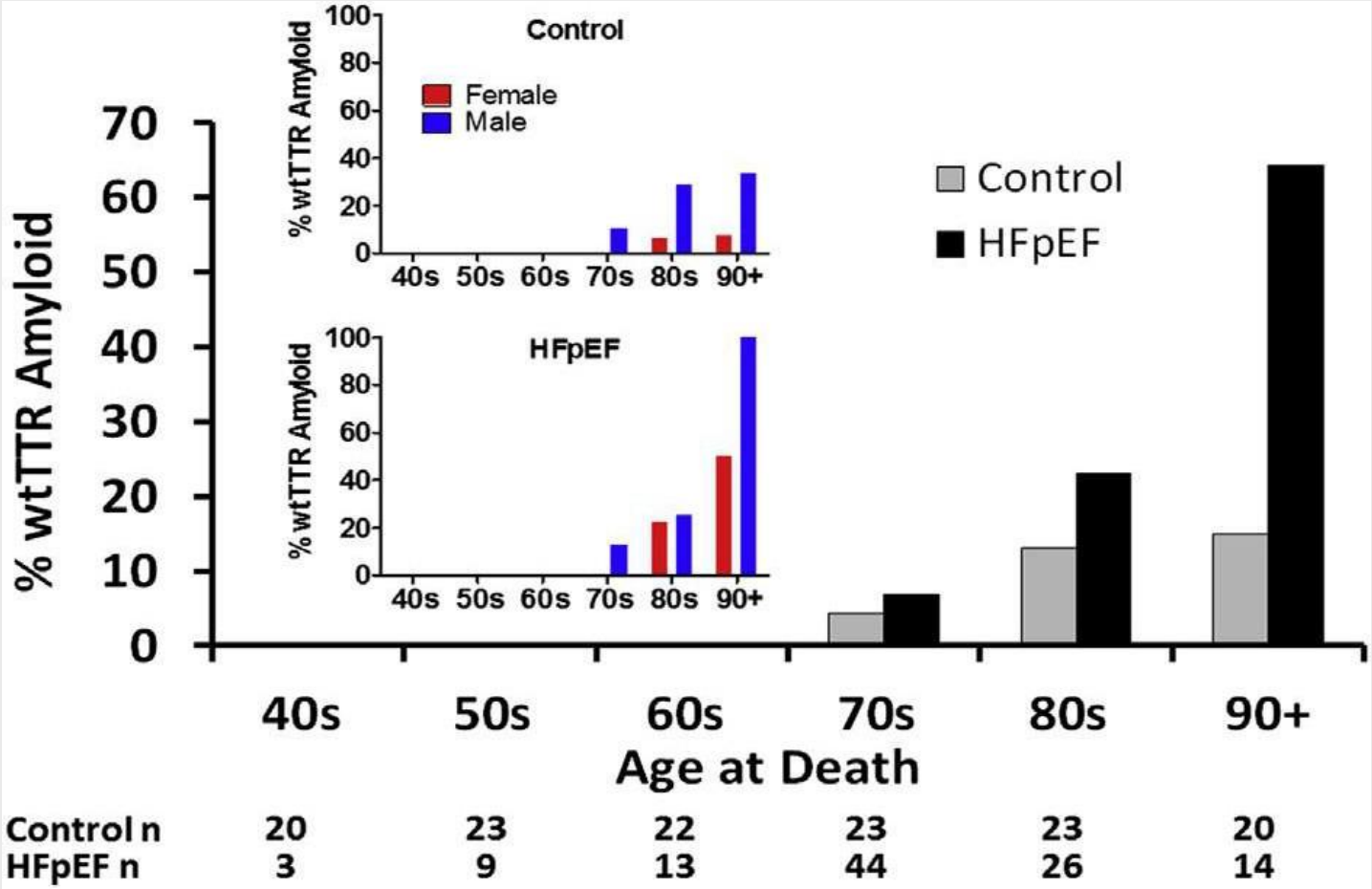
TETRAMER **FOLDED MONOMER** **MISFOLDED PROTEINS** **AMYLOID FIBRILS**



Mutationsbedingte Instabilität

1.Hammarström P et al. *Science.* 2003;299:713–716
2.Sekijima Y et al. *Curr Pharm Des*. 2008;14:3219–3230
3.Benson MD et al. *Mus Nerve* 2007;36:411–423

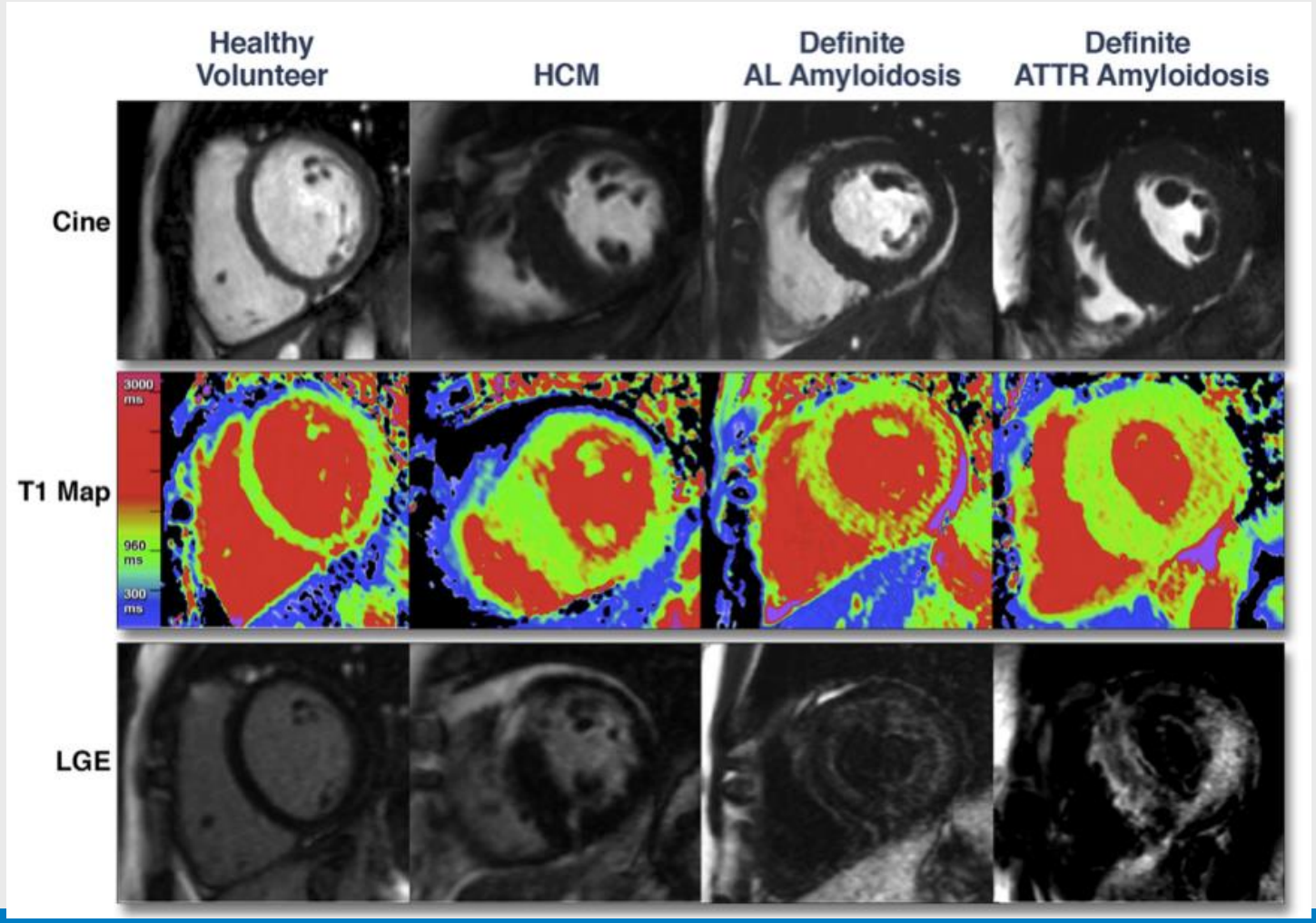
30% der Männer im Alter mit HFpEF haben eine wtATTR



MRT Diagnostik bei Amyloidosen

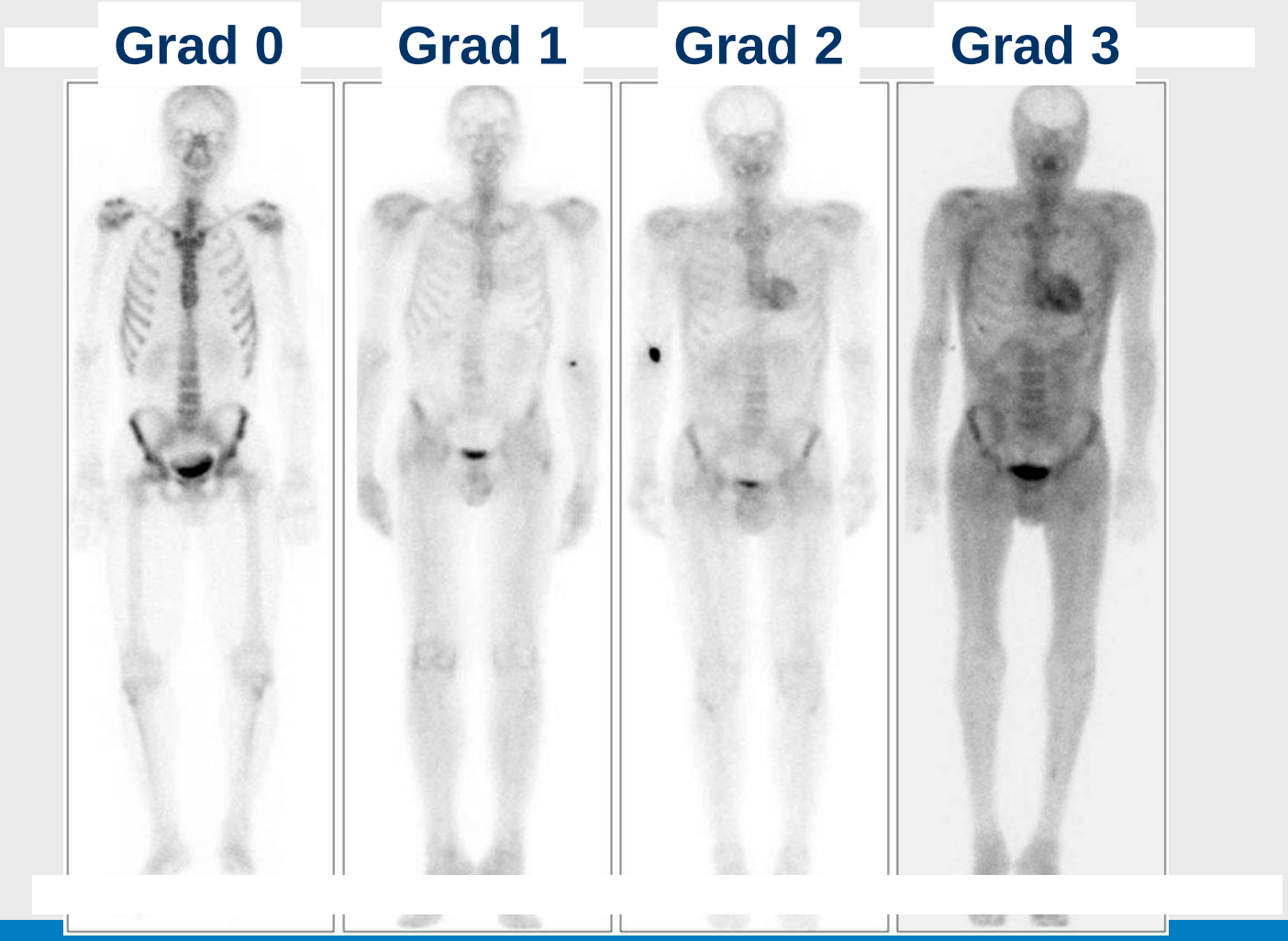
Kardio-MRT
T1 Mapping

Fontana et al. JACC Cardiovasc Imaging 2014



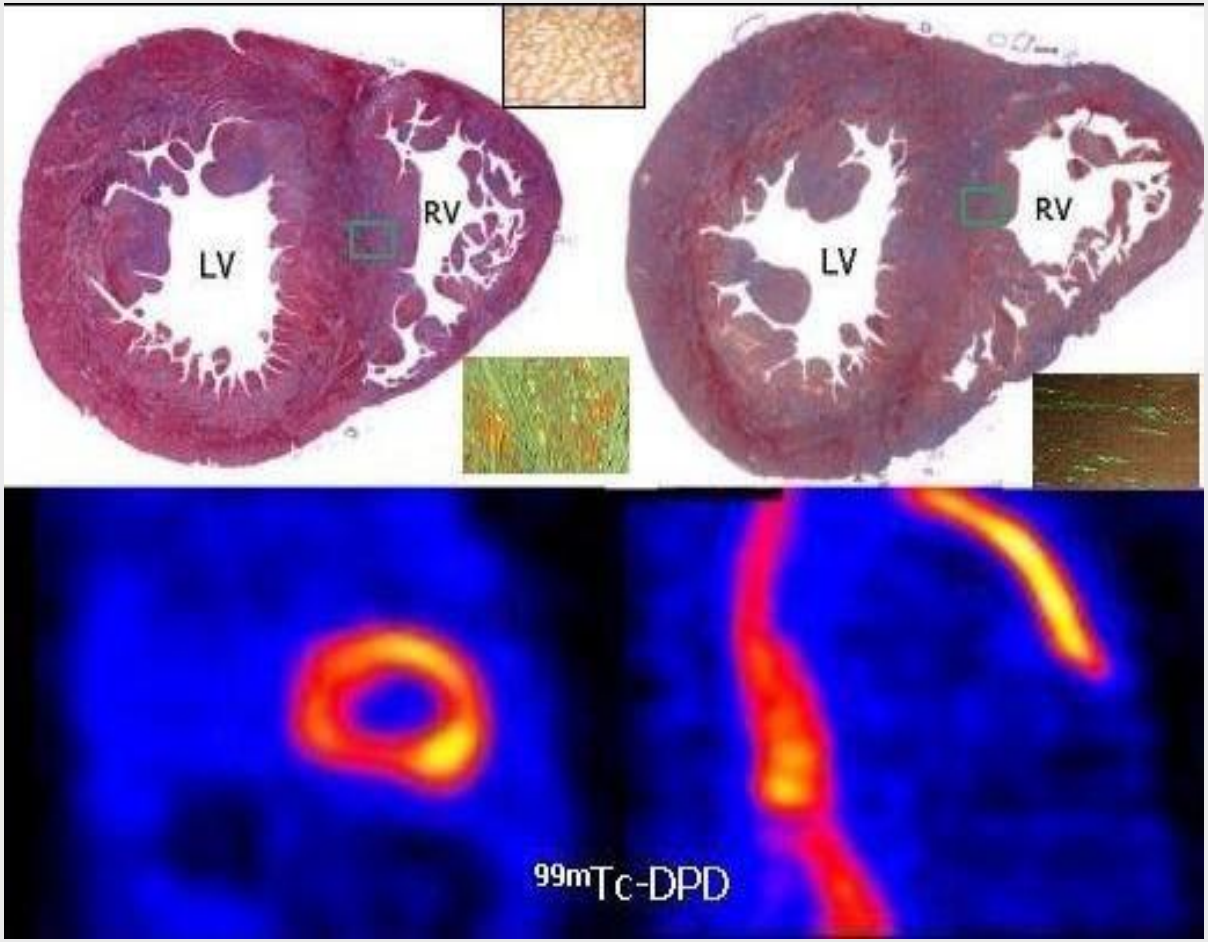
Semiquantitative Analyse der Herzretention

Glaudemans AW et al. Amyloid 2014



Korrelation einer positiven 99mTc-DPD Szintigraphie bei WT ATTR vs. AL

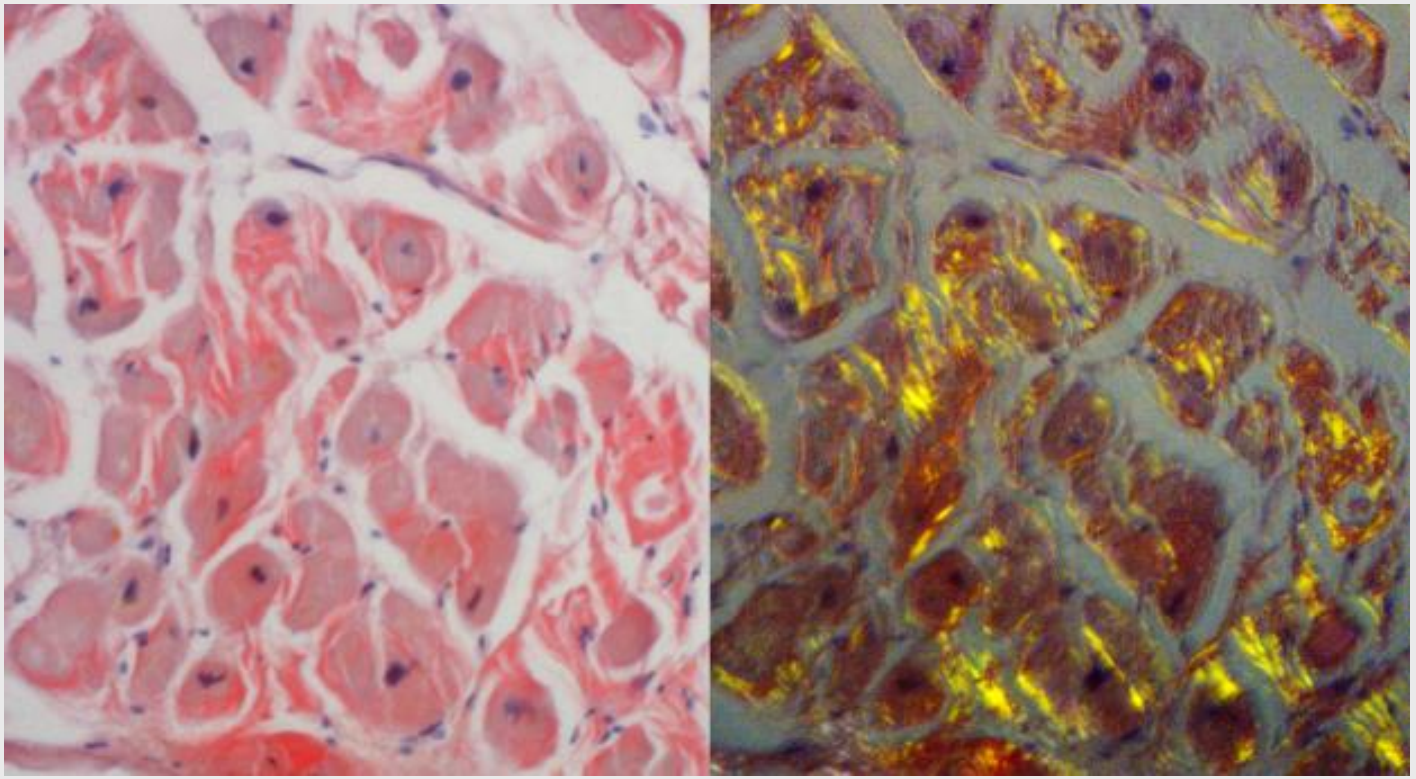
ATTR



AL

Rolle der Biopsie:
Amyloidose: eine histologische Diagnose

Kongorot **polarisiertes Licht**



Limitationen der Biopsieanalysen

- **Niedrige Sensitivität Extrakardialer Biopsien**

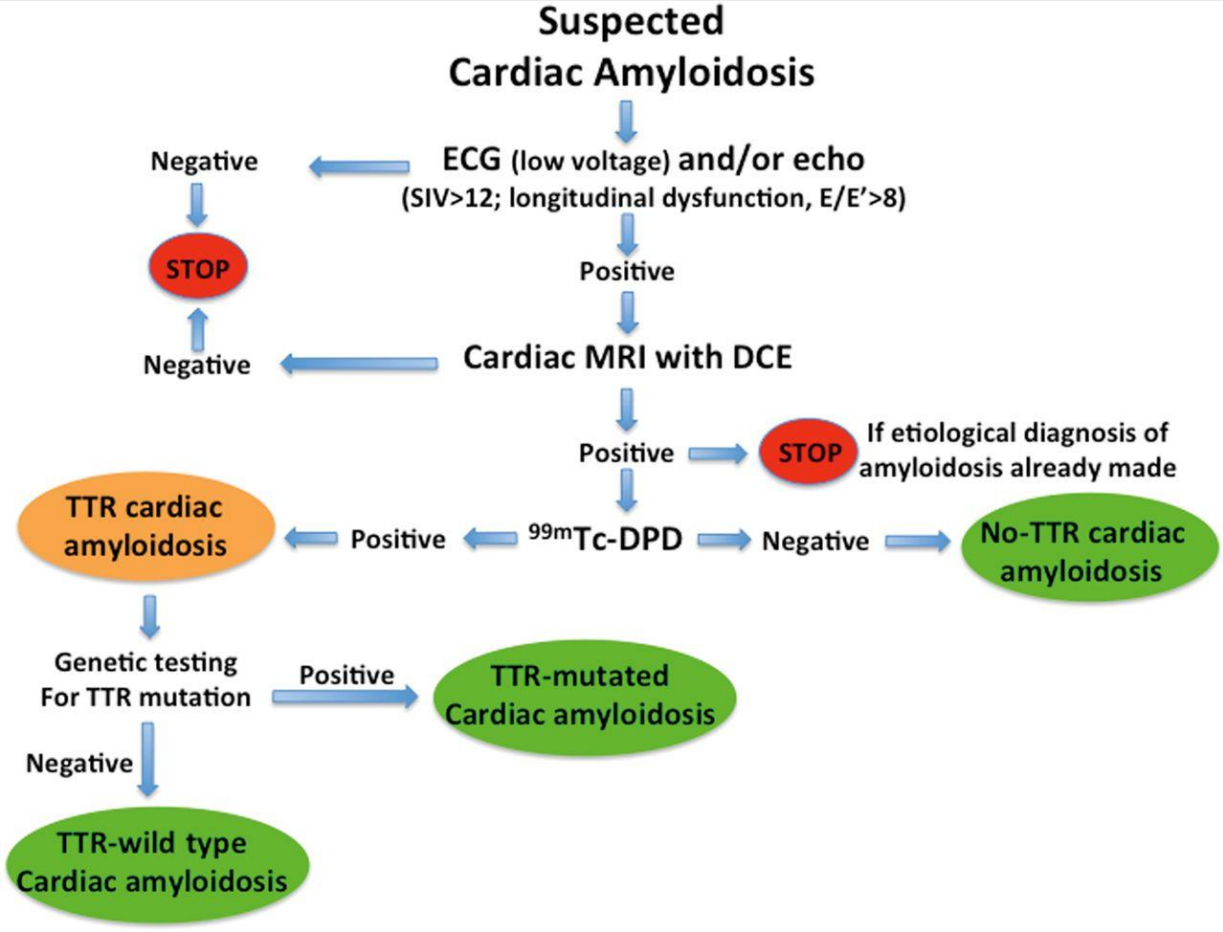
AL ≥80%
TTR 30% -50%

- **Niedrige Spezifität der reinen Immunhistologie (AL und ATTR of gemeinsam positiv)**

- **Massenspektrometrie notwendig**

Suggested workflow diagram in the non-invasive diagnostic imaging workup of suspected cardiac amyloidosis

Gianluca Di Bella et al. Eur Heart J Cardiovasc Imaging 2014



Fazit für die Praxis

- **30% der LVH oder HFpEF Pat haben eine Amyloidose**

- **Früherkennung ist entscheidend (AL vs ATTR)**

- **Low VolatageEKG, apikaler Strain, Szinitigraphie, Biopsie wie für ATTR**

- **Therapie bei WT-ATTR: in Studien zu Small Molecules/Tafamides/Grünem Tee Extrakt**

- **Lebertransplantation bei Mutations-ATTR**

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