SARKOİDOZ VE AMİLOİDOZDA VT ABLASYONU

DR BARIŞ AKDEMİR

YENİ YÜZYIL ÜNİVERSİTESİ TIP FAKÜLTESİ

TIP FAKÜLTESİ HASTANESİ

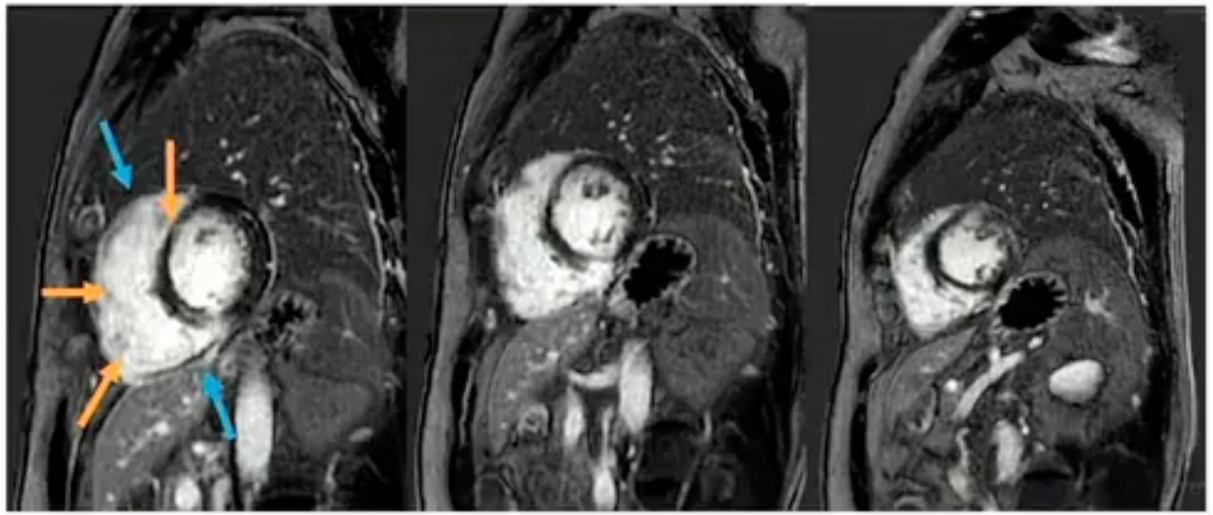
OLGU 1

- 52 YAŞ ERKEK HASTA
- TENİS OYNARKEN SENKOP
- SON 2 AYDA 4 DEFA SENKOP (HEPSİ TENİS OYNARKEN)
- AİLEDE ANİ ÖLÜM ÖYKÜSÜ YOK

OLGU 1

- ACİL EKG : VENTRİKÜLER TAŞİKARDİ
- BASAL EKG : SR 1.DERECE AV BLOK PR 240 MSEC VE IVCD 140 MSEC
- EKOKARDİYOGRAFİ: EF %54 HAFİF MY , ORTA TY , KONSANTRİK LV, NORMAL RV
- KORONER ANGİOGRAFİ: NORMAL KORONERLER

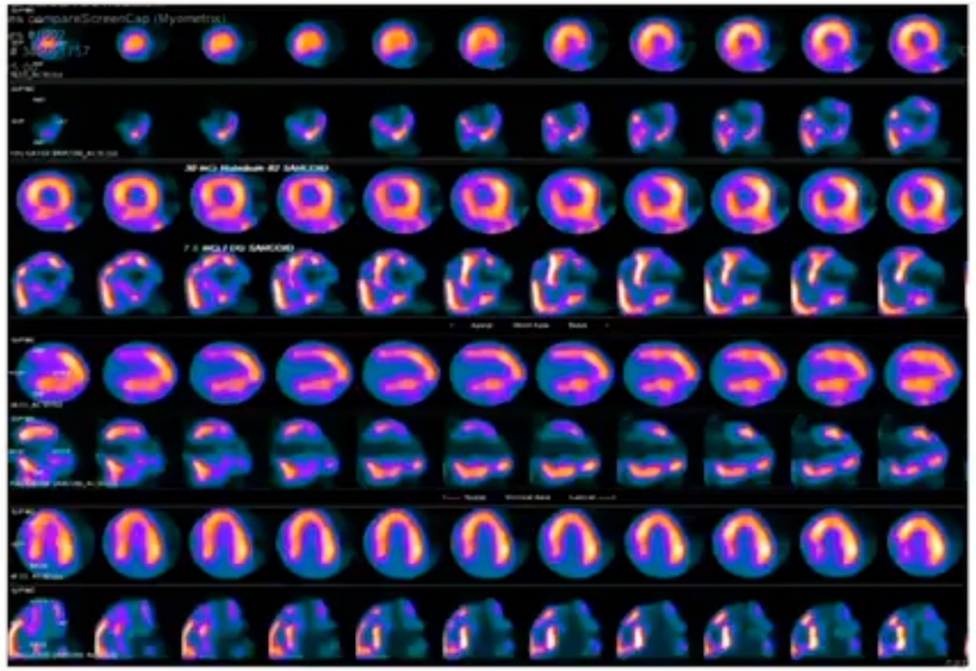
CARDIAC MRI



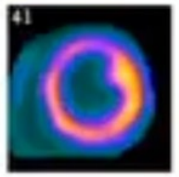
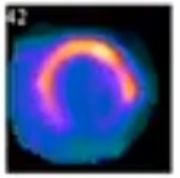
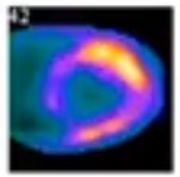
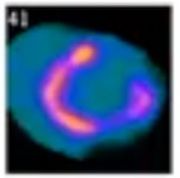
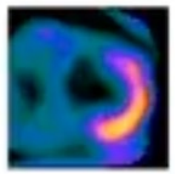
- Extensive, patchy myocardial LGE involving the septum, lateral LV, and lateral RV (orange arrow)
- T2 hyperintensities suggestive of edema (blue arrow)
- R greater than L axillary lymphadenopathy

FDG PET

- Intense and heterogeneous FDG uptake in heart, including right ventricle
- Partial corresponding areas of rubidium hypoperfusion
- Hypermetabolic axillary and mediastinal lymphadenopathy



FDG PET IMAGE PATTERNS & CARDIAC SARCOID DISEASE STAGING

	PERFUSION	METABOLISM	
Normal			Normal perfusion No FDG uptake
Mild or Early Disease			No or mild perfusion defect FDG uptake defect
Moderate or Progressive Disease			Moderate perfusion defect FDG uptake defect
Severe or Fibrous Disease			Severe perfusion defect No or minimal FDG uptake

Bokhari S, Lin JC, Julien HM. FDG-PET is a superior tool in the diagnosis and management of cardiac sarcoidosis. *Expert Analysis Am College of Cardiology*. 2019.

BU AŞAMADA TEDAVİDE NE YAPARSINIZ ?

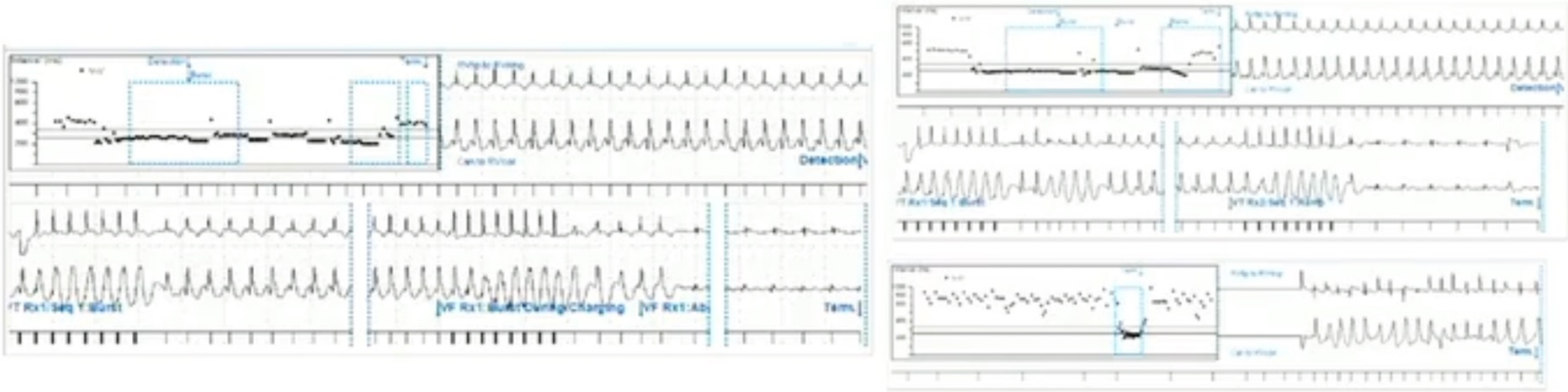
- A- ICD (CRT) + BETABLOKER
- B- AMIODARONE + STEROID
- C- ICD + BETABLOKER + STEROID
- D- VT ABLASYONU + AMIODARONE
- E- ICD (CRT) + BETABLOKER + STEROID

BU AŞAMADA TEDAVİDE NE YAPARSINIZ ?

- A- ICD (CRT) + BETABLOKER
- B- AMIODARONE + STEROID
- C- ICD + BETABLOKER + STEROID
- D- VT ABLASYONU + AMIODARONE
- **E- ICD (CRT) + BETABLOKER + STEROID**

- METOPROLOL 25 MG VE PREDNISONE 40 MG
- CRT-D İMPLANTE EDİLDİ

2 months later, he has ventricular tachycardia terminated with ATP

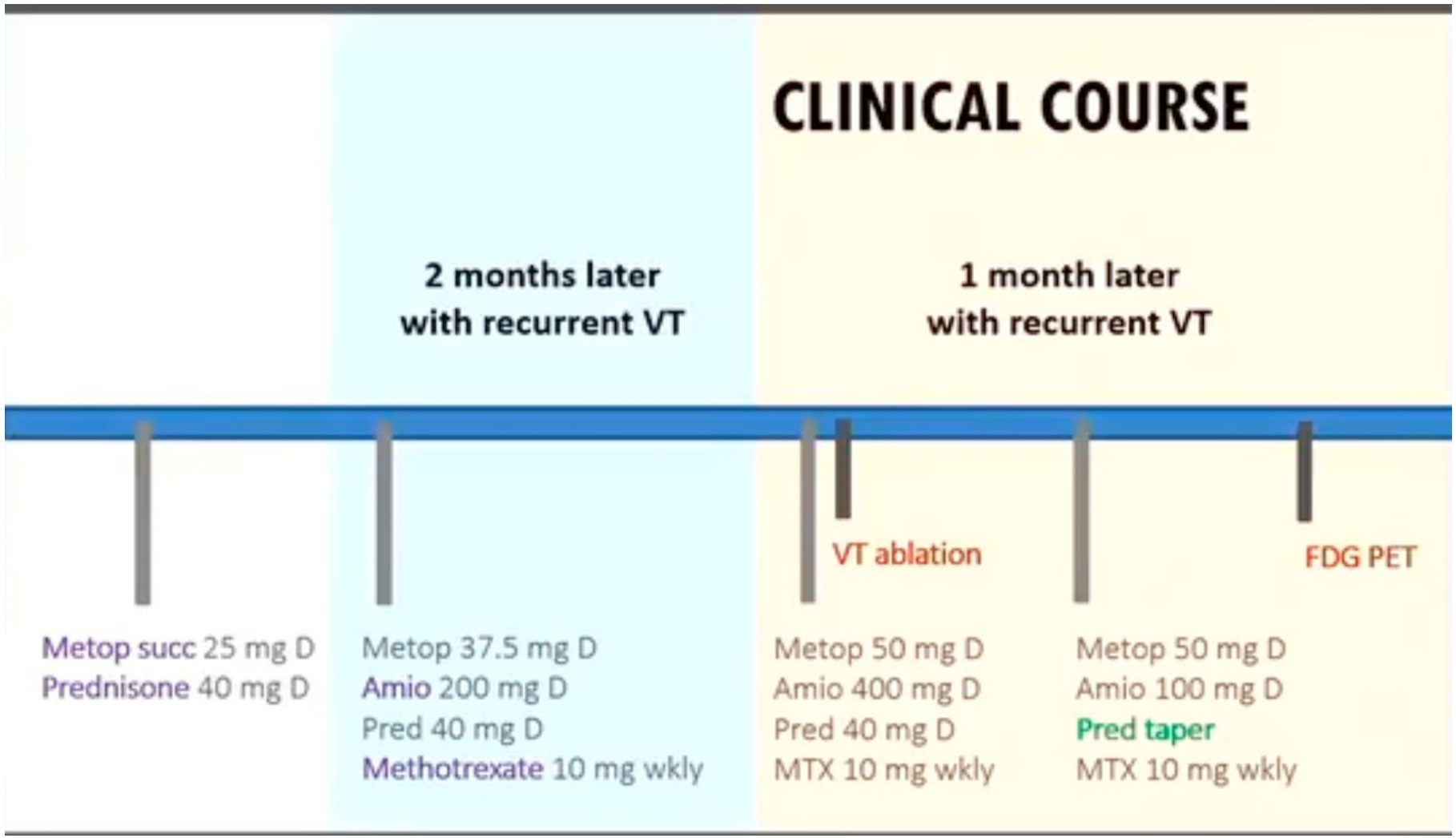


ŞİMDİ NE YAPALIM ?

- A- PET SCAN TEKRARI
- B- ANTİARİTMİK (AMİODARONE) EKLEYELİM
- C- BİYOLOJİK DMARD EKLEYELİM
- D- VT ABLASYONUNA YÖNLENDİRELİM
- E- B VE C

ŞİMDİ NE YAPALIM ?

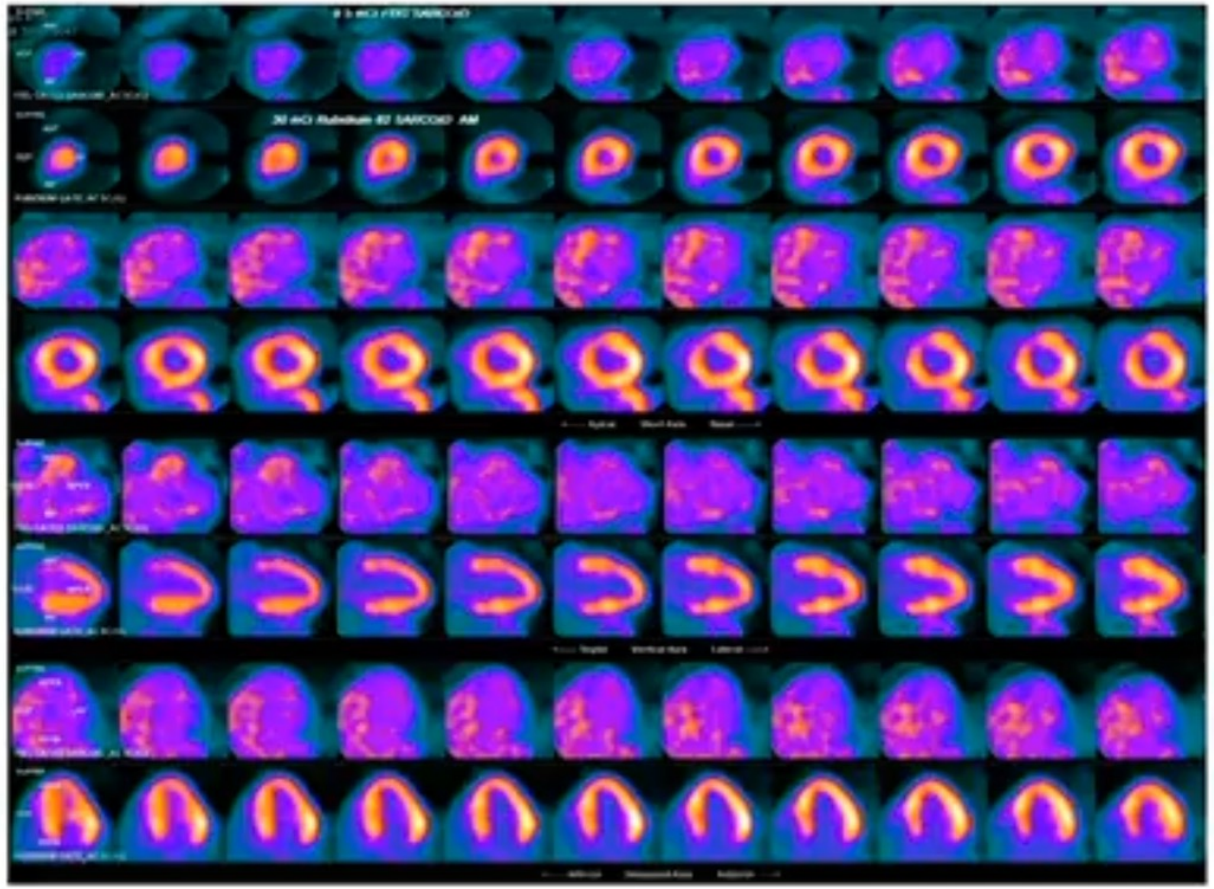
- A- PET SCAN TEKRARI
- B- ANTİARİTMİK (AMİODARONE) EKLEYELİM
- C- BİYOLOJİK DMARD EKLEYELİM
- D- VT ABLASYONUNA YÖNLENDİRELİM
- **E- B VE C**

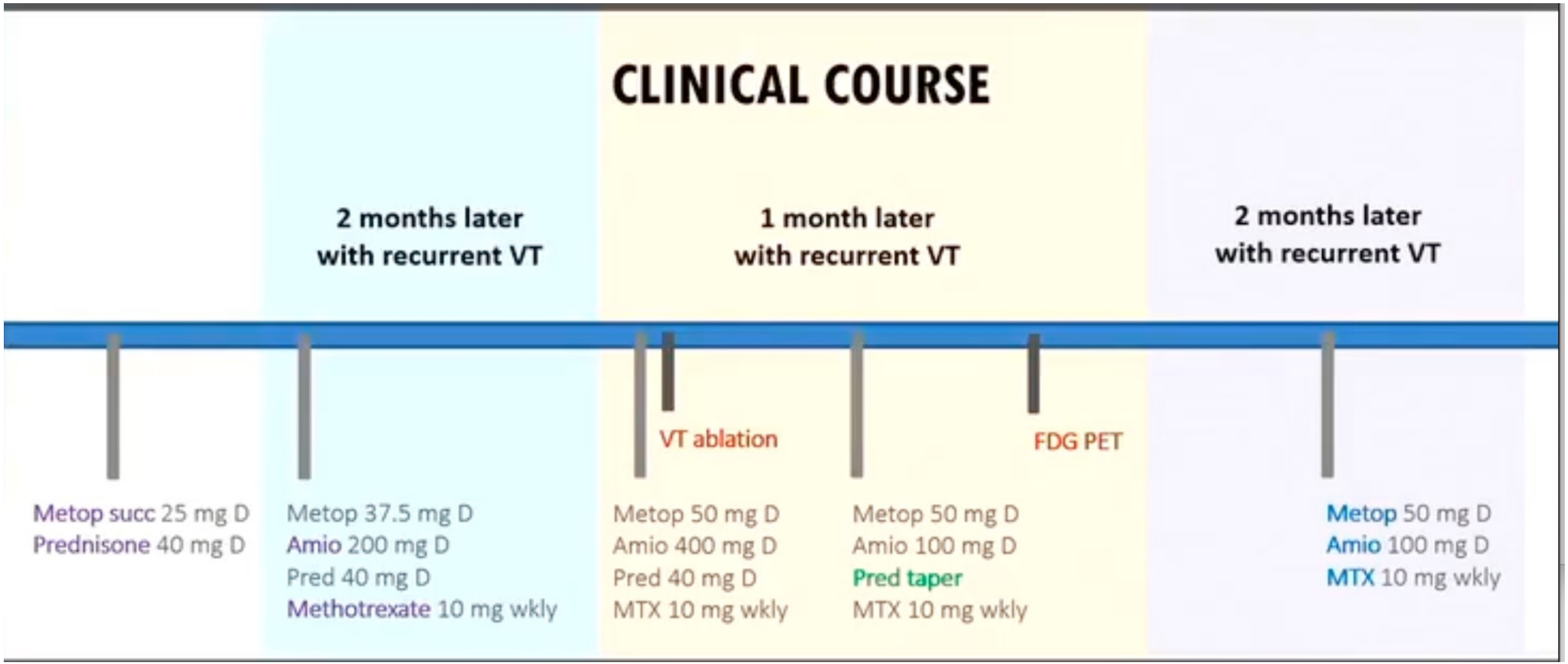


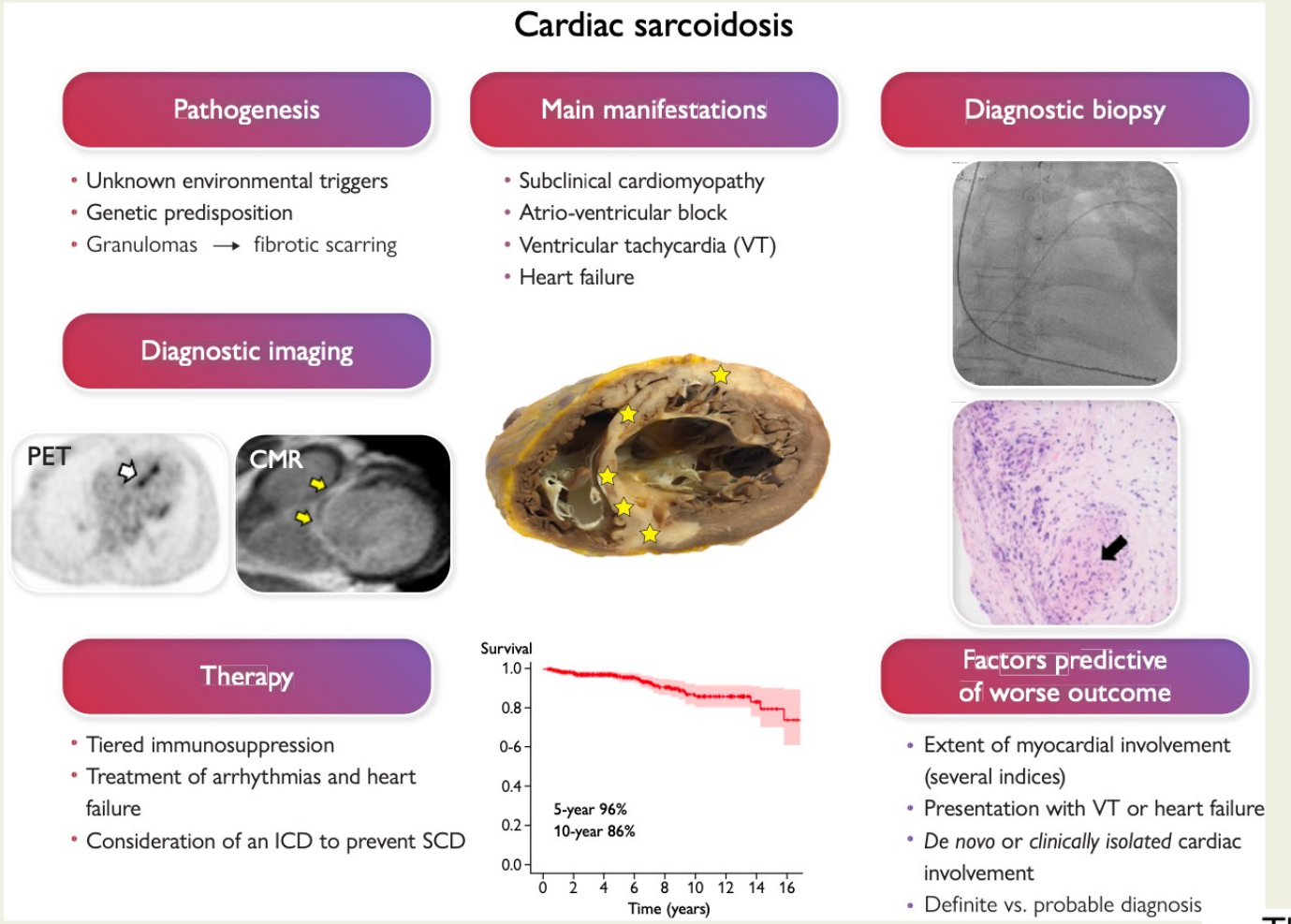
FDG PET

5 months after initial FDG PET

- Complete resolution of FDG uptake in myocardium
- Markedly improved rubidium perfusion with minimal hypoactivity







The manifestations of CS (*Table 1*) depend on the location and extent of granulomas, with high-grade atrioventricular block (AVB) and VAs being the most common initial signs.[8,22–25] Sustained ventricular tachycardia (VT) results from re-entry circuits in inflamed and scarred myocardial areas, but automatic and triggered arrhythmias are also possible.[26] Multiple VT morphologies are common. Heart failure reflects

Table 3 **The heart rhythm society's criteria for the diagnosis of cardiac sarcoidosis**[4]

1. Histological diagnosis from myocardial tissue, *definite cardiac sarcoidosis* *requires presence of non-necrotizing granulomas with no alternative cause*
2. Clinical diagnosis from noninvasive and invasive studies, *probable cardiac sarcoidosis* *requires histologic diagnosis of extracardiac sarcoidosis and presence of one or more of the following:*
—cardiomyopathy or atrioventricular block responsive to immunosuppression
—unexplained reduced left ventricular ejection fraction (<40%)
—unexplained sustained ventricular tachycardia (spontaneous or induced)
—2nd degree (Mobitz type II) or 3rd degree heart block
—patchy uptake on dedicated cardiac 18-F fluorodeoxyglucose PET[a]
—late gadolinium enhancement on CMR[a]
—positive gallium uptake[a]
and exclusion of other causes for the cardiac manifestations

CMR indicates cardiac magnetic resonance; PET, positron emission tomography.
[a]in a pattern consistent with cardiac sarcoidosis.

Table 4 Current recommendations by expert societies for an implantable cardioverter-defibrillator in patients with cardiac sarcoidosis

Class[a]	2014 HRS Consensus Statement on Management of Arrhythmias in Cardiac Sarcoidosis[4]	2017 AHA/ACC/HRS Guideline for Management of Ventricular Arrhythmias and Prevention of Sudden Cardiac Death[153]	2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death[154]
I	Prior aborted cardiac arrest, documented spontaneous sustained ventricular tachycardia, or LVEF ≤ 35%[b,c]		
IIa	LVEF > 35% with an indication for permanent pacemaker		
	History of syncope compatible with arrhythmogenic etiology		
	Inducible sustained ventricular arrhythmia at PES		Inducible sustained monomorphic ventricular arrhythmia at PES in a patient with LVEF 35%–50% and minor LGE at CMRI
		LVEF > 35% with evidence of myocardial scar (or 'extensive scar') by CMRI or PET[c]	LVEF >35% with significant myocardial LGE at CMRI after resolution of acute inflammation
IIb	LVEF 36%–49% or RVEF < 40%[b]		

ACC indicates American College of Cardiology; AHA, American Heart Association; CMRI, cardiac magnetic resonance imaging; ESC, European Society of Cardiology; HRS, Heart Rhythm Society; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; PES, programmed electrical stimulation; PET, positron emission tomography; RVEF, right ventricular ejection fraction.

[a]Class I is recommended ('is useful/indicated/beneficial', 'should be performed'); Class IIa, modest recommendation ('can be useful/beneficial', 'should be considered'); and Class IIb, weak recommendation ('usefulness is unknown/uncertain', 'may/might be considered').

[b]2014 HRS guidance presupposes optimal medical therapy and a period of immunosuppression in the presence of active inflammation.

[c]2017 ACC/AHA/HRS guideline presupposes meaningful expected survival ≥1 year.

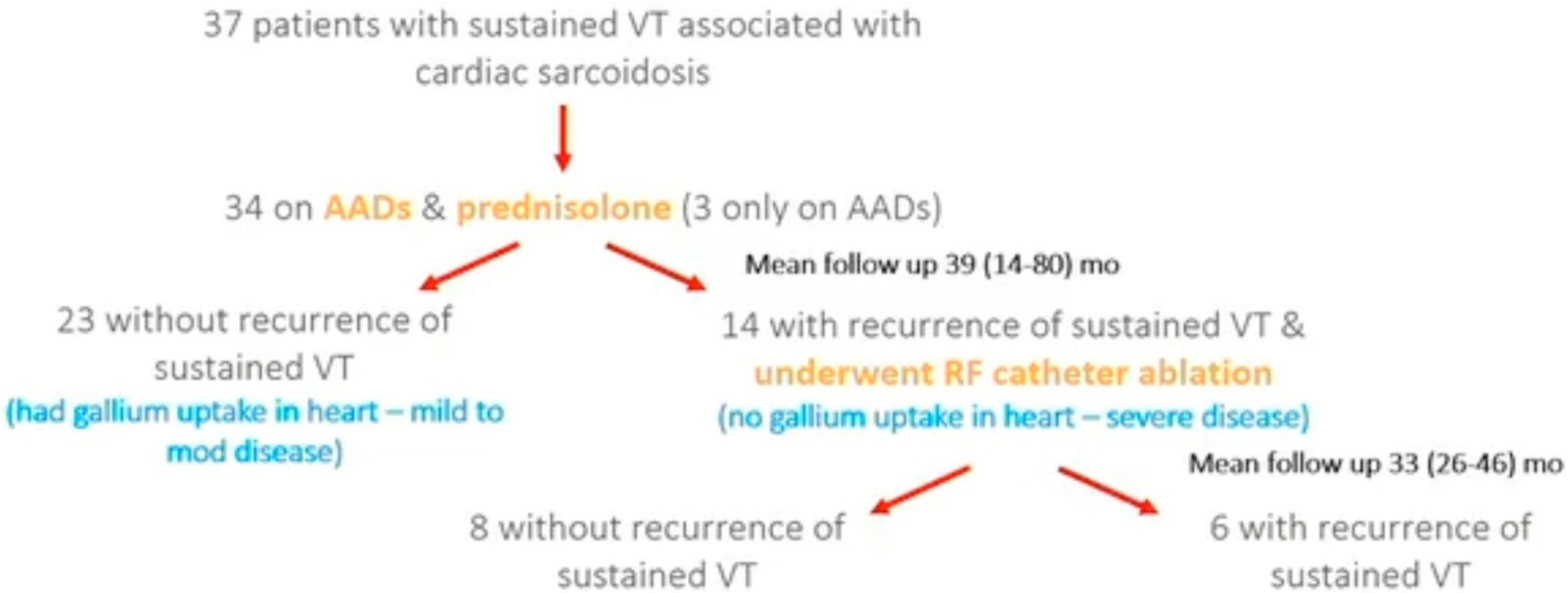
Ventriküler aritmiler için tedavi sırası

- Steroid + Antiaritmik (amiodarone veya sotalol)
- Medikal tedavi başarısız olursa veya VT fırtınası var ise – ABLASYON
- Ablasyon ve Medikal tedavi başarısız olur ise – Sempatektomi ?

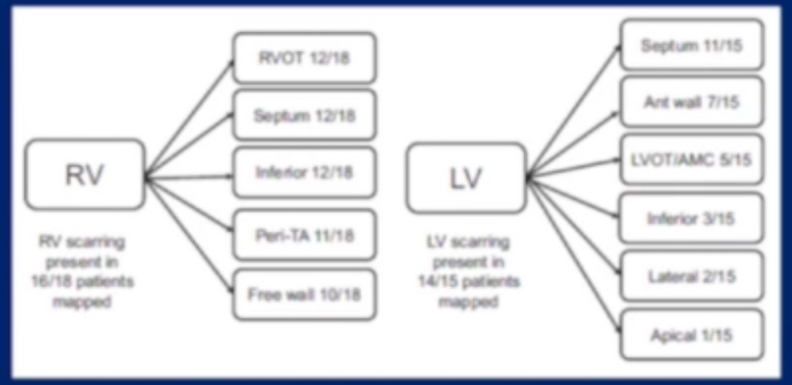
*** 15 çalışmanın metaanalizinde (>400 ablasyon)
- tek işlemde VT rekürensi olmayan hasta oranı %43.
-tekrarlayan işlemlerde %63 .

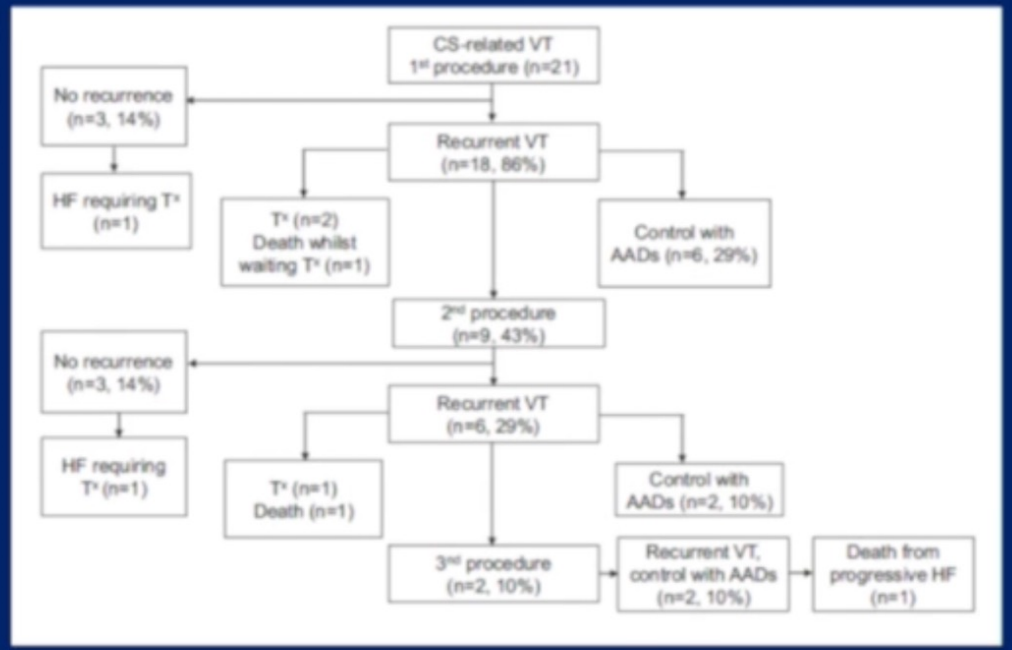
Retrospective study in Japan

Naruse Y et al. Systematic treatment approach to ventricular tachycardia i
cardiac sarcoidosis. *Circ Arrhythm Electrophysiol*. 2014;7:407-413



ABLATION OF SARCOID RELATED VT

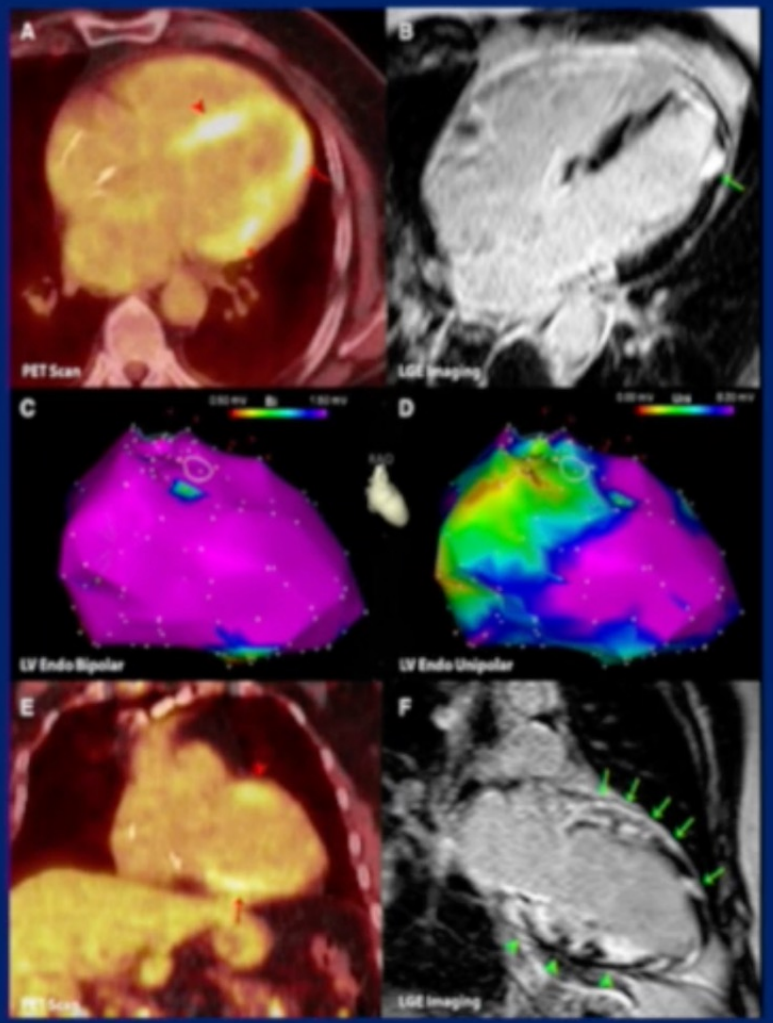




- 21 pts, 5% of all NICM
- 18/21 treated with IS therapy
- Diverse RV and LV substrate
- 1 year VT free survival
  - 14% single proc
  - 37% multiple procs

Kumar, Stevenson et al, Circ A&E 2015. 8:87-93

ABLATION OF SARCOID RELATED VT



- 31 pts with ablation, 75% with MRI or PET

	LGE on MRI			Abnormal FDG Uptake on PET		
	K (95% CI)	*P* Value	Strength of Agreement	*K* (95% CI)	*P* Value	Strength of Agreement
Endocardial bipolar LVA (≤1.5 mV)	0.34 (0.23–0.45)	<0.001	Fair	0.25 (0.14–0.36)	<0.001	Fair
Endocardial unipolar LVA (≤8.3 mV for the LV and ≤5.5 mV for the RV)	0.44 (0.36–0.53)	<0.001	Moderate	0.27 (0.18–0.36)	<0.001	Fair
Epicardial bipolar LVA (≤1.0 mV)	0.53 (0.38–0.67)	<0.001	Moderate	0.20 (0.06–0.33)	<0.01	Poor

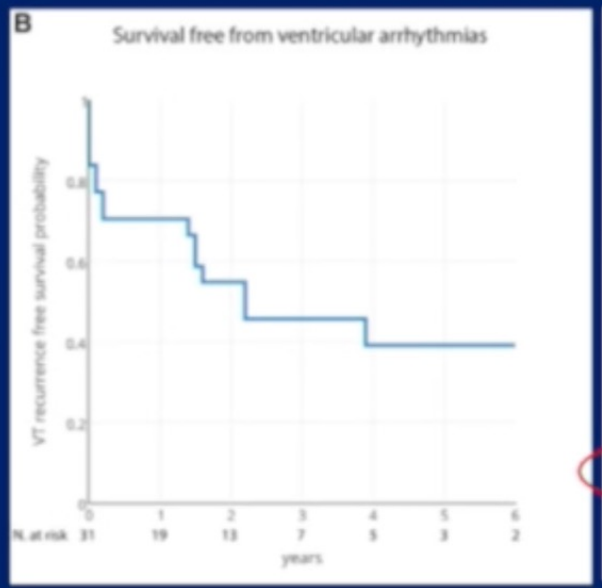


Table 6. Single-Variable Cox Proportional Hazards Analysis of Baseline Covariates in Relation to Outcome Events

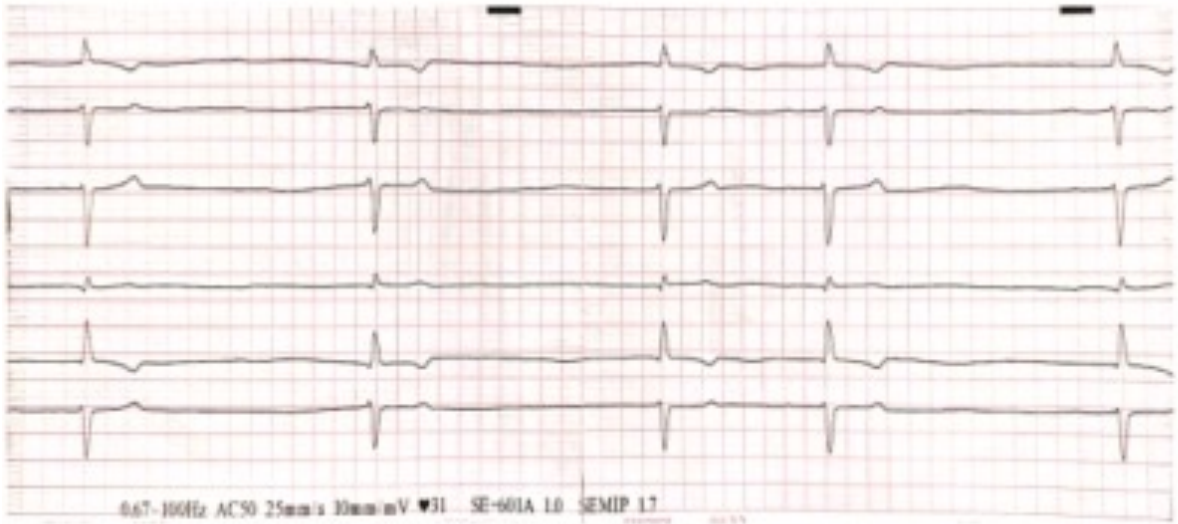
	Sustained VT Recurrence	
	HR (95% CI)	*P* Value
Age, y	0.97 (0.92–1.02)	0.19
Male sex	3.38 (0.77–14.95)	0.12
LVEF (per each 10% decrease)	1.69 (1.14–2.51)	0.01
Moderate to severe RV dysfunction	1.83 (1.08–3.10)	0.03
Moderate to severe diastolic dysfunction	1.19 (0.43–3.32)	0.74
Chronic kidney disease	2.74 (0.75–10.11)	0.13
History of syncope	1.24 (0.46–3.35)	0.67
NYHA class III/IV	2.43 (1.26–4.68)	0.01
VT storm at presentation	1.45 (0.18–11.48)	0.73
Amiodarone therapy	1.58 (0.48–5.09)	0.60
Positive baseline PET	3.86 (1.01–14.74)	0.05
Failed PET improvement after immunosuppressive therapy	2.08 (1.16–3.73)	0.01
>5 segments involved by LGE on MRI	5.02 (1.25–20.16)	0.02
Septal substrate	1.10 (0.41–2.96)	0.85

Muser, Marchlinski et al Circ A&E, July 2016

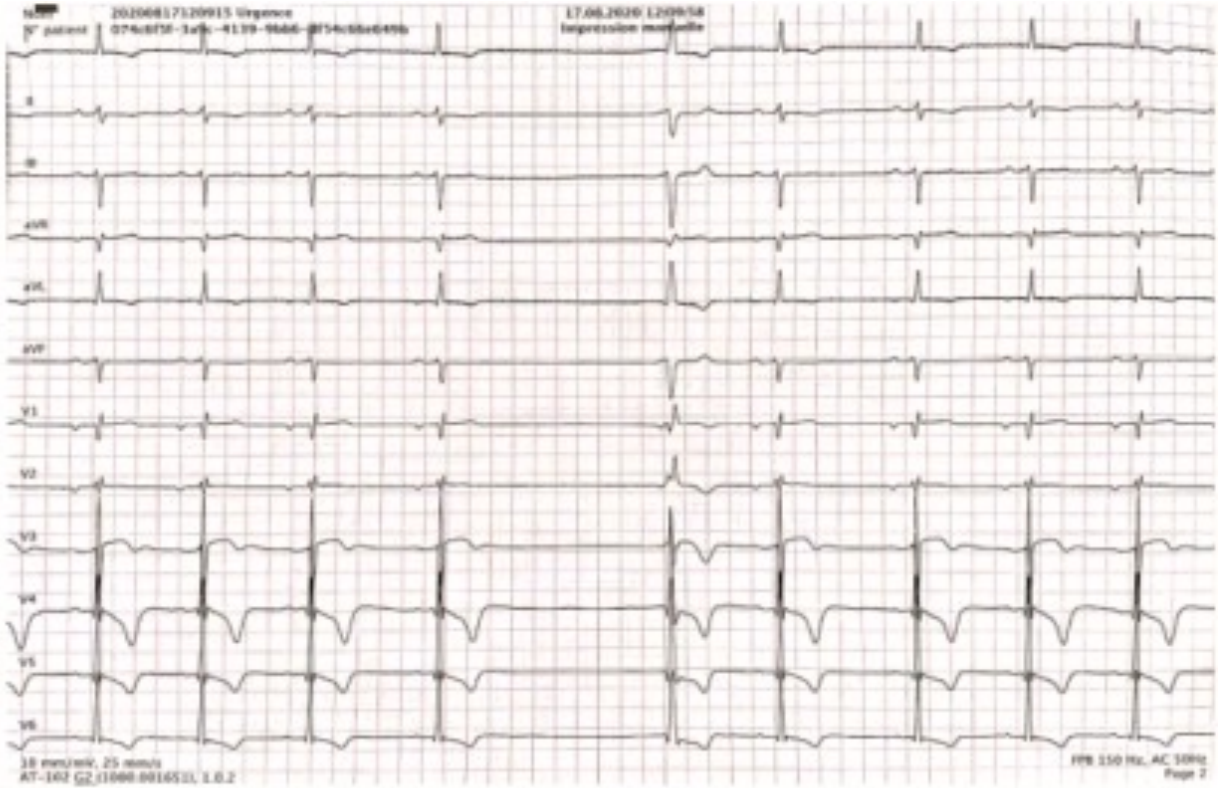
OLGU 2

- 59 yaş erkek hasta
- Acile nefes darlığı ve halsizlik şikayeti ile başvuruyor.
- NHYA KLASS III
- FM: Bradikardik , sistolik üfürüm

ACİL EKG



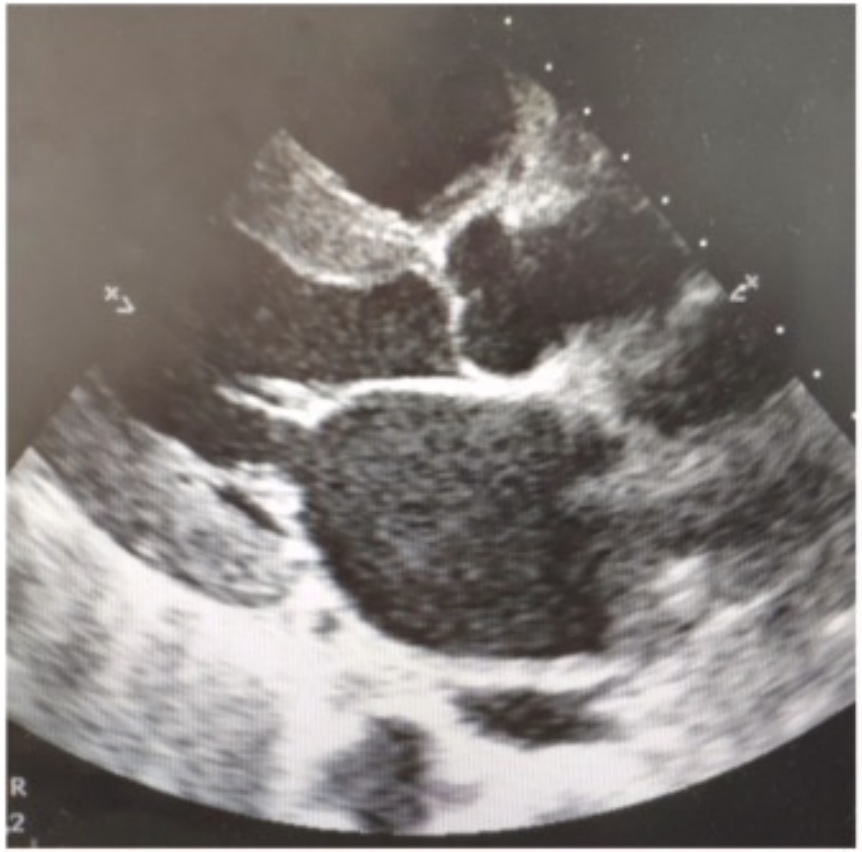
A

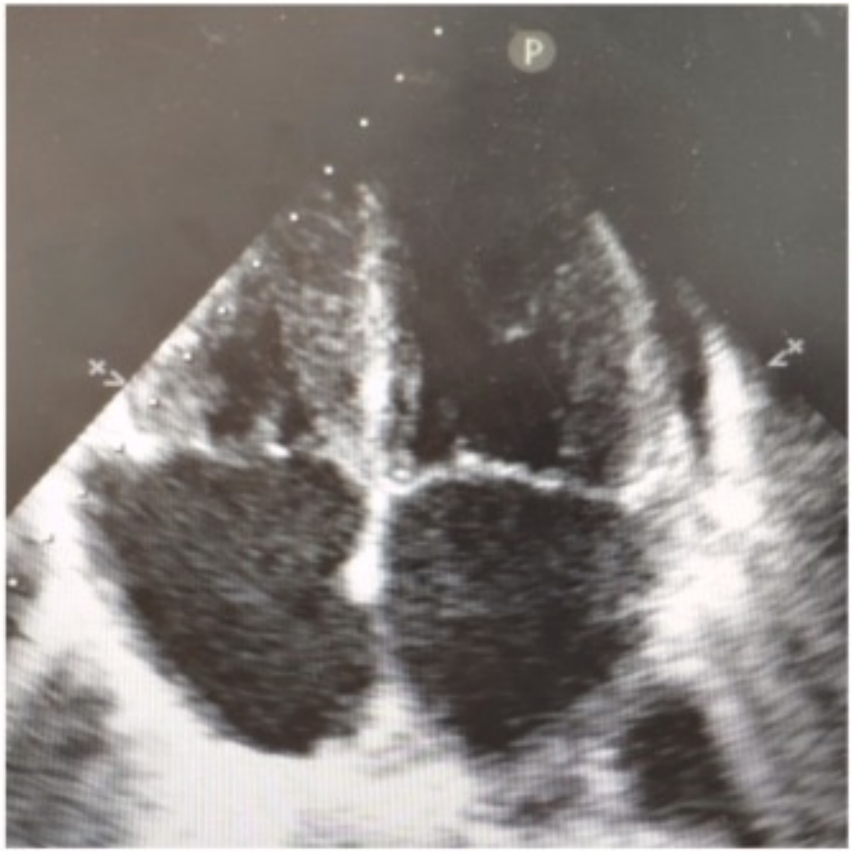


B

TIP FAKÜLTESİ HASTANESİ

EKOKARDİYOGRAFİ





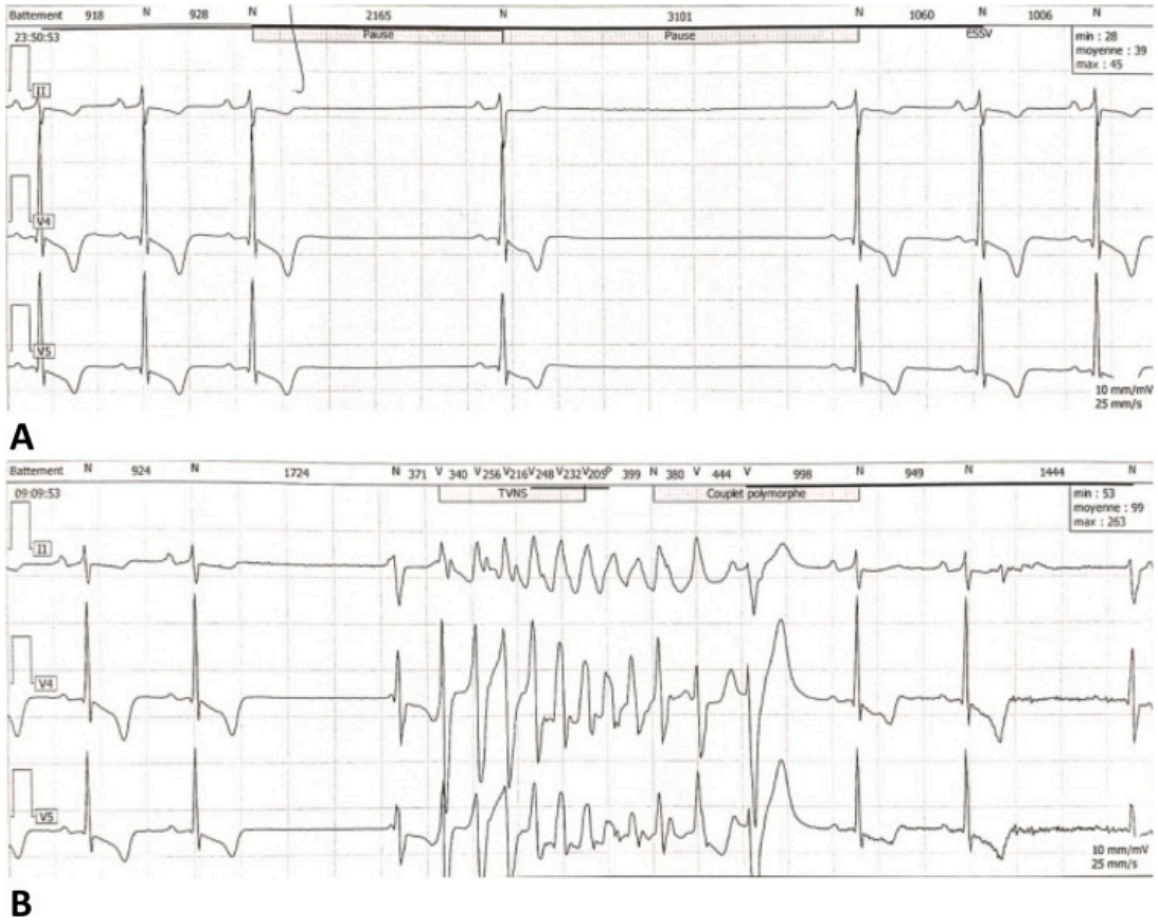
Kardiyak MRI- Biopsi

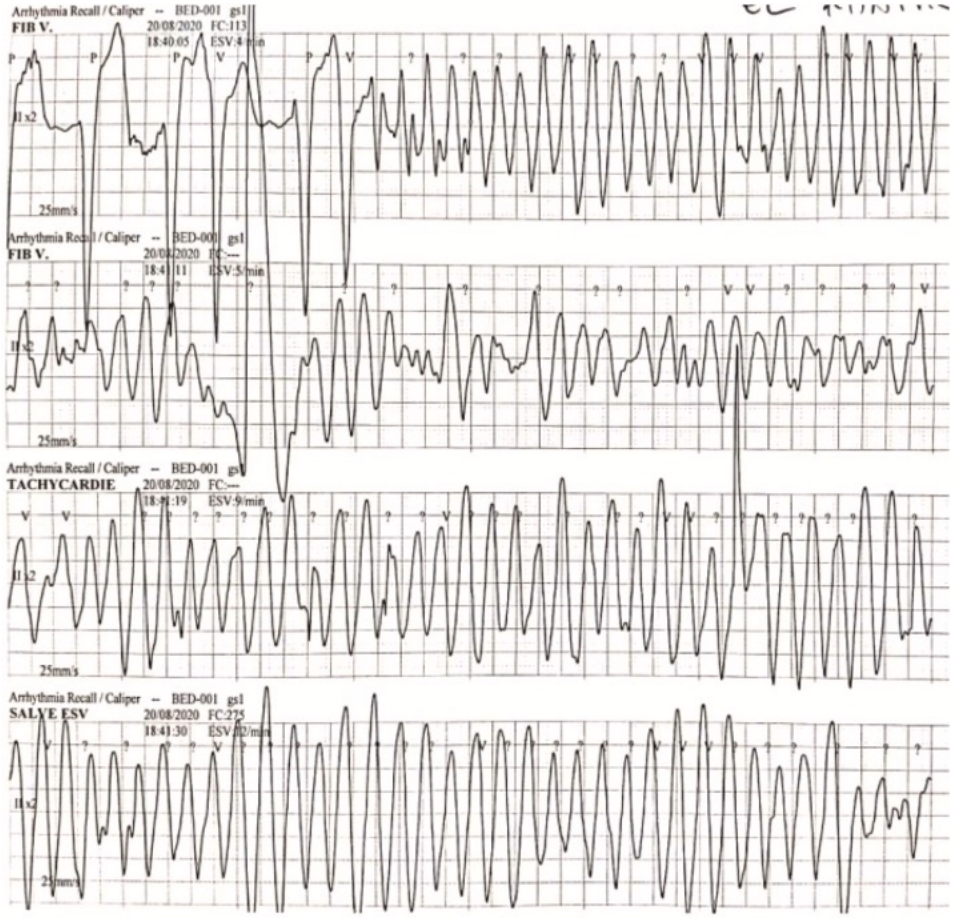
- Yaygın geç gadolinium tutulumu

*** Kardiyak amyloidosis şüphesi ile extrakardiyak biopsi

- AL- AM.

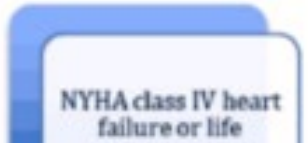
HOLTER



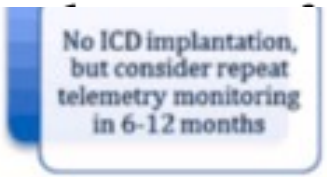


ICD ENDİKASYONU

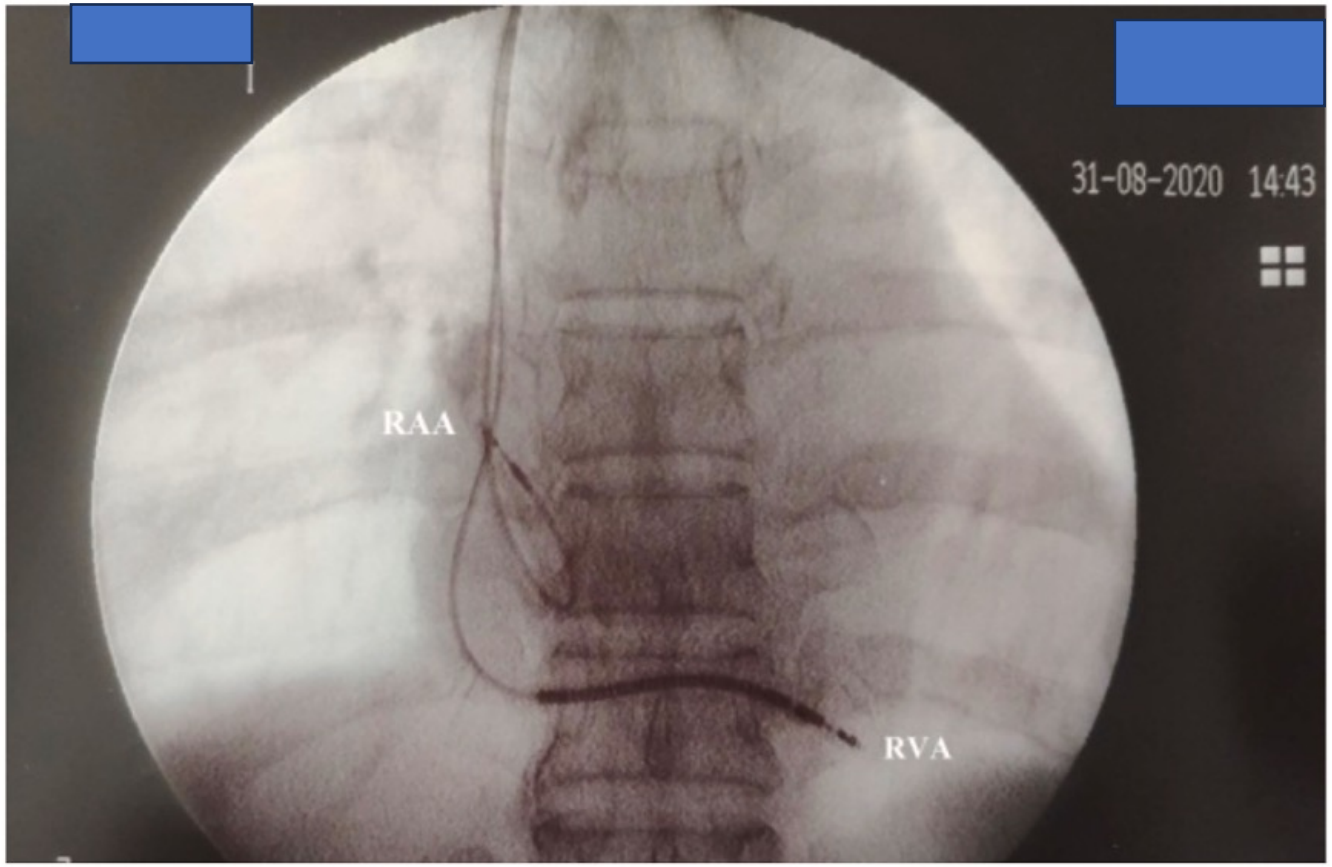
ICD ENDİKASYONU



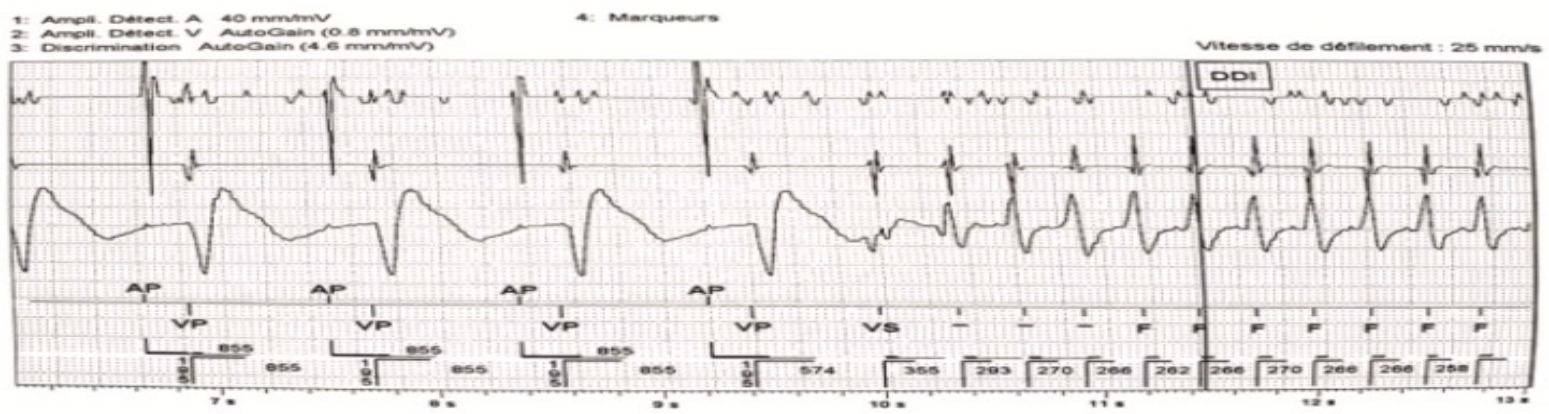
limited for mainly two reasons [6]: 1) Electromechanical dissociation or agonal bradycardia from end-stage heart failure represent the most frequent documented mechanism of sudden death in CA [7,8]; 2) The worst outcome and low life expectancy in this population. As a result, there has been very little enthusiasm for the ICD in patients with CA. Based on such limited data, The current guidelines [9] consider that ICD implantation should be considered in secondary prevention, in patients with a life expectancy > 1year and good functional status, but predictors of survival in patients with CA and ICD are very poorly understood.

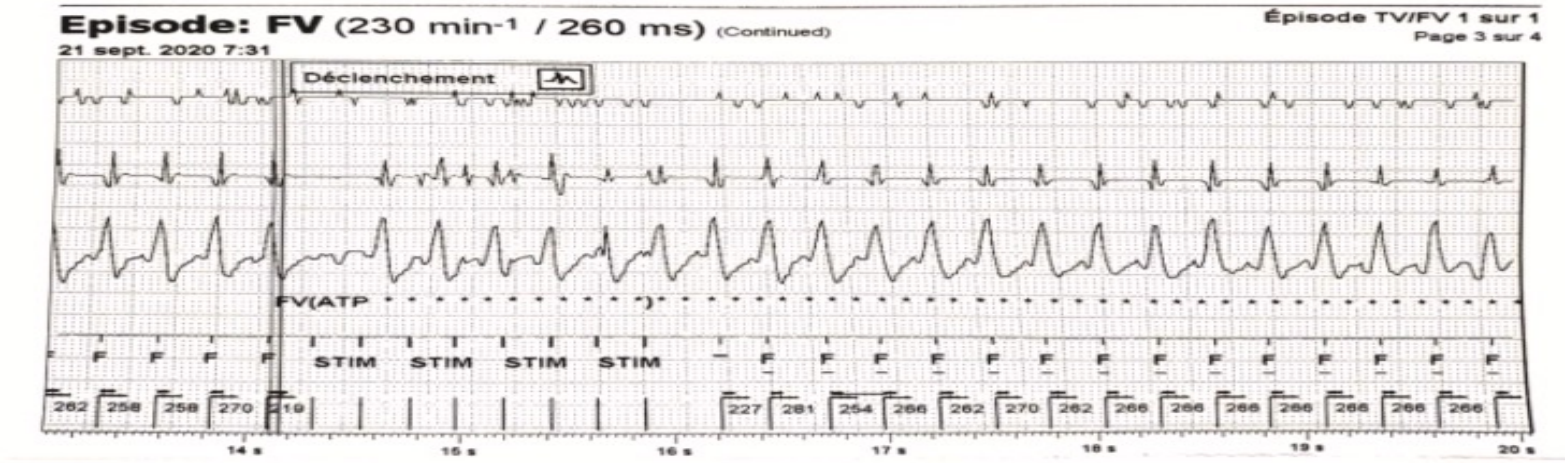


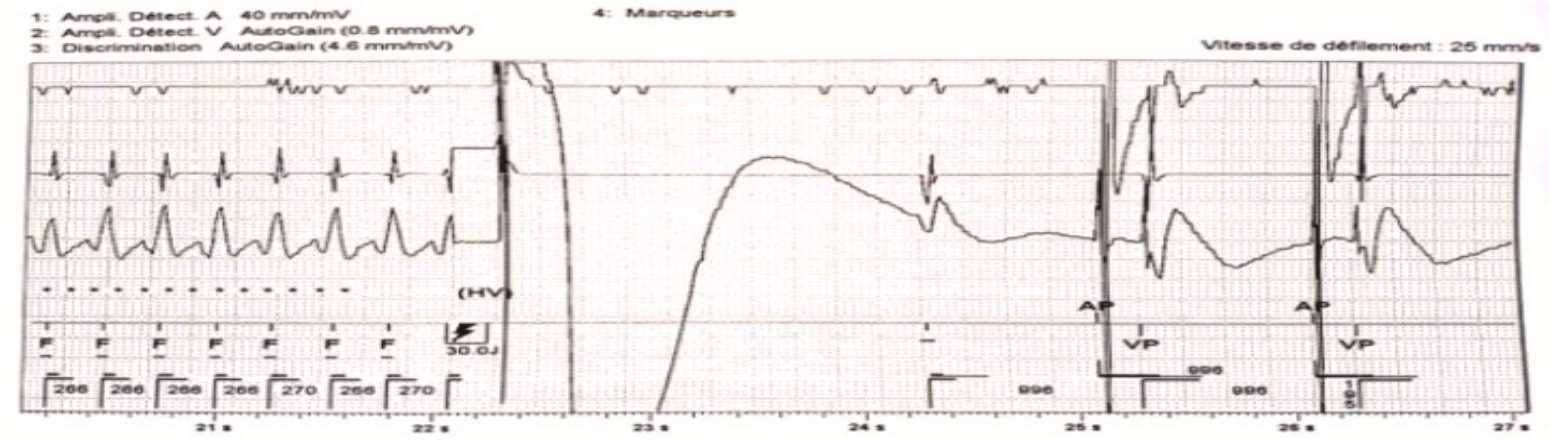
ICD implantasyonu



ICD ŞOK

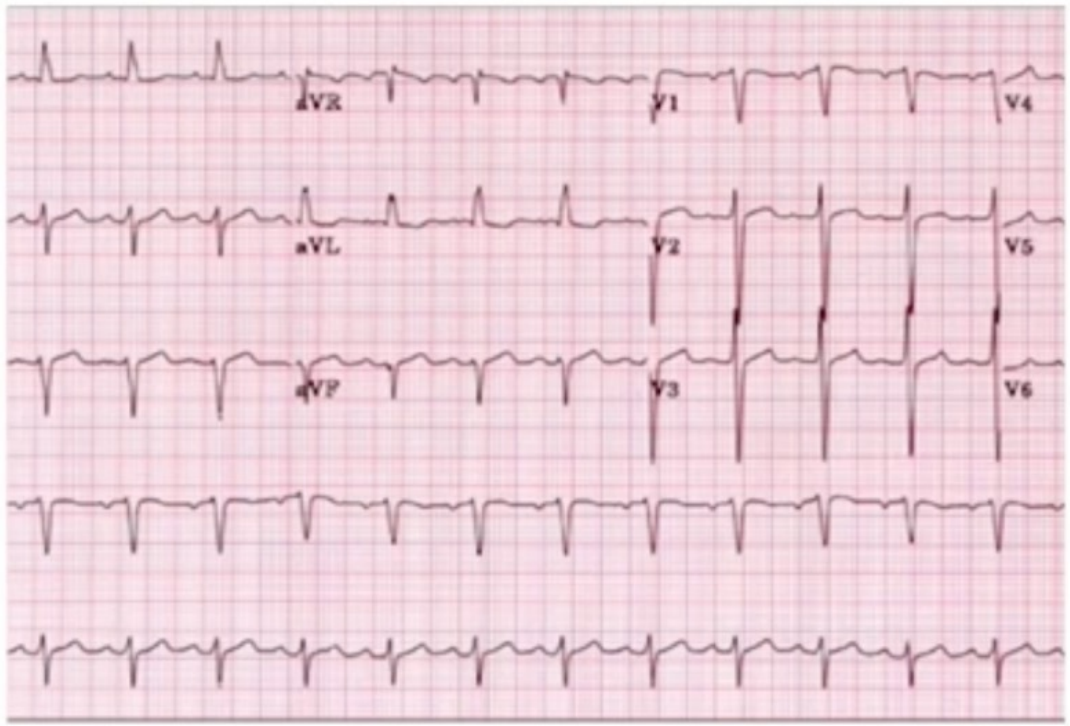


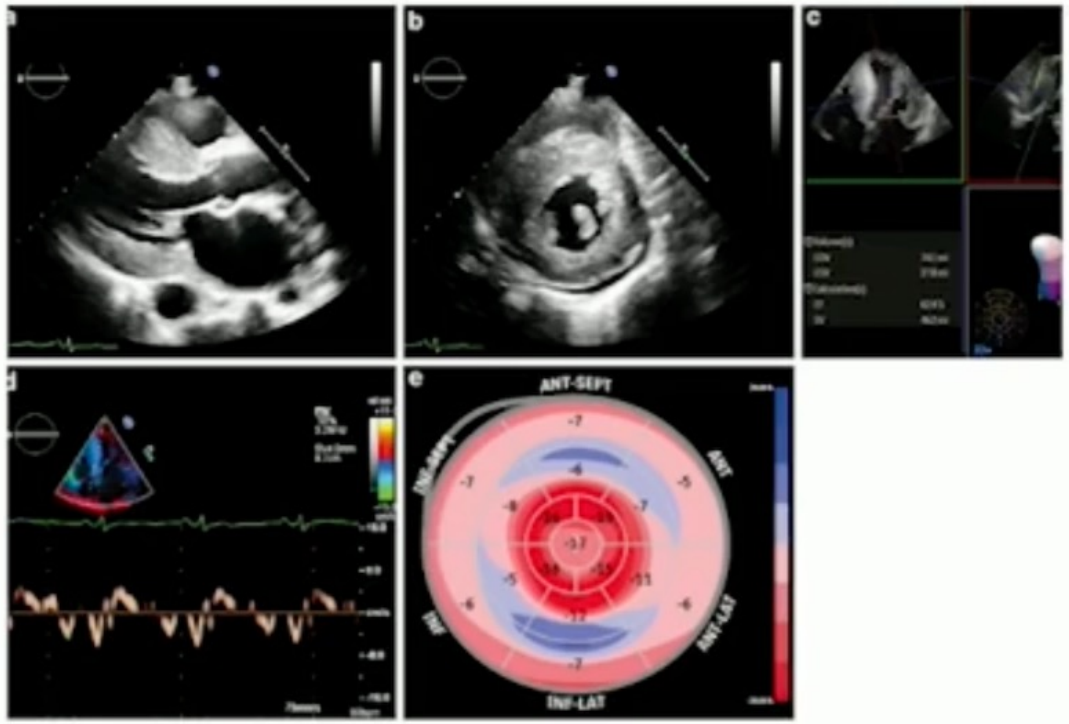




OLGU 3

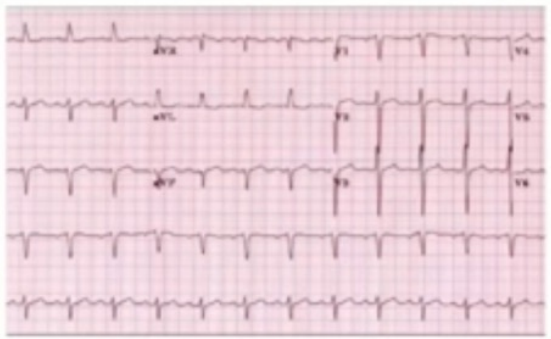
- 65 YAŞ ERKEK HASTA
- SCD SURVIVOR
- 5 YILDIR BILATERAL KARPAL TÜNEL SENDROMU TANISI MEVCUT.
- AİLEDE ANİ ÖLÜM ÖYKÜSÜ YOK

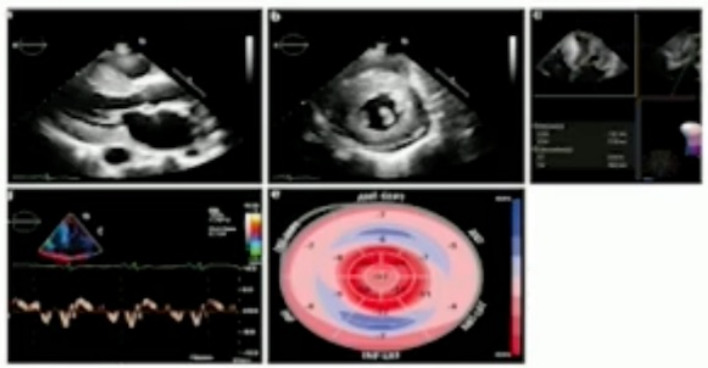




Patient case:

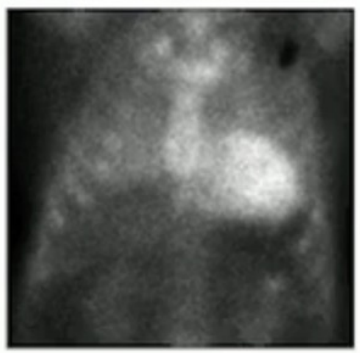
- JS
- 65 y/o AAM, presents via EMS after SCD at the supermarket
- PMH: bilateral carpel tunnel syndrome for 5 years





High suspicion for Amyloidosis:

1) SPIE, UPIE, SFLC all negative
2) PYP scan obtained:

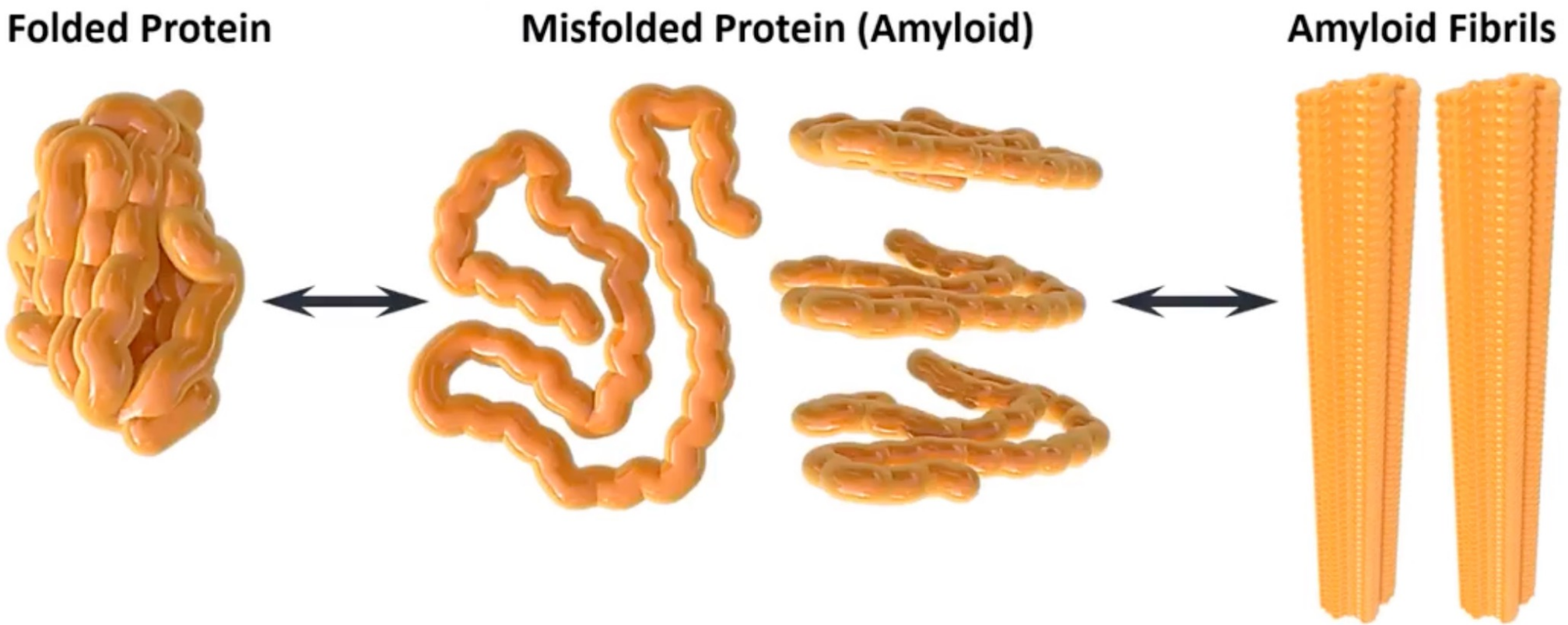


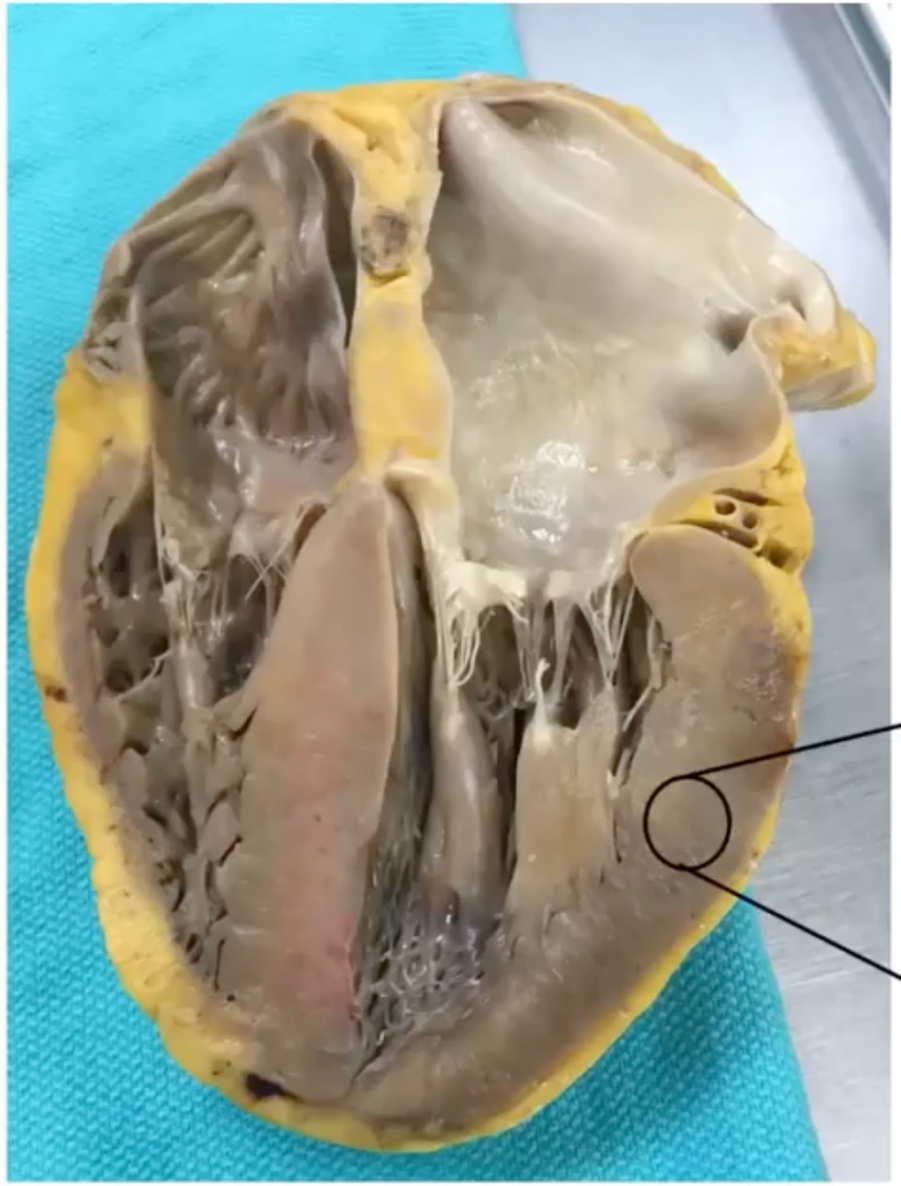
3) Genetic testing: +V122I mutation

Dx: hATTR CM and neuropathy

Rx: Tafamidis + Patisiran

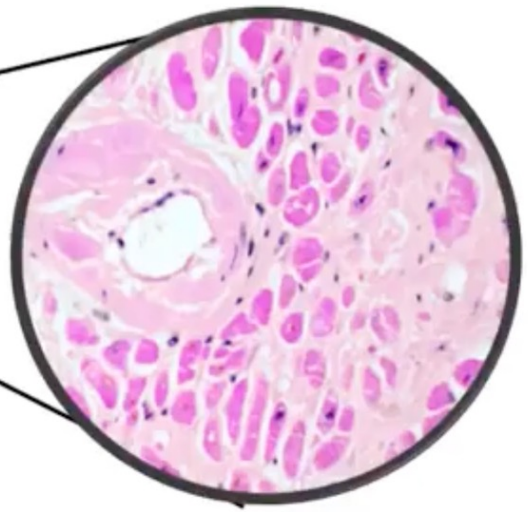
Protein Misfolding Disorder



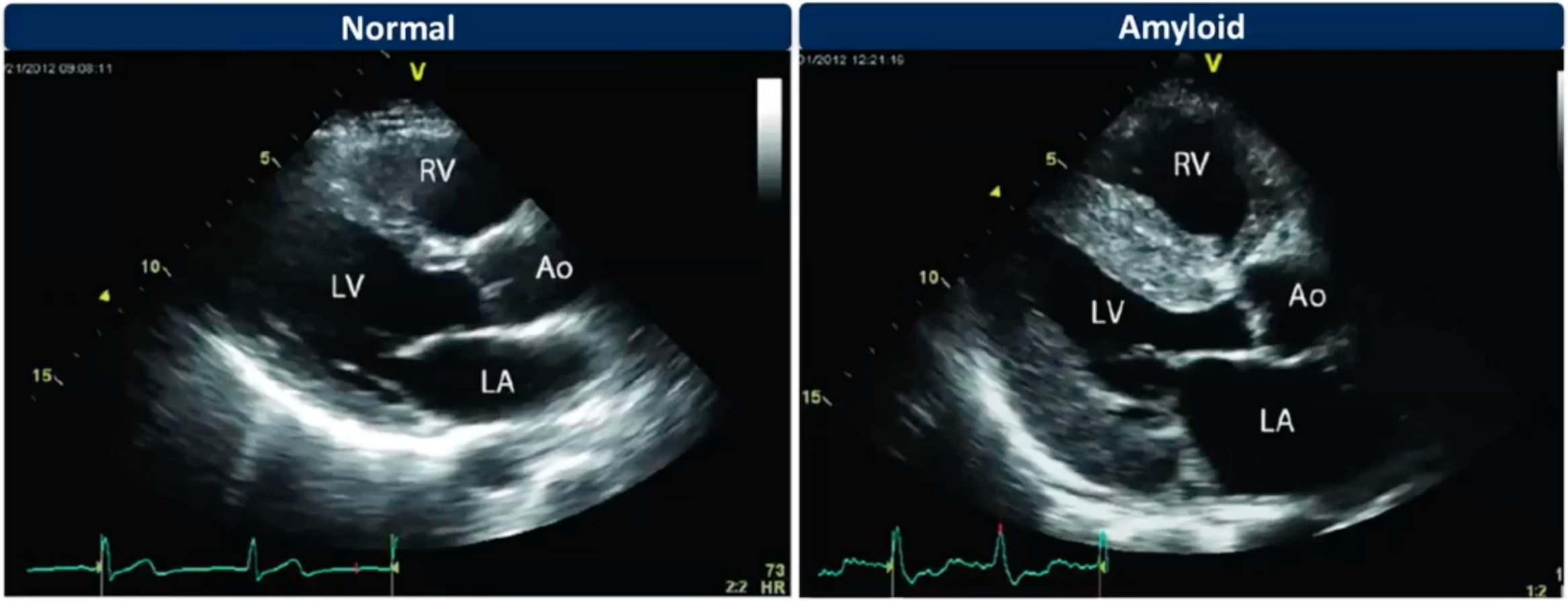


Pathology: Diffuse involvement

- Increase in LV mass w/out dilatation
- Atrial infiltration impairing atrial contraction
- Conduction system
- Mitral and Tricuspid valve thickening
- Microvascular ischemia

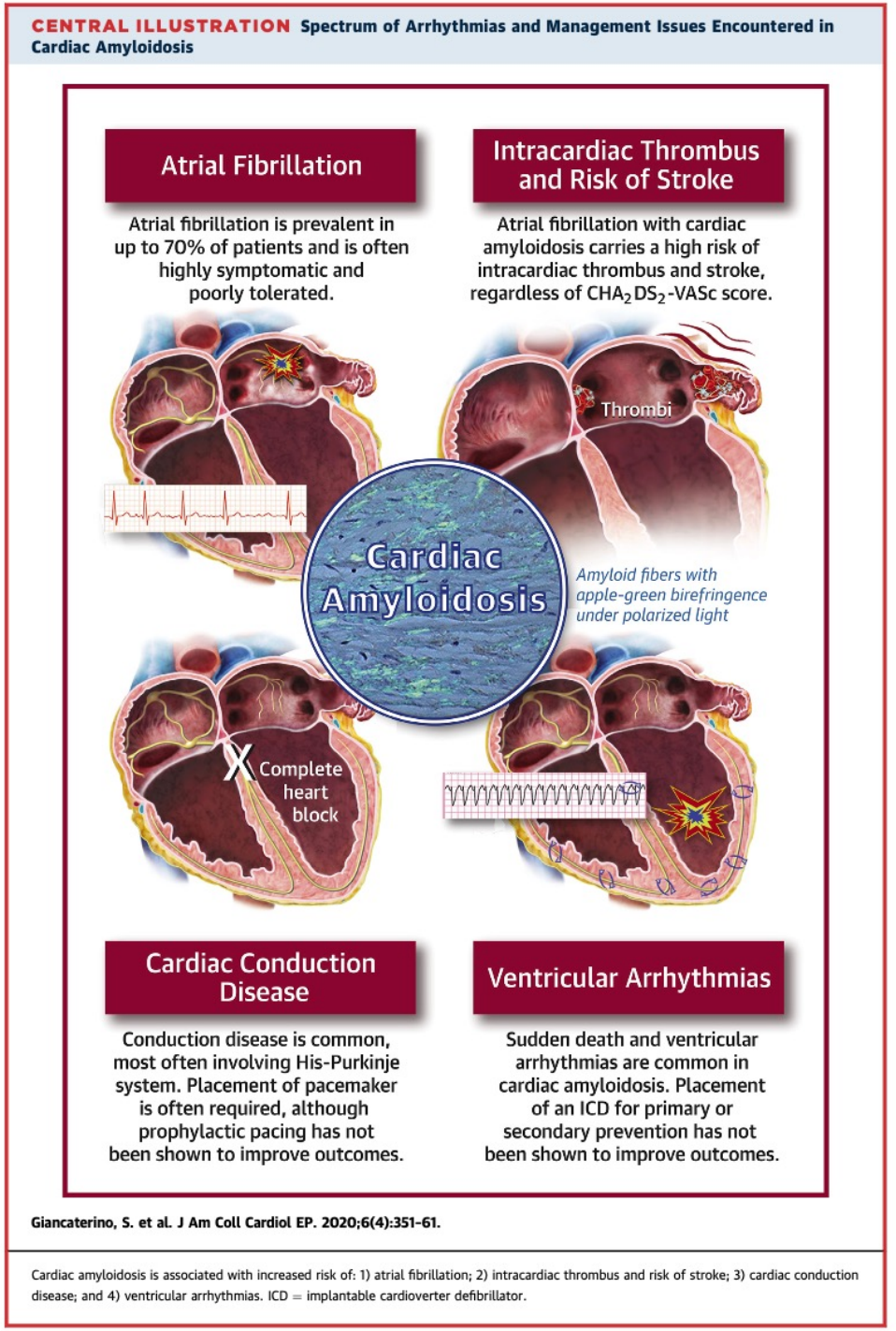


Echocardiogram: Prompts Suspicion

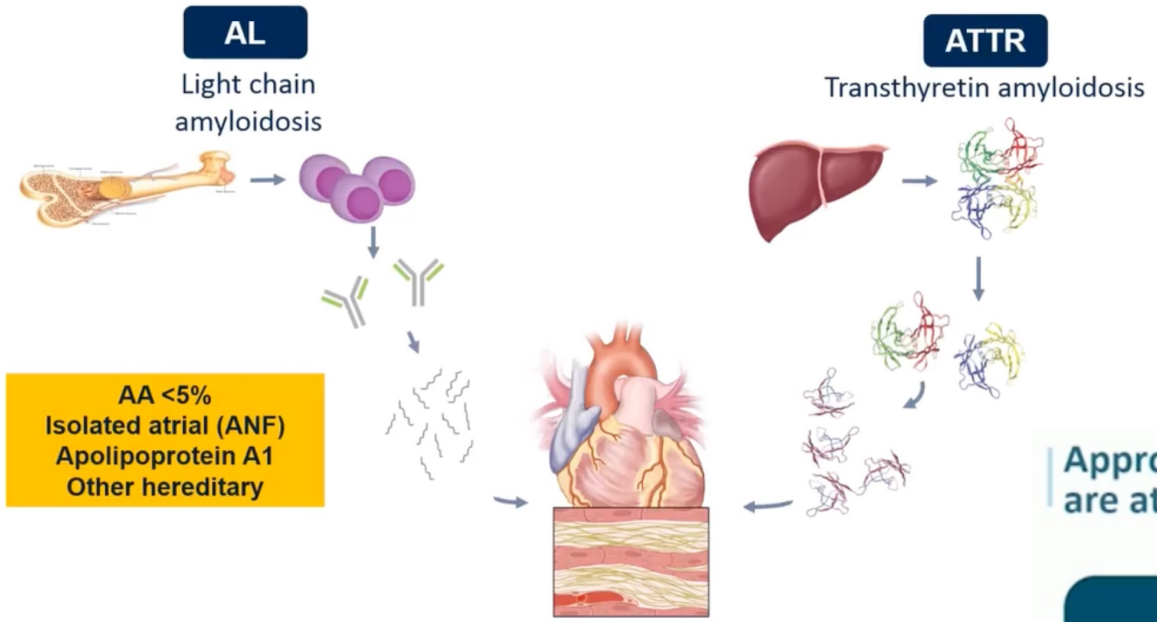


AMİLOİDOZ şüphesi yaratan durumlar

- LVH ile düşük voltaj QRS uyumsuzluğu
- Azalmış strain (Apex hariç)
- Düşük akım düşük gradient Aort Darlığı
- MRI da yaygın geç gadolinium tutulumu
- HFpEF >60 yaş
- Atriyoventriküler blok, Ventriküler taşikardi (LVH ile beraber)
- Standard kalp yeterziliği tedavilerine intolerans
- Karpal Tünel sendromu
- Otonomik sinir sistemi disfonksiyonu



Two Main Types of Amyloid That Affect the Heart



Approximately 95% of all cardiac amyloidosis diagnoses are attributed to AL or ATTR amyloidosis

CARDIAC AMYLOIDOSIS[1-4]

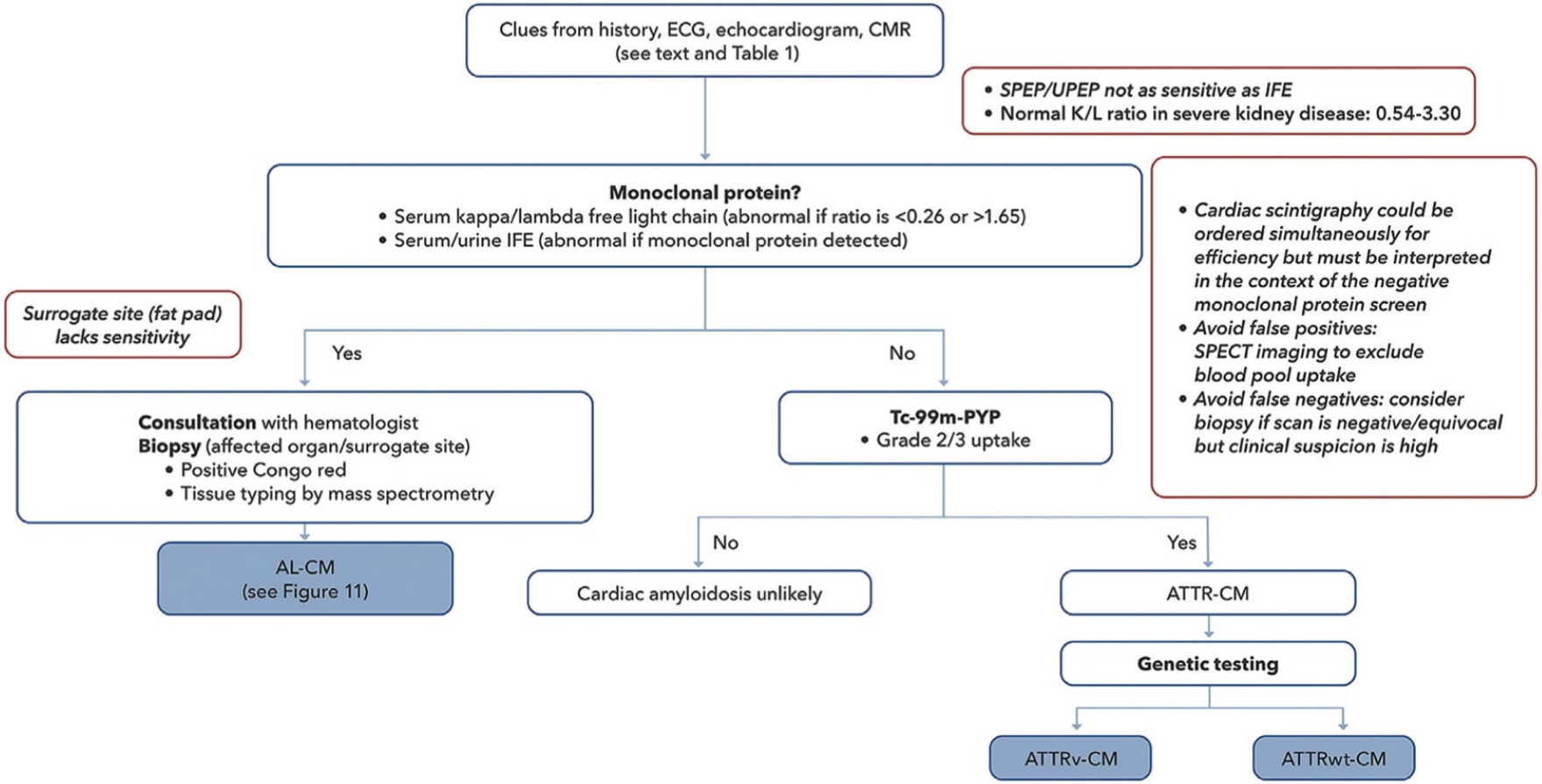
Immunoglobulin (or amyloid) light-chain (AL) amyloidosis1-4*	Transthyretin amyloid cardiomyopathy (ATTR-CM)[1-3]	**Others including[2,3]** Serum amyloid A Apolipoprotein A1 Immunoglobulin heavy chain Fibrinogen alpha chain Gelsolin

Account for more than 95% of all cardiac amyloidosis diagnoses[2]

***It is important to clinically differentiate between ATTR and AL, since they have different clinical courses. AL requires immediate treatment, as it is considered a hematologic emergency, and the treatment regimen is very different from that for ATTR.[2]**

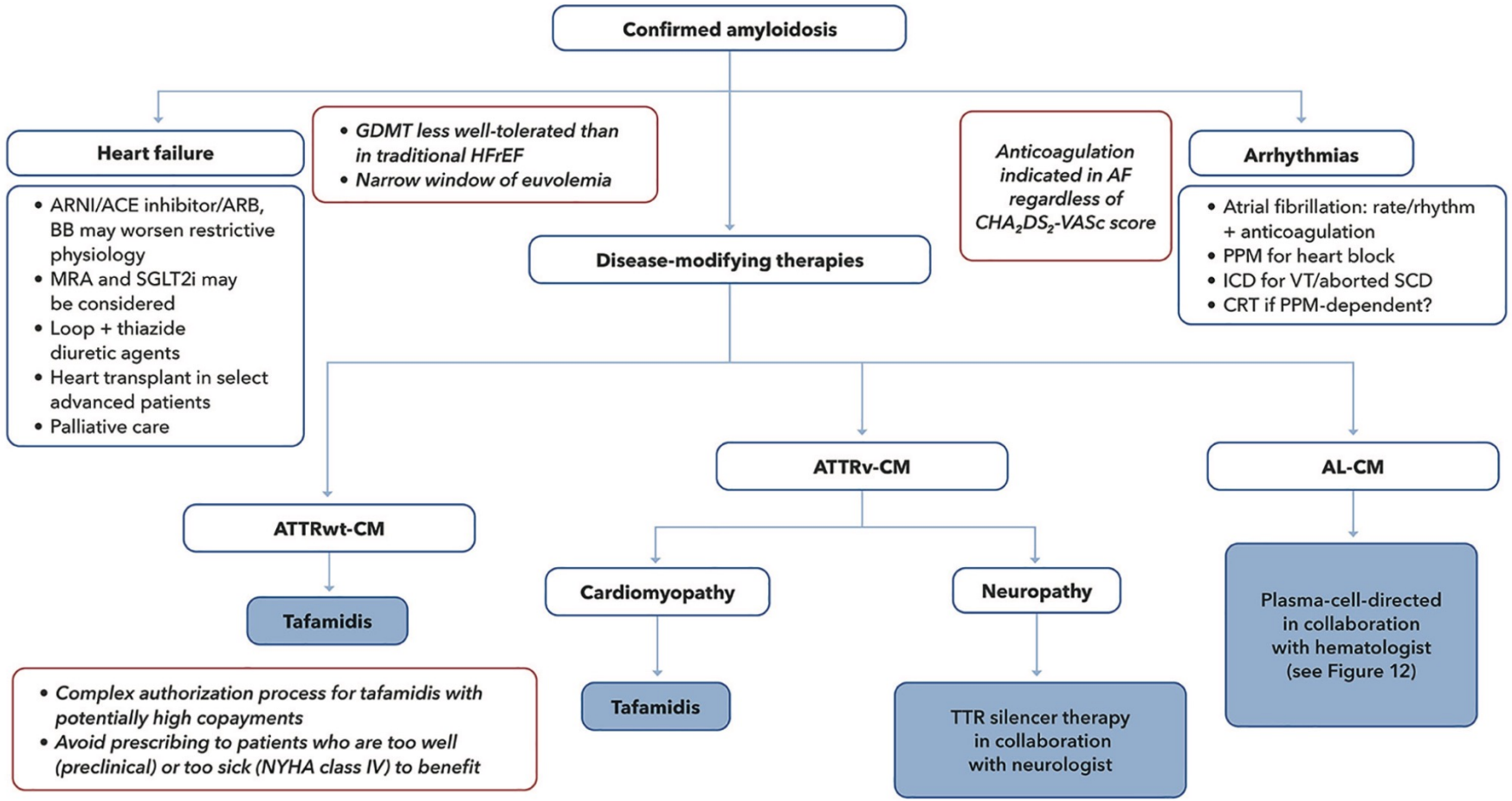
1. Siddiqi OK, et al. *Trends Cardiovasc Med.* 2018;28:10-21. 2. Donnelly J, et al. *Cleve Clin J Med.* 2017;84(12 suppl 3):12-26. 3. Kholová I, et al. *J Clin Pathol.* 2005;58:125-133. 4. Rapezzi C, et al. *Circulation.* 2009;120:1203-1212.

FIGURE 3 Diagnostic Algorithm for Cardiac Amyloidosis



AL-CM = amyloid monoclonal immunoglobulin light chain cardiomyopathy; ATTR-CM = amyloid transthyretin cardiomyopathy; ATTRv-CM = variant transthyretin amyloid cardiomyopathy; ATTRwt-CM = wild-type transthyretin amyloid cardiomyopathy; CMR = cardiac magnetic resonance; ECG = electrocardiogram; IFE = immunofixation electrophoresis; K/L = kappa/lambda; PYP = pyrophosphate; SPECT = single-photon emission computed tomography; SPEP/UPEP = serum/urine protein electrophoresis.

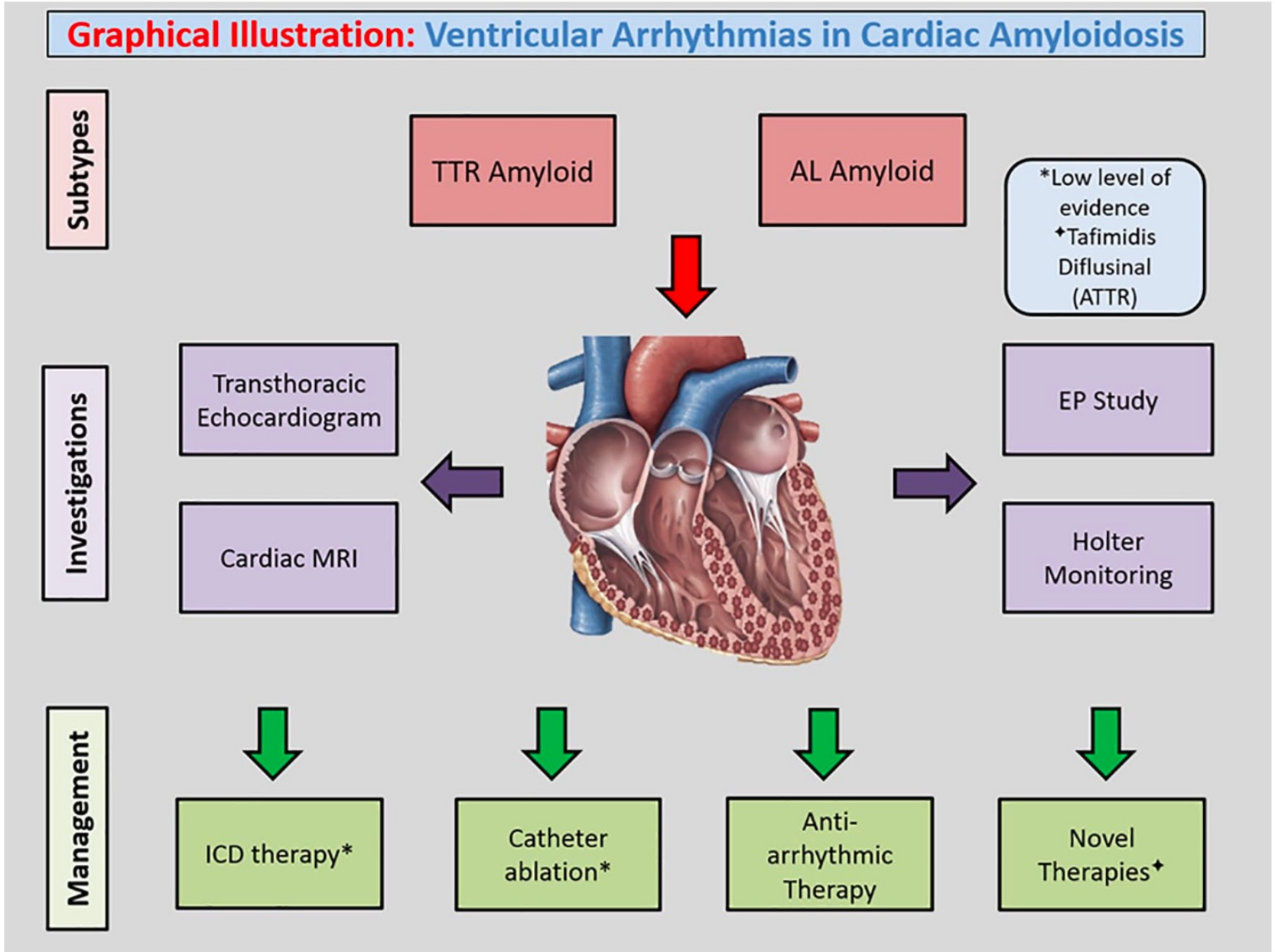
FIGURE 4 Overview of Management of Cardiac Amyloidosis



AF = atrial fibrillation; ARNI/ACE inhibitor/ARB = renin-angiotensin system inhibitors; AL-CM = amyloid monoclonal immunoglobulin light chain; ATTR = amyloid transthyretin; ATTRv-CM = variant transthyretin amyloid cardiomyopathy; ATTRwt-CM = wild-type transthyretin amyloid cardiomyopathy; BB = beta-blocker; CRT = cardiac resynchronization therapy; HFrEF = heart failure with reduced ejection fraction; GDMT = guideline-directed medical therapy; ICD = implantable cardioverter-defibrillator; MRA = mineralocorticoid receptor antagonists; NYHA = New York Heart Association; PPM = permanent pacemaker; SCD = sudden cardiac death; SGLT2i = sodium glucose cotransporter 2 inhibitor; TTR = transthyretin; VT = ventricular tachycardia.

Table 1. Summary of studies investigating the prevalence of ventricular tachy-arrhythmias in cardiac amyloidosis.

STUDY SUMMARY	NUMBER OF PATIENTS	TYPE OF CARDIAC AMYLOID	METHOD OF MONITORING	NON-SUSTAINED VT IN % OF PATIENTS	OTHER RELATED FINDINGS
Palladini et al[7]	51	AL	24-hour Holter monitoring	Non-sustained VT in 18% of patients.	Ventricular tachycardia was a significant prognostic determinant for survival ($P=0.04$).
Sayed et al[8]	20	AL with symptoms of pre-syncope or syncope	Implantable loop recorder	Non-sustained VT in 5% of patients	Terminal syncopal event was marked by bradycardia, not tachycardia, in every available recording.
Murtagh et al[9]	127	AL	Electrocardiogram	Non-sustained VT in 1% of patients	Premature ventricular contractions were noted in 13% of patients.
Goldsmith et al[10]	24	AL monitored peri autologous stem cell transplantation	Telemetry, average of 24 days	Non-sustained VT in 100% of patients	In the deceased patients (n=3), VT/VF events were the highest of all 24 patients. There was a correlation between VT and serum BNP levels before SCT (r=0.47, $P=0.019$) and during admission for SCT (r=0.62, $P=0.0012$), serum creatinine before SCT (r=0.62, $P=0.001$), and inverse relationship with cardiac output (r=−0.72, $P<0.001$)
Dubrey et al[12]	232	AL	24-hour Holter monitoring	Non-sustained VT in 26.7% of patients	Ventricular tachycardias were not associated with increased risk of sudden cardiac death.
Hörnsten et al[11]	30	ATTR (ATTR Val30Met trait), before liver transplant	24-hour Holter monitoring	Non-sustained VT in 16.7% of patients	–
Varr et al[45]	31	AL 77%, ATTR 23% (V122I mutation 10%, wild type 13%)	ICD, permanent pacemaker, telemetry	VT in 74% of patients	ICD therapy was successful in most patients, with therapy in 4 of 5 (80%) patients resulting in the termination of the arrhythmia.
Kristen et al[13]	19	AL with ICD insitu	ICD	VT/VF in 11% of patients	Ventricular extra beats (grade IVa or higher) were present more often in non-survivors than in survivors ($P<0.05$).
Hamon et al[49]	45	Familial ATTR 60%, AL 27%, senile ATTR 13%. All with ICD in situ	ICD	VT/VF in 27% of patients	Inappropriate shocks was uncommon and occurred in 2 patient (4.4%).



Graphical Illustration: Ventricular Arrhythmias in Cardiac Amyloidosis.

ÖZET

- VT tedavisinde steroid ve antiaritmikler tek başına yeterli olmayabilir.
- VT fırtınasında ablasyon düşünülebilir onun haricinde öncelikle medikal takip etmek gerekiyor.
- Biyolojik DMARD lar tedavide etkin bir yer alabilirler . Hem steroid dozunu azaltmak hem de steroide yanıt vermeyenlerde ikincil tedavi olarak.
- Amiloidozda prognoz genellikle kötü olduğu için ön planda antiaritmik tedaviler ile ventriküler taşikardileri kontrol etmek önemli. Yine sarkoidozda olduğu gibi fırtına esnasında ablasyon düşünülebilir.

TEŞEKKÜRLER.....

TIP FAKÜLTESİ
HASTANESİ