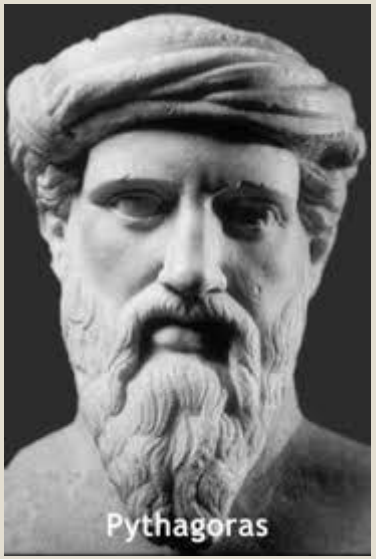
ΠΡΟΛΗΨΗ ΑΙΦΝΙΔΙΟΥ ΚΑΡΔΙΑΚΟΥ ΘΑΝΑΤΟΥ

ΑΝΝΑ Π. ΑΝΤΩΝΙΟΥ
ΔΙΕΥΘΥΝΤΡΙΑ ΚΑΡΔΙΟΛΟΓΟΣ
Γ.Ν.Α. «ΑΛΕΞΑΝΔΡΑ»

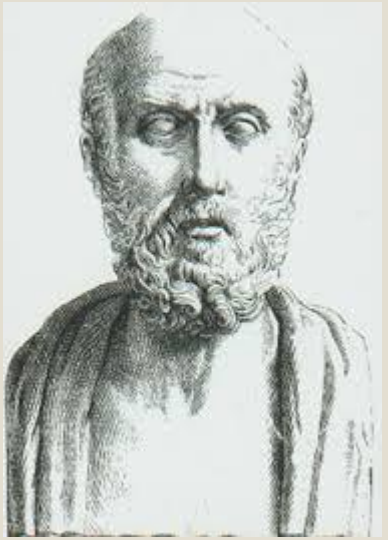
"Καρδίην μή εσθίειν..."
Μην «τρως» την καρδιά σου

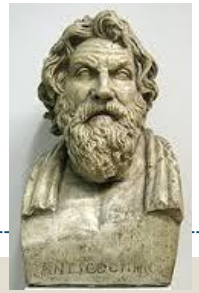
Πυθαγόρας



«Κάλλιον το προλαμβάνειν ή το θεραπεύειν»

Ιπποκράτης





«Αρχή παιδεύσεως η των ονομάτων επίσκεψις»
Αντισθένης, 445-366 μ.Χ.

- **Αιφνίδιος καρδιακός θάνατος**= η ξαφνική και μη αναστρέψιμη παύση όλων των βιολογικών λειτουργιών του ανθρώπινου οργανισμού που οφείλεται σε καρδιακά αίτια και επέρχεται εντός της πρώτης ώρας από την εκδήλωση των οξέων συμπτωμάτων.

- **Καρδιακή ανακοπή** = η αιφνίδια και απρόβλεπτη διακοπή της μηχανικής δραστηριότητας της καρδιάς, η οποία χαρακτηρίζεται από την απουσία σφυγμικού κύματος και αναπνευστικής λειτουργίας, με αποτέλεσμα την ανεπαρκή παροχή οξυγονωμένου αίματος στα ζωτικά όργανα.

Causes of SCD

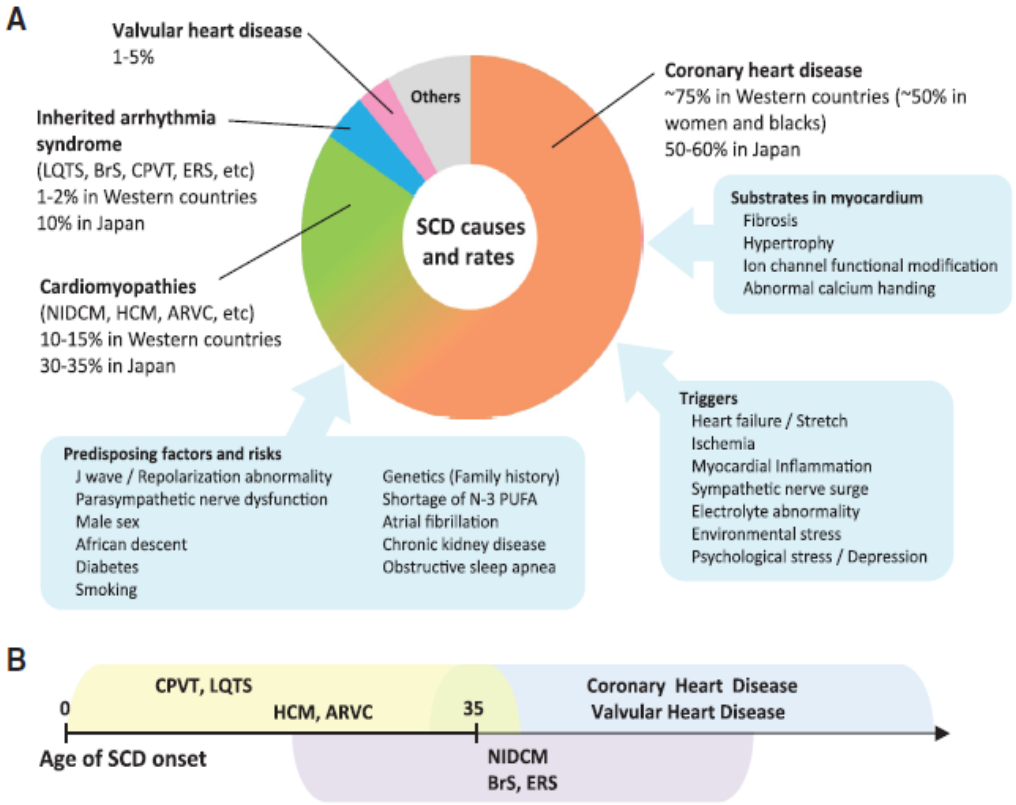


Figure 2. Causes of sudden cardiac death (SCD) and rates (A) and age of SCD onset in each disease (B). A, Coronary heart disease is the leading cause of SCD, but the rates of baseline heart disease differ between Western countries and Japan. **B**, SCDs occur in elderly populations in coronary heart disease and valvular heart disease, whereas most SCDs in catecholaminergic polymorphic ventricular tachycardia (CPVT) and long-QT syndrome (LQTS) develop at age <35 years. ARVC indicates arrhythmogenic right ventricular cardiomyopathy; BrS, Brugada syndrome; ERS, early repolarization syndrome; HCM, hypertrophic cardiomyopathy; NIDCM, non–ischemic dilated cardiomyopathy; and PUFA, polyunsaturated fatty acids.

Circ Res 2015;116:1887-1906

Causes of SCD: age-related variations

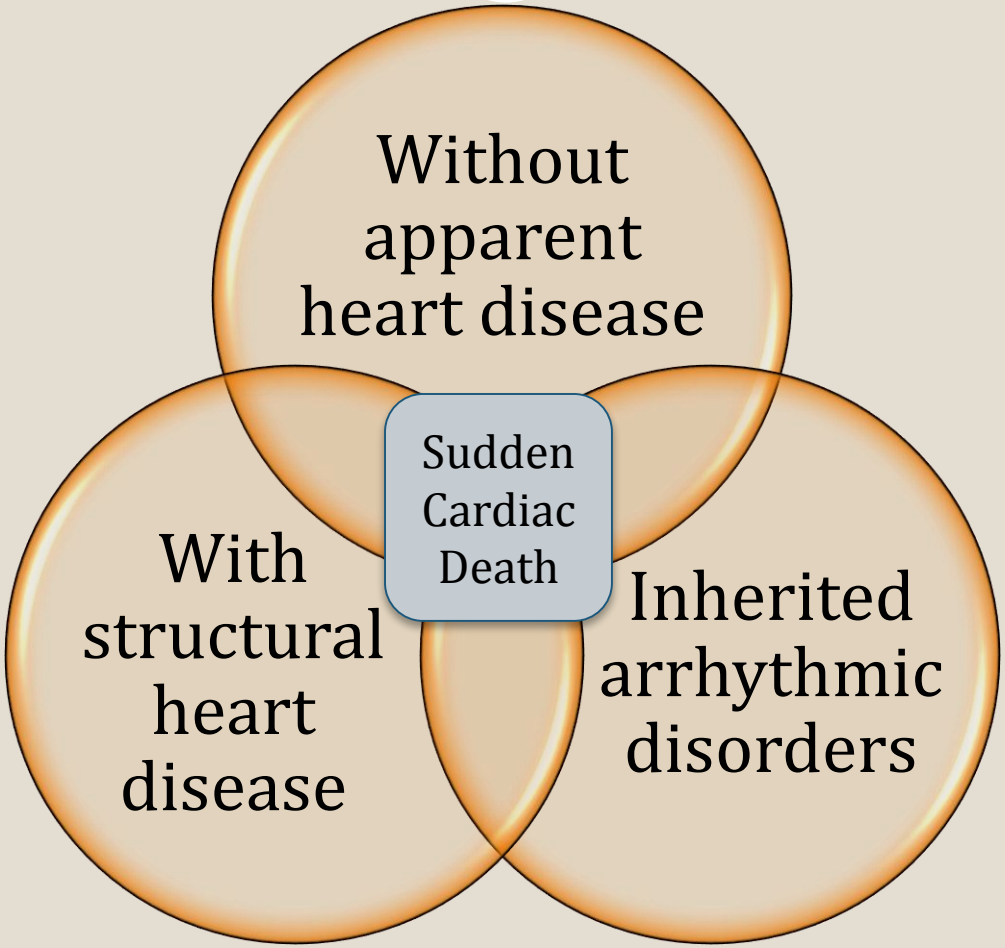
- In **adults aged >35 years**, particularly among white men, coronary heart disease is responsible for ≈70%–75% of SCDs.

Circulation. 2012;125:1043–1052

- In **young adults and children aged <35 years**: hypertrophic cardiomyopathy (HCM), coronary artery anomalies, myocarditis, arrhythmogenic right ventricular cardiomyopathy (ARVC), and primary ion channelopathies.

Circulation. 2011;123:1911–1918

SCD prevention



ΠΡΟΛΗΨΗ ΑΙΦΝΙΔΙΟΥ ΚΑΡΔΙΑΚΟΥ ΘΑΝΑΤΟΥ

ΣΕ ΑΤΟΜΑ ΧΩΡΙΣ ΓΝΩΣΤΗ ΔΟΜΙΚΗ Ή ΗΛΕΚΤΡΙΚΗ ΚΑΡΔΙΑΚΗ ΝΟΣΟ

Individuals without apparent heart disease (1)

- Risk factors for CHD are associated with SCD risk in the population

  (hypertension, diabetes mellitus, hypercholesterolemia, obesity, and smoking)
- ***Hypertension*** and resultant left ventricular hypertrophy seem to be particularly important markers of SCD risk in blacks.
- ***Diabetes mellitus*** is a particularly strong risk factor for SCD, even in higher risk populations.
- ***Smoking*** confers marked elevations in SCD risk, especially among women.
- ***Serum cholesterol*** seems to be more strongly related to SCD at younger ages.

Individuals without apparent heart disease (2)

Family History of SCD

- Several studies have demonstrated a familial predisposition to SCD and VF.
- A parental history of fatal MI had no effect on SCD risk.

SCD and Atrial Fibrillation

- In patients with established AF treated with anticoagulation, SCD accounts for >20% of all deaths.
- Patients with AF have on average a 2.5-fold increased risk of SCD100 or VF as compared with those without AF.
- ***Why***? coexisting HF, antiarrhythmic medications

Recommendations for cardiovascular risk assessment

Recommendations	Class[a]	Level[b]
Systematic CV risk assessment is recommended in individuals at increased CV risk, i.e. with family history of premature CVD, familial hyperlipidaemia, major CV risk factors (such as smoking, high BP, DM or raised lipid levels) or comorbidities increasing CV risk.	I	C
It is recommended to repeat CV risk assessment every 5 years, and more often for individuals with risks close to thresholds mandating treatment.	I	C
Systematic CV risk assessment may be considered in men >40 years of age and in women >50 years of age or post-menopausal with no known CV risk factors.	IIb	C
Systematic CV risk assessment in men <40 of age and women <50 years of age with no known CV risk factors is not recommended.	III	C

ESC Guidelines for Cardiovascular Disease Prevention, 2016

ΠΡΟΛΗΨΗ ΑΙΦΝΙΔΙΟΥ ΚΑΡΔΙΑΚΟΥ ΘΑΝΑΤΟΥ

ΣΕ ΑΤΟΜΑ ΜΕ ΓΝΩΣΤΗ ΔΟΜΙΚΗ Ή ΗΛΕΚΤΡΙΚΗ ΚΑΡΔΙΑΚΗ ΝΟΣΟ

SCD in the Patient Populations With Structural Heart Disease

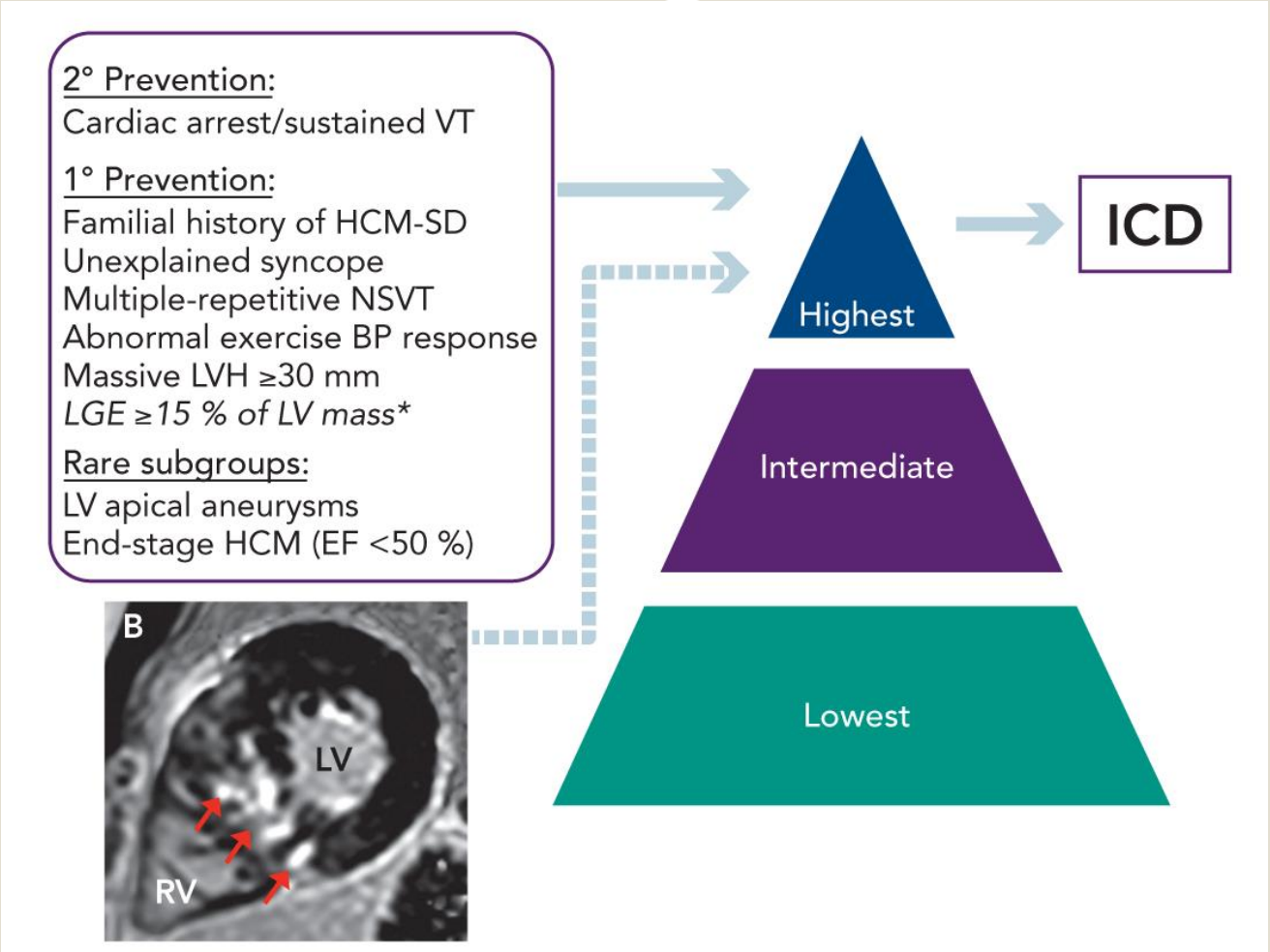
- During or after acute MI
- Provoked by coronary ischemia without MI
- In the presence of myocardial structural alterations (fibrosis, scar, left ventricular dilatation) secondary to prior MI or chronic ischemia.

Inherited Arrhythmia Syndromes

- **Structural diseases with risk of arrhythmias**
  - Hypertrophic (obstructive) cardiomyopathy (HOCM, HCM)
  - Familial Dilated Cardiomyopathy (DCM)
  - Arrhythmogenic right-ventricular cardiomyopathy / dysplasia (ARVC / D)

- **Primary arrhythmia syndromes (channelopathies)**
  - Long-QT syndrome (LQTS)
  - Short-QT syndrome
  - Brugada syndrome
  - Catecholaminergic polymorphus ventricular tachycardia (CPVT)
  - Early Repolarization syndrome (ERS)
  - Idiopathic VF

Risk Stratification of HCM for Sudden Death Prevention



Rowin EJ and Maron MS. Arrhythmia & Electrophysiology Review 2016;5(3):197–202

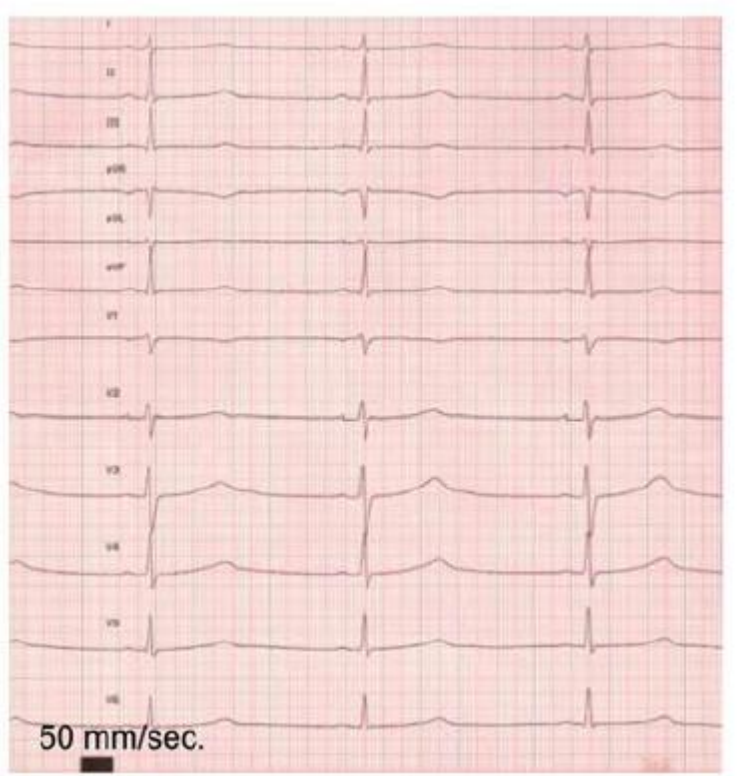
ARVC

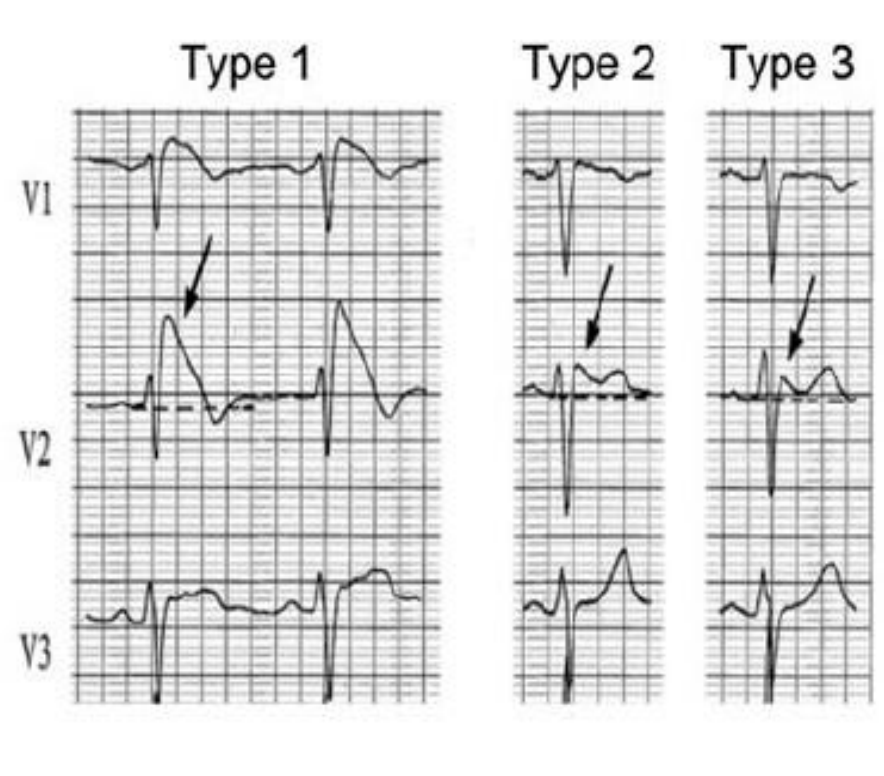
- SCD is a common cause of death in patients with ARVC especially in those in the fourth decade of life or younger, and it may be the first arrhythmic event in up to 50% of cases.

- Predictors of appropriate ICD therapy include:
  - history of a cardiac arrest or VT with hemodynamic compromise
  - younger age
  - LV involvement
  - unexplained syncope
  - presence of non–sustained VT
  - inducibility during electrophysiology study

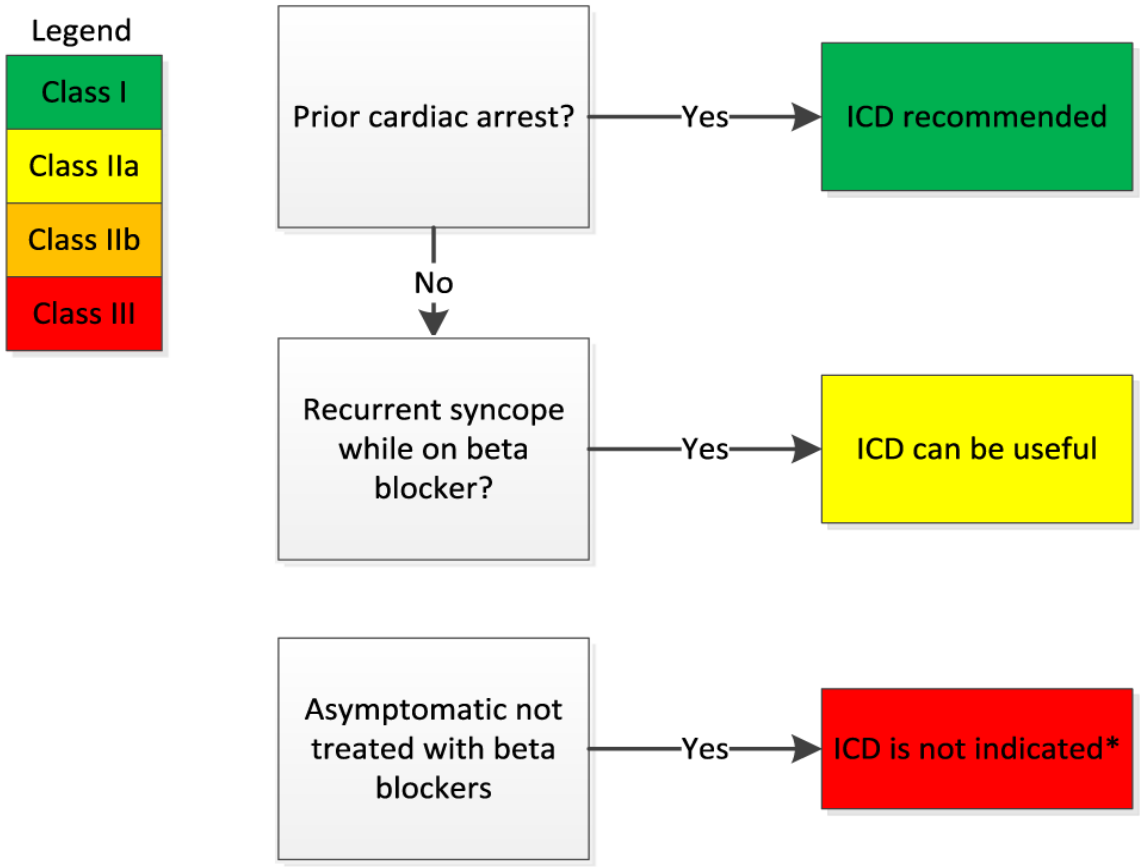
- ACC/AHA/HRS guidelines: prophylactic use of an ICD in those who have ≥1 risk factors for SCD (class IIa).

Long QT – Brugada syndrome





ICD in long QT syndrome



Priori SG et al. Heart Rhythm, 2013.

Brugada Syndrome

- Guidelines recommend an ICD in:
  1. Patients who have suffered a SCA (class I)
  2. Patients with syncope and a spontaneous type 1 ECG pattern (Class IIa)
  3. Patients with inducible arrhythmias (class IIb)

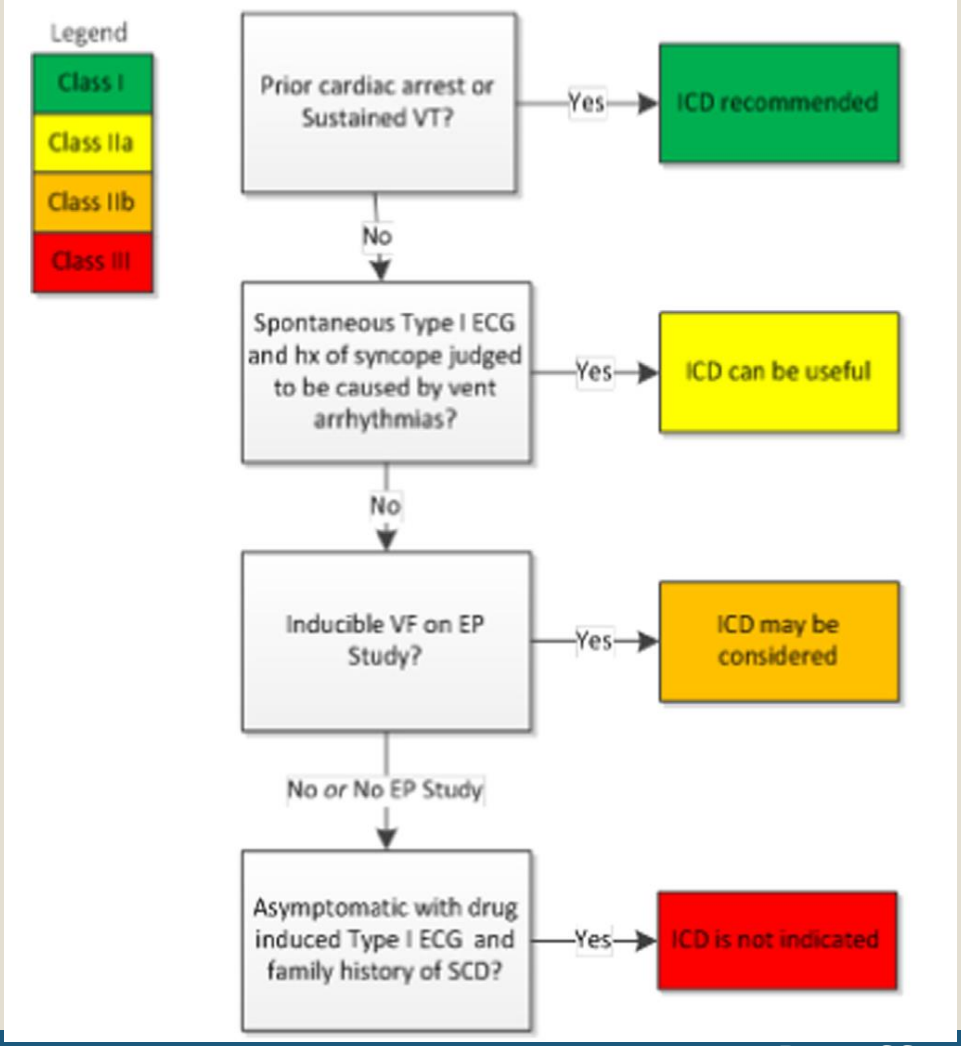
- Asymptomatic Brugada Syndrome

  Spontaneous type 1 ECG pattern and :

  Presence of sinus node disease or

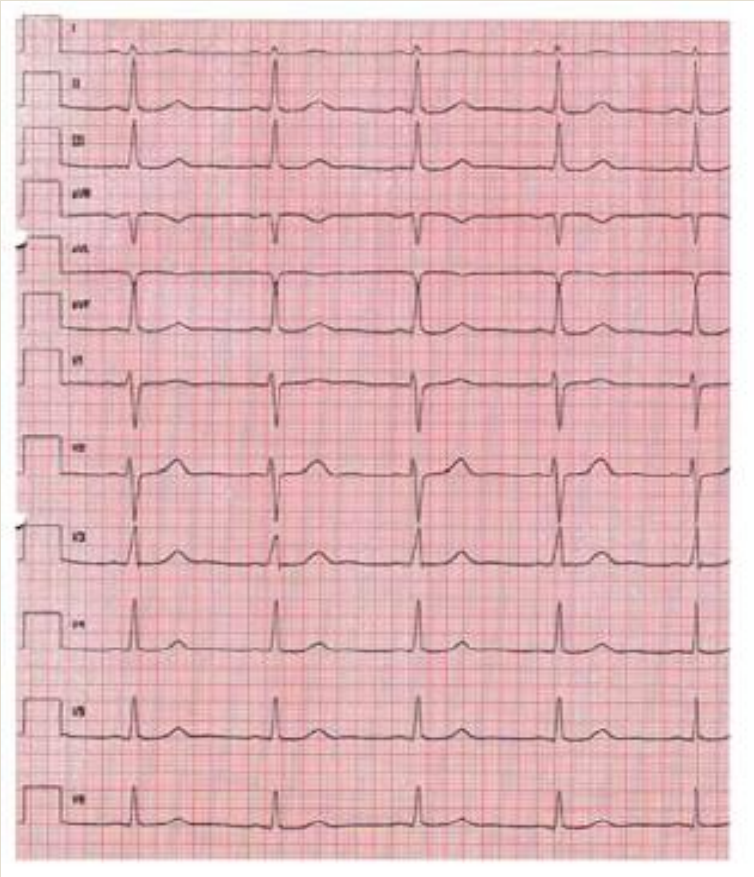
  Inducible VAs during programmed electrical stimulation

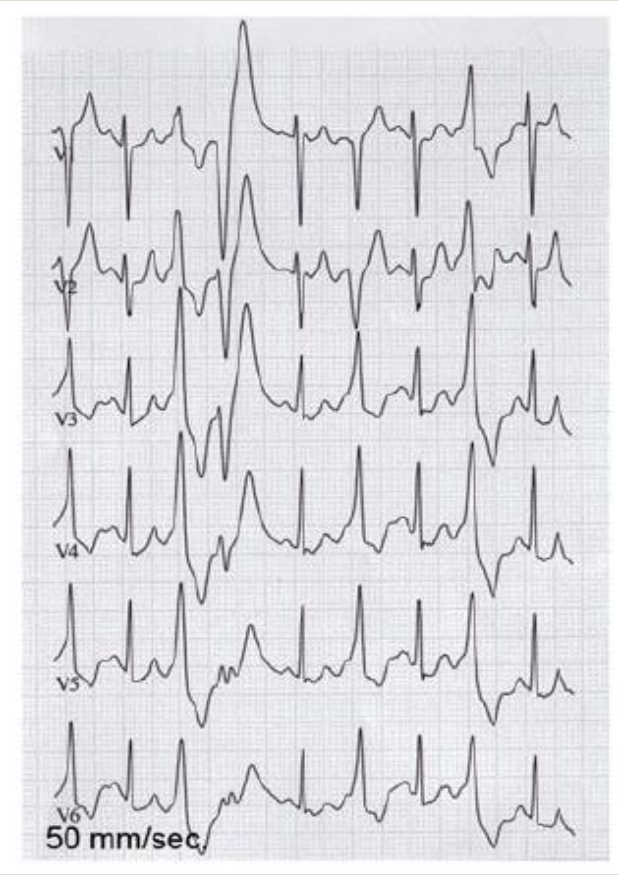
ICD in Brugada syndrome



Priori SG et al. Heart Rhythm, 2013.

Catecholaminergic Polymorphous Ventricular Tachycardia (CPVT)





Beckmann BM et al. Deutsches Ärzteblatt International | Dtsch Arztebl Int 2011; 108(37): 623–34

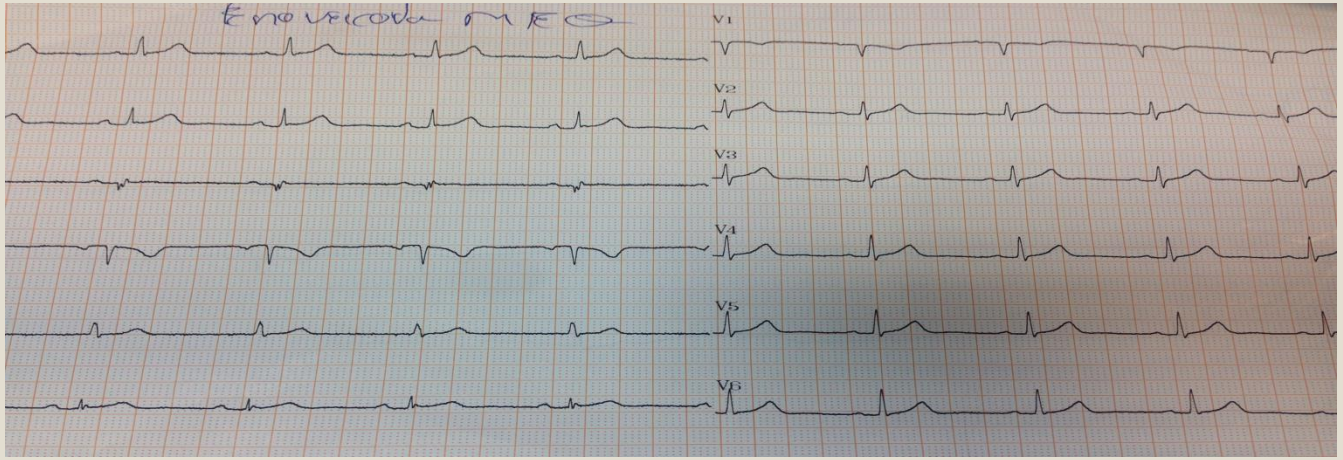
CPVT

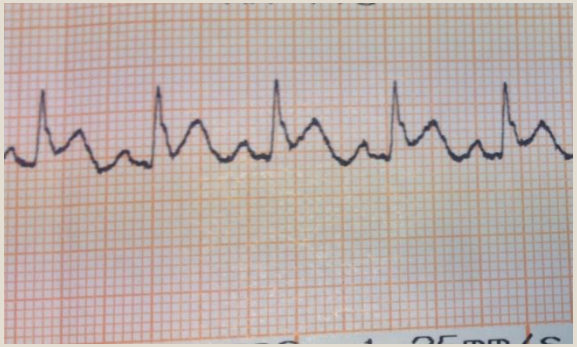
- The affected patients usually develop arrhythmic events (syncope, aborted cardiac arrest, or SCD) during adrenergic activity in the first or second decade of life.
- No detectable cardiac morphological abnormalities, and the ECG is normal except for a lower heart rate at rest.
- The clinical course is considered to be highly malignant. Without proper treatment such as **β-blockers**, **flecainide**, and **ICDs**, mortality reaches >30% by the age of 30 years
- The estimated 8-year fatal or aborted SCA event rate after the diagnosis is 13%.

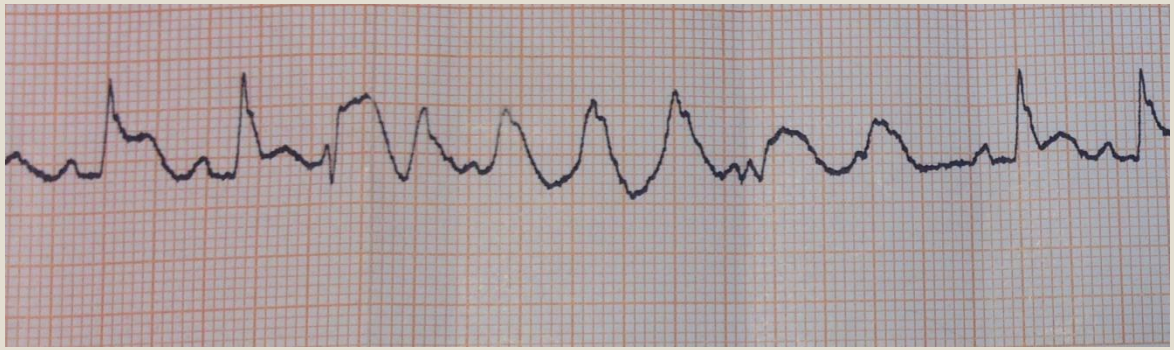
Early Repolarization (ERP) Syndrome

- ERP in the inferior and lateral leads is more commonly found in patients with idiopathic VF as compared with controls.
- **ERP** =the presence of J point elevation ≥0.1 mV in ≥2 contiguous inferior and lateral leads,
- **ERP syndrome** =the presence of ERP in a patient resuscitated from otherwise unexplained VF/polymorphic VT or autopsy negative SCD victim with a previous ECG demonstrating ERP.

Early Repolarization (ERP) Syndrome







Prevention of SCD
Primary Arrhythmia Syndromes

Congenital long-QT syndrome
Brugada syndrome
CPVT
ERS (early repolarization syndrome)

ICD is recommended as secondary prevention

Brugada syndrome
Type 1 ECG manifestation
syncope or suspected VT

ICD is recommended as primary prevention

ΠΡΟΛΗΨΗ ΑΙΦΝΙΔΙΟΥ ΚΑΡΔΙΑΚΟΥ ΘΑΝΑΤΟΥ

ΤΙ ΣΥΣΤΗΝΟΥΝ ΟΙ ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ ΣΧΕΤΙΚΑ ΜΕ ΤΗΝ ΤΟΠΟΘΕΤΗΣΗ ΣΥΣΚΕΥΩΝ

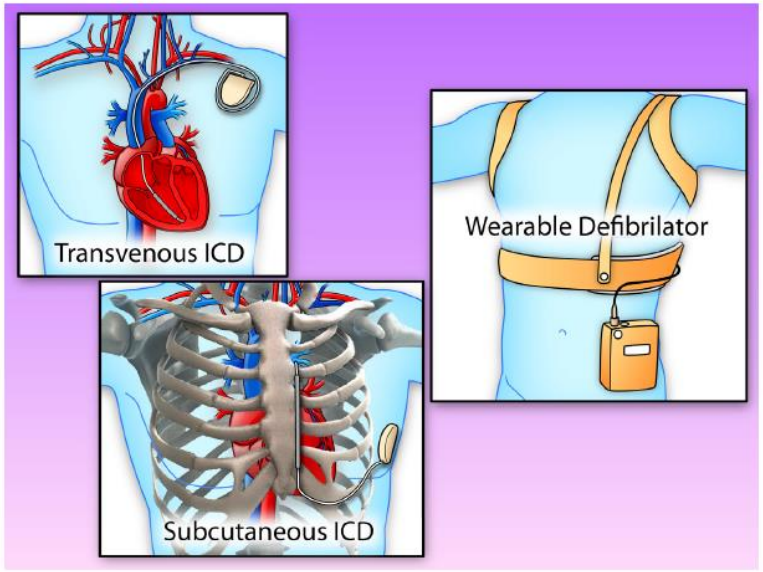


Figure. Types of implantable and wearable defibrillators. ICD indicates implantable cardioverter-defibrillator (Illustration credit: Ben Smith).

Αιφνίδιος καρδιακός θάνατος

- Η **πρωτογενής πρόληψη** στοχεύει σε ασθενείς που ανήκουν σε ομάδα υψηλού κινδύνου για αιφνίδιο καρδιακό θάνατο, οι οποίοι δεν έχουν ακόμα εμφανίσει κακοήθης κοιλιακές αρρυθμίες.

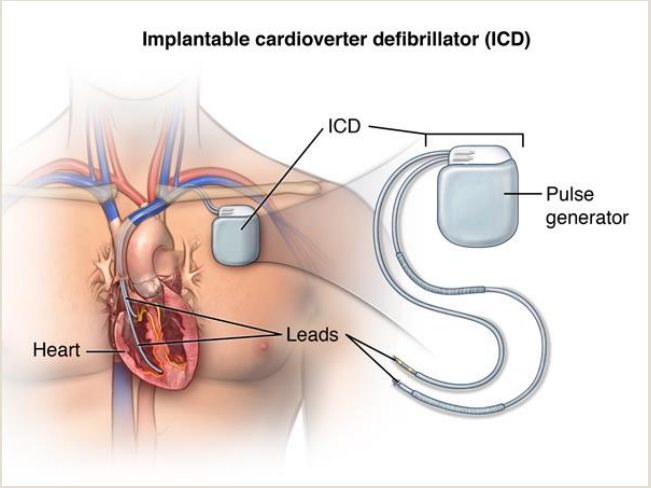
- Η **δευτερογενής πρόληψη** αφορά σε ασθενείς οι οποίοι επιβιώσαν καρδιακής ανακοπής / κακοήθων κοιλιακών ταχυαρρυθμιών, καθώς και σε ασθενείς υψηλού κινδύνου με ιστορικό ανεξήγητων συγκοπτικών επεισοδίων.

Ischemic Heart Disease
Secondary Prevention ICD

Clinical Trials of Secondary Prevention ICD

Trials	Follow-Up Analysis (Mean)	Inclusion Criteria	No. of Patients	LVEF	All-Cause Mortality		Relative Risk Reduction	NNT
					Control	ICD		
Secondary prevention								
AVID (1997)	18 mo	VF or VT with Syncope VT with LVEF </= 40%	1016	32%	24%	16%	–27% (*P*<0.02)	12
CIDS (2000)	36 mo	VF, resuscitated out of hospital cardiac arrest secondary to VF or VT, symptomatic VT with LVEF≤35% Unwitnessed syncope with subsequent or inducible VT	659	34%	10%/y	8%/y	–20% (*P*=0.142)	…
CASH (2000)	57 mo	VF and VT	288	46%	44%	36%	–23% (*P*=0.081)	…
Connolly et al,[46] Meta-Analysis (2000)	…	Eligible patients from AVID, CIDS, CASH database	1866	34%	12%/y	9%/y	–28% (*P*=0.0006)	29

ICD for Secondary Prevention



ICD for the secondary prevention of sudden cardiac death and ventricular tachycardia

Recommendations	Class[a]	Level[b]	Ref.[c]
ICD implantation is recommended in patients with documented VF or haemodynamically not tolerated VT in the absence of reversible causes or within 48 h after myocardial infarction who are receiving chronic optimal medical therapy and have a reasonable expectation of survival with a good functional status >1 year.	I	A	151–154
ICD implantation should be considered in patients with recurrent sustained VT (not within 48 h after myocardial infarction) who are receiving chronic optimal medical therapy, have a normal LVEF and have a reasonable expectation of survival with good functional status for >1 year.	IIa	C	This panel of experts
In patients with VF/VT and an indication for ICD, amiodarone may be considered when an ICD is not available, contraindicated for concurrent medical reasons or refused by the patient.	IIb	C	155, 156

ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Ischemic Heart Disease
Primary Prevention ICD

Clinical Trials of Primary Prevention ICD

Trials	Follow-Up Analysis (Mean)	Inclusion Criteria	No. of Patients	LVEF	All-Cause Mortality		Relative Risk Reduction	NNT
					Control	ICD		
Primary prevention; ischemic cardiomyopathy								
MADIT (1996)	27 mo	Previous MI w/LVEF≤35%; NYHA classes I, II, III	196	26%	39%	16%	–54% (*P*=0.009)	4
CABG-Patch (1997)	32 mo	LVEF≤35% with abnormal SAECG undergoing CABG	900	27%	21%	23%	+7% (*P*=0.64)	…
MUSTT (1999)	39 mo	LVEF≤40%; CAD; NSVT; inducible VT	704	30%	55%	24%	–58% (*P*<0.001)	3
MADIT-II (2002)	20 mo	LVEF≤30%, previous MI >1 mo	1232	23%	20%	14%	–31% (*P*=0.016)	18
DINAMIT (2004)	30 mo	LVEF<35%, MI in the past 6–40 days	674	28%	17%	19%	+8% (*P*=0.66)	…
Primary prevention; nonischemic cardiomyopathy								
DEFINITE (2004)	29 mo	NICM w/LVEF ≤36%, NYHA classes I–III, NSVT or PVC	458	21%	18%	12%	–35% (*P*=0.08)	…
Primary prevention; ischemic and nonischemic cardiomyopathy								
SCD-HeFT (2005)	46 mo	LVEF<35% with NYHA class II or III	2521	25%	29%	22%	–23% (*P*=0.0007)	14

Timing of implantable cardioverter defibrillator placement after myocardial infarction. Assessment of left ventricular ejection fraction

Recommendations	Class[a]	Level[b]	Ref.[c]
Early (before discharge) assessment of LVEF is recommended in all patients with acute myocardial infarction.	I	C	286–288
Re-evaluation of LVEF 6–12 weeks after myocardial infarction is recommended to assess the potential need for primary prevention ICD implantation.	I	C	286–288
ICD implantation or temporary use of a WCD may be considered <40 days after myocardial infarction in selected patients (incomplete revascularization,[d] pre-existing LVEF dysfunction, occurrence of arrhythmias >48 h after the onset of ACS, polymorphic VT or VF).	IIb	C	170, 273
ICD implantation for the primary prevention of SCD is generally not indicated <40 days after myocardial infarction.	III	A	274, 275

ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

Implantable cardioverter defibrillator in patients with left ventricular dysfunction

Recommendations	Class[a]	Level[b]	Ref.[c]
ICD therapy is recommended to reduce SCD in patients with symptomatic HF (NYHA class II–III) and LVEF ≤35% after ≥3 months of optimal medical therapy who are expected to survive for at least 1 year with good functional status:			
– Ischaemic aetiology (at least 6 weeks after myocardial infarction).	I	A	63,64
– Non-ischaemic aetiology.	I	B	64,316, 317

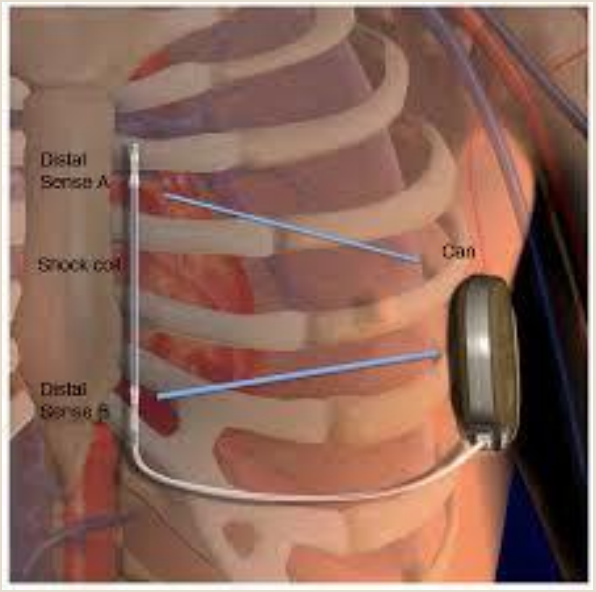
HF = heart failure; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; SCD = sudden cardiac death.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

Subcutaneous Defibrillator



Subcutaneous implantable cardioverter defibrillator

Recommendations	Class[a]	Level[b]	Ref.[c]
Subcutaneous defibrillators should be considered as an alternative to transvenous defibrillators in patients with an indication for an ICD when pacing therapy for bradycardia support, cardiac resynchronization or antitachycardia pacing is not needed.	IIa	C	157, 158
The subcutaneous ICD may be considered as a useful alternative to the transvenous ICD system when venous access is difficult, after the removal of a transvenous ICD for infections or in young patients with a long-term need for ICD therapy.	IIb	C	This panel of experts

ICD = implantable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Wearable Cardioverter Defibrillator/WCD

Wearable cardioverter defibrillator

Recommendation	Class[a]	Level[b]	Ref.[c]
The WCD may be considered for adult patients with poor LV systolic function who are at risk of sudden arrhythmic death for a limited period, but are not candidates for an implantable defibrillator (e.g. bridge to transplant, bridge to transvenous implant, peripartum cardiomyopathy, active myocarditis and arrhythmias in the early post-myocardial infarction phase).	IIb	C	167, 168

LV = left ventricular; WCD = wearable cardioverter defibrillator.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Automated External Defibrillators

Public access defibrillation

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended that public access defibrillation be established at sites where cardiac arrest is relatively common and suitable storage is available (e.g. schools, sports stadiums, large stations, casinos, etc.) or at sites where no other access to defibrillation is available (e.g. trains, cruise ships, airplanes, etc.).	I	B	173, 174
It may be considered to teach basic life support to the families of patients at high risk of SCD	IIb	C	This panel of experts

SCD = sudden cardiac death.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Μηνύματα

- Συνιστάται η εμφύτευση ICD για **δευτερογενή πρόληψη** σε επιβιώσαντες επεισοδίου κοιλιακής μαρμαρυγής ή κοιλιακής ταχυκαρδίας με αιμοδυναμική αστάθεια.
- Ασθενείς με ΟΕΜ και χαμηλό ΚΕ, πρέπει να λάβουν φαρμακευτική αγωγή και να επανεκτιμηθούν **6-12 εβδομάδες μετά το ΟΕΜ**. Συνιστάται εμφύτευση ICD για **πρωτογενή πρόληψη** όταν παραμένει ↓ ΚΕ (≤ 30%).
- Συνιστάται η εμφύτευση ICD για **πρωτογενή πρόληψη** σε ασθενείς με **καρδιακή ανεπάρκεια** και ΚΕ ≤ 35% μετά βέλτιστη φαρμακευτική αγωγή.
- Τα θύματα αιφνιδίου καρδιακού θανάτου πρέπει να υποβάλλονται σε εμπεριστατωμένη νεκροψία/νεκροτομή για την ταυτοποίηση πιθανόν κληρονομικού νοσήματος. Συνιστάται γενετική ανάλυση υλικού από τα θύματα, όταν υποπτευόμαστε ως αιτία κληρονομούμενες μυοκαρδιοπάθειες ή καναλοπάθειες (σύσταση Class I).

Risk factors for SCD in patients with established CHD

- Left ventricular systolic dysfunction and severity of HF symptoms are currently the strongest predictors of SCD risk among patients with prior MI and ischemic cardiomyopathy.
- ICD therapy is recommended for patients with ischemic dilated cardiomyopathy, prior MI, NYHA class II and III HF, and LVEF ≤35%.
- In contrast, ICD therapy does not reduce mortality in the early post-MI period (within 40 days), possibly because of a predominance of nonarrhythmic causes of death during this time window.

Early Repolarization (ERP) Syndrome

- Ethnic, racial, and sex differences in the relationship between the ERP and SCD (Europeans/Japanese, White, Women).

- The calculated *relative risks* for sudden arrhythmic death associated with a J point elevation of 0.1 mV are modest and the *absolute risk* of arrhythmic death in asymptomatic individuals with the ERP on ECG is extremely low.

J Am Coll Cardiol 2008;52:1231–1238
Eur Heart J. 2011;32:3098–3106

Cardiomyopathies: DCM, HCM, ARVC

- Non–ischemic cardiomyopathies are the second most frequent cause of SCD in the United States and European countries, which account for ≈10% to 15%

- The prevalence of cardiomyopathies in young autopsied SCD victims aged ≤35 years is higher and is reported to be 15% to 30%.

Inherited Arrhythmic Disorders: LQTS, BrS, CPVT, ERPS

- Among patients with autopsy negative SCD, ≈50% will have inherited arrhythmic syndromes.
- Performing **molecular autopsies** in cases with autopsy-negative SCD and **cascade screening of families** is important to establish the cause of death and to identify relatives potentially at high SCD risk.
- In cases of sudden unexplained death, where a diagnosis is not made either by antemortem or postmortem analysis, **genetic testing** of family members reveals a possible disease-causing mutation in 31% of families, and inherited arrhythmic syndromes comprise 30% of these mutations.

Eur Heart J. 2008;29:1670–1680
Circ Arrhythm Electrophysiol. 2013;6:588–596
Circulation. 2013;128:1513–1521

LQTS: therapy and SCD prevention

- **β-Blockers**
- **ICDs** are generally reserved for patients who have experienced a cardiac arrest.

Heart Rhythm. 2013;10:1932–1963

Individuals without apparent heart disease (2)

- **Diet:**
  - Consuming ***fish*** ≈1 to 2X/wk has been associated with significant 42%–50% reductions in SCD risk, with minimal impact of risk of non–fatal MI.
  - ***Magnesium*** intake: each 0.25 mg/dL (1 SD) increment in plasma magnesium was associated with a 41% reduced risk of SCD
  - A ***Mediterranean-style diet*** pattern (higher intake of vegetables, fruits, nuts, whole grains, fish, and low intake of red/processed meat) may also lower SCD risk among women.
  - ***Alcohol intake***: U-shaped associations between recent alcohol intake and SCD with reduced risks at levels of 0.5 to 1 drink/d and no reduction at ≥2 drinks/d. Heavy levels of alcohol consumption (>6 drinks/d) have also been associated with increased risk for SCD.

LQTS: Risk Factors

- 25% to 35% of genetically affected patients have a normal or borderline QTc at rest, requiring exercise or a catecholamine infusion to disclose the masked QT interval.
- The estimated incidence of cardiac arrest or SCD before the age of 40 years in untreated patients is estimated to be 0.30%/y, 0.60%/y, and 0.56%/y in LQT1, LQT2, and LQT3, respectively.
- Most arrhythmic events developed during exercise or emotional stress in LQT1, at rest or with sudden noises in LQT2, and at rest or during sleep in LQT3.
- Other risk factors for arrhythmic events in LQTS include prior history of syncope, significant QTc prolongation, and location and number of mutations.

Αιφνίδιος Καρδιακός Θάνατος ≠ Καρδιακή Ανακοπή

- Σε αντίθεση με τον ΑΚΘ ο οποίος αποτελεί **μη αναστρέψιμη κατάσταση**, η καρδιακή ανακοπή είναι **εν δυνάμει αναστρέψιμη** αν και εφόσον γίνουν οι απαραίτητες παρεμβάσεις στον ελάχιστο κρίσιμο χρόνο.