

# **Syncope and Sudden Cardiac Death**

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**The symptom of syncope and the event of sudden cardiac death are closely intertwined. This lecture will review the relationship of syncope to sudden cardiac death in several different cardiac disorders.**

# Syncope

*“Those who suffer from frequent and severe fainting often die suddenly.”*

*Hippocrates, 1000 BC*



**This tight relationship has been noted as far as back as 1,000 B.C. when Hippocrates made the comment “those who suffer from frequent and severe fainting often die suddenly.” This profound observation frames our concern when patients present with syncope and the need to sort out their risk for sudden cardiac death.**

# Magnitude of Syncope

- 30-40% of population will experience syncope
- More than 500,000 new patients per year



**1-6% of admissions**

**3% of emergency room visits per year**

National Disease and Therapeutic Index on Syncope and Collapse: ICD-9-CM 780.2, IMS America, 1997

Gendelman HE et al: NY State J Med, 1983

Day SC et al: Am J of Med, 1982

Kapoor W: Medicine 69:160-75, 1990

**Syncope is a common disorder with 30-40% of the population in the United States experiencing syncope at some time during their life time, and more than 500,000 new patients with syncope per year. This accounts for 1-6% of all hospital admissions and 3% of emergency room visits per year.**

# **Syncope**

## **Annual Mayo Experience**

- **800-1,000 ER patients**
- **2,000-2,500 outpatients**
- **400 hospital admissions**
- **30% of EP practice**

**500 consults**

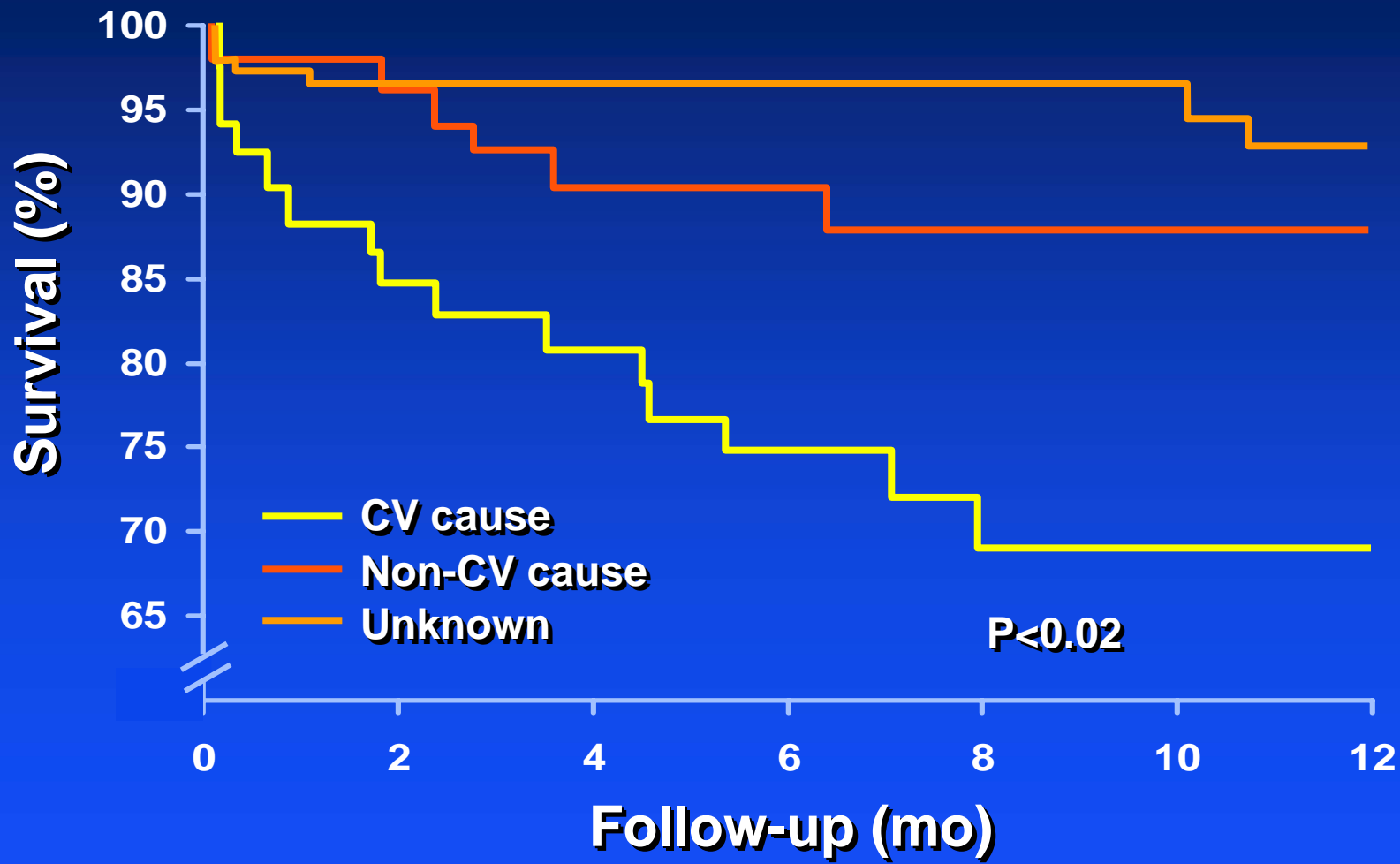
**125 EP studies**

**300 tilt tests**

**Annually, at Mayo Clinic, 800-1,000 patients are seen in the emergency room for syncope; 2,000-2,500 outpatients; 400 hospital admissions; and syncope accounts for 30% of the electrophysiology (EP) practice. In EP, we do approximately 500 consults, 125 EP studies, and 300 tilt tests on patients whose primary problem is syncope.**



# Cumulative Survival in Patients with Syncope

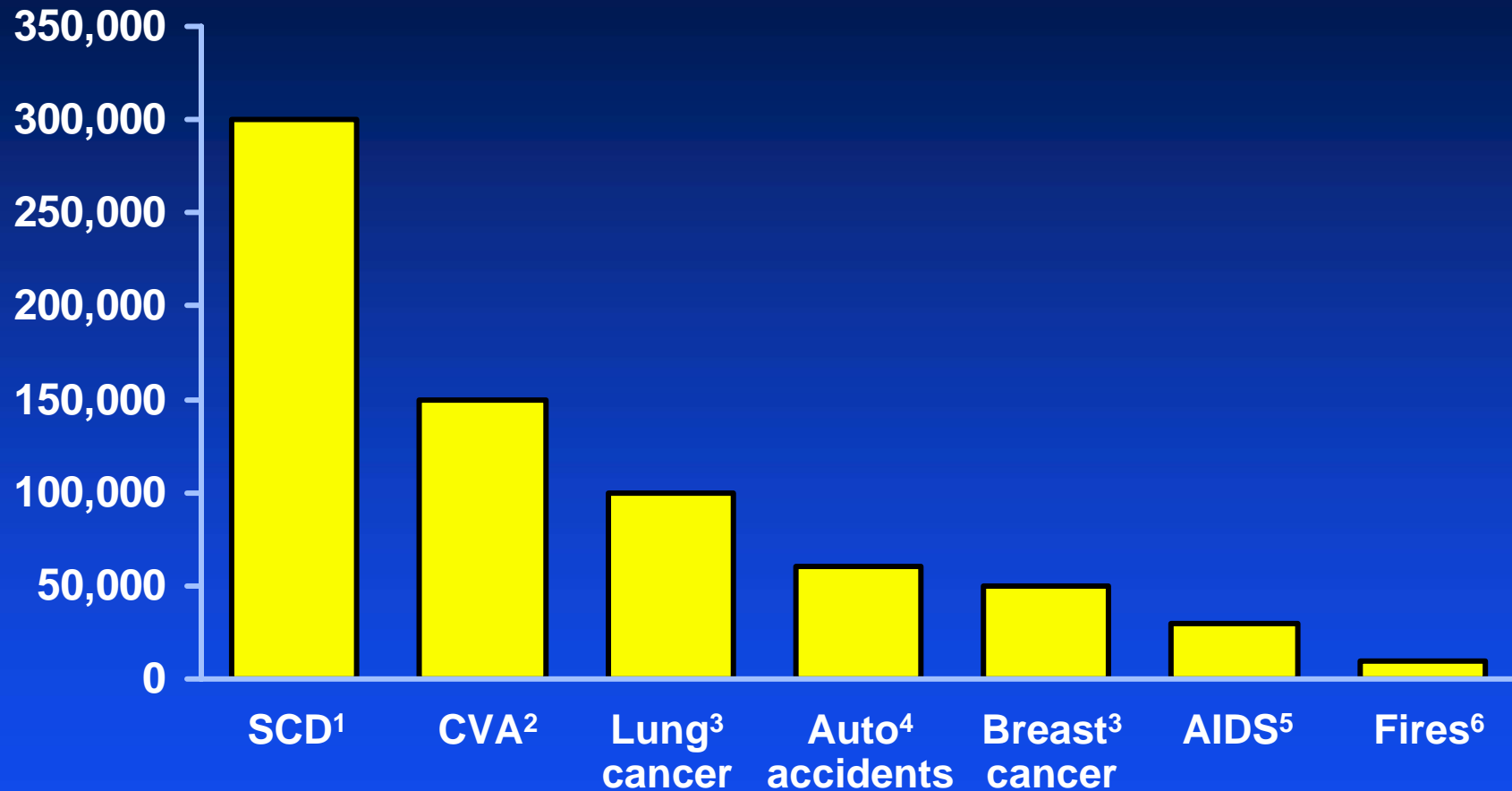


Kapoor, 1983

**A landmark study by Kapoor and associates in 1983 showed that patients with a cardiovascular cause for syncope had worse survival compared to patients with a non-cardiovascular cause or an unknown cause. The majority of patients with an “unknown” cause would now be determined to have neurocardiogenic syncope. The patients with a cardiovascular cause for syncope include those with structural heart disease and significant valvular heart disease.**

***Syncope may represent a self-terminating episode of sudden death -- especially in patients with associated heart disease***

# Annual Deaths in the U.S.

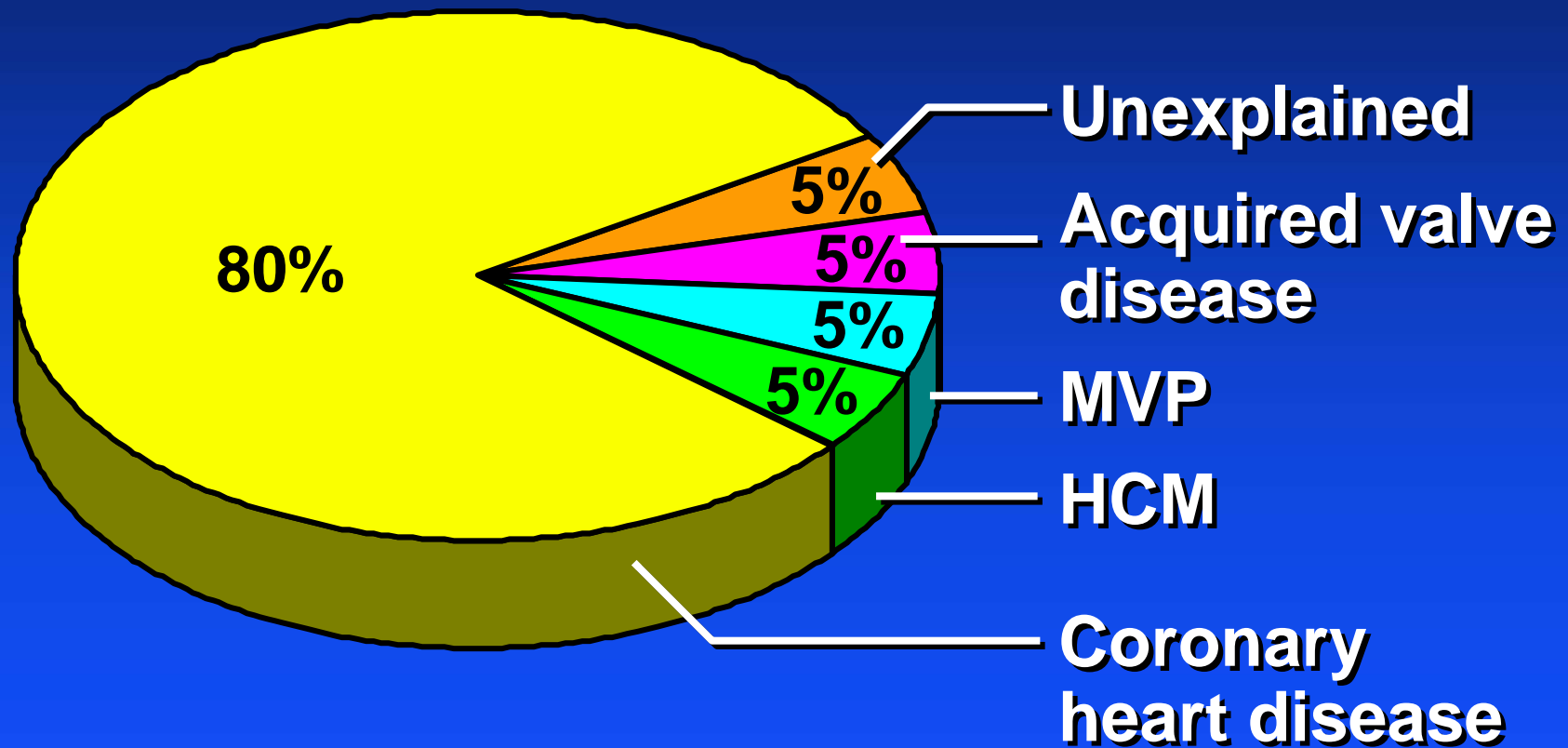


<sup>1</sup>NASPE, May 2000; <sup>2</sup>American Heart Association 2000;  
<sup>3</sup>National Cancer Institute 2001; <sup>4</sup>National Transportation Safety Board, 2000;  
<sup>5</sup>Center for Disease Control 2001; <sup>6</sup>NFBA, US Facts & Figures, 2000

**The concern with syncope is that it may represent a self-terminating episode of sudden death – especially in patients with associated heart disease. Sudden cardiac death accounts for nearly 300,000 deaths in the United States and exceeds the number of deaths caused by stroke, lung cancer, automobile accidents, breast cancer, and AIDS. Sudden cardiac death is a major health problem and may be heralded by syncope only later to have the patient experience sudden death.**

# Causes of Sudden Death

**≥35 years old**

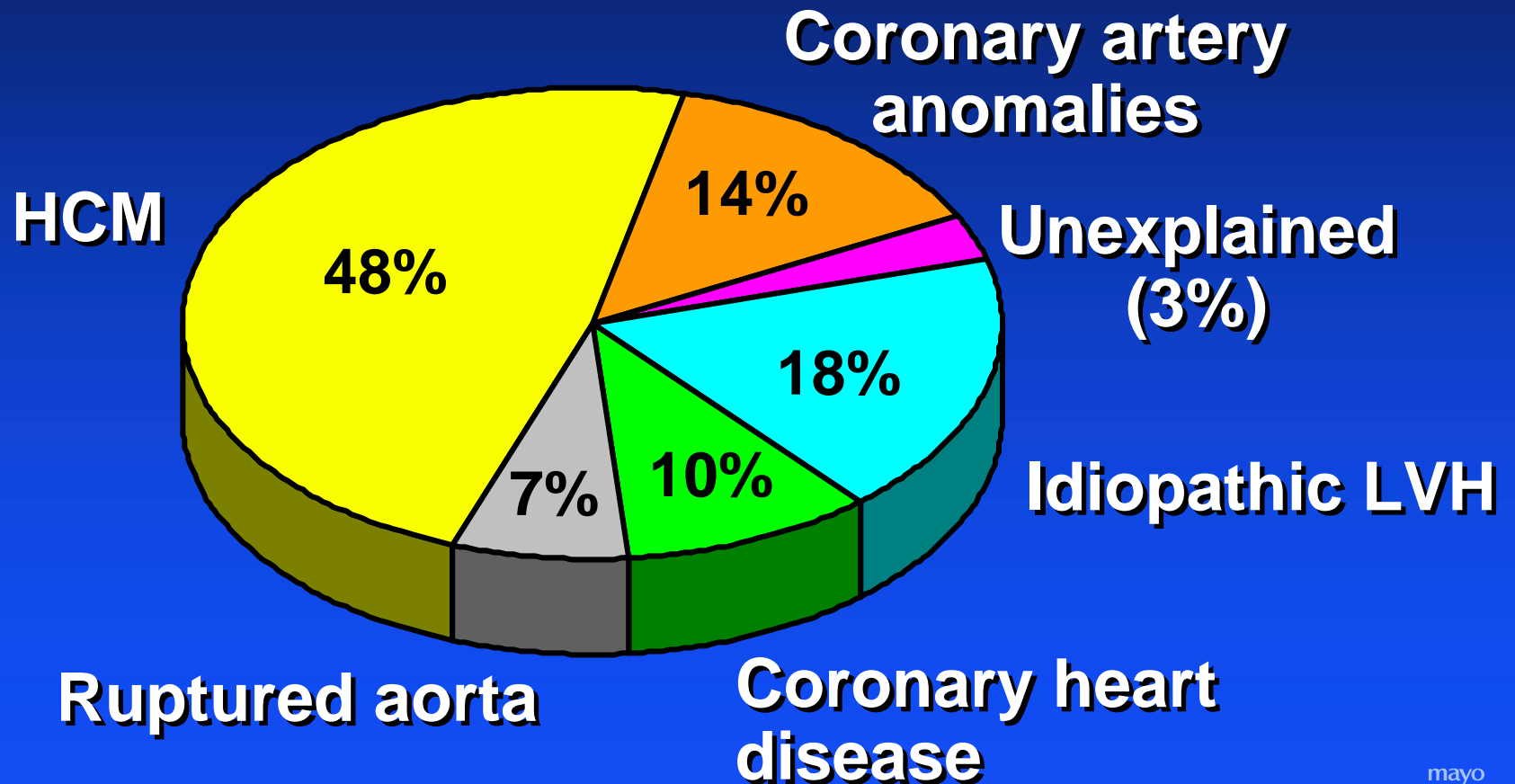


Maron et al: JACC, 1986

**The causes of sudden cardiac death in 80% of athletes exceeding the age of 35 years is coronary artery disease. The remaining 20% have hypertrophic cardiomyopathy, mitral valve prolapse, acquired valvular heart disease, or unexplained findings at the time of autopsy.**

# Causes of Sudden Death

**<35 years old**



Maron et al: JACC, 1986



**This is in contrast to athletes under age 35 in whom approximately 50% have hypertrophic cardiomyopathy at the time of autopsy; 7% a ruptured aorta; 14% coronary artery anomalies; 18% idiopathic left ventricular hypertrophy; 10% coronary artery disease; 3% no identifiable abnormalities.**

# Sudden Unexpected Death

## Ages 20-40 Years, Olmsted County

**54 deaths**

<b>CAD</b>	<b>18</b>	<b>HCM</b>	<b>2</b>
<b>Myocarditis</b>	<b>4</b>	<b>Seizure</b>	<b>6</b>
<b>Stroke</b>	<b>3</b>	<b>PE</b>	<b>2</b>
<b>CNS infection</b>	<b>1</b>	<b>Aortic dis</b>	<b>2</b>
<b>1<sup>o</sup> arr</b>	<b>6</b>	<b>Unknown</b>	<b>7</b>

Shen et al: AJC, 1995

**Shen and associates reviewed the causes of sudden unexpected death in patients age 20-40 years in Olmsted County, Minnesota. In this county, over 95% of the health care is provided by the Mayo Clinic and nearly 100% of patient records are available for long term evaluation. In this group, there were 54 deaths: 18 had coronary artery disease, 4 had myocarditis, 3 had stroke, 1 had CNS infection, 6 had primary arrhythmia, 2 had hypertrophic cardiomyopathy, 6 had seizure, 2 had pulmonary embolus, 2 had aortic dissection, and 7 had unknown cause.**

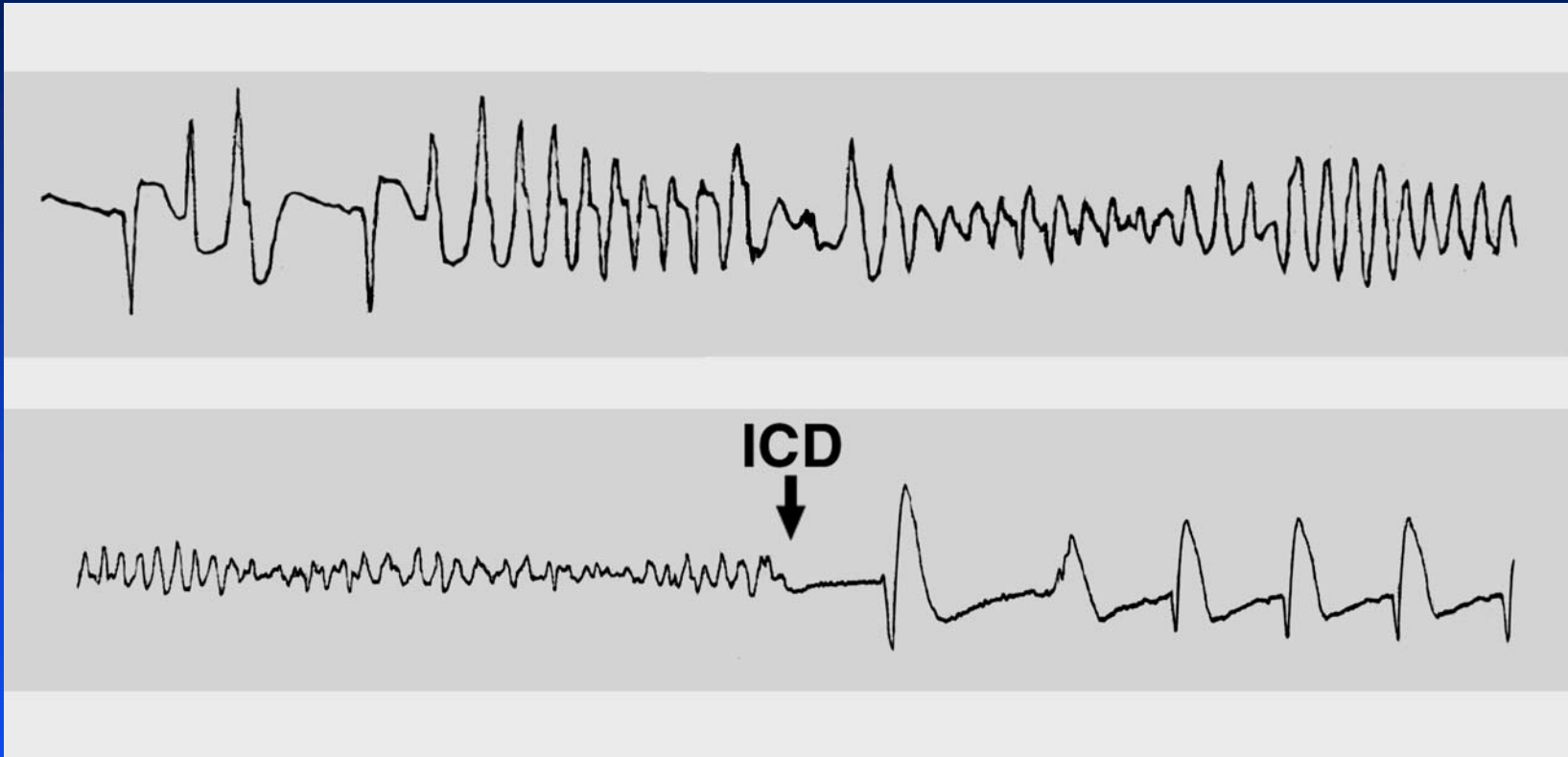
# **Sudden Unexpected Death Ages 20-40 Years, Olmsted County**

- **54 deaths**
- **ARVD features in 9  
(17%)**
- **6 of the 9 had another  
potential cause**

**Of the 54 deaths, 9 patients (or 17%) had features of arrhythmogenic right ventricular dysplasia but six of the nine had another potential cause of sudden death. Therefore, sudden cardiac death in young adults in Minnesota is due to a wide spectrum of causes.**

***The ICD is an effective treatment  
to prevent sudden death from VT or VF  
in patients with syncope***

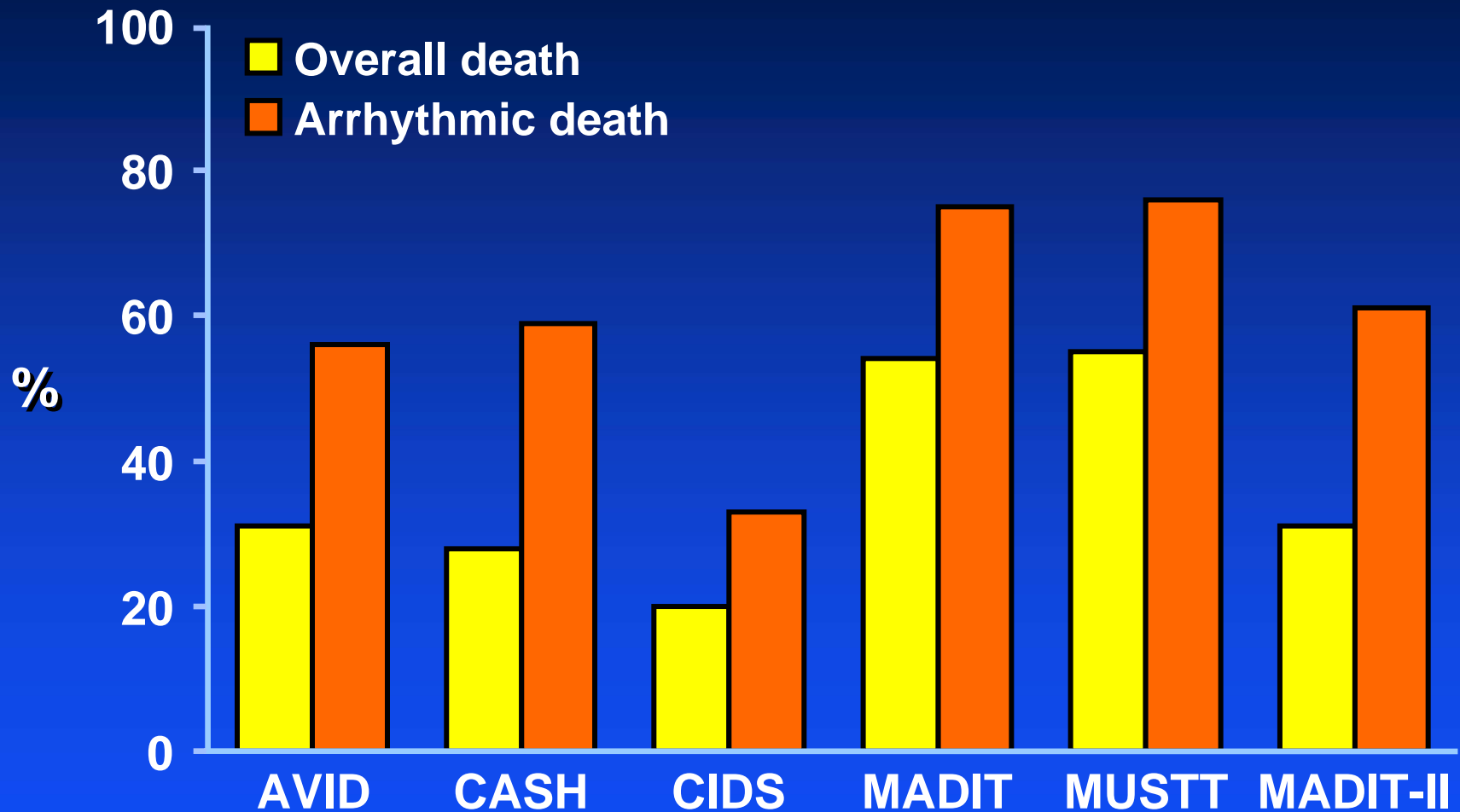
**The implantable cardioverter defibrillator (ICD) has proven to be an effective treatment to prevent sudden death from ventricular tachycardia or ventricular fibrillation in patients who initially present with syncope. The use of this device has improved our care of these high risk patients.**





**This is an example of a patient with polymorphic ventricular tachycardia degenerating to ventricular fibrillation successfully converted with the ICD with subsequent backup ventricular pacing until sinus rhythm returned.**

# Mortality Reduction with ICD Treatment



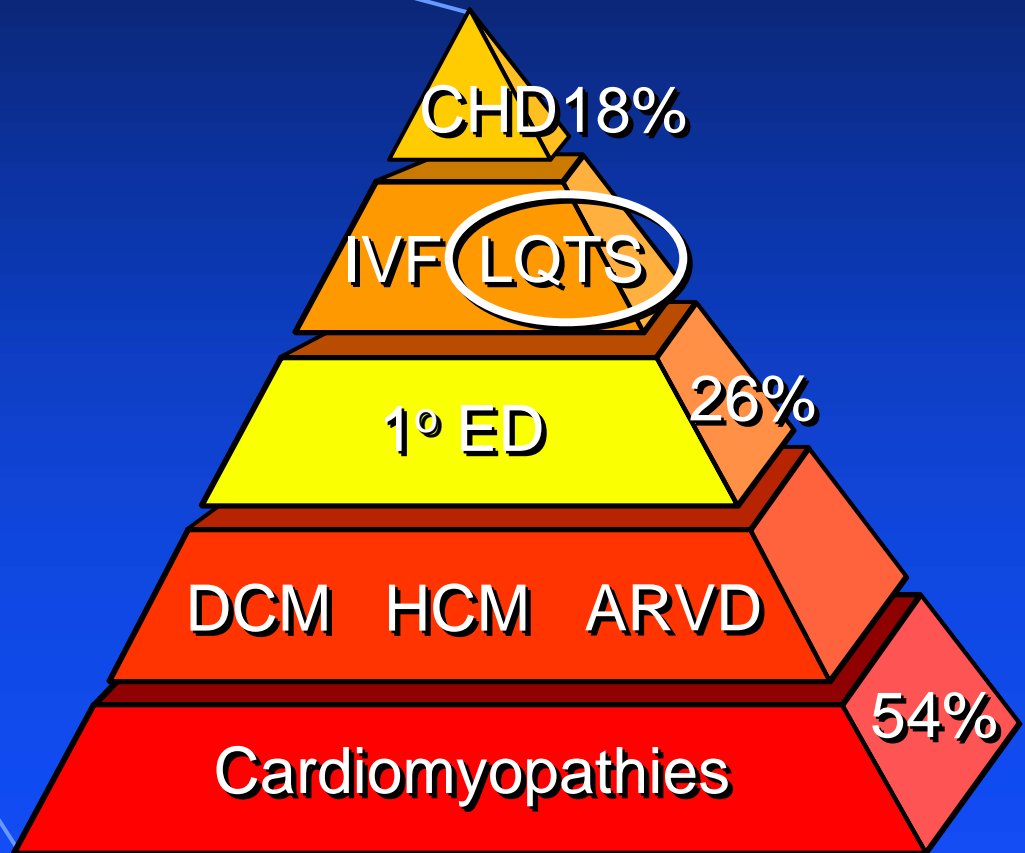
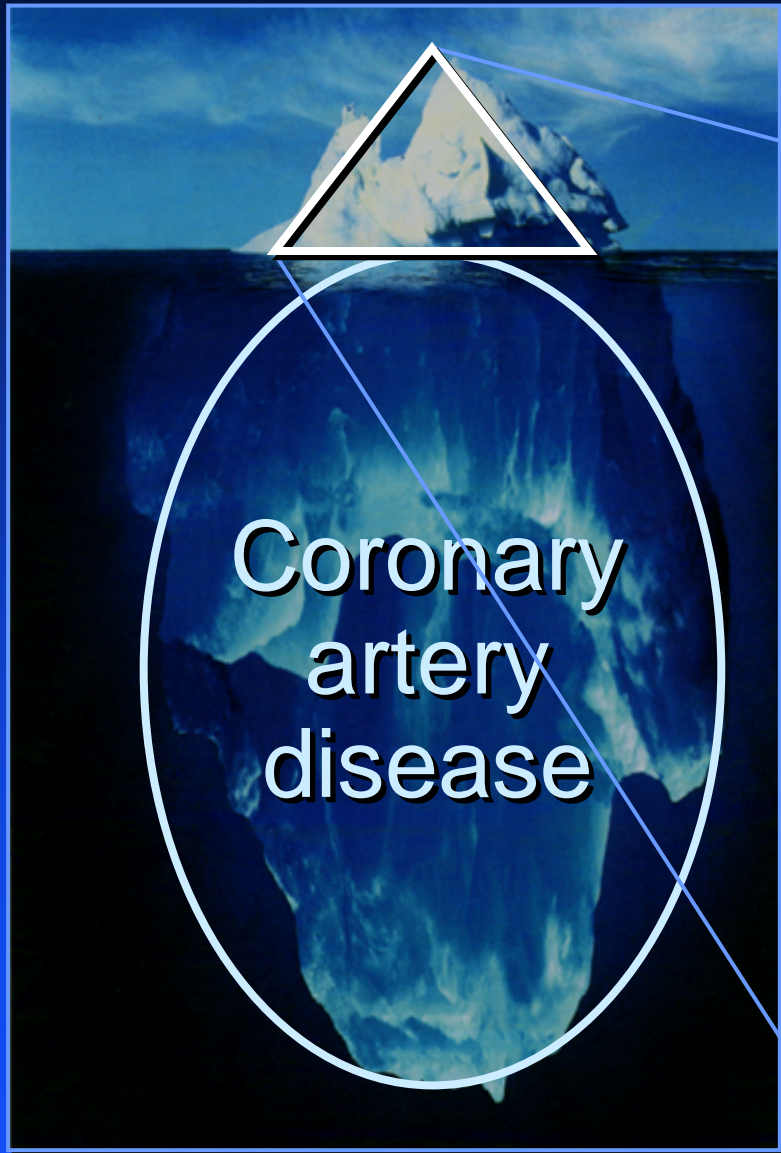
**Secondary  
Prevention**

**Primary  
Prevention**

**The ICD has been associated with significant mortality reduction with regard to overall death and arrhythmic death in studies evaluating the therapy as primary prevention and secondary prevention of sudden cardiac death. Many of the patients who received the ICD for secondary prevention had syncope with a subsequently inducible ventricular arrhythmia.**

***Spectrum of Cardiac Causes  
in SCD Survivors***

# Spectrum of Cardiac Causes in SCD Survivors

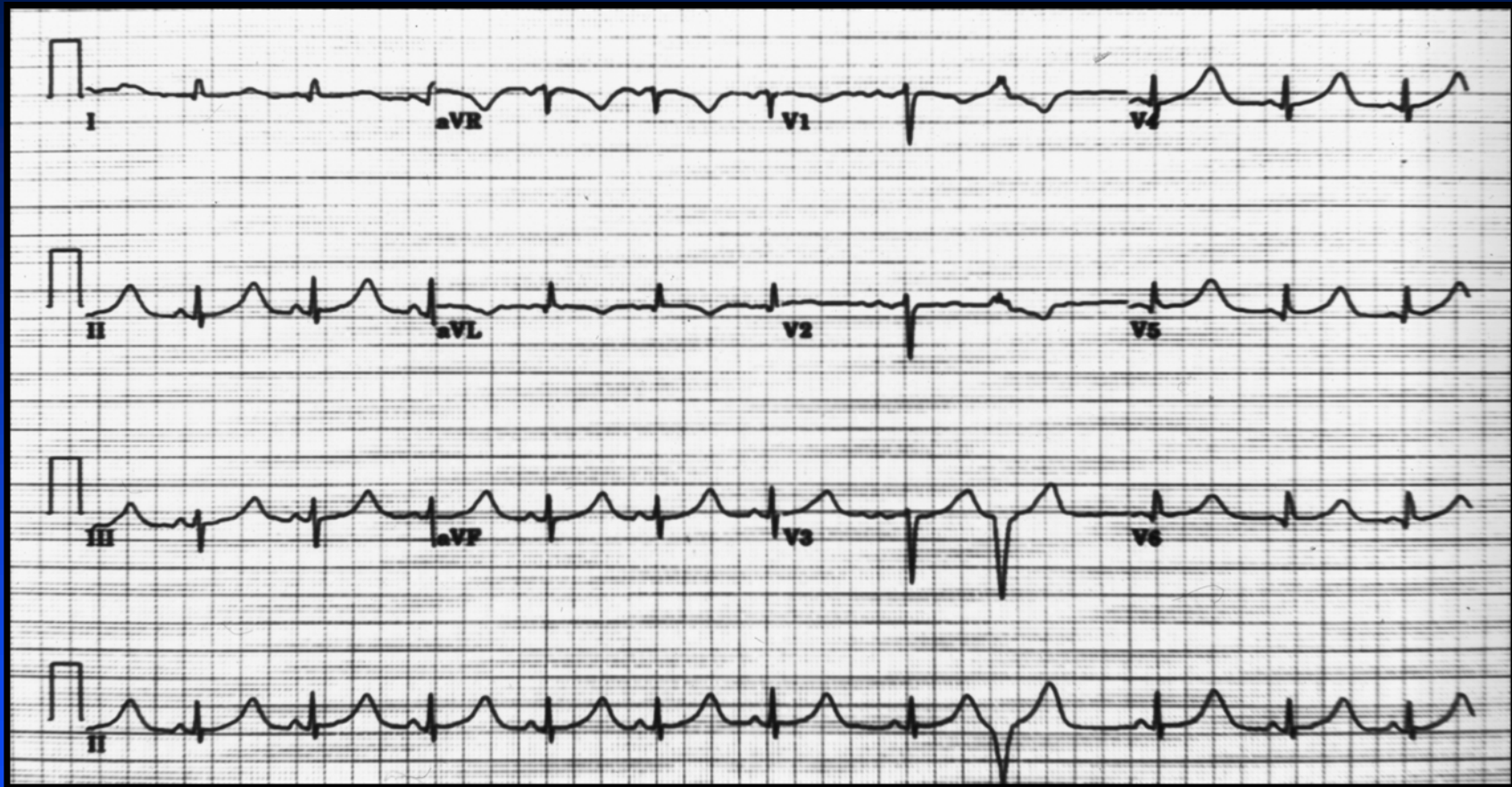


**There is a wide spectrum of cardiac causes of sudden cardiac death in those who survive the event. Coronary artery disease causes the majority of sudden deaths but the tip of the iceberg is represented by dilated, hypertrophic, and arrhythmogenic right ventricular cardiomyopathy in 54%; primary electrical disease in 26%; and idiopathic ventricular fibrillation, long QT syndrome, and congenital heart disease in 18% of patients.**

# 19-Year-Old Female

- Admitted after syncope with an automobile accident
- No prior medical problems
- Positive family history of sudden death
- Only medication BCP
- Normal physical, routine labs, CXR, Echo, EEG
- ECGs →

# 19-year-old female Admission ECG, 7/16





**The awareness of long QT syndrome as a cause of sudden death has increased significantly over the last several years. This is an example of a 19 year old female who was admitted after syncope with an associated automobile accident. She had no prior medical problems but did have a positive family history of sudden cardiac death in a sister, age 24, and a cousin, age 37. Her only medication was birth control pills and her physical examination and routine laboratory testing were entirely normal. Her ECG showed significant QT prolongation with a QT interval approaching 600 msec at a heart rate of 75 bpm.**

# Long QT Syndrome

## Clinical Features

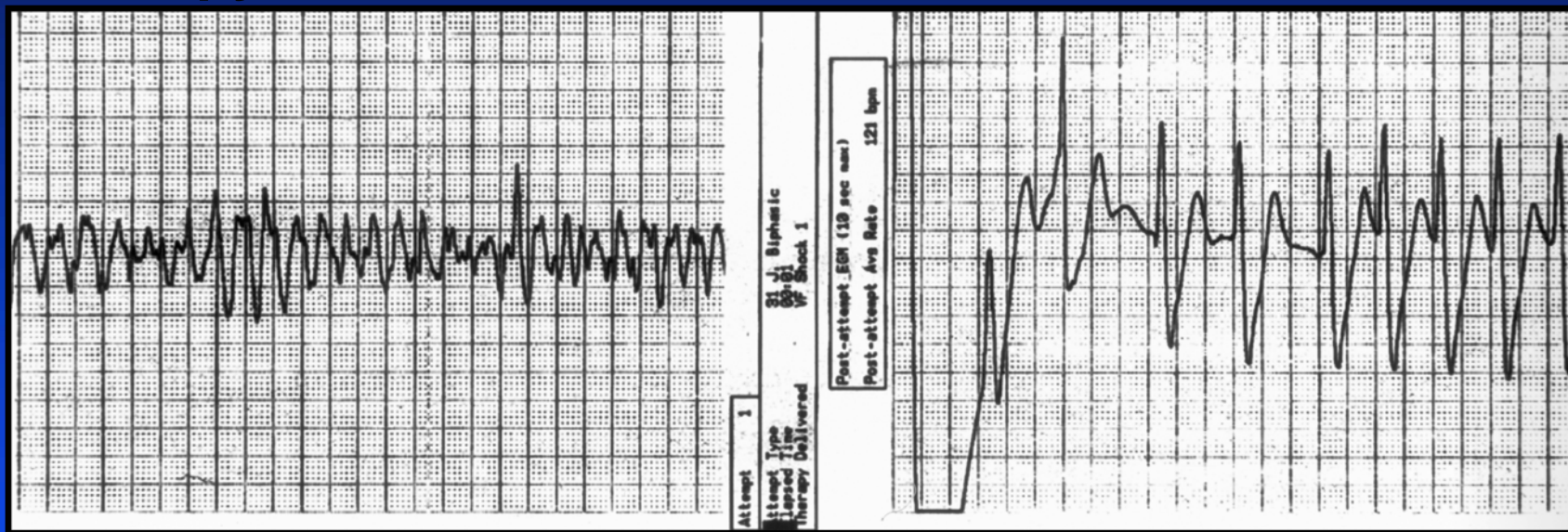
- QT prolongation, T and U wave abnormality
- QTc  $>0.46$  sec (occasionally 0.41-0.45)
- **Recurrent syncope** (torsades de pointes)
- Spells misdiagnosed as seizure or vasovagal
- Sudden death

**The clinical features of long QT syndrome include: QT prolongation and T wave and U wave abnormalities on the ECG with the QTc exceeding 0.46 sec. Occasionally patients with genetically proven long QT syndrome have a corrected QT interval of 0.41-0.45 sec. Patients often present with recurrent syncope due to torsades de pointes, and the spells are often misdiagnosed as seizure or vasovagal. Unfortunately, patients can experience sudden cardiac death.**

# 19-Year-Old Female

- Full recovery
- Genetic mutation: **KVLQT 1**
- ICD placed

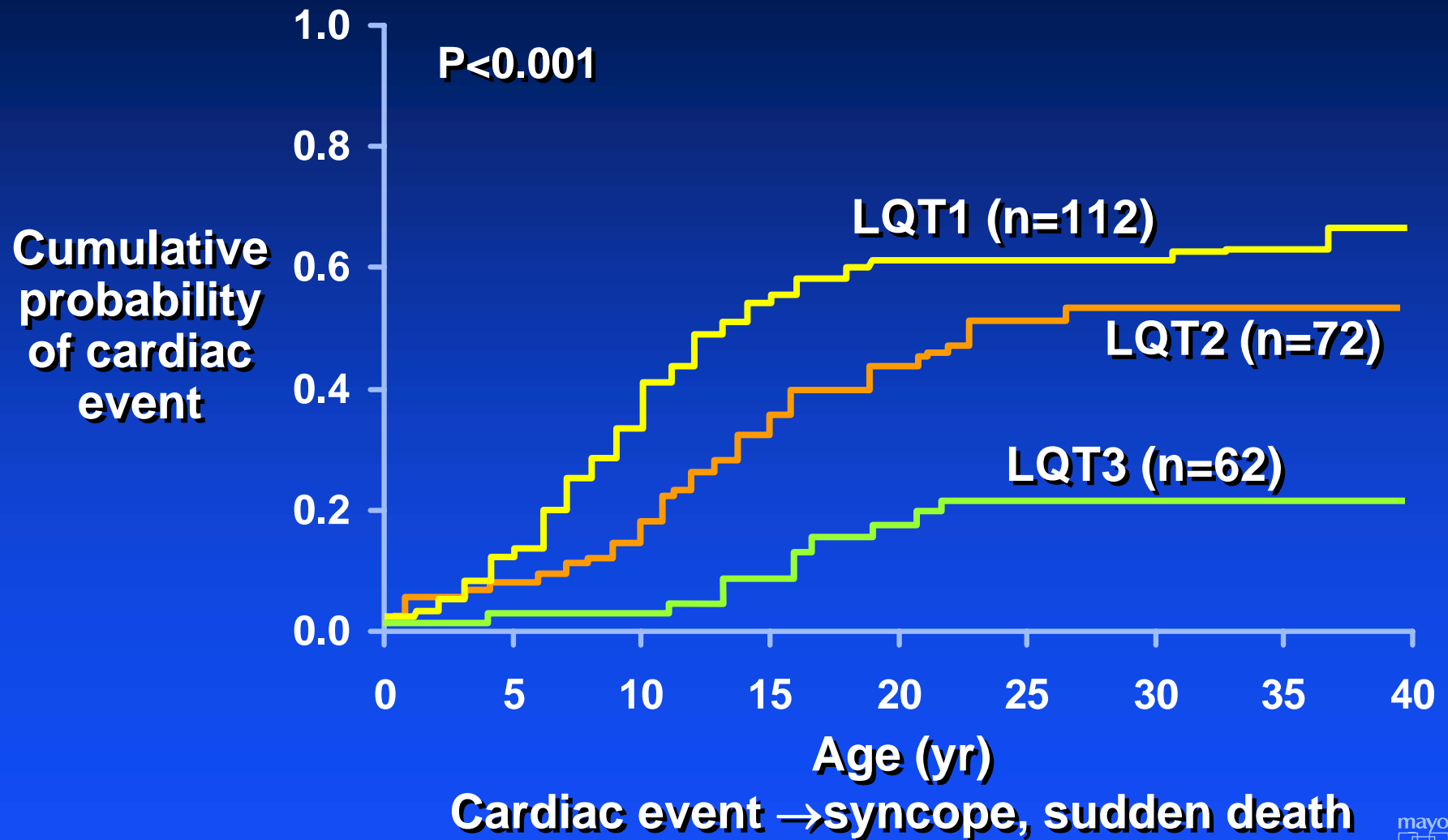
# 19-year-old female (now 21) Therapy



**This patient had a full recovery, genetic evaluation showed an abnormality of KVLQT1 and an ICD was placed. At age 21, two years after placement of the ICD, she had a documented episode of ventricular fibrillation successfully detected and terminated by the ICD.**

# Long QT Syndrome

## Influence of Genotype on Clinical Course



Zareba for the INT LQTS Registry: NEJM, 1998



CP985319-49

**The genotype in long QT syndrome can significantly influence the clinical course. The cumulative probability of a cardiac event, which includes syncope or sudden death, is worse in patients with long QT1 than patients with long QT2 or long QT3. This is helpful data for prognosis and risk stratification of patients with long QT syndrome.**

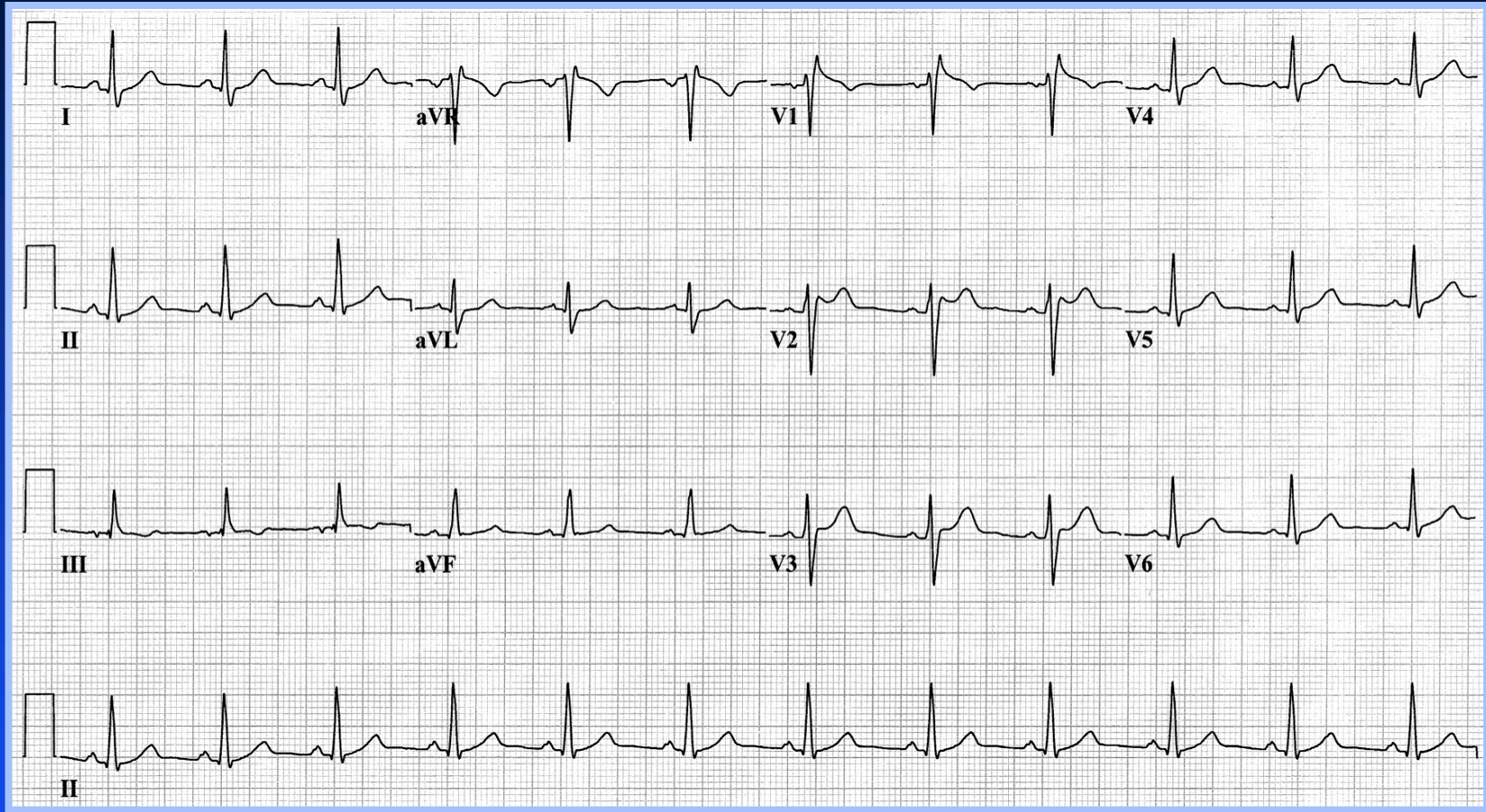


***Other causes of syncope and sudden death in patients with a structurally normal heart include:***

- **Brugada syndrome**
- **WPW**
- **Catecholaminergic polymorphic VT**

**Other causes of syncope and sudden death in patients with a structurally normal heart include Brugada syndrome, Wolff-Parkinson-White, and catecholaminergic polymorphic ventricular tachycardia.**

# 53 year-old male with syncope and Brugada Syndrome



**Syncope is an independent risk factor for sudden death and patients should be treated with an ICD.**

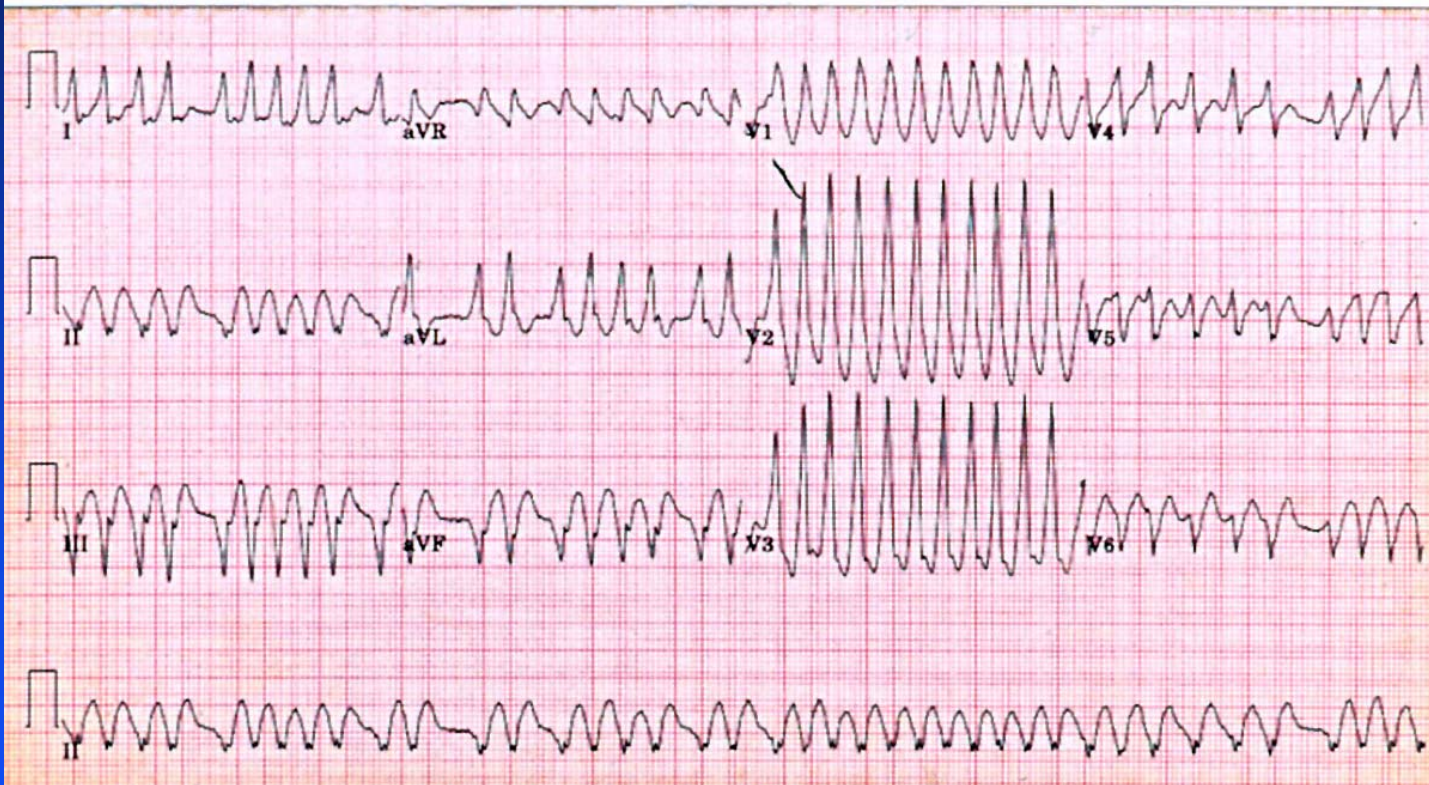
Antzelevitch et al. JACC 2003

**This 53 year old male presented with syncope and an ECG consistent with Brugada syndrome. Syncope is an independent risk factor for sudden cardiac death in patients with Brugada syndrome and strong consideration should be given to placing an ICD.**



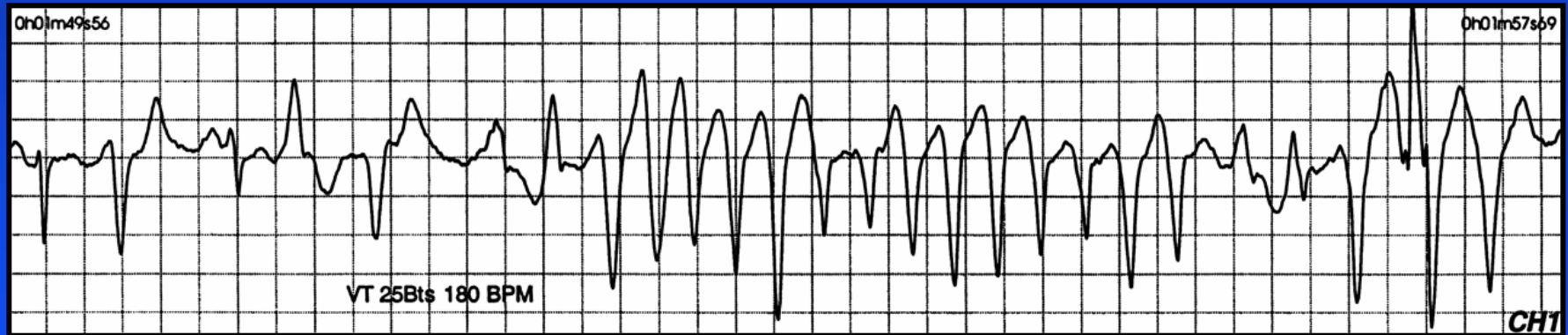
# WPW with a rapid ventricular rate during atrial fibrillation

26-YEAR-OLD MALE WITH NEAR SYNCOPE PLAYING BASKETBALL. NO PRIOR MEDICAL PROBLEMS.



**Patients with WPW can develop a rapid ventricular rate during atrial fibrillation which may degenerate into ventricular fibrillation and sudden death. Occasionally these patients will present with syncope, although the frequency of syncope in such patients is not clearly defined as syncope can also occur with orthodromic reentrant tachycardia. Nonetheless, these patients are appropriately treated with radiofrequency catheter ablation to eliminate conduction over the accessory pathway.**

**45-year-old woman with 31 prior event recorder transmissions when she felt palpitations, faint, weak, etc – all 31 showed sinus rhythm with occasional PACs or PVCs, but none were done during a “bad spell” except this one, #32**



**Catecholaminergic polymorphic ventricular tachycardia typically occurs during exercise in patients with an otherwise normal heart. This is an ECG recorded by an event monitor in a 45 year old woman who had episodes of palpitations, faintness, and weakness with essentially a normal recording. However, none of these were “a bad spell” until the final recording documented polymorphic ventricular tachycardia. This rhythm can be provoked with isoproterenol or epinephrine during EP testing and treatment usually requires use of the implantable defibrillator.**



# Hypertrophic Cardiomyopathy

- Annual rate of sudden cardiac death is 1-1.5%
- Syncope is an independent risk factor for sudden death

Elliott et al. JACC, 2000  
Kofflard et al. JACC, 2003

**Patients with hypertrophic cardiomyopathy have an annual rate of sudden cardiac death approaching 1-1.5%. Early studies at tertiary referral centers showed a higher rate of sudden death but in the more general population the rate is lower. Syncope is an independent risk factor for sudden death in such patients.**

***EP testing for  
evaluating syncope***

# **Syncope**

## **Who to Refer for EP Testing**

- **If the ECG shows conduction disease or there is associated heart disease--**

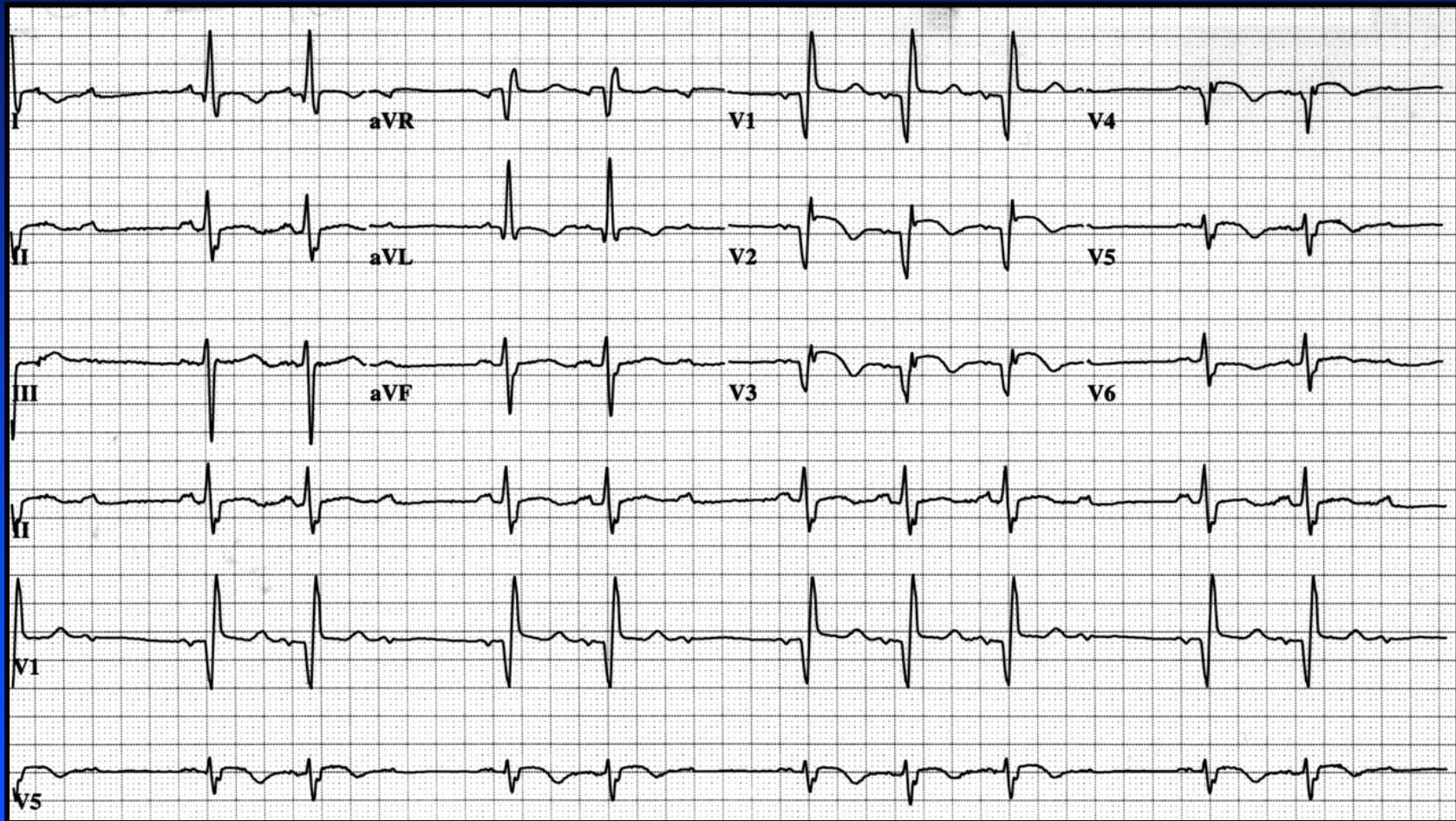
**Diagnostic yield is 40-65%**

- **If the ECG is normal and no associated heart disease--**

**Diagnostic yield is 5-15%**

**The role of EP testing for patients with syncope has been better defined over the last several years. Patients who should be referred for EP testing are those with syncope in whom their ECG shows conduction system disease or there is associated heart disease. In these patients the diagnostic yield of the EP study is 40-65%. If the ECG is normal and there is no associated heart disease, the diagnostic yield is extremely low at 5-15%.**

# 68-year-old man with MI 3 months earlier, EF 45%, presents with syncope



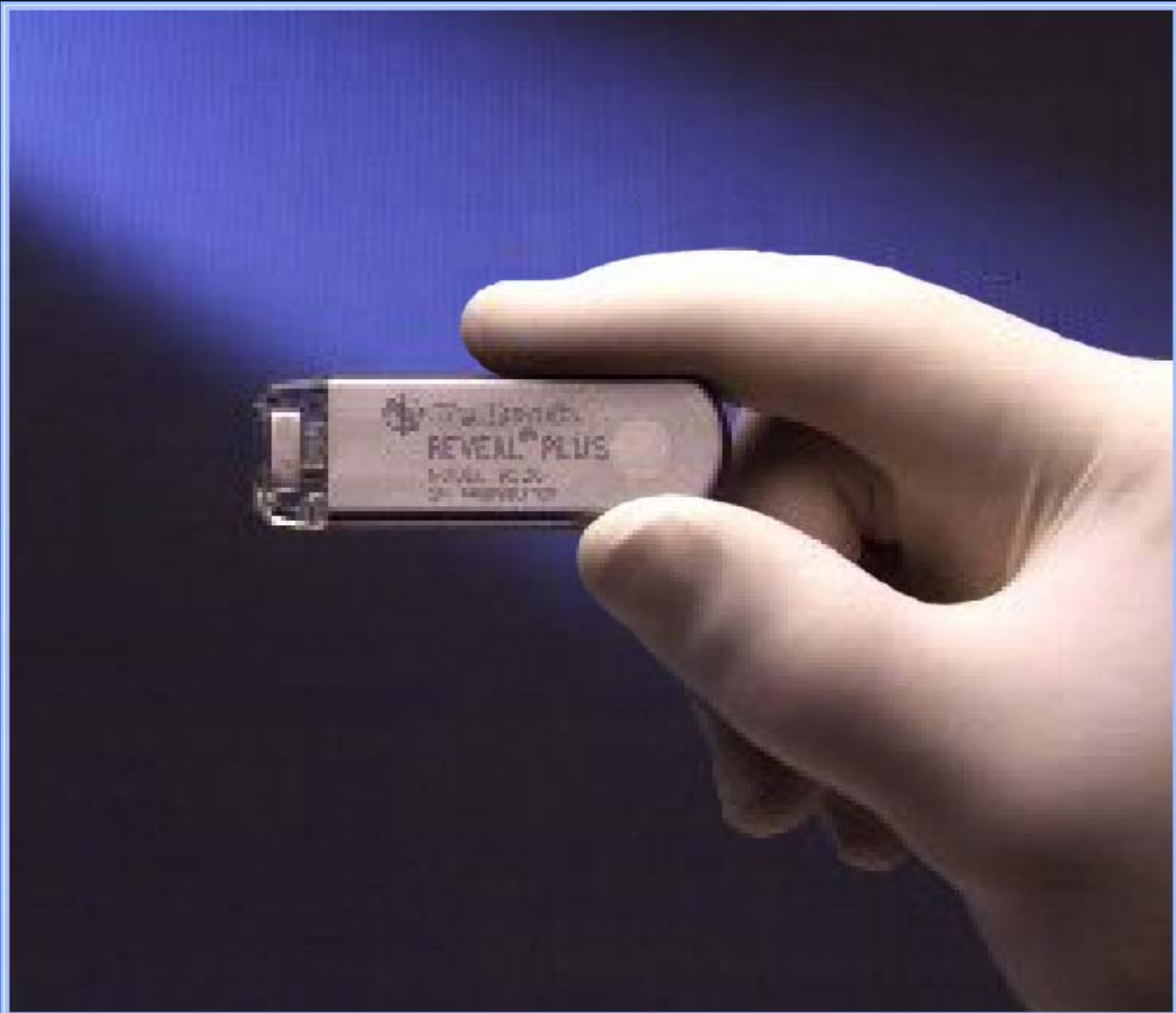
**This 68 year old man with a myocardial infarction three months earlier and an ejection fraction of 45% presented with syncope. His ECG shows several abnormalities which are associated with syncope. These include an anterior myocardial infarction and persistent ST elevation consistent with left ventricular scar or aneurysm both of which increase the risk for ventricular tachycardia. In addition, there is conduction disease with Mobitz II block which increases the risk for heart block. EP testing is appropriate to decide if this patient is best treated with a pacemaker or an ICD.**

***Extended ECG monitoring of  
patients with syncope***



# Holter Monitors and External Loop Recorders--Problems

- **Excellent tools for patients with frequent symptoms**
- **Few symptoms during monitoring period**
- **Patient noncompliance**
  - Not wearing device during symptoms**
  - Failure to operate device**
- **Operational failure**
  - Poor electrode contact**
- **Failure to record**
- **Poor telephone transmission**



**Extended ECG monitoring in patients with syncope can be done by 24 hour Holter recording and external loop recorders. Unfortunately, these recording systems have problems which limit their usefulness. They are excellent tests for patients with frequent symptoms but often there are few symptoms that occur during the period of cardiac monitoring. The use of the implantable loop recorder has improved our ability to obtain an ECG at the time of an event in patients with infrequent symptoms. This device is placed underneath the skin and can record for up to 15 months. It records both in an automatic mode storing ECGs associated with significant bradycardia or tachycardia or a patient-activated mode. In the patient-activated mode it can be programmed to store over 20 minutes of ECG data prior to the activation.**

# 28-Year-Old Male

## Background

Numerous syncopal episodes over past year

Multiple falls with bruising

Feared falling and driving

Many frustrating trips to ER without diagnosis

## Workup and treatment

Holter monitor, external event recorder, ECG & carotid sinus massage—negative

EP study within normal limits

Tilt test showed slight abnormality

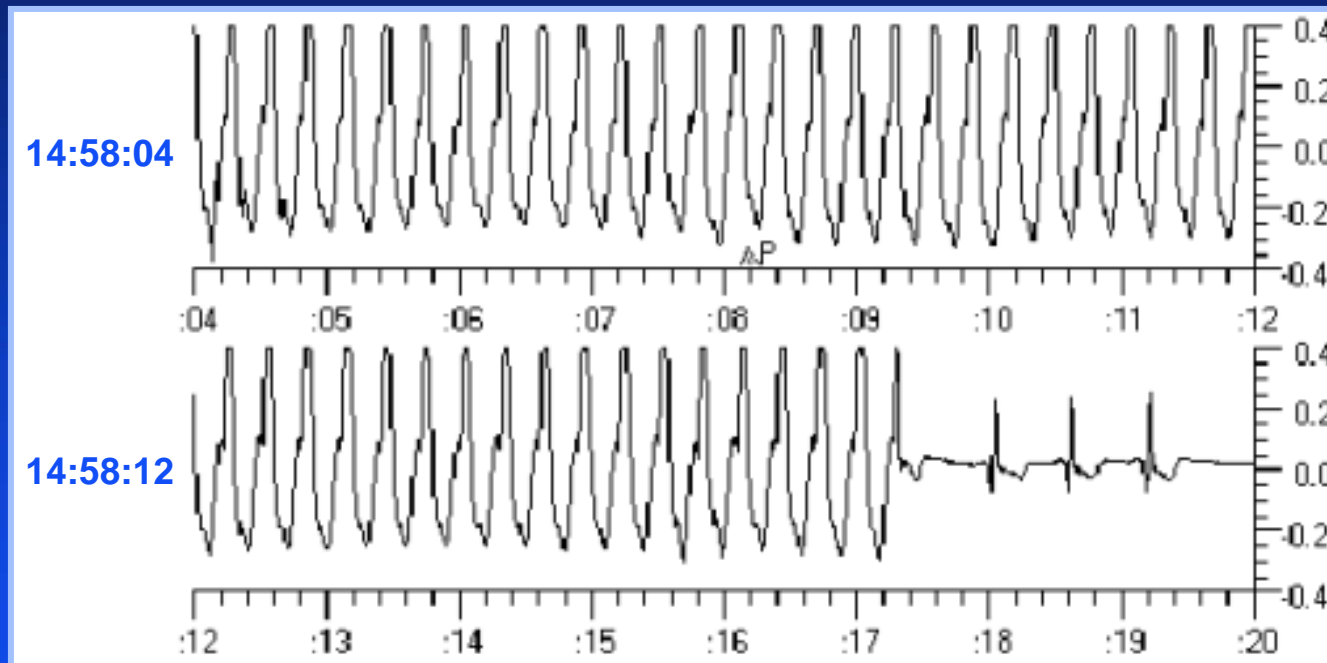
Physician suspected psychological disorder

ILR was implanted

**This is an example of a 28 year old male with numerous syncopal episodes over the previous year resulting in falls. He stopped driving and evaluations in the emergency room were normal. An extensive workup was performed which was normal and included Holter monitor, event recorder, tilt test, EP study, and psychological evaluation. The implantable loop recorder was subsequently placed.**

# 28-Year-Old Male

**Within 1-month post-implantation, a rhythm strip was captured after a syncopal episode**



- **100-beat run of ventricular tachycardia over 190 bpm**
- **Patient was ablated and medicated**
- **Patient has been symptom free for more than 6 months**

**Within one month following implantation, a rhythm strip was captured after a syncopal event showing monomorphic ventricular tachycardia at a rate of over 190 bpm. This was successfully treated with ablation and beta blocker.**

# Unexplained Syncope Implantable Loop Recorder

- 66 patients with unexplained syncope
- No orthostatic changes, negative Holter, EF  $\geq 35\%$
- Randomized to ILR vs conventional
- Conventional: Event recorder 2-4 weeks, tilt, EP

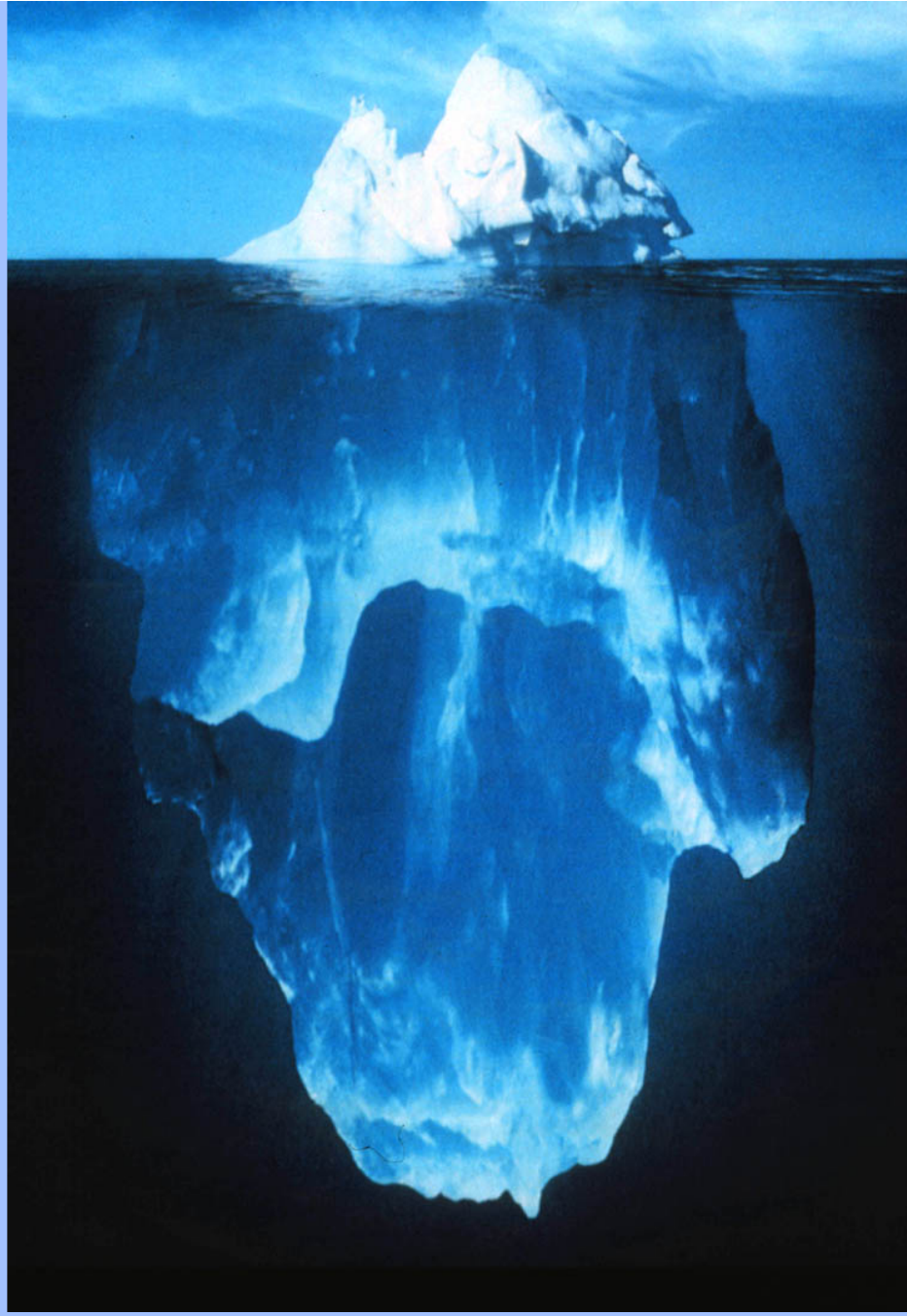


# Unexplained Syncope Implantable Loop Recorder

	<b>ILR</b>	<b>Tilt/EPS</b>	<b>P</b>
Initial diagnosis (%)	52	20	0.012
Crossover diagnosis (%)	62	17	0.069
<b>Overall (%)</b>	<b>55</b>	<b>19</b>	<b>0.004</b>
<b>Diagnosis</b>			
Brady	14	3	
SVT	3	1	
VT	0	1	
Vagal	3	2	
Seizure	2	0	

Krahn et al: Circ, 2001

**Use of the implantable loop recorder in patients with unexplained syncope has been reported by Krahn and associates. They describe 66 patients with unexplained syncope who had no orthostatic changes, a negative Holter, and an ejection fraction 35% or greater. They were randomized to the implantable loop recorder or conventional therapy. Conventional therapy included an event recorder for 2-4 weeks, tilt testing, and EP testing. During followup the implantable loop recorder achieved overall diagnosis in 55% of patients compared to 19% of patients with conventional therapy. Potential causes of syncope that could eventually lead to sudden death were few in this group of patients.**



**Understanding the  
relationship between  
syncope and sudden  
death --**

**Making progress  
but still more to  
discover**

**Our understanding of the relationship between syncope and sudden death has increased significantly over the last several years. Patients with structural heart disease and certain ECG abnormalities have been identified to have increased risk of sudden death and often the initial presentation is an episode of syncope.**