SYNCOPE

WHEN IS IT A SIMPLE FAINT AND WHEN IS IT NOT?

75 year old female presents from airport with a collapse/LOC – now back to normal.

- 1. *What history and physical examination data help to risk-stratify her?*
- 2. *What diagnostic testing data help to risk-stratify her?*
- 3. *Should she be admitted?*
- *4. What if she was 25?*

WHAT WE ARE GOING TO COVER

- DEFINITION – WHAT IT IS, WHAT IT ISN'T
- AETIOLOGY, INCIDENCE
- WHAT DO I NEED TO DO WHEN I SEE THE PATIENT ACUTELY ?
- WHEN DO I NEED TO BE WORRIED IN A YOUNG PERSON ?

SYNCOPE

- "..A SYMPTOM COMPLEX THAT IS COMPOSED OF A BRIEF LOSS OF CONSCIOUSNESS ASSOCIATED WITH AN INABILITY TO MAINTAIN POSTURAL TONE THAT SPONTANEOUSLY AND COMPLETELY RESOLVES WITHOUT MEDICAL INTERVENTION"
- IT IS DISTINCT FROM VERTIGO, SEIZURES, COMA, STATES OF ALTERED CONSCIOUSNESS

AETIOLOGY

- **CARDIAC: OBSTRUCTION TO OUTFLOW**
  - Aortic stenosis
  - Hypertrophic cardiomyopathy
  - Pulmonary embolus
- **CARDIAC: ARRYTHMIAS**
  - Sustained ventricular tachycardia
  - Sick-sinus syndrome
  - 2nd and 3rd degree AV block
  - Other electrophysiological abnormalities, e.g. pacing-induced infranodal block; sinus node recovery time > 3 seconds; H-V interval > 100m
- **NONCARDIAC**
  - Reflex-mediated vasovagal ('drop attack') – neurocardiogenic/neurally mediated; situational (micturition, defecation, cough)
  - Orthostatic hypotension
  - Drug-induced
  - Carotid sinus hypersensitivity
  - VBI

SYNCOPE

- 1-1.5% ED VISITS ANNUALLY
- 6% HOSPITAL ADMISSIONS
- IN USA, MORE THAN 2 BILLION DOLLARS A YEAR SPENT ON HOSPITALISATION OF PATIENTS WITH SYNCOPE
- INITIAL EVALUATION ONLY HAS DIAGNOSTIC RATE 20-50%
- EVEN WITH EXTENSIVE INVESTIGATION, 15-30% REMAIN UNDIAGNOSED

THEREFORE, ROLE OF PRIMARY DOCTOR IS

- IDENTIFY THE IMMEDIATELY LIFE-THREATENING CAUSES, E.G. ARRYTHMIAS, PE, AORTIC DISSECTION OR ANEURYSM RUPTURE, SAH, ACUTE CORONARY SYNDROME, OCCULT HEMORRHAGE
- RISK STRATIFY TO IDENTIFY THOSE WHO MAY BENEFIT FROM INPATIENT ASSESSMENT, THOSE WHO CAN BE INVESTIGATED AS AN OUTPATIENT AND THOSE WHO NEED NO FURTHER INVESTIGATION
- DEFINITIVE DIAGNOSIS IS NOT NECESSARY AND MAY BE HARMFUL BY CAUSING 'PREMATURE CLOSURE'

EVIDENCE EXAMINED TO ANSWER THREE QUESTIONS

- 1. *What history and physical examination data help to risk-stratify patients with syncope ?*
- 2. *What diagnostic testing data help to risk-stratify patients with syncope ?*
- 3. *Who should be admitted after an episode of syncope of unclear cause ?*

RECOMMENDATIONS

- *LEVEL A:* Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e. based on Class I or overwhelming Class II studies
- *LEVEL B:* …may identify strategy or range of management strategies that reflect moderate clinical certainty (i.e. based on Class II studies that directly address the issue, decision analysis… or strong consensus of ..Class III studies.
- *LEVEL C:* Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus

LITERATURE CLASSIFICATION

Design /Class	**Therapy**	**Diagnosis**	**Prognosis**
I	Randomized, controlled trials or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
II	Nonrandomised trial	Retrospective observational	Retrospective cohort; Case control
III	Case series Case report Other (consensus, review)	Case series Case report Other (consensus. Review)	Case series Case report Other (consensus, review)

1. What history and physical examination data help to risk-stratify patients with syncope?

- ***LEVEL A:*** Use history or physical examination findings consistent with heart failure to help identify patients at higher risk of an adverse outcome
- ***LEVEL B:***

1. Consider old age, structural heart disease, or a history of coronary artery disease as risk factors for adverse outcome
2. Consider younger patients (<35) with syncope that is non-exertional, without history or signs of cardiovascular disease, a family history of sudden death, and without co-morbidities to be at low risk of adverse events

- ***LEVEL C:*** None specified

HISTORY AND EXAM FACTORS THAT INCREASE RISK

- AGE
- ABNORMAL ECG
- NO PRODROME
- SIGNS OR SYMPTOMS HEART DISEASE
- VASOACTIVE DRUGS: Antihypertensives, Vasodilators for angina, erectile dysfunction, antiarrythmics, diuretics, CNS agents, QT prolongers

PEARLS

- Mild brief tonic-clonic activity may accompany syncope of any aetiology but tongue-biting unusual
- Prolonged confusion unusual
- Trauma may occur as a result of falling, complicating picture
- Absent or brief prodrome makes arrythmia more likely
- When checking for orthostatic hypotension, presence or absence of symptoms more important than actual degree of drop (may be present in up to 40% asymptomatic patients over age 70 and 23% <60))
- Eyewitness accounts may be useful
- Family history of sudden death may be useful in young (see later)
- Persistent hypoperfusion or hypotension suggest another diagnosis
- Murmurs should suggest further investigation, e.g. echo
- Beware occult gastrointestinal haemorrhage which can cause syncope from vagal simulation rather than volume loss – you need a good reason for not PRing the syncope patient.

2. What diagnostic testing data help to risk-stratify patients with syncope?

- *LEVEL A:* Obtain a standard 12-lead ECG in patients with syncope
- *LEVEL B:* None specified
- *LEVEL C:* Laboratory testing and advanced investigative testing such as echo cardiography or cranial CT scanning need not be routinely performed unless guided by specific findings in the history or physical examination

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PEARLS

- ECG yield is low (<5%) but noninvasive, inexpensive and useful in picking rare potentially fatal causes in young (see later)
- ?What is an abnormal ECG: nonsinus, new changes, abnormality rhythm or conduction, ventricular hypertrophy, previous infarction (excluding nonspecific ST-T changes)
- Strong suspicion arrythmia should prompt inpatient or ambulatory monitoring
- Blood tests – low yield but one study showed haematocrit <30% a useful predictor in unselected presenters.
- Echo: history or exam suggests structural cardiac disease, abnormal ECG, particularly if aortic stenosis suspected

3. Who should be admitted after an episode of syncope of unclear cause?

- *LEVEL A:* None specified
- *LEVEL B:*

1. Admit patients with syncope and evidence of heart failure or structural disease
2. Admit patients with syncope and other factors that lead to stratifications as high-risk for adverse outcome.

- *LEVEL C:* None specified

HIGH-RISK FACTORS

- OLDER AGE & ASSOCIATED CO-MORBIDITIES (Age is a continuous variable – no specific age)
- ABNORMAL ECG (Acute ischemia, arrythmia, significant conduction abnormalities)
- HCT < 30 (if obtained)
- HISTORY OR PRESENCE HEART FAILURE, CORONARY ARTERY DISEASE, OR STRUCTURAL HEART DISEASE

PEARLS

- Reason for admitting is that risk assessment puts patient at risk of significant arrythmia or sudden death
- Value of short-term admission in preventing adverse outcomes not proven
- Other medical and social problems may impact on decision to admit, as may need for further investigation & treatment

What about the young person, when do I need to be worried?

- ***BRUGADA SYNDROME***
- ***HYPERTROPHIC CARDIOMYOPATHY***
- ***PROLONGED QT***

BRUGADA SYNDROME

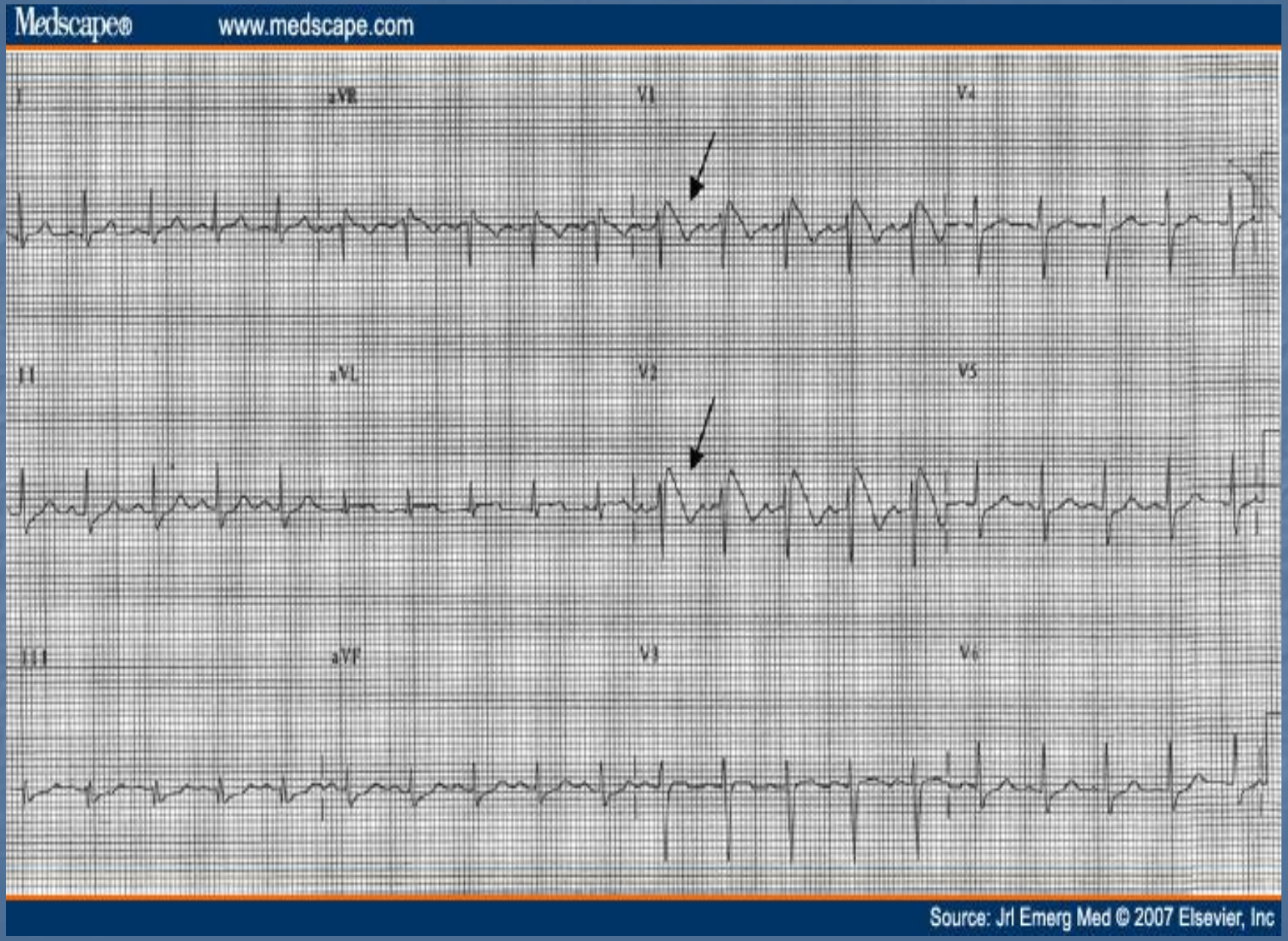
- ECG changes recognised since 1953 but a group of 8 cases described in 1992 by Pedro and Josep Brugada
- Responsible for 4-12% all sudden deaths & 20% deaths in patients with structurally normal hearts
- Incidence 5 per 10,000
- Leading cause death in men <50 in regions world where inherited syndrome is endemic
- 58% cases in literature of Asian origin – known in Philippines as *bangungut* ("to rise and moan in sleep"); in Thailand as *lai tai* ("death during sleep")
- Linked to mutations in SCN5A, gene encoding for alpha subunit of the sodium channel

BRUGADA SYNDROME – ECG FEATURES

- An accentuated J wave appearing principally in right precordial leads (V1-3) & taking form of an ST-segment elevation, often followed by a negative T wave
- Very closely coupled extrasystoles
- Rapid polymorphic VT, which may be indistinguishable from VF
- ST elevation may display a saddleback appearance, and rarely VT may be monomorphic

ECG CHANGES MAY NOT BE PRESENT ON 'ROUTINE ECG' & MAY BE UNMASKED OR ACCENTUATED BY:

- SODIUM CHANNEL BLOCKERS: Flecainide, disopyramide
- FEVER
- VAGOTONIC AGENTS
- ALPHA AGONISTS
- BETA-BLOCERS
- TRICYCLICS
- ANTIHISTAMINES
- COCAINE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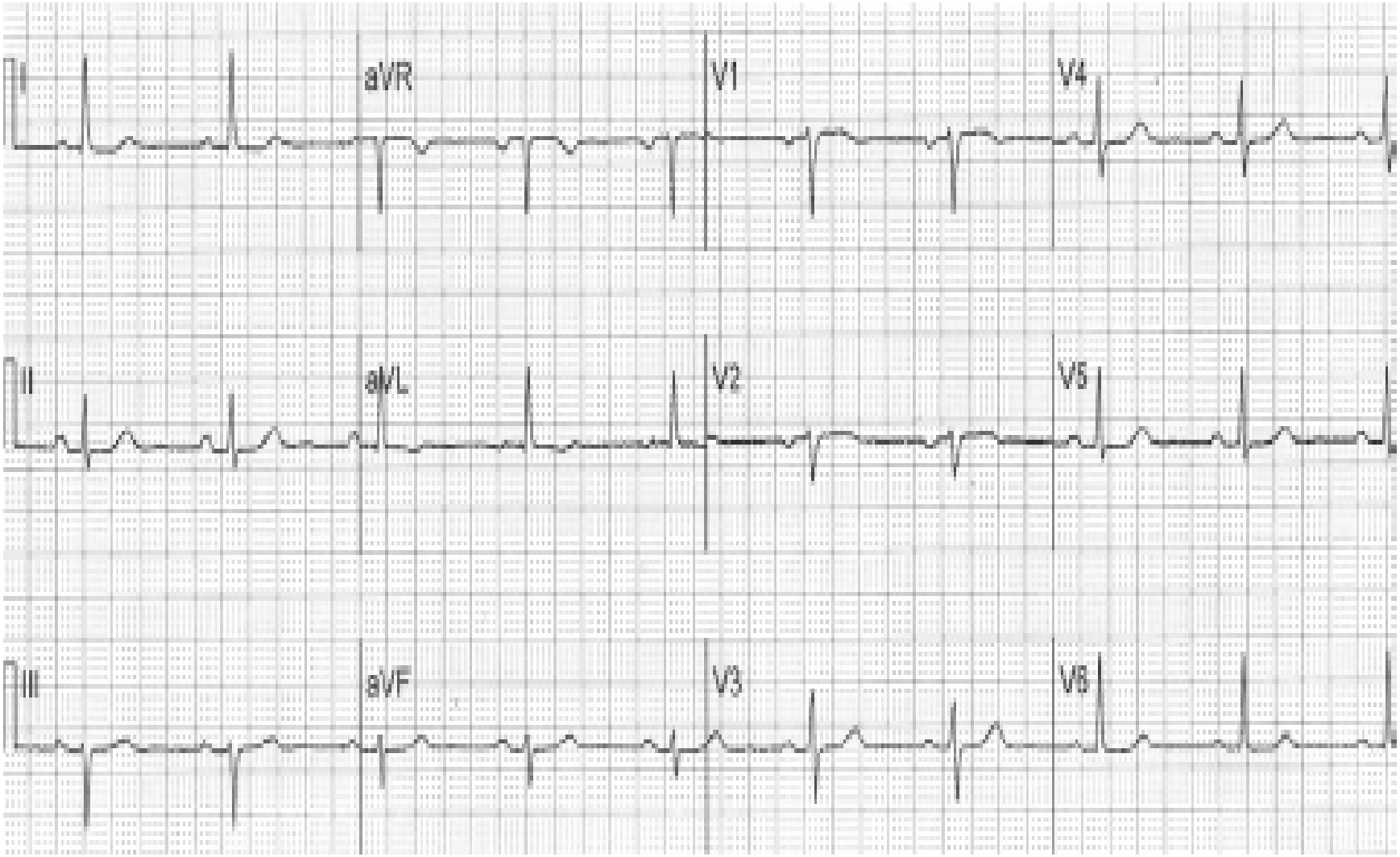


OTHER FEATURES OF BRUGADA

- Patients presenting with aborted sudden death have 69% risk recurrence
- Syncope & spontaneously appearing ECG abnormalities have 19% risk
- Those with changes only after provocation have minimal risk sudden death
- Autosomal dominant
- Mechanisms: failure sodium channel to express; reduced current due to shift in voltage & time dependence of sodium channel current activation, inactivation or reactivation; reduced contribution of sodium current during early phases of action potential resulting from accelerated inactivation – premature inactivation noted at higher temperatures

BRUGADA - MANAGEMENT

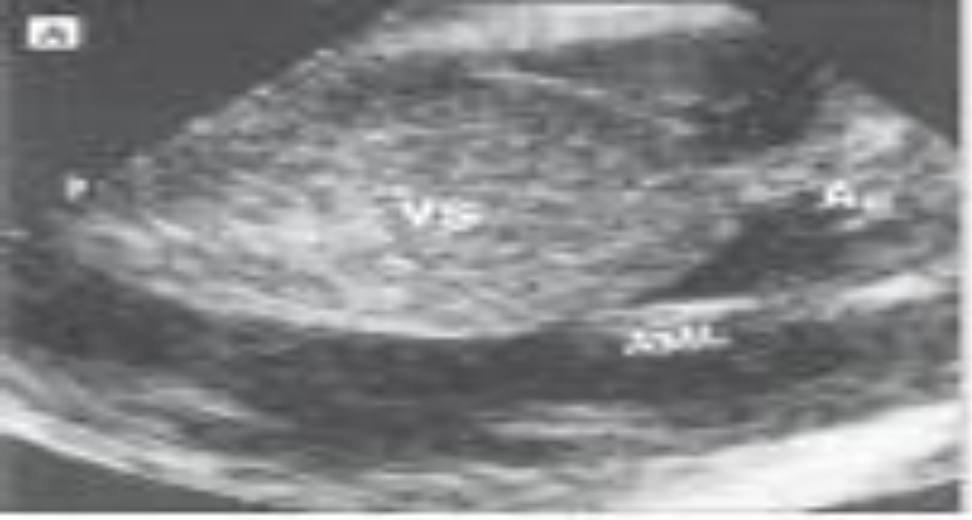
- IMPLANTED DEFIBRILLATOR – ONLY PROVEN EFFECTIVE TREATMENT
- DRUGS – some evidence for Quinidine (blocking transient outward current); new phosphodiesterase III inhibitor, *Cilostazol* (normalises ST by reducing sodium current secondary to increase in HR and by augmenting calcium channel current)

HYPERTROPHIC CARDIOMYOPATHY

- PREVALENCE 1:500 – MOST COMMON GENETIC CARDIOVASCULAR DISEASE
- INCLUDES OBSTRUCTIVE & NONOBSTRUCTIVE (75%) FORMS
- AUTOSOMAL DOMINANT, CAUSED BY MUTATIONS IN 1 OF 10 GENES, EACH ENCODING PROTEINS OF CARDIAC SARCOMERE
- HETEROGENOUS IN CLINICAL EXPRESSION, NATURAL HISTORY AND PROGNOSIS
- MOST COMMON CAUSE OF SUDDEN DEATH IN YOUNG (INCLUDING COMPETETIVE ATHLETES)
- OVERALL, ANNUAL MORTALITY 1% & IN MOST CONFERS LITTLE MORBIDITY OR DECREASE IN LIFE-EXPECTANCY
- SUBSETS WITH HIGHER MORBIDITY/MORTALITY LINKED TO SUDDEN DEATH, PROGRESSIVE HEART FAILURE, ATRIAL FIBRILLATION WITH EMBOLIC STROKE
- REMODELLING WITH SPONTANEOUS APPEARANCE OF HYPERTROPHY MAY NOT APPEAR UNTIL ADOLESCENCE OR EVEN LATER

HCM - DIAGNOSIS

- *ECHOCARDIOGRAPHY*: HYPERTROPHIED BUT NONDILATED LV, IN ABSENCE OF OTHER CARDIAC OR SYSTEMIC DISEASE (E.G. HYPERTENSION OR AORTIC STENOSIS) CAPABLE OF PRODUCING MAGNITUDE OF HYPERTROPHY EVIDENT
- MAY BE SUSPECTED BECAUSE OF HEART MURMUR, POSITIVE FAMILY HISTORY, NEW SYMPTOMS, ABNORMAL ECG
- CLINICAL SIGNS (MURMUR, BIFID PULSE) MAY BE LIMITED TO SUBGROUPS WITH OUTFLOW OBSTRUCTION
- LVH CAN APPEAR AT ANY AGE AND INCREASE OR DECREASE DYNAMICALLY THROUGHOUT LIFE.
- LVH IS HETEROGENOUS WITH DIFFUSE OR FOCAL AND ASYMMETRIC PATTERNS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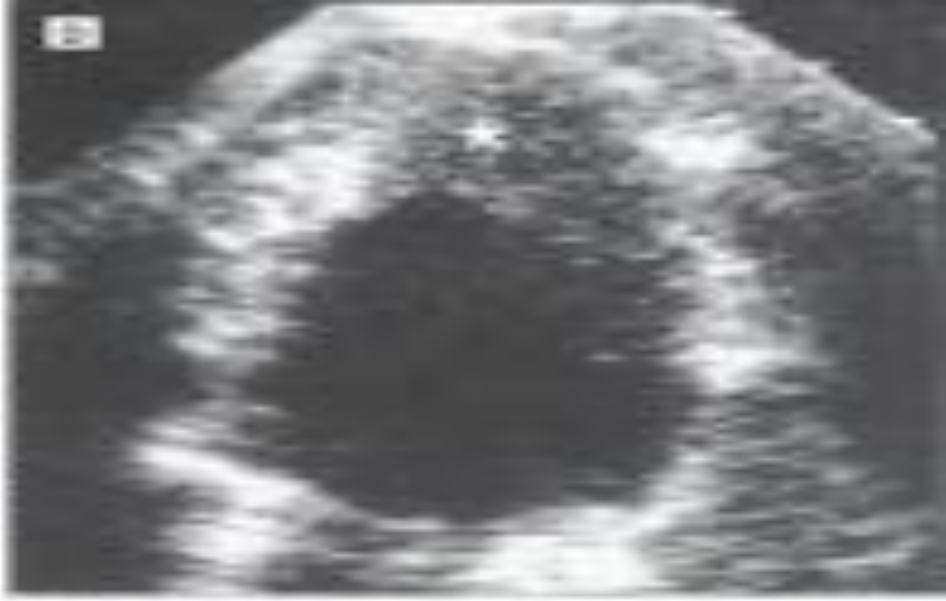
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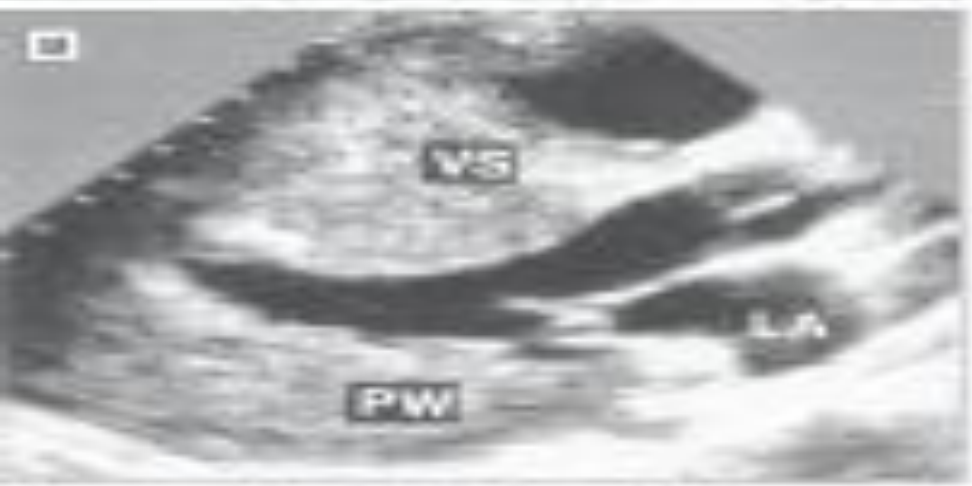
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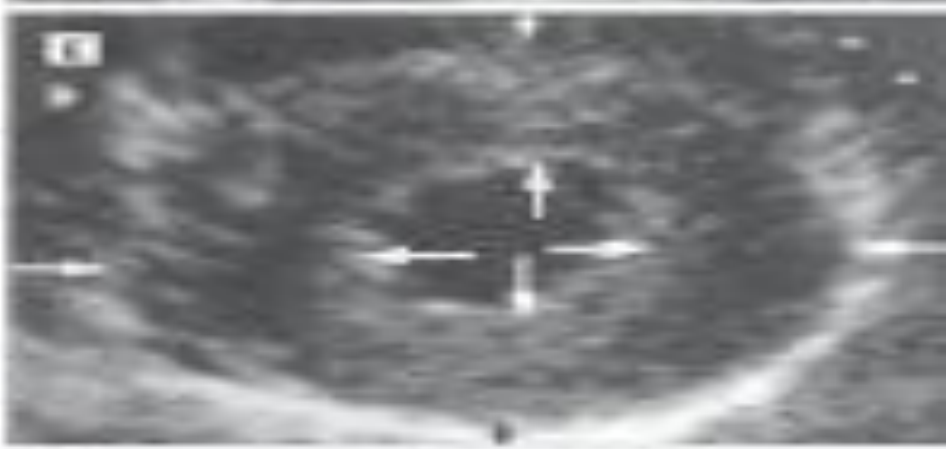
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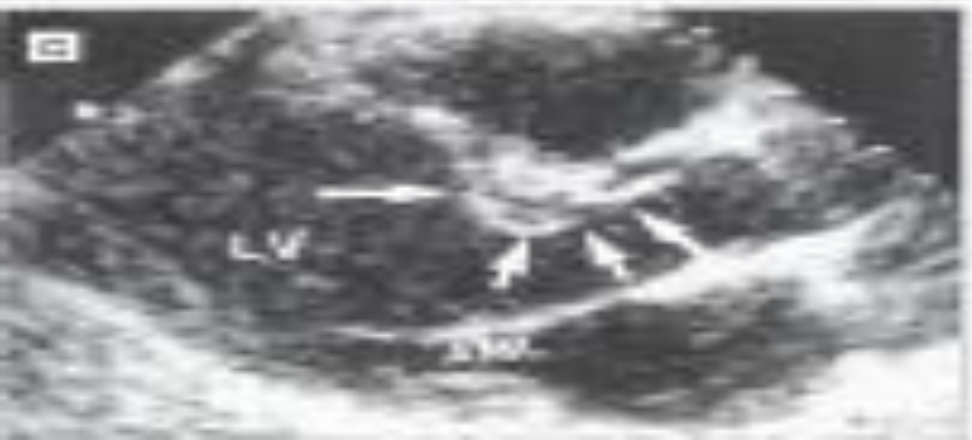
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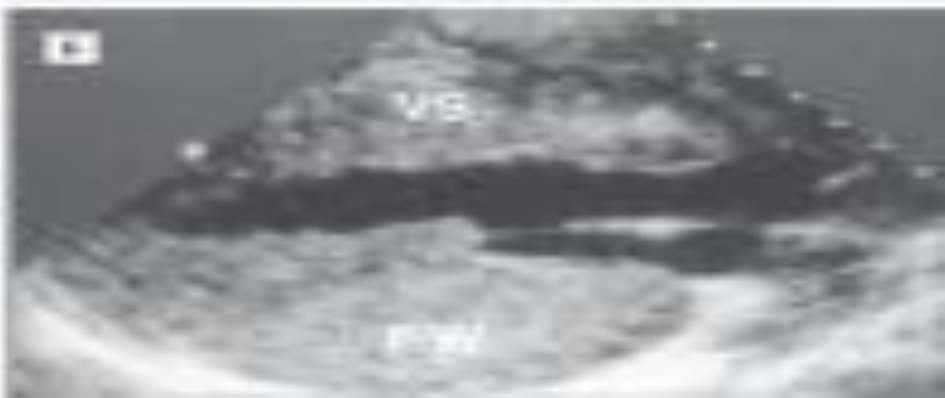
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HCM – CLINICAL COURSE

- MAY PRESENT AT ANY AGE
- MANY MAY HAVE MINIMAL OR NO SYMPTOMS
- ADVERSE PATHWAYS:

1. HIGH RISK OF SUDDEN DEATH
2. CONGESTIVE HEART FAILURE WITH EXERTIONAL DYSPNOEA AND FUNCTIONAL DISABILITY, USUALLY IN THE PRESENCE OF PRESERVED LV FUNCTION
3. ATRIAL FIBRILLATION, POSSIBLY WITH EMBOLIC STROKE

HCM – SUDDEN DEATH

- MAY BE THE INITIAL MANIFESTATION
- MORE COMMON IN YOUNG BUT CAN OCCUR AT ANY AGE
- MAY OCCUR DURING EXERTION
- 10-20% HCM POPULATION SEEM TO BE AT RISK
- RISK FACTORS:
  - Prior cardiac arrest or sustained VT
  - Family history of HCM related sudden death, particularly if close relatives or multiple
  - Syncope or near-syncope – particularly if exertional or recurrent, or in young, when documented arryhthmia-related or clearly unrelated to neurocardiogenic mechanisms
  - Multiple and repetitive or prolonged bursts of nonsustained VT on ambulatory ECG recordings
  - Hypotensive blood pressure response to exercise, particularly in those < 50 years
  - Extreme LVH with maximum wall thickness >/= 30mm, particularly in young
  - Certain gene mutations, e.g. some Beta-myosin heavy chain & troponin T mutations

HCM - MANAGEMENT

- *PREVENTION*
  - Little evidence for value of drugs in preventing sudden death from arrythmias
  - Implanted Cardioverter-defibrillator
  - Avoid competitive sports
- *ATRIAL FIBRILLATION*
  - Common – 20-25% HCM patients
  - Associated embolic stroke, progressive heart failure
  - Drugs – rate control (Beta-blockers, Verapamil), reducing occurrences (amiodarone), AV nodal ablation with pacing, anticoagulation
- *HEART FAILURE*
  - May occur independent of LV contractility or outflow obstruction
  - Progress variable – only 15-20% progress to Classes III-IV
  - Symptoms seem to be result of diastolic dysfunction
  - Chest pain a common symptom (with normal coronary arteries)
- *DRUGS*
  - Beta-blockers and verapamil (disopyramide if severe outflow obstruction)
  - Diuretics, vasodilators, digoxin
  - If outflow obstruction present, consider prophylactic antibiotics where bacteremia a risk
- *SURGERY*
  - Severe symptomatic outflow obstruction (peak gradient >/= 50mmHg) unresponsive drugs
  - Ventricular septal myotomy-myectomy
  - Heart transplant
- *ALTERNATIVES*
  - Chronic dual-chamber pacing
  - Alcohol septal ablation

LONG QT SYNDROME

- CONGENITAL DISORDER CHARACTERISED BY A PROLONGATION OF THE QT INTERVAL ON ECG AND A PROPENSITY TO VENTRICULAR TACHYARRHYTHMIAS, WHICH MAY LEAD TO SYNCOPE, CARDIAC ARREST OR SUDDEN DEATH

QT INTERVAL

- MEASURED FROM BEGINNING QRS TO END OF T WAVE
- REPRESENTS DURATION OF ACTIVATION AND RECOVERY OF THE VENTRICULAR MYOCARDIUM
- QT INTERVALS CORRECTED FOR HEART RATE (QTc) LONGER THAN 0.45 SECONDS ARE GENERALLY ABNORMAL BUT IN FEMALES UP TO 0.46 ALLOWED
- BAZETT EQUATION USED TO CALCULATE: QTc = QT/ROOT OF R-R
- LONGEST QT USUALLY OBSERVED IN RIGHT PRECORDIAL LEADS

PATHOPHYSIOLOGY

- QT REPRESENTS DURATION OF ACTIVATION & RECOVERY OF VENTRICULAR MYOCARDIUM
- PROLONGED RECOVERY INCREASES LIKELIHOOD DISPERSING REFRACTORINESS
- IN LQTS, TRANSMURAL DISPERSION OF REPOLARISATION (TDR) INCREASES AND CREATES FUNCTIONAL SUBSTRATE FOR TRANSMURAL REENTRY
- QT PROLONGATION CAN LEAD TO POLYMORPHIC VT OR TORSADES DE POINTES WHICH MAY TRIGGER VF
- TORSADES DE POINTES IS THOUGHT TO BE TRIGGERED BY REACTIVATION OF Ca CHANNELS, REACTIVATION OF DELAYED Na CURRENT OR DECREASED OUTWARD K CURRENT THAT RESULTS IN EARLY AFTERDEPOLARISATION (EAD).
- TDR NOT ONLY SERVES AS FUNCTIONAL REENTRY SUBSTRATE TO MAINTAIN TORSADES BUT ALSO INCREASES THE LIKELIHOOD OF EAD, THE TRIGGERING EVENT, BY PROLONGING THE TIME WINDOW FOR Ca CHANNELS TO REMAIN OPEN

GENETICS

- EIGHT GENES IDENTIFIED, VARIOUSLY AFFECTING SODIUM, CALCIUM AND POTASSIUM CHANNELS
- MAIN SYNDROMES:
  - Romano-Ward – 6 types, autosomal dominant
  - Jervell and Lang-Nielsen – autosomal recessive, deafness
  - Andersen
  - Timothy

LQTS

- ARRHYTHMIAS MAY OCCUR SPONTANEOUSLY OR BE PRECIPITATED BY ADRENERGIC STIMULI, E.G EXERCISE, EMOTION, COLD WATER, LOUND NOISE
- 10-15% GENE CARRIERS HAVE NORMAL QTc
- INCIDENCE 1:10,000
- THOUGHT CAUSE 4000 DEATHS/YR IN USA
- CUMULATIVE MORTALITY 6% BY AGE 40
- SUDDEN DEATH MAY OCCUR WITH FIRST SYNCOPE IN 30%
- NO RACE RELATIONSHIP
- NEW CASE DIAGNOSED MORE COMMONLY IN FEMALES (60-70%)
- CORRELATION OF CARDIAC EVENTS WITH MENSES & POST-PARTUM
- USUALLY DIAGNOSED AFTER A SYNCOPE OR CARDIAC ARREST, OR A FAMILY MEMBER DIES
- LQ3 USUALLY HAVE EVENTS DURING SLEEP
- DRUGS MAY ALSO CAUSE LQTS AND PRECIPITATE TORSADES – GENETIC OR NONGENETIC
- APART FROM DRUGS, OTHER DISEASES, E.G. MYOCARDIAL INFARCTION OR CEREBRAL HEMORRHAGE MAY ALSO PROLONG QT

EXAMPLES OF DRUGS THAT PROLONG QT WITH RISK OF TORSADES

- Amiodarone
- Chloroquine
- Chlorpromazine
- Cisapride
- Clarithromycin
- Disopyramide
- Domperidone
- Droperidol
- Erythromycin
- Haloperidol
- Methadone
- Pentamidine
- Procainamide
- Quinidine
- Sotalol
- Thioridiazine

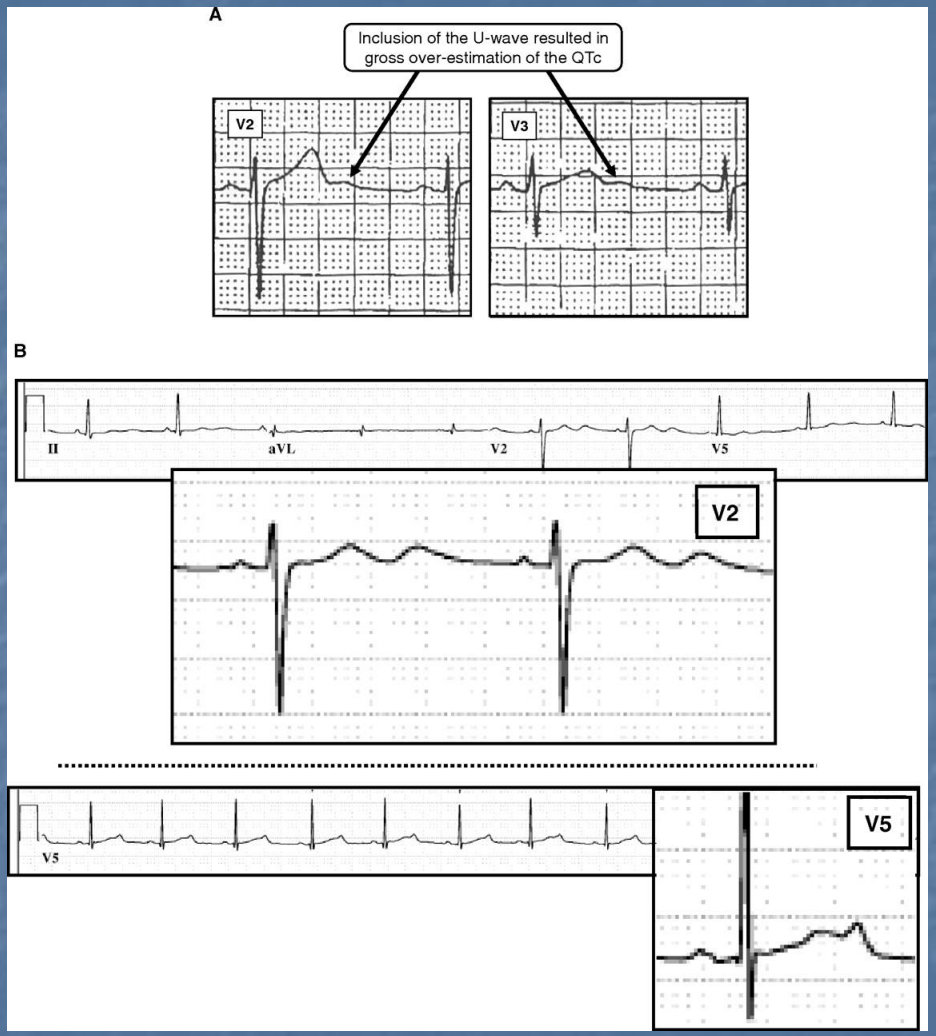
OTHERS WITH POSSIBLE RISK

- AMANTADINE
- AZITHROMYCIN
- CLOAZAPINE
- FLECAINIDE
- INDAPAMIDE
- LEVOFLOXACIN
- LITHIUM
- MOXIFLOXACIN
- OCTREOTIDE
- ONDANSETRON
- QUETIAPINE
- RISPERIDONE
- ROXITHROMYCIN
- TAMOXIFEN
- VENLAFAXINE

LQTS - MANAGEMENT

- CORRECT POTASSIUM AND MAGNESIUM DEFFICIENCIES
- BETA-BLOCKERS – EFFECTIVE IN PREVENTING CARDIAC EVENTS IN 70%
- ICDs – ABORTED CARDIAC ARREST OR RECURRENT CARDIAC EVENTS NOT RESPONSIVE BETA-BLOCKERS OR STRONG FAMILY HISTORY SUDDEN DEATH
- PACEMAKERS MAY ALSO BE USEFUL TO TREAT BRADYCARDIAS AND DCREASE REPOLARISATION HETEROGENEITY, REDUCING RISK TORSADES
- STELLECTOMY
- AVOID EXERCISE, SWIMMING
- PATIENT AND FAMILY EDUCATION
- 40% PATIENT DIAGNOSED WITH LQTS MAY NOT HAVE IT

Erroneous U-wave inclusion in the QTc calculation



Taggart, N. W. et al. Circulation 2007;115:2613-2620

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TREATMENT OF TORSADES DE POINTS

- DEFIBRILLATE
- MAGNESIUM
- OVERDRIVE PACING
- CORRECT POTASSIUM AND MAGNESIUM

SUMMARY – YOUNG PATIENTS WITH SYNCOPE

- *BRUGADA SYNDROME* – refer for urgent EPS and ICD placement
- *HYPERTROPHIC CARDIOMYOPATHY* – refer for urgent echocardiography and definitive diagnosis
- *PROLONGED QT SYNDROME* – Suspect torsades de pointes as cause of syncope