Syncope and high risk

- Cardiac conditions not the most common cause, but associated with highest mortality
- Up to 50% of all cases presenting with syncope have a cardiac cause—especially with increasing age

Initial assessment should focus on:
- Is there evidence of risk associated?
- Should this patient be admitted?
- Of secondary importance is determining:
  - The cause
  - Appropriate treatment

Conflicts and Sources

- No conflicts to declare
- Thanks to Professor Kenny for sharing slides
- 2018 ESC Guidelines for the diagnosis and management of syncope: Unexplained syncope in patients at high risk of SCD
- 2018 ESC Guidelines on Syncope – Michele Brignole & Angel Moya EHJ Doi:10.1093/eurheartj/ehy037
- Vincent PROBST, MD, PhD, l’institut du thorax, Nantes, France

Reducing incidence of syncope and potential SCD

- Appropriate therapy
  - Medication
    - largely unhelpful (except some hereditary conditions)
    - May be pro-arrhythmic
  - ICD
    - Low risk of device failure (? 1 per 300,000)
    - Significant risk of complications
      - Implant complications
      - Device rust
      - Lead and/or device revision
    - Surgical (or percutaneous) intervention
      - Aortic stenosis, HCM has a definite role
      - Reversal of cardiac ischaemia may have a role
      - Left cervical sympathetic denervation
  - Identification of at-risk patients

Features that suggest increased risk

- History of IHD or heart failure
- Occurs during exertion (but not post exercise)
- Signs of heart failure or structural cardiac disease
- Abnormal ECG
- Occurs without warning, > 65 years
- Family history of hereditary cardiac condition or sudden cardiac death
- New or unexplained SOB (? PE)
Hypertrophic Cardiomyopathy
- Left ventricular hypertrophy (concentric or asymmetric) in the absence of physiological cause
- HCM or HOCM
  - 25% have obstruction
  - Genetic cause - Gene mutation in > 1 in 500 population
  - Familial transmission in 90% of cases
  - Sporadic in 10%
  - 14 genes associated
    - Majority sarcomeric protein genes
    - Metabolic causes
      - Fabry disease
      - AMP Kinase
      - Danon disease
    - Genetic test identifies cause approx 60% of affected cases

Syncope in HCM
- Mechanical obstruction
  - Systolic anterior motion of AMVL causes gradient across LVOT
  - Conditions of stress or exercise increase myocardial oxygen demand, increase gradient and reduce output (and coronary flow)
  - Sometimes precipitated by post-prandial state or vasodilators (alcohol, GTN, phosphodiesterase inhibitors)

Syncope in HCM - Arrhythmia
- Conditions for arrhythmia in HCM
  - Pro-arrhythmic substrate
    - Myofibre disarray
    - Fibrosis
  - Trigger
    - Relative ischaemia
      - Exercise (microvascular disease, mismatch supply and demand, LVOT obstruction)
      - Arrhythmia (paroxysmal A Fib, SVT)
    - Emotion

Arrhythmia and sudden death in HCM
- Overall 1% per year
- Higher rates in probands
- Lower rates in family screening services
- 9 - 50% of all sudden cardiac deaths aged 1-35 years
- Are high-risk patients identifiable?
- Is sudden death preventable?

ESC-hosted: http://www.doc2ibo.com/hcm/webHCM.html
Familial DCM and arrhythmia

- Idiopathic DCM is familial in perhaps 25% of cases
- 100 different genetic causes, including sarcomeric mutations
  - Current gene panels offered are 28-96 genes
  - Cost (in Oxford) £1020 for index case
- Gene mutation identified 5-30%
  - Titin mutations may account for 25%
- Risk stratification as per SCD HeFT
  - NYHA Class II-III symptoms
  - LV ejection fraction ≤ 35%
- Only approx 20% of this population receive ICD therapy within 5 years of implant
- Recent studies (subgroup analysis DANISH, Sanjay Prasad et al this week’s JACC Imaging) suggest presence of LGE (+/- Extent or location) the most reliable predictor of arrhythmia in non-ischaemic DCM

Special cases with DCM

- Higher arrhythmic risk with near-normal LV EF in
  - Lamin A/C disease (association of conduction disease and premature SCD +/- PAF)
  - Myotonic dystrophy
    - Presence of atrial arrhythmia (sustained atrial tachycardia, flutter or fibrillation)
    - Severe ECG abnormality (PR ≥ 240 msec, QRS ≥ 120 msec, 2nd or 3rd degree A-V block)
    - Prolongation of A-H and H-V interval on EPS
  - Muscular dystrophies
  - LV variant ARVC

Arrhythmogenic (right ventricular) cardiomyopathy (ARVC/D)

- Myocardial cell death and replacement with fat and fibrosis (causing arrhythmia and heart failure RV>LV)
- Inherited in > 50%
- Prevalence unknown – estimated at 1 in 5000 but may be more frequent
- Wide variation is penetrance and disease severity
- Risk of sudden death again ~ 1%/year
- 5 disease-causing desmosomal mutations known, accounting for 30-40% clinically-diagnosed patients
- Diagnosis relies on TFC (originally 1994, revised 2010) – no gold standard for diagnosis

Sudden death in ARVC

- Initially thought to be 2% per year (pre-ICD)
- Family studies suggest overall incidence <<1% per year
- Risk stratification in ARVC
  - In USA clinical diagnosis usually considered indication for ICD
  - In Germany documented ventricular arrhythmia often treated pharmacologically
  - Clinical risk factors
Clinical risk factors ARVC

- Major morphological abnormalities of RV
  - Severe dilatation +/- systolic impairment +/- aneurysm
  - Significant LV involvement
  - Documented ventricular arrhythmia (especially if poorly tolerated haemodynamically)
  - Unexplained syncope
  - Strong family history SCD

- Pharmacological therapy
  - B-blockers no anti-arrhythmic benefit
  - Sotalol / amiodarone some benefit

- EPS and ablation – usually only post-ICD
  - ICD may have higher complication rate in those with thinned and fibrosed RV (apex part of ‘triangle of dysplasia’)

Long QT syndrome

- Prevalence may be 1 in 2000, Autosomal dominant
- Not detectable after death (unless DNA)
- Diagnosis
  - Abnormal T-wave morphology +/- QT prolongation
  - Inappropriate bradycardia for age
  - Inappropriate QT response to exercise (brisk standing)
  - Circumstances of arrhythmia may alter between types
    - LQT1 (SCN5A) – events occur during exercise/emotion
    - LQT2 (KCNH2) – events occur when startled (telephone, alarm)
    - LQT3 (KCNE1) – events occur at rest / during sleep
  - LQT1 patients more likely to be symptomatic (40%) but self-limiting syncope more common
  - SCD risk higher in LQT3, LQT2

LQT ECG

Brugada syndrome

- True prevalence unknown
- Ventricular arrhythmia (polymorphic VT) + ST elevation V1-V3
- South-East Asian males
- Events usually at rest/during sleep
- Sodium channel mutation found in 20%
- 4 other genes recently discovered
- Characteristic ECG not always present at rest
  - May be unmasked by infusion of Na-channel inhibitors (Flecainide / Ajmaline)
- Management
  - VT stim
  - ICD
Risk stratification controversial

- Priori et al
  - High risk if:
    - Type 1 (coved pattern) present at rest
    - Syncope

- Brugada brothers
  - EP VT stimulation studies
    - Weak positive predictive value
    - Strong negative predictive value

- Management
  - ICD
  - No Med Rx
  - Quinidine may be effective at reducing arrhythmia (Adjunct to ICD if frequent events)

Other Forms

Due to a lack of studies examining unexplained syncope in other forms of inheritable arrhythmic diseases such as catecholaminergic polymorphic VT, early repolarization syndrome, and short QT syndrome, this Task Force is unable to give specific recommendations for the investigation and treatment of unexplained syncope.

Catecholaminergic Polymorphic VT

- Syncope or sudden death during exercise / emotion
- ? 1 in 10,000 population
- Normal / near-normal resting ECG
- Bi-directional ectopy / VT when HR > 110/min
- 2 gene mutations identified (Ryanodine 2 receptor, Calsequestrin)
  - Disease of calcium handling

- Management
  - B-blockers (Nadolol may be most effective, very difficult to source in Ireland)
  - Avoid precipitant
  - ICD if events on-treatment (often high discharge rate)
  - Left Cervical Sympathetic Denervation
In summary

- Cardiac conditions not the most common cause, but associated with highest mortality
- Up to 16% of all cases presenting with syncope have a cardiac cause (especially with increasing age)
- Initial assessment should focus on:
  - Is there evidence of risk associated?
  - Should this patient be admitted?
- Unexplained syncope in individuals with underlying cardiac conditions often indicates increased mortality risk
  - Should prompt consideration of ICD implant
  - ILR now included on syncope guidelines as reasonable option for individuals in whom features of underlying condition do not otherwise suggest ICD indicated