2011년 순환기관련학회 춘계통합학술대회

Noninvasive Predictors of Sudden Cardiac Death

영남대학교 의과대학 순환기내과학교실
신 동 구

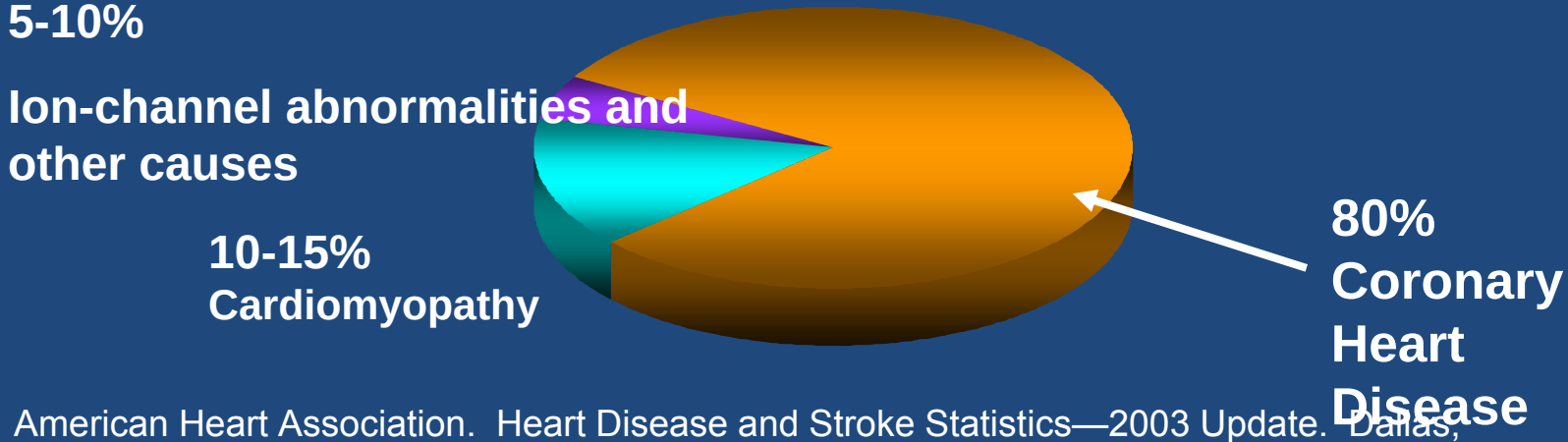
Diseases associated with SCD

- Previous SCD event
- Prior episode of ventricular tachyarrhythmia
- Previous myocardial infarction
- Coronary artery disease (CAD)
- Heart failure
- Hypertrophic cardiomyopathy
- Genetic diseases including LQTS or Brugada…
- A combination of these risk factors

Coronary Heart Disease

- An estimated 13 million people had CHD in the U.S. in 2002.[1]
- Sudden death was the first manifestation of coronary heart disease in 50% of men and 63% of women. [1]
- CHD accounts for at least 80% of sudden cardiac deaths in Western cultures.[3]

Etiology of Sudden Cardiac Death[2,3]

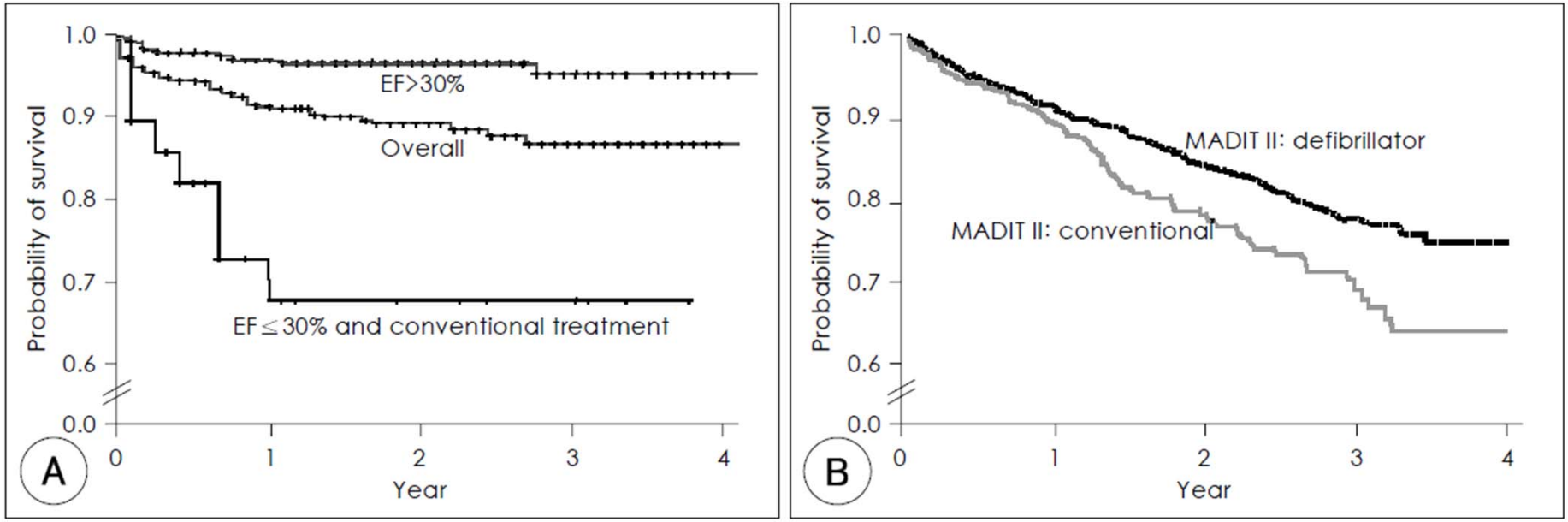


[1] American Heart Association. Heart Disease and Stroke Statistics—2003 Update. Dallas, Tex.: American Heart Association; 2002.

[2] Adapted from Heikki et al. N Engl J Med, Vol. 345, No. 20, 2001.

[3] Myerberg RJ. Heart Disease, A Textbook of Cardiovascular Medicine. 6th ed. P. 895.

Post-MI Cardiac Mortality in Korean PMI Pts
Comparison with MADIT II pts



Korean Circulation J 2006;36:431-436

Are MADIT II Criteria Suitable for Chinease Patients?

Siu CW et al. J Cardiovascular Electrophyiol 2010; 21:231-235

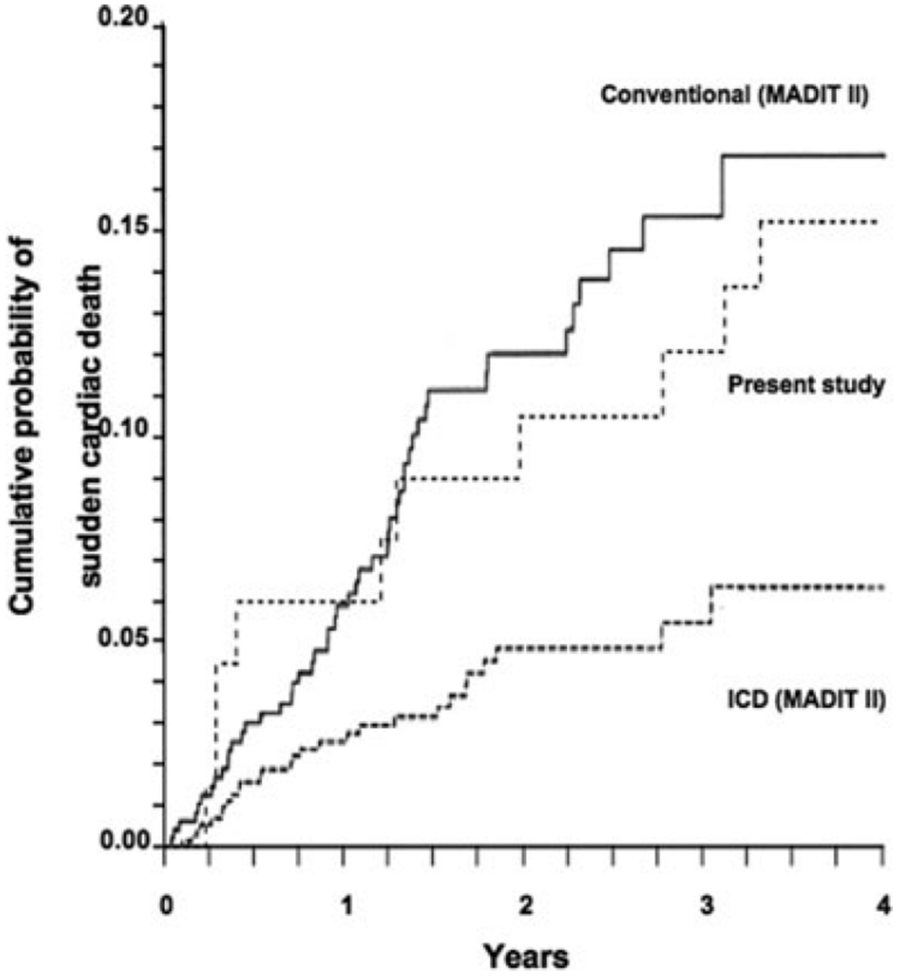
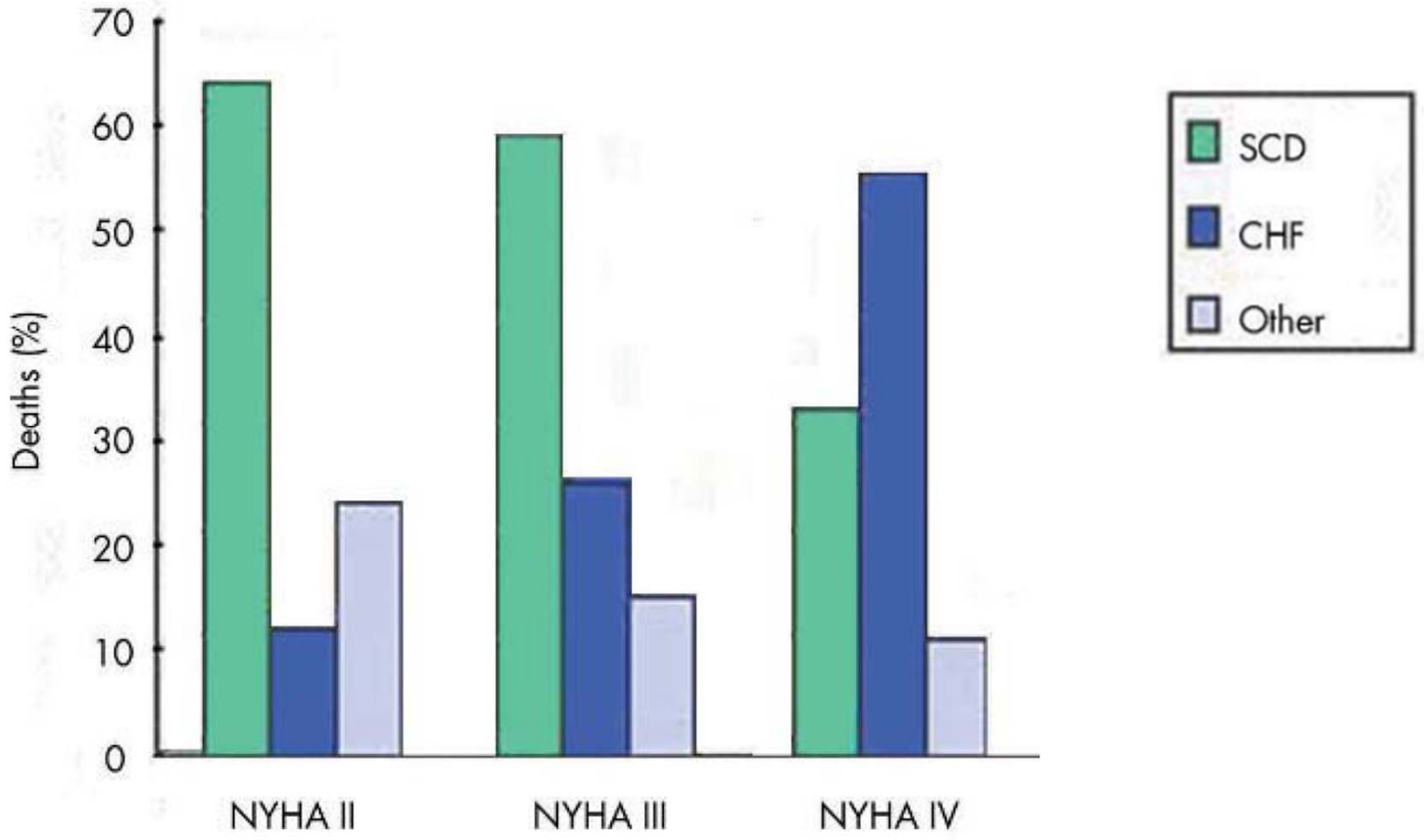


Figure 3. *Kaplan-Meier estimates of the probability of SCD of patients in MADIT-II and the present study.*

Severity of HF and the Mode of Death in the MERIT-HF study

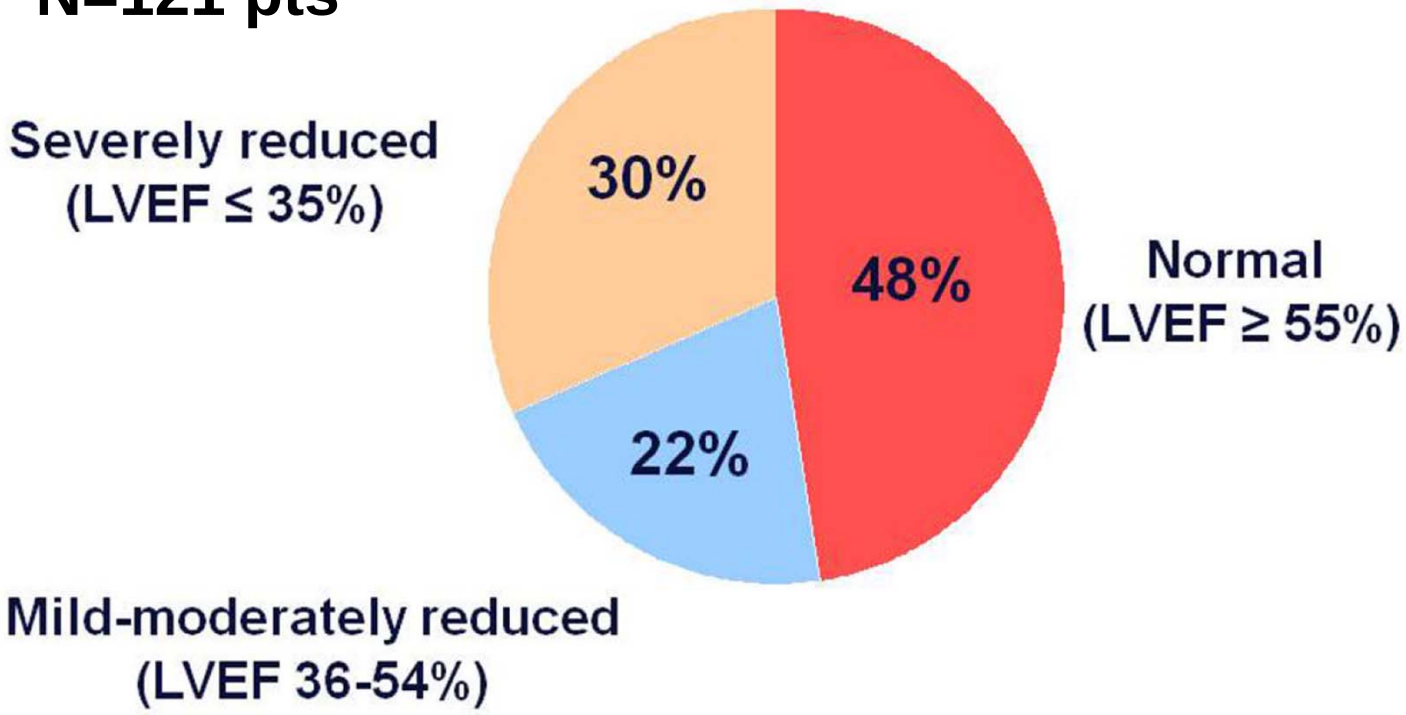


MERIT-HF, metoprolol CR/XL randomized intervention trial in heart failure
Adapted from MERIT-HF Study Group. Lancet 1999;353:2001–7

Contribution of Severe LV systolic Dysfunction to SCD in the General Population

The Need to Go Beyond the LVEF

N=121 pts



Population-Based Analysis of SCD With and Without Left Ventricular Systolic Dysfunction; Two-Year Findings from the Oregon Sudden Unexpected Death Study. J Am Coll Cardiol 2006;47:1161– 6

Implantable Cardioverter-Defibrillators

ICD therapy is indicated in patients with LVEF less than or equal to **35%** due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III.

ICD therapy is indicated in patients with nonischemic DCM who have an LVEF less than or equal to **35%** and who are in NYHA functional Class II or III.

ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less than or equal to **30%**, and are in NYHA functional Class I.

ICD therapy is indicated in patients with nonsustained VT due to prior MI, LVEF less than or equal to 40%, and inducible VF or sustained VT at electrophysiological study.

All primary SCD prevention ICD recommendations apply only to patients who are receiving optimal medical therapy and have reasonable expectation of survival with good functional capacity for more than 1 year.

Phenotypes associated with SCD risk

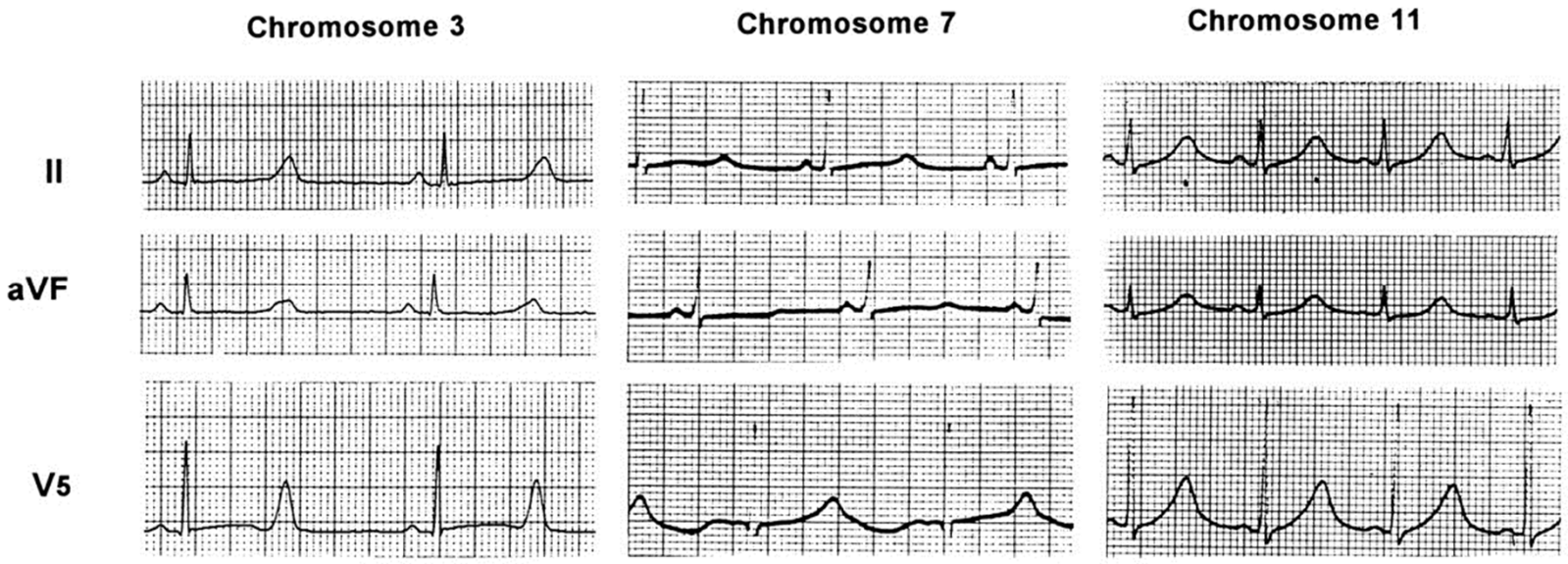
- LV hypertrophy[1]
- Prolonged QTc interval [2,3]
- RCA or left circumflex coronary artery involvement
- Fragmented QRS complex
- Alterations in heart rate
- Low socioeconomic status
- Diabetes
- Gender-specific

1. Haider AW et al. J Am Coll Cardiol 1998;32:1454–1459
2. The Rotterdam study. Straus SM, et al. J Am Coll Cardiol 2006;47:362–367.
3. The Oregon-Sudden Unexpected Death Study. Stecker EC, et al. J Am Coll Cardiol 2006;47:1161–1166.

Assessment of SCD risk: Specific Tests

- Left ventricular ejection fraction
- New York Heart Association class
- Nonsustained ventricular tachycardia
- Microvolt T-wave alternans
- Measures of cardiac autonomic modulation
  - Heart rate variability(HRV)
  - Baroreflex sensitivity(BRS)
  - Heart rate turbulence(HRT)
  - Deceleration capacity of heart rate(DC)
- QT interval, QT dispersion, and QT variability
- Signal-averaged ECG
- Imaging studies
- Genetic testing
- Serum markers
- Electrophysiology study

ECG recordings from leads II, aVF, and V5 in three patients from families with long QT syndrome linked to genetic markers on chromosomes 3, 7, and 11



Moss, A. J. et al. Circulation 1995;92:2929-2934

Genetic Contribution to SCD

Evidence of Familial Aggregation

- The Paris Prospective Study[1]
- The Finnish Genetic Study of Arrhythmic Events[2]
- Friedlander Y, et al.[3]
- Dekker LR, et al.[4]

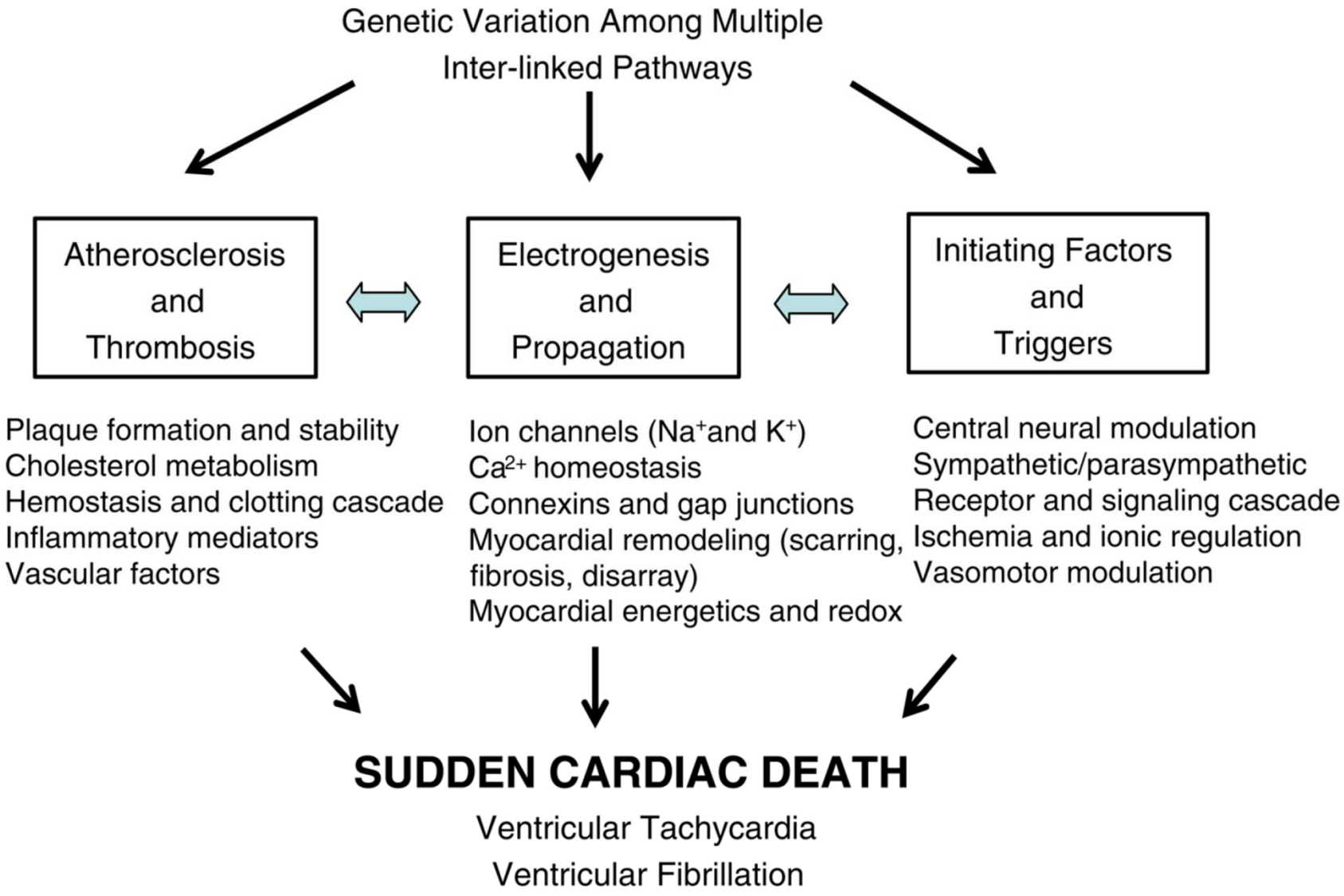
1. Jouven X, et al. Eur Heart J. 2005;26:2142–2147
2. Kaikkonen KS, et al. Circulation 2006;114:1462–1467
3. Family history as a risk factor for primary cardiac arrest. Circulation 1998;97:155–160
4. Familial sudden death is an important risk factor for primary ventricular fibrillation: a case-control study in acute myocardial infarction patients. Circulation 2006;114: 1140–1145

Genetic susceptibility to SCD

- GPC5 SNP that codes for glypican-5
- Cardiac ion channel genes associated with SCD
  2 common intronic variants in KCNQ1 and SCN5A
  - rs2283222 OR 1.36, P=0.0002
  - rs11720524 OR 1.31, P=0.0005

Genetic Susceptibility to SCD

Potential contributors



Biomarkers

- **CRP[1]**

  Men, the highest vs. the lowest quartile (OR 2.78, 95% CI 1.35–5.72)

- **NT-proBNP[2]**

  Women, 2× higher SCD in the highest quartile than in the lowest quartile (RR 2.37, P = 0.05)

- **Markers of membrane stability[3,4]**

  Non-esterified fatty acids, n-3 fatty acids, trans fatty acids

  Increased risk; trans isomer of linoleic acid (trans-18:2) (OR 2.34, 95% CI 1.27 to 4.31)

  Decreased risk with the trans isomer of oleic acid(OR 0.18, 95% CI 0.06–0.54).

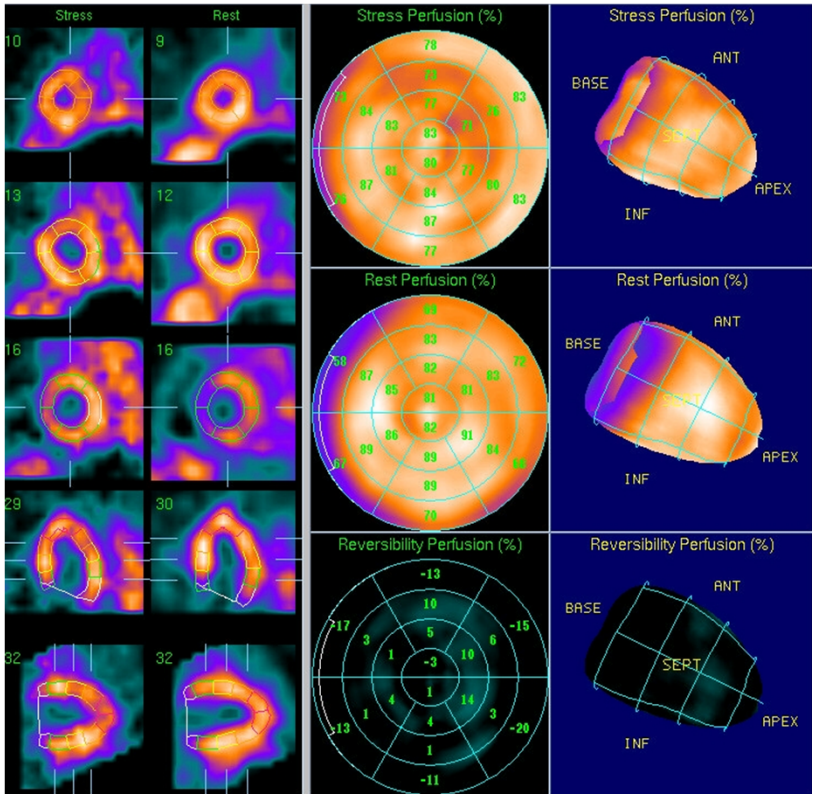
1. Physician's Health Study. Albert CM, et al. Circulation 2002;105:2595–99
2. Nurses' Health Study. Korngold EC, et al. Circulation 2009;119:2868–76
3. Jouven X, et al. Circulation 2001;104:756–761
4. Lemaitre RN, et al. Circulation 2002;105:697–701.

Imaging to Detect Risk of SCD

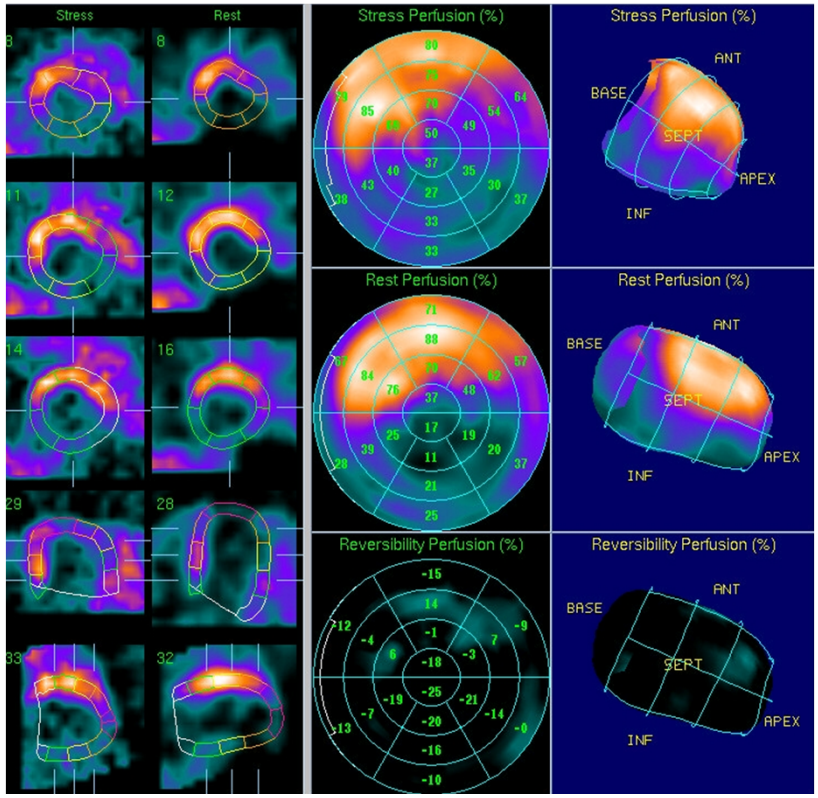
- MRI; Conventional gadolinium-based contrast agent
- MRI;Cardiomyocyte apoptosis imaging with annexin-labeled magneto-fluorescent nanoparticle
- ^{123}I-metaiodobenzyl-guanidine (MIBG) scintigraphy
- [^{11}C]methylquinuclidinyl benzilate ([11C]MQNB)

I^{123}-MIBG finding

Control

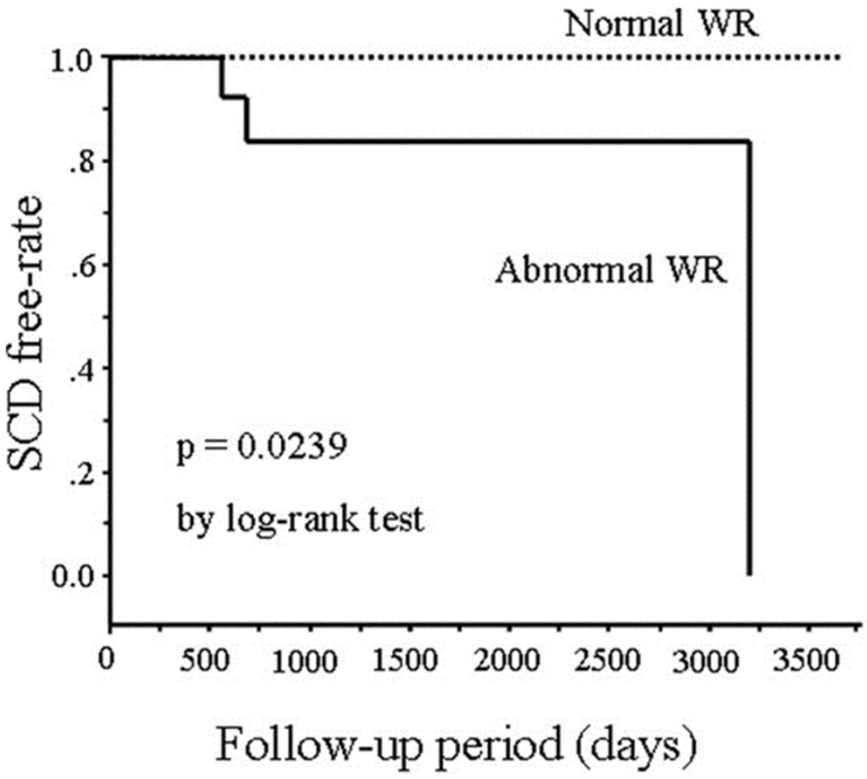


Idiopathic DCM

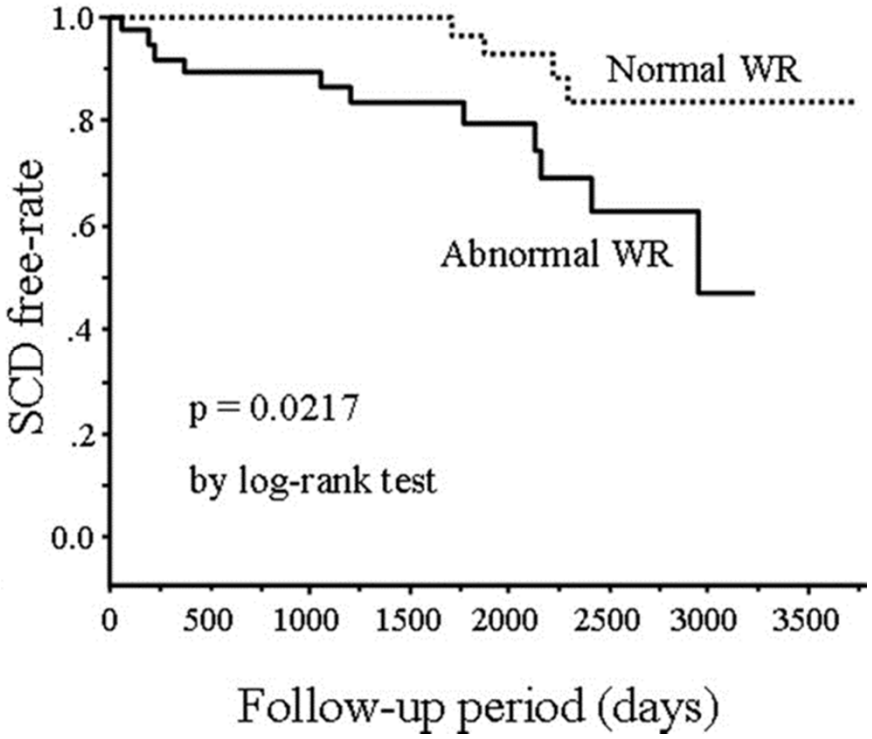


Cardiac 123Iodine-MIBG Imaging Predicts SCD

Kaplan-Meier SCD-Free Curves



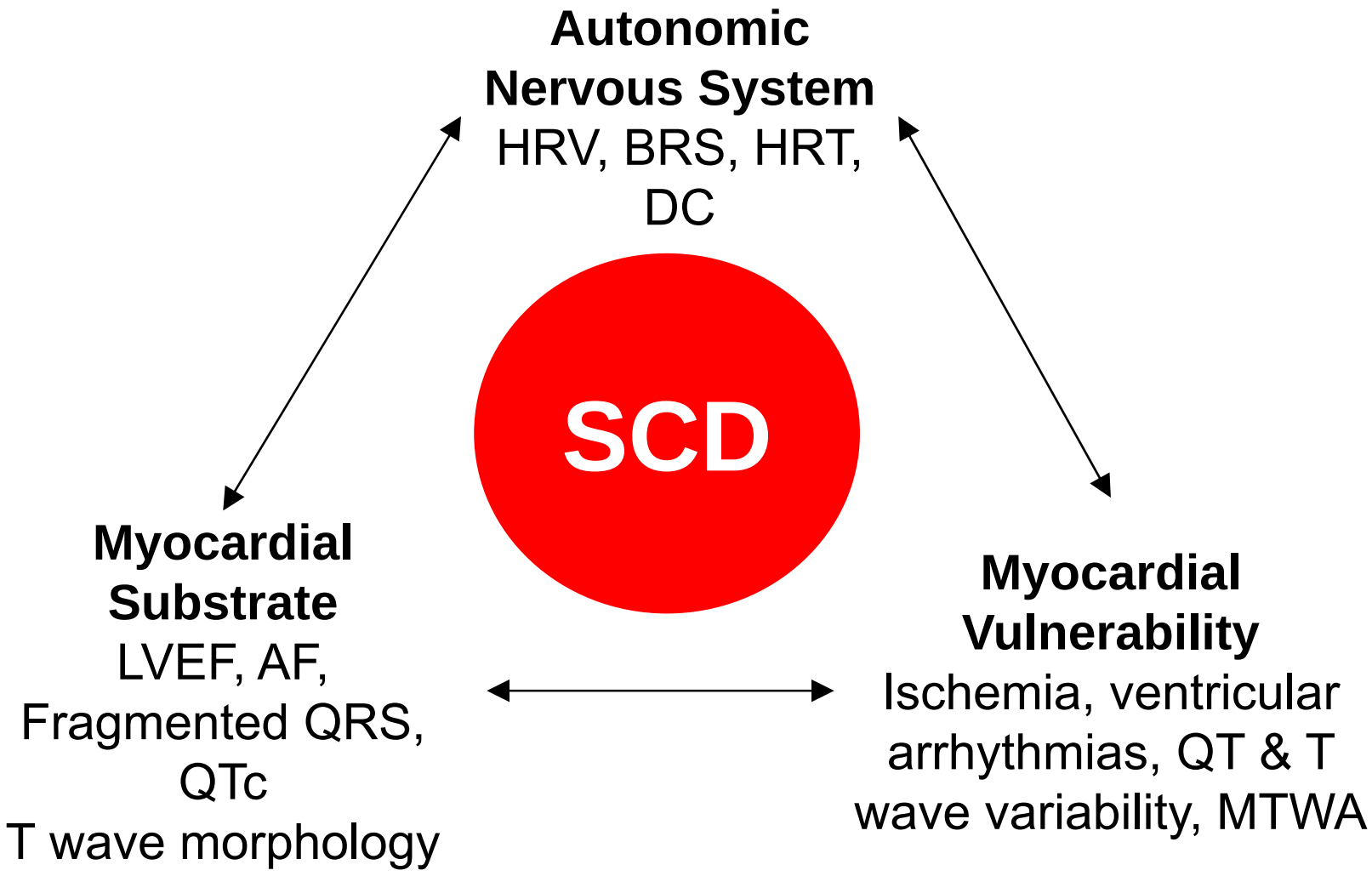
LVEF >35%

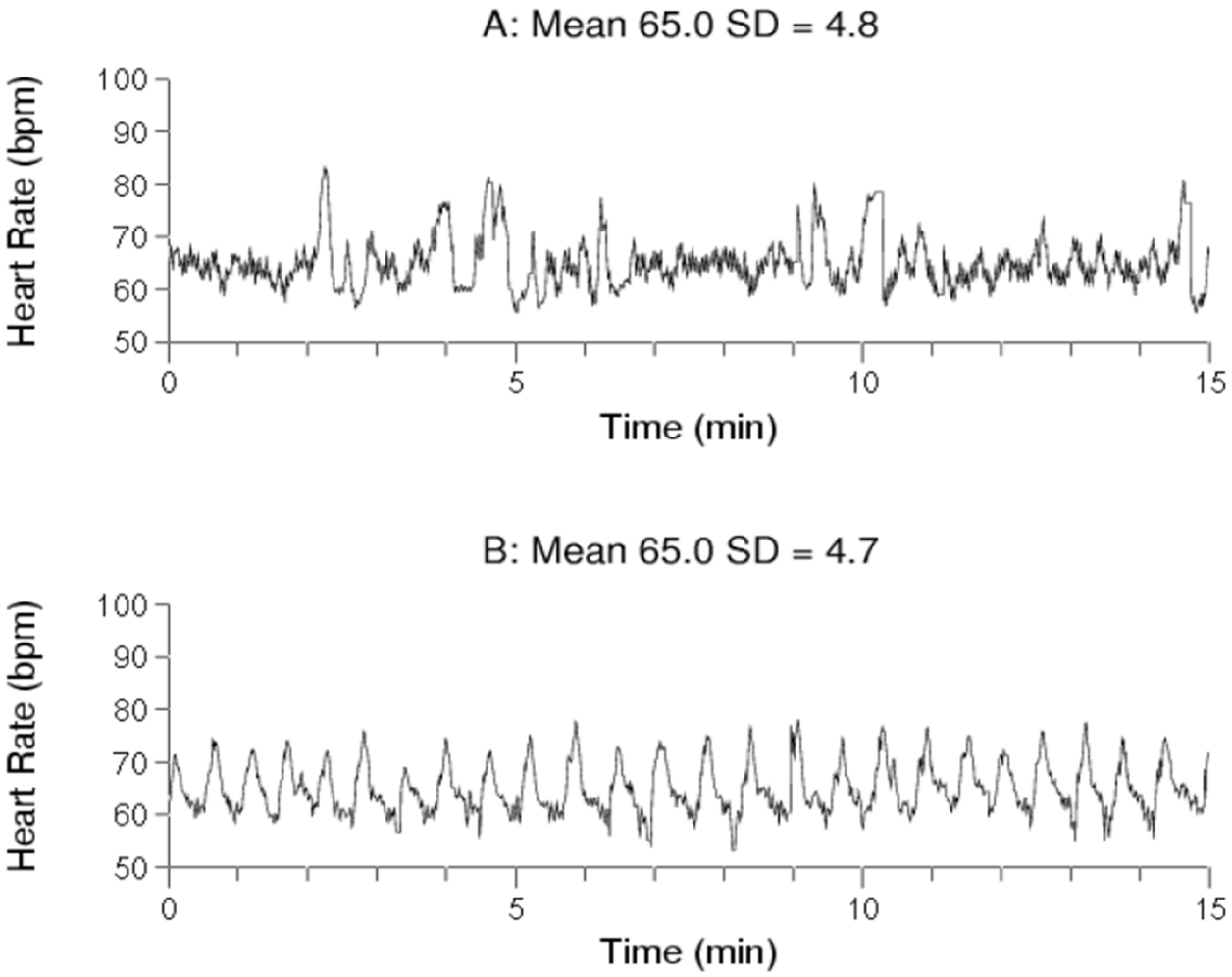


LVEF ≤35%

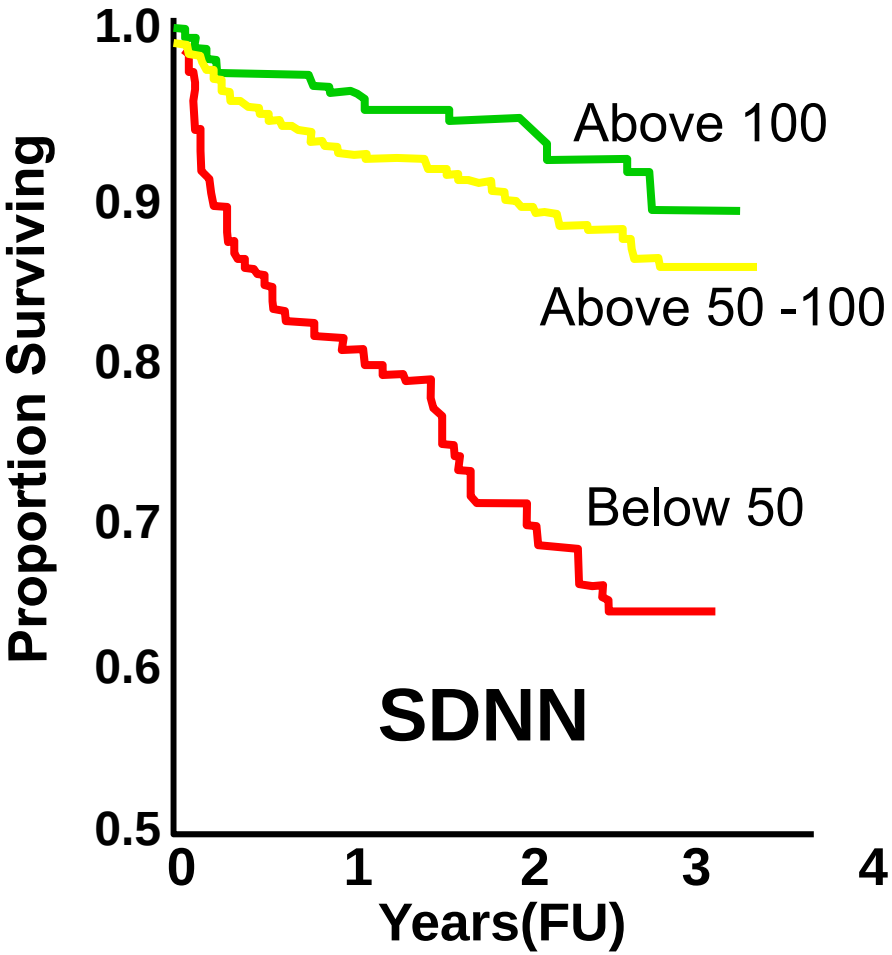
J Am Coll Cardiol 2009;53:426–35

Factors contributing to SCD and respective Holter-derived ECG parameterss




A: Mean 65.0 SD = 4.8
Heart Rate (bpm)
100
90
80
70
60
50
0
5
10
15
Time (min)
B: Mean 65.0 SD = 4.7
Heart Rate (bpm)
100
90
80
70
60
50
0
5
10
15
Time (min)

Heart Rate Variability

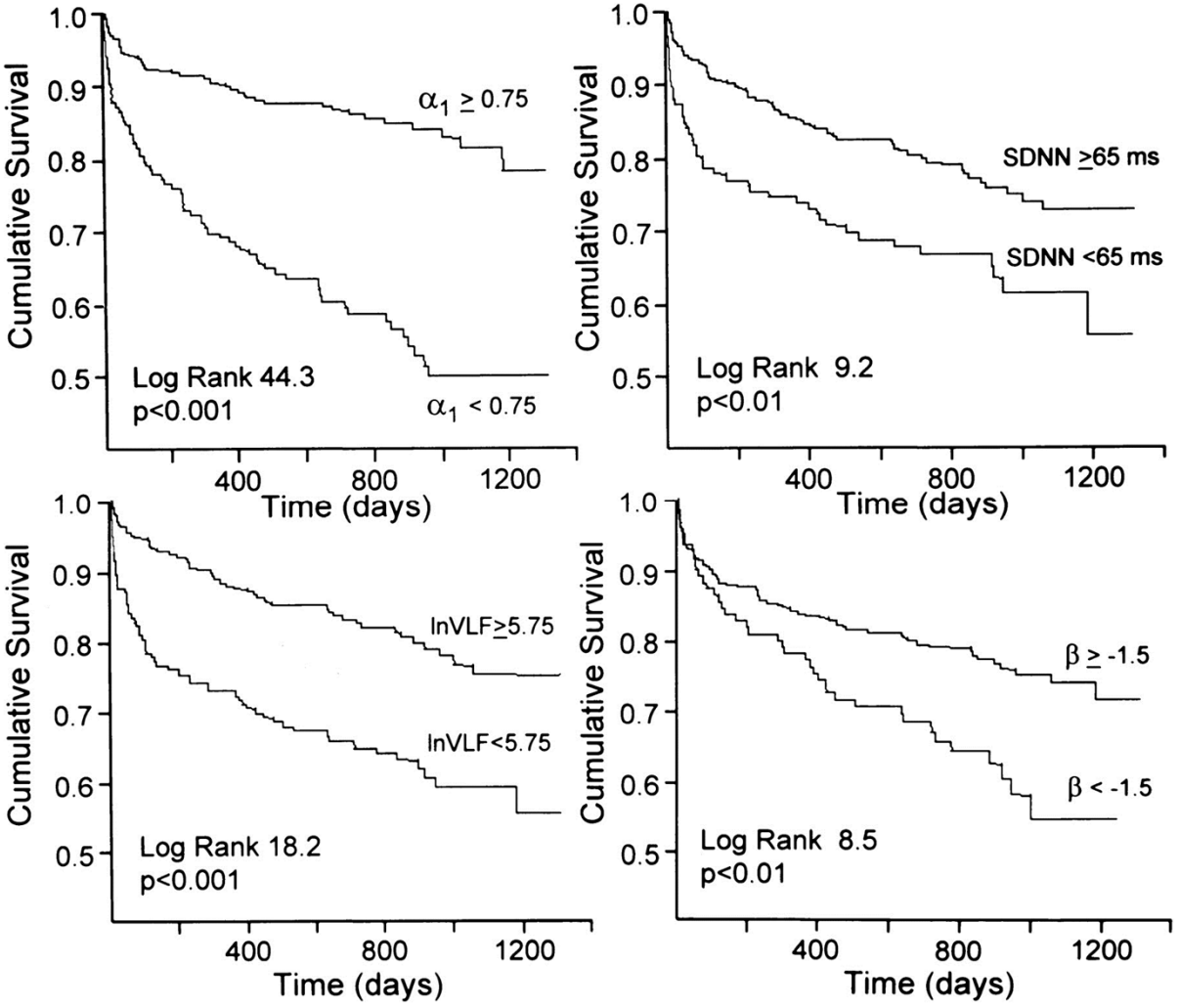


Cumulative survival of patients after MI. Survival of patients stratified according to 24-hour SDNN values into three groups with cutoff points of 50 and 100 ms

***Kleiger et al. Am J Cardiol.* 1987;59:256-262**

Values of HRV measurements are dependent on:

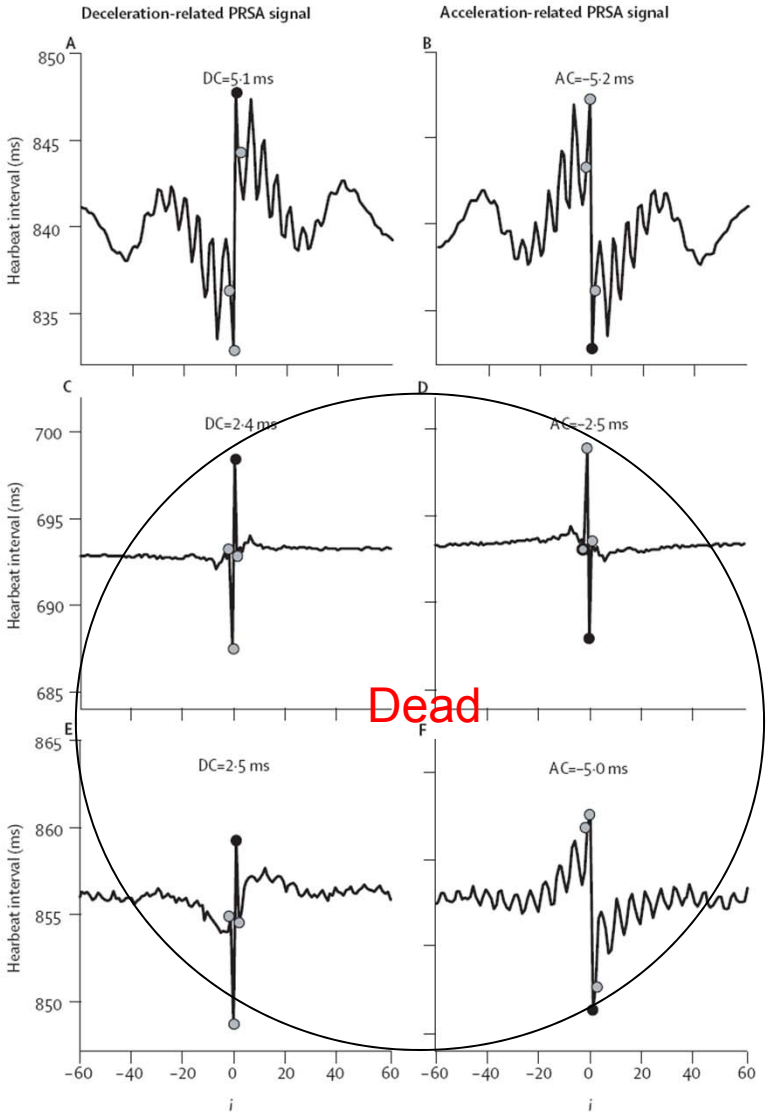
- Data length
- Age
- Physical conditioning
- Activity
- Sleep/wake cycle
- Disease
- Drug effects
- Gender

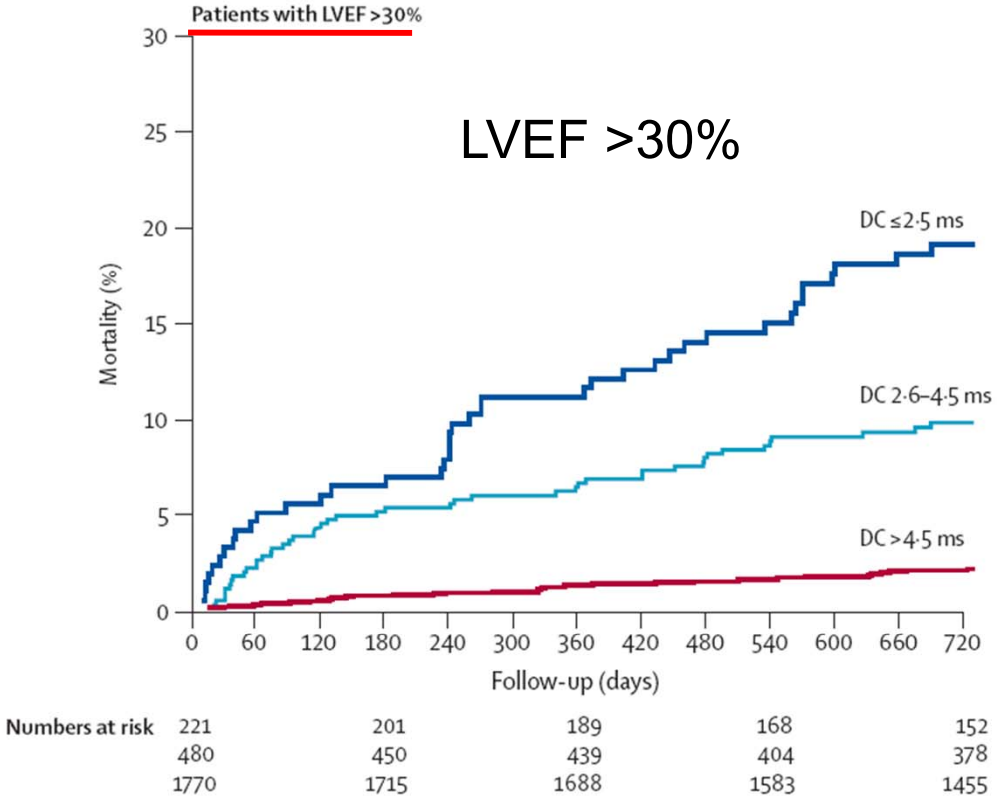


Huikuri, H. V. et al. Circulation 2000;101:47-53

Kaplan-Meier survival curves of patients with a scaling exponent {alpha}1 >=0.75 and <0.75, respectively (top left); patients with SDNN of >=65 and <65 ms, respectively (top right); patients with natural logarith m of very-low-frequency spectral component (ln VLF) of >=5.75 and <5.75, respectively (bottom left); an d scaling exponent {beta} of >=-1.5 and <-1.5 (bottom right)

Deceleration Capacity(DC)



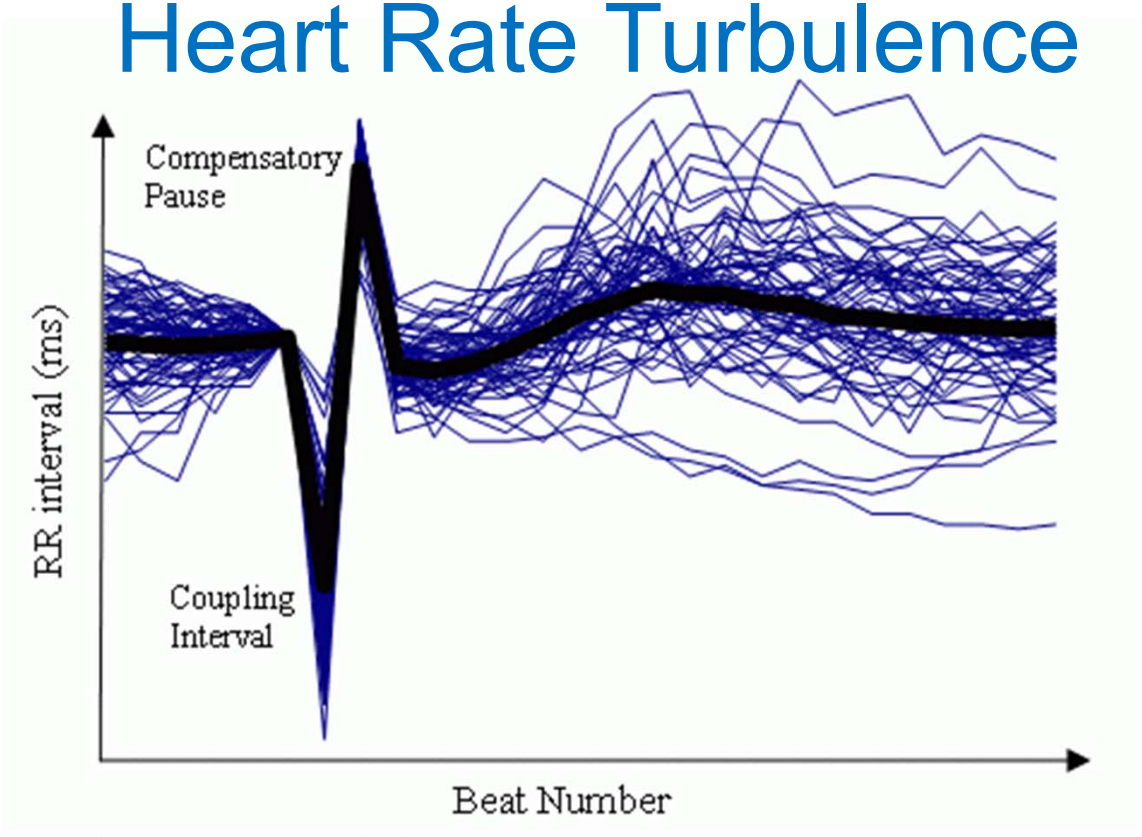


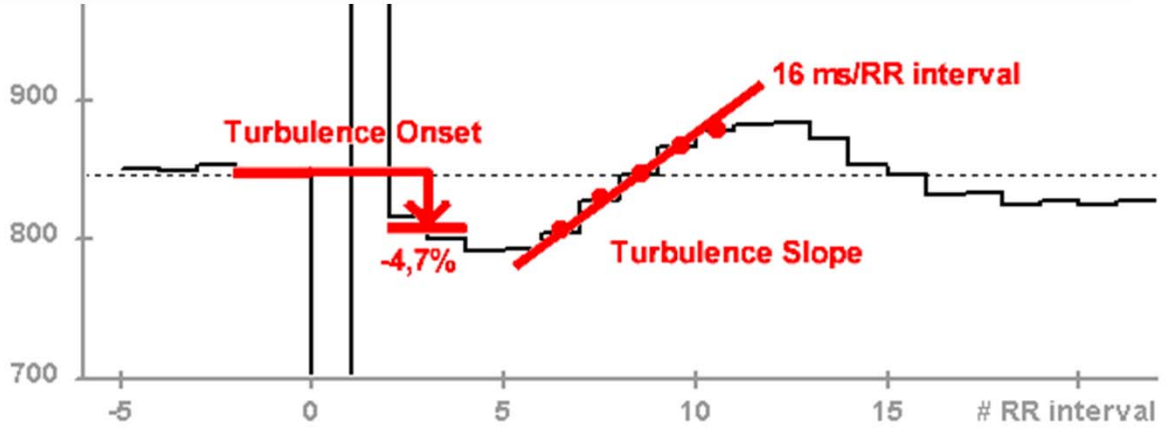
LVEF >30%

Schmidt G et al. Lancet Vol 367, 2006

http://h-r-t.org/prsa/en/

Heart Rate Turbulence

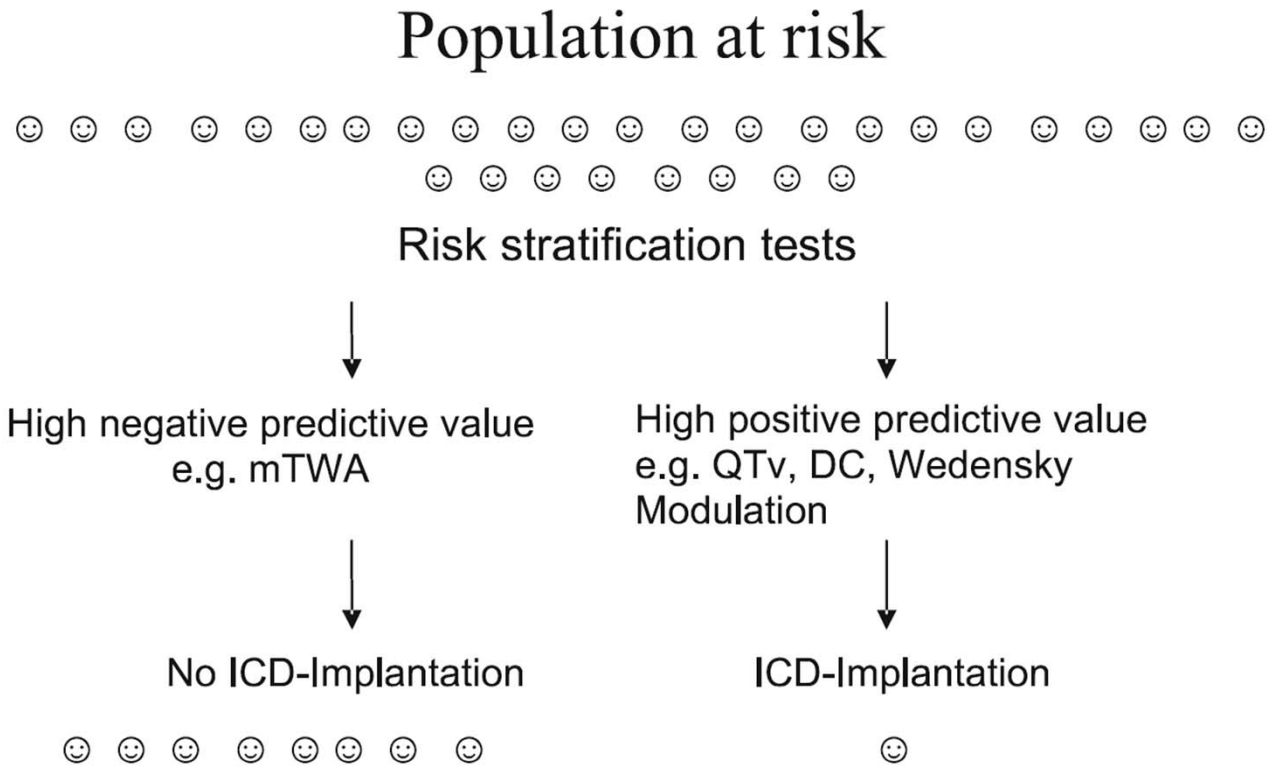




TO > 0 and TS > 2.5 are normal

The Current

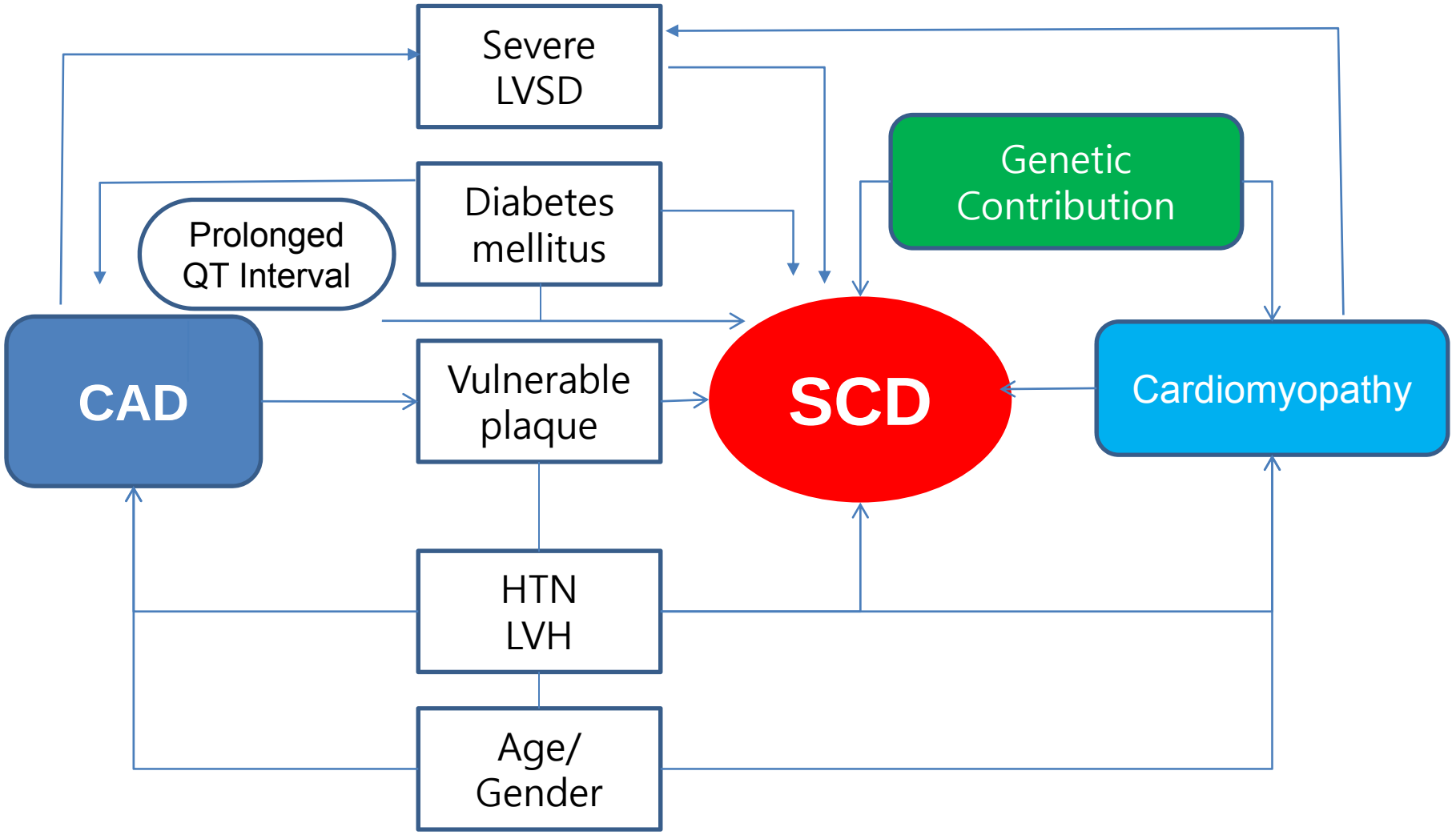
Multi-component Risk Stratification Strategy



DC deceleration capacity, mTWA microvolt T-wave alternans, QTv QT variability

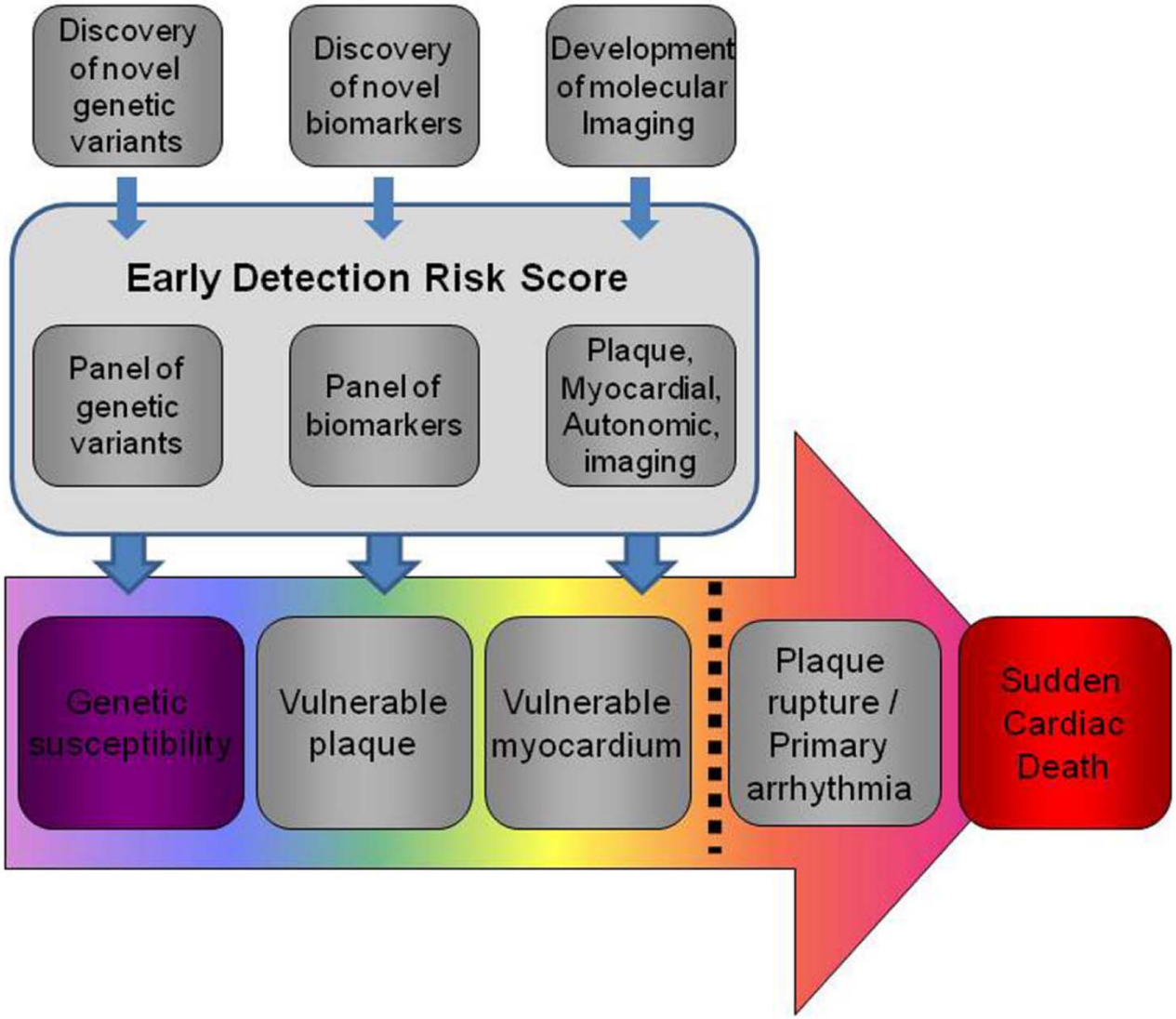
Challenges of Early SCD Risk Prediction

Risk factors associated with SCD in patients with CAD



The Future

Development of an Early Detection Risk Score for SCD



Closing Remark

- To date, no single test reliably predicts arrhythmic risk
- The LVEF is the only major risk factor utilized in clinical practice
- Integration of potential genetic, clinical, molecular and imaging risk predictors
- An integrated and inter-disciplinary approach for identification of early risk predictors
- Unfortunately, we do not have data available yet

경청해주셔서 감사합니다