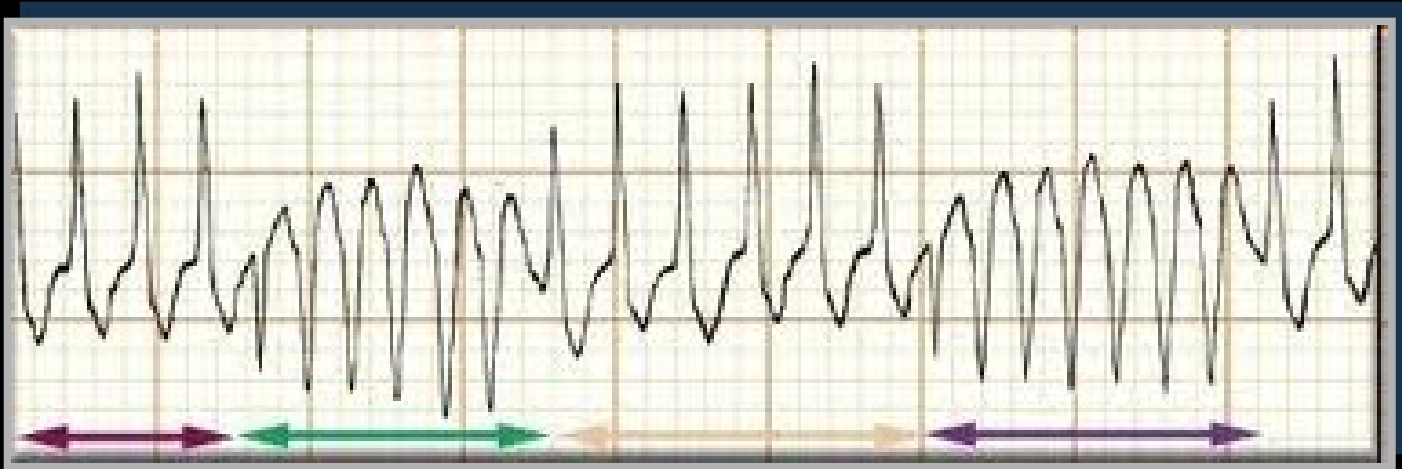


Arrhythmias in women



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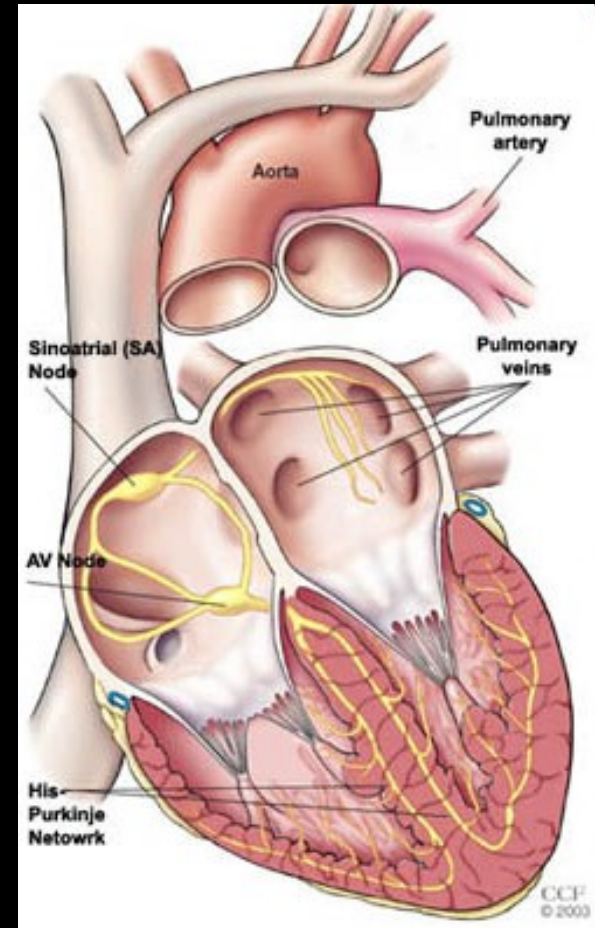
Arrhythmias in women



- There are important gender differences in cardiac electrophysiology that affect
 - Epidemiology
 - Presentation
 - Prognosis in various arrhythmias
- The sex differences can have important clinical and therapeutic implications
 - the risks of pharmacological therapy are different in men and women

Heart rate and rhythm differences between men and women

- Women tend to have a faster baseline heart rate
 - shorter sinus node refractory time
- Women's ECG readings may be different
 - QT interval is shorter in men than in women, beginning after puberty with a linear increase through the major part of adulthood to at least age 55.
 - androgen and estrogen levels may explain the gender differences in QT interval
- Lower QRS voltages than man
 - /lower sensitivity for left ventricular hypertrophy/



-Mishel J., et al. Am J of Cardiol, 2008; vol.01(9); 1291-96

-Curtis A.B, et all.Clin Cardiol35,3,166-171 (2012)

Symptoms of irregular heart rhythms

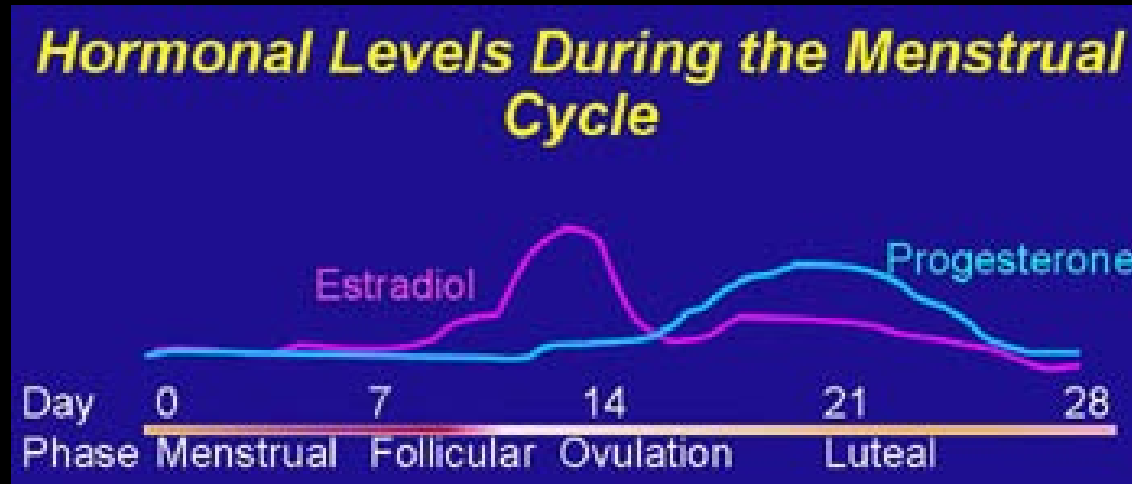
- Silent
- Pounding in chest
- Shortness of breath
- Dizziness, light headace
- Chest discomfort
- Weakness or fatigue

Symptoms of palpitation represent 15-25 % of all the symptoms reported by female heart patients.

They are associated with:

- Premenstrual syndrome
- Pregnancy
- Perimenopausal period

Hormones and Irregular Heart Beats



The rise of progesterone and the fall of estrogen correspond with:

- More frequent episodes of various supraventricular tachycardia (SVT)
- More symptoms associated with SVT
- More frequent and longer lasting episodes of SVT
- Increased frequency of ventricular ectopic beats

Menopause and rhythm disturbances

- **During perimenopause** (the time period before menopause), there is a marked decrease in ovarian estrogen production
 - increase in heart rate (sinus tachycardia), and
 - increase frequency in palpitations and non-threatening arrhythmias, such as premature ventricular contractions or PVCs.
- **Menopause** (women 40 -64 years) causes a further decline in estrogen as the menstrual cycle stops
 - irregular heart beats,
 - palpitations,
 - spasmodic chest pain and nightmares

Heart and Estrogen/Progestin Replacement Study (HERS)

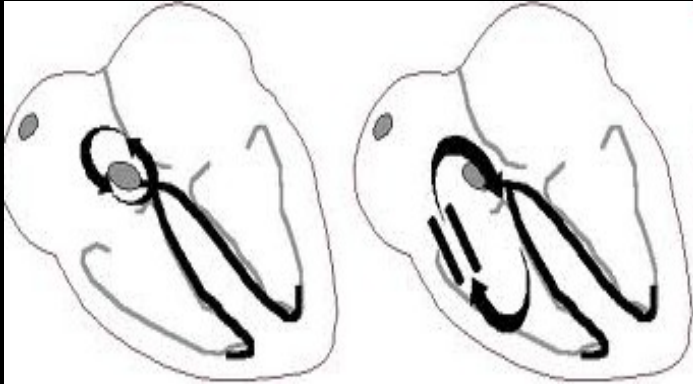
- No benefit in use of hormone replacement therapy to reduce cardiovascular events, and hormone replacement therapy may even increase risk of thromboembolism (blood clot) during the first year
- HRT is also associated with lengthening of the QT interval, although the relevance of this finding is not known

- HRT may decrease palpitations and other symptoms such as hot flashes, insomnia, and sweating
- it may be considered as a treatment option in low risk female patients to relieve symptoms of palpitations

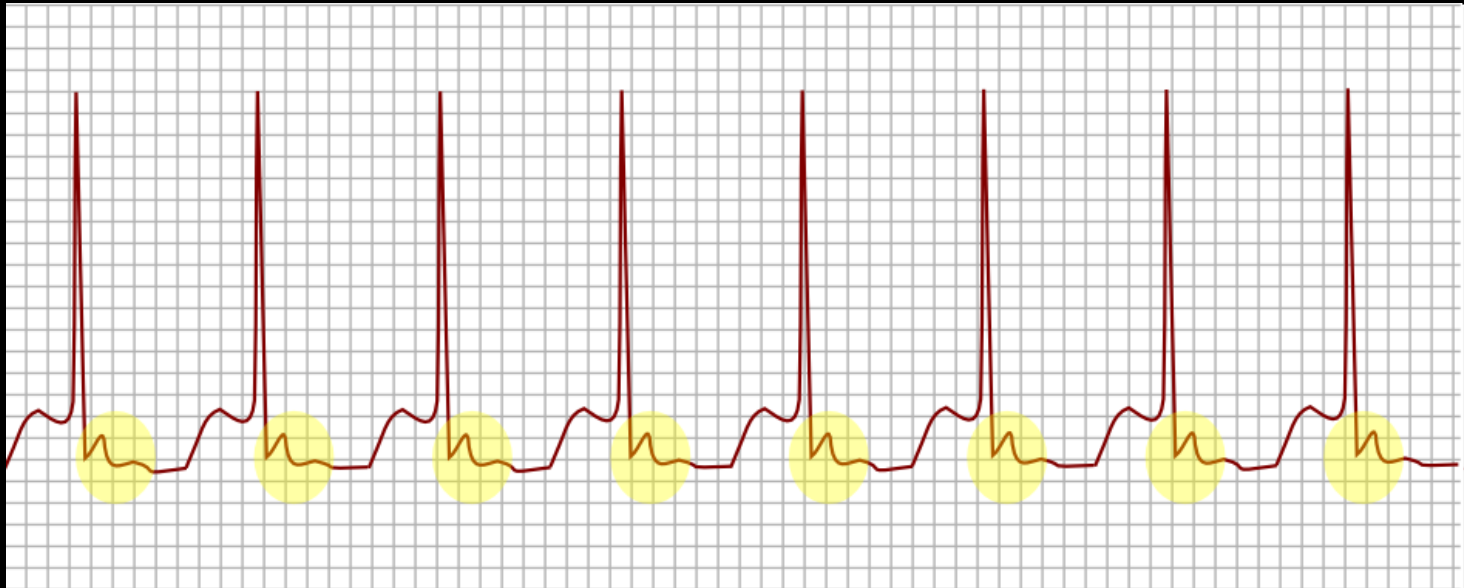
Arrhythmias more prevalent in women

- **Supraventricular Tachycardia (SVT) or Paroxysmal SVT (PSVT) –**
- **Sinus Node Dysfunction (SSSy)**
- **AV Nodal Re-entry Tachycardia (AVNRT)**
- **Long QT Syndrome**
- **Postural Orthostatic Tachycardia Syndrome (POTS)**

AV Nodal RE-entry Tachycardia



women : men = 2 : 1

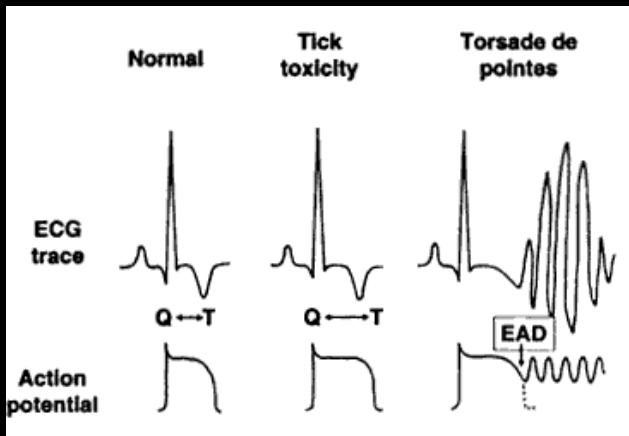
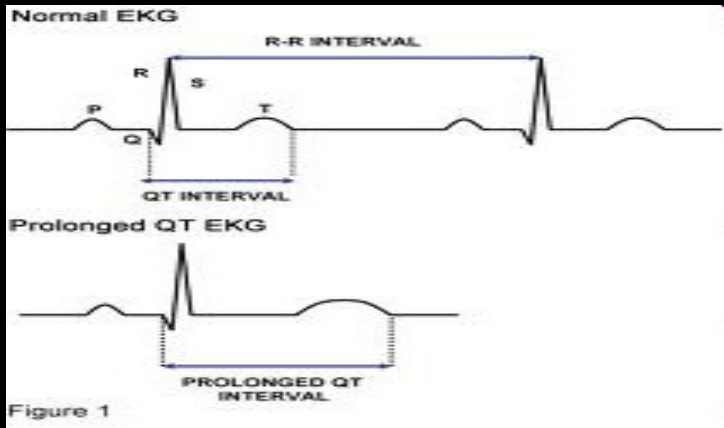


Long QT Syndrome

a familiar disorder with delayed ventricular repolarization due to mutation in cardiac ion channels

- Increases the risk for life threatening forms of VT (torsades de pointes)

- Greater risk than men of developing TdP when given drugs that prolong cardiac repolarisation



QTc 0,42

$$QTc = \frac{QT}{\sqrt{RR}} = \frac{0.71}{\sqrt{1.11}} = 0.67 \text{ seconds}$$

Postural Orthostatic Tachycardia Syndrome (POTS)

- Abnormal response to change in position, related to the autonomic nervous system
 - Drop in blood pressure
 - Rise in heart rate
 - Syncope
 - Dizziness or lightheadedness

Arrhythmias more prevalent in men presenting differently in women

- Atrial fibrillation

- Sudden cardiac death

Arrhythmias more prevalent in men presenting differently in women

Atrial fibrillation

- Men and women increase incidence of AFF with age
- Men have AFF more often than women, but the absolute number of women with AFF is equal or greater than men in the older age groups
- Women with AFF have
 - more symptomatic episodes,
 - frequent recurrences,
 - longer episodes (>24 hours) and
 - significantly higher ventricular rate

Independent Risk Factors for Atrial Fibrillation in a Population-Based Cohort

The Framingham Heart Study

- To determine the independent risk factors for AFF
- 2090 male, 2641 female, age 55 to 94,
- free of history of AFF
- 38 years follow up

men had a 1.5 times greater risk of developing atrial fibrillation than women

Independent Risk Factors for Atrial Fibrillation in a Population-Based Cohort

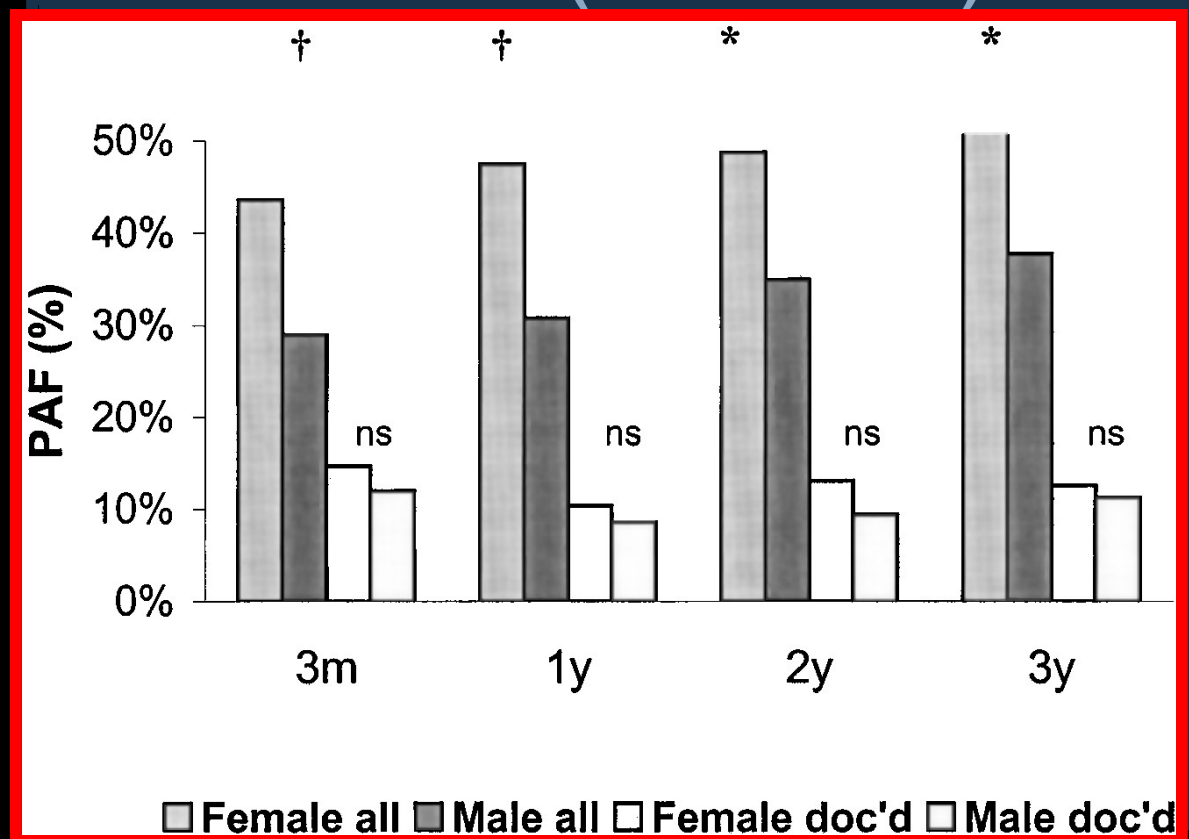
The Framingham Heart Study

Variable /odds ratio	men	women
Age(/10y)	2,2	2,1
Cigarette smoking	1,2	1,4
Diabetes	1,4	1,6
LVH	1,4	1,3
HTA	1,5	1,4
Heart failure	4,5	5,9
AIM	1,4	1,2
Valve diseases	1,8	3,4

The Canadian Registry of Atrial Fibrillation (CARAF)

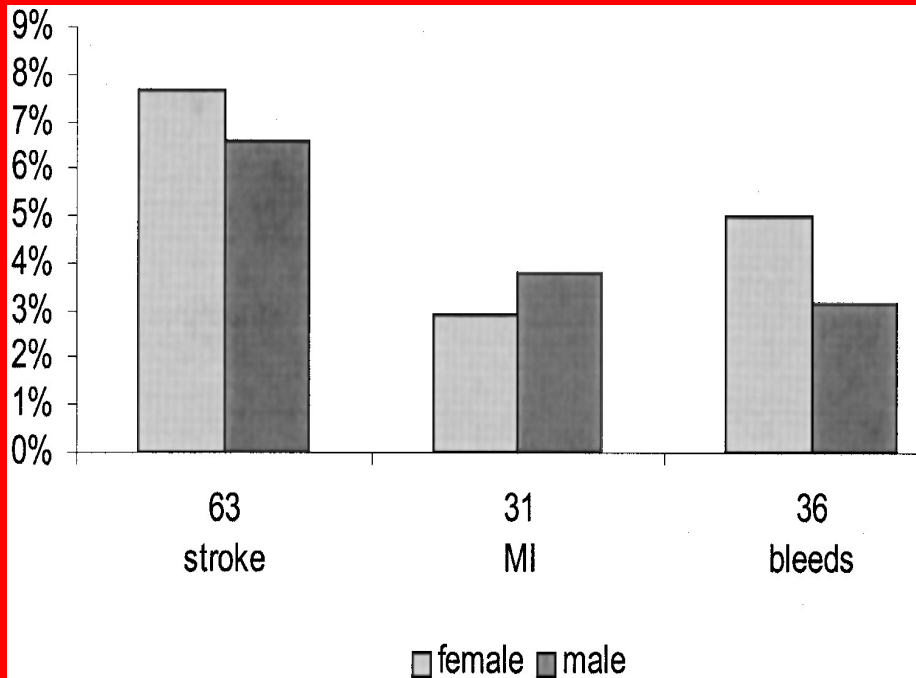
- **New onset AF: sex differences in presentation, treatment and outcome**
- Enrolled subjects at the time of first ECG confirmed diagnosis of AF
- 339 female (38%) and 560 male were followed for 4.14 \pm 1.39 years, on the 3-rd moths, at the year and annually

The Canadian Registry of Atrial Fibrillation (CARAF)



- ✓ Recurrences of AF at each follow up visit were significantly greater in women than men
- ✓ Women had more impaired quality of life compared to man

The Canadian Registry of Atrial Fibrillation (CARAF)



- Total stroke, MI and major bleeding did not vary by sex, but there was a significant interaction between sex and Warfarin,
- women on Warfarin were 3.35 times more likely to experience a major bleed than men
- 9 of 10 women who experienced major bleeding were aged >75 years

Circulation, May 15, 2001;103:2365-2370

ATRIA study and 3 SPAF trials reported similar rates of major hemorrhage in both sexes with no independent major bleeding risk for women

✓ ATRIA study showed additional risk for stroke, especially for those women older than 75 years

Atrial fibrillation

- **People with diabetes have 44% higher prevalence of atrial fibrillation**
- **Women with type 2 diabetes have 26% increased risk of developing AFF**
- **Diabetes was a stronger predictor of AFF than obesity and elevated blood pressure**

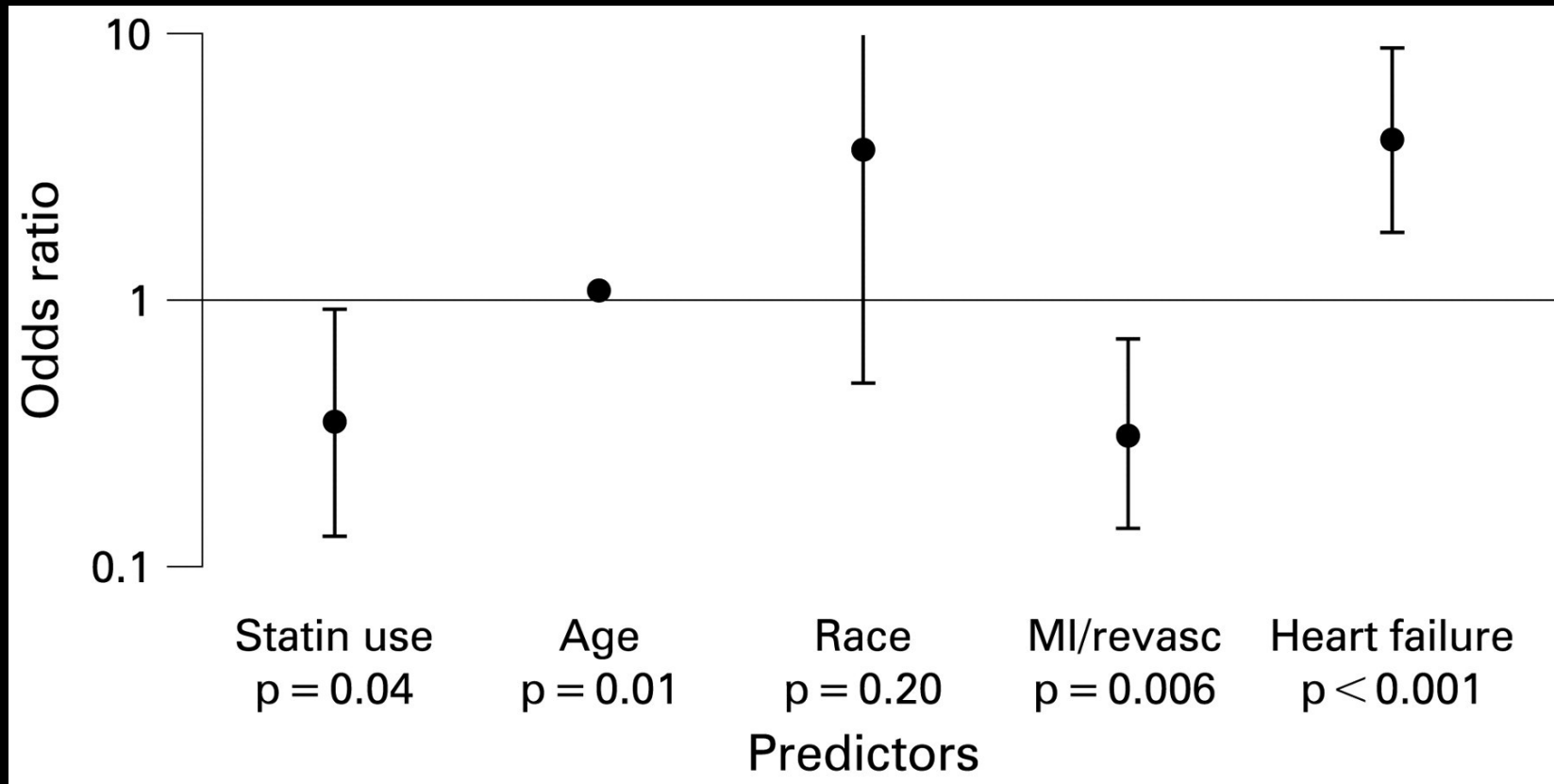
Copenhagen Heart Study

- It analyzes the gender-specific effect of atrial fibrillation (AF) on the risk of stroke and cardiovascular death during 5 years of follow-up.
The effect of **AF on the risk of stroke** was 4.6-fold **greater in women** (hazard ratio 7.8, 95% confidence interval 5.8 to 14.3) than in men (hazard ratio 1.7, 95% confidence interval 1.0 to 3.0).
- The independent **effect of AF on cardiovascular mortality** rate was 2.5-fold **greater in women** (hazard ratio 4.4, 95% confidence interval 2.9 to 6.5) than in men (hazard ratio 2.2, 95% confidence interval 1.6 to 3.1).
- **CONCLUSION: AF was independently associated with a higher cardiovascular mortality rate in women (hazard ratio 4,4 as compared to man 2,2)**

Statin use is associated with lower risk of atrial fibrillation in women with coronary disease: the HERS trial

- 2673 Postmenopausal women with coronary disease
- AF prevalence at baseline and incident AF over a mean follow-up of 4.1 years.

Prevalence of atrial fibrillation at baseline based on the presence of predictors.



Statin use was associated with 55% lower incidence of AFF

AFF treatment

- Euro Heart Survey study – treatment for AF was more conservative in women, with significantly less rhythm control than man
- Canadian Registry – the men were more likely to undergo electrical cardioversion than women
 - Cardioversion to normal sinus rhythm was equally successful in both genders (75,9% in women and 79,3% in men)
- European study showed that women were under-referred and referred later for AF ablation after failing treatment with antiarrhythmic drugs
 - Women were older, with more hypertensive pats and larger dimension of LA
 - Immediate success rates and complications were similar in both

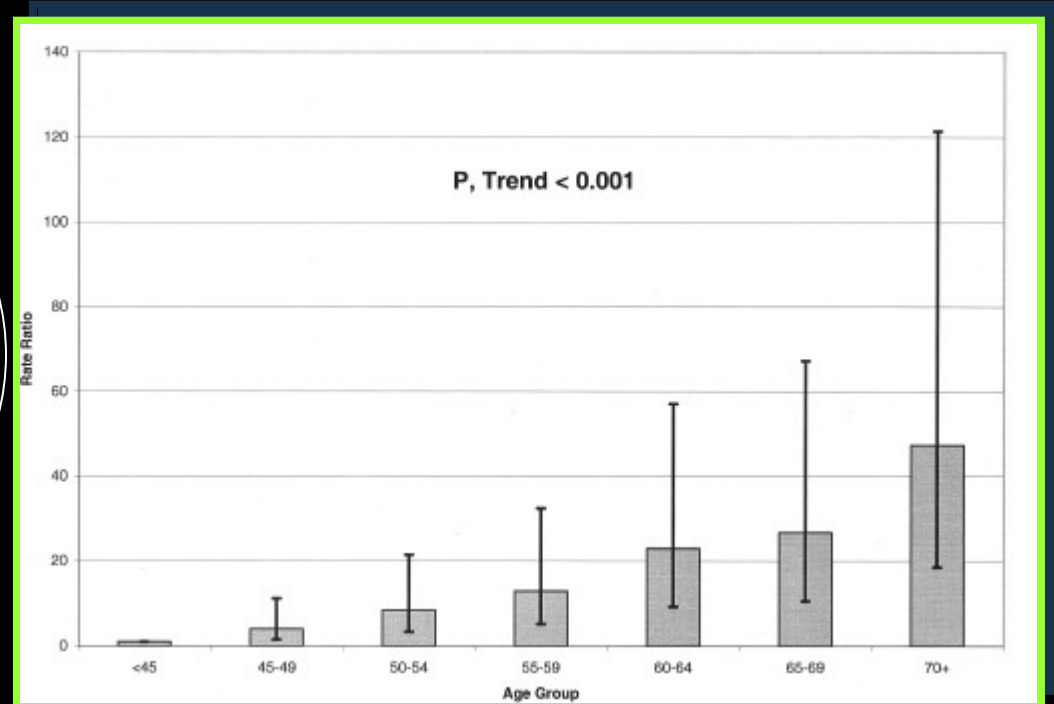
Sudden cardiac death

- Sudden cardiac death (SCD) occurs less frequently in women
- The Nurses' Health Study showed that while the majority of women who had SCD had
 - no prior history of cardiovascular disease before death,
 - they had at least one cardiac risk factor (smoking, hypertension and diabetes had the greatest impact).
 - Family history also played a role in increased risk if one parent died of heart disease before age 60
- The majority of SCD in women is related to an abnormality of the heart rhythm

Prospective Study of SCD among women

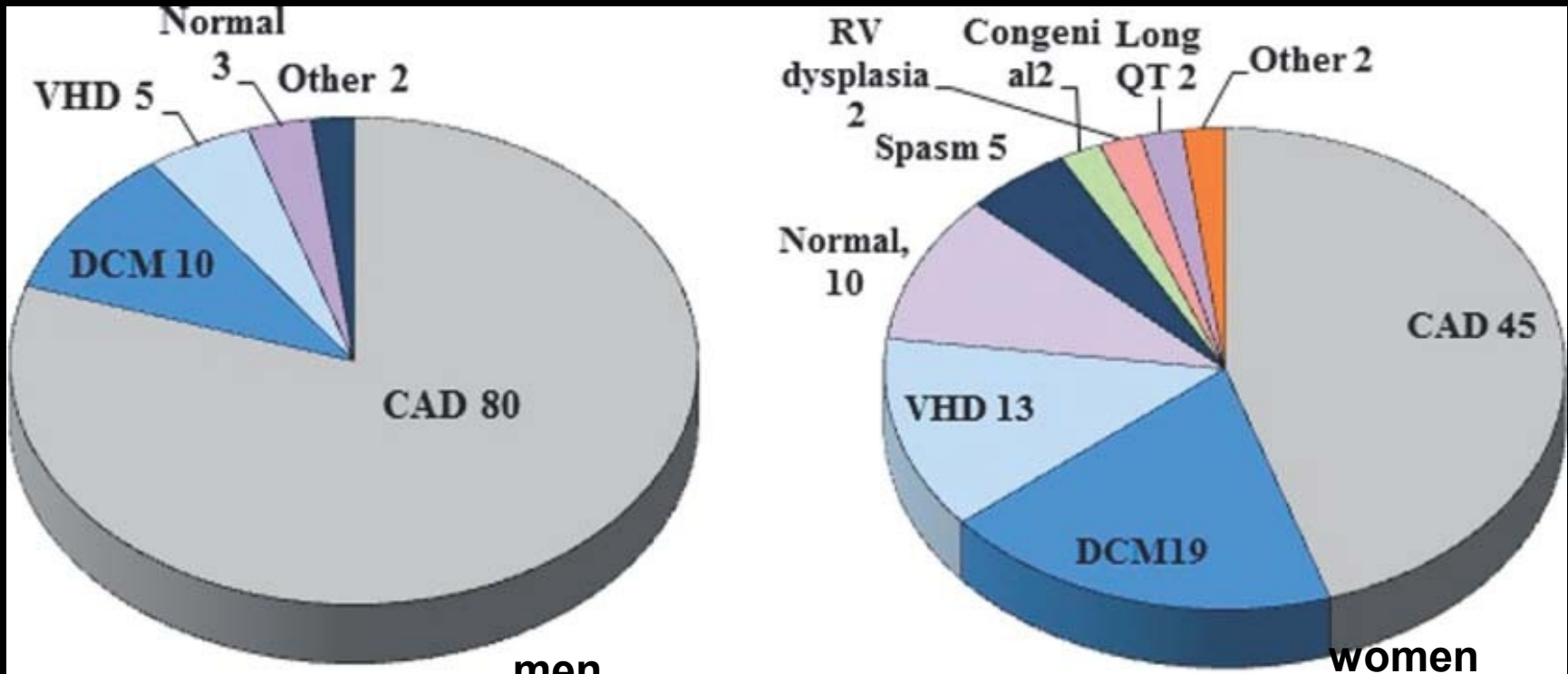
- Prospective cohort of 121 701 women aged 30 to 55 years at baseline.
- From 1976 to 1998, 244 SCDs were identified

- ♥ markedly increased with age
- ♥ 69% no history of cardiac diseases before death
- ♥ 94% had at least 1 CAD risk factor (HTA,DM,smoking)
- ♥ 88% were classified as arrhythmic



Arrhythmias in Women

Framingham Study – Sudden cardiac death



The Incidence of SCD increased with age in both sexes, although the annual rate of SCD in women was around half of that in men in all ages combined

- **SCD in women is more difficult to predict, and therefore to prevent**
- Although SCD is less common among women, it remains an important cause of mortality that requires more intensive primary preventive efforts.
- **Less women than men were treated with ICD in primary and secondary prevention of sudden cardiac death**
- **ICD offer similar benefits in men and women**

Arrhythmias and pregnancy

Arrhythmias may occur more frequently during pregnancy due to changes in hormones, changes in autonomic tone, changes in circulating blood volume which can increase myocardial irritability during pregnancy

- an increased heart rate provides a protective effect on the QT interval

Arrhythmias and pregnancy

- Premature atrial beats occur in about 50 percent of women during pregnancy, although most are harmless and do not last.
- Those who have supraventricular tachycardia or paroxysmal SVT, the symptoms are worsening in 20 percent of those cases with SVT
- An increased incidence of 34% for the new onset of SVT
- Women who have had congenital heart defects repaired have an increased risk of arrhythmias during pregnancy

Treatment of arrhythmias in pregnancy

- Arrhythmias in pregnancy are treated conservatively.
 - rest and vagal maneuvers
 - Digoxin or a beta blocker – ACC/AHA/ESC Guid.recommendation
- No anti-arrhythmic medication is completely safe during pregnancy;
 - medications are avoided during the first trimester if possible to limit risk to the fetus
 - Propranolol, metoprolol, digixin, and adenosine have been tested and shown to be well tolerated and safe during the second and third trimester .



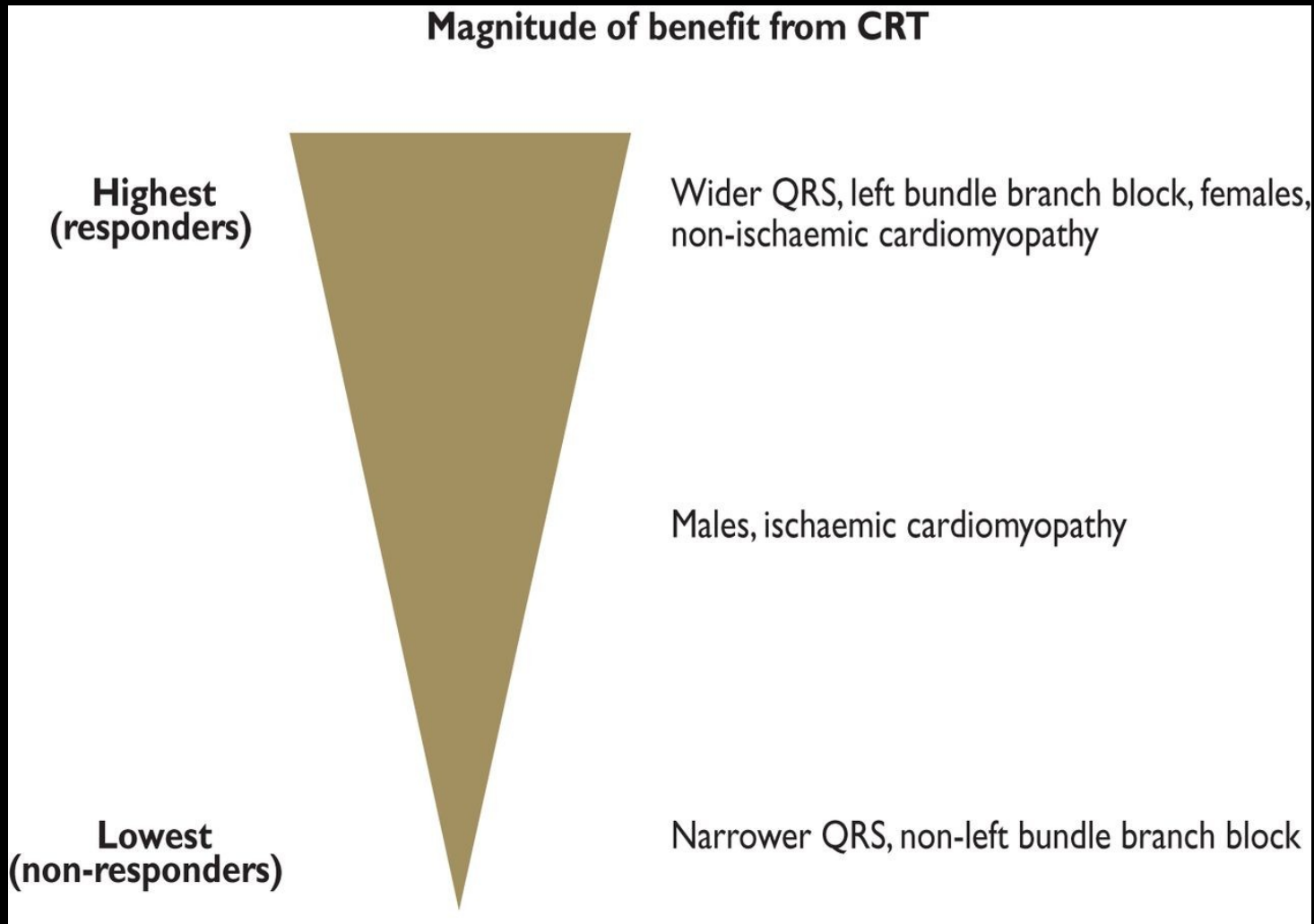
Cardioversion is safe during all trimesters of pregnancy and can be used if necessary



Pregnancy in ICD implanted women

- Women who have an ICD who become pregnant do not have an increased risk for ICD discharges or ICD complications.
- A woman who has an ICD can safely become pregnant, unless she has an underlying heart condition that would increase health risks during pregnancy

Clinical factors influencing the likelihood to respond to CRT.



Authors/Task Force Members et al. Eur Heart J
2013;34:2281-2329

Arrhythmia therapy in women

- Women have increased risk of drug related torsades de pointes
- Women are more susceptible than men to proarrhythmia (Tdp) from QT-interval prolonging agents (class 1a quinidine, procainamide and disopyramide; class III sotalol, rare amiodarone)

- weight-dependant drug dosing (higher level in women)
- metabolic enzymes exhibit varying gender effects (group cytochrome p450 enzymes differences in men and women)
- renal excretion is greater in men (10% GFR in men)
- some medicine (exp.sotalol) is level dependent for proarrhythmias
- differences in drug induced QT prolongation

Conclusions

- Women tend to have a faster baseline heart rate - shorter sinus node refractory time
- QT interval is shorter in men than in women, androgen and estrogen levels may explain the gender differences in QT interval
- Arrhythmias more prevalent in women: SVT, AVRNT, Long QT
- Arrhythmias more prevalent in men: AFF, SCD
- Men more often have AFF associated with CHD, women more often with *valve diseases*
- SCD in women is more difficult to predict, and therefore to prevent
- No anti-arrhythmic medication is completely safe during pregnancy
- Women are more susceptible than men to proarrhythmia



Thank you for attention