Women and Arrhythmias

Kara J. Quan, M.D.
Director, Cardiac Electrophysiology

Gender Gap Increases Women's Heart Risks

"The data suggest there is a disconnect in the way physicians diagnose and treat heart disease in women versus men."

Gender Differences

- Mortality
- Arrhythmias
- QT interval and AADs
- Pregnancy
- Devices and trial data

Background

- The pathophysiologic mechanisms by which gender influences cardiac arrhythmias are poorly understood.
- Current knowledge stems from clinical and electrocardiographic observations with sparse experimental data.
- Contributors to the gender gap
  - Hormonal effects on expression and function of ion channels
  - Autonomic tone

Gender Differences

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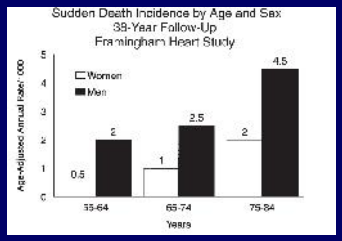
Sudden Cardiac Death: *Incidence by Age and Gender*

- SCD is more common in men.
- In women, incidence of SCD ~doubles with each decade.



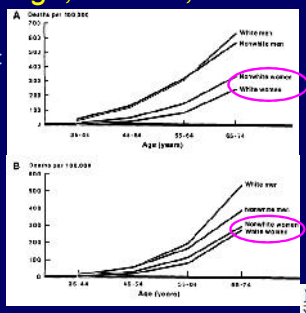
Question:

After cardiac arrest, which gender has a better overall survival?

(1) Men
(2) Women
(3) No Difference

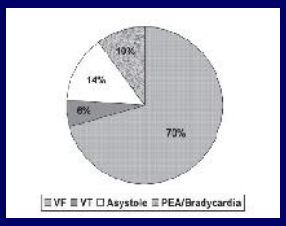
Mortality Rates:
Effect of Age, Gender, and Race

- Out of Hospital Arrest
- In-Hospital Arrest



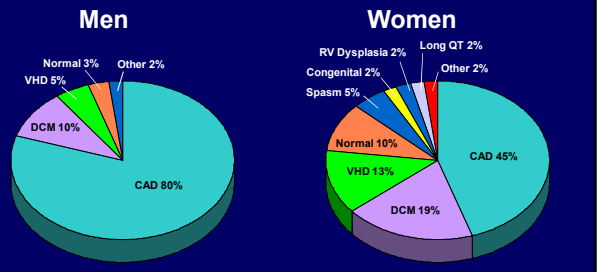
Arrhythmic Death
Documented Rhythm

- VF or VT constitutes 76% of first cardiac rhythm post arrest.
- No gender difference



Albert CM et al. Circulation 2003;107:2096-2101

Structural Heart Disease in Cardiac Arrest Survivors



Albert CM, et al. Circ. 1996;93:1170-1176.

Gender Differences

- Mortality
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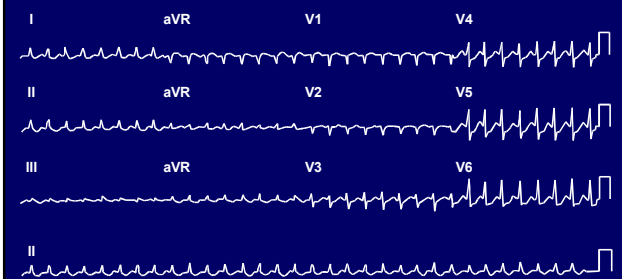
Case Study: AVNRT

- 27 year old woman
- Palpitation x 10 years
  - ↑ frequency x 2 years
  - Episodes now last several hours
  - Associated dyspnea, dizziness
  - Patient unable to coach children's soccer, afraid to travel
- Therapy
  - Failed beta blockers
  - Treated with verapamil

Case Study: AVNRT



Courtesy of Dr. Helen Barold.

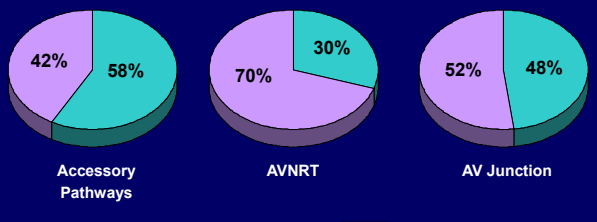
Frequency of Arrhythmias
Gender Differences

Arrhythmia	Male	Female
Bradyarrhythmia	AV block Carotid Sinus Syncope	Sinus Node Dysfunction
Supraventricular Arrhythmias	APCs Atrial fibrillation AVRT WPW	Inapprop Sinus Tachycardia AVNRT
Ventricular Arrhythmias	PVCs VT SCD Brugada	Congenital and Acquired LQTS RVOT VT

Adapted from Rodriguez L, et al. Am J Cardiol. 1992;70:1213-1215

Catheter Ablation of Accessory Pathways, AVNRT, and AV Junction:

Gender Distribution %



Calkins H, et al. Circ. 1999;99:262-270.

Question

- With atrial fibrillation, which gender is at a higher risk of stroke?
  - (1) Men
  - (2) Women
  - (3) No Difference

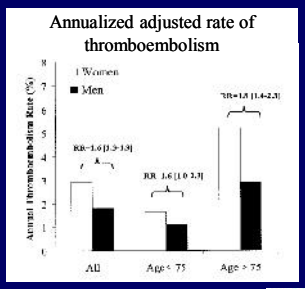
Atrial Fibrillation

- Women who have atrial fibrillation are more likely to have a life-threatening stroke.
- Atrial fibrillation diminishes the female advantage in survival.

Benjamin EJ, et al. Circ. 1998;98:946-952.

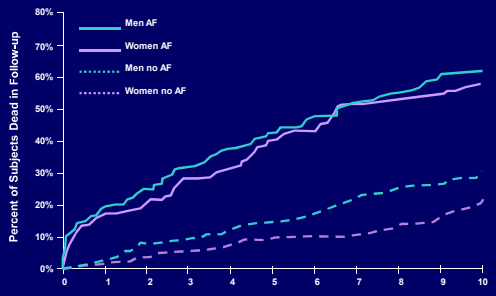
Atrial Fibrillation
Stroke Risk

- ATRIA study
- Women at higher stroke risk



Fang, M et al. Circulation 2005;112:1687-1691

Atrial Fibrillation and Risk of Death

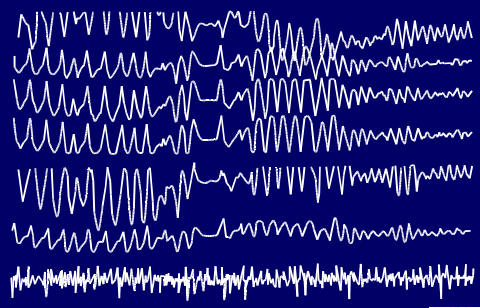


Adapted from Benjamin EJ, et al. Circ. 1998;98:946-952.

Case Study

- 42 year old woman
  - Exercise induced palpitation
  - Normal echocardiogram
  - Event monitor as follows:

RVOT VT



Courtesy of Dr. Brian Olshansky.

Right Ventricular Outflow Tract (RVOT) Tachycardia in Women

- Exacerbated by gender specific hormonal fluctuation that can occur with menopause, gestation, and menstrual cycle
- Not always precipitated by exercise

Deely M, et al. JACC. 1998;31:Suppl A:91A.

Postulated Mechanisms for Gender Differences

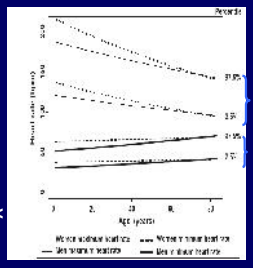
Effects on Cellular Electrophysiology	Presence of estrogen receptors Modulation of L-type Ca receptors Modulation of potassium channels (IKR, IKI)
Autonomic Modulation	Basal heart rate disparity Heart rate variability Baroreceptor sensitivity Muscle sympathetic nerve activity Dispersion of repolarization Nitric oxide expression
Combinations	M cells Long QT syndromes Dispersion of repolarization

Question

- Which gender has a higher age-adjusted resting heart rate?
  - (1) Men
  - (2) Women
  - (3) No Difference

Resting Heart Rate
Gender Differences

- 1920s Bazett observed a higher resting heart rate in women
- CARDIA study n=5116 HR in women 3-5 bpm> men
- CSNRT and SNRT< Women
- IST> Women

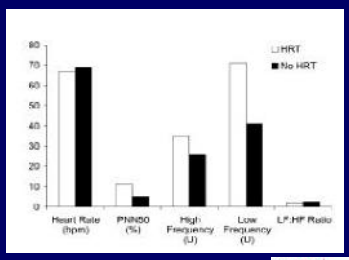


N=625

Silva De Paula et al. IJC 2005; 105;152-158

Heart Rate Variability
Relationship to HRT

- Women after HRT have improved HRV.



Huikuri et al. Circulation 1996; 94;122-5

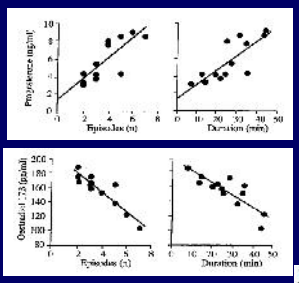
Effect of Ovarian Hormones in Palpitation

- Ovarian hormonal levels vary during the menstrual cycle
- Estradiol has calcium-antagonistic (verapamil-like) properties
  - Protective mid-cycle
  - Reduces incidence of SVTs
  - Effect lost premenstrual

Rosano GMC, et al. Int J Fertil. 1997;42:94-100.

Hormonal Effects on PSVT
Estrogen and Progesterone

- With increased Progesterone level
  - ↑ frequency and duration of PSVT
- With increased Estradiol level
  - ↓ frequency and duration of PSVT



Rosano et al. Lancet 1996 347;786-88

Palpitation in Women: *Diagnosis*

- Work up indicated for:
  - Documented episodes associated with syncope
  - Or inappropriately rapid pulse during symptoms
- Methods of Diagnosis:
  - 12 lead ECG
  - Holter monitor / Event monitor
  - Echocardiogram
  - Exercise testing
  - Referral to an electrophysiologist

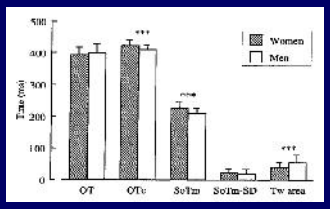
Gender Differences

- Mortality
- Arrhythmias
- QT interval and AADs
- Pregnancy
- Devices and trial data

Question

- Which gender has a longer age-adjusted QTc interval?
  - (1) Men
  - (2) Women
  - (3) No Difference

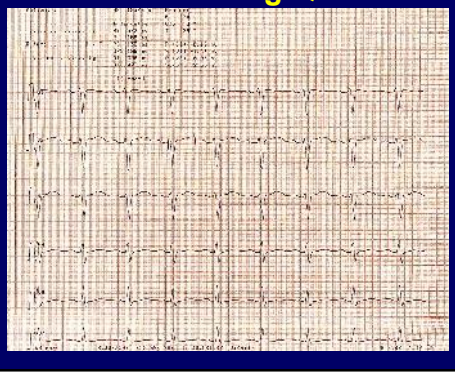
Ventricular Repolarization *Gender Differences*



*200 women and 233 men (age 10–81 years, median age 35 years) in 12-lead electrocardiogram (ECG) ***P , 0.0001.*

Merri M et al. Circulation 1989;80:1301-1308

Long QT



Congenital Long QT

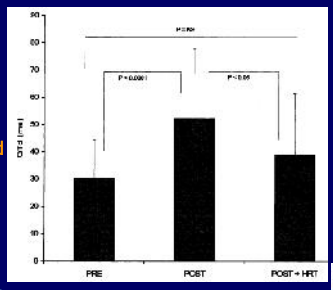
- Unexplained female prevalence in Long QT
- Women more likely than men to have a cardiac event
- Risk of cardiac events
  - Males until puberty
  - Females during adulthood
- Inheritance not sex-linked
  Genotypes – same
  Phenotypes – different
  Female carriers have longer QTc than male carriers

Locati EH, et al. Circ. 1998;97:2237-2244.

Ventricular Repolarization

Effect of Low Estrogen States in Healthy Women

- QT dispersion based on estrogen levels
  - Low estrogen state increased QTd



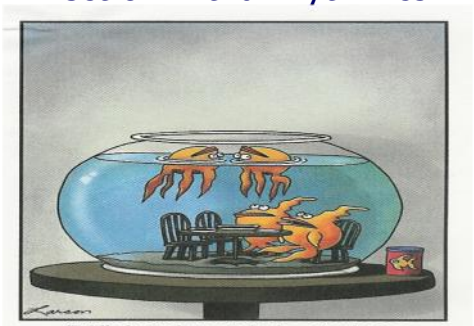
Saba S et al. AJC 2001: 354-356

Acquired Long QT

- QTc is 10-20 ms longer in women than men.
- In 332 reported cases of PMVT associated with antiarrhythmic drug therapy – 70% were women.
- QTc prolongation was not related to changes in the menstrual cycle, CAD, or LV dysfunction.

Makkar RR, et al. JAMA. 1993;270:2590-2597.

Effect of Anti-arrhythmics??



"Well, the Parkers are dead. ... You had to encourage them to take thirds, didn't you?"

Long QT Resulting in Torsades de Pointes

Comparison of Observed vs. Expected Torsades de Pointes : Female Prevalence

			Observed		Expected	
			Female Prevalence		Female Prevalence	
Drug	No.	Median Age (yrs)	%	95% CI	%	P
Quinidine	108	64	60	50-70	43	<.002
Procainamide	39	66	49	32-66	38	.21
Disopyramide	49	66	86	72-94	63	<.002
Amiodarone	28	64	68	47-85	32	<.001
Sotalol	21	65	76	52-92	50	<.04
Bepridil	27	73	74	53-89	50	<.02
Phenylamine	23	71	78	56-93	50	<.02
Two drugs	19	66	89	63-99	NA	NA

Adapted from Makkar RR, et al. JAMA. 1993;270:2590-2597.

Sotalol Proarrhythmia

- Reported risk factors:
  - Daily sotalol dose
  - Female gender
  - Corrected QT interval > 550 ms
  - History of heart failure
- Gender differences in renal clearance and body composition may result in ↑ proarrhythmia in women
- Female patients have an ↑ risk of proarrhythmia and should receive lower doses of sotalol

Basta MN, et al. Aust NZ J Med. 1996;26:167-170.

Gender Differences

- Mortality
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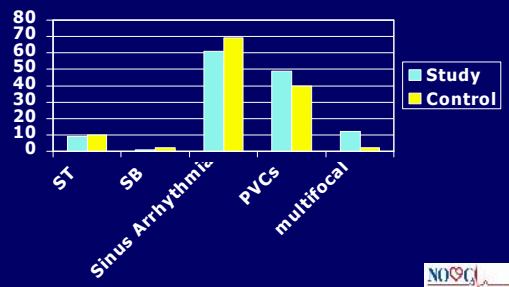
Palpitation During Pregnancy

- Clinical experience suggests that pregnancy may be arrhythmogenic in women with and without heart disease
- Some patients with complaints of palpitation improve during pregnancy
- Palpitation in most cases are due to sinus tachycardia and related to circulatory adaptations in pregnancy

Rosano GMC, et al. Int J Fertil. 1997;42:94-100.

Pregnancy and Arrhythmias

Holter Monitoring N=162



Shotan A et al. AJC 1997;1061-1064

FDA Pregnancy Risk Classification

Category A	Controlled studies show no risk
Category B	No evidence of risk in pregnant women. Either animal studies show risk but human studies do not, or animal studies do not show risk but no adequate studies in humans have been conducted
Category C	Studies in pregnant women are lacking, and animal studies are either positive for fetal risk or lacking as well
Category D	Positive evidence of risk. Investigational or post-marketing data show risk to the fetus

Adapted from Chow T, et al. Am J Cardiol. 1998;82:581-621.

Antiarrhythmic Drugs in Pregnancy

Drug	FDA Class	Placental Transfer	Adverse Effects	Teratogenic	Breast Milk	Risk
Quinidine	C	Y	Thrombocytopenia	N	Y*	Minor
Procainamide	C	Y	None	N	Y*	Minor
Disopyramide	C	Y	Uterine contraction	N	Y*	Minor (L)
Lidocaine	C	Y	Bradycardia, CNS side effects	N	Y*	Minor
Mexiletine	C	Y	Bradycardia, low weight, APGAR, sugar	N	Y*	Minor (L)
Tocainide	C	Unknown	Unknown	Unknown	Unknown	Minor (L)
Flecainide	C	Y	None	N	Y*	Minor (L)
Propafenone	C	Y	None (L)	N	Unknown	Minor (L)

* American Academy of Pediatrics considers drug to be "usually compatible with breast feeding."
L = Limited experience

Adapted from Page RL, Am Heart J. 1995;130:871-876.

Antiarrhythmic Drugs in Pregnancy

Drug	FDA Class	Placental Transfer	Adverse Effects	Teratogenic	Breast Milk	Risk
Propranolol	C	Y	Growth retardation, bradycardia, apnea, hypoglycemia	N	Y*	Minor
Sotalol	B	Y	ß-blocker effects	N	Y*	Minor (L)
Amiodarone	D	Y	Hypothyroidism, growth retardation, premature birth, large fontanelle	Y ?	Y*	Significant
Verapamil	C	Y	Bradycardia, heart block, hypotension	N	Y*	Moderate
Diltiazem	C	N	Unknown	Unknown	Y*	Moderate (L)
Digoxin	C	Y	Low Birth Weight	N	Y*	Minor
Adenosine	C	N (L)	None	N	Unknown	Minor (L)

* American Academy of Pediatrics considers drug to be "usually compatible with breast feeding."
L = Limited experience

Adapted from Page RL, Am Heart J. 1995;130:871-876.

Adenosine Use in Pregnancy

- Limited experience suggests adenosine is safe and effective for treatment of SVT in pregnancy.

Hagley MT, Cole PL. Annals of Pharmacotherapy. 1994;28:1241.

Arrhythmias in Pregnancy: Management of Reentrant SVT

Vagal Maneuvers

- No effect → Adenosine 6 mg → No effect → Adenosine 12 mg → No effect or hemodynamic instability → Sedate → Cardiovert
- Terminates → No additional therapy

Burkart TA, Conti JB. ACC Current Journal Review. 1999;8:41-44.

Arrhythmias in Pregnancy: Atrial Flutter and Atrial Fibrillation

- Rare in women of childbearing age with no underlying heart disease
- Cardioversion (if needed) should be performed early to avoid the need for anticoagulation
- Fetal monitoring recommended during and following cardioversion

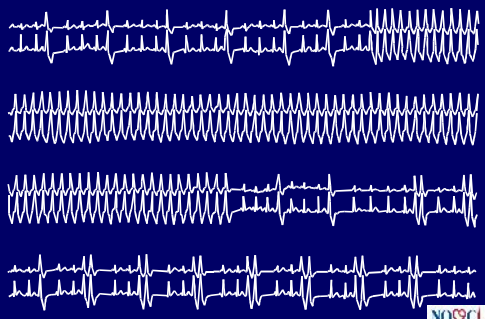
Burkart TA, Conti JB. ACC Current Journal Review. 1999;8:41-44.

Arrhythmias in Pregnancy: Atrial Fibrillation

- Anticoagulate chronic AF in patients with risk factors:
  - Diabetes
  - Hypertension
  - Congestive heart failure
  - Previous stroke or rheumatic heart disease
- Warfarin therapy contraindicated during the first trimester
- High-dose SQ heparin is recommended, particularly for the first trimester

Burkart TA, Conti JB. ACC Current Journal Review. 1999;8:41-44.

Monomorphic Ventricular Tachycardia



Wolbrette D. Current Opinions in Cardiology. 1999;14:36-43.

Arrhythmias in Pregnancy: Ventricular Tachycardia

- If therapy is required, beta-blockers are the drug of choice
- Beta blockers are well tolerated but risk/benefit ratio for mother and fetus must be considered
- DC cardioversion appropriate for hemodynamically unstable VT
- Stable VT – Lidocaine is the acute drug of choice

Burkart TA, Conti JB. ACC Current Journal Review. 1999;8:41-44.

ICDs and Pregnancy

- Multicenter retrospective study involving 44 women patients who became pregnant
- Therapies during pregnancy:
  - 33 (75%) No shocks
  - 8 (18%) One shock
  - 3 (7%) Multiple shocks
- Outcome
  - 39 (89%) Healthy babies
  - 1 (2%) Stillborn
  - 2 (4%) Small for gestational age

Natale A, et al. Circ. 1997;96:2808-2812.

Pregnancy and Arrhythmias
Use of ICD's

- Conclusions:
  - Pregnancy does not increase the risk of major ICD-related complications or result in a high number of ICD discharges
  - The presence of an ICD should not deter a women from becoming pregnant unless underlying structural cardiac disease is a contraindication

Natale A, et al. Circ. 1997;96:2808-2812.

Gender Differences

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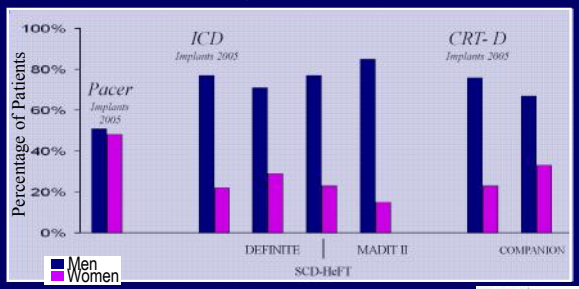
ICD's Class I Indications:

- Primary Prevention
  - CAD or NIDCM, LVEF ≤ 35%, inducible VT on EP study
  - Prior MI, LVEF < 30%, NYHA class II/III
  - NIDCM, LVEF ≤ 30%, NYHA class II/III
  - Syncope of unknown origin with clinically relevant hemodynamically significant sustained VT/VF induced when drug therapy is ineffective, not tolerated, or not preferred
- Secondary Prevention
  - Prior spontaneous sustained VT or VF
  - Chronic HF and low LVEF with syncope of unknown origin

2005 ACC/AHA guidelines

ICD Implants and Clinical Trials:
Under-representation of Women



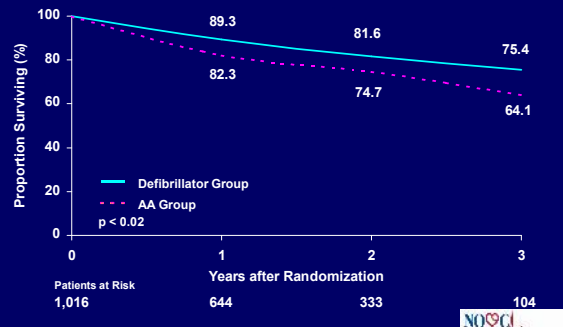
Source: Definite, ScdHeft, Madit2 and Companion

Gender Differences in Patients with ICDs

- Women who receive ICDs were:
  - Younger (50 vs 61 yrs)
  - ↓Ischemic (38% vs. 78%) p < .001
  - ↑Survival
- Recurrent VT/VF was nearly as common in women as men.
- ICD Rx can benefit women whose mortality may be more closely linked to recurrent VT/VF than underlying heart disease.

Kuderchuk PJ, et al. Circ. 1994;90:Suppl:I-655.

AVID Overall Survival



AVID Investigators. N Engl J Med. 1997;337(22):1576-1583.

Gender Differences in Patients With Life-Threatening Ventricular Arrhythmias (AVID)

- Female clinical characteristics:
  - Younger
  - Less CAD
  - More non-ischemic DCM
  - More idiopathic VF
  - Better ejection fraction
  - More congestive heart failure
- Female coronary risk factors:
  - More hypertension and diabetes
  - Smoked less
- Female index arrhythmia:
  - VF is more common the VT (58% vs 48%) p = 0.05

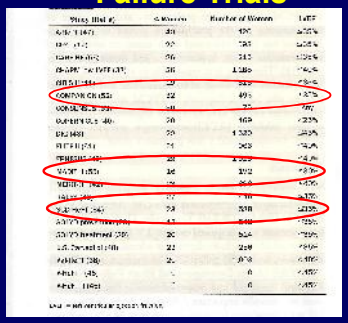
Engelstein ED, et al. Circ. 1997;96:Suppl: I-720.

Gender Differences in Patients With Life-Threatening Ventricular Arrhythmias (AVID)

- **Despite differences in gender profile, antiarrhythmic drug therapy and survival were similar in men and women with life-threatening ventricular arrhythmias.**

Engelstein ED, et al. Circ. 1997;96:Suppl: I-720.

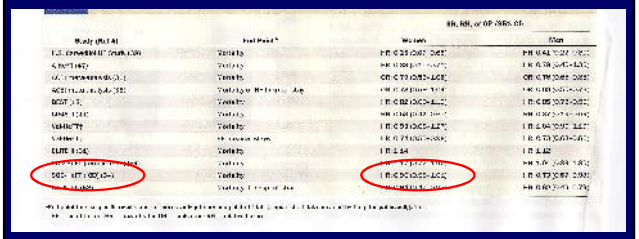
Female Participants in Chronic Heart Failure Trials



Few trials have gender specific data

Hsich, JACC, 54, 1009, 491-8

Risk of Mortality and / or Hospital Stay in Female Heart Failure Patients



Not powered enough to detect gender differences
No clear mortality benefit for women

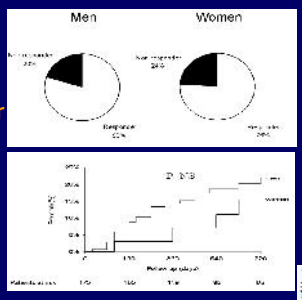
Hsich, JACC, 54, 1009, 491-8

Question

- **Which gender has a higher responder rate to CRT therapy?**
  - **(1) Men**
  - **(2) Women**
  - **(3) No Difference**

Response to CRT
Gender Difference

- No significant difference in responder rate based on gender (men 80% vs women 76% responders; p=NS)



Bleeker G et al. PACE 2005;28:1271-1275

COMPANION Study
(Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure)

- **Included 299 women**
  - **LVEF ≤ 0.35**
  - **NYHA III to IV despite optimal medical therapy**
  - **QRS ≥ 120 ms**
- **ICD decreased total mortality or hospital stay for any cause compared with medical therapy**

CARE-HF Study
(Cardiac Resynchronization Heart Failure)

- Included 215 women
  - LVEF ≤ 0.35
  - NYHA III to IV
  - LVEDD ≥ 30 mm
  - QRS ≥ 120 ms
- Trend for improvement in total mortality and hospital stay with CRT compared with medical therapy alone

MADIT CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) n=1,820

- Ischemic or nonischemic cardiomyopathy
- Class I or II HF
- QRS ≥ 130 ms
- All candidates for ICD
- Randomized to ICD + CRT or ICD alone
- Largest ever % women in any device trial

NEJM online 2009 Sept 1

MADIT CRT

- Demographics
  - Women more likely to have nonischemic CM than men
  - Women more likely to have LBBB than men
- Results
  - Women with better result from CRT-D therapy than men
  - 70% relative risk reduction in HF in women (vs. 35% in men, p 0.001)
  - 69% relative risk reduction in death or HF (vs. 28% in men, p 0.001)

Arshand A, Moss AJ, et. Al. JACC, 2011; 57:813-820

Conclusions

- Major influences of hormones and ANS in arrhythmogenic substrate
- Major differences in mortality, arrhythmia occurrence, response to common AADs, and event rate in LQTS
- Adenosine and beta blockers effective in pregnancy
- Devices beneficial for recurrent VT/VF and for heart failure
- Trial data sparse

Thank you.

Backup Slides

Mechanism of SVT and Gender

Type of Arrhythmia	Male	Female	Odds Ratio (M/F)
Atrial tachycardia	12	18	0.66
AV nodal reentrant tachycardia			
Typical	51	109	0.4
Atypical	0	5	0.0
Accessory pathways			
Manifest	211	106	1.99
Concealed	61	31	1.96
Circus movement tachycardia	81	49	1.31
Atrial fibrillation	51	15	1.58
Ventricular fibrillation	11	1	5.06

Adapted from Rodriguez L, et al. Am J Cardiol. 1992;70:1213-1215.

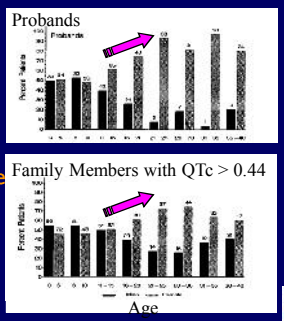
Management of Arrhythmias in Pregnancy

- Document arrhythmia
- Need for treatment must be clear
  - Sinus tachycardia is common in pregnancy
- In patients c/o palpitation without a documented arrhythmia (non-invasive testing), likelihood is low for a life-threatening arrhythmia
- Clinician must consider risk/benefit ratio for both mother and fetus

Burkart TA, Conti J. ACC Current Journal Review. 1999;8:41-44.

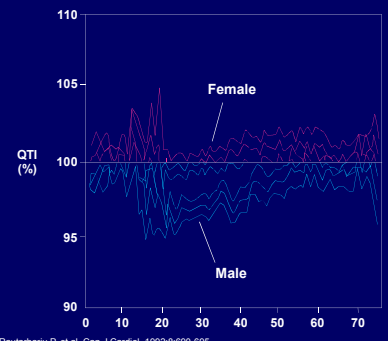
Gender Influences In LQTS

- Comparison of LQTs in Probands and those with Familial history
  - Females more affected by LQTs after the age of 15 than males



Locati EH, et al. Circ. 1998;97:2237-2244.

Shortening of QT in Males After Puberty



Adapted from Rautarharju P, et al. Can J Cardiol. 1992;8:690-695.

Echocardiographic Catheter Placement in Pregnancy

Lee MS, et al. J Am Soc Echo. 1994;7:182-186.

Arrhythmias in Pregnancy: Ventricular Tachycardia

- If ICD implantation or invasive EP testing is necessary consider echocardiographic guidance to prevent radiation exposure to the fetus

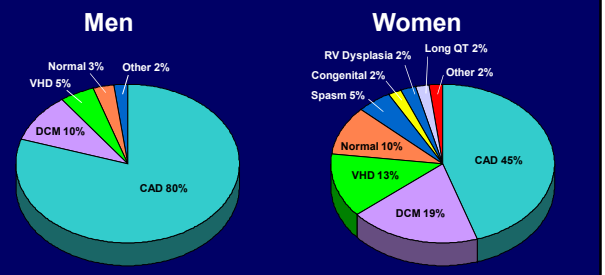
Lee MS, et al. J Am Soc Echo. 1994;7:182-186.

Bradycardia in Pregnancy

- Vasovagal syncope is one of the most common causes of symptomatic bradycardia in women of childbearing age
- Vasovagal syncope is rare during pregnancy

Burkart TA, Conti JB. ACC Current Journal Review. 1999;8:41-44.

Structural Heart Disease in Cardiac Arrest Survivors



Albert CM, et al. Circ. 1996;93:1170-1176.

PVCs As a Risk Factor in Women

- PVCs in men associated with ↑ risk of SCD
- PVCs in women not associated with ↑ risk of SCD
- Women with SCD were less likely to have CAD (45% vs. 80%)

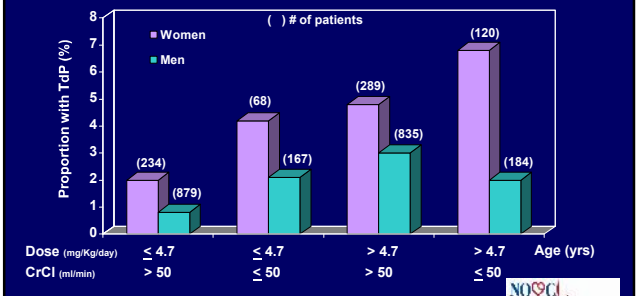
Albert C. In Julian DG, ed. Women and Heart Disease. St. Louis. Mosby. 1997:363-372.

Devices and Mammography

- Device may hinder mammogram interpretation (10% of women)
- Recommendation – implant the device contralateral to any suspicious areas on prior mammograms
- Consider future mammograms during implant

Roelke M, et al. JACC. 1997;29:Suppl A:511A.

Prevalence of Torsades de Pointes With d, l-Sotalol by Creatinine Clearance



Lehman MH, et al. Circ. 1996;94:2534-2541.

Device Implantation Techniques in Women

- Incision site cosmetically chosen – (option) vertical rather than horizontal incision
- Submammary (under breast)
  - Controversial
  - May interfere with mammogram interpretation
- Future mammography
  - Allow for adequate visualization of the breast tail
  - Implant more lateral than medial

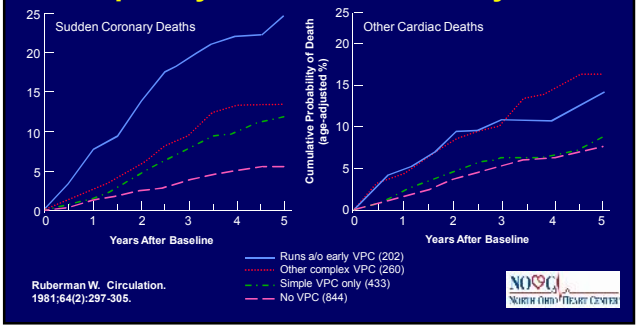
Device Teaching and Follow-up in Women

- Provide adequate counseling in regards to altered body image
- Mammography:
  - Patients should follow the recommended guidelines for breast cancer prevention
  - Provide reassurance that mammography does not hurt the device
  - Radiologists may need to make certain adequate shots of breast tissue are obtained

ICD Patients
Gender Considerations

Sudden Cardiac death	*Women vs. Men*
Incidence	Lower
VF prevalence	Lower
Resuscitation rate	Higher
CAD	Lower
NICM	Higher
EF	Higher
Inducibility at EP	Lower

Risk of Sudden Death in Relation to Complexity of Ventricular Arrhythmia



Ruberman W. Circulation. 1981;64(2):297-305.

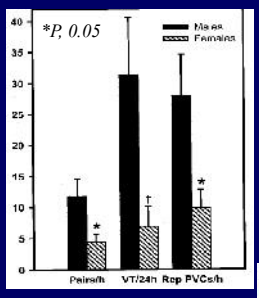
Clinical Characteristics of Long QT Patients with Cardiac Events

	Female Probands (n=259)	Male Probands (n=107)	P
Clinical History			
Age at first cardiac event, yrs	14 ± 10	8 ± 7	0.0001
First event age <15 yrs; n (%)	130 (60)	98 (92)	0.0001
Median No. of cardiac events	6	4	0.002
Median event rate per year	0.24	0.27	NS
Ventricular tachyarrhythmias	150 (58)	41 (38)	0.001
Baseline ECG parameters			
Age at ECG, yrs	21 ± 12	13 ± 11	0.0001
Heart rate, bpm	71 ± 19	73 ± 22	NS
QT_c ms	519 ± 61	519 ± 58	NS
QT_c > 470 ms, n (%)	205 (79)	95 (89)	NS
QT_c > 500 ms, n (%)	117 (45)	52 (49)	NS

Locati EH, et al. Circ. 1998;97:2237-2244.

Arrhythmic Events in HF
Gender Differences

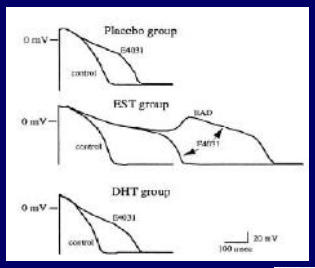
- Patients admitted for decompensated HF
  - All measures of ventricular ectopy were markedly lower in women



Aronson D et al. PACE 2002 25: 1206-1211

Ventricular Repolarization
Cellular Effects of Hormones

- Estradiol (EST) and DHT response in ovariectomized rabbits



Hara et al. JPE 1998;285: 1068-72

Long QT: Torsades de Pointes

- Torsades de pointes – PMVT occurring in the setting of a lengthened QT interval
- Reflects prolonged cardiac repolarization
- May cause syncope or even precipitate VF and cardiac arrest
- May be congenital but most common as an acquired disorder (drugs, hypokalemia)

SVT: *Inducibility During Menstruation*

- Premenstrual clustering of spontaneous arrhythmia has been observed in women with SVT
- Scheduling elective EP procedures at times of low estrogen levels may facilitate successful procedures

Myerburg RJ, et al. Am J Cardiol. 1999;83:1049-1054.

Palpitation During Menopause or Perimenopause

- Treatment:
  - Not required
- Improvement of symptoms:
  - Beta blockers if palpitation persist after initiation of ERT
  - Progesterone may trigger cardiac arrhythmia in certain patients

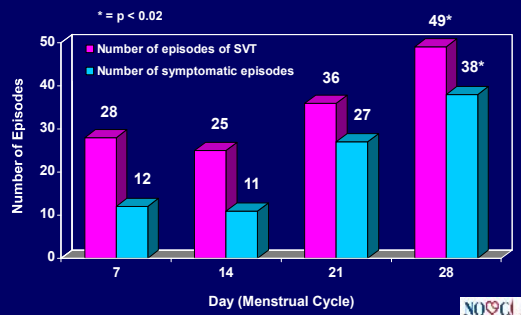
Rosano GMC, et al. Int J Fertil. 1997;42:94-100.

Palpitation During Menopause or Perimenopause

- Menopause:
  - ↓ estradiol production
  - Associated with ↑ and uncontrolled adrenergic activity
  - Palpitation frequent CV complaint
- Perimenopause:
  - Palpitation often due to sinus tachycardia
  - Related to ↑ sympathetic drive

Rosano GMC, et al. Int J Fertil. 1997;42:94-100.

Cyclical Variation in SVT in Women



Rosano GMC, et al. The Lancet. 1996;347:786-788.

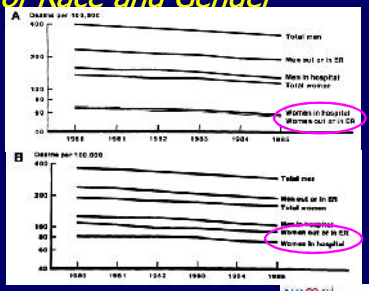
Estrogen Modulation in Mice

- Estrogen modulates autonomic inputs into murine SA and AV nodes
- Normal estrogen states increase sympathetic input
- Low estrogen decrease AVN conduction times and RV refractory periods
- Estrogen replacement restores these parameters
- ? Clustering of arrhythmias around menses

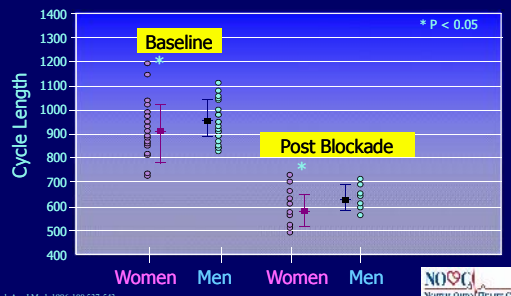
Saba et al. ANE 2004; 9:142-148

Mortality Trends (Age-Adjusted)
Effect of Race and Gender

- Out of Hospital Arrest
- In-Hospital Arrest

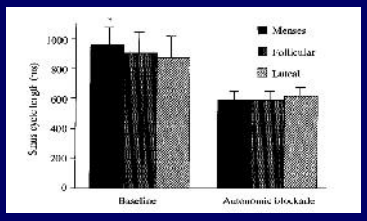


Autonomic Blockade
Gender Differences



Burke JH, et al. Am J Med. 1996;100:537-543.

Response to Autonomic Blockade:
Menstrual Effects



*The sinus cycle length was significantly longer (*P <0.03) during the menstrual phase of the cycle at baseline*

Burke JH, et al. Am J Med. 1996;100:537-543.

Palpitation in Women

- **Palpitation represent 15-25% of symptoms reported by female cardiology patients**
- **Occur frequently during the luteal phase of the menstrual period, pregnancy, and perimenopause**

Rosano GMC, et al. Int J Fertil. 1997;42:94-100.

Palpitation in Women:
Associations

- **Young women and rapid HR**
  - **Frequently re-entrant tachycardias**
  - **Associated with mitral valve prolapse**
- **Pregnancy**
  - **SVT may be due to mechanical stimuli or possible arrhythmogenic effects of pregnancy**
- **Perimenopause**
  - **Usually benign**
  - **May be due to ↑ sympathetic activity in menopause**

Rosano GMC, et al. Int J Fertil. 1997;42:94-100.