Rhythms of the HEARTLAND

15th Annual Heart Rhythm Symposium:
Rhythms of the Heartland

Management of PVCs From the Healthy to CHF Clinic

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February 2018

Objectives

- To understand the range of symptoms and presentations of patients with frequent PVCs
- To illustrate the importance of defining prognosis in these patients
- To outline the therapeutic options to suppress or eliminate ventricular ectopy
- To illustrate the role of ablative therapy in PVC management

Which of these statements are TRUE?

A) "PVCs are benign…"

B) "PVCs are a sign of underlying heart disease…"

C) "PVCs can lead to heart failure…."

D) "PVCs can be life threatening…

E) All of the Above

"True" statements

- "PVCs are benign…"
- "PVCs are a sign of underlying heart disease…"
- "PVCs can lead to heart failure…."
- "PVCs can be life threatening…"

History

"…Occasional pulse irregularities did not predict an adverse outcome."

"However, frequent irregularities(1 in 10 beats) was associated with an ominous prognosis…often resulting in death within one year."

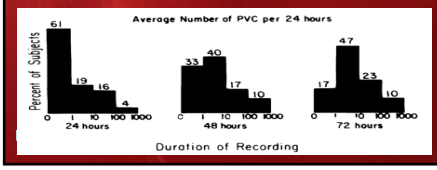
-Chinese Physician Pien Ts'Io ~ 600 BC

PVCs are common

TABLE 2. *Probability (%) of Observing a Given Number of Premature Ventricular Complexes During a Given Length of Observation in Subjects with Normal Hearts*

	No. of PVCs						
	0	≥1	>5	>10	>50	>100	>500
1 hour (9–10 a.m.)	85	15	3	2	1	0	0
3 hours (9 a.m.–12 noon)	78	22	9	5	2	0	0
6 hours (9 a.m.–3 p.m.)	74	26	14	8	3	1	0
8 hours (9 a.m.–5 p.m.)	72	28	15	10	3	2	0
12 hours (9 a.m.–9 p.m.)	64	36	22	15	5	3	0
24 hours	61	39	25	20	9	4	1

Abbreviation: PVC = premature ventricular complex.



Kostis JB. Circulation 1981; 63: 1351-6

PVCs are common

TABLE 3. *Effect of Age on the Probability (%) of Having More Than a Given Number of Premature Ventricular Complexes per 24 Hours in Subjects with Normal Hearts*

Age (years)	n	No. of PVCs >0	>50	>100
10–29	6	16.7	0	0
30–39	11	18.2	0	0
40–49	29	27.6	3.5	0
50–59	39	51.3	12.8	5.1
60–69	12	58.3	25.0	16.7

Abbreviation: PVC = premature ventricular complex.

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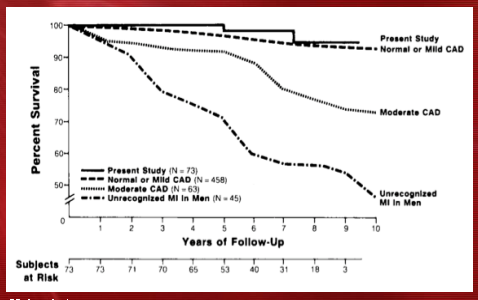
Kostis JB. Circulation 1981; 63: 1351-6

PVCs are benign…



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Kennedy HL NEJM 1985

…except when they are not benign.

- In pts with prior infarction, frequent or complex PVCs are associated with increased mortality
  - » Hallstrom AP et al. JACC 1992; 20: 259-64
  - » Ruberman W et al. NEJM 1977; 297: 750-7
- Hypertension is associated with frequency and/or complexity of PVCs
  - » Abdalla IS et al. Am J Cardiol 1987; 60: 1036-42.
  - » Simpson RJ et al. Am Heart J 2002; 143: 535-40
  - » Bikkina M et al. Ann Intern Med 1992; 117: 990-6
- In pts with LVH, frequent PVCs are associated with increased mortality
  - » Bikkina M et al. JACC 1993; 22: 1111-16

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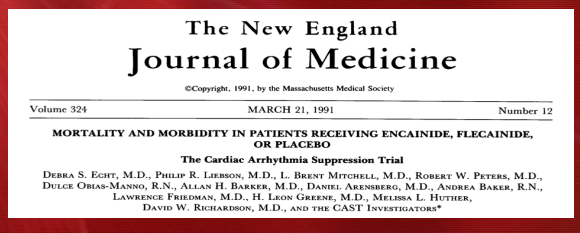
CAST: A cautionary tale



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MORTALITY AND MORBIDITY IN PATIENTS RECEIVING ENCAINIDE, FLECAINIDE, OR PLACEBO

The Cardiac Arrhythmia Suppression Trial

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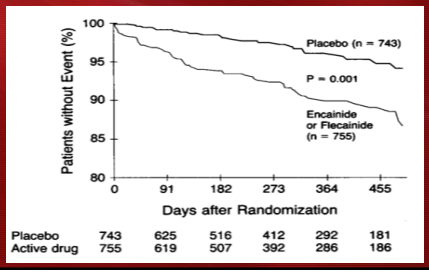
CAST Trial

- PVCs may be associated with adverse outcomes in MI patients…but PVC *treatment* can cause more harm than good



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PVCs and "Normal" hearts

Benign Prognosis

- ✓ Circulation 1971; 44: 617-25
- ✓ Chest 1973; 64: 564-9
- ✓ Cardiology 1983; 70 (Suppl 1): 82-7
- ✓ Eur Heart J 1983; 4: 338-46
- ✓ Am J Cardiol 1992; 70: 748-51
- ✓ Jpn Circ J 1994; 58: 190-8
- ✓ N Eng J Med 1985; 312:193-7
- ✓ J Intern Med 1999; 246: 363-72
- ✓ J Am Coll Cardiol 2001; 38: 364-70
- ✓ Heart 2009; 95: 1230-7

Adverse Outcomes

- ✓ Am Heart J 1981; 101: 135-42
- ✓ Am J Cardiol 1987; 60: 1036-42
- ✓ Eur Heart J 1991; 12: 597-601
- ✓ Ann Intern Med 1992; 117: 990-6
- ✓ Am J Cardiol 2006; 97: 1351-7
- ✓ J Cardiol 2010; 56: 23-6
- ✓ Am J Cardiol 2011; 107: 151-5

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Approach: General Principles

- Assess for symptoms and triggers
- Confirm PVC diagnosis (12 lead PLEASE!)
- Quantify PVC burden (HOLTER)
- Temporal correlation: Arrhythmia→Symptoms
- Assess for presence of structural heart disease
- Counsel patient on likely prognosis
- Decide if treatment necessary
- Determine reasonable level of aggression for treatment

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Symptoms and PVCs

Asymptomatic

↓

Nonspecific

(Fatigue, Weakness, Exercise intolerance)

↓

Typical

(Palpitations, Irregular and/or "pounding" Heart Beat)

↓

Overt

(Heart Failure, Syncope/Cardiac Arrest from PVC-induced VT/VF)

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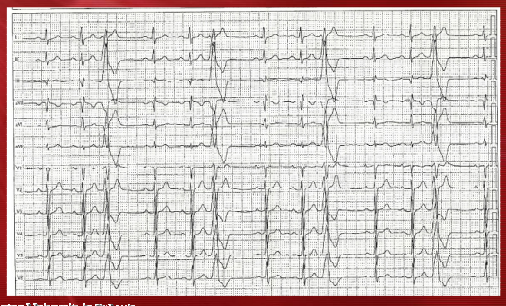
Confirm Diagnosis: 12 Lead ECG



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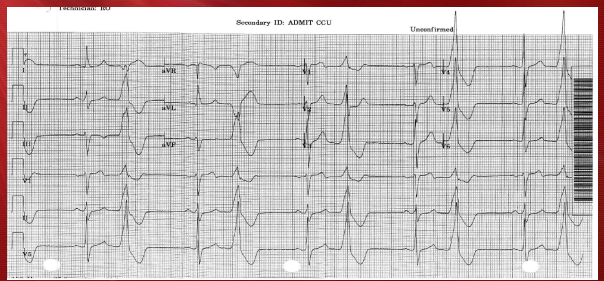
Confirm Diagnosis: Vent. Bigeminy



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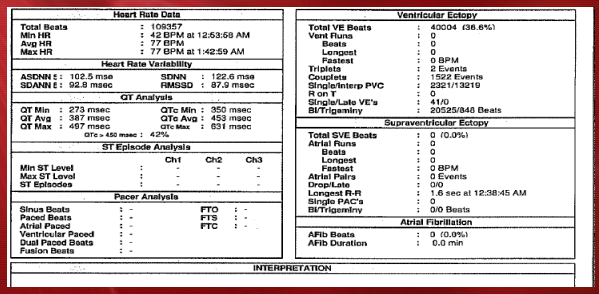
Quantify PVC Burden: Holter



Heart Rate Data		Ventricular Ectopy	
Total Beats	108357	Total VE Beats	40004 (36.6%)
Min HR	42 BPM at 12:53:58 AM	Vent Runs	
Avg HR	77 BPM	Beats	0
Max HR	77 BPM at 1:42:59 AM	Longest	0
Heart Rate Variability		Fastest	0 BPM
ASDNN ε	102.5 mse	Triplets	2 Events
SDANN ε	92.8 msec	Couplets	1522 Events
SDNN	122.6 mse	Single/Interp PVC	2221/13219
RMSSD	87.9 msec	R on T	0
QT Analysis		Single/Late VE's	41/0
QT Min	273 msec	Bi/Trigeminy	20525/846 Beats
QT Avg	387 msec	QTc Min	350 msec
QT Max	497 msec	QTc Avg	453 msec
QTc > 450 msec	42%	QTc Max	631 msec
ST Episode Analysis		**Supraventricular Ectopy**	
	Ch1 Ch2 Ch3	Total SVE Beats	0 (0.0%)
Min ST Level	- - -	Atrial Runs	
Max ST Level	- - -	Beats	0
ST Episodes	- - -	Longest	0
Pacer Analysis		Fastest	0 BPM
Sinus Beats	-	Atrial Pairs	0 Events
Paced Beats	-	Drop/Late	0/0
Atrial Paced	-	Longest R-R	1.6 sec at 12:38:45 AM
Ventricular Paced	-	Single PAC's	0
Dual Paced Beats	-	Bi/Trigeminy	0/0 Beats
Fusion Beats	-	**Atrial Fibrillation**	
FTO	-	AFib Beats	0 (0.0%)
FTS	-	AFib Duration	0.0 min
FTC	-		
INTERPRETATION			

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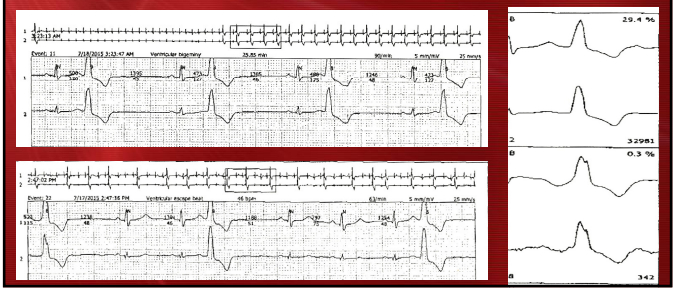
Holter Monitor

1. Basic Rhythm: Sinus. Rate 40 to 100/m. Average 70/m.
2. PVCs – mostly in the form of bigeminy – some interpolated – few couplets/salvos/No V tach. Total of 30% of beats scanned.
3. Rare PACs.
4. No ST-T wave changes.
5. Activity Log – No correlationship.



Symptoms and Arrhythmia

- *Temporal* relationship between PVCs and symptoms helps dictate management
- 12 lead ECG may be insufficient
- Continuous Monitoring
  - 24-72 hour HOLTER Monitor
    - If symptoms are *frequent*
  - 30 day Event Recorder
    - If symptoms are *less frequent*
  - Implantable loop recorder (ILR)
    - *Rare*, but significant events

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Noninvasive imaging

- Transthoracic Echocardiography
  - Assess ventricular function
  - Rule out valvular heart disease
  - Other: HCM, infiltrative CM
- Exercise treadmill test
  - Especially, if exercise-induced
  - Elevated heart rate often suppresses "benign" PVCs
  - PVCs may be more prevalent during recovery
  - Dynamic ST changes or exercise induced multifocal PVCs or NSVT may indicate ischemic heart disease
- Echo or nuclear imaging can be combined with exercise in patients with higher suspicion of CAD

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Noninvasive imaging

- Other:
  - Cardiac CT
  - Cardiac MRI
  - Positron-emision Tomography
- Reserved when suspicion of specific, less common disorders is present
  - HCM
  - Cardiac Sarcoid
  - Infiltrative Cardiomyopathy
  - ARVC

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PVCs with Structural Heart Disease

- Coronary Disease
  - PVC origin is commonly from ischemic tissue or scar
  - Reperfusion arrhythmias are common
  - Can increase likelihood of sustained VT/VF
  - Remember CAST!
- Nonischemic Cardiomyopathy
  - Epicardial and basal LV origins are common
- ARVC
  - PVCs are common with RV origin from regions of fibrofatty replacmeent of tissue
- Frequent PVCs may interfere with biventricular pacing (CRT)

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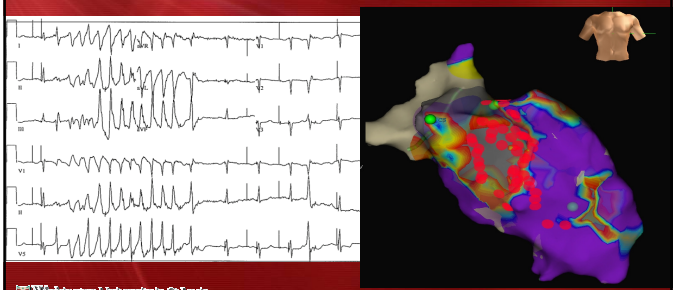
"Malignant" PVCs



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PVCs without Structural Heart Disease

- Ventricular outflow tracts are most common sites of origin
  - RVOT >>> Aortic Cusps/LVOT
  - Common Embryologic Origin
  - Other: Mitral/Tricuspid Annulus, Aortomitral continuity, papillary muscles, Purkinje fibers
- Triggered Activity
- Catecholamine sensitive
- Catheter ablation can be curative

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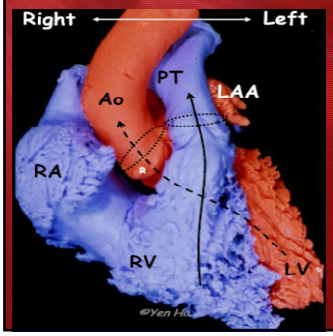
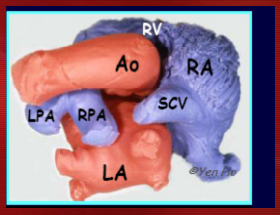
Idiopathic VT/PVCs: Anatomy





Points of Emphasis

- The RVOT runs anterior, leftward, and superior to the LVOT
- Tight Quarters: Many potential sites of origin requiring different approaches

PVC-Induced Cardiomyopathy

First Evidence of Premature Ventricular Complex-Induced Cardiomyopathy: A Potentially Reversible Cause of Heart Failure

- 22 y/o Female with Fatigue/Palpitations
- Holter: 25-50,000 PVCs/24 hrs
- Echo: LVEF 43%, globally dilated LV
- Successful elimination of PVCs (Ablation)
- 6 months follow up: Normal LV, LVEF

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Chugh SS et al. JCE 2000; 11: 328

Which patient is most likely to develop a PVC-Induced Cardiomyopathy?

A) Symptomatic with 50,000 PVCs (50%), PVC ~ 135ms

B) Asymptomatic with 3000 PVCs (3%), PVC ~ 165ms

C) Symptomatic with 42,000 PVCs (42%), PVC ~ 140ms

D) Asymptomatic with 42,000 PVCs (42%), PVC ~ 180 ms

E) Symptomatic with 42,000 PVCs (42%), PVC ~ 185ms

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Which patient is most likely to develop a PVC-Induced Cardiomyopathy?

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C) Symptomatic with 42,000 PVCs (42%), PVC ~ 140ms

D) *Asymptomatic with 42,000 PVCs (42%), PVC ~ 180 ms*

E) Symptomatic with 42,000 PVCs (42%), PVC ~ 185ms

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PVC-Induced Cardiomyopathy

- PVC Burden > 24% associated with overtly diminished LV function

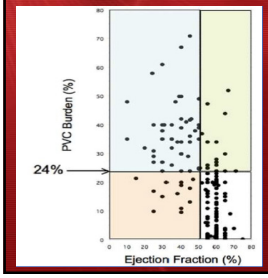

Table 3 Cutoff data for the PVC burden based on data from the ROC curves with combined sensitivity and specificity

PVC burden (%)	Sensitivity (%)	Specificity (%)
10	100	46
16	90	58
21	80	75
27	70	88
30	60	91
34	50	91
35	40	94
39	30	95
41	20	96
50	10	99

ROC = receiver-operator characteristic; other abbreviations as in Table 2.

Bauman TS et al. Heart Rhythm 2010; 7: 865-69

PVC-Induced Cardiomyopathy

- Cardiomyopathy is reversible if PVC burden is substantially reduced

Patients With Repetitive Monomorphic Ventricular Ectopy and Depressed Left Ventricular Function

Age, y	Sex	Presenting Symptom	Origin of CMP	Cardiac Medications	PVC Origin in RVOT	RFA Success	Initial Holter, PVCs/24 h	F/U Holter, (PVCs/24 h	Initial EF, %	F/U EF, %
37	F	Dyspnea	Idiopathic	β-Blockers	Anterior	Yes	5502	44	38	65
51	M	None	Idiopathic	β-Blockers	Posteroseptal	Yes	26 491	1893	45	60
80	M	Presyncope	Idiopathic	None	Anteroseptal	Yes	35 664	1100	35	55
51	M	Palpitations	Idiopathic	None	Anterior	Yes	9791	5	35	60
71	F	Palpitations	Idiopathic	β-Blockers	Posteroseptal	Yes	23 352	117	43	65
62	M	Presyncope	Idiopathic	β-Blockers	Posterolateral	Yes	...*	332	45	65
47	M	Palpitations	Idiopathic	None	Posterolateral	Yes	16 362	55	45	65
68	F	Palpitations	Idiopathic	β-Blockers	Posterior	No	5626	12 883	30	35

Yarlagadda RK et al CIRC 2005; 112: 1092

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PVC Induced Cardiomyopathy

- Asymptomatic patients are more likely to develop cardiomyopathy
  - » Yokokawa M et al. Heart Rhythm 2012: 9:92-95
  - » Del Carpio Munez F. JCE 2011: 22: 791-98
- PVC Burden greater than 15-20% have been associated with CM…but it has also been seen with lower burdens (4%).
  - » Lee et al. Circ AE 2012; 5: 229-36
  - » Yarlagadda RK. CIRC 2005; 112:1092
  - » Kanei Ann Noninvasive Electrocardiol 2008; 13: 81-85
- Subtle cardiac dysfunction likely exists in most patients with frequent PVCs and preserved EF…reversible after elimination.
  - » Wijnmaalen PA et al. Heart 2010; 96:1275
- Wide PVC duration (>150ms), epicardial origin, and shorter coupling intervals also associated with cardiomyopathy
  - » Yokokawa M et al. Heart Rhythm 2012: 9: 1460
  - » Moulton KP et al CIRC 1990; 81: 1245
  - » Sun Y et al. J Cardiobasc Imaging 2003; 19: 295

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Treatment: Lifestyle changes

- Typical Advice
  - Avoid excessive caffeine
  - Avoid smoking
  - Avoid excessive alcohol
  - Avoid triggers if present
- Data is lacking to support behavior modification…but a reasonable start while further work-up initiated

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Medical Therapy: Beta Blockers

- *Mainstay* of conventional medical therapy in symptomatic patients
- Particularly useful and indicated in patients with heart failure or CAD
- Beware the side effects…esp in young pts.
  - Fatigue, depressed mood, sexual dysfunction

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Medical Therapy: Calcium-Channel Blockers

- Commonly used in young patients without structural heart disease
- Common Side Effect: Constipation
- Avoid in patients with significant LV systolic dysfunction

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Medical Therapy: Antiarrhythmics

- Remember CAST!
- Sotalol
  - Class III AAD
  - Beta blocker and Potassium Channel Blocker
  - Monitor QT +/- hospitalization
- Amiodarone
  - "Class III AAD "
  - Diverse effects on various ion channels
  - QT prolongation is of less concern
  - Effective, but side effect concerns (short and long-term)
    - Thyroid, Liver, Lungs, Skin, Eyes

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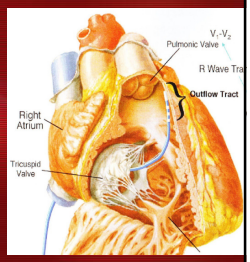
Catheter Ablation

- Patient sedated in fasting state
- Multiple, steerable catheters are placed via femoral access sites
- High burden of PVCs desirable to allow for precise mapping
  - Activation Mapping
  - Pace-mapping
- Ablation is performed at sites with "earliest" activation and/or "perfect" pacemaps



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Ablation versus Drugs

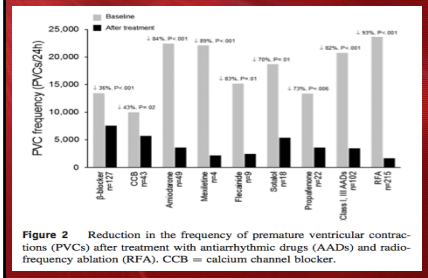

Figure 2 Reduction in the frequency of premature ventricular contractions (PVCs) after treatment with antiarrhythmic drugs (AADs) and radiofrequency ablation (RFA). CCB = calcium channel blocker.

Ablation most effective modality for PVC reduction…

…but drugs aren't terrible.

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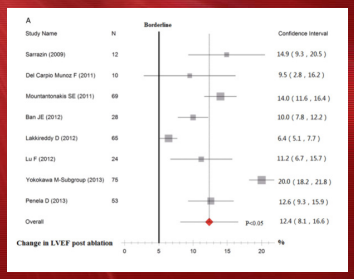
Zhong L et al. Heart Rhythm 2014; 11: 187

Catheter Ablation



Ablation improves LV function…

…and is often curative!

~ Success rate 70-90 %
~ Complication rate 1-3 %
~ Duration 2-6 hrs

Zang M et al. Heart 2014; 100: 787

Bias Alert!!!

"He that is good with a Hammer tends to think everything is a nail."

-- Maslow's Maxim: Law of the Instrument

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"Real World" Translation

- Most PVCs are benign…but not all.
- Ablation should be offered to patients with a substantial PVC burden (>20-25%) and diminishing EF for presumed PVC-induced cardiomyopathy.
  - If asymptomatic with normal EF, it is reasonable to follow with annual TTE.
- Ablation can be considered in patients with symptomatic PVCs that are refractory to CCB or BB.
- PVCs that induce malignant arrhythmias (PMVT, TdP, VF) and are refractory to AAD, should be targeted with ablation.

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