Nonsurgical Septal Reduction Therapy for Hypertrophic Obstructive Cardiomyopathy

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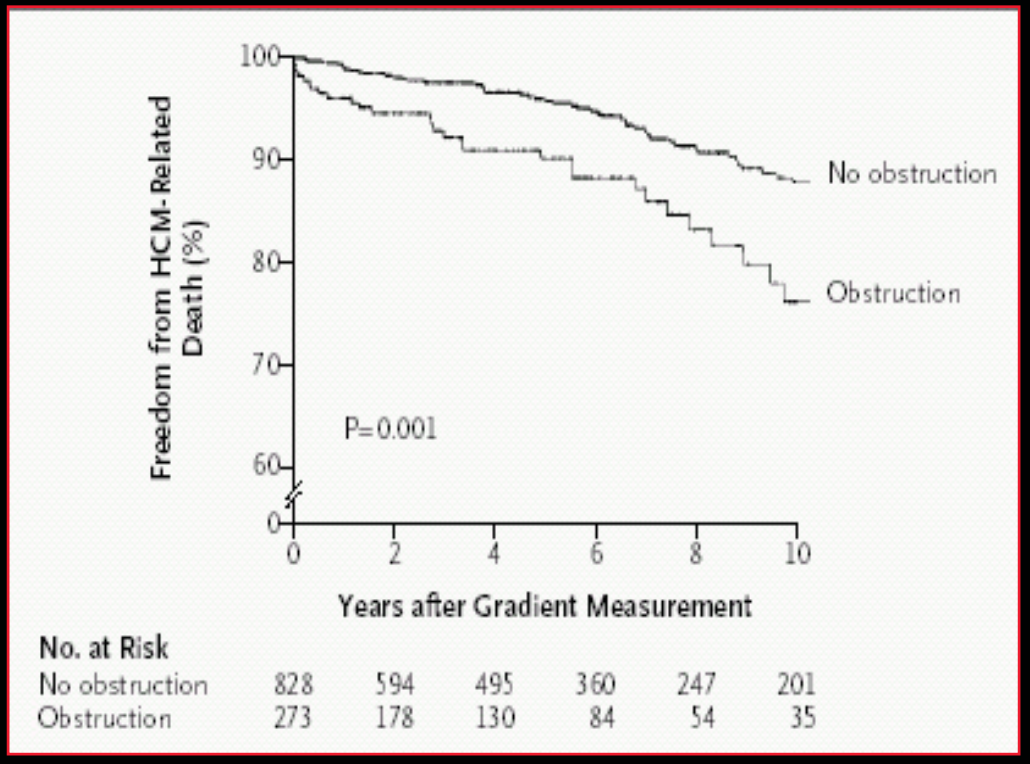
Hypertrophic Obstructive Cardiomyopathy(HOCM)

- Left ventricular(LV) outflow obstruction : an important determinant of symptoms
- Therapies that reduce the LV outflow perssure gradient : may improve LV filling pressure and symptoms

Hypertrophic Obstructive Cardiomyopathy(HOCM)



In patients with HOCM, left ventricular outflow tract obstruction at rest is a strong, independent predictor of progression to severe symptoms of heart failure and of death.

NEJM, 2003; 348 : 295-303

Therapies that reduce LV outflow obstruction

- Surgical myectomy or myotomy
- DDD pacemaker therapy
- Nonsurgical septal reduction therapy(NSRT) : introduced by Sigwart et al

Surgical Myectomy

- Symptomatic improvement : ≈ 70%
- Operative mortality : 2 - 5 %

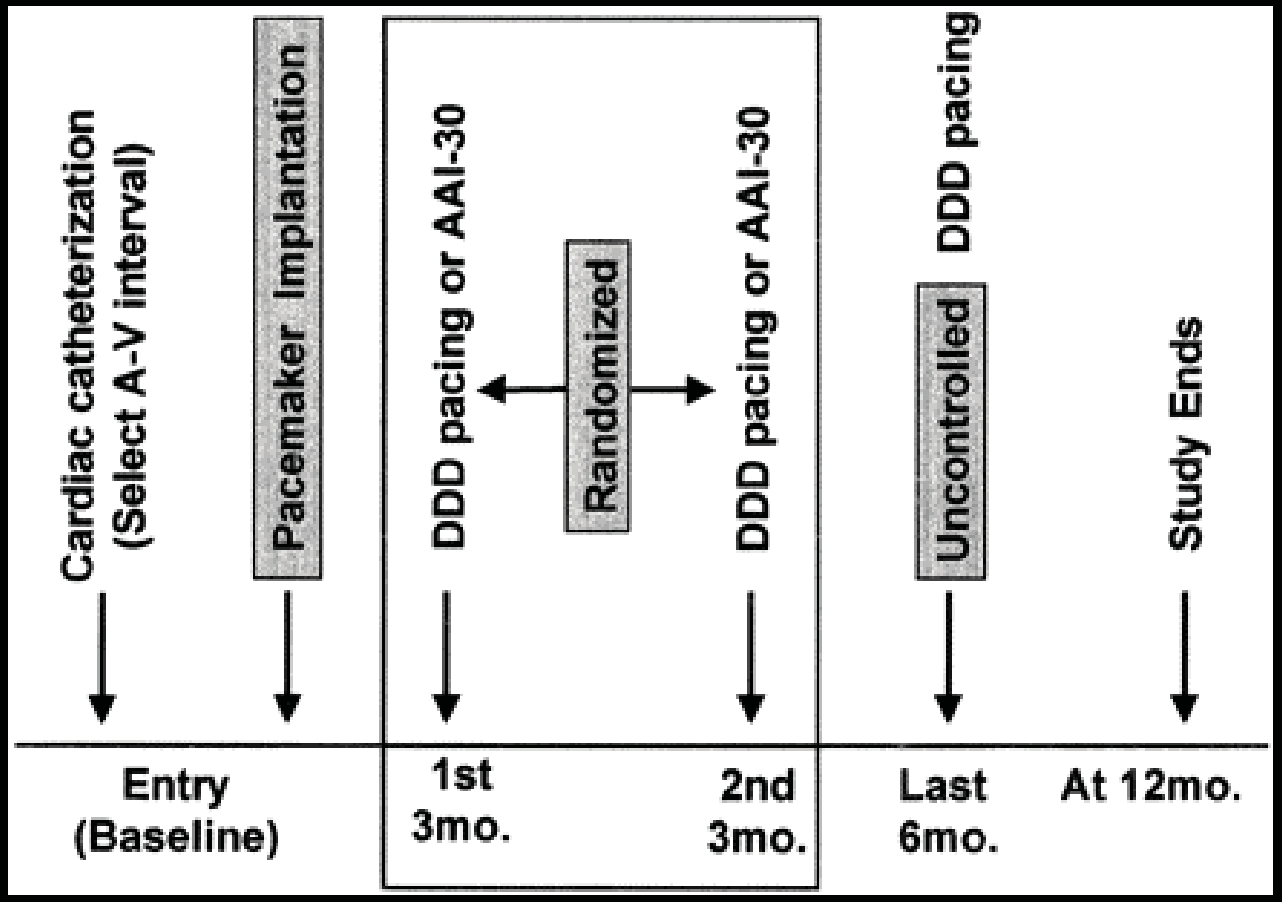
  Complications : VSD, arrythmia, LV dysfunction
- Few centers have adequate experience with this procedure

DDD Pacemeker

- Early and uncontrolled studies : may reduce LVOT gradient and symptoms
- Recent observations :
  - less uniform and mixed results
  - further impairment of LV diastolic function by the shortening of AV interval

M-PATHY Study

A randomized, double-blind, crossover study



N=48

Circulation 1999; 99:2927-33

M-PATHY Study

A randomized, double-blind, crossover study

- Symptoms : 25%↑, no difference between groups
- Exercise capacity : no improvement
- LVOT pressure gradient : 40% ↓ in DDD group

Conclusion : Pacing cannot be regarded as a primary treatment for HOCM

Merits of NSRT

- Nonsurgical technique for septal myocardial reduction
- Hemodynamic improvement : more dramatic in NSRT than in pacemaker therapy
- Technically easy to interventional cardiologists

Current Indications for NSRT

Symptomatic HOCM

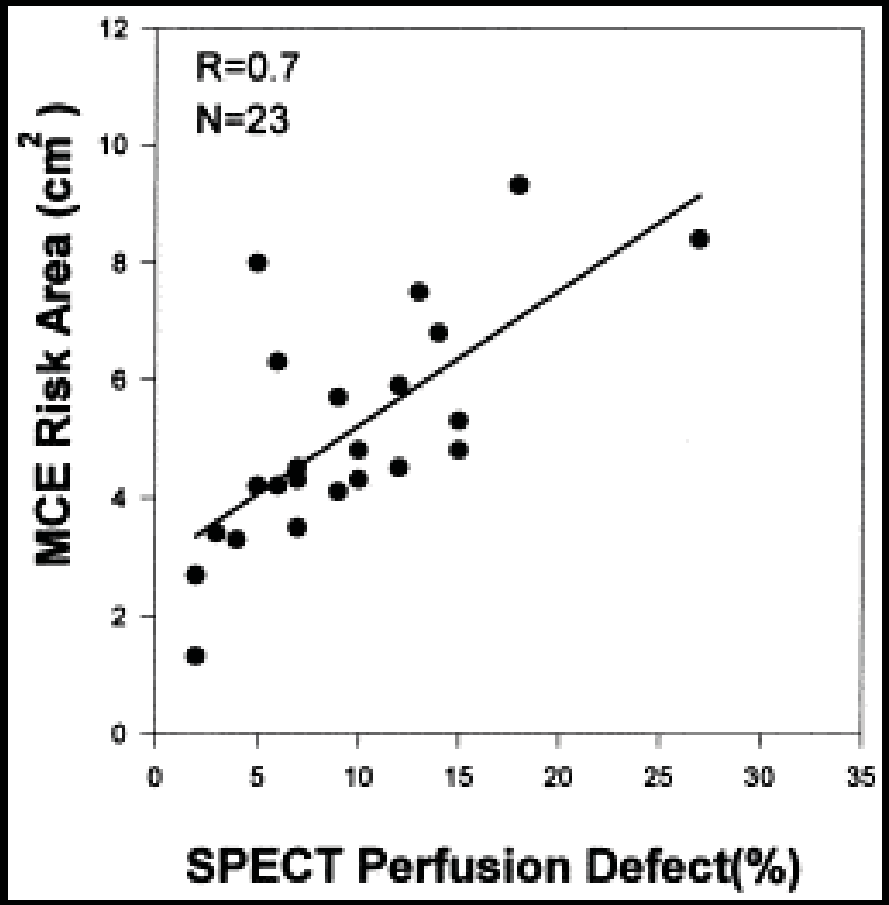
- unresponsive to medical therapy
- unresponsive to DDD pacemaker therapy or surgical myectomy

Technical Consideration

Selection of target artery("culprit vessel")

- 1st or 2nd septal artery : usually selected for intracoronary ethanol injection
- Hemodynamic testing by probatory balloon occlusion : low predictive value
- Myocardial contrast echocardiography

Myocardial Contrast Echocardiography



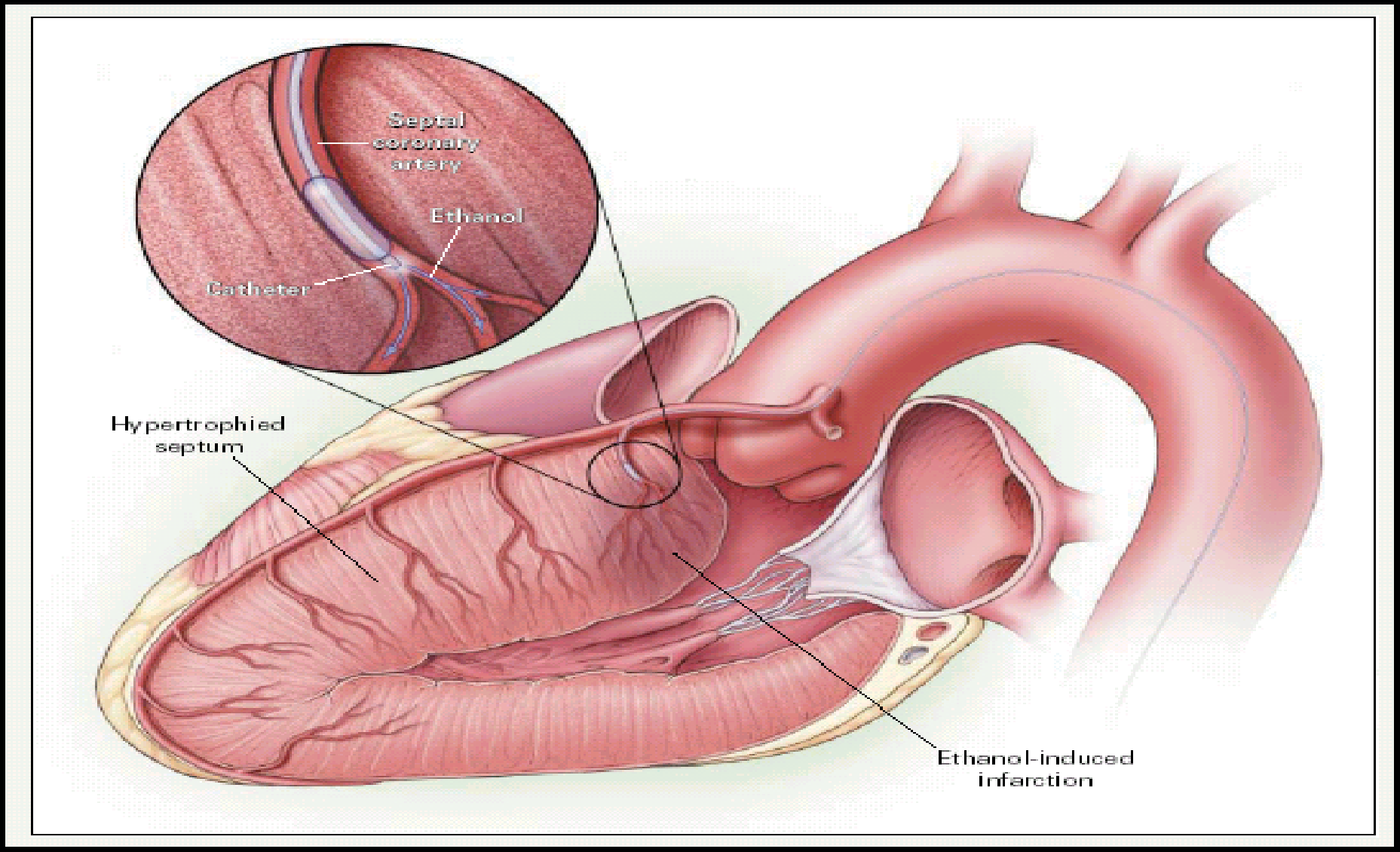
- Estimation of the size of the septal vascular territory with MCE is accurate, safe and feasible in patients during NSRT.

JACC 1998; 32 : 225-9

Procedure of NSRT

- Temporary pacemaker insertion
- Hemodynamic measurements
- 8F guiding catheter into the left main ostium
- Angioplasty balloon(1.5 - 3 mm) positioned at proximal portion of the septal artery

Procedure of NSRT



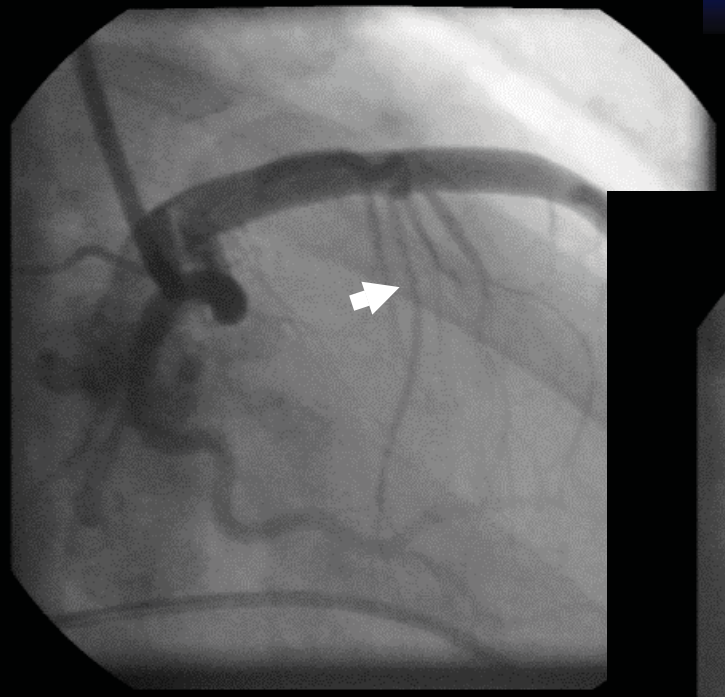
Procedure of NSRT

- Myocardial contrast echocardiography for proper localization and quantification of septal infact after enthanol injection
- Exclusion of dye reflux into the LAD

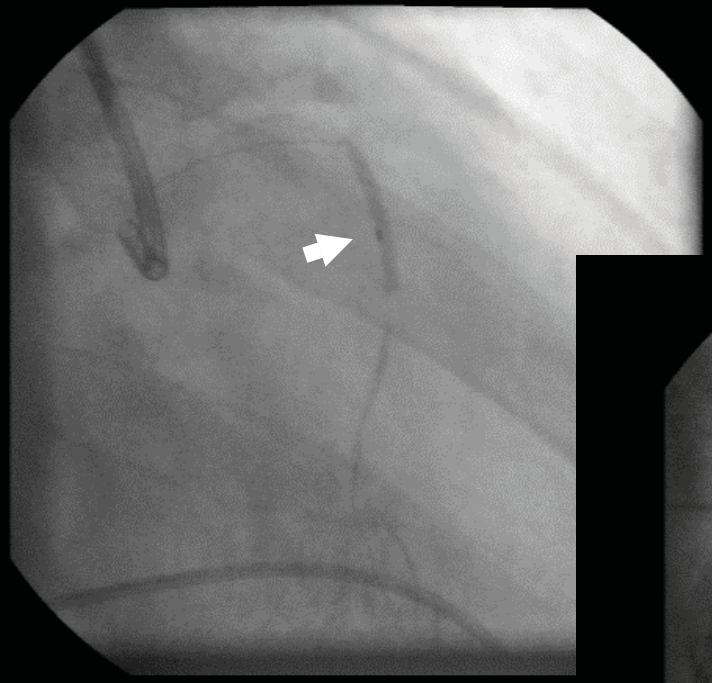
Procedure of NSRT

- 4-8 mg morphine IV for pain control
- Absolute alcohol(2 - 5 ml) is slowly injected through the lumen of the inflated balloon into the septal artery and left for 5 minutes before the balloon is deflated.

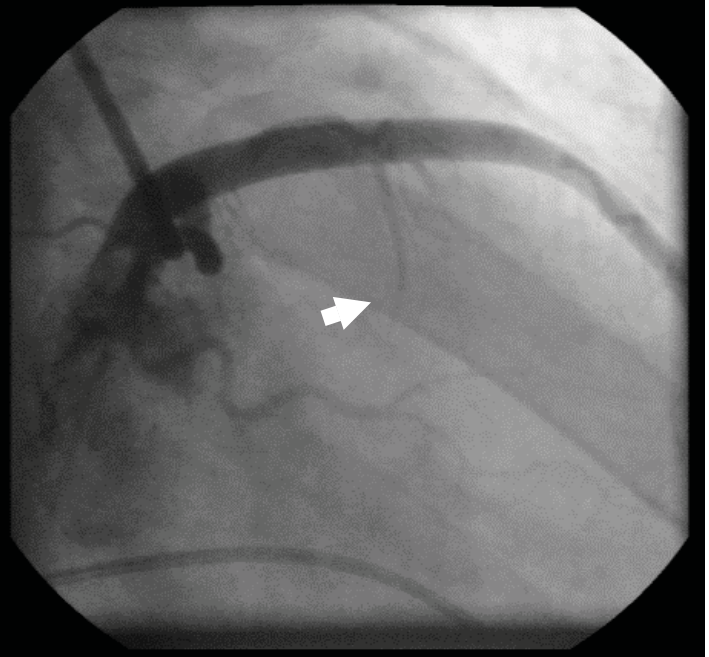
Procedure of NSRT



Target Artery

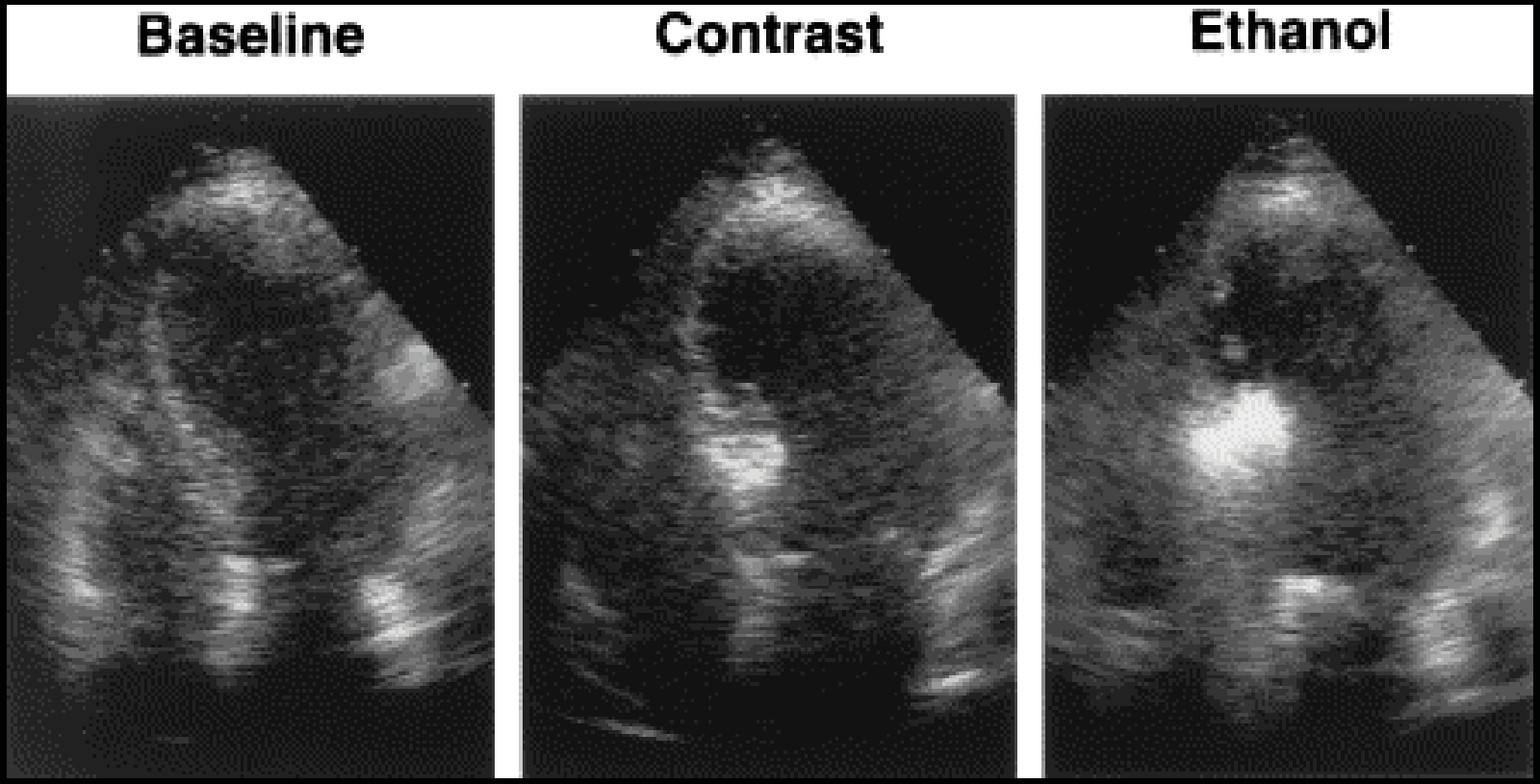


Balloon

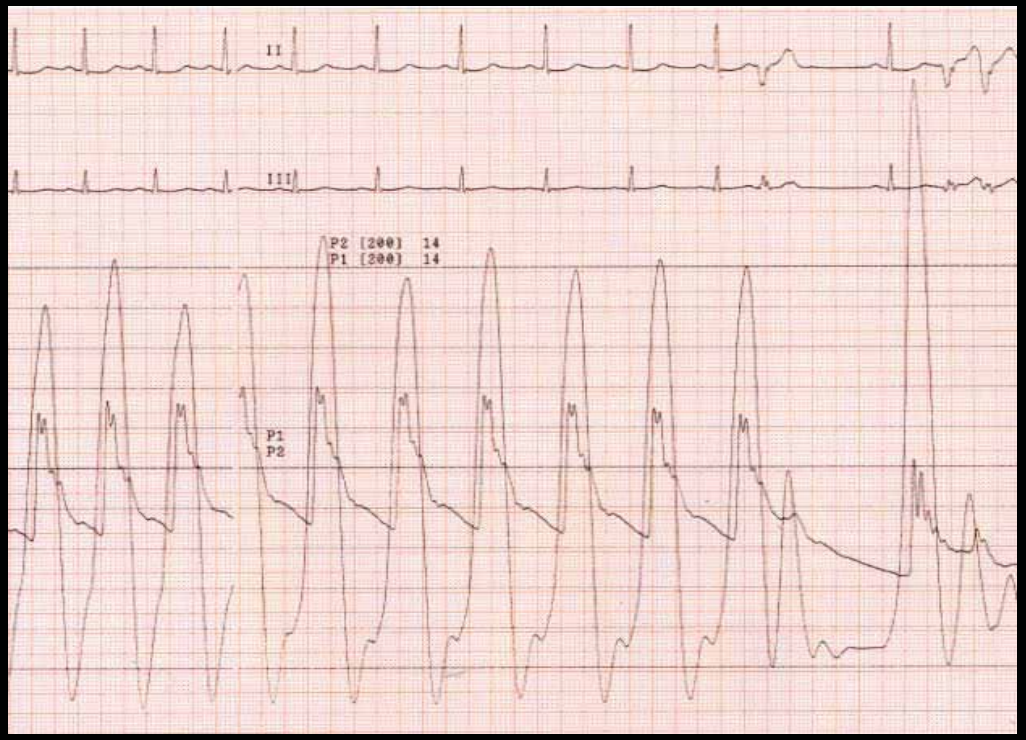


No Reflow

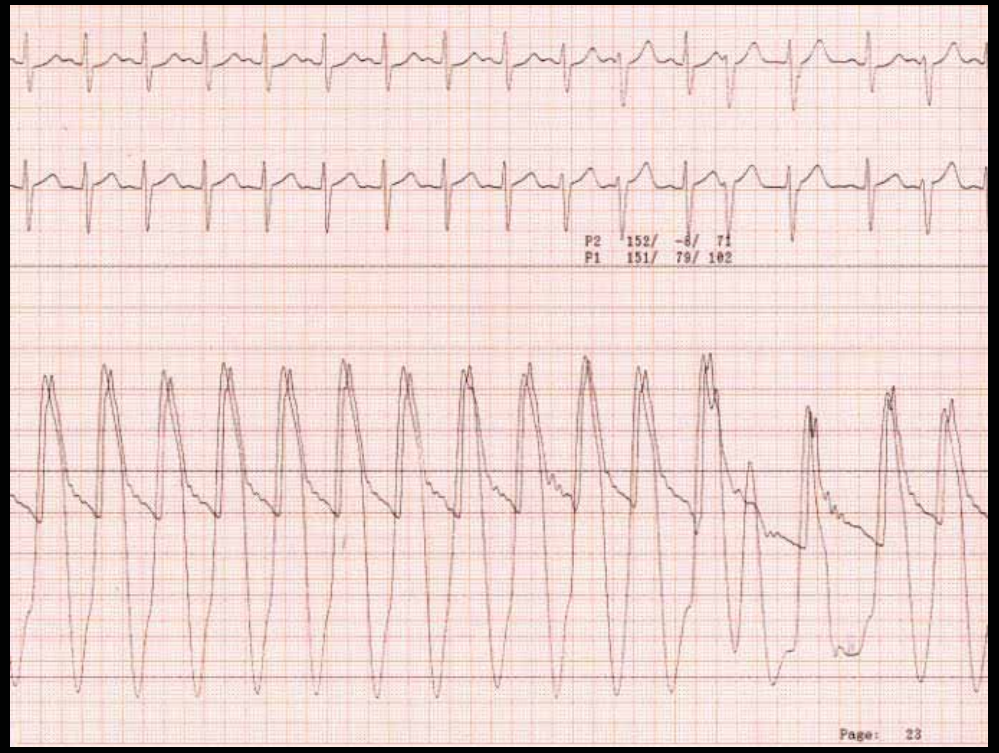
Myocardial Contrast Echocardiography



Pressure Recording



Before Ablation



After Ablation

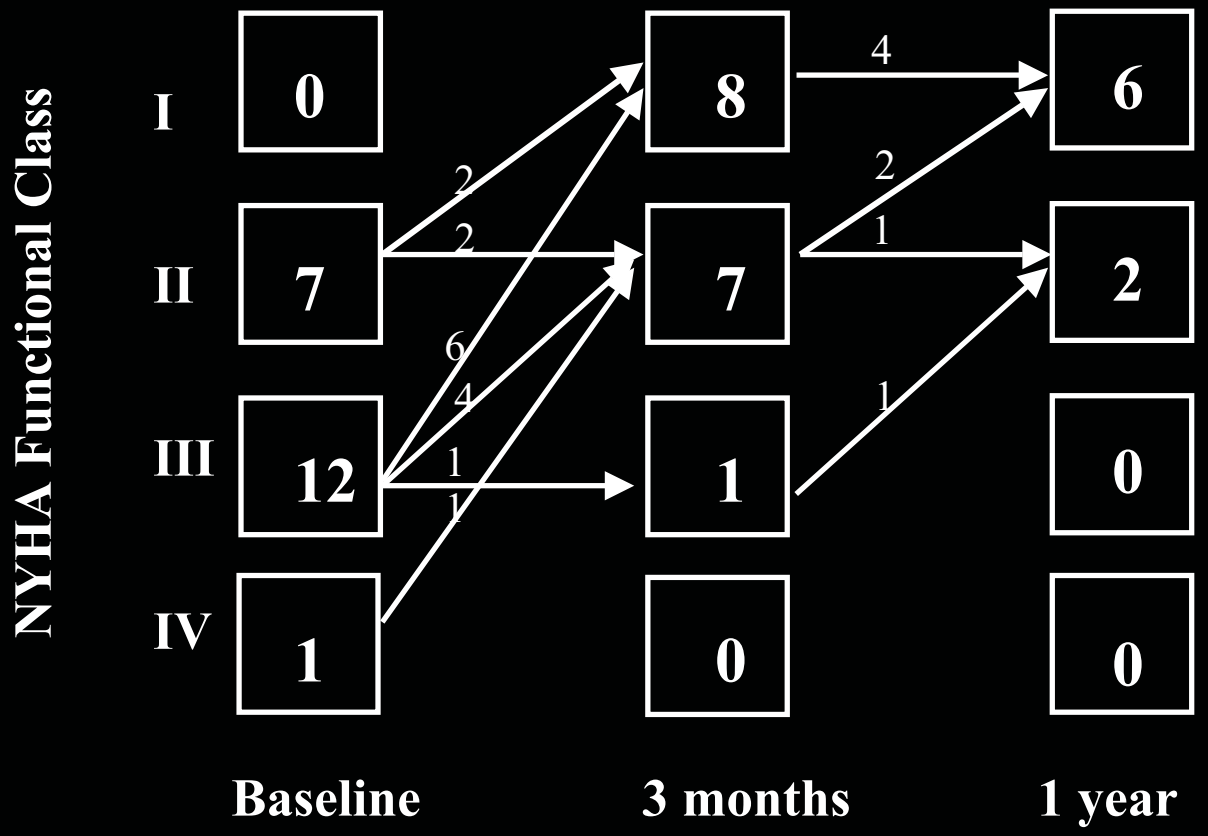
Postablation Management

- Admission to CCU for careful ECG monitoring and cardiac enzymatic assays for 1 - 3 days
- Discharge : usually 7 days after the NSRT

Therapeutic Effects

AMC Data

Symptomatic improvement in the majority of patients after NSRT (≈ 80%)



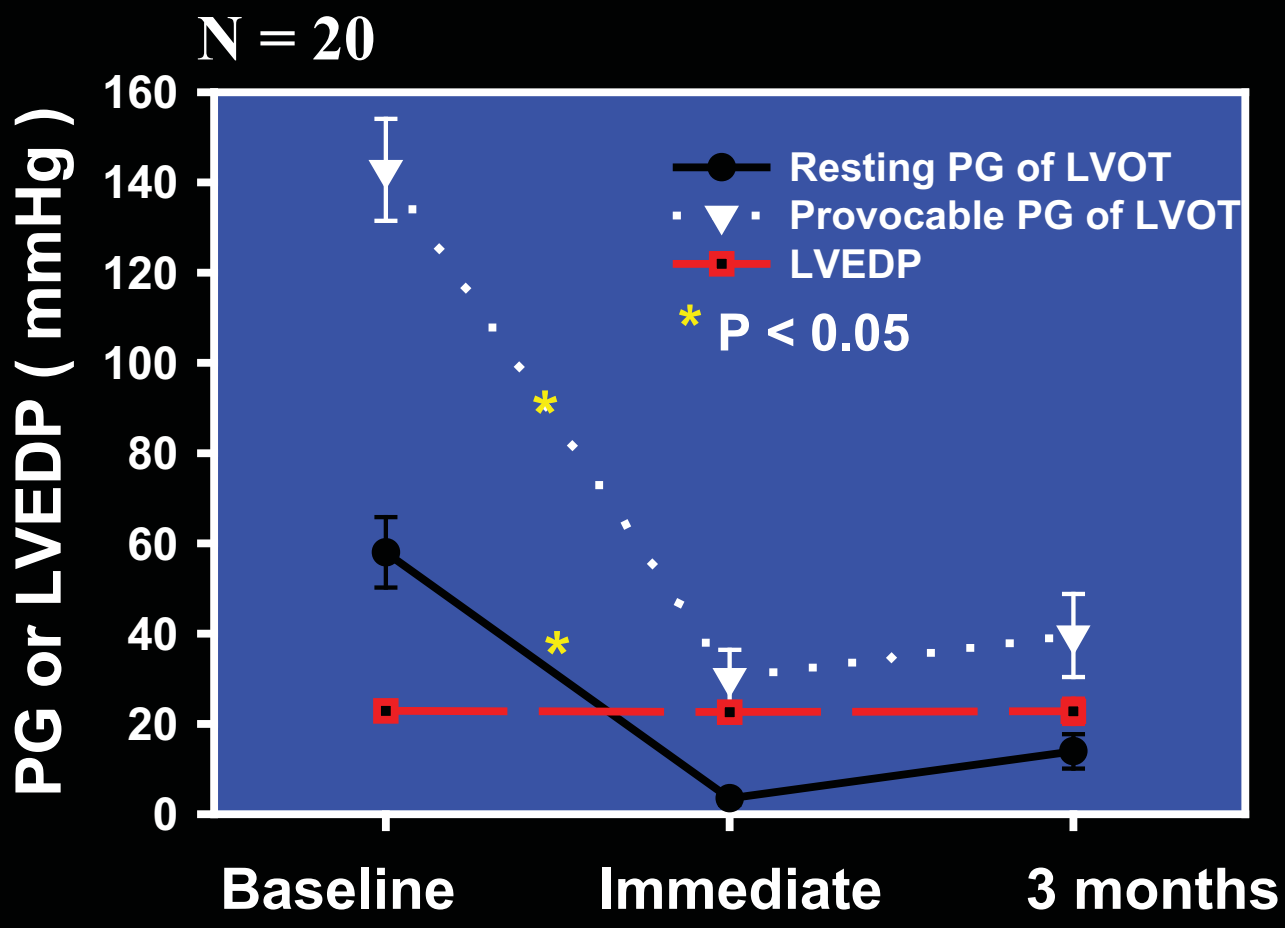
Symptomatic Improvement

	Baseline	Follow-up
Knight et al(n=18)	**2.6 ± 0.6**	1.1 ± 0.8*
Seggewisa (n=25)	**2.8 ± 0.6**	1.4 ± 1.1*
Kim (n=20)	2.7 ± 0.6	1.6 ± 0.6*
Faber (n=91)	**1.8** ± 0.9	**1.3** ± 0.9*

***p<0.05 vs Base, NYHA Functional Class**

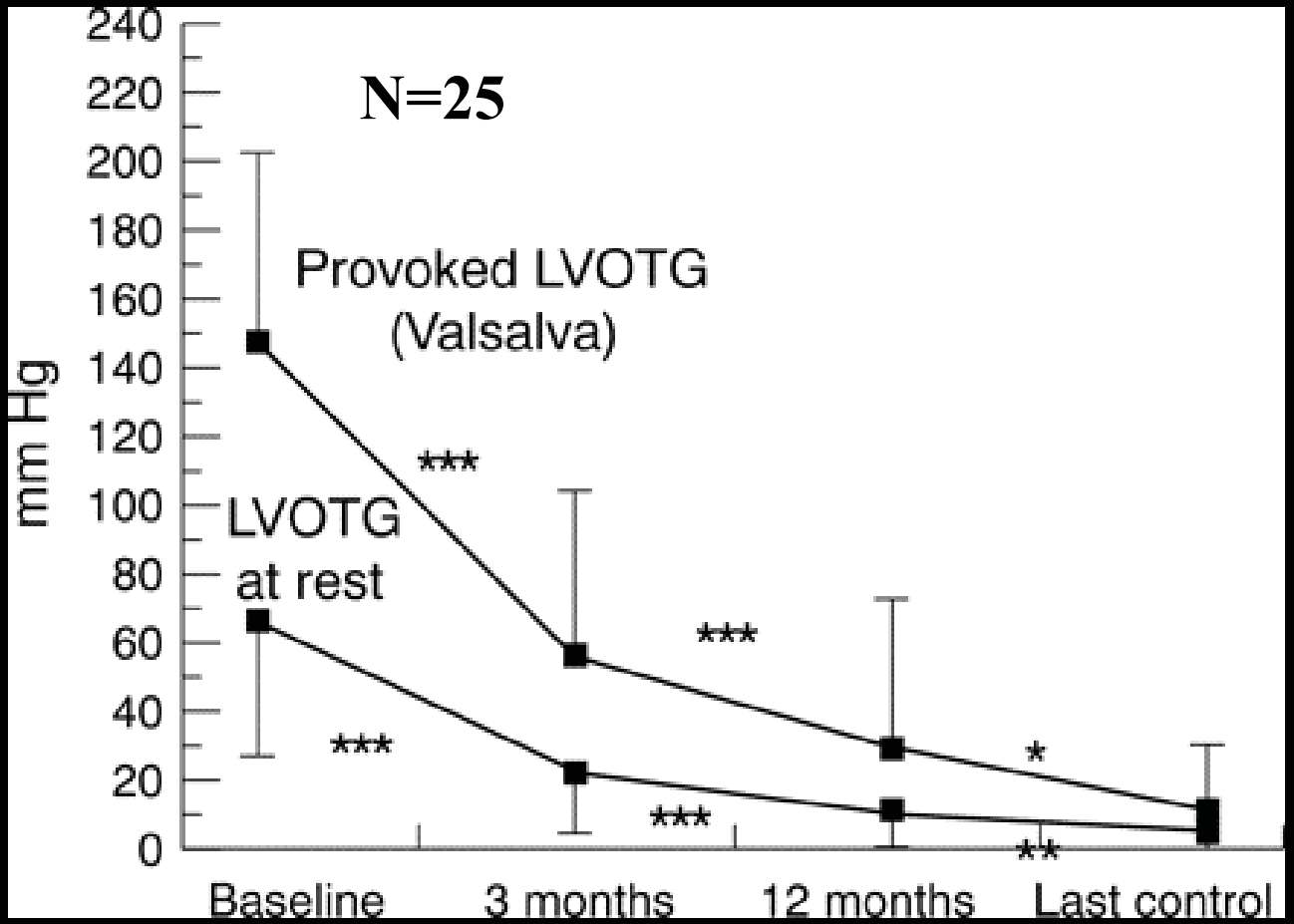
Hemodynamic Effects

AMC Data



LVOT gradient is markedly reduced immediately after NSRT & maintained at follow-up

Evolution of LVOT PG Estimated By Doppler Echo



LVOT gradient is progressively decreased after the NSRT

Heart 2000; 83 : 326-31

Exercise Test

AMC Data

	Base(n=20)	3 months	1 year
Exercise time(s)	573 ± 47	742 ± 46†	763±58†
Peak HR	137 ± 11	142 ± 6	139 ± 76
Peak SBP(mmHg)	132 ± 10	160 ± 5†	166 ± 7†
VO_2 at rest(ml/min)	238 ± 13	268 ± 11*	271 ± 18*
VO_2max(ml/min/kg)	18.5 ± 1.5	22.6 ± 1.3†	22.9 ± 1.8†

HR : heart rate, SBP : systolic blood pressure *p<0.05 and †p<0.01 vs baseline

NSRT leads to significant improvement of overall exercise capacity as well as symptomatic improvement.

Echocardiography

AMC Data

	Base(n=20)	3 months	1 year
EF(%)	**66 ± 2**	**63 ± 3**	**64±3**
Septal thickness	**28.3 ± 1.2**	**27.4 ± 0.9**	**25.2 ± 1.3***
LVEDD (mm)	**41.7 ± 1.7**	**43. ± 2.0**	**42.3 ± 2.2**
MR, grade	**1.7 ± 1.2**	**0.8 ± 0.7***	**0.6 ± 0.5***
SAM, grade	**2.5 ± 0.6**	**1.0 ± 0.7***	**0.8 ± 0.8***

***p<0.05 vs Base**

Echocardiography

Faber L et al

	Base(n=91)	Acute	3 months
EF(%)	79.2 ± 9.2		76.6±11.3*
Septal thickness	21.1 ± 3.3		17.1 ± 3.6*
LVEDD (mm)	47.3 ± 5.3	45.7 ± 5.3	48.6 ± 5.3*
MR, grade	0.8 ± 0.5	0.6 ± 0.5*	0.4 ± 0.5*
SAM, grade	2.4 ± 0.7	1.3 ± 0.7*	0.8 ± 0.8*

*p<0.05 vs Base

Circulation1999; 98 : 2415-2421

Mechanisms of Therapeutic Benefits (1)

- Septal infarction : thin the ventricular septum with contractile dysfunction and widens the LV outflow tract -> relief of the LV outflow obstruction

Mechanisms of Therapeutic Benefits (2)

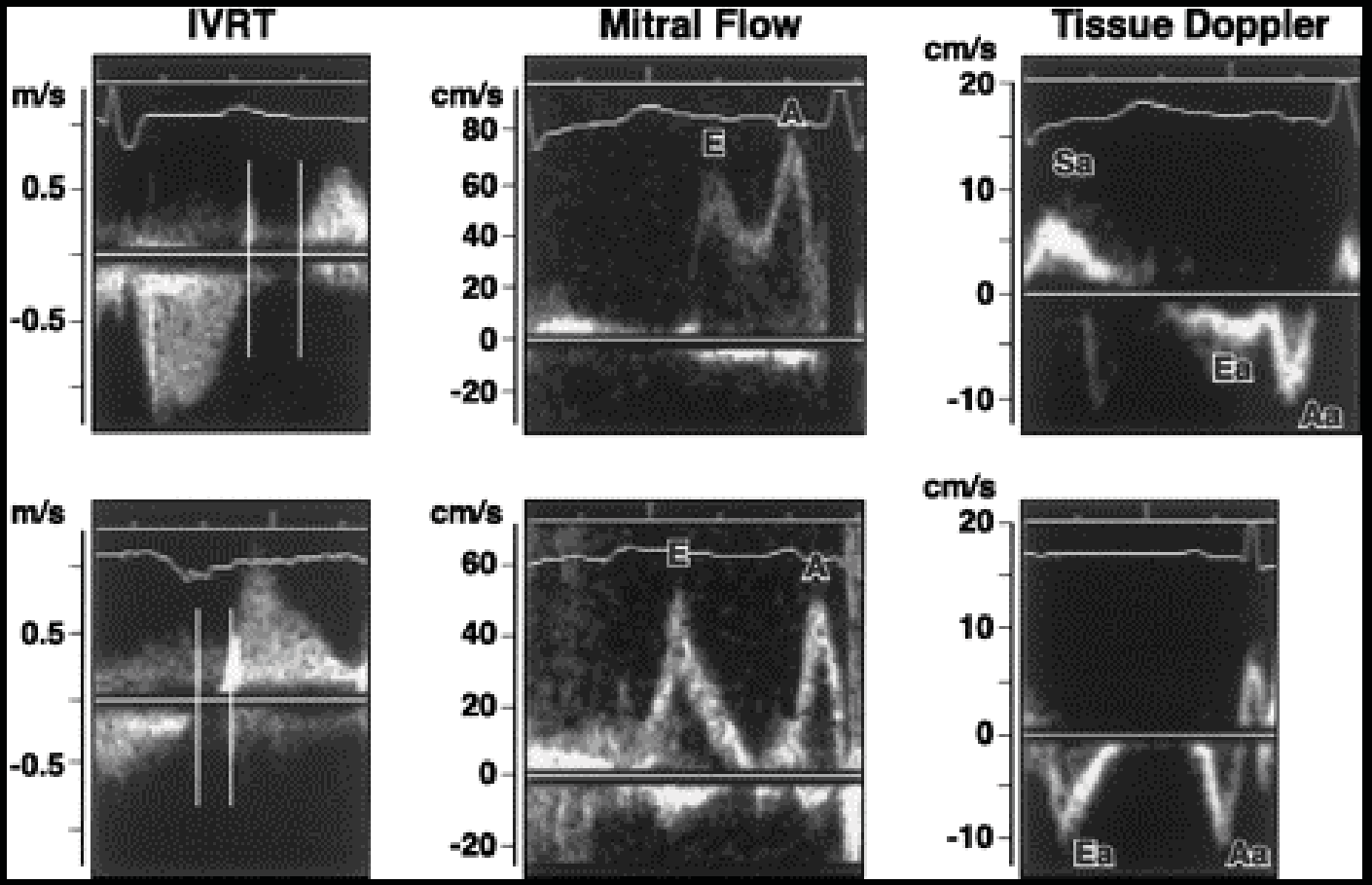
- Echocardiography study :

  - LV relaxation and compliance may improve after NSRT.

  - a reduction in LA size, ejection force and kinetic energy

JACC 1999; 34 : 1123-8

LV Diastolic Function



Baseline

6 Months

NSRT improves LV relaxation and compliance

Circulation 1999; 99:344-347

Change in LV Filling and LA Function

	Baseline	6 Months
LA max volume,ml	89 ± 36	66 ± 21*
LA min volume,ml	34 ± 22	14 ± 15*
LA ejection force	23 ± 14	15.8± 10.3*
LA kinetic energy	58.4 ± 25	36.1 ± 22.6*

NSRT results in an increase in LV passive filling volume and a reduction in LA size, ejction force and kinettic energy.

*p<0.05

JACC 1999; 34 : 1123-8

Early Complications

- Complete AV block : transient
  permanent
- Ventricular arrhythmia : VT/VF
- No reflow

Complete heart block : predictors, clinical impact

	Odds Ratio	95% CI	p Value
LBBB	39	3.6-416	0.002
> 2 septals injected	4.6	1.3-16	0.016
Bolus injection of ethanol	51	3.5-735	0.004
First-degree AV block	14	3-69	0.001
Female gender	4.3	1.3-1.5	0.02

JACC 2003; 42 : 296-300

Complete heart block : predictors, clinical impact

	PPM	No PPM	p Value
Number of patients	31	31	
NYHA class improvement	1.76±0.63	1.48±0.8	0.11
Septal reduction	0.82±0.67	0.5±0.7	0.08
Rest LVOTPG reduction	56±42	39±45	0.06
Increase in exercise time	68±149	132±116	0.13

Patients with complete heart block derive similar clinical and hemodynamic benefit to patients who did not require PPM

JACC 2003; 42 : 296-300

Complications

Pooled Data : 1.5%

	CAVB	VT/VF	Death
Knight et al(n=18)	0 %	11.1 %	0 %
Seggewisa (n=25)	20	4	4
Kim (n=20)	0	10	3
Faber (n=91)	11	2	2
Nagueh (n=29)	27.5	0	0

CAVB : complete AV block requiring permanent pacemaker insertion,
VT/VF : requiring DC cardioversion
Death : procedure related death (intractable VF)

Infarct Size

- **Cardiac enzyme(CK) :** *99' AMC Data*

  2,000 ± 500 (800 - 7,600 IU/L)

- **SPECT : 9.5 ± 6% (3 - 27%)**

Late Complications

- remain uncertain
- the potential risk of arrhythmia-related cardiac events (an arrhythmogenic substrate)
- progression of LV dysfunction ?

Long-Term Follow-Up

n=64 3.0±1.3 years (2.1-5.9)

	Baseline	6 weeks	3 years
Exercise time	6.1 ± 2.8	9.5 ± 3.4*	10.0 ± 3.2#
LA diameter, cm	4.2 ± 0.7	4.2 ± 0.6	4.0 ± 0.7#
LVEDD, cm	4.2 ± 0.7	4.8 ± 0.7*	4.8 ± 0.8
Resting PG, mmHg	64 ± 36	16 ± 14*	16 ± 15
Stress PG, mmHg	132 ± 34	46 ± 20*	45 ± 19
LV mass	410 ± 195	331 ± 127*	287 ± 108#

*p<0.05 versus Baseline value # p<0.05 versus 6 weeks

NEJM, 2002; 347 : 1326-33

Long-Term Follow-Up

- Significant reduction of LV outflow tract pressure gradient up to 3 years
- Improve exercise capacity

Caveat

- A steep learning curve for physicians
- Mortality rate is low (up to 4%)
- Complete AV block (up to 25%)
- Massive myocardial infarction as complcation
- NSRT does not permit correction of MR

Need For Rigorous Studies

- No controlled studies
- Long-term effects : remain uncertain
- NSR : should be reserved for patients who are not responding to medical therapy

Conclusions

- NSRT is a promising nonsurgical technique for septal myocardial reduction in HOCM
- Further follow-up studies may be needed to recommend NSRT as a primary therapy for HOCM.