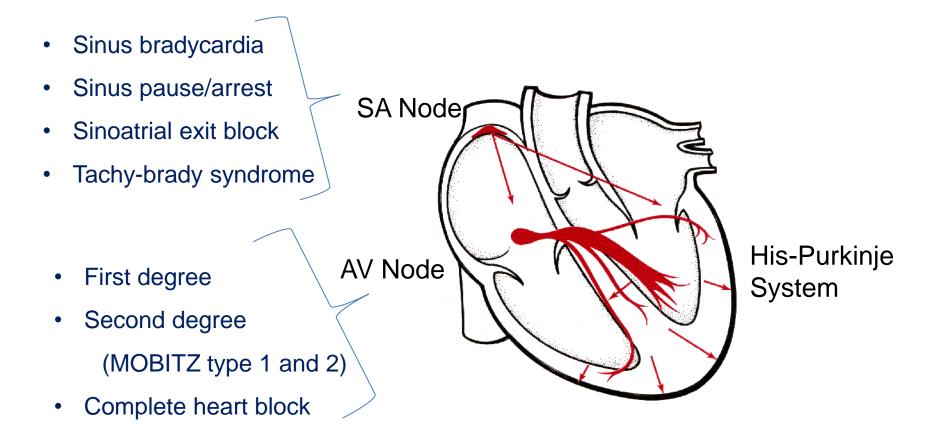
Bradycardia: Hemodynamic Impact and Revisited Pacemaker Indication in Children

부산대학교병원 조민정

When is bradycardia a bad thing?

- Extrinsic factors acting on a normal heart and its conduction system
- Intrinsic dysfunction or injury to the heart's conduction system



When is bradycardia a bad thing?

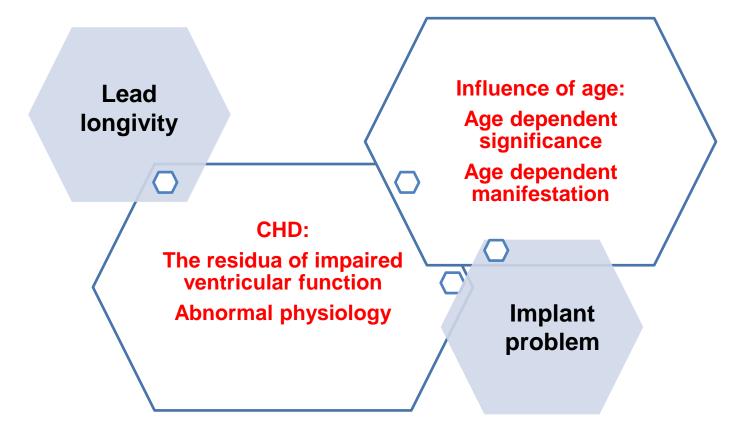
- Impaired ceret
- Significantly co
- Loss of AV sy

 To treat symptoms
 To improve ventricular dysfunction
 Prophylactic pacing ncope, near-syncope, okes-Adams attacks zziness htheadedness nfusion

or feeding thargy ilure to thrive tigue ercise intolerance

• Sudden death

What we need to consider before pacing in children?



Current indications for pacing therapy in children and patients with CHD

ACC/AHA/HRS 2012 Task Force on Practice Guidelines: the same contents with 2008 guidelines

third-degree AV block associated with symptomatic bradycardia, ventricular

2. Permanent pacemaker implantation is indicated for SND with correlation of

symptoms during age-inappropriate bradycardia. The definition of bradycardia

3. Permanent pacemaker implantation is indicated for postoperative advanced

4. Permanent pacemaker implantation is indicated for congenital third-degree

5. Permanent pacemaker implantation is indicated for congenital third-degree

congenital heart disease and sinus bradycardia for the prevention of recurrent

AV block with a wide QRS escape rhythm, complex ventricular ectopy, or

AV block in the infant with a ventricular rate less than 55 bpm or with

1. Permanent pacemaker implantation is reasonable for patients with

episodes of intra-atrial reentrant tachycardia; SND may be intrinsic or

4. Permanent pacemaker implantation is reasonable for patients with

2. Permanent pacemaker implantation is reasonable for congenital third-

degree AV block beyond the first year of life with an average heart rate less

than 50 bpm, abrupt pauses in ventricular rate that are 2 or 3 times the basic

cycle length, or associated with symptoms due to chronotropic incompetence. 3. Permanent pacemaker implantation is reasonable for sinus bradycardia with

complex congenital heart disease with a resting heart rate less than 40 bpm or

bradycardia with the longest relative risk interval less than 3 seconds and a

congenital heart disease and a ventricular rate less than 70 bpm.

second- or third-degree AV block that is not expected to resolve or that

dysfunction, or low cardiac output.

ventricular dysfunction.

varies with the patient's age and expected heart rate.

persists at least 7 days after cardiac surgery.

secondary to antiarrhythmic treatment.

pauses in ventricular rate longer than 3 seconds.

European Society of Cardiology (ESC) 2013 Guidelines

Recommendations	Class ^a	Level ^b
I) Congenital AV block. Pacing is indicated in high degree and complete AV block in symptomatic patients and in asymptomatic patients with any of the following risk conditions: ventricular dysfunction, prolonged QTc interval, complex ventricular ectopy, wide QRS escape rhythm, ventricular rate <50 b.p.m., ventricular pauses >three-fold the cycle length of the underlying rhythm.	I	с
2) Congenital AV block. Pacing may be considered in asymptomatic patients with high degree and complete AV block in absence of the above risk conditions.	ПЬ	с
3) Postoperative AV block in congenital heart disease. Permanent pacing is indicated for postoporative advanced second.	I	в

Congenital AV block

Evidence: C

Evidence: B

Evidence: B

Evidence: B

Evidence: C

Evidence: C

Evidence: B

Level of

Evidence: C

Postoperative AV block

CLASS

CLASS

CLASS IIa

Sinus node dysfunction

second-degree AV block. 4. Permanent pacemaker implantation is not indicated for asymptomatic sinus

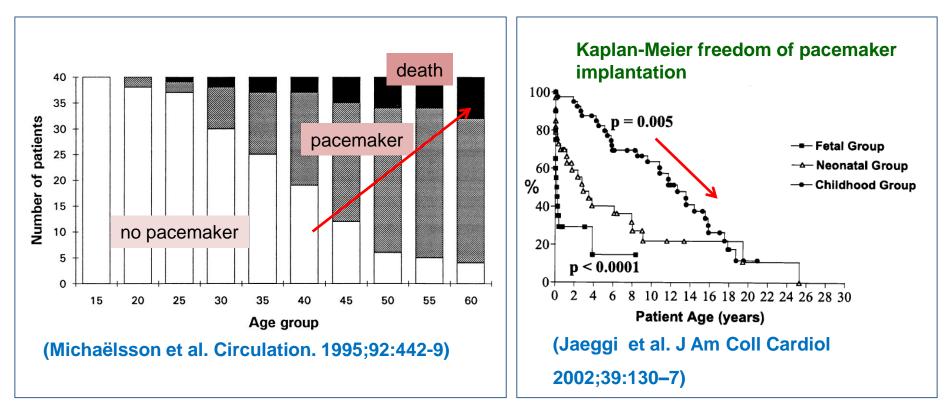
minimum heart rate more than 40 bpm.

Evidence: C Level of Evidence: C for asymptomatic resting heart rate <40 b.p.m. or ventricular pauses lasting >3 sec.

IIb

Causes

- 1/2: Passively acquired autoimmune disease from mother
 - SLE (90~99%)
 - Sjogren syndrome, rheumatoid arthritis, scleroderma...
- 1/3: Anomalous conduction tissue ass. with CHD
 - corrected TGA, AVSD, left atrial isomerism, Ebstein anomaly...
- Genetic mutation in NKX2.5,
 SCN5A, Holt-Oram syndrome....
- Many of them are diagnosed in utero or at birth.
 - AV block develops months or years after birth.



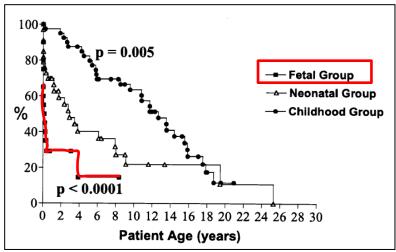
 \rightarrow Post-natal degenerative disorder of the specialized conduction system.

- Progressive.
- Spontaneous recovery cannot be expected.

Mortality of non-paced patients with isolated complete AVB

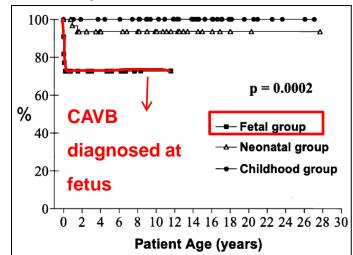
- 8 ~16 % in infants
- 4 ~ 8 % in children and adults

Kaplan-Meier freedom of pacemaker implantation



- High mortality.
- Especially in fetal and neonatal group.

Mortality



(Jaeggi ET et al. J Am Coll Cardiol 2002;39:130-7)

- Risk of developing dilated cardiomyopathy.
 - Prevalence of DCMP: 5 ~ 30 % of CCAVB diagnosed in utero or at birth
 - Hypothetical causes:
 - May be a sequela of in utero autoimmune myocarditis or due to its

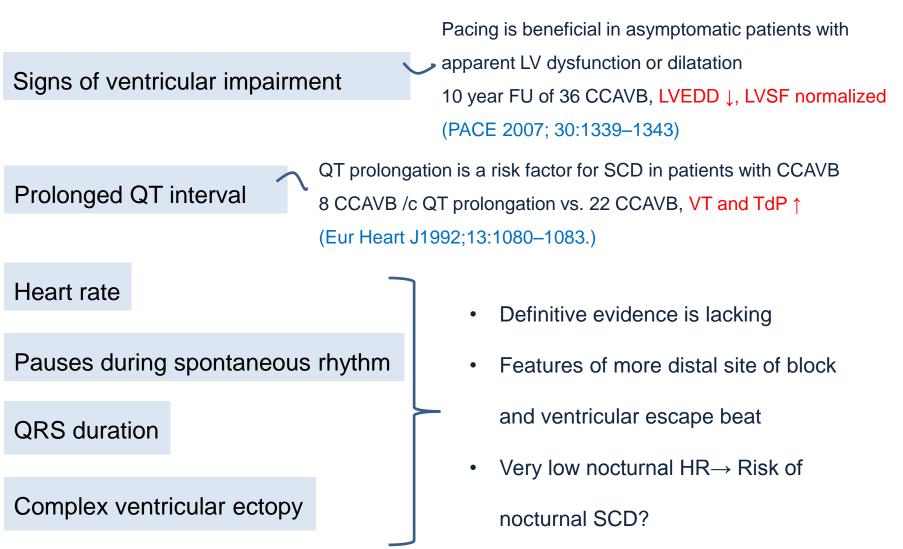
postnatal reactivation

 RV pacing induced myocardial dystrophic changes and adverse remodeling caused by ventricular desynchronization

> J Am Coll Cardiol 2001;37:1129–1134. Circulation 2004;110:3766–3772. J Am Coll Cardiol 2001;37:238–242.

Onset	Congenital AV block Early onset Lifelong pacemaker! Implant problem, Lead longevity
Progression	Progressive
Morbidity and mortality	 High mortality. Especially in fetal and neonatal group. Affected by level of block.
Recovery	 No spontaneous recovery
Special considerations	Risk of DCMP

Risk assessing parameters in "asymptomatic" patients



Congenital AV block: Pacemaker indication

AHA 2008, 2012 (Class I, IIa)	국내 인정 기준
• Permanent pacemaker implantation is indicated for ad vanced second- or third degree AV block associated w	 증상이 있는 서맥이나 심실성 부정맥을 초래하는 3도 또는 고도 2도 방실 차단
ith symptomatic bradycardia, ventricular dysfunction, or low cardiac output. (Class I: C)	 무증상의 지속성 3도 방실 차단에서 (1) 심비대, (2) 좌심실 기능저하, (3) 방실 결절 아래 부위의 차단이 있는 경우
• Permanent pacemaker implantation is indicated for congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. (Class I: B)	 각성상태에서 증상이 없는 3도 또는 고도 2도 방실 차단에 서 (1) 3초 이상 무수축 심정지가 증명, (2) 이탈박동이 40 회 미만, (3) 방실 결절 아래 부위에서 나오는 이탈박동이 있는 경우
• Permanent pacemaker implantation is indicated for congenital third-degree AV block in the infant with a ventricular rate less than 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm (Class I: C)	서 각성 시 심박수가 55회/분 미만인 경우 • 선천성 3도 또는 고도 2도 방실 차단이 동반된 선천성 심기
 Permanent pacemaker implantation is reasonable for c ongenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, ab rupt pauses in ventricular rate that are 2 or 3 times th e basic cycle length, or associated with symptoms due to chronotropic incompetence. (Class IIa: B) 	의 소아에서 (1) 각성 상태 시 심실 박동수가 50회/분 미만, (2) 심실 휴지기가 평상시 심박동수 주기의 2배 이상으로 발생한 경우

- Postoperative conduction tissue damage, inflammation, edema, bleeding...
- s/p VSD, AVSD, LVOT obstruction, discordant atrioventricular (AV) connections
- Incidence of early postop heart block: 0.7% ~ 3%
- Under the influence of
 - 1. The residua of impaired ventricular function
 - 2. Abnormal physiology

 May result in symptoms at milder bradycardia or AV dyssynchrony.

- High mortality especially within 1 year after the cardiac op.
- The 1-year postop mortality rate for patients with persistent

postop. CAVB: 28 ~ 100 %

(Lillihei CW et al. J Thorac Cardiovasc Surg. 1963;46:436-56.)

(Hofschire PJ et al. Am J Cardiol 1977;39:559 –562)

(Murphy DA et al. Lancet 1970;1:750 –752.)

 High mortality and high risk for sudden cardiac death.

May resolves spontaneously

in 43% to 92% of cases

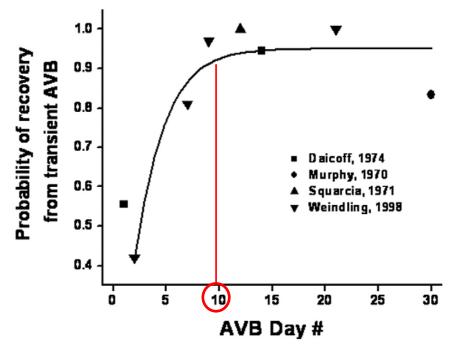
Usually within 7 to 14 days

of onset

- Often, the heart block is transient.
- Especially within 7~10 days of onset.

Cumulative probability of recovery from transient

postop-AVB, based on published studies



Gross et al. (Heart Rhythm 2006;3:601-604)

(Angela et al. J Thorac Cardiovasc Surg 2010;140:158-60)

- Retrospective review of s/p VSD, AVSD, TOF
- n = 922
- Early postop. AVB: 21 (2.3%)
- Persistent AVB: 0.9 %
- Delayed AVB: 0.3% to 0.7%.

 Late onset of CAVBs after open heart surgery are existed.

	AV canal	TOF	VSD
	(n = 197)	(n = 222)	(n = 503)
Transient	3 (1.5%)	4 (1.8%)	6 (1.2%)
Pacemaker implanted	2 (1%)	3 (1.4%)	3 (0.6%)

Patient	s with dela	yed AV block (n=3)	
Patient	Diagnosis	Age at surgery (mo)	Postoperative transient heart block	Interval to pacemaker (mo)
1	CAVC	2	No	2
2	VSD	4	Yes	8
3	TOF	6	Yes	16

	Postoperative AV block
Onset	 Postoperative. Late onset may possible
Progression	· (-)
Morbidity and mortality	 Highest mortality. Symptoms at milder bradycardia or AV dyssynchrony. Key determinant of pacemaker
Recovery	 May resolves spontaneously within 7~14 days of onset implantation: "duration" of postoperative heart block.
Special considerations	

Late onset AV block: Any predictable factor?

• 1988 and 2006

Liberman et al. Pediatr Cardiol (2008) 29:56–59

- 15 patients with late-onset heart block
- From op. ~ pacemaker: 6.8 ± 7.3 years.
- Fatigue/exercise intolerance (n=4), Syncope (n=2), Heart failure (n=2),

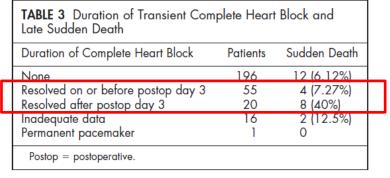
irritability (n=1), Diagnosed during routine follow-up (n=6)

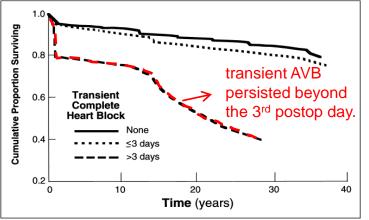
- Complete RBBB and left superior axis in 2 of 15
- PR interval longer than 200 ms in 3 of 15 (20%)
- Hx of transient postop heart block in 3 of 13 (23%)

Seems not very useful predicting factor....

Late onset AV block: Associated with transient CAVB?

- s/p TOF (n=288) \rightarrow 28 year F/U
- Sudden death: 26 of the 288 (9%)





(Hokanson et al. Am J Cardiol 2001;87:1271-7)

- 5662 cardiac op for CHD
- 72 persistent postop. CAVB → pacemaker implantation
- 7 of 72 (9.6%) \rightarrow recovered
 - Median 41 days (18-113 days) after the initial op.
 - No late recurrence during FU (mean: 4.4±2.6 years)

(Batra et al. J Thorac Cardiovasc Surg 2003;125:1291-3)

Transient CAVB with residual bifascicular block: risk of late-onset CAVB

Meta-analysis of the prognostic significance of fascicular block ECG

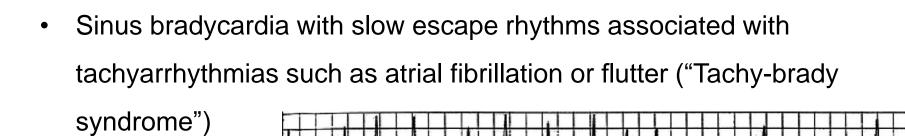
patterns following CHD surgery.

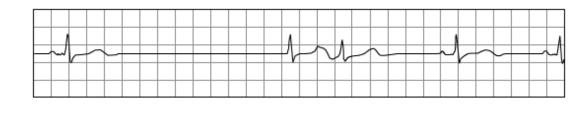
- 1,856 patients / 8 series
- 81 transient AVB \rightarrow late recurrence: 4 of 81 (5%)
- Incidence of late CAVB or sudden death
 - 1.5 % in 204 bifascicular block /s transient CAVB
 - 29 % (n=16) in 56 bifascicular block after transient CAVB

Postoperative AV block: Pacemaker indication

AHA 2008, 2012 (Class I, IIa)	국내 인정 기준
Permanent pacemaker implantation is indicated fo	심장 수술 후 발생한 3도 또는 고도 2도 방실 차단이 호
r postoperative advanced second- or third-degree	전되기를 기대하기 어렵거나, 수술 후 <mark>지속</mark> 되는 경우
AV block that is not expected to resolve or that pe	· 방실 접합부에 대한 전극도자절제술을 시행 후 발생한 3
rsists at least 7 days after cardiac surgery. (Class I	도 또는 고도 2도 방실 차단
: B)	
Permanent pacemaker implantation is reasonable	· 만성 2섬유속 차단에서 (1) 고도 2도 방실 차단, (2) 간헐
for unexplained syncope in the patient with prior	적인 3도 방실 차단, (3) 2도 🛛 형 방실 차단, (4) 각차단이
congenital heart surgery complicated by transient	교대로 발생하는 경우
complete heart block with residual fascicular bloc	• 만성 2섬유속 차단 에서 실신, 현기증 의 원인이 심 전기생
k after a careful evaluation to exclude other cause	리학적 검사를 포함한 진단적 검사로도 심실 빈맥과 같
s of syncope. (Class IIa: B)	은 다른 원인은 배제되고 방실 차단에 의한 것으로 판단
	되는 경우

- Sinus bradycardia with slow escape rhythm
 - Profound sinus bradycardia
 - Sinus pauses
 - Sinus arrest
 - SA nodal exit block
 - Chronotropic incompetence



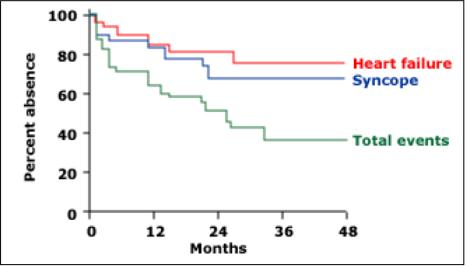


Causes of SND in the pediatric age group

- Ion channelopathies, malignancies, infammatory disorders, cardiomyopathies
- Structural heart disease especially, with left isomerism
- After surgical repair (Fontan, Mustard, Senning)
- Readily reversible causes: hypothyroidism, hypothermia, and medications

- Depends on the function of the remaining cardiac conduction system,
 & depend on age
- Infant Poor feeding, lethargy, and failure to thrive
- Older children Fatigue, shortness of breath, syncope, CHF, or IART
- Rarely, sudden death
- Many patients tolerate well chronic bradycardia. (asymptomatic)
 - Progressive.
 - Gradual loss of sinus rhythm

35 patients with SND > 45 years old



(Menozzi C et al. Am J Cardiol 1998;82:1205.)

17 y.o with fatigue. sinus bradycardia

	aVR			V1			V4			
~				Pause	3.07sec					
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Phase		Time	Speed	Grade	Workload	HR	BP	RPP	VE	Comment
	Stage Name	Time in Stage	Speed (km/h)			HR (bpm)				Comment
Phase Name	Stage Name	in Stage	Speed (km/h)	Grade (%)	Workload (METS)	(bpm)	BP (mmHg)	RPP (*100)	VE (/min	Comment
 Phase		in Stage 01:17	Speed (km/h) 0.00	Grade (%) 0.00	Workload (METS) 1.0	(bpm) 53	BP	RPP	VE (/min	Comment
Phase Name	I Stage Name SUPINE	in Stage	Speed (km/h)	Grade (%)	Workload (METS)	(bpm)	BP (mmHg)	RPP (*100)	VE (/min	Comment
Phase Name PRETEST	Stage Name SUPINE STANDING	in Stage 01:17 00:29	Speed (km/h) 0.00 0.00	Grade (%) 0.00 0.00	Workload (METS) 1.0 1.0	(bpm) 53 89	BP (mmHg)	RPP (*100) 62	VE (/min	Comment
Phase Name PRETEST	Stage Name SUPINE STANDING STAGE 1	in Stage 01:17 00:29 00:11	Speed (km/h) 0.00 0.00 2.70	Grade (%) 0.00 0.00 10.00	Workload (METS) 1.0 1.0 1.3	(bpm) 53 89 84	BP (mmHg) 117/55	RPP (*100)	VE	Comment

- Chronotropic incompetence: Risk factor for the subsequent development of IART
 - 42 with AFL onset \geq 6 months postoperatively
 - No difference of minimum HRs (pts vs. controls)
 - HR acceleration in response to exercise was significantly more blunted in AFL cases than in matched controls

	Estimate of	least squares mea	ins (±SE)			
	Unadjusted			Adjusted ^a		
	Cases	Controls	Р	Cases	Controls	Р
Min HR (bpm)	54 ± 2	52 ± 2	0.38	54 ± 2	55 ± 3	0.73
Average HR (bpm)	75 ± 2	81 ± 2	0.02	76 <u>+</u> 2	83 ± 2	0.01
Max HR (% of predicted for age)	67 ± 2	80 ± 2	<0.001	66 <u>+</u> 1	73 <u>+</u> 2	<0.001
Chronotropic index	66 ± 3	76 ± 3	0.01	60 ± 4	65 <u>+</u> 4	0.08

Table 3 Summarized HR data, with least squares means estimates (±SE) and P-values obtained from mixed linear regression analysis

(Anand N et al. Eur Heart J 2006;27:2069-73)

All data shown are adjusted for repeated measures. Minimum (Min) and average HR are from Holter recordings. Maximum (Max) HR calculation is based on the formula (maximum predicted HR = 220 – age in years) applied to maximum HR data recorded on Holter recordings and GXT. Chronotropic index is calculated from GXT data using the formula $[(HR_{stage} - HR_{rest})/(220 - age - HR_{rest})] \times 100$, where HR_{stage} and HR_{rest} are defined as peak exercise-induced sinus HR and baseline resting HR, respectively. SE, standard error.

^aAdjusted for sex and for age, permanent pacing, and medication use at the time of test for all analyses except chronotropic index which excludes paced patients and is adjusted for sex, age, and medication use.

(Garson A et al. J Am Coll Cardiol 1985;6:871-8)

collaborative study in 19 institutions

380 patients with atrial flutter (1 ~ 25 years, mean 10.3)

60% had repaired CHD

13% palliated CHD

8% unoperated CHD

Follow up: 14.5 years (1.2 to 38.4 yr)

48.6 % Treated AFL

17% died

10% sudden death

Substantial morbidity

 and mortality in
 patients with
 recurrent or chronic
 IART, with the loss of
 sinus rhythm

1 case: AFL resulted in sudden death

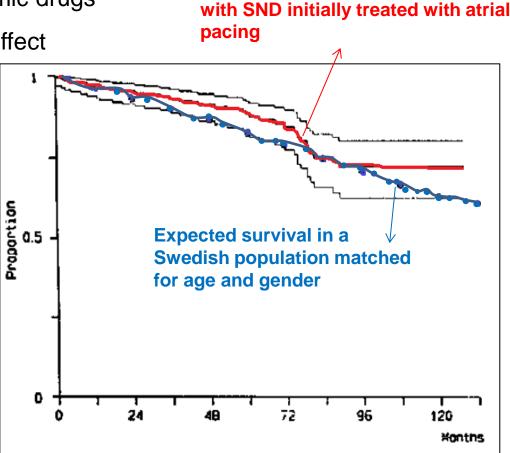
4 cases: pacemaker implanted state →
 tachyarrhythmia may causes sudden death.

 Those with pacemaker (7%) vs. without pacemaker (11%) → no statistical difference.

pacing may...

- alleviate symptoms as fatigue
- permit treatment with antiarrhythmic drugs
- have a favorable hemodynamic effect

 While pacemakers may reduce morbidity, they have not been shown to reduce mortality.



Survival during FU of 213 patients

(Brandt J et al. J Am Coll Cardiol 1992;20:633-9)

	Sinus Node Dysfunction
Onset	Gradual onset
Progression	Progressive.
Morbidity and mortality	 Usually asymptomatic or nonspecific symptoms Affected by function of remaining cardiac conduction system Tachy-brady syndrome → risk of SCD
Recovery	 No spontaneous recovery
Special considerations	 Pacemakers may not reduce mortality.

- Any prophylactic effect of PM without documented IART before implant?
 - Use and efficacy of ATP in pts with CHD, single center
 - 80 implants on 72 patients
 - Median 2.9 years FU

(Kamp et al. Congenit Heart Dis. 2015 epub.)

Table 2. Antitachycardia Pacing Resu	ults
Follow-up >3 months	n = 56
Follow-up, median (range) AT	2.8 years (0.3-10.7)
Prior to ATPM implant	41 (73%)
Post-ATPM implant	35 (63%)
Antiarrhythmic therapy after implant	29 (52%)
Successful ATP	20 (36%)
AT post-ATPM implant, n = 35	(57%)
Time to first successful ATP, median (range)	1.3 years (0–6.5)
Number of successful ATP, n = 20	
<5	6 (30%)
5–15	1 (5%)
>15	13 (65%)
DC cardioversion required after ATPM implant Pre: 3	8(14%)
AT, atrial tachycardia; ATP, antitachycardia pacin pacemaker.	ng; ATPM, antitachycardia

Table 3.Clinical Factors Associated with tachycardia Pacing	Successful	Anti-
Follow-up >3 months	n = 56	Р
Successful ATP, $n = 20$ Two-ventricle repair, $n = 38$ One-ventricle palliation, $n = 18$	17 (45%) 3 (17%)	.04
Atrial tachycardia prior to implant, $n = 41$ No atrial tachycardia prior to implant, $n = 15$	19 (46%) 1 (7%)	.006
Atrial switch procedure, n = 21 Other congenital heart surgery, n = 35	9 (43%) 11 (31%)	NS
Preimplant AT, successful ATP, n = 19 Atrial switch procedure, n = 12 Other congenital heart surgery, n = 7	8 (67%) 2 (28%)	.01
AT, atrial tachycardia; ATP, antitachycardia pacing.		

Sinus Node Dysfunction: Pacemaker indication

AHA 2008, 2012 (Class I, IIa)	국내 인정 기준
• Permanent pacemaker implantation is indicated for SN D with correlation of symptoms during age-inappropria te bradycardia. The definition of bradycardia varies wit h the patient's age and expected heart rate. (Class I: B)	 연령에 따른 심박수가 부족한 동서맥(age-inappropriat e sinus bradycardia)으로 인한 증상이 있는 경우 증상을 동반한 서맥이나 증상을 동반한 동휴지가 각성 상태에서 입증된 경우 증상을 동반한 심박수변동 부전(chronotropic incomp etence)이 있는 경우
 Permanent pacemaker implantation is reasonable for p atients with congenital heart disease and impaired hem odynamics due to sinus bradycardia or loss of AV synch rony. (Class IIa: C) 	인한 방실 조화(AV synchrony) 소실에 의한 혈역학적
 Permanent pacemaker implantation is reasonable for p atients with congenital heart disease and sinus bradyca rdia for the prevention of recurrent episodes of intra-at rial reentrant tachycardia; SND may be intrinsic or seco ndary to antiarrhythmic treatment. (Class IIa: C) 	입성 기전 빈맥 (intra-atrial reentrant tachycardia)
• Permanent pacemaker implantation is reasonable for si nus bradycardia with complex congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. (Class IIa: C)	

	Congenital AV block	Postoperative AV block	Sinus Node Dysfunction
Onset	Earliest onset	Postoperative.Late onset may possible	Gradual onset
Progression	Progressive		Progressive.
Morbidity and mortality	 High mortality. Especially in fetal and neonatal group. Affected by level of block. 	 Highest mortality. Symptoms at milder bradycardia or AV dyssynchrony. 	 Tachy-brady syndrome → risk of SCD Usually asymptomatic or nonspecific symptoms Affected by function of remaining cardiac conduction system
Recovery	 No spontaneous recovery 	 May resolves spontaneously within 7~14 days of onset 	 No spontaneous recovery
Special considerations	Risk of DCMP		 Pacemakers may not reduce mortality.

경청해 주셔서 감사합니다.