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Title: Myocardial Scintigraphy Findings in Congenital Complete Atrioventricular Block after Pacemaker Implantation

Running title: Myocardial Scintigraphy in CCAVB patients

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Abstract

Background: Patients with isolated Congenital Complete Atrioventricular Block (CCAVB) occasionally develop dilated cardiomyopathy (DCM), despite early pacemaker implantation. However, the etiology of the DCM and its relationship to permanent ventricular pacing are not fully understood.

Objectives: The purpose of this study was to investigate myocardial perfusion using scintigraphy in patients with CCAVB.

Methods: Twenty five patients with CCAVB underwent ^{99m} technetium (Tc) myocardial perfusion scintigraphy. Thirty myocardial scintigraphy images were obtained and divided into three groups; Group 1: CCAVB before pacemaker implantation (PMI) (n=11), Group 2: CCAVB after PMI who did not subsequently develop DCM, Group 3: CCAVB after PMI who subsequently developed DCM.

Results: Perfusion defects on SPECT of myocardial scintigraphy were identified in group 1, 0%; group 2, 85%; and group 3, 100%. In groups 2 and 3, in patients with right ventricular pacing the perfusion defects were mainly in the septum or between the apex and septum. On 20 segment polar maps, the distribution of %uptake showed a similar pattern in groups 2 and 3; the degree of decreasing %uptake and the number of segments with decreased %uptake being more severe in group 3.

Conclusions: Artificial left bundle branch block pattern myocardial contraction induced by right ventricular pacing decreased myocardial perfusion around the apex and

septum. Some patients with CCAVB will develop left ventricular dysfunction caused by artificial LBBB induced interventricular asynchrony.

Key Words: congenital complete atrioventricular block, pacemaker implantation, dilated cardiomyopathy, myocardial scintigraphy, left bundle branch block

Most patients with isolated congenital complete atrioventricular block (CCAVB) eventually require pacemaker implantation (PMI) and the prognosis has been considered relatively benign. Recent evidence suggests that a subset of patients with CCAVB develop dilated cardiomyopathy (DCM) despite early pacemaker implantation. We report our myocardial scintigraphy findings in patient with CCAVB.

Methods

Study group: Twenty-five patients (15 male and 10 female) with CCAVB without associated structural heart disease underwent ^{99m} technetium (Tc)-tetrofosmin myocardial scintigraphy between January 1995 and March 2004 in the Department of Pediatrics, National Cardiovascular Center. We obtained thirty SPECT films of myocardial scintigraphy and divided them into three groups; Group 1: CCAVB before pacemaker implantation (n=11), Group 2: CCAVB after pacemaker implantation with no subsequent DCM (n=13), Group 3: CCAVB after pacemaker implantation who subsequently developed DCM (n=6). All 6 patients who developed DCM presented with decreased cardiac contractility after pacemaker implantation. No patient was diagnosed as having DCM when their CCAVB was first diagnosed. Five of the 25 patients underwent myocardial scintigraphy before and after pacemaker implantation.

Myocardial scintigraphy: A weight-adjusted dose of ^{99m}Tc-tetrofosmin (Nihon Medi-Physics Co.) calculated according to recommendations of the European Association of Nuclear Medicine was injected into a peripheral vein in each patient.

Forty-five minutes later, SPECT was performed using a dual-head angular rotating γ-camera equipped with a low-energy general-purpose collimator. Image acquisition parameters were 180° (30 steps: 6° per step) using a 64×64 matrix and a 20% main window centered at the photopeak energy of ^{99m}Tc (140 KeV). Four patients in Group 1, 11 patients in Group 2 and 5 patients in Group 3 underwent gated SPECT.

Two experienced nuclear medicine physicians independently read all studies. We assessed myocardial perfusion abnormalities using segmental perfusion polar maps that showed pixels corresponding to the maximum ventricular perfusion to be equal to 100% of the summed gating data.

Statistical analysis: Data are expressed as the mean value ± SD. Differences between the two means were compared by the unpaired t test. A p value<0.05 was considered as statistically significant.

Result

Patient characteristics (Table 1)

There was no significant difference in the mean age and gender distribution between the three groups. Although there was no significant difference in either age at pacemaker implantation or pacing mode, the duration of pacing in Group 3 was shorter than in Group 2 ($p<0.05$). Perfusion defects on SPECT of myocardial scintigraphy were identified in 0%, 85% and 100% in groups 1, 2 and 3, respectively. In Group 2, 8 of 9 patients receiving RV epicardial pacing, 2 of 3 receiving LV epicardial pacing and one

receiving RV endcardial pacing myocardial scintigraphy revealed perfusion defects. In Group 3, all 6 patients had perfusion defects.

Perfusion defect's characteristics on myocardial scintigraphy (Figure 1)

In Group 2, the short axis image of ^{99m}Tc-tetrofosmin myocardial SPECT showed decreased septal uptake without left ventricular dilatation. RV epicardial and endocardial pacing patients had perfusion defects mainly in the septum or between the apex and septum. Patients paced with LV epicardial leads had perfusion defects on SPECT at the apex or anteriorly.

In Group 3, the short axis image of ^{99m}Tc-tetrofosmin myocardial SPECT showed that uptake between the septum and the inferior myocardium was widely decreased with left ventricular dilatation. RV epicardial pacing was associated with a wide range of perfusion defects between the apex, septum and inferior myocardium.

Gated SPECT and % uptake of 20 segments' polar map (Figure 2, Figure 3)

LVEF calculated by gated SPECT in Group 3 was 18.0±5.5, significantly lower than that in Group 1 (58.0±11.7, $p<0.001$) or in Group 2 (66.3±9.8, $p<0.001$). Total %uptake of the apex, septum and inferior myocardium on a polar map in Group 3 was significantly lower than in Group 1. Total %uptake of the apex and inferior myocardium on polar map in Group 3 was also significantly lower than in Group 2. Total %uptake of the septum in Group 3 showed a tendency to be low compared with Group 2. The number of segments in which %uptake was less than 60% in Group 3 was significantly more than that in

Group 1 and 2. Although the distribution of %uptake on the polar map had a similar pattern in Group 2 and Group 3, the degree of decreased %uptake and the number of segments with decreased %uptake were greater than in Group 3.

Discussion

The prognosis for children diagnosed with CCAVB *in utero* or CCAVB associated with structural cardiac disease is generally poor. In contrast the prognosis for children with isolated CCAVB has been considered relatively benign, with a normal life-expectancy, although most patients require pacemaker implantation at some stage[1)-3)]. Recently, evidence has emerged that a subset of patients with isolated CCAVB develops chronic heart failure resembling DCM despite early pacemaker implantation[4)-7)]. Moak et al[5)]. described dilated cardiomyopathies developing in 16 patients with CCAVB and who were ventricular paced. Consequently, the long term prognosis for isolated CCAVB is now less certain. One of the mechanisms of CCAVB is thought to be autoimmune injury of the fetal conduction system by maternally-derived IgG antibodies (anti-SSA/Ro, anti-SSB/La). Significantly, these antibodies react, not only with the fetal conducting system but also with all fetal myocardial tissue [1)2)]. Despite this observation, the etiology of isolated CCAVB with DCM and the relationship between the development of DCM and ventricular pacing are not fully understood.

Recently, it has been proposed that interventricular conduction abnormalities may

themselves impair cardiac function through ventricular asynchrony leading to cardiac failure. As a result, biventricular or left ventricular pacing is emerging as a treatment for patients with severe heart failure or DCM with ventricular asynchrony[8)-12)]. In patients with an interventricular conduction abnormality such as LBBB, the isolated LBBB itself caused global ventricular abnormalities manifested by a shortening of diastolic filling times, changes in heart sounds, abnormal interventricular septal motion, and reduced left ventricular ejection fraction[12)]. Myocardial scintigraphical studies of isolated LBBB patients demonstrated perfusion defects in the septum without coronary artery disease. LBBB per se may reduce myocardial perfusion and glucose uptake in the septum, because the interventricular asynchrony associated with LBBB causes excess systolic thickening and augmented intramyocardial pressure in the septum [13)]. In addition, in patients with right ventricular pacing, a high incidence of myocardial perfusion defects in the septum associated with pacing induced artificial LBBB has been reported[10)14)]. In our study myocardial scintigraphy also demonstrated a high incidence of perfusion defects in the apex and septum associated with right ventricular pacing and distribution of perfusion defects were widely distributed in CCAVB with DCM.

Karpawich P et al[15)]. described a significant increase in histopathological abnormalities in biopsy samples from patients who had had apical right ventricular pacing and speculated that chronic apical right ventricular pacing may adversely alter

myocellular growth at the cellular and subcellular level, potentially contributing to the diminished function observed clinically.

We speculate that, in some CCAVB patients, artificial LBBB induced by right ventricular pacing decrease local myocardial perfusion of the apex and septum, further contributing to previous functional impairment in myocardium affected by maternal anti-SSA/Ro and anti-SSB/La antibodies. In patients with CCAVB and right ventricular pacing, the developments of decreasing cardiac function or perfusion defects on myocardial scintigraphy are indications for changing the pacing site.

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Table 1: Patient characteristics and perfusion defects in myocardial scintigraphies

Group		Group 1 (n=11)	Group 2 (n=13)	Group 3 (n=6)	p-value
Age (year)		7.6 (0.4~30.1)	8.2 (0.1~29.3)	4.5 (2.4~13.4)	NS
Gender	M	6	9	3	NS
	F	5	4	3	
Age at PMI (day)		-	163 (0~4693)	368 (0~3511)	NS
Duration of pacing (day)		-	2,543 (24~6536)	1,166 (128~1717)	p<0.05
Pacing mode	VVI	-	10	4	
	DDD		2	2	NS
	VDD		1	0	
PD		0 (0%)	11 (85%)	6 (100%)	p<0.001
PD/Pacing site	RV epicardium	-	8/9	6/6	
	LV epicardium	-	2/3	-	NS
	RV endocardium	-	1/1	-	

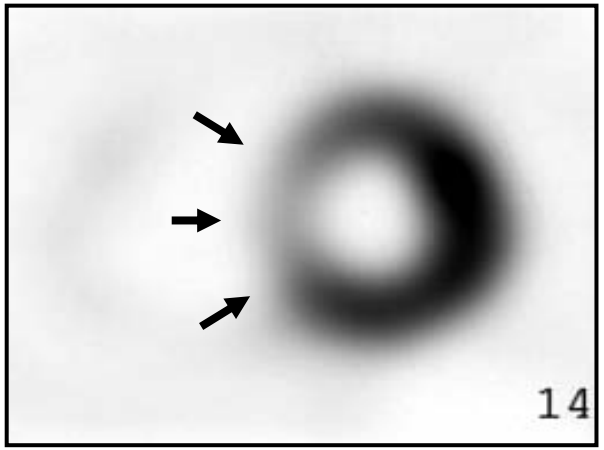
Median (minimum~maximum)

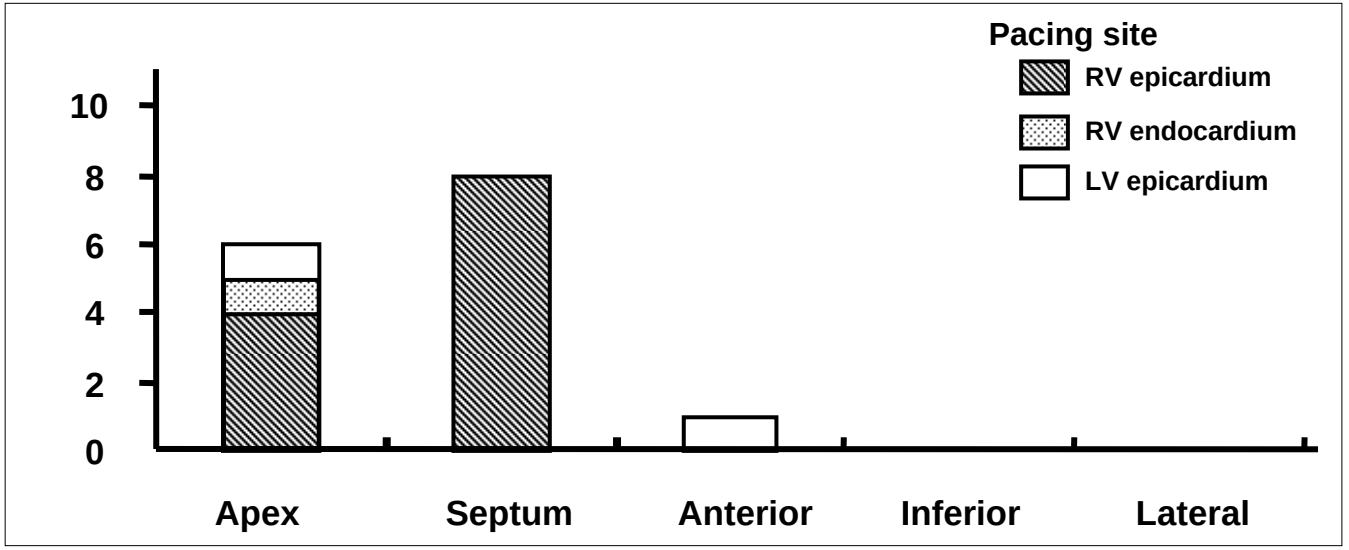
Group 1: CCAVB before pacemaker implantation, Group 2: CCAVB after pacemaker implantation who did not subsequently develop DCM, Group 3: CCAVB after pacemaker implantation who subsequently developed DCM

CCAVB: congenital complete atrioventriculer block, DCM: dilated cardiomyopathy, F: female, M: male, PMI: pacemaker implantation, PD: perfusion defect, RV: right ventricle, LV: left ventricle

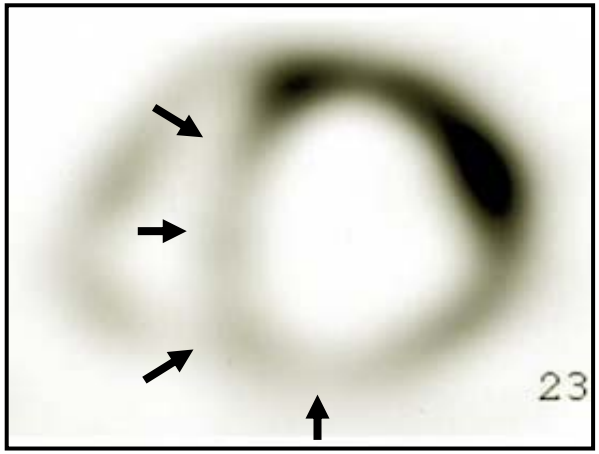
Figure 1: Perfusion defect characteristics on SPECT of myocardial scintigraphy

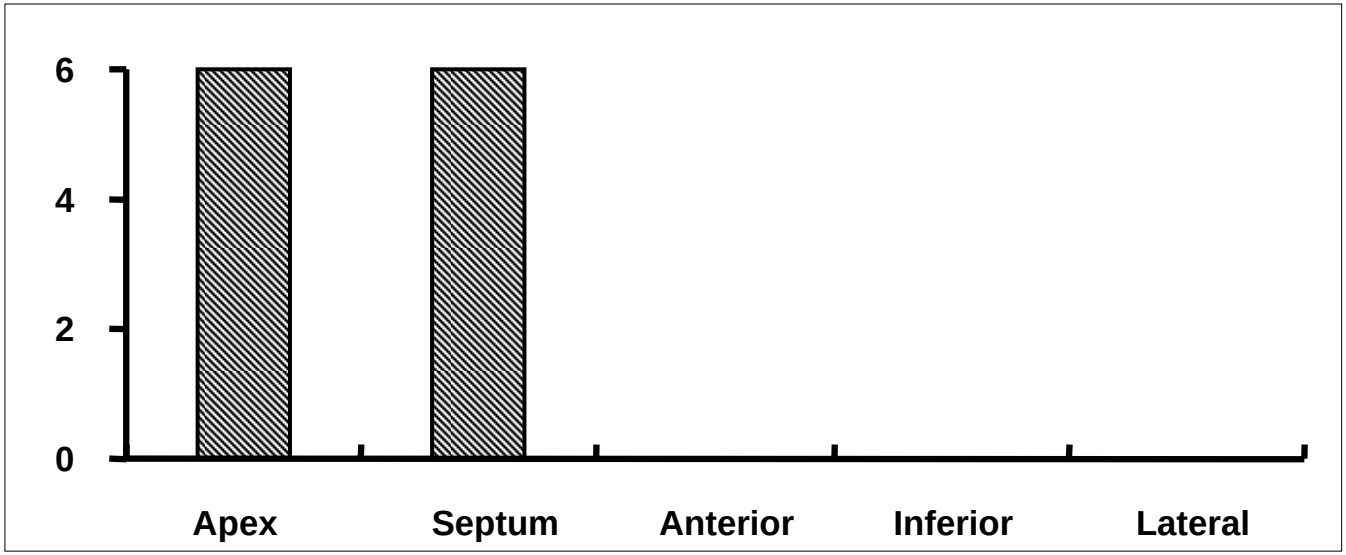
Group 2





Group 3





SPECT: , RV: right ventricle, LV: left ventricle

Figure 2: Perfusion defect characteristics on Bull's eye map (20 segments)

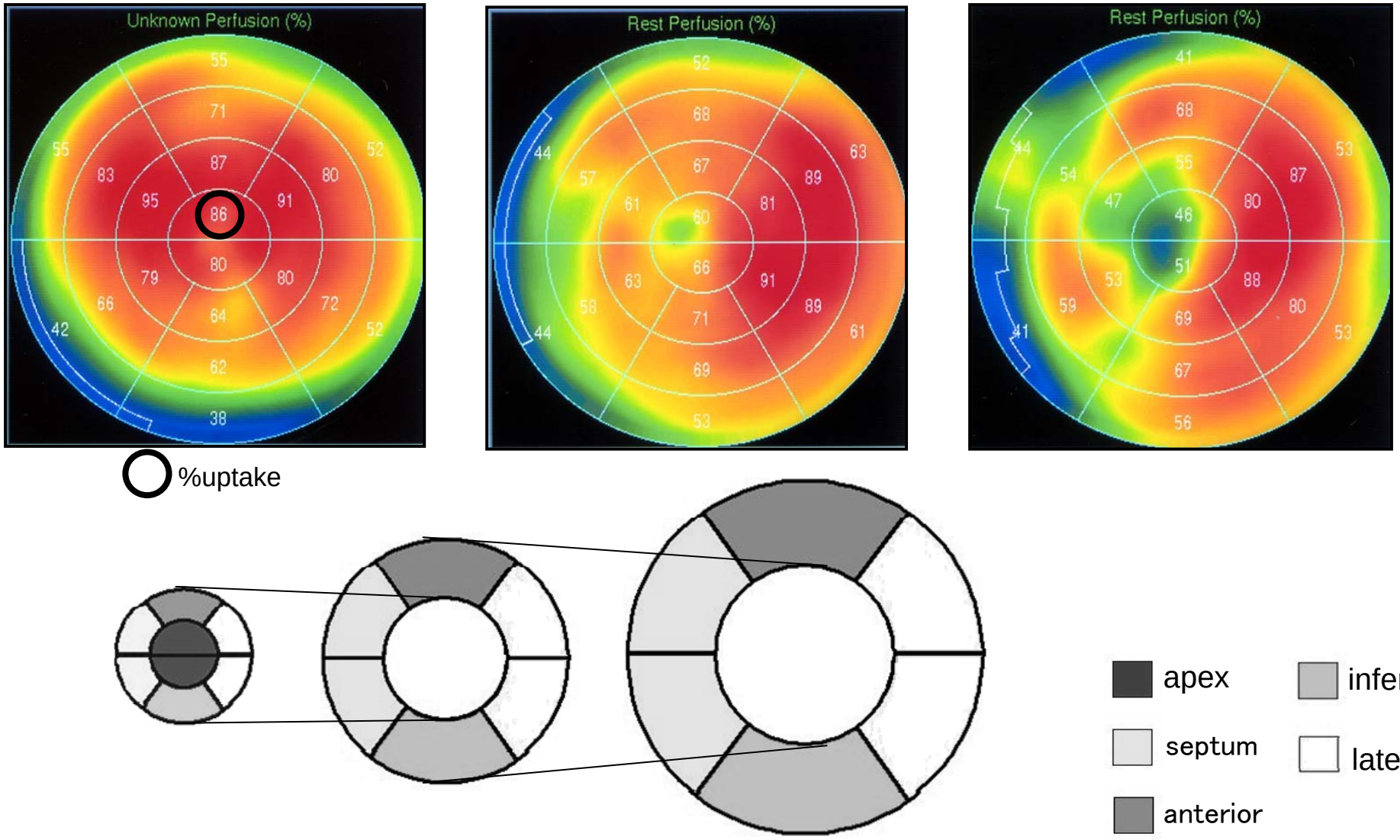


Figure 3: Gated SPECT and polar map %uptake