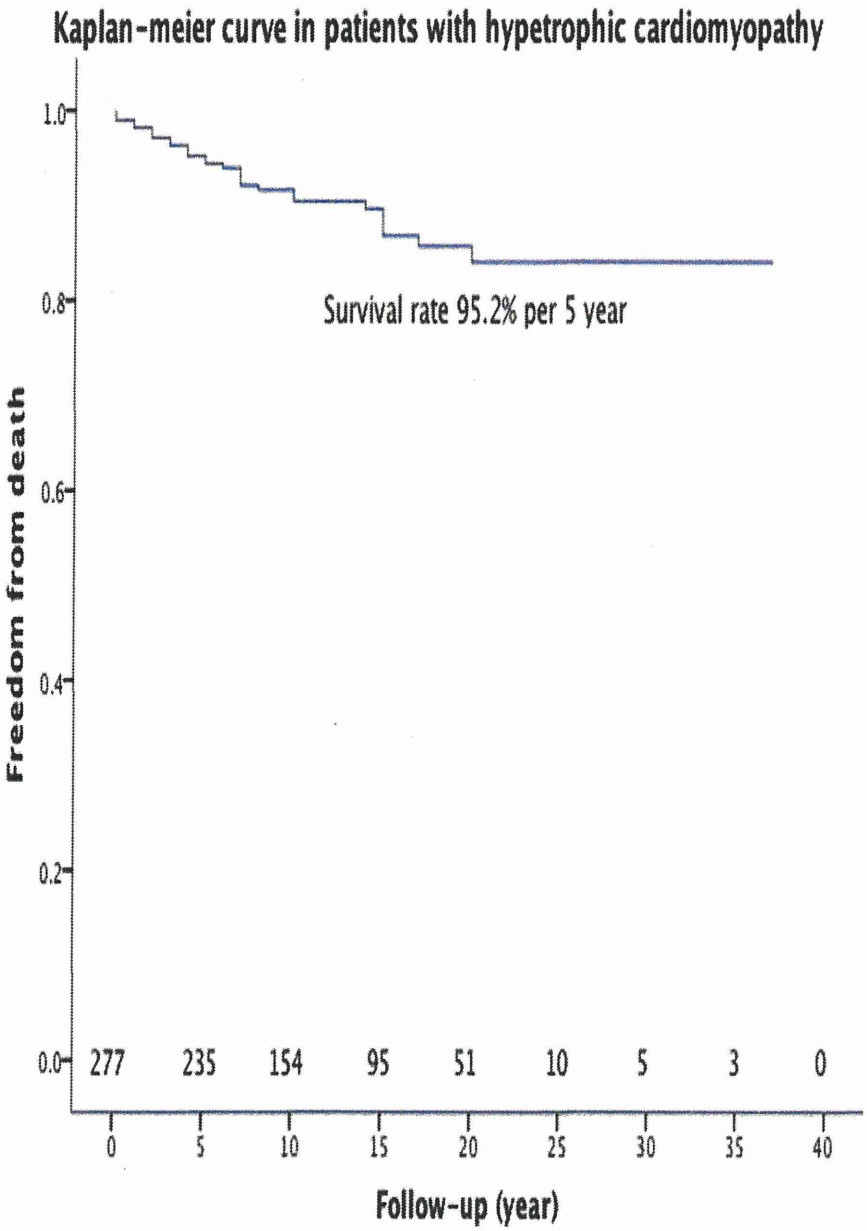
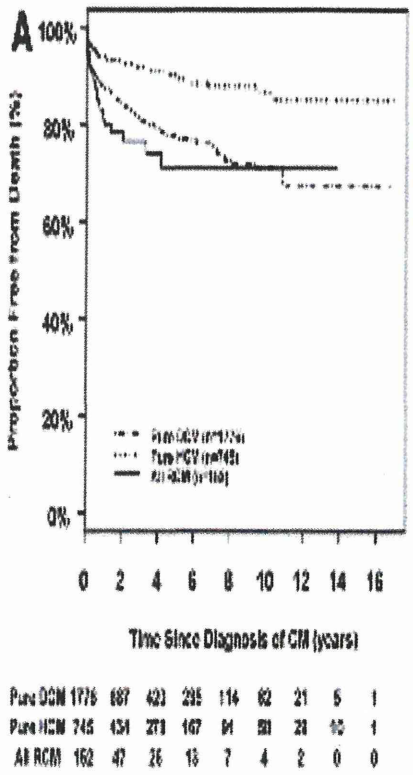
小児心筋症の予後
世界のデータと
今回の調査

我が国のデータ:
肥大型心筋症:
死亡回避率



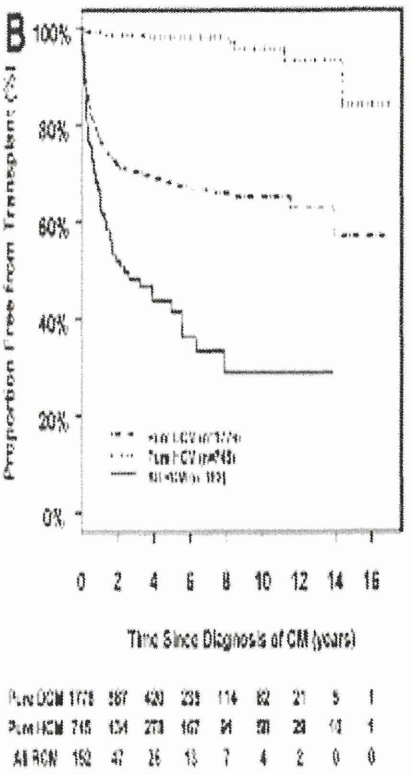
日本



USA

我が国のデータ:
肥大型心筋症:
移植回避率

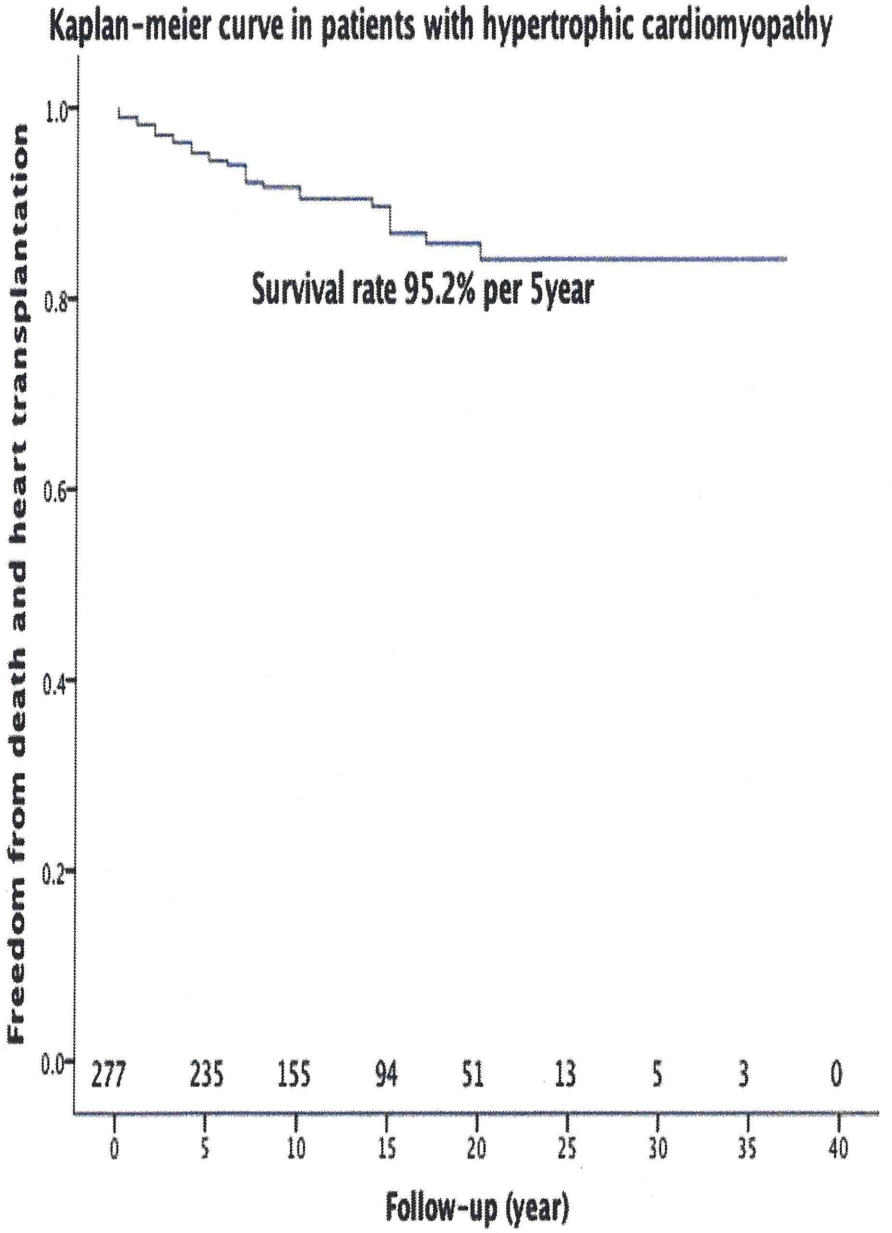
- 我が国では、移植は無し



USA

日本

我が国のデータ:
肥大型心筋症:
死亡ないし移植回避率



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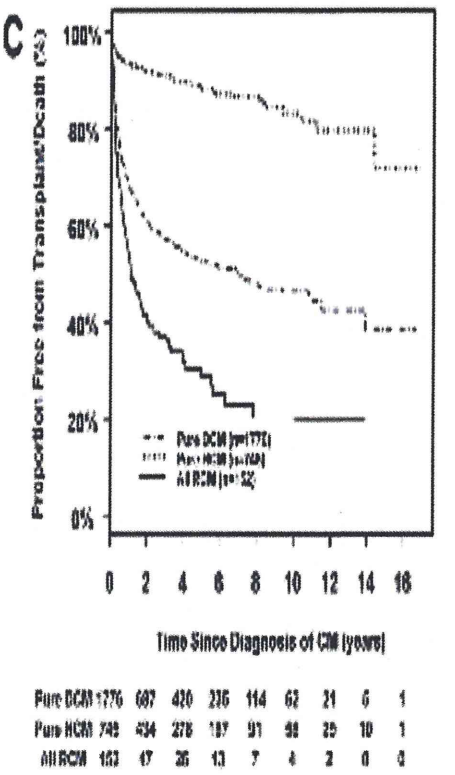
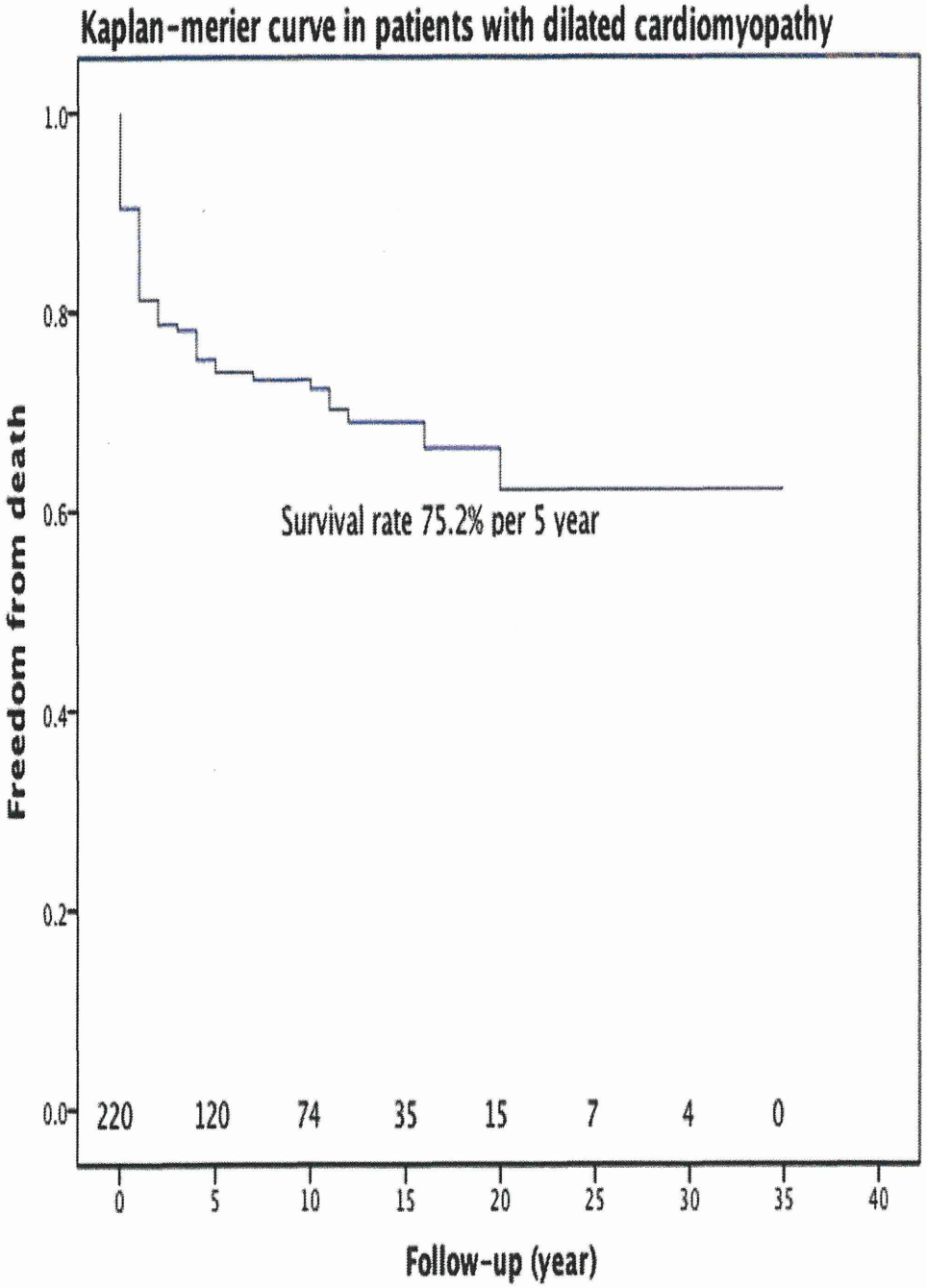


USA

我が国のデータ:
拡張型心筋症:
死亡回避率



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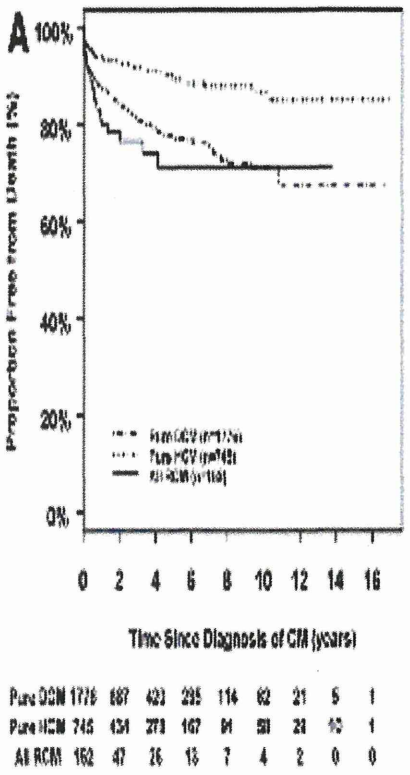
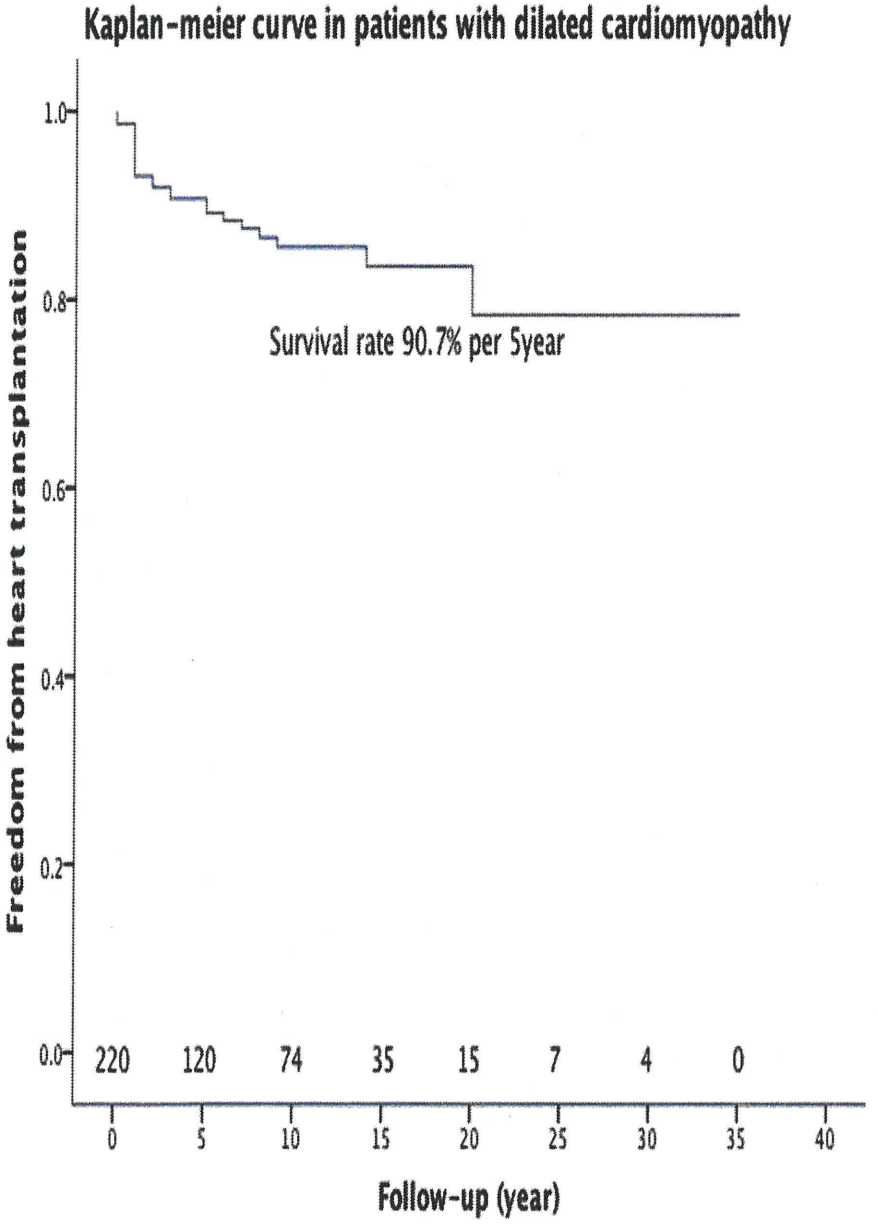


USA

我が国のデータ:
拡張型心筋症:
移植回避率



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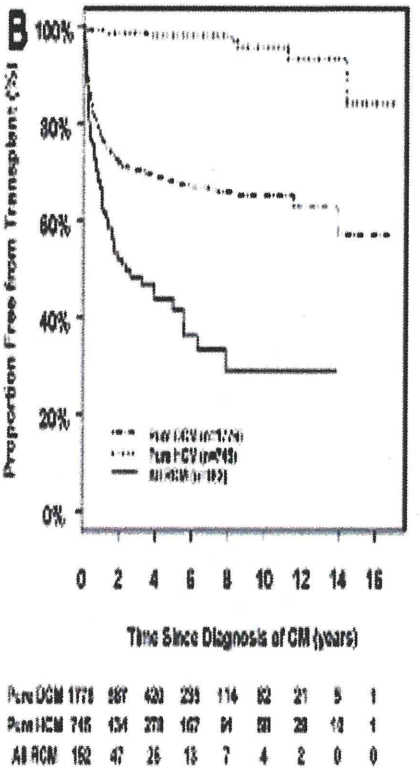
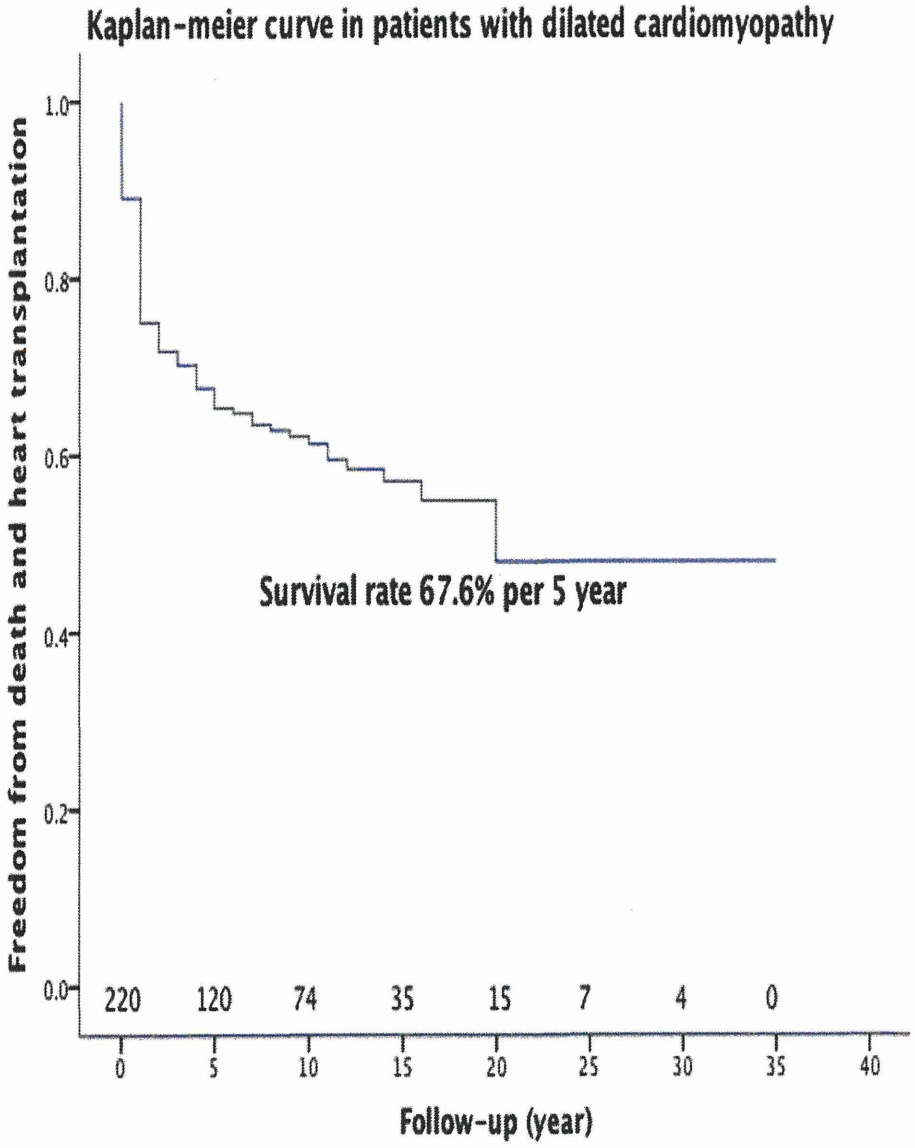


USA

我が国のデータ:
拡張型心筋症:
死亡ないし移植回避率



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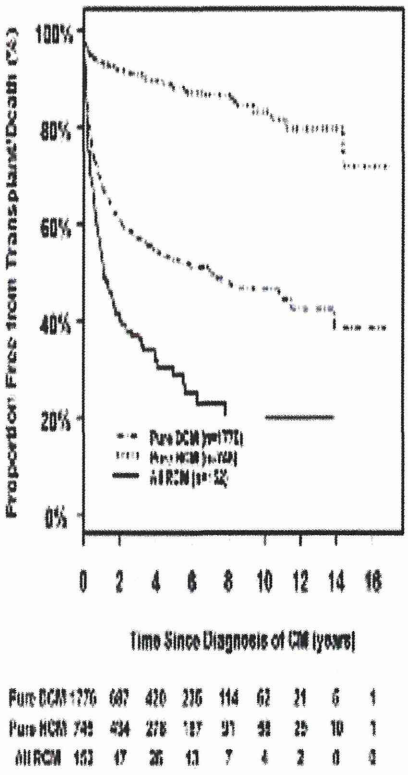
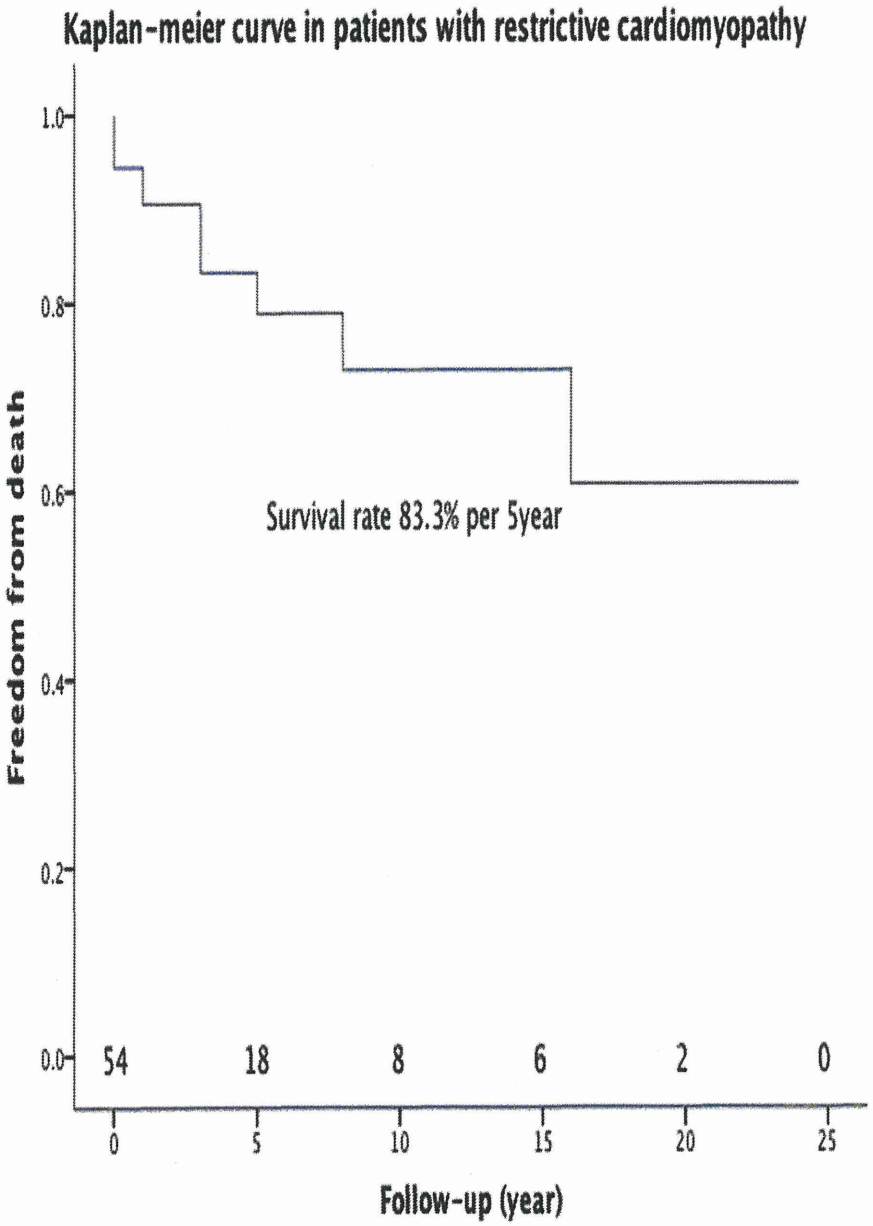
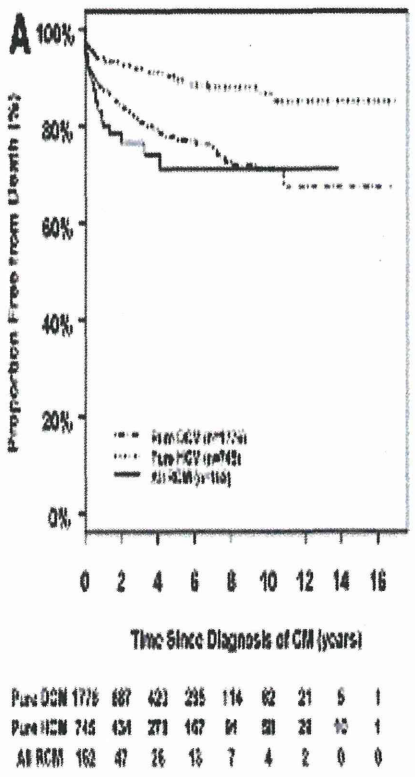


USA

我が国のデータ:
拘束型心筋症:
死亡回避率

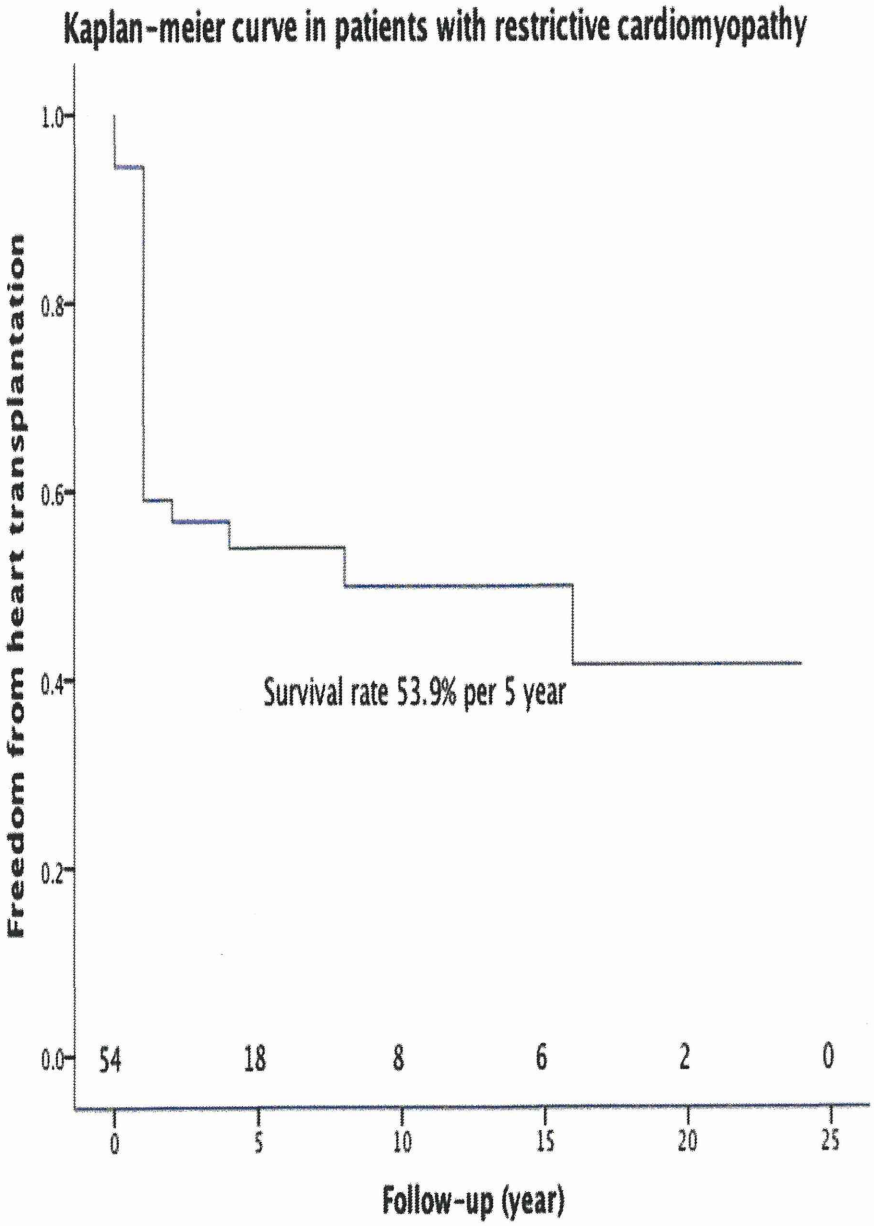


日本

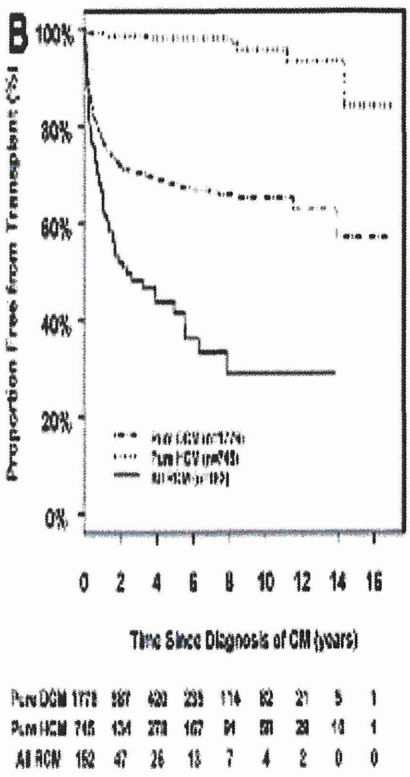


USA

我が国のデータ:
拘束型心筋症:
移植回避率

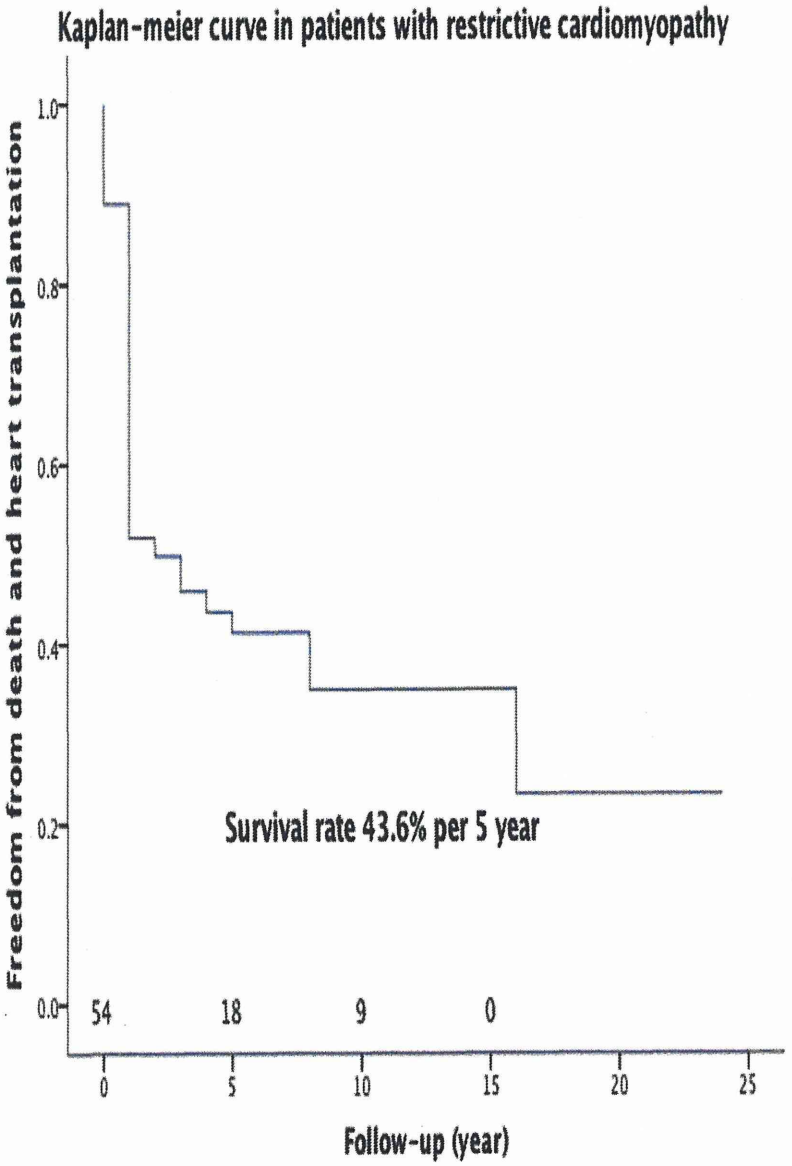


日本



USA

我が国のデータ:
拘束型心筋症:
死亡ないし移植回避率



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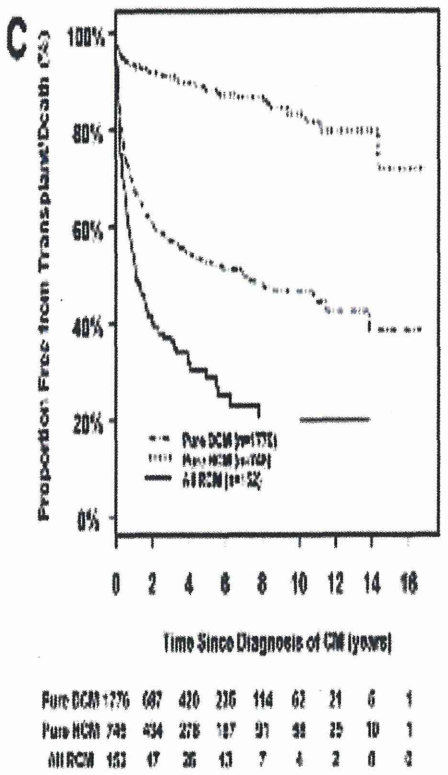


USA

遺伝子解析を行った77例の検討

遺伝子検索

- A total 77 idiopathic cardiomyopathy patients diagnosed at age 16 years or younger.
- A screening test for myofilament gene mutations by direct sequencing of 8 genes, including β-myosin heavy chain (βMHC), cardiac myosin binding protein C (MyBPC), cardiac troponin T (TNNT2), cardiac troponin I (TNNI3), α-tropomyosin (TPM1), regulatory and essencial light chains (MYL2, MYL3), and cardiac α-actin (ACTC).

Results

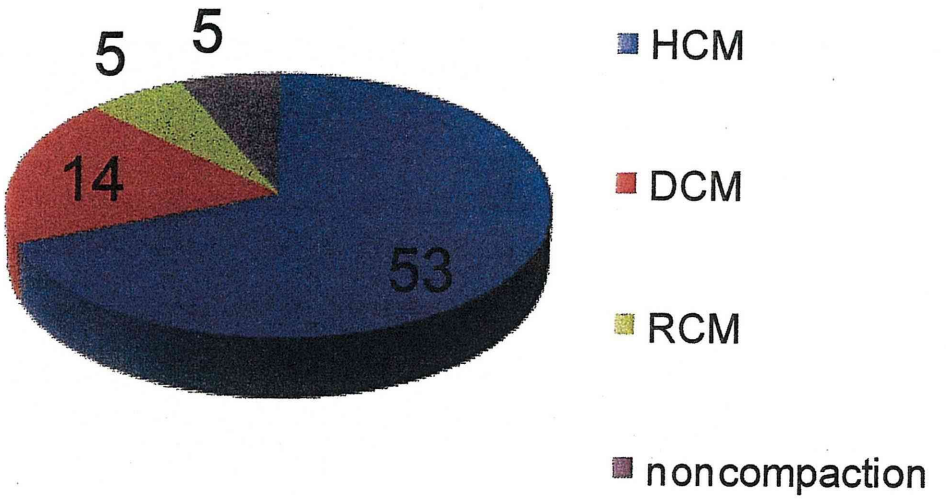
◆ Baseline characteristics

Variable	All patients (n=77)
Male / Female	36 / 41
Age at diagnosis (year)	8.8 (quartile range 1.17-12.6)
Follow-up duration (year)	6.8 (quartile range 1.35-15.3)
Family history of IM	54% (42/77)
Family history of sudden death	26% (20/77)
Brain natriutetic peptide (pg/ml)	330 (quartile range 33.8-860.6)
Arrhythmia	20% (15/77)
Disease-causing gene mutation	42% (32/77)

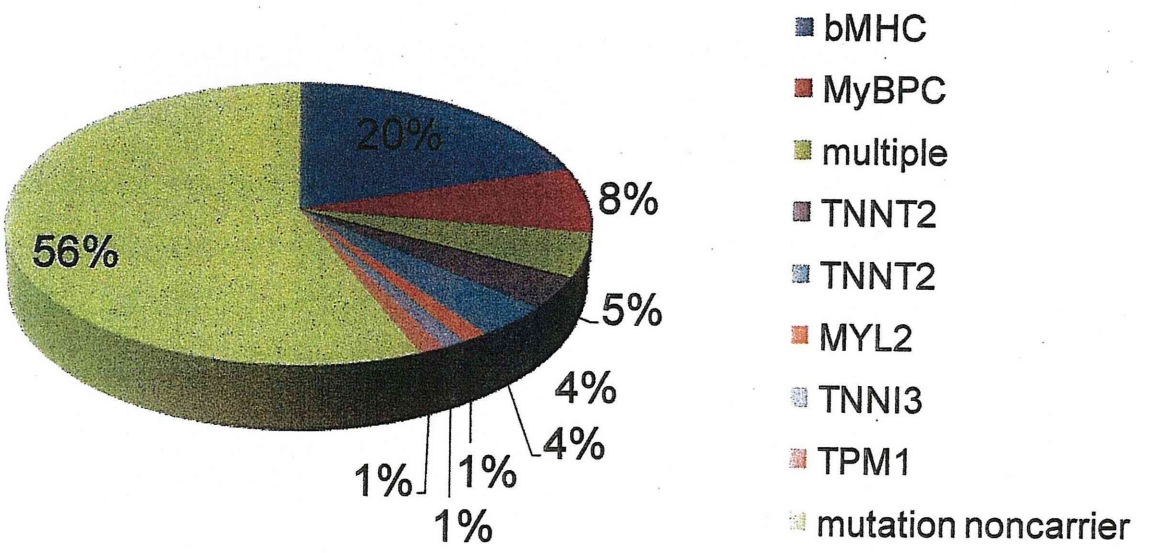
Patients (<16 yrs old) (n=77)

NYHA at last visit	number
I	26
II	18
III	3
IV	1
Post transplant	3
Died	12
Unknown	14

Type of cardiomyopathy

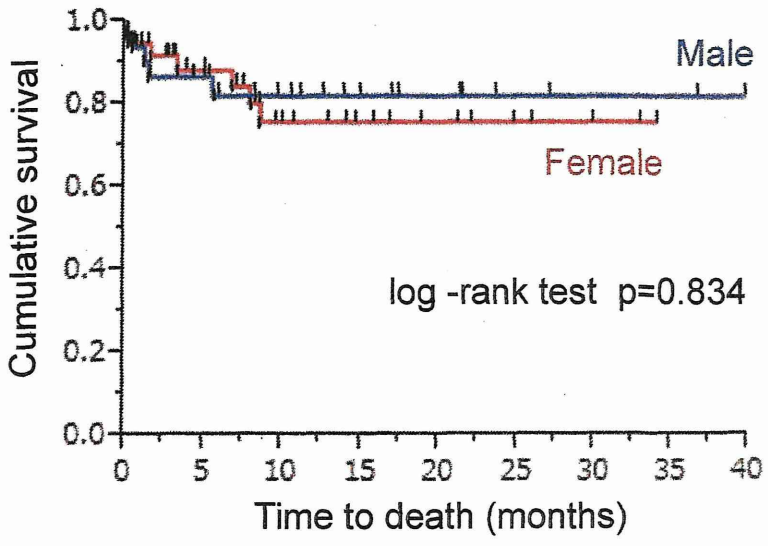


Gene mutation in 77 patients



Genes	HCM	DCM	RCM	Non compaction	total
βMHC	14	1	1	0	16
MyBPC	5	1	0	0	6
TNNT2	3	0	0	0	3
TNNI3	0	0	1	0	1
TPM1	0	0	0	1	1
MYL2	1	0	0	0	1
MYL3	0	0	0	0	0
ACTC	0	0	0	0	0
Multiple mutation	4	0	0	0	4
Mutation negative	26	12	3	4	45
total	53	14	5	5	77

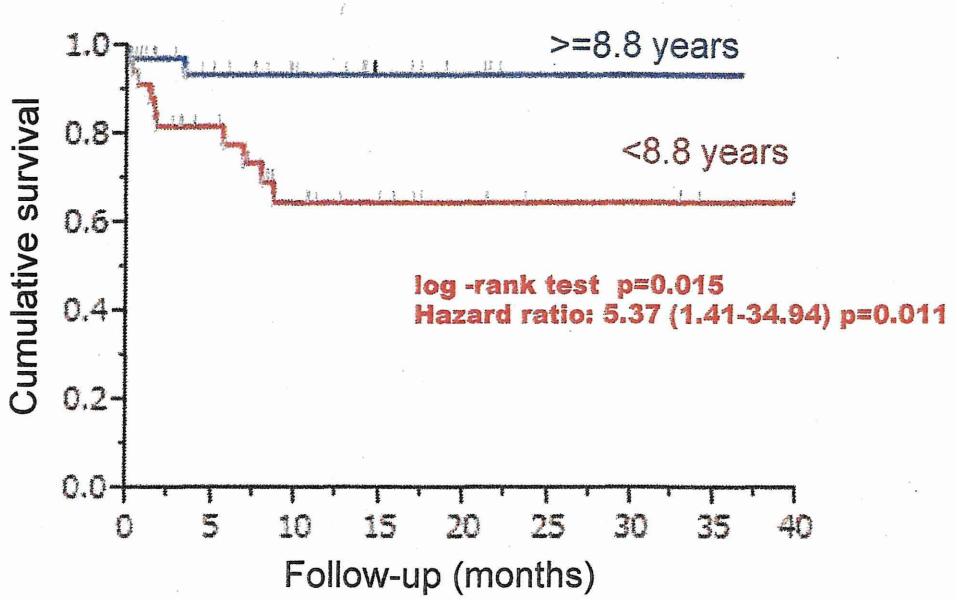
Overall survival by gender



Gene mutation and phenotypes

	Mutation negative (n=45)		Mutation positive (n=32)		p value
Gender, male / female	23 / 22		13 / 19		0.363
Age at diagnosis (year)					
Mean±SD	6.2±0.8		10.2±0.9		0.001
Median(interquartile range)	4.8 (0.5, 12.3)		12.0 (8.2, 13.0)		0.004
Follow up period (year)	5.1 (0.5, 11.85)		9.6 (3.23, 17.4)		
Family history					
Cardiomyopathy					
Yes, %	22	44.4	22	68.8	0.0532
No, %	23	51.1	10	31.3	
Unknown, %	2	4.4	0	0.0	
Sudden death					
Yes, %	9	20.0	11	34.4	0.2155
No, %	33	73.3	21	65.6	
Unknown, %	3	6.7	0	0.0	
BNP at first					
Arrhythmia					
Yes, %	7	15.6	8	25.0	0.293
No, %	23	51.1	18	56.3	
Unknown, %	15	33.3	6	18.8	
NYHA at last follow-up					
I, %	13	28.9	13	40.6	0.162
II, %	9	20.0	9	28.1	
III, %	2	4.4	1	3.1	
IV, %	0	0.0	1	3.1	
Heart transplant	3	6.7	0	0.0	
Death, %	10	22.2	2	6.3	
Unknown, %	8	17.8	6	18.8	

Survival by age at diagnosis



遺伝子解析を行った77例

- 18歳以下で発症した心筋症患者77例の臨床データを集計した。
- 全例で、βミオシン重鎖(βMHC)、ミオシン結合蛋白(MyBPC)、トロポニンT (TNT),トロポニンI (TNI),トロポミオシン(TPM1)、ミオシン軽鎖(MYL2, MYL3)、αアクチン(ACTC)の8個の遺伝子変異の有無をダイレクトシーケンス法で調べた。
- 心筋症の内容は、肥大型53例、拡張型14例、拘束型5例、左室緻密化障害5例であった。
- 遺伝子変異の内容は、βミオシン重鎖(βMHC)16例、ミオシン結合蛋白(MyBPC)6例、トロポニンT (TNT)3例,トロポニンI (TNI)3例,トロポミオシン(TPM1)1例、ミオシン軽鎖(MYL2, MYL3)1例、重複した変異4例であった。
- 拡張型、拘束型心筋症の予後は悪かったが、遺伝子変異による予後の差は認めなかった。
- トロポニンT変異の家系に突然死を認めた。

Myofilament Gene Mutations and Phenotype Correlation in Childhood

Pediatric Cardiology, Tokyo Women's Medical University, Tokyo, Japan
Toshio Nakanishi, Ayako Chida, Kei Inai

Backgrounds

- Many genetic abnormalities associated with idiopathic cardiomyopathy have been identified in recent years.
- However, genotype-phenotype correlation in idiopathic cardiomyopathy is still unclear, especially in childhood.

Objectives

- To assess gene mutation causing childhood idiopathic cardiomyopathy
- To investigate the prognosis of patients according to the affected genes.
- I will present results of our study and review previous studies.

Our study

- A total 77 idiopathic cardiomyopathy patients diagnosed at age 16 years or younger.
- A screening test for myofilament gene mutations by direct sequencing of 8 genes, including β-myosin heavy chain (βMHC), cardiac myosin binding protein C (MyBPC), cardiac troponin T (TNNT2), cardiac troponin I (TNNI3), α-tropomyosin (TPM1), regulatory and essencial light chains (MYL2, MYL3), and cardiac α-actin (ACTC).
- Their clinical presentation and outcomes (phenotypes) were evaluated.

Patients (<16 yrs old) (n=77)

Male/female	36:41
Age at presentation (years)	8.8 (median, range 1.2-12.6)
Follow-up (years)	6.8 (median, range 1.3-15.3)
Family histoly	55% (42/77)
Family histoly of sudden death	26% (20/77)
BNP at presentation	330 (median, range 33-860)

Results

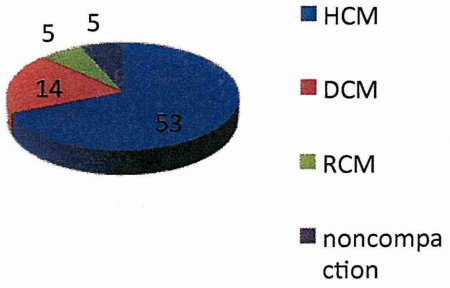
◆ Baseline characteristics

Variable	All patients (n=77)
Male / Female	36 / 41
Age at diagnosis (year)	8.8 (quartile range 1.17-12.6)
Follow-up duration (year)	6.8 (quartile range 1.35-15.3)
Family history of IM	54.5% (42/77)
Family history of sudden death	26.0% (20/77)
Brain natriutetic peptide (pg/ml)	330.2 (quartile range 33.8-860.6)
Arrhythmia	19.5% (15/77)
Disease-causing gene mutation	41.6% (32/77)

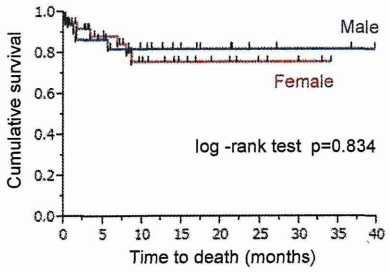
Patients (<16 yrs old) （n=77）

NYHA at last visit	number
I	26
II	18
III	3
IV	1
Post transplant	3
Died	12
Unknown	14

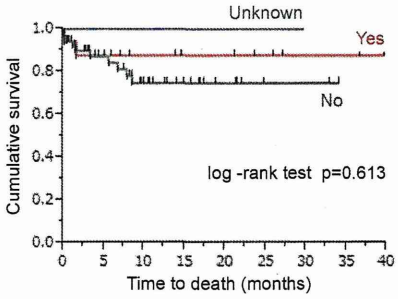
Cardiomyopathy type



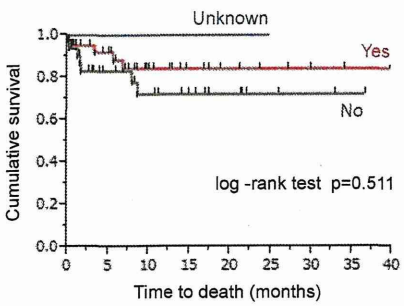
◆ Overall survival by gender



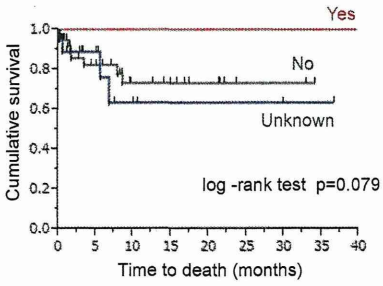
◆ Overall survival by family history of sudden death



◆ Overall survival by family history of cardiomyopathy



◆ Overall survival by arrhythmia



Gene mutation and phenotypes

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Median(interquartile range)	4.8 (0.5, 12.3)		12.0 (8.2, 13.0)		0.004
Follow up period (year)	5.1 (0.5, 11.85)		9.6 (3.73, 17.4)		
Family history					
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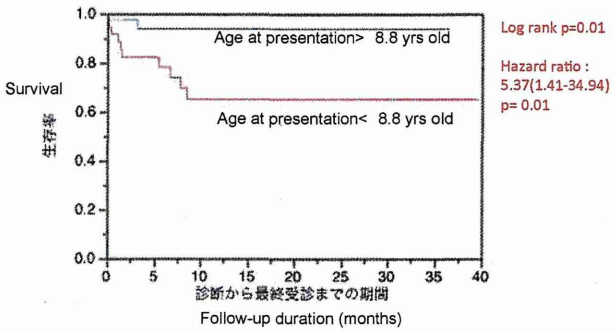
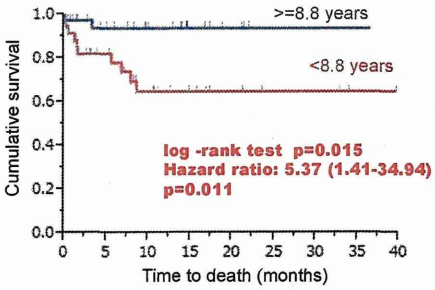
Yes, %	22	44.4	22	68.8	0.0532
No, %	23	51.1	10	31.3	
[redacted]	[redacted]		[redacted]		
Sudden death					
Yes, %	9	20.0	11	34.4	0.2155
No, %	33	73.3	21	65.6	
[redacted]	[redacted]		[redacted]		
BNP at first					
Arrhythmia					
Yes, %	7	15.6	8	25.0	0.293
No, %	23	51.1	18	56.3	
Unknown, %	15	33.3	6	18.8	
NYHA at last follow-up					
I, %	13	28.9	13	40.6	0.162
II, %	9	20.0	9	28.1	
III, %	2	4.4	1	3.1	
IV, %	0	0.0	1	3.1	
Heart transplant	3	6.7	0	0.0	
Death, %	10	22.2	2	6.3	
Unknown, %	8	17.8	6	18.8	

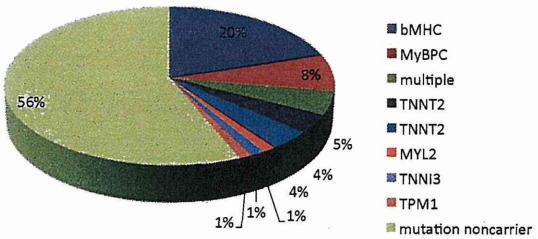
Age at presentation and prognosis



◆ Overall survival by age at diagnosis



Gene mutaion (n=77)



Genes	HCM	DCM	RCM	Non compaction	total
βMHC	14	1	1	0	16
MyBPC	5	1	0	0	6
TNNT2	3	0	0	0	3
TNNI3	0	0	1	0	1
TPM1	0	0	0	1	1
MYL2	1	0	0	0	1
MYL3	0	0	0	0	0

● Multiple mutations (4 patients)

Proband	Cardio myopathy	Double mutations	Compound mutations
1	HCM	MyBPC	-
2	HCM	MyBPC	-
3	HCM	MyBPC	-
4	HCM	-	βMHC, MyBPC