Effects of glucose-induced insulin on ST-Segment elevation in Brugada Syndrome

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Background

*** Changes of ST-segment elevation in patients with the Brugada syndrome are known to fluctuate from time to time influenced by multiple factors.**

*** Insulin has been shown to affect QT dispersion in healthy volunteers as well as abnormality of ventricular repolarization in patients with the congenital long QT**

*** However, no studies have explored effects of plasma insulin level after glucose load on ST-segment elevation in patients with the Brugada syndrome.**

Objective

This study was designed to determine whether patients with the Brugada syndrome exhibit an increased abnormality in ST-segment of right precordial leads V1-V3 in response to plasma insulin level.

Methods

Study patients

1) Brugada syndrome :

* ECG with either persistent or transient RBBB pattern and ST segment elevation (? 2mm) of coved or saddle-back type morphology in leads V1 to V2 or V3
* 20 men, mean age 51 ± 10years
* Symptomatic:14 pts (70%), Family history of sudden cardiac death:7pts(35%)
* Electrophysiological Study :
  Induction of ventricular fibrillation -- 20 pts (100%)
* Pharmacological provocation with intravenous Flecainide or pilsicainide:
  Augmentation of ST-segment elevation (>1.0mm)-- 20 pts (100%)

2) Control subjects :

* 20 healthy volunteers with normal ST segment and QT interval
* 20 men, mean age 52 ± 17 years

Oral glucose tolerance test (OGTT)

*** An oral glucose tolerance test was done in each patients according to WHO guideline.**

*** Blood sample were taken during fasting (baseline), and 30, 60, 120 and 180 min after a 75 g oral glucose load.**

*** Measurement: plasma glucose, immunoreactive insulin concentration (IRI) and potassium level.**

12-lead surface ECG during OGTT

*** All standard 12-lead ECGs :**

- A speed of 25 and 50 mm/sec

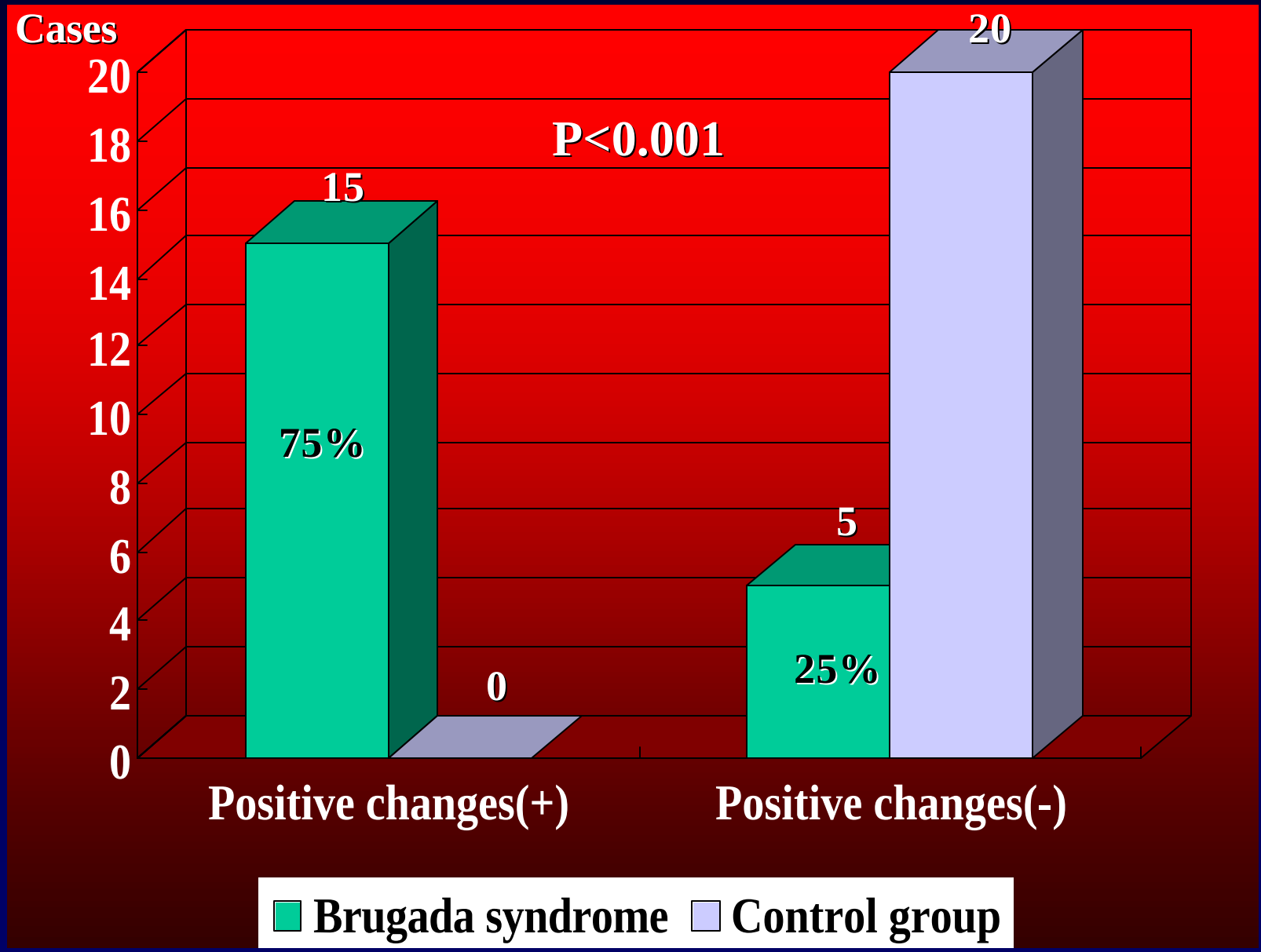
- During fasting, and 30, 60, 120 and 180 min after glucose load

Positive ECG changes during OGTT

* Augmentation (>1.0mm) of ST segment elevation in leads V1 to V3

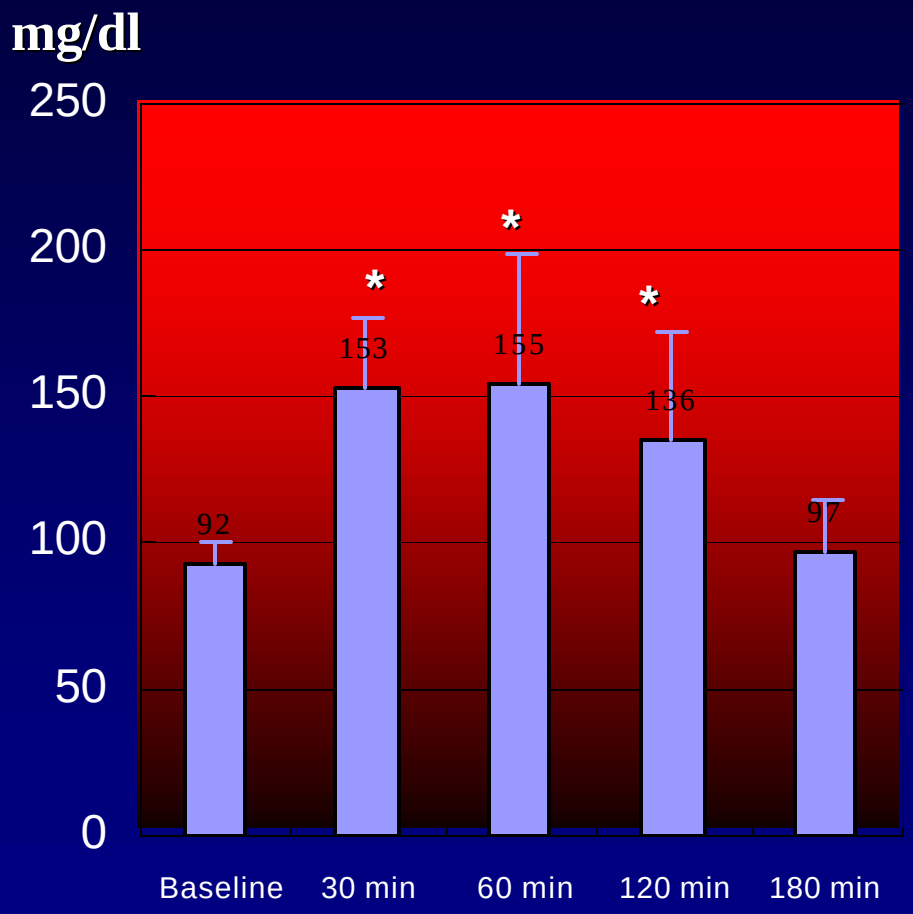
* Morphology change : A distinctly visible alteration of ST-segment morphology such as transformation from saddle-back to coved type and new development of negative T wave

Positive ECG changes during OGTT

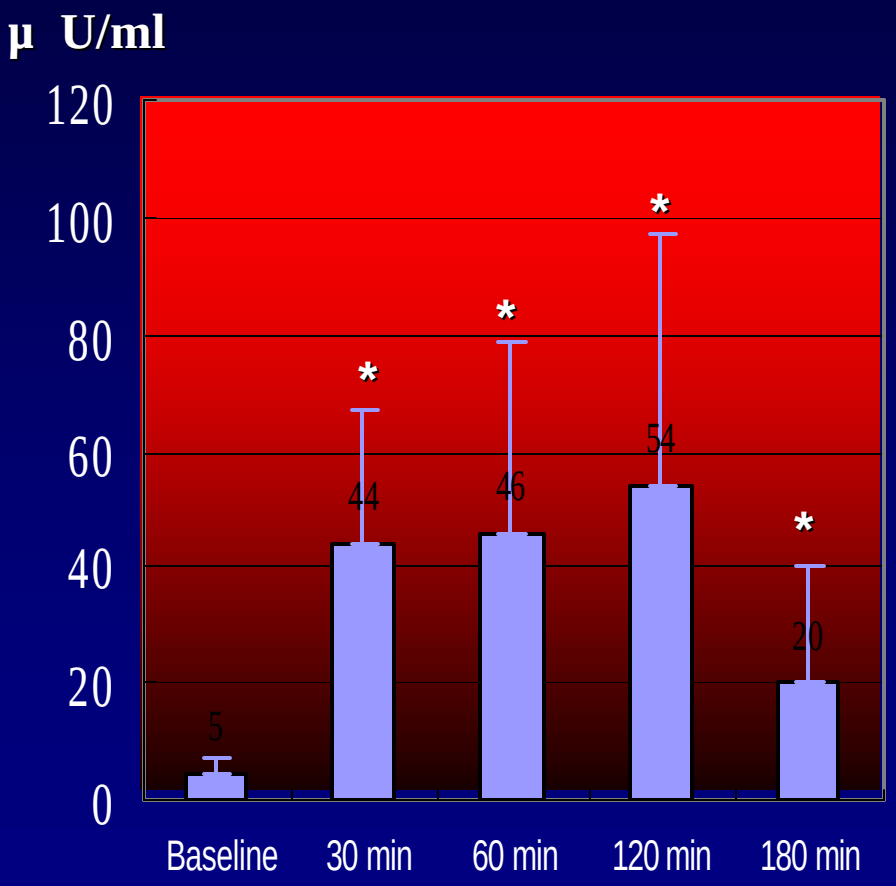


Results of Oral glucose tolerance test in Brugada syndrome

Plasma glucose

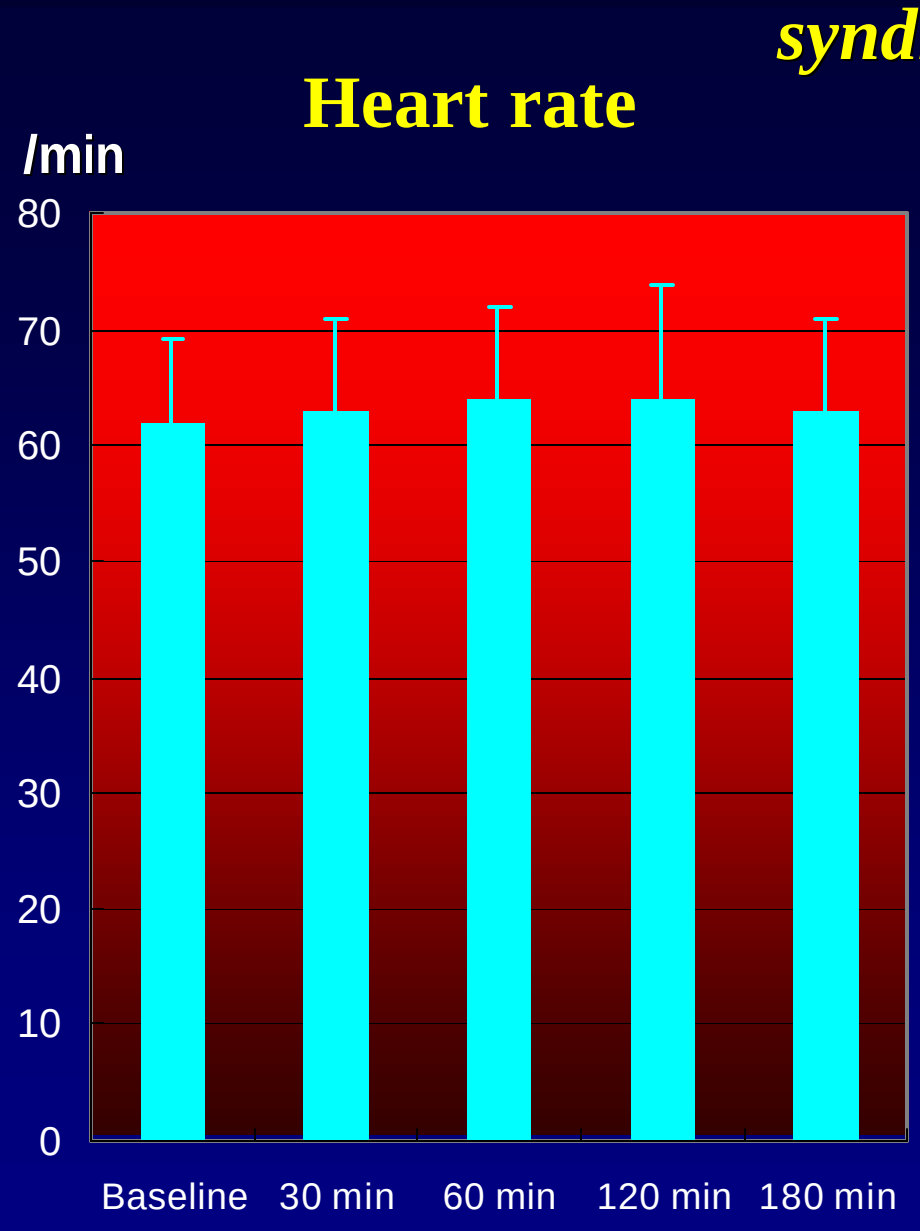


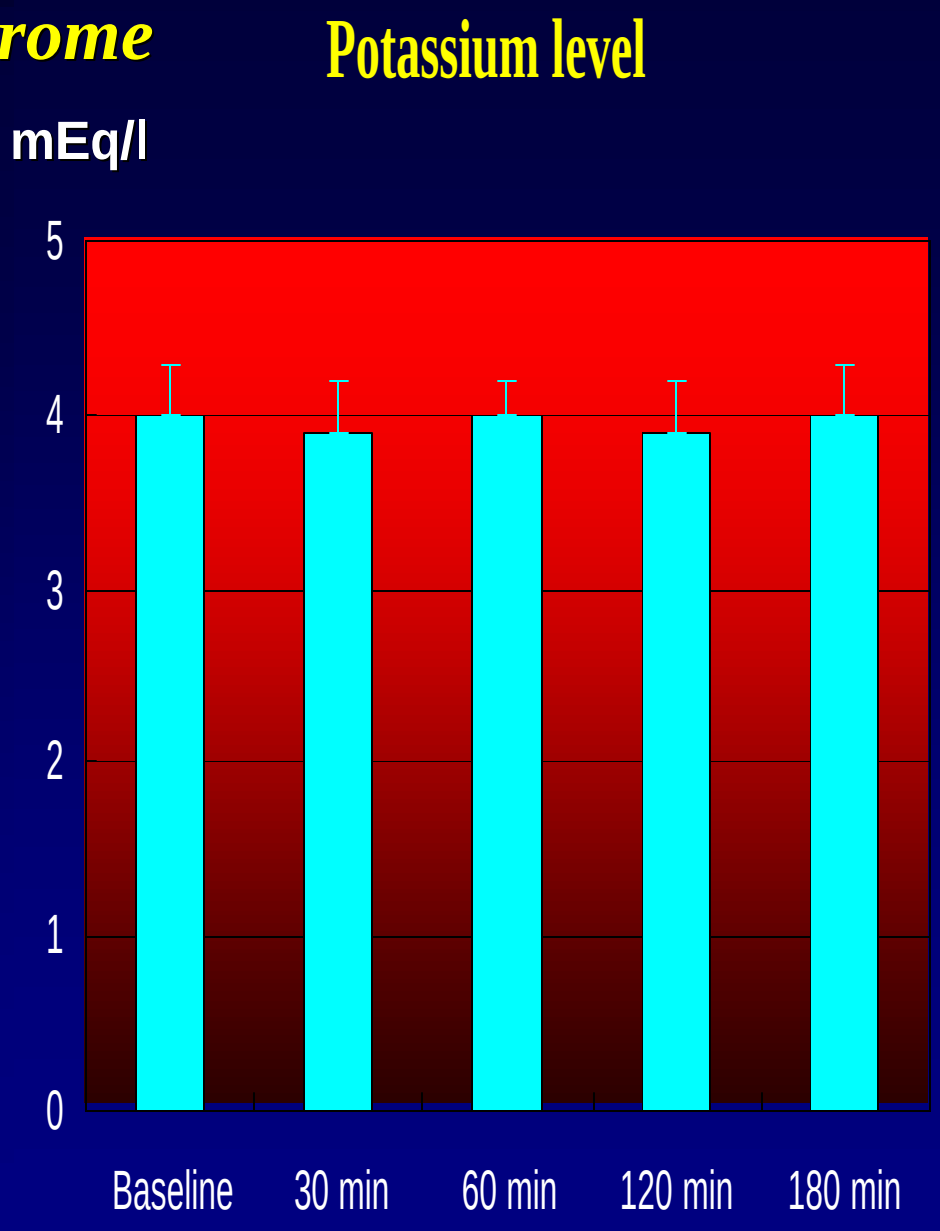
Immuno reactive insulin (IRI)



*** P<0.01 vs Baseline**

Results of Oral glucose tolerance test in Brugada syndrome





Results of Glucose Tolerance Test

	Brugada syndrome (n=20)	Control group (n=20)	P value
Potassium level (mEq/L)			
Fasting	4.0 ± 0.3	4.0 ± 0.3	NS
30 min	3.9 ± 0.3	3.9 ± 0.4	NS
60 min	4.0 ± 0.2	4.0 ± 0.3	NS
120 min	3.9 ± 0.3	4.0 ± 0.2	NS
180 min	4.0 ± 0.3	4.0 ± 0.3	NS
Plasma glucose (mg/dl)			
Fasting	92 ± 8	93 ± 9	NS
30 min	153 ± 24**	158 ± 27**	NS
60 min	155 ± 44**	165 ± 31**	NS
120 min	136 ± 36**	126 ± 31**	NS
180 min	97 ± 18	97 ± 28	NS
IRI (μ U/ml)			
Fasting	5 ± 2	7 ± 5	NS
30 min	44 ± 23**	50 ± 31**	NS
60 min	46 ± 33**	60 ± 31**	NS
120 min	54 ± 43**	48 ± 23**	NS
180 min	20 ± 20**	22 ± 19*	NS

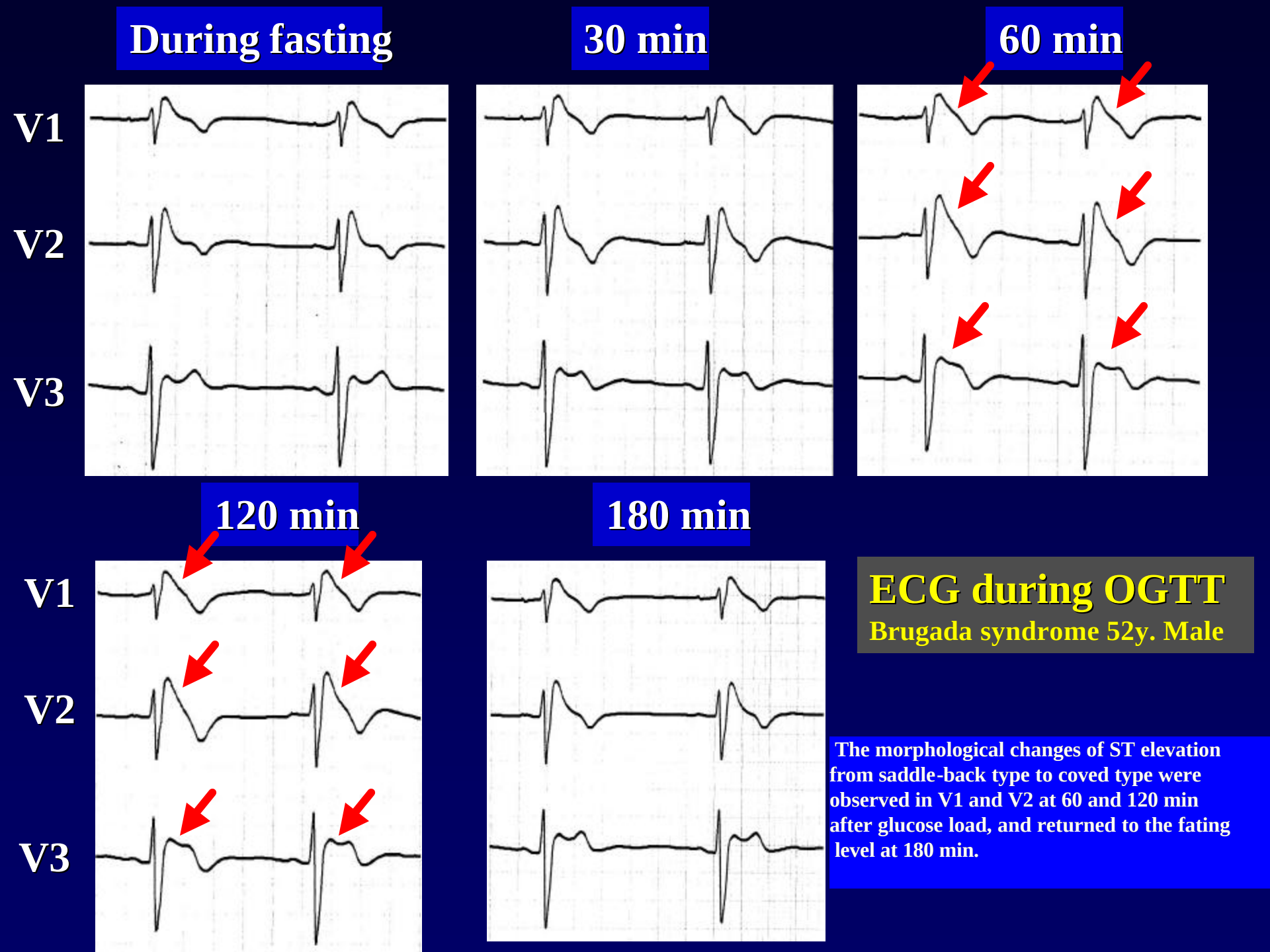
** P<0.01 vs. Fasting,
*P<0.05 vs. Fasting

Changes of ST segment, QT intervals and QT dispersion during Glucose Tolerance Test

	Brugada syndrome (n=20)	Control Group (n=20)	P Value
Changes of ST segment (% of patients)	75%	0%	<0.01
QT maximum (ms)			
Fasting	428±48	420±20	NS
30min	448±66	421±24	NS
60min	445±61*	422±31	NS
120min	432±47	419±27	NS
180min	424±47	411±25*	NS
QT minimum (ms)			
Fasting	374±25	389±22	NS
30min	374±22	380±27*	NS
60min	370±25	375±24**	NS
120min	368±28	376±23**	NS
180min	366±32*	380±28	NS
QT dispersion (ms)			
Fasting	51±30	30±8	<0.01
30min	75±52 **	41±17	<0.05
60min	75±45**	47±22*	<0.05
120min	64±34*	42±8**	<0.05
180min	57±29	30±8	<0.01

* P<0.05 vs. Fasting

** P<0.01 vs. Fasting



ECG during OGTT

Brugada syndrome 52y. Male

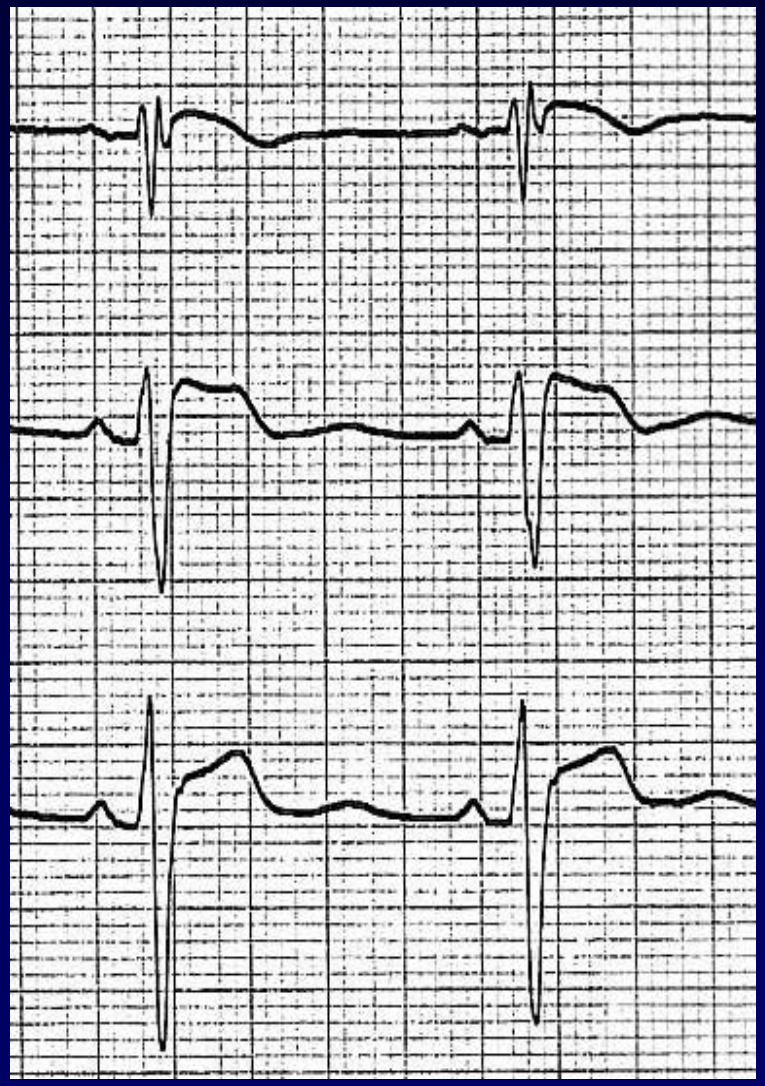
The morphological changes of ST elevation from saddle-back type to coved type were observed in V1 and V2 at 60 and 120 min after glucose load, and returned to the fating level at 180 min.

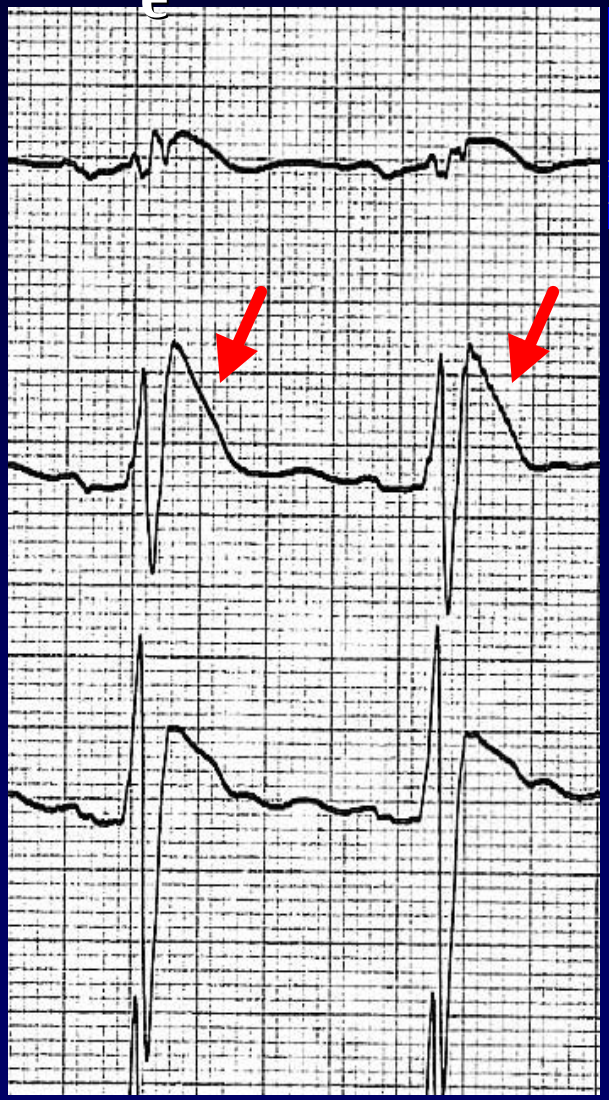
(1) ECG after administration of pilsicainide

Brugada syndrome
57y. Male.

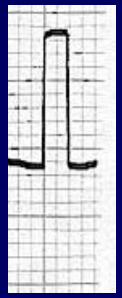
Baseline

Pilsicainide



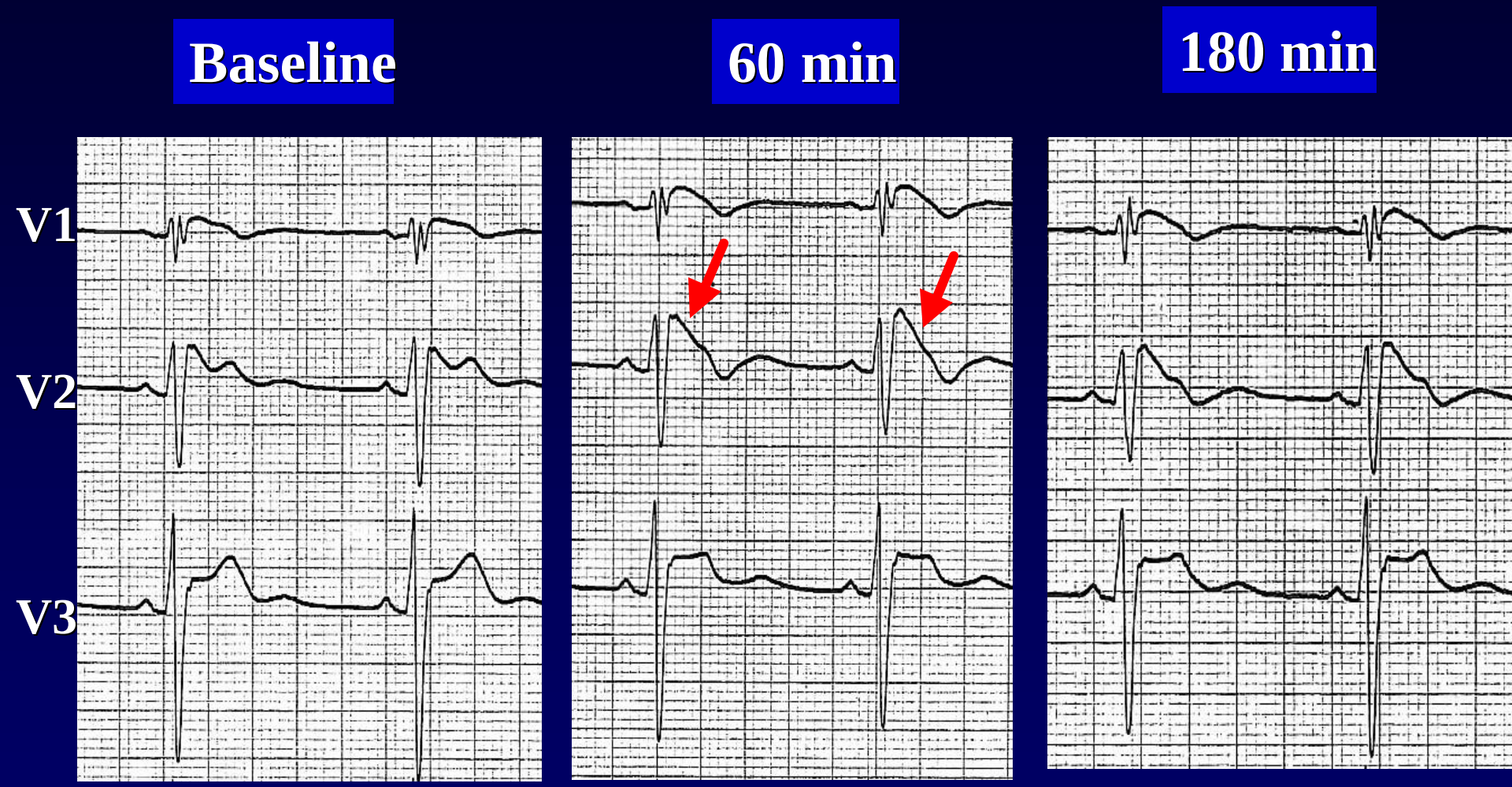


After pilsicainide, marked ST elevation and change of ST-segment morphology from saddle-back to coved type were observed in V2-



(2) ECG during OGTT

Brugada syndrome
57y. Male



ST-segment elevation in leads V1 to V3 changed distinctively at 60 min after glucose load, which was similar to those after pilsicainide. Configuration of ST-segment in lead V2 at 60 min showed typical coved-type ST-Segment elevation.

Results

*** Augmentation (>1 mm) or morphology change of ST segment elevation was frequently observed in response to insulin level during OGTT in patients with Brugada syndrome, but none during OGTT in control group (P<0.01).**

*** These changes of ST segment elevation was observed more frequently in patient with coved type (8/8 pts:100%) than those with saddle-back type or transient normalization of ST segment elevation (7/12 pts:58%, P<0.05). Moreover, these changes returned to baseline at 180 min after glucose load in 9 of 15 patients with Brugada syndrome.**

*** The maximal QT interval and QT dispersion increased significantly and returned to baseline level in response to IRI after glucose load in Brugada syndrome.**

*** There was no significant difference in glucose, IRI and potassium level during OGTT between the 2 groups.**

Conclusions

These findings suggest that glucose-induced insulin secretion play a role for change of ST segment elevation in Brugada syndrome, and may provide a clue to add diagnostic evaluation of the ST elevation in this syndrome.