CATHETER ABLATION FOR BRUGADA SYNDROME
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12th ASIA PACIFIC HEART RHYTHM SOCIETY SCIENTIFIC SESSION
24-27 OCTOBER 2019 / BANGKOK, THAILAND

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Figure 2: Map of Thailand demonstrated higher prevalence of BrS in Northeastern region of Thailand according to previous studies from Makarawate et al. in Khon Kaen University, our previous study in Buriram hospital and our current study in EGAT cohort.
Worldwide Prevalence of Brugada Syndrome: A Systematic Review and Meta-Analysis

Wasawat Vuthikraivit,1 Pattara Rattanawong,2 Prapaipan Putthapiban,3 Weera Sukhumthammara,3 Prin Vathesatogkit,4 Tachapon Ngarmukos4 and Ammarin Thakkinstin5

Potentially relevant articles identified from search of MEDLINE (n=670) and EMBASE database (n=227) and screened for retrieval

Exclusion of 204 duplications

Title and abstract review of potentially relevant articles (n=693)

628 articles were excluded because
- 375 articles were no outcome of interest
- 108 articles were case report
- 45 articles were letter
- 23 articles were non-human
- 8 articles were non-English

65 articles underwent full-length article review

28 articles were excluded because of non-population base study

2 articles were excluded because of patient duplication

5 articles were excluded because of unclear BrP definition

28 articles underwent meta-analysis
Worldwide Prevalence of Brugada Syndrome: A Systematic Review and Meta-Analysis

Note: Hawaii

Vutthikraivit W. Acta Cardiol Sin 2018;34:0E0
Medical therapy for Brugada Syndrome

**Ineffective or Proarrhythmic**
- Amiodarone 126
- β Blockers 126
- Class IC antiarrhythmics
  - Flecaïnide 10
  - Propafenone 184
- Disopyramide 127
- Class IA antiarrhythmics
  - Procainamide 9

**Effective for Treatment of Electrical Storms**
- β Adrenergic agonists – isoproterenol 16, 162, danopamine 144, orciprenaline 140, 156
- Phosphodiesterase III Inhibitors cilostazol 155

**Effective General Therapy**
- Quinidine 100, 132-134, 145-147
- Bepridil (I$_{to}$-blocking and I$_{Na}$-gaining effect?) 177
- Cilostazol combined with bepridil 172

**Experimental Therapy**
- $I_{to}$ Blockers - cardioselective and ion channel specific
  - Quinidine 100
  - 4-aminopyridine 100
  - Tedisamil 150
  - AVE0118 154
  - PDE-III-inhibitors
  - Cilostazol – Increases I$_{CaL}$ and inhibits I$_{to}$ 174, 185
  - Milrinone - I$_{CaL}$-boosting 174, 185
- Herbal extracts
  - Wexin Keli - combined I$_{to}$-blocking and tyramine-like effect 130
Drugs

quinidine is the only one that has been extensively studied and has been shown to be effective in the prevention of cardiac events.
Problem…
Quinidine Is Inaccessible in Many Countries

- Survey of 273 physicians from 131 countries
- Quinidine was readily available in
  - 19 countries (14%)
  - not accessible in 99 countries (76%)
  - special procedure in 13 countries (10%)
Other Treatments for Brugada Syndrome
Unpublished Treatment of Brugada Syndrome in Thailand

- Lai Tai
- SUDS
- “The Widow Ghost”
Treatment for Brugada Syndrome

- **Device**
  - Proven to decrease mortality
  - Easier to get one
  - More expensive
  - Problem with device, QOL
  - Limited indications

- **Ablation**
  - Proven to decrease ICD shock
  - Harder to fine a doctor
  - Repeat/Risks procedure
  - Short follow up
  - May apply to more patient
Devices
DEFibrillator vs. β-blockers for Unexplained death in Thailand

Kaplan-Meier survival curves for the 2 treatment arms. The primary end point was mortality.

Nademanee K, Circulation. 2003;107:2221
DEfibrillator vs. /3 blockers for Unexplained death in
Thailand

- Cumulative proportion of the VF/death occurrence using the composite end points of recurrent VT/VF or cardiac arrest from which the patient was resuscitated or death.
Ablation
N=7 (4 men; age, 38±7 years; 4 with long-QT and 3 with Brugada syndrome) with VF or PMVT & frequent PVC

- PVC originated from
  - HPJ system in 4 (1 Brugada right & 3 long-QT left) associated with variable Purkinje-to-muscle conduction times (30 to 110 ms)
  - RVOT 3

F/U 17±7 months using ambulatory monitoring and defibrillator memory interrogation, no patients had recurrence of symptomatic ventricular arrhythmia but 1 had persistent PVC.
Regional Substrate Ablation Abolishes Brugada Syndrome

• 43 y/o with syncope FHx of SCD

• Brugada ECG

• ICD implanted with multiple shock

• VT induced by RVOT ectopic

• No PVC was induced during EP study, pace mapping and ablation of the anterolateral RVOT.

• During RF VF was induced

• Area around the RF site were ablated

Successful Radiofrequency Catheter Ablation for Electrical Storm of Ventricular Fibrillation in a Patient With Brugada Syndrome

Nakagawa E. Circ J 2008; 72: 1025 – 1029
Short-term normalization of ventricular repolarization by transcatheter ablation in a patient with suspected Brugada Syndrome

- 30 y/o with VF arrest
- Propafenone induced PVCs
- RF ablation of PVC from RVOT & LV posterior septum transiently normalised ST elevation in V1
- No ICD for financial reason
Short-term normalization of ventricular repolarization by transcatheter ablation in a patient with suspected Brugada Syndrome

Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium

Koonlawee Nademane, Guanpanart Veerakul, Pakorn Chandanamattha, Lertlak Chaothawee, Aekarach Ariyachaipanich, Kriengkrai Jirasirirojanakorn, Khanchit Likittanasombat, Kiertijai Bhuripanyo and Tachapong Ngarmukos

*Circulation* 2011;123;1270-1279; originally published online Mar 14, 2011; DOI: 10.1161/CIRCULATIONAHA.110.972612

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Epicardial
late fractionate potential at RVOT
Prevention of VF Episodes in Brugada Syndrome by Ablation Over the Anterior RVOT Epicardium

- 9 symptomatic BrS (all men; median age 38 years)
- recurrent VF episodes (median 4 episodes) per month
- All patients had typical type 1 Brugada ECG pattern and inducible VT/VF
- abnormal low voltage (0.94±0.79 mV), prolonged duration (132±48 ms), and fractionated late potentials (96±47 ms beyond QRS complex) clustering exclusively in the anterior aspect of the RVOT

Nademanee et al. Circulation; 2011; 123; 1270-1279
Prevention of VF Episodes in Brugada Syndrome by Ablation Over the Anterior RVOT Epicardium
Prevention of VF Episodes in Brugada Syndrome by Ablation Over the Anterior RVOT Epicardium
Endocardial Mapping and Catheter Ablation for Ventricular Fibrillation Prevention in Brugada Syndrome

- N=10 BrS (all men; median age 36.5 years) with VF storm (group I, n = 4) and no VF storm (group II, n = 6) were enrolled in the study between August 2007 and December 2008

- All patients underwent electrophysiological study using noncontact mapping.

- The isopotential map in sinus rhythm and the region that had electrical activity occurring during J point to +60 (J+60) milliseconds interval of the V1 or V2 of surface ECG was considered as the late activation zone (LAZ) and also the substrate for ablation

- Endocardial catheter ablation of the LAZ modified Brugada ECG pattern in 3 of 4 patients (75%) and suppressed VF storm in all 4 patients in group I during long-term follow-up (12–30 months)
Endocardial Mapping and Catheter Ablation for Ventricular Fibrillation Prevention in Brugada Syndron
Mechanisms Underlying Epicardial Radiofrequency Ablation to Suppress Arrhythmogenesis in Experimental Models of Brugada Syndrome

Effect of Ajmaline

Sacher et al. Heart Rhythm 2013:0:1–3
Epicardial ablation for prevention of ventricular fibrillation in a patient with Brugada Syndrome.
Epicardial ablation for prevention of ventricular fibrillation in a patient with Brugada Syndrome
Ablation of the Epicardial Substrate in the RVOT in a Patient With Brugada Syndrome Refusing ICD

- A 31-year-old male patient with recurrent short lasting paroxysmal palpitations, once leading to syncope,
Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

• N=14 with BrS, median age 39 years (30.3–42.3) with ICD

• Substrate identification consisted in mapping right ventricle epicardial surface before and after flecainide (2 mg/kg per 10 minutes)

• After radiofrequency ablation, flecainide and remap confirmed elimination of abnormal substrate, BrS ECG pattern, and ventricular tachycardia/ventricular fibrillation indelibility

• Flecainide testing was performed at each monthly follow-up visits ≤6 months.
Low-voltage areas (<1.5 mV) were commonly identified on the anterior RV and RVOT, which increased after flecainide from 17.6 cm$^2$ (12.1–24.2) to 28.5 cm$^2$ (21.6–30.2; $P=0.001$)
Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

- areas with abnormal electrograms increased after flecainide from 19.0 (17.5–23.6) to 27.3 cm (24.0–31.2; \(P=0.001\))
Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

• After 23.8 minutes (18.1–28.5) of RFA, abnormal electrograms disappeared, whereas low-voltage areas were replaced by scar areas (<0.5 mV) of 25.9 cm² (19.6–31.0).

• Substrate elimination resulted in BrS ECG pattern disappearance and no VT/VF inducibility without complications.

• After a median follow-up of 5 months (3.8–5.3), ECG remained normal despite flecainide.
Brugada Syndrome
Phenotype Elimination by Epicardial Substrate Ablation

A&B baseline
C&D immediate post ablation
E&F follow up

Brugada J. Circ Arrhythm Electrophysiol. 2015:8:1373–1381
Electrical Substrate Elimination in 135 Consecutive Patients With Brugada Syndrome

- A total of 135 symptomatic Brugada syndrome patients having ICD were enrolled
- 63 (group 1) VT/VF & Brugada syndrome–related symptoms
- 72 (group 2) having inducible VT/VF without ECG documentation at the time of symptoms.
- 3D maps before and after ajmaline determined the arrhythmogenic electrophysiological substrate (AES)
- Primary end point was identification and elimination of AES leading to ECG pattern normalization and VT/VF noninducibility.
- Radiofrequency ablation eliminated AES leading to ECG normalization and VT/VF noninducibility in all patients. During a median follow-up of 10 months, the ECG remained normal even after ajmaline in all except 2 patients who underwent a repeated effective procedure for recurrent VF.
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How to do BrS ablation?
Epicardial substrate ablation for Brugada syndrome

- Target for ablation
  - Abnormal EGM are defined as EGM that have
    - low voltage (≤1 mV)
    - split electrograms or fractionated electrograms with multiple potentials with ≥2 distinct components
    - with >20 ms isoelectric segments between peaks of individual components:
      - long duration (>80 ms) or late potentials, with distinct potentials extending beyond the end of the QRS complex.

Nademanee K. Heart Rhythm 2017;14:457-461
Epicardial substrate ablation for Brugada syndrome

- Importance of sodium channel blockers in identifying subtle substrate sites
  - Ajmaline IV 50–80 mg over 5 minutes
  - Procainamide (750–1000 mg over 20–30 minutes) infusion

Nademane K. Heart Rhythm 2017;14:457–461
Epicardial substrate ablation for Brugada syndrome

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Nademanee K. Heart Rhythm 2017;14:457–461
Epicardial substrate ablation for Brugada syndrome

An irrigated-tip catheter that provides force measurement is recommended.

- With good contact > 5g, RF power between 20 and 45 W
- If RF energy is effective in creating the lesion, the recorded EGM voltage amplitude will be drastically reduced and the mid and late components of the fractionated potentials will disappear
- The best and only end point is to eliminate all substrate areas that harbor abnormal low-voltage fractionated signals detected after sodium channel blocker challenge,

Nademanee K. Heart Rhythm 2017;14:457–461
Summary?
Ablation in Brugada Syndrome for the Prevention of VF (BRAVE)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified September 2016 by Pacific Rim Electrophysiology Research Institute

Sponsor:
Pacific Rim Electrophysiology Research Institute

Collaborator:
Academisch Medisch Centrum - Universiteit van Amsterdam (AMC-UvA)

Information provided by (Responsible Party):
Koonlawee Nademanee, MD, Pacific Rim Electrophysiology Research Institute

ClinicalTrials.gov Identifier:
NCT02704416

First received: February 18, 2016
Last updated: September 26, 2016
Last verified: September 2016

Purpose

This trial aims to develop evidence based curative treatment with optimal net benefit for patients with Brugada syndrome.

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<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
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<tr>
<td>Brugada Syndrome</td>
<td>Procedure: Catheter Ablation</td>
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Hybrid thoracoscopic epicardial ablation of right ventricular outflow tract in patients with Brugada syndrome.
Thank You Very Much
For Your Attention
The End
Thank you very much for your attention

See you in Bangkok
October 24-27, 2019
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Hybrid thoracoscopic epicardial ablation of right ventricular outflow tract in patients with Brugada syndrome

In 36 BrS (26 men (72.2%); mean age 36.66 ± 15.8 years; range 3–63 years) who underwent hybrid thoracoscopic epicardial ablation of RVOT from January 2016 to April 2018 were included in this study.

- Two expert electrophysiologists analyzed the EGMs during ajmaline challenge and guided the surgeon to perform ablation.
- Ajmaline challenge was repeated after 1 month to assess the absence of the BrS electrocardiographic pattern.
- Patients were followed by remote monitoring and outpatient visits every 6 months.

Salghetti F. Heart Rhythm 2019;16:879–887
Hybrid thoracoscopic epicardial ablation of right ventricular outflow tract in patients with Brugada syndrome

Salghetti F. Heart Rhythm 2019;16:879–887
Hybrid thoracoscopic epicardial ablation of right ventricular outflow tract in patients with Brugada syndrome
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FIGURE 6. J-Wave and Maximal Action Potential Notch Area Recorded at Each Step of the Epicardial Ablation Experiments in the 2 Models
Addition of the provocative agents, NS5806 + verapamil (NS + Ver; n + 6) or ajmaline + pinacidil (Ajm + Pin; n + 4), significantly increased, whereas epicardial ablation significantly decreased J-wave area (A) and maximal action potential notch area (B). *p < 0.001 versus control. †p < 0.001 versus pre-ablation. ‡p = 0.027 versus control. §p = 0.017 versus pre-ablation.
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