Supraventricular Tachycardia (SVT)

Bruce Stambler, MD

Piedmont Heart
Atlanta, GA
Supraventricular Tachycardia

Objectives

• Types and mechanisms
  – AV nodal reentrant tachycardia (AVNRT)
  – AV reciprocating tachycardia (AVRT)

• Treatment options
  – Acute
    • New investigational nasal spray (etripamil)
  – Chronic
    • Catheter ablation
Paroxysmal supraventricular tachycardia (PSVT)
Supraventricular Tachycardia (SVT) Terminology

- **Supraventricular** - a rhythm process in which the ventricles are activated from the atria or AV node/His bundle region.
- Usually **paroxysmal**, i.e., starts and stops abruptly; in which case, called **PSVT**.
- QRS typically **narrow**; thus, also termed **narrow complex tachycardia**.
Supraventricular Tachycardia
Not all SVTs have a narrow QRS complex

WCT at 185 bpm $\rightarrow$ AVNRT with right bundle branch block
Supraventricular Tachyarrhythmias

- Paroxysmal Supraventricular Tachycardia
- Atrial Flutter
- Atrial Fibrillation
- Paroxysmal Supraventricular Tachycardia
Primary Mechanisms of PSVT

AVNRT
70%
Atrioventricular Nodal Reentrant Tachycardia

AVRT
20%
Atrioventricular Reciprocating Tachycardia

AT
10%
Atrial Tachycardia
Paroxysmal supraventricular tachycardia (PSVT)

• In the U.S., there are:
  – 600,000 persons with PSVT.
  – 90,000 new cases per year
  – 50,000 emergency department visits per year

Influence of Age on SVT Mechanism

Influence of Gender on SVT Mechanism

CAFFEINE
NECTAR
ALCOHOL
NICOTINE
Prospective Placebo Controlled Randomized Study of Caffeine in Patients with SVT Undergoing Electrophysiologic Testing

• Moderate caffeine intake associated with:
  – significant increases in systolic and diastolic BPs
  – no effect on heart rate, cardiac conduction or refractoriness
  – no effect on induction of SVT or more rapid rates of induced tachycardias.

• Moderate caffeine intake should not be:
  – considered to cause cardiac arrhythmias.
  – restricted in patients with a history of arrhythmias.

J Cardiovasc Electrophysiol, Vol. 26, pp. 1-6, January 2015
Supraventricular Tachycardia

Diagnosis

- ECG is cornerstone
- Tachycardia rate
- Wide vs. narrow QRS
- Relationship of P wave and QRS complex
- Morphology of P wave
- Zones of transition for clues to mechanism:
  - onset
  - termination
  - slowing, AV nodal block
  - bundle branch block
Differential Dx of Regular SVT

Sinus Rhythm

Short RP Interval

Long RP Interval
Differential Dx of Regular SVT

- Short RP tachycardia
  - AV nodal reentrant tachycardia (AVNRT)
  - AV reciprocating (AVRT) [ORT (Orthodromic reciprocating tachycardia)]
  - Atrial tachycardia with slow AV nodal conduction

Short RP interval
Differential Dx of Regular SVT

- Long RP tachycardia
  - Atrial tachycardia
  - Sinus tachycardia
  - Sinus node reentry
  - Atypical AV nodal reentrant tachycardia
  - Permanent form of junctional reciprocating tachycardia

Long RP interval
Supraventricular Tachycardia

Mode of Tachycardia Termination

No P-wave

AT unlikely
Intracardiac Electrophysiology

Electrode catheters:
- High right atrium (HRA)
- His bundle (His)
- Right ventricle (RV)
- Coronary sinus (CS)

Ablation catheter
History of Electrophysiology

1929 Cardiac catheterization (Forssman)
1945 Intracardiac electrogram
1968 Surgical ablation of accessory pathway (Cobb)
1969 Catheter recording of His bundle signal (Scherlag)
1971 Programmed ventricular stimulation (Wellens)
1981 Catheter ablation in human (Scheinman)
1986 Radiofrequency current catheter ablation
1989 FDA approval IV adenosine for PSVT
1995 Electroanatomic mapping techniques
45 yo Female with Palpitations & “Panic Attacks”
• **Origin:** AV nodal region

• **Mechanism:** Reentry

• **Tachycardia Rate:** 100 – 280 BPM (most around 170 bpm)

• **ECG:** QRS normal, P-wave not seen during tachycardia (within QRS).

• **Clinical Characteristics:** most common SVT in adults, females > males, can occur at any age (commonly in mid-40s), not associated with heart disease, catecholamine-sensitive
AV Nodal Reentry Tachycardia (AVNRT)

Note fixed, short RP interval mimicking r' deflection of QRS
AVNRT: Dual AV Node Physiology

AVNRT Normal Sinus Rhythm

During sinus beats
- conduction via fast pathway
- conduction via slow pathway blocked

Sinus Rhythm

Atrium → Slow → Fast → Ventricle
Normal AVN Conduction Curve

Normal Decremental AV Nodal Conduction
Dual AVN Physiology

≥50 ms AH interval with atrial extrastimulus decremented by 10-ms

Slow Pathway

Fast Pathway

AH INTERVAL (ms)

A1A2 COUPLING INTERVAL (ms)

Baseline

AVNRT
AVNRT: Dual AV Nodal Pathways
AVNRT: Initiation of Tachycardia

AVNRT (Atrioventricular Nodal Reentrant Tachycardia) is a type of arrhythmia characterized by a reentrant circuit involving the AV node. The diagram illustrates the sequence of events:

- **AS**: Sinus P wave
- **AP**: PAC (Premature Atrial Contractions)
- **AR**: Retrograde P wave

The diagram shows the progression from the atria (Atria) through the AV node (AV Node) and into the ventricles (Vent.). The sequence is marked by the notation of time (Time) and the flow of impulses.
AVNRT: Initiation of SVT

500  310  250

H    A    A
H    H
V    V

200 ms
328 msec
Septal VA interval < 70 ms
AV Nodal Reentrant Tachycardia

- Sometimes terminated by vagal maneuvers
- Highly responsive to AV nodal blocking agents:
  - Adenosine IV
  - Beta blockers IV
  - \(\text{Ca}^{2+}\) channel blockers
    - Diltiazem, verapamil IV
    - Etripamil Nasal Spray (Investigational).
- Recurrences common on medical therapy
• Slow Pathway Ablation
  - posterior approach (close to CS os)
  - preferred technique
  - does not affect normal AV conduction
  - risk of AV block ~ 0.5-1%
    – 95-99% successful
AVNRT: Slow Pathway Ablation
35 yo Male with Palpitations in the ER
AV Reciprocating Tachycardia
“Orthodromic” AVRT (ORT)

Retrograde P wave
AVRT: WPW syndrome: Preexcitation 12-Lead ECG

Incidence: 1-2/500 have an accessory pathway
~50% symptomatic with WPW syndrome
Wolff-Parkinson-White Pattern: Ventricular Preexcitation

ECG requirements for diagnosis of WPW Pattern

- P-R interval < 120 ms
- Normal P wave vector (to exclude junctional rhythm)
- Presence of a delta wave
- QRS duration > 100 ms

WPW ECG pattern + SVT = WPW syndrome
Wolff-Parkinson-White (WPW) Syndrome

The American Heart Journal

Vol. V August, 1930 No. 6

Original Communications

BUNDLE-BRANCH BLOCK WITH SHORT P-R INTERVAL IN HEALTHY YOUNG PEOPLE PRONE TO PAROXYSMAL TACHYCARDIA

Atrioventricular bypass tracts, or accessory pathways, can be found anywhere along the muscular portion of the posterior and lateral aspects of the mitral and tricuspid annuli. They can be classified by their anatomic location as either

- **left-sided** (50%)
- **posteroseptal** (25%)
- **right-sided** (15%)
- **mid, anteroseptal** (10%)

Multiple APs: 2-10% of pts.

AP: histologically strands of NL myocardium
Concealed Accessory Pathway

Sinus beat

No Delta wave during NSR (but AP capable of retrograde conduction)
AVRT: Reentrant Circuits

Sinus Rhythm

Orthodromic AVRT
(Narrow Complex)

Antidromic AVRT
(Wide Complex)

Atrium

AV node

Ventricle

95%

5%

ORT

ART
Preexcited Atrial Fibrillation
WPW Syndrome
WPW: Atrial fibrillation with rapid ventricular response

Risk of Sudden Cardiac Death in WPW:
- Symptomatic WPW: lifetime risk 3-4%
- Asymptomatic WPW: risk <1:10,000 (Class IIa indication catheter ablation)
Diagnosis of Orthodromic AVRT in the EP Lab
Orthodromic AVRT: Mechanism
Orthodromic AVRT: Initiation of SVT

VA = 100 ms (>70 ms)
Treatment of AP-Mediated Tachycardias

• **Acute Termination of ORT:**
  - AV nodal blockade:
    - Vagal maneuvers
    - IV adenosine 6, 12 mg
    - IV verapamil; diltiazem
    - IV beta-blocker
    - NS etripamil (investigational)

*Avoid digoxin*
Treatment of AP-Mediated Tachycardias

- **Wide complex tachycardia (WPW syndrome):**
  - AF with Preexcitation
  - Antidromic tachycardia
    - NO AV nodal blockers
    - IV procainamide, ibutilide
    - Electrical cardioversion

*Avoid digoxin*
Treatment of AP-Mediated Tachycardias

- **Chronic therapy:**
  - Class IC (flecainide)
    + AV nodal blocker

- ORT
- ART
- AF

*Avoid digoxin*
AVRT: Catheter ablation of accessory pathway
WPW Catheter Ablation
Left Lateral Accessory Pathway

Trans-septal sheath
His
Ab
CS

LAO

I.R. 08/11/06
WPW Catheter Ablation
Left Lateral Accessory Pathway

RF ON
AP GONE
## Catheter Ablation of Accessory Pathways

<table>
<thead>
<tr>
<th>AP Location</th>
<th>Success Rate (%)</th>
<th>Recurrence Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left free wall</td>
<td>&gt;95</td>
<td>2-5</td>
</tr>
<tr>
<td>Right free wall</td>
<td>85-90</td>
<td>10-15</td>
</tr>
<tr>
<td>Posteroseptal</td>
<td>93-98</td>
<td>3-6</td>
</tr>
<tr>
<td>Anteroseptal, midseptal</td>
<td>95-98</td>
<td>3-6</td>
</tr>
</tbody>
</table>

**Complication rate:** 1-4% (AV block ~1-3%, esp with septal APs)
Acute Treatment of PSVT

Regular SVT

Vagal maneuvers and/or IV adenosine (Class I)

If ineffective or not feasible

Hemodynamically stable

Yes

IV beta blockers, IV diltiazem, or IV verapamil (Class IIa)

If ineffective or not feasible

Synchronized cardioversion* (Class I)

No

Synchronized cardioversion* (Class I)

2015 ACC/AHA/HRS Guideline for the Management of Adult Patients with SVT
Heart Rhythm 2016 13, e136-e221DOI: (10.1016/j.hrthm.2015.09.019)
Etripamil

- Novel, L-type calcium channel antagonist with rapid metabolism
- Rapid onset of action
- Short-acting
- Administered as a nasal spray
- Being developed as a self-administered therapy to terminate PSVT outside of the emergency room or hospital.
Etripamil Nasal Spray for Rapid Conversion of Supraventricular Tachycardia to Sinus Rhythm

Bruce S. Stambler, MD, Paul Dorian, MD, Philip T. Sager, MD, Douglas Wight, MSc, Philippe Douville, PhD, Diane Potvin, MSc, Pirouz Shamszad, MD, Ronald J. Haberman, MD, Richard S. Kuk, MD, Dhanunjaya R. Lakireddy, MD, Jose M. Teixeira, MD, Kenneth C. Bilchick, MD, Roger S. Damle, MD, Robert C. Bernstein, MD, Wilson W. Lam, MD, Gearoid O’Neill, MD, Peter A. Noseworthy, MD, Kalpathi L. Venkatachalam, MD, Benoit Coutu, MD, Blandine Mondésert, MD, Francis Plat, MD
MULTI-CENTER, PLACEBO-CONTROLLED, DOUBLE-BLINDED, DOSE-RANGING PHASE II ELECTROPHYSIOLOGICAL STUDY OF INTRANASAL ADMINISTRATION OF ETRIPAMIL FOR THE CONVERSION OF INDUCED PSVT (NODE-1)

Clinicaltrial.gov ID: NCT02296190
ELIGIBILITY CRITERIA

• Subjects who met all of the following inclusion criteria were eligible to participate:
  – Male or female, aged $\geq$18 years;
  – History of PSVT;
  – Scheduled to undergo EP study and possible catheter ablation;
  – Provided written informed consent.
**Objectives:** Demonstrate superiority of intranasal etripamil over placebo in terminating SVT induced in the EP Lab and perform a dose ranging trend analysis.

- **Pre-ablation visit**
  - Double blind randomization
- **100 Patients with PSVT undergoing a planned ablation**
- **Study drug administration**
  - Placebo, n=20
  - Etripamil 35 mg, n=20
  - Etripamil 70 mg, n=20
  - Etripamil 105 mg, n=20
  - Etripamil 140 mg, n=20
- **Primary endpoint:** conversion within 15 min
  - >80% power to show a 50% absolute difference
  - (30% placebo & 80% etripamil conversion rates)
Primary Efficacy Endpoint

Conversion rate of PSVT#

*within 15 min of study drug administration  *p<0.05 vs placebo
## Primary Endpoint

<table>
<thead>
<tr>
<th>Study drug</th>
<th>Placebo</th>
<th>Etripamil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>0 mg</td>
<td>35 mg</td>
</tr>
<tr>
<td>Subjects converted at T15</td>
<td>7/20 35%</td>
<td>13/20 65%</td>
</tr>
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</table>

### Treatment comparisons (vs. placebo)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Etripamil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio</td>
<td>3.45</td>
<td>12.38</td>
</tr>
<tr>
<td>95% CI of odds ratio</td>
<td>(0.79, 15.46)</td>
<td>(2.28, 82.26)</td>
</tr>
<tr>
<td>Fisher's exact test p-value (vs placebo)</td>
<td>0.1128</td>
<td>0.0006</td>
</tr>
<tr>
<td>Cochran-Armitage test p-value (trend test)</td>
<td></td>
<td></td>
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</tbody>
</table>
Median time to conversion was 2-3 minutes.
## Adverse Events

### NASAL DISCOMFORT

- Placebo (N = 20): 1 (5.0)
- Etripamil 35 mg (N = 20): 12 (60.0)
- Etripamil 70 mg (N = 23): 11 (47.8)
- Etripamil 105 mg (N = 20): 7 (35.0)
- Etripamil 140 mg (N = 21): 8 (38.1)

### NASAL CONGESTION

- Placebo (N = 20): 0 (0.0)
- Etripamil 35 mg (N = 20): 5 (25.0)
- Etripamil 70 mg (N = 23): 6 (26.1)
- Etripamil 105 mg (N = 20): 9 (45.0)
- Etripamil 140 mg (N = 21): 8 (38.1)

### THROAT IRRITATION

- Placebo (N = 20): 2 (10.0)
- Etripamil 35 mg (N = 20): 9 (45.0)
- Etripamil 70 mg (N = 23): 8 (34.8)
- Etripamil 105 mg (N = 20): 7 (35.0)
- Etripamil 140 mg (N = 21): 4 (19.0)

### COUGH

- Placebo (N = 20): 0 (0.0)
- Etripamil 35 mg (N = 20): 0 (0.0)
- Etripamil 70 mg (N = 23): 4 (17.4)
- Etripamil 105 mg (N = 20): 3 (15.0)*
- Etripamil 140 mg (N = 21): 2 (9.5)

### Serious Adverse Event

* Severe cough occurred in one subject treated with etripamil 105 mg
Systolic Blood Pressure (SBP)

Mean Changes in SBP (mmHg)

- Placebo
- Etripamil 35 mg
- Etripamil 70 mg
- Etripamil 105 mg
- Etripamil 140 mg

Time since study drug administration (minutes)

T0 = subject in SVT

Comparison vs T0

*P < 0.05
**P < 0.01
***P < 0.001
• The NODE-1 study supports development of intranasal etripamil in a “real world” setting of patient self-administration to terminate PSVT.

• If successful, etripamil could provide a fast-acting nasal spray that can safely terminate acute PSVT without the need for an urgent care visit and could change the treatment paradigm for acute management of PSVT.
Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Efficacy, and Safety Study of Etripamil Nasal Spray for the Termination of *Spontaneous* Episodes of Paroxysmal Supraventricular Tachycardia

The NODE-301 Trial

ELIGIBILITY CRITERIA

- Subjects who meet all of the following inclusion criteria are eligible to participate:
  - Male or female, aged \( \geq 18 \) years;
  - ECG documented PSVT;
  - History suggestive of sustained episodes (lasting \( \sim 20 \) min or longer);
  - Signed written informed consent.