ABSTRACT

Purpose: The present study aimed to compare the demographic, medical history, clinical features, and treatment management of paroxysmal supraventricular tachycardia (PSVT) in the emergency department of a teaching hospital in Riyadh, Saudi Arabia. A secondary purpose was to evaluate Adenosine response among numerous variables that might be used as predictors of the conversion.

Methods: All PSVT cases presented to the Department of Emergency Medicine at King Khalid University Hospital, during the period from January 1, 2016, until December 31, 2016, were included in the study. Patients were assigned into two groups: adenosine sensitive (AS-group) and adenosine resistant (AR-group) according to adenosine conversion response.

Results: A total of 38 patients were admitted during the study period. Fisher’s exact test results showed that there were no significant (P > 0.05) differences among the AS-group and AR-group in the demographics, past medical history and clinical features, and post-ablation condition, except for the previous usage of the other anti-arrhythmic drugs to convert the last PSVT in the AR-group. The first bolus of adenosine had higher sensitivity and specificity, compared to the second bolus. Further, the second bolus of adenosine was not specific for short-term treatment of PSVT.

Conclusions: Differences in adenosine sensitivity among PSVT patients were independent of demographic, past medical history, and clinical features of PSVT patients. Thus, the difference in adenosine response among groups may be attributed to the heterozygosity in conducting pathways. The first bolus of adenosine had high sensitivity and specificity, compared to the second bolus, and their optimal levels were predictable by HR deceleration.

Key words: Adenosine; arrhythmia; receiver operating characteristic; sensitivity; specificity; supraventricular; tachycardia

Introduction

Paroxysmal supraventricular tachycardia (PSVT) is a common arrhythmia seen in emergency medical services. Its incidence rate is about 35 cases per 100,000 person-years, and peak incidence occurs in the middle age and occurs as twice as much in women than men.1-2 PSVT is characterized by regular tachycardia with sudden onset, abrupt termination, and a narrow QRS and P wave may not be identifiable on electrocardiogram.3 The mechanism for PSVT involves current reentry at the sinoatrial node, atrium, atrioventricular junction, and accessory pathways.
and also includes enhanced automaticity in the atrium or atrioventricular node.[4,16]

Adenosine is a unique agent for the short-term treatment of PVST. It is a nucleoside that slows down conduction through the atrioventricular node by activating the outward potassium current in the cell membrane. It has been reported that adenosine converts PSVT in 72%–90% of cases.[7‑10] Hence, it is recommended by the American Heart Association as the drug of choice.[10,11] However, repeated dose bolus of adenosine increases the chance of side effect and complication and may result in asystole.[12‑13] The controversial step arising regarding the efficacy and safety of the repeated third dose of Adenosine or to escalate it to 18 mg, or to switch earlier to the rate control medication e.g., (Diltiazem, Verapamil, Metoprolol).[4,14‑15] Another medical treatment of PVST has been reported with amiodarone, procainamide, flecainide, propafenone, propranolol, sotalol, and quinidine, either alone or in combination.[11,16‑17] There is a lack of data regarding the demographics, past medical history, clinical features, and Adenosine response in patients with PSVT in the Middle East region. Differential assessment of patients in whom the first bolus of adenosine was effective while patients in whom adenosine failed to convert PSVT should provide a clue to predict who might have high resistance to adenosine and benefit from other medications, hence avoiding the failed response and the associated side effect or complication of repeated doses. Furthermore, at present, there is no information to describe the demographics, clinical features, past medical history, and treatment modalities among different types of PSVT conversion.

Given the review presented above, the present study aimed primarily to describe and analyze the demographics, past medical history, clinical features, and short-term and long-term treatment modalities of PSVT in the patients in Riyadh city. A secondary purpose was to evaluate adenosine response, sensitivity, and specificity model, using heart rate (HR) as a predictor.

Materials and Methods

Study design

A retrospective design was conducted and then categorized into two groups of PSVT patients according to the adenosine response. Patients with Adenosine sensitive were designated as (AS-group) in whom PSVT was converted to normal sinus rhythm (NSR) following the injection the first or the second bolus of adenosine, with a dose of 6 mg and 12 mg according to advanced cardiac life support guideline. A second group whom the first (6mg) and the second bolus (12 mg) of Adenosine failed to convert the PSVT to NSR designated as the Adenosine resistant group (AR-group). Patients who aborted PSVT spontaneously, by vasovagal stimulation maneuver, cardioversion, or rate control medication were included in the descriptive parts but not in the Adenosine response analysis since they did not receive Adenosine.

Participants

All cases of PSVT presented to the Department of Emergency Medicine (DEM) at King Saud University Medical City (KSU-MC), from January to December 2016, triaged as category two to Resuscitation Area. The IRB Committee of KSU-MC approved the protocol of the present study.

Measurements

PSVT was diagnosed using international classification of diseases, tenth revision. Retrospectively reviewing the ED logbook in the resuscitation area, all patients presented as SVT or palpitation or arrhythmia listed. Then, the data retrieved throughout the patient name, file number, and the date of presentation to select the PSVT cases. A different person repeated the diagnosis confirmation and the analysis of the data to conduct a good data quality. several measures have been studied such as general demographics and the clinical characteristics and the management.

Adenosine dosages

The current practice following ACC/AHA/HRS 2015 Guideline for the Management of Adult Patients with SVT is a rapid administration of a 6 mg bolus given in one or 2 s through a large peripheral vein (mainly left antecubital vein) followed by a 20-mL saline flush and elevation of the arm. All efforts were made for rapid injection to minimize systemic cellular uptake. If the arrhythmia was not converted within 1 min, a second bolus of 12 mg was injected as described previously.[18‑20]

Statistical analysis

Descriptive analysis was generated to differentiate the frequency of occurrences among variables of interests. Fisher’s exact test was carried out to determine the difference in observed and expected frequencies among groups. The receiver operating characteristic (ROC) curve procedure was used to compare the efficacy of adenosine. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

Results

Descriptive findings

The descriptive clinical presentations, medical history, and care delivery measures are summarized in Table 1.
Table 1 revealed that there was an equal proportion of male and female patients. The mean age of patients was 40.9 ± 13.67.

We found that among circadian rhythm distribution (morning, afternoon, evening, and night), the afternoon time (12 pm to 5 pm) has the maximum number of PSVT visits, with 13 patients (34%), but it is not a statistically significant finding.

Regarding the clinical presentation, we found that all patients (100%) reported palpitation followed by dyspnea (36.8), chest pain (31.6%), and dizziness (26.3%) and less than 20% of them reported other symptoms such as syncope, Diaphoresis, and chest discomfort [Table 1]. From the past medical history, there were 25 patients (66%), have a previous episode of PSVT but only 7 patients (28%) of them did the ablation. In addition, the proportion of comorbidities, including HTN, diabetes, CRF, hypothyroidism, and hyperthyroidism, was <20%.

We found that the Vagal maneuver was only tried in 9 out of the 38 patients and 2 patients successfully converted to NSR without any pharmacological intervention. The remaining 36 patients who received a sequence of pharmacological treatment are summarized in Figure 1. The success percentage for conversion of the first and second dose of adenosine is 35% and 52%, respectively. The total number of patients received rate control drug is 12 patient and successfully convert 11 patients to NSR with success percentage of 91%. Among all the 38 patients, 19 patient (50% of PSVT) converted by the first or second dosage (AS-group) whereas in 8 patient (21%) were not converted even after of the second dosage (AR-group).

About the disposition, there were 29% of patients completely managed and discharged by the emergency physician [Table 1] whereas there were about 34% discharged by the cardiologist and 37% have been admitted.

The descriptive blood chemistry and hemodynamic measures are summarized in Table 2. All hemodynamic measures were within normal range, except HR. In addition, about 42% patients with PSVT blood were extracted for chemistry analysis and measures were also within normal range, except for blood glucose which considered a Borderline high level; however, the fasting state of patients was not reported.

Demographic, past medical history, and past medications
Chi-square test failed to show statistically significant ($P > 0.05$) differences between AS-group and AR-group groups.

Table 1: Participants characteristics, clinical presentations, medical history, and delivery

| Measures                        | Frequency (%) |
|---------------------------------|---------------|
| **Gender**                      |               |
| Male                            | 19 (50)       |
| Female                          | 19 (50)       |
| **Clinical presentations**      |               |
| Palpitation                     | 38 (100)      |
| Dizziness                       | 10 (26.3)     |
| Dyspnea                         | 14 (36.8)     |
| Chest discomfort                | 6 (15.8)      |
| Chest pain                      | 12 (31.6)     |
| Nausea                          | 2 (5.3)       |
| Syncope                         | 4 (10.5)      |
| Diaphoresis                     | 4 (10.5)      |
| Others                          | 9 (23.7)      |
| **Duration of symptom (h) ($n=33$)** |             |
| $\leq 2$                        | 12 (31.6)     |
| 2-4                             | 8 (21.1)      |
| 4-6                             | 3 (7.9)       |
| $>6$                            | 10 (26.3)     |
| **Past medical history**        |               |
| PSVT/(post-ablation)            | 25 (66%)/(7) (18%) |
| Arrhythmia (other than PSVT)    | 6 (15.8)      |
| Cardiac disease*                | 12 (31.6)     |
| Diabetes mellitus               | 7 (18.4)      |
| HTN                             | 7 (18.4)      |
| Hypothyroidism                  | 0 (0)         |
| Hyperthyroidism                 | 1 (2.6)       |
| Chronic renal failure           | 0 (0)         |
| Drug abuse                      | 1 (2.6)       |
| Smoking                         | 1 (2.6)       |
| **Past medications history**    |               |
| Rate control drugs (beta blocker or calcium channel blocker) | 16 (42.1) |
| Other antiarrhythmic drugs      | 2 (5.3)       |
| Other antihypertensive drugs    | 2 (5.3)       |
| Carbamazepine                   | 0 (0)         |
| Others                          | 7 (18.4)      |
| **Disposition**                 |               |
| Discharged by emergency physicians | 11 (29)     |
| Referred to cardiologist and discharged | 13 (34) |
| Admitted                        | 14 (37)       |
| **Time of presentation**        |               |
| Morning (5 am to 11:59 am)      | 7 (18)        |
| Afternoon (12 pm to 4:59 pm)    | 13 (34.1)     |
| Evening (5 pm to 8:59 pm)       | 6 (15.7)      |
| Night (9 pm to 4:59 am)         | 11 (29)       |

*Ischemic heart disease, heart failure, structural heart disease. PSVT: Paroxysmal supraventricular tachycardia, HTN: Hypertension
in the baseline characteristics, including age, gender, and the comorbidities. Furthermore, the results of independent t-test showed that there were no significant (\( P > 0.05 \)) differences between AS-group and AR-group with regard to age and hemodynamic variables that included HR, mean arterial blood pressure (MAP), and systolic blood pressure. AR-group had higher mean glucose level compared to AS-group (\( P = 0.001 \)). However, in addition, there was also a significant statistical difference between the two groups in terms of hemoglobin level (\( P = 0.03 \)). There were no significant (\( P > 0.05 \)) differences between the two group in the vital sign and blood laboratory investigations including as white cell count, potassium, and Troponin. also, there were no statistically significant differences between both groups regarding the ablation therapy.

There were no significant differences (\( P > 0.05 \)) between AS-group and AR-group, with regard to the adenosine or vagal stimulation maneuver, or cardioversions were used to convert the previous PSVT, Fisher’s exact test also shown that there were about 63% of the patients in AR-group in whom other antiarrhythmic drugs (other than adenosine or rate control medication such as amiodarone, procainamide, or flecainide) have been used to convert their past PSVT after unsuccessful adenosine, and this finding is significant statistical finding as \( P = 0.001 \).

**Clinical presentation of the current paroxysmal supraventricular tachycardia**

There was no difference between the two groups in terms of the type of symptoms and symptoms duration. Even with a percentage of 50% of patients in AR-group reported for more than 6 h, as compared with 22.2% in AS-group but the difference was not statistically significant (\( P > 0.05 \)).

**Sensitivity and specificity analysis for adenosine**

The efficacy of adenosine in the adenosine-sensitive group was conducted using ROC curve [Figure 2a and b]. Besides larger area under the ROC curve (73%) for the first bolus of Adenosine, an optimal level of sensitivity of 68% was associated with the optimal level of specificity (75%); (1–0.25 = 0.75) in panel A. Whereas in panel B of [Figure 2] revealed a small area of 0.167 under the curve, which implied poor characteristics, associated with 58% sensitivity and less than 20% specificity for the second bolus of the Adenosine. Thus, the second bolus of adenosine is not specific for the short-term treatment of PSVT, regardless of 68% sensitivity. Fundamentally, poor specificity indicated more chance for more specific drugs, as compared to the second bolus of adenosine.

Based on the ROC curve, the corresponding critical target HR, before the first bolus of Adenosine, was found to be at 176 bpm [Table 3]. These findings indicate an important clinical application that may help the clinicians to decide whether to give the second bolus of adenosine or to switch to other antiarrhythmic drugs. That is if the first bolus of adenosine failed to convert PSVT of a rate of 176 or below, there is no need to use a second or third bolus and a decision for switching to another antiarrhythmic or rate control drug should be recommended.

**Type of medication on discharge**

As shown in Table 4, all of the AR-group cases were discharged on antiarrhythmic drugs whereas only 52% of AS-group discharged on antiarrhythmic drugs (rate control drugs) with a significant result (\( P < 0.05 \)).

**Discussion**

The findings of the present study showed that there were no major differences between AS-group and AR-group in the demographic factors, age, past medical history, current medications used by the patient, types of symptoms, and symptoms duration. In a large population study, it was reported that patients with PSVT fall into two distinct clinical subsets: those with other CVD and those without CVD.[21] Patients with PSVT, without heart diseases, are more likely to be females, to be younger, to have had an earlier onset of symptoms, and have faster PSVT rates.[22–24] Our findings clarify that the characteristics of patients in both groups of PSVT patients are the middle age with an equal proportion of male and female, the majority of which had a previous PSVT episode, but without chronic cardiac diseases such as Ischemic heart disease, heart failure, and structural heart disease. Thus, both AS-group and AR-group in our study might be classified as homogeneous PSVT groups, with heterogeneous etiology for PSVT because of lack of

| Table 2: Blood chemistry and hemodynamics measures of patients |
|----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                | Age    | HR     | SBP    | MAP    | Temperature | Glucose | WBC    | Hb      | K      | Na     | Troponin |
| n              | 38     | 38     | 38     | 38     | 35           | 15      | 16     | 17      | 16     | 16     | 4        |
| Mean           | 40.92  | 184.82 | 120.00 | 90.91  | 36.83        | 7.97    | 9.59   | 13.17   | 4.15   | 137.00 | 0.08     |
| SEM            | 2.657  | 4.980  | 3.595  | 3.013  | 0.069        | 1.324   | 0.599  | 8.956   | 0.103  | 0.926  | 0.025    |
| SD             | 16.376 | 30.701 | 22.163 | 18.576 | 0.406        | 5.129   | 2.397  | 36.929  | 0.412  | 3.706  | 0.049    |

SD: Standard deviation; SEM: Standard error of mean; HR: Heart rate; SBP: Systolic blood pressure; MAP: Mean arterial pressure; WBC: White cell count; Hb: Hemoglobin
Table 3: Coordinate of the receiver operating characteristic curve using heart rate as the test results measure for sensitivity and specificity

| Positive if greater than or equal to (HR) | Sensitivity | 1 - Specificity |
|----------------------------------------|------------|----------------|
| 127                                    | 1          | 1              |
| 141                                    | 0.889      | 1              |
| 156                                    | 0.889      | 0.875          |
| 164                                    | 0.889      | 0.750          |
| 170                                    | 0.778      | 0.750          |
| 171                                    | 0.778      | 0.625          |
| 176                                    | 0.667*     | 0.25*          |
| 181                                    | 0.556      | 0.250          |
| 183                                    | 0.556      | 0.125          |
| 192                                    | 0.556      | 0              |
| 206                                    | 0.333      | 0              |
| 217                                    | 0.222      | 0              |
| 228                                    | 0.111      | 0              |
| 234                                    | 0.000      | 0              |

*Critical value for adenosine first bolus at sensitivity of 68% and specificity of 75%.
HR: Heart rate

In general, two major types of PSVT are classified owing to a site of origin: the first originates from sinoatrial and the second comes from the atria. As previously noted from electrophysiological and surgical studies, the presence of one or more accessory atrioventricular pathways exists near the AV node create special channel with lower refractory period or bypass tract that allows the electrical impulse to enters this pathway and starts traveling in a circular pattern without resistant and therefore stimulates the ventricles to beat rapidly and regularly.

Adenosine slows down conduction, through the atrioventricular node, by activating the outward potassium current in the cells of the atrium, sinus, and atrioventricular nodes. The inability of Adenosine to convert the PSVT in the AR-group might be attributed the possibility of PJRT as the electrophysiological mechanism which is considered as one of the causes of refractory PSVT. Medical treatment with amiodarone, procainamide, flecainide, propafenone, propranolol, sotalol, quinidine, and verapamil had been reported. We believe that electrophysiological studies with radiofrequency ablation should be considered in patients of suitable age on the appearance of symptoms related to PSVT.

Regarding PSVT circadian pattern occurrence, we found that among circadian rhythm distribution, the afternoon time (12 pm to 5 pm) has the maximum number of PSVT visit in the emergency room, 13 patient, 34%, and despite the consistency with previous study but it is not statistically significant finding in our study.

Although there was no difference between the two groups in the comorbidity including DM we found from the blood chemistry measures that hyperglycemia and anemia were associated with AR-group. Because the majority of cases in our study managed without laboratory investigation we cannot attribute the association to the Adrenergic effect.
leading to hyperglycemia with high metabolism rate that interferes with Adenosine action or even the Arrhythmogenic effect of anemia until larger prospective study conducted.

From the previous history of management for the last PSVT episode, we found that 63% of the patients in AR-group has been given other Antiarrhythmic drugs, such as amiodarone, procainamide or flecainide, to convert their previous PSVT episode as a third line management after the adenosine and rate control medication. therefore we highly recommend reviewing the management of the previous PSVT episode to predict the Adenosine response and to guide the management of the current episode. These findings support the heterogeneity in the pathogenesis of PSVT and can be used as a predictor for adenosine effect.

The findings of the present study assessed the responses to adenosine using ROCs analysis. ROC model allowed enables us to predict an optimal efficacy of the first bolus of adenosine that corresponded to the optimal sensitivity and specificity. Based on the coordinate of the ROC curve, we were able to predict, the corresponding critical target HR, before the first bolus of adenosine to be 176 bpm, for this specific age group. These findings have an important clinical application that may help clinicians decide whether to give the second bolus of adenosine or to switch to other antiarrhythmic drugs. In other words, if the first bolus of adenosine did not convert HR of 176 or below, it would not be necessary to use the second, nor the third bolus adenosine and a decision should be made for switching to another antiarrhythmic or rate control drugs. This is the first report that described the efficacy of adenosine using ROC for adenosine, using HR as a predictor. These findings have an important predictor value for adenosine sensitivity, using which response must occur within few seconds to accomplish a target HR of 176 bpm in PSVT patients. Although the model was not done before, previously reported works that described the association between HR and PSVT conversion supported it. However, our ROC model remains delimited to the group being studied and cannot be generalized, until larger population-based with more representative sample conducted.

From the discharge medication, we found all AR-group cases discharged on antiarrhythmic drugs whereas only 52% of AS-group discharged on rate control drugs (rate control drugs) with a significant difference. Although it was an expected finding, it raises questions regarding the association between the adenosine response, the recurrence rate, and the indication of antiarrhythmic drugs to prevent the recurrence of the PSVT episode that can be answered by larger prospective studies.

### Study limitations and recommendations

There were several limitations of this study:

1. The sample for this study was limited to the Emergency Medicine DEM at KSU-MC, Saudi Arabia. Therefore, further research is highly recommended to be obtained to cover different hospitals and regions
2. The sample size was limited. Thus, further research is highly recommended to be obtained considering increasing sample size
3. The study sample was selected from the patients with PSVT presented to (KKUH DEM) at King Khalid University Hospital (KKUH), during the period of January 1, 2016 to December 31, 2016
4. The findings of this study were not generalizable to the entire Saudi Arabian PSVT population.

### Conclusions

Differences in adenosine sensitivity among PSVT patients were independent of demographic, past medical history, and clinical features of PSVT patients. Thus, the difference in response to adenosine among groups was attributed to the presence of heterogeneous conducting pathways. The first bolus of adenosine had high sensitivity and specificity, compared to the second bolus, and their optimal levels were predicted at HR of 176 bpm.

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Conflicts of interest
There are no conflicts of interest.

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