STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Comparison of Single-Syringe vs. Double-Syringe Techniques for Adenosine Administration in Paroxysmal Supraventricular Tachycardia: A Randomized Controlled Trial

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Sponsor	Hormozgan University of Medical Sciences
Principal investigator	Farima Roshanasan
Study site	Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
Ethics approval	IR.HUMS.REC.1403.152
Study design	Single-center, open-label, parallel-group randomized controlled trial

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1. Administrative information

Official study title	Comparison of Single-Syringe vs. Double-Syringe Techniques for Adenosine Administration in Paroxysmal Supraventricular Tachycardia: A Randomized Controlled Trial
Brief title	Comparison of Single-syringe vs. Double-syringe Techniques for Adenosine Administration in PSVT
Unique protocol ID	PSVT management techniques
Registry	ClinicalTrials.gov
Registration number	NCT07554170
Registration status	Retrospectively registered and first posted in April 2026
Sponsor	Hormozgan University of Medical Sciences
Study site	Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
Principal investigator	Farima Roshanasan
Protocol date/version	August 2026/Version 1.0
Funding	No external funding

2. Background and rationale

Paroxysmal supraventricular tachycardia (PSVT) is a regular narrow-complex tachyarrhythmia that commonly presents to emergency departments and may cause palpitations, chest discomfort, dyspnea, dizziness, or presyncope. In hemodynamically stable patients who do not respond to vagal maneuvers, intravenous adenosine is a first-line pharmacological treatment because of its rapid onset and very short half-life.

The conventional double-syringe technique (DST) administers adenosine as a rapid intravenous bolus followed immediately by a rapid normal-saline flush from a second syringe. The single-syringe technique (SST) combines adenosine and normal saline in one syringe, potentially simplifying administration and improving drug delivery in the emergency setting. This trial compared the efficacy and safety of SST with DST for terminating PSVT.

3. Objectives and hypotheses

3.1 Primary objective

To compare the first-dose PSVT termination rate between adenosine administered using SST and DST.

3.2 Secondary objective

To compare the cumulative adenosine dose required to achieve successful PSVT termination between the two groups.

3.3 Exploratory objectives

Additional exploratory analyses included overall PSVT termination, time to treatment response, adverse events, and post-treatment hemodynamic parameters. These variables were collected during the study but were not registered as primary or secondary outcomes in the initial ClinicalTrials.gov record; accordingly, they are reported as exploratory outcomes.

3.4 Hypothesis

The study was initially designed to evaluate whether the single-syringe technique was non-inferior to the double-syringe technique. However, the final analysis did not use a prespecified non-inferiority margin and was conducted as a between-group comparative analysis. Accordingly, the final analyses evaluated differences between SST and DST in first-dose PSVT termination and cumulative adenosine dose.

4. Study design and setting

This was a single-center, open-label, parallel-group randomized controlled trial conducted in the emergency department of Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Eligible participants were allocated in a 1:1 ratio to SST or DST.

Recruitment start date	21 May 2024
Recruitment end date	21 December 2025
Primary completion date	21 December 2025
Study completion date	21 December 2025
Planned enrollment	134
Actual randomized enrollment	134

5. Participants

5.1 Inclusion criteria

- Age 18–80 years.
- Presentation to the emergency department between May 2024 and December 2025.
- PSVT requiring adenosine administration after failure of two Valsalva maneuvers lasting 15–30 seconds each.
- PSVT was defined as a narrow-QRS tachyarrhythmia with a heart rate ≥150 beats/min and absent or retrograde P waves on ECG.

5.2 Exclusion criteria

- Wide QRS complex with an irregular R-R interval on ECG
- Known allergy to adenosine.
- Recent ingestion of dipyridamole, carbamazepine, or theophylline.
- Caffeine ingestion within the previous 2 hours.
- Acute asthma attack.
- Previous heart transplantation.
- Systolic blood pressure <90 mmHg.

- Previous inclusion in the trial with a second episode of re-entry tachycardia occurring less than 4 hours after the first episode.
- Clinically too unstable to give consent.

6. Recruitment and informed consent

Potential participants were screened in the emergency department. Eligible patients received an explanation of the study and provided written informed consent before enrollment and randomization. Standard initial care included measurement of vital signs, continuous ECG monitoring, establishment of intravenous access in an antecubital vein, and laboratory testing as clinically indicated. The diagnosis of PSVT was confirmed by an emergency medicine specialist and an emergency medicine resident.

7. Randomization, allocation concealment, and blinding

7.1 Sequence generation

Participants were randomized in a 1:1 ratio using a computer-generated allocation sequence.

7.2 Allocation concealment

Allocation was concealed using sealed opaque envelopes prepared according to the randomization sequence.

7.3 Blinding

Because the two adenosine administration techniques were visibly different, investigator blinding, although initially intended, could not be reliably maintained during study conduct. Participants, nurses, treating clinicians, and investigators involved in treatment assessment could therefore become aware of group allocation. The primary outcome was determined objectively based on electrocardiographic evidence of rhythm conversion, reducing the likelihood of assessment bias. Accordingly, the masking classification in the ClinicalTrials.gov PRS record was revised from “Single (Investigator)” to “None (Open Label)” to more accurately reflect the conduct of the trial.

8. Interventions

8.1 Single-syringe technique group

A single syringe containing 6 mg of adenosine (2 mL) diluted with 18 mL of normal saline to a total volume of 20 mL was administered rapidly. If PSVT persisted, a second dose containing 12 mg of adenosine (4 mL) diluted with 16 mL of normal saline to the same total volume of 20 mL was administered; a third 12-mg dose could be administered in the same manner if needed.

8.2 Double-syringe technique group

Adenosine was administered as a rapid intravenous bolus (6 mg) followed immediately by a 20-mL normal-saline flush using a second syringe. If PSVT persisted, a second 12-mg dose was given in the same manner; a third 12-mg dose could be administered if needed.

8.3 Concomitant and prohibited therapies

Before study treatment, patients received standard emergency care. Drugs known to interact with adenosine and recent caffeine use were addressed through the exclusion criteria. Other acute therapies were permitted only as rescue treatment after failure of the study adenosine regimen.

9. Management of treatment failure and monitoring

Patients who did not respond to the maximum adenosine regimen were managed according to the treating physician’s clinical judgment, including other pharmacologic therapy (e.g., a non-dihydropyridine calcium-channel blocker) or synchronized electrical cardioversion, when clinically indicated.

After adenosine administration, all participants were monitored for adverse events, including hypotension, dyspnea, flushing, bradycardia, and chest pain. Vital signs and clinical status were assessed every 15 minutes for 30–60 minutes after administration.

10. Outcome measures

10.1 Primary outcome

The primary outcome in the ClinicalTrials.gov record was defined as successful PSVT termination within 3 minutes after the first 6-mg adenosine dose, with restoration of sinus rhythm and a heart rate <140 beats/min. During study conduct, treatment response was assessed using ECG-confirmed conversion to sinus rhythm within 2 minutes after the first 6-mg dose, which was the definition used for the final analysis and manuscript. The ClinicalTrials.gov record was subsequently updated to reflect the outcome definition actually used in the study.

10.2 Secondary outcome

Total cumulative adenosine dose: the cumulative dose of adenosine required to achieve successful PSVT termination.

10.3 Exploratory outcomes

- Overall PSVT termination rate.
- Treatment response time.
- Adverse events, including hypotension, bradycardia, dyspnea, flushing, and chest pain.
- Post-treatment hemodynamic parameters.

10.4 Safety definitions

Hypotension was defined as systolic blood pressure <90 mmHg, and bradycardia as heart rate <60 beats/min. Dyspnea, flushing, and chest pain were recorded based on patient-reported symptoms during the post-administration observation period.

11. Data collection and management

Data were collected using a standardized case-report form and included demographic characteristics, medical history, home medications, baseline vital signs, ECG findings, intravenous-access characteristics, treatment details, treatment-response time, post-treatment vital signs, adverse events, rescue therapy, and disposition. Data were reviewed for completeness and consistency before statistical analysis.

12. Sample size

The sample size was determined a priori for comparison of first-dose PSVT termination between the two treatment groups using a one-sided significance level of 0.05 and a statistical power of 80%. During the predefined study period, 134 eligible patients were enrolled, randomized, and all randomized participants were included in the intention-to-treat (ITT) analysis.

13. Statistical analysis plan

13.1 Analysis populations

Efficacy and safety outcomes were analyzed according to the ITT principle, with participants analyzed according to their randomized group. Time to treatment response was analyzed only among patients who achieved successful PSVT termination.

13.2 Descriptive analysis

Continuous variables were summarized as mean ± standard deviation when approximately normally distributed and as median with interquartile range when non-normally distributed. Categorical variables were summarized as number and percentage. Distributional assumptions were assessed using the Shapiro–Wilk test.

13.3 Baseline comparisons

Continuous baseline variables were compared using an independent-samples t test when normally distributed and the Mann–Whitney U test when non-normally distributed. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

13.4 Primary outcome analysis

The primary outcome (first-dose PSVT termination) was compared between the two treatment groups using Fisher's exact test. The treatment effect was reported as an odds ratio (OR) with a corresponding 95% confidence interval (CI).

13.5 Secondary and exploratory analyses

- Cumulative adenosine dose was compared using an independent-samples t-test.
- Overall termination rates and individual adverse events were compared using chi-square or Fisher's exact tests.
- Time to treatment response was compared using an independent-samples t test among participants who achieved successful PSVT termination.
- Post-treatment hemodynamic parameters were compared between groups using an independent-samples t test.

13.6 Missing data

No missing outcome data occurred during the study. Therefore, no imputation or other missing-data handling procedure was required. No specific imputation method had been prespecified.

13.7 Multiplicity, interim analysis, and software

The primary and secondary outcomes were defined separately, while additional outcomes were considered exploratory. No adjustment for multiple comparisons was planned or performed. No interim analysis was planned or performed. Statistical significance was defined as a two-sided $P<0.05$. Analyses were performed using IBM SPSS Statistics version 26 and R software version 4.5.1.

14. Safety reporting

Adverse events were systematically assessed in all participants during the 30–60-minute observation period following adenosine administration. Recorded adverse events included hypotension, bradycardia, dyspnea, flushing, and chest pain. Hypotension was defined as systolic blood pressure <90 mmHg and bradycardia as heart rate <60 beats/min, whereas dyspnea, flushing, and chest pain were recorded based on patient-reported symptoms. Adverse events were summarized by randomized group as the number and percentage of participants experiencing each event and any adverse event.

15. Ethical considerations

The study was approved by the Ethics Committee of Hormozgan University of Medical Sciences and the participating hospital (approval code IR.HUMS.REC.1403.152) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment. Participant confidentiality was protected through coded identifiers and restricted access to study data. The trial was retrospectively registered at ClinicalTrials.gov (NCT07554170) and first posted in April 2026.

16. Dissemination and protocol amendments

The study findings are intended for dissemination through peer-reviewed publication. Study results will also be submitted to ClinicalTrials.gov. Clarifications and corrections identified after completion of the study were documented and incorporated into the updated ClinicalTrials.gov PRS record. These updates were made to accurately reflect the conduct and reporting of the trial. Any substantive differences from the original protocol or initial ClinicalTrials.gov record are described in the relevant sections of this document.

Appendix A. Summary of Corrections and Clarifications to the ClinicalTrials.gov PRS Record

The following revisions were made to the ClinicalTrials.gov Protocol Registration and Results System (PRS) record to correct data-entry and terminology errors, complete missing administrative information, and align the record with the actual conduct of the trial and the final manuscript. These revisions document post-completion corrections and clarifications to the PRS record and do not represent prospective modifications to the conduct of the completed trial.

PRS Section	Current public entry	Corrected PRS Entry pending release	Rationale for revision	Effect on study conduct
Official title	Comparison of Single-syringe vs. Double-syringe Techniques for Adenosine Administration in Supraventricular Tachycardia: A Randomized Clinical Trial	Comparison of Single-Syringe vs. Double-Syringe Techniques for Adenosine Administration in Paroxysmal Supraventricular Tachycardia: A Randomized Controlled Trial	The title was revised to specify paroxysmal supraventricular tachycardia (PSVT) as the target arrhythmia and to describe the randomized controlled trial design more precisely. Minor formatting and capitalization inconsistencies were also corrected.	None; editorial clarification only
Unique Protocol ID	SVT management techniques	PSVT management techniques	Terminology was revised from SVT to PSVT to more accurately specify the target arrhythmia and to maintain consistent terminology	None; editorial clarification only

			throughout the study record.	
Study Description	“stable supraventricular tachycardia (SVT)” / “regular narrow complex SVT”	“paroxysmal supraventricular tachycardia (PSVT)” / “regular narrow-complex PSVT”	Terminology was revised from SVT to PSVT to more accurately specify the target arrhythmia and to maintain consistency with the revised study title and manuscript.	None; terminology clarification only
Study Description – Study objective	“The study aims to determine if the SST method is non-inferior to the DST method.”	“The study aims to compare the efficacy of SST and DST for PSVT termination.”	The initial PRS record described the study objective as non-inferiority. However, the final analysis did not use a prespecified non-inferiority margin and was conducted as a between-group comparative analysis. The wording was therefore revised to accurately reflect the analytical approach used in the study.	None; this correction reflects the actual analytical framework and does not represent a change in study procedures or collected outcomes.
Eligibility criteria	Exclusion criteria included wide QRS complex with an irregular R-R interval,	Exclusion criteria were: (1) wide QRS complex with an irregular R-R interval	The initial PRS entry did not fully reflect the eligibility criteria	None; this revision documents the eligibility criteria applied during the

	known allergy to adenosine, recent ingestion of dipyridamole, carbamazepine, or theophylline, caffeine ingestion within the previous 2 hours, clinical instability precluding informed consent, and systolic blood pressure <90 mmHg.	on ECG; (2) known allergy to adenosine; (3) recent ingestion of dipyridamole, carbamazepine, or theophylline; (4) caffeine ingestion within the previous 2 hours; (5) acute asthma attack; (6) previous heart transplantation; (7) systolic blood pressure <90 mmHg; and (8) previous inclusion in the trial with a recurrent episode of re-entry tachycardia occurring <4 hours after the first episode.	applied during the study. The entry was revised to accurately document the exclusion criteria used for participant selection during the trial and reported in the final manuscript.	study and does not represent a post hoc change in participant selection.
Masking	Single(investigator) masking	None (open-label)	The PRS record initially classified the study as “Single (Investigator).” During study conduct, participants, treating personnel, investigators, and outcome assessors were aware of treatment allocation. The masking classification	None; this correction reflects the actual conduct of the trial and did not alter study procedures.

			was therefore corrected to "None (Open Label)" to accurately reflect the conduct of the trial.	
Actual enrollment	131 participants	134 participants	The previously entered enrollment value of 131 did not reflect the final randomized sample. The enrollment value was updated to 134 participants based on the final study database and participant flow records.	None; no change in recruitment or participant inclusion
Study location	Duplicate location entries	One study location	A duplicate entry for the same study site was removed. The trial was conducted at a single center.	None; administrative correction only
Arms and Interventions	The 12-mg second and third adenosine doses were described as being mixed with 18 mL of normal saline.	The initial 6-mg dose was diluted with 18 mL of normal saline to a total volume of 20 mL. The second and third 12-mg doses were each diluted with 16 mL of normal saline to the	The previously entered volume of 18 mL of normal saline for the 12-mg doses did not reflect the preparation used during the trial. The 12-mg dose (4 mL of	None. This correction reflects the intervention as actually administered and does not represent a change in the study procedure.

		same total volume of 20 mL.	adenosine) was administered with 16 mL of normal saline, resulting in a total syringe volume of 20 mL.	
Outcome measures	The primary outcome was described as first-dose successful termination of SVT to normal sinus rhythm with a heart rate <140 within 3 minutes. The secondary outcome was listed as total administered dose.	The primary outcome was revised to first-dose PSVT termination, defined as ECG-confirmed conversion to sinus rhythm within 2 minutes after the initial adenosine dose. The secondary outcome was clarified as the total cumulative adenosine dose required for successful PSVT termination.	The initial PRS record defined the primary outcome using a 3-minute assessment window. The revised entry reflects the ECG-confirmed 2-minute assessment window used during study conduct and in the final analysis. The secondary outcome terminology was also clarified to specify the cumulative adenosine dose required for successful PSVT termination.	None; the corrections reflect the outcomes and assessment procedures actually used during the study and do not represent retrospective changes in data collection or study procedures.
Record verification date	April 2026	August 2026	The verification date was updated after reviewing the	None

			study record and confirming that the revised information was accurate and current.	

PRS: Protocol Registration and Results System. The revisions listed above document corrections and clarifications to the registered information after completion of the trial and are intended to accurately reflect the study as conducted and analyzed. They do not represent changes made to participant management or study procedures after completion of the trial.