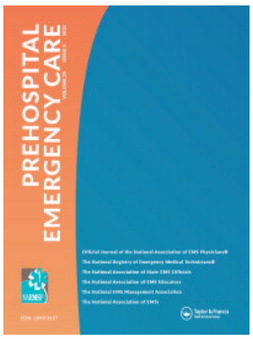

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Comparing Prehospital Adenosine Initial Dosing of 6 mg Versus 12 mg for Presumed Paroxysmal Supraventricular Tachycardia (PSVT)

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ABSTRACT

Objectives: Adenosine is a common prehospital treatment for paroxysmal supraventricular tachycardia (PSVT); however initial dosing varies and the optimal first dose is unknown. To evaluate the association of the two common initial adenosine dosing regimens (6 mg and 12 mg) with prehospital patient improvement, hospital admission, complications, and death.

Methods: This retrospective observational study included all 9-1-1 responses with prehospital adenosine administration between 1/1/2022 and 12/31/2022 from the ESO Data Collaborative. Outcomes included EMS clinician documented patient response (improved v. unchanged/worse) to the initial dose, emergency department (ED) dispositions, compressions/cardioversion/pacing after adenosine administration, and death. Descriptive statistics and adjusted odds ratios (OR) were used to compare outcomes for patients who received an initial adenosine dose of 6 mg versus 12 mg.

Results: We analyzed 11,245 patients that received adenosine from 1,350 EMS agencies. Most received an initial dose of 6 mg (70%, $n=7,825$), while 30% (n = 3,314) received an initial dose of 12 mg. Initial pulse rate and systolic blood pressure were similar between groups. Nearly half in the 6 mg group (48%, $n=3,746$) received additional doses, compared to 25% ($n=815$) in the 12 mg group. An initial dose of 12 mg was associated with 65% increased odds of prehospital improvement (OR: 1.65, 95%CI: 1.49–1.82). Complications including cardioversion (5%, $n=481$), pacing (<1%, $n=2$), and cardiopulmonary resuscitation (CPR) (<1%, $n=20$) were rare. There was no difference in the need for cardioversion, pacing, or CPR between groups ($p>0.05$). Amongst EMS transported patients, 25% (n = 2,732) had available ED dispositions. An initial dose of 12 mg was associated with a 28% reduction in odds of admission (OR: 0.72, 95%CI: 0.59–0.87). In total, 2% (n = 48) who received prehospital adenosine and had available outcome data died. Of those, 70% (n = 32) were in the 6 mg group and 30% (n = 14) were in the 12 mg group.

Conclusions: An initial prehospital adenosine dose of 12 mg was associated with less re-dosing, greater rates of patient improvement, and lower rates of hospital admission compared to an initial dose of 6 mg. Complications requiring interventions and death were rare and similar across dosing regimens.

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Introduction

Cardiac related conditions comprise approximately 13% of all requests for Emergency Medical Services (EMS) in the United States (U.S.) (1) and there are approximately 89,000 new cases of paroxysmal supraventricular tachycardia (PSVT) annually (2). Adenosine has been described as a therapy for PSVT in the U.S. since 1990 (3) when it was approved by the FDA (4); studies describing its use in the emergency department (ED) began in 1991 (5) and in the prehospital setting in 1992 (6). Adenosine has been has been the recommended medication in the American Heart Association (AHA) Guidelines for PSVT since 1992 (7). Although the Guidelines have recommended an initial adult dose of 6 mg followed by 12 mg, supporting evidence appears limited. The initial 1990 Food and Drug Administration (FDA) approval recommended an initial dose of 6 mg (4). A 1990 study documented a 57.4% conversion rate using an initial dose of 6 mg and a 93.4% conversion using one 6 mg dose followed by a single 12 mg dose if necessary (3). A 1999 cost efficiency study reported a 65% conversion rate for an initial 6 mg dose but concluded that additional conversions that could be achieved at 12 mg were not worth the additional cost; they recommended 6 mg as the most cost effective dose of adenosine (8). In 1996 Brady et al., did the first similar analysis for the prehospital setting with comparable results: 36% conversion for 6 mg dose, and 63% conversion for 6 or

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6 + 12 mg doses. Many other prehospital studies have documented adenosine overall conversion rates between 68% and 89% (6,9–14), but none studied the impact of specific dose ranges. Morrison et al., did the first prehospital dosage comparison study between 6 mg and 12 mg initial doses in a small before/after study and found a 33% conversion rate at 6 mg and 46% at 12 mg (15). A more recent, randomized controlled study demonstrated a 70% conversion rate for 6 mg and an additional 8% conversion following 12 mg. They also found that prehospital administration of adenosine shortened time to ED discharge from nearly 4 h to about 2 h compared to patients who received their first dose of adenosine in the ED (16). No studies have explored more long-term outcomes such as mortality or hospital admission.

Paroxysmal supraventricular tachycardia is not benign. Beyond commonly causing patient discomfort, palpitations, chest pain, dyspnea, syncope and sweating (17), PSVT is associated with hemodynamic instability, ischemic stroke (18), and sudden cardiac death (19,20). Imprecise initial dosing may fail to convert PSVT to sinus rhythm, increasing the risk of complications. Delays in conversion may also necessitate synchronized cardioversion which carries serious risks including pain, thromboembolic events, dysrhythmias, heart failure, complete heart block and cardiac arrest (21,22). Evidence-based dosage guidelines for adenosine could improve patient safety and comfort by increasing the likelihood of rapid conversion while minimizing complications. To date, no large-scale studies have compared the conversion success rate and patient outcomes associated with adenosine dosing strategies for treatment of PSVT.

This study evaluated the association of the two common EMS adenosine dosing regimens (6 mg and 12 mg) with prehospital patient improvement, hospital admission, complications, and death.

Methods

Study Design and Setting

We conducted a retrospective analysis of prehospital patient care records from January 1, 2022 to December 31, 2022. Data were obtained from the ESO Data Collaborative public use dataset. The institutional review board at St. David's HealthCare determined that this study was exempt.

The ESO Data Collaborative consists of data from EMS agencies, fire departments, and hospitals that have agreed to allow use of their de-identified records for research purposes. ESO is one of the largest EMS electronic health record (EHR) clinicians in the U.S. (23). The EHR software facilitates the collection of prehospital dispatch information, patient demographics, clinical presentation and course, interventions, treatments, and outcomes at transfer of care. Emergency Medical Services personnel are responsible for all data entered into the EHR. The software's data variables and values are standardized across EMS agencies and follow the National Emergency Medical Services Information System (NEMSIS) data standard (24). Additionally, EMS agencies may use the ESO health data exchange (HDE) software product to directly receive hospital outcomes including disposition and diagnosis that are then linked to the patient's prehospital EHR.

Selection of Participants

We evaluated records for all emergency (9-1-1) EMS responses with documented prehospital administration of adenosine. Interfacility transfers and records missing the dose of adenosine were excluded.

Measures

Patient outcomes following prehospital adenosine administration included EMS clinician reported patient response to the initial dose (improved vs unchanged/worse), transport disposition, ED disposition, hospital disposition, and mortality.

Indication for adenosine administration was assessed using the EMS clinician primary impression data field. Indications were collapsed into three categories: cardiopulmonary, injury, or other. (Supplemental File Table 1) Total adenosine dose during the EMS encounter was reported as a total dose in milligrams (mg).

The patient's response to the medication was documented by the EMS clinician as improved, unchanged, or worse, as required by the NEMSIS data standard (25,26). Complications evaluated included cardioversion, pacing, or cardiopulmonary resuscitation (CPR) following adenosine administration. Patient transport disposition was categorized as transported by EMS, released on scene (both against medical advice (AMA) and per protocol), or dead on-scene.

Emergency department dispositions were collapsed into four categories: admitted, discharged/AMA, died in the ED, or transferred to another facility. For admitted patients, in

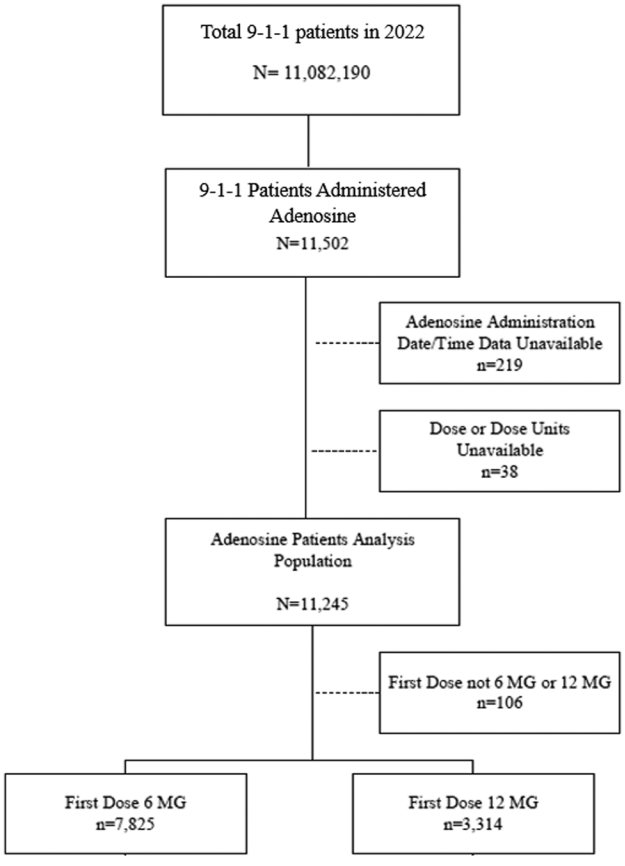

Figure 1. Inclusion of patients.

hospital dispositions were collapsed into three categories: discharged/left AMA, died in hospital, or transferred to another facility. In-hospital patient mortality was obtained from available ED and hospital dispositions. Mortality data was categorized as alive at the end of the study period (discharged from the ED, left against medical advice, discharged from the hospital, or documented hospital disposition of "still a patient") or deceased (died in the ED or died in the hospital). Mortality data was unavailable for patients transferred to another facility or if a hospital disposition was not documented for admitted patients.

Data Analysis

Descriptive statistics including frequencies, percentages, medians and interquartile ranges are reported. Missing data for each variable were omitted. Crude and adjusted odds ratios (adjusted for patient age, sex, race/ethnicity, first systolic blood pressure, first heart rate, primary impression) were calculated using logistic regression modeling to evaluate the odds of patient improvement following adenosine administration, hospital admission from the ED, and death for initial adenosine doses of 6 mg or 12 mg. Analysis was completed using STATA IC version 18.0 (StataCorp LP; College Station, TX).

Results

During the study period, 11,245 patients received adenosine from 1,350 EMS agencies. Most received an initial dose of 6 mg (70%, $n = 7{,}825$), while 30% (3,314) received an initial dose of 12 mg (Figure 1). Demographics were similar between the two groups (Table 1). The majority of adenosine administrations were for cardiopulmonary EMS impressions/indications (88%, $n = 9{,}926$), while 1% were for injury EMS impressions/indications, and 10% were for other EMS impressions/indications.

Indications and initial vital signs were similar between those who had an initial adenosine dose of 6 mg and those

Table 1. Patient and encounter characteristics for all records with documented out-of-hospital adenosine administration.

Variable name %(n)	Overall $N = 11{,}245$	Initial dose 6mg $n = 7{,}825$	Initial dose 12mg $n = 3{,}314$	Missing data
Sex				
Female	54.3% (6,093)	55.6% (4,345)	51.3% (1,700)	16
Male	45.7% (5,136)	44.4% (3,466)	48.7% (1,613)	
Race/Ethnicity				
Asian, not hispanic/latino(a)	1.6% (164)	1.6% (113)	1.5% (48)	1,088
Black or African American, not hispanic/latino(a)	16.7% (1,698)	15.3% (1,063)	19.9% (618)	
Hispanic/latino(a)	8.5% (861)	8.2% (569)	8.7% (271)	
Other Race, not hispanic/latino(a)	0.8% (80)	0.7% (48)	1% (31)	
White, not hispanic/latino(a)	72.4% (7,354)	74.2% (5,164)	68.9% (2,140)	
Age, years				
Median (Interquartile Range)	60 (45–72)	60 (46–72)	59 (45–71)	0
Initial Pulse Rate				
Median (Interquartile Range)	179 (160–198)	179 (160–198)	179 (160–198)	13
Initial Systolic Blood Pressure				
Median (Interquartile Range)	128 (108–148)	129 (108–148)	126 (106–146)	97
EMS Primary Impression/Indication				
Cardiopulmonary	88.3% (9,926)	88.7% (6,938)	87.4% (2,897)	0
Injury	1.2% (138)	1.2% (90)	1.4 (45)	
Other	10.5% (1,181)	10.2% (797)	11.2% (372)	
Patient Response to Initial Administration				
Improved	58.6% (5,253)	55.0% (3,280)	65.4% (1,903)	2,286
Unchanged	41.2% (3,687)	44.8% (2,669)	34.3% (999)	
Worse	0.2% (19)	0.2% (12)	0.2% (7)	
Number of Doses				
One dose	59.2% (6,656)	52.1% (4,079)	75.4% (2,499)	0
Two doses	21.6% (2,423)	25.3% (1,978)	13.0% (431)	
Three or more doses	19.3% (2,166)	22.6% (1,768)	11.6% (384)	
Total Dose				
Median (Interquartile Range)	12mg (6 mg – 18 mg)	6mg (6 mg–18mg)	12mg (12 mg–12mg)	0
Prehospital Complications (*not mutually exclusive*)				
Cardioversion	4.3% (481)	4.1% (319)	4.9% (161)	0
Pacing	<0.1% (2)	<0.1% (2)	0.0% (0)	
CPR	0.1% (20)	0.2% (12)	0.2% (7)	
EMS Disposition				
Transported	98.4% (11,061)	98.2% (7,687)	98.6% (3,269)	0
Treated released/transferred care to non-EMS	1.6% (183)	1.8% (138)	1.3% (44)	
Died on-scene	<0.1 (1)	0.0% (0)	<0.1% (1)	
ED Disposition (among 2,732 records with linked outcomes)				
Discharged	56.5% (1,543)	54.7% (1,001)	60.0% (528)	8,513
Admitted	42.5% (1,162)	44.4% (812)	39.1% (344)	
Transferred	0.8% (23)	0.8% (15)	0.8% (7)	
Died in the ED	<0.1% (4)	<0.1 (1)	0.1 (1)	
Overall Mortality				
Lived	98.2% (2,684)	98.2% (1,798)	98.3% (866)	8,512
Died	1.8% (49)	1.8% (32)	1.7% (15)	

Table 2. Univariable and adjusted odds ratios for study outcomes.

	Univariable odds ratios	95% Confidence interval	Adjusted odds ratios*	95% confidence interval
Patient Improvement Following Adenosine Administration				
6 MG		Referent		Referent
12 MG	1.55	1.41–1.69	1.65	1.49–1.82
Hospital Admission from ED				
6 MG		Referent		Referent
12 MG	0.8	0.68–0.95	0.72	0.59–0.87
Death				
6 MG		Referent		Referent
12 MG	0.91	0.48–1.71	0.84	0.42–1.69

Adjusted for Patient Age, Sex, Race/Ethnicity, First Systolic Blood Pressure, First Heart Rate, Primary Impression.

with an initial dose of 12 mg. After adjustment, an initial dose of 12 mg was associated with 65% increased odds (OR: 1.65, 95%CI: 1.49–1.82) of prehospital improvement (Table 2). Patients administered an initial dose of 12 mg were more likely to receive a single dose of adenosine compared to those given an initial dose of 6 mg (75% vs. 52%, respectively). Further, there was a higher percentage of patients that received 3 or more doses among those that had an initial dose of 6 mg (12% vs. 23%, respectively). Documented prehospital complications following adenosine administration were rare. Less than 5% of patients received cardioversion following adenosine administration and less than 1% had pacing performed (Table 1). There were 41 total patients that had CPR performed with 21 having CPR performed prior to adenosine administration and 20 having CPR performed following adenosine administration (Supplemental File Table 2). Of the 20 patients with CPR performed following adenosine administration, 10 had missing data that prevented the calculation of total CPR time. Among those with CPR performed following adenosine administration and data available to calculate CPR time, 9 of 10 had resuscitation times of less than 4 minutes with a median time of 2 minutes (Interquartile range: 1–3 minutes). There was one patient that had a total CPR time of 40 minutes following adenosine administration. There was no difference in the need for cardioversion, pacing, or CPR following adenosine administration between groups (p-value > 0.05) (Table 1).

Almost all patients (98%) were transported by EMS. Amongst EMS transported patients, 25% (2,732) had available ED dispositions. After adjustment, an initial dose of 12 mg was associated with reduced odds (OR: 0.72, 95%CI: 0.59–0.87) of admission (Table 2). Finally, in total, 2% (48) who received prehospital adenosine and had available outcome data died. Of those, 70% (32) were in the 6 mg group and 30% (14) were in the 12 mg group. After adjustment, there was no statistically significant difference in the odds of mortality between adenosine dose groups (OR: 0.84, 95%CI: 0.42–1.69).

Discussion

In this study of more than 11,000 patients who received prehospital adenosine we found that an initial dose of 12 mg was associated with significantly better patient outcomes compared to a 6 mg dose. Specifically, patients who received 12 mg were less likely to require additional dosing, demonstrated greater improvement in the prehospital setting and had a substantial reduction in odds of hospital admission.

While this study did not evaluate the initial electrocardiogram (ECG) interpretation, the median initial pulse rate of 179 is consistent with cardiac tachydysrhythmia indications for adenosine administration (27). These results are aligned with reports that EMS clinicians correctly identify cardiac rhythm indications for adenosine administration in 88%-98% of cases (12,15,16,28). Nearly all patients were transported to the hospital, and almost half the patients were admitted.

Consistent with AHA Guidelines the majority of patients received an initial dose of 6 mg. Although the clinical presentation of patients who received a 6 mg initial dose was similar to that of those who received a 12 mg initial dose, those who received 12 mg were more likely to improve during the EMS encounter. While prehospital studies directly comparing patient improvement associated with various doses of adenosine are limited, a number of papers described improvements in conversion rates when adenosine dosage exceeded 6 mg (3,9,15,29–31).

Complications following adenosine administration were rare and did not differ between dosing groups. Notably, there were 21 records that indicated CPR was performed prior to adenosine administration. While this may have been due to documentation errors, the rationale for adenosine administration following CPR should be investigated. The resuscitation time was short among those that received CPR following adenosine administration, potentially indicating the patient experienced a post-adenosine pause in many cases.

Patients who received an initial dose of 12 mg were also less likely to require repeat doses of adenosine in the field. The need to administer repeat doses represents prolongation of an abnormal rhythm which is associated with patient discomfort, hemodynamic instability, and serious cardiovascular complications (18–20). The benefits of the higher dose of adenosine were observed beyond the prehospital portion of the EMS encounter as patients who received an initial dose of 12 mg with available ED dispositions also had a 28% reduction in the odds of hospital admission. Importantly as this study is unable to determine causation, other explanations for this association warrants further exploration. For example, the reduction in hospital admissions may be related to a decrease in negative cardiovascular consequences associated with prolonged episodes of PSVT rather than a direct consequence of the dose.

Limitations

This large retrospective analysis evaluated prehospital patient care records and linked hospital outcomes containing data entered by EMS and hospital personnel during the routine course of public safety and healthcare activities. Emergency Medical Service clinicians self-reported the patient response to adenosine into three nationally defined categories (improved, unchanged, or worse) which are subjective and could not be quantified. We were unable to evaluate patient ECGs to determine actual conversion rates. We did not evaluate the

intravenous (IV) site used to administer the adenosine; one previous study found that the odds of rhythm conversion doubled when the IV was placed in the antecubital space rather than the lower arm or hand (12). This study is limited by the lack of availability of hospital outcomes for the entire study population. Missing data could not be obtained because data were not abstracted for a registry but rather obtained directly from the electronic patient care record as documented by the EMS clinician or hospital staff.

Conclusions

In this large-scale analysis of EMS administration of adenosine for patients with PVST, an initial dose of 12 mg was associated with fewer re-doses, increased prehospital patient improvement, and reduced rates of hospital admission compared to the more commonly used 6 mg initial dose. Complications were few and similar between dosing groups. Collectively, these findings underscore the importance of optimizing initial adenosine dosing in the prehospital setting and suggest that further research is warranted.

Authors' Contributions

All authors made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; including drafting the work and reviewing it critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Generative AI in Scientific Writing

The authors did not use a generative artificial intelligence (AI) tool or service to assist with preparation or editing of this work. The author(s) take full responsibility for the content of this publication.

Disclosure Statement

ARF, SSB, RPC, AT, and JBM are employed by ESO.

Data Availiability Statement

ESO Data Collaborative datasets are made freely available for scholarly research purposes following an external proposal and review process. For more information see: https://www.eso.com/data-and-research/

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