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Peer-reviewed author version

Lodewyckx, Eric & BERGS, Jochen (2021) Effectiveness of the modified Valsalva manoeuvre in adults with supraventricular tachycardia: a systematic review and meta-analysis. In: European journal of emergency medicine, 28 (6) , p. 432-439.

DOI: 10.1097/MEJ.0000000000000862

Handle: <http://hdl.handle.net/1942/34805>

PREPRINT

Effectiveness of the modified valsalva manoeuvre in adults with supraventricular tachycardia: A systematic review and meta-analysis

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Abstract

Background and importance: Cardiac arrhythmia, specifically paroxysmal supraventricular tachycardia (SVT), accounts for a substantial proportion of emergency medical services resources utilisation. Reconversion requires increasing the atrioventricular node's refractoriness, which can be achieved by vagal manoeuvres, pharmacological agents, or electrical cardioversion. There are multiple variants of vagal manoeuvres, including the Valsalva Manoeuvre (VM). While the effectiveness of the standard VM has already been systematically reviewed, there has been no such analysis for the modified VM.

Objective(s): Compare the effectiveness of the modified VM *versus* the standard VM in restoring the normal sinus rhythm in adult patients with supraventricular tachycardia.

Design: Systematic review with meta-analysis of published randomised controlled trials

Outcome measures: The primary outcome was the reconversion to a sinus rhythm. Secondary outcomes included: medication use, adverse events, length of stay in the emergency department, and hospital admission.

Main results: Five randomised controlled trials were included, with a combined total of 1,181 participants. The meta-analysis demonstrated a significantly higher success rate for reconversion to sinus rhythm when using the modified VM compared to the standard VM in patients with an SVT (OR = 4.36; 95 per cent c.i. 3.30 to 5.76; $P < .001$). More adverse events were reported in the modified VM group, although this difference is not significant (RR = 1.48; 95 per cent c.i. 0.91 to 2.42; $P = .11$). The available evidence suggests that medication use was lower in the modified VM group than the standard VM group. However, medication use could not be generalised across the different studies. None of the included studies showed a significant difference in length of stay in the emergency department. Only one study reported on hospital admission, with no significant difference between the two groups.

Conclusions The available evidence is highly suggestive to support the use of the modified VM compared to the standard VM in the treatment of adult patients with SVT. Meta-analysis showed a higher success rate, required less medication use, and resulted in an equal number of adverse events. However, these results cannot be regarded as definitive in the absence of higher-quality studies.

Keywords: Valsalva Maneuver; Tachycardia; Meta-analysis

ARTICLE

Citation: Lodewyckx E & Bergs J. Effectiveness of the modified valsalva manoeuvre in adults with supraventricular tachycardia: A systematic review and meta-analysis. *European Journal of Emergency Medicine*. 2021;28:432-439. doi: 10.1097/MEJ.0000000000000862

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Data Availability Statement:

Data and research materials supporting the results in the article are available upon request.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Introduction

Cardiac arrhythmia, specifically paroxysmal supraventricular tachycardia (SVT), accounts for a substantial proportion of emergency medical services resources utilisation (1). Restoring a normal sinus rhythm (reconversion) should be done quickly and effectively. Reconversion requires increasing the atrioventricular node's refractoriness, which can be achieved by vagal manoeuvres, pharmacological agents, or electrical cardioversion.

The Valsalva Manoeuvre (VM) is a commonly used non-invasive reconversion method (2-7). The VM increases myocardial refractoriness by increasing intrathoracic pressure for a brief period, thus stimulating baroreceptor activity in the aortic arch and carotid bodies, resulting in increased parasympathetic (vagus nerve) tone (7, 8). The effectiveness of conventional vagal manoeuvres in terminating SVT, when correctly performed, shows a considerable variation ranging from 19.4% to 54.3% (9). To improve the effectiveness of the VM, the Modified Valsalva Manoeuvre (MVM) was introduced (7, 10). While the standard VM is performed when the patient is in a sitting position (45° - 90°), the modified VM involves having the patient sit up straight and perform a forced expiration for about 15 seconds, after which the patient is brought into a supine position with the legs raised (45°) for another 15 seconds. This modification should increase relaxation, phase venous return, and vagal stimulation (10-12).

While the effectiveness of the standard VM has been systematically reviewed, there has been no such analysis for the modified VM (9). Therefore, this systematic review aimed to compare the effectiveness of the modified VM *versus* the standard VM in reconversion to a normal sinus rhythm in adult patients with supraventricular tachycardia.

Methods

This paper describes a systematic review with meta-analysis, the PRISMA standards for reporting a systematic review were applied during the preparation of this manuscript (13). A review protocol was used, which is available in Appendix S1 (Appendix S1).

Search strategy

The Cochrane Library, MEDLINE, EMBASE, CENTRAL, and Web of Science databases were searched systematically for all publications until February 2021. The following medical subject heading (MeSH) search terms and keywords were used, either individually or in combination: Tachycardia [MeSH]; tachycard*[tiab]; supraventricular tachycard*[tiab]; Valsalva Maneuver [MeSH]; valsalva* [tiab]. The MEDLINE search strategy (Appendix S2) was adjusted to the other databases' dictionaries as appropriate. Besides, bibliographies of included articles were hand-searched for other relevant articles. During the preparation of the manuscript, the MEDLINE strategy was consulted weekly to identify new publications. Grey literature was not considered.

Study selection

Only randomised clinical trials comparing the standard VM and modified VM's effectiveness in achieving cardiac reconversion in adults with supraventricular tachycardia (*i.e.*, QRS duration less than 120ms and a rate more than 100 bpm) were included. Patients with sinus tachycardia, atrial flutter, atrial fibrillation, or age <18 years were excluded. There were no further restrictions regarding the population, language, or publication date. The study selection process was recorded in a structured format (Appendix S3).

Data extraction

After the removal of duplicates, the first selection of references was made based on title and abstract. Papers selected for full-text review were screened according to the inclusion and exclusion criteria. Two independent reviewers carried out data extraction. Study setting, design, selection and measurement bias, baseline outcome measurements and characteristics, risk of contamination, data analysis, selective outcome reporting, other risks of bias, and generalisability and sustainability issues were extracted and recorded. The primary outcome was the reconversion to a sinus rhythm (reconversion success). Secondary outcomes included the need for medication use (*e.g.*, adenosine, verapamil, diltiazem, or beta-blockers), length of stay in the emergency department, adverse events, and hospital admission.

Risk of bias assessment

Assessment for risk of bias and critical appraisal was conducted using the Cochrane Collaboration's Effective Practice and Organisation of Care Group guidelines. For assessing the risk of bias, the Cochrane Risk of Bias Tool was used (14). The critical appraisal was performed independently by two reviewers. A third reviewer was consulted in case of disagreements until consensus was reached.

Data analysis

Primary or secondary outcomes discussed in the selected studies were included in the narrative synthesis. Meta-analysis was performed for three main patient outcome measures: reversion success, medication use, and adverse events.

A random-effects meta-analysis using the DerSimonian-Laird estimator obtained odds ratios (ORs) and 95 per cent confidence intervals (CIs) for achieving sinus rhythm after one minute. Risk ratios (RRs) with 95 per cent CIs were calculated as a summary estimate for medication use and adverse events.

The study results' heterogeneity was assessed by using the Cochran Q test and the Higgins I^2 test. The following thresholds were used to quantify heterogeneity: $P < .10$ in Cochran's Q test and an I^2 value exceeding 50 per cent were considered to show significant heterogeneity ($I^2 \leq 25\%$ for low, $25\% < I^2 < 50\%$ for moderate, and $I^2 \geq 50\%$ for high heterogeneity). Funnel plots were used to assess publication bias.

Data were analysed using R (a language and environment for statistical computing) (15); more specifically, the meta package was used (16). All reported P values are two-sided; $P < .05$ was considered to indicate statistical significance.

Results

The search identified 152 studies, of which 141 studies were excluded (details are provided in Figure 1). The full texts of the remaining 11 studies were retrieved for evaluation; of which four studies were excluded due to study design (12, 17-19), and two studies (6, 20) were excluded because they did not compare the modified VM *versus* the standard VM. A total of five studies were included in the systematic review. Figure 1 shows the PRISMA flow diagram of the study selection.

[INSERT FIGURE 1]

Included studies

Characteristics of the included studies (11, 21-24) are presented in Table 1. The full extraction of the retrieved data can be found in Appendix S4. The studies were conducted in three different countries (*i.e.*, United Kingdom, Turkey, and China) with a total of 1,181 participants. Not all included studies reported all the selected secondary outcomes, *e.g.*, medication use, length of stay, adverse events, and hospital admission. Two studies reported on multicentre trials (11, 21), the other three studies reported on single-centre trials (22-24).

[INSERT TABLE 1]

Risk of bias assessment

The complete assessment of the risk of bias can be found in Table 2. Overall, the risk of bias ranged from low to some concerns. All studies used a randomisation process; however, two studies did not provide a detailed description of their randomisation plan (21, 24). Patients and caregivers were not blinded to the intervention in the included studies. However, given the nature of the intervention, the effect of blinding participants and caregivers was probably limited. In two studies, the assessors of the outcome were other blinded investigators (11, 21). The registration of missing data was limited, and if there was missing data, it was processed correctly, so attrition bias was limited.

[INSERT TABLE 2]

Effects of the modified Valsalva manoeuvre

An overview of the included outcomes reversion success, medication use, and adverse events is displayed in Table 3.

[INSERT TABLE 3]

Reversion success

Five studies reported data on reversion to sinus rhythm. Three studies defined reversion success as the presence of sinus rhythm after one minute (11, 21, 24); one study also reported reversion after

five minutes (24). Two studies did not specify the time to reconversion but described reconversion success during admission at the emergency department (22, 23). When multiple times were available, sinus rhythm after one minute was used, which was the most reported outcome. All studies reported a significant difference between standard VM and modified VM in favour of the latter: 17 *versus* 43 per cent ($P < .001$) (11), 12.1 *versus* 37.5 per cent ($P < .001$) (24), 16 *versus* 46 per cent (95 per cent c.i. 2.5 to 5.9) (21), 10.7 *versus* 42.9 per cent ($P = .007$), 15.47 *versus* 19.89 per cent ($P < .001$).

Pooled analysis showed a success rate of 15.8 per cent (91 successful reconversions in 575 patients) for the standard VM group compared to a success rate of 45 per cent (258 successful reconversions in 573 patients) for the modified VM group. On average, 3.4 patients would have to be treated with modified VM (instead of standard VM) for one additional patient to have a successful reconversion.

Meta-analysis for reconversion success across five studies yielded an OR of 4.36 (95 per cent c.i. 3.30 to 5.76; $P < .001$). The results showed no significant heterogeneity (Cochran's $Q = 1.12$, 4, d.f., $P = .89$; $I^2 = 0\%$) (Fig. 2).

[INSERT FIGURE 2]

Adverse events

Four studies reported adverse events (11, 21-23). Specific adverse events per study can be found in Appendix S4. No significant difference was found in adverse events between standard VM and modified VM: 4 *versus* 6 per cent ($P = .32$) (11), 0.8 *versus* 1.6 per cent ($P > .05$) (21), 7.1 *versus* 7.1 per cent ($P > .05$) (22), 7.78 *versus* 11.12 per cent ($P > .05$) (23). Meta-analysis for adverse events yielded a RR of 1.48 (95 per cent c.i. .91 to 2.42, $P = .11$). The results showed no significant heterogeneity (Cochran's $Q = 0.28$, 3, d.f., $P = .96$; $I^2 = 0\%$) (Fig. 3).

[INSERT FIGURE 3]

Medication use

Three studies (11, 21, 22) reported medication use as a secondary outcome. However, only two studies specified the medication used (*i.e.*, adenosine or antiarrhythmics) (11, 22), the other study reported medication use without specifically stating which ones (21). Due to uncertainty about the methodological heterogeneity between studies, it was decided not to perform a meta-analysis.

All the included studies showed a difference in the use of antiarrhythmic medication between the standard VM and the modified VM group, favouring the modified VM. Two studies showed a difference in the need for adenosine, both favouring the modified VM group: 69% *versus* 50%; $P < .001$ (11) and 30.4% *versus* 19.6% (95%CI - 14 to 34) (22). For the use of other antiarrhythmic medication, the same trend was observed: 80% *versus* 57% ($P < .001$) (11), 71% *versus* 45% (95%CI - .33 to .69) (21), 32.1% *versus* 14.3% (95%CI - 6.7 to 40) (22). The available evidence, summarised in Table 2, suggests that medication use was lower in the modified VM group compared to the standard VM group.

Emergency department length of stay

Length of stay in the emergency department was reported in two studies (11, 21). One study noted a median length of stay of 2.83 hours (IQR 1.95–3.62) for the standard VM group and 2.82 hours (IQR 1.95 – 3.77; $P = .31$) for the modified VM group (11). Another study showed a median of 2.88 hours (IQR 1.96 – 3.78) for the standard VM group and 2.79 hours (IQR 1.94–3.78; 95 per cent c.i. .77 to 1.12) for the modified VM group (21). In summary, none of the included studies showed a significant difference in the time spent at the emergency department between the standard VM group and the modified VM group.

Hospital admission

One study reported on hospital admission; there was no significant difference between the standard VM group *versus* the modified VM group regarding the proportion of patients discharged home from the emergency department (68% *versus* 63%; $P = .28$) (11).

Discussion

This was the first systematic review and meta-analysis to compare the difference in the effectiveness of the standard VM *versus* the modified VM. A total of five randomised controlled trials were included, with a combined total of 1,181 participants. The meta-analysis demonstrated a significantly higher success rate for reconversion to sinus rhythm when using the modified VM compared to the standard VM in patients with an SVT (OR = 4.36; 95 per cent c.i. 3.30 to 5.76; $P < .001$). There were more adverse events reported in the modified VM group, although this difference is not significant (RR = 1.48; 95 per cent c.i. .91 to 2.42; $P = .11$). Adverse events were mainly described as clinical manifestations (*e.g.*, dizziness, chest

pain); none of the included studies reported actual patient safety incidents. The available evidence suggests that medication use was lower in the modified VM group compared to the standard VM group. However, medication use could not be generalised across the different studies. Despite being more effective, none of the included studies showed a significant difference in the length of stay in the emergency department between the standard VM group and the modified VM group. This is easy to explain as there is no difference in the care patients receive after reversion. One aspect that could result in decreased length of stay is the time between the onset of SVT and the application of the VM. Only one study reported on hospital admission, with no significant difference between the two groups.

The VM is considered safe and is internationally recommended as a first-line emergency treatment for SVT (25). However, a Cochrane review found insufficient evidence to support or refute its utility (9). In this study, a pooled analysis showed significantly higher success rates for reversion to sinus rhythm in adults with SVT when using the modified VM. These findings strengthen the position of VM as a first-line treatment for SVT. Hence, the current evidence suggests that both manoeuvres are safe with the modified VM being more effective, but these results cannot be regarded as definitive in the absence of higher-quality studies. Research on how to decrease the time between onset and application of the VM could improve the health economic advantages of vagal manoeuvres. The use of mobile health applications could provide the means for early detection. At the same time, programs aimed at the education and empowerment of patients and family members could improve the timely application. If it can be done safely, early termination of the arrhythmia should be performed in the prehospital setting. Besides, training of prehospital personal (*i.e.*, nurses, paramedics, and emergency medical technicians) in using the modified VM could improve its applicability. However, differences in laws and legislation between countries must be kept in mind. The SVM, medication treatment, and shock therapy are already applied in the prehospital setting (26). Future research can show whether the MVM is also safe and efficient in the prehospital setting.

Despite training being available (27), application in practice seems limited. As with many interventions, it is the implementation that determines the real-world success of an intervention. Therefore, research into the factors influencing procedure adherence and the contextual factors that influence the successful execution of the modified VM is essential.

Limitations

The overall risk of bias was low; however, there were some reservations regarding the randomisation process because not all studies reported a description of their randomisation plan. Another limitation is the fact that this review only included five studies causing a relatively small population size. Besides, the included population was limited to adult with SVT, other causes of tachycardia are not included. Future research should include a broader population to reduce potential selection bias. A limitation related to the primary outcome was that time to reversion was defined differently over the studies. The registration of secondary outcomes, like adverse events, did not run identically across the different studies. In addition, there existed some vagueness about the use of medication because some studies did not specify which medication was used. Therefore, more data is needed to investigate adverse events. Finally, three out of five studies were carried out at a single centre.

Conclusion

The available evidence is highly suggestive to support the use of the modified VM compared to the standard VM in the treatment of adult patients with SVT. Meta-analysis showed a higher success rate, required less medication use, and resulted in an equal number of adverse events. However, these results cannot be regarded as definitive in the absence of higher-quality studies.

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Figures

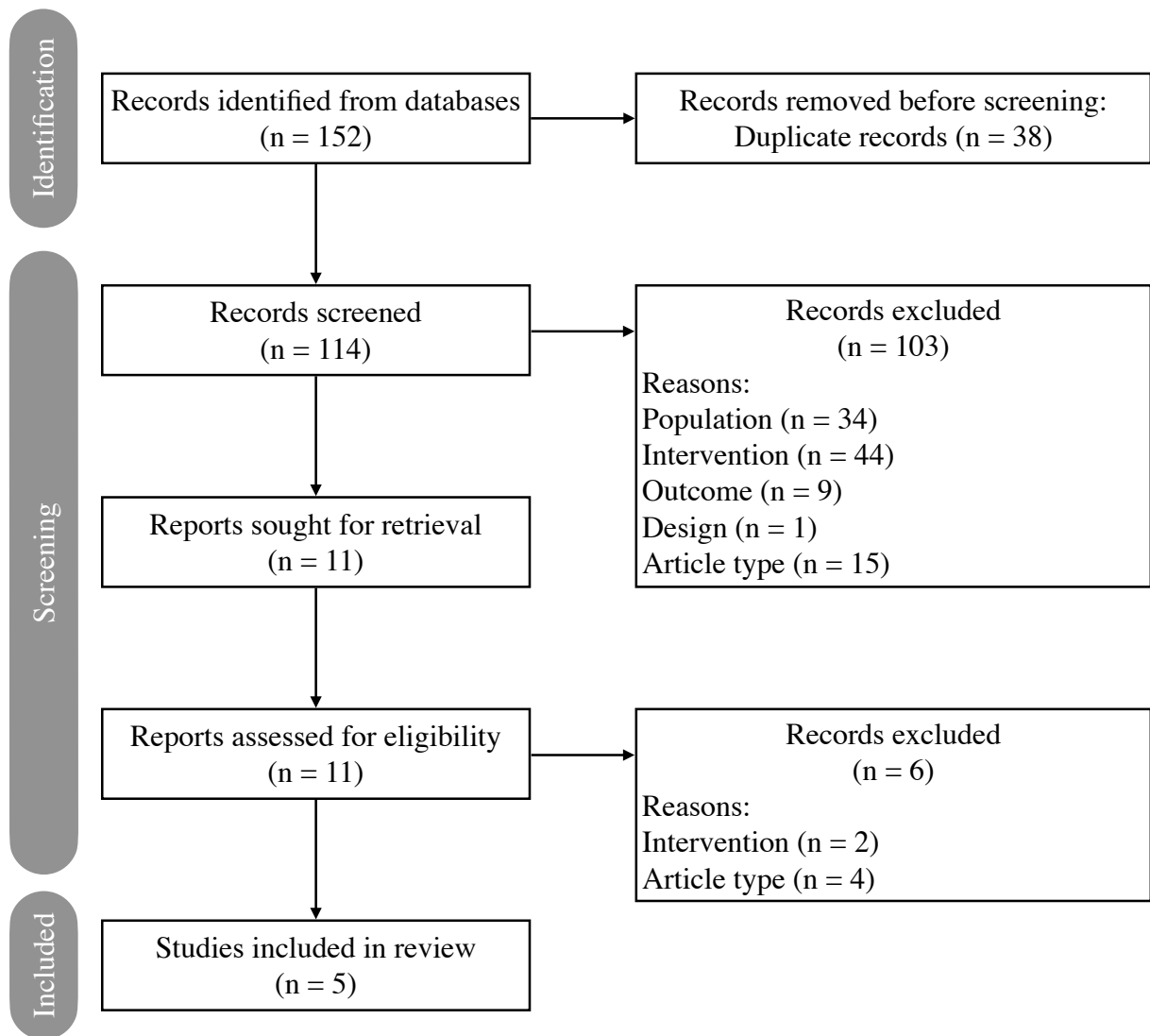


Figure 1 PRISMA flow diagram

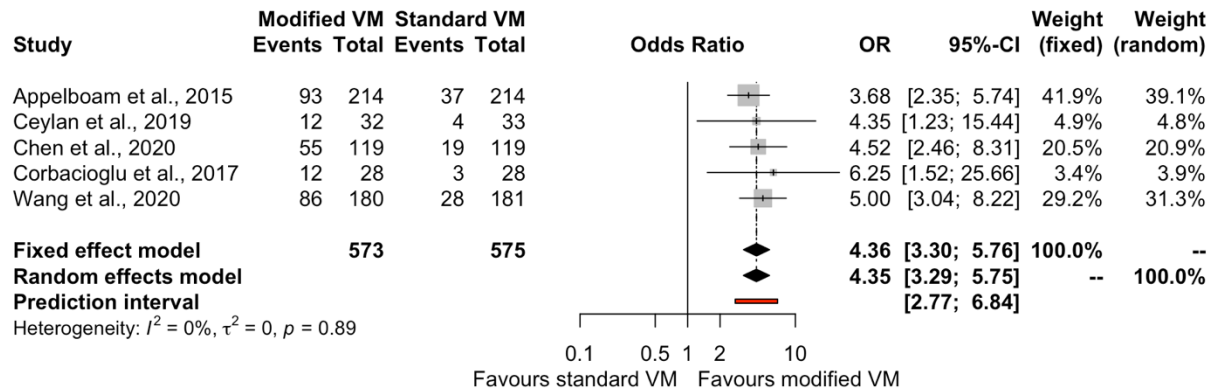


Figure 2 Forest plot reversion success

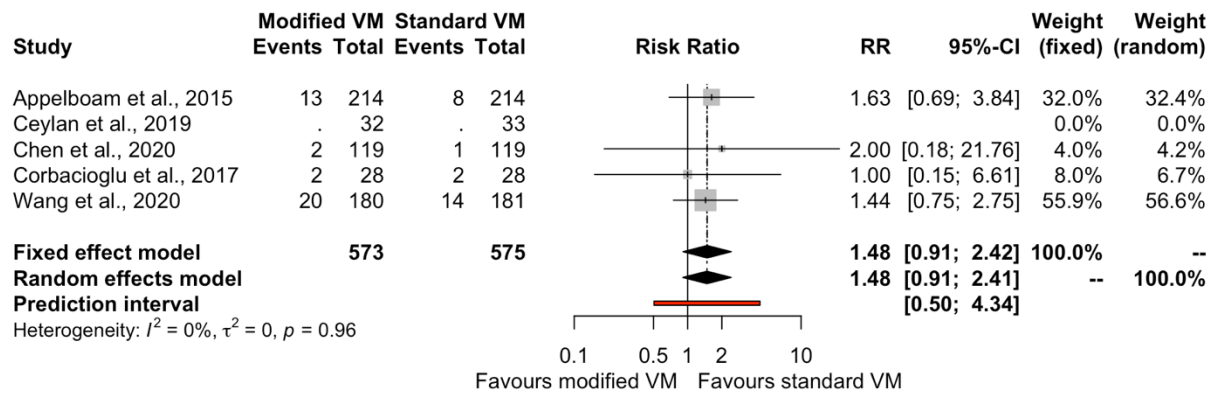


Figure 3 Forest plot adverse events

Tables

Table 1 Study characteristics

Authors publication date	country, study design	number of participants (n=)	characteristics of participants respectively SVM - MVM	
			Data are n (%) or mean (SD)	
			SVM	MVM
Appelboom et al. 2015	United Kingdom, multicenter RCT	428 SVM: 214 MVM: 214	<ul style="list-style-type: none"> Men 80 (37%) Age (years) 54-5 (16.8) Previous SVT (undiagnosed) 57 (27%) Previous SVT (diagnosed) 103 (48%) Previous ablation treatment 15 (7%) Ischaemic heart disease 7 (3%) Diabetes 18 (8%) Hypertension 36 (17%) Valvular heart disease 5 (2%) Pneumonia 4 (2%) COPD 7 (3%) Systolic BP (mm Hg) 124 (22) Diastolic BP (mm Hg) 82 (18) Pulse (beats per minute) 179 (29) O2 saturation (%) 97.9 (2.1) 	<ul style="list-style-type: none"> Men 89 (42%) Age (years) 55-1 (16.3) Previous SVT (undiagnosed) 63 (29%) Previous SVT (diagnosed) 97 (45%) Previous ablation treatment 19 (9%) Ischaemic heart disease 11 (5%) Diabetes 25 (12%) Hypertension 47 (22%) Valvular heart disease 1 (<1%) Pneumonia 2 (1%) COPD 2 (1%) Systolic BP (mm Hg) 125 (23) Diastolic BP (mm Hg) 83 (19) Pulse (beats per minute) 172 (29) O2 saturation (%) 98.0 (1.9)
Ceylan et al. 2019	Turkey, single- center RCT	98 SVM:33 MVM: 32 CSM:33	<ul style="list-style-type: none"> Age (years), median (IQR) 61 (46–67) Male, n (%)14 (31.1) Family history of SVT 2 (18.2) SVT history 19 (43.2) Coronary artery disease 7 (30.4) Diabetes mellitus history: 3 (15.8) Hypertension history 13 (32.5) Anemia history 4 (33.3) Hyperthyroidism history 0 (0.0) Malignancy history 5 (62.5) 	<ul style="list-style-type: none"> Age (years), median (IQR) 50 (36–61) Male, n (%) 17 (37.8) Family history of SVT 3 (27.3) SVT history 11 (25.0) Coronary artery disease 6 (26.1) Diabetes mellitus history: 4 (21.1) Hypertension history 8 (20) Anemia history 1 (8.3) Hyperthyroidism history 1 (25.0) Malignancy history 1 (12.5)
Chen et al. 2020	China, multicenter RCT	238 SVM: 119 MVM: 119	<ul style="list-style-type: none"> Long RP VS Short RP 	
Corbacioglu et al. 2017	Turkey, single- center RCT	56 SVM: 28 MVM: 28	<ul style="list-style-type: none"> Age (years) 48.4 (40–60) Male 13 (46.4%) Ischemic heart disease 3 (10.7%) Diabetes mellitus history 4 (7.1%) Hypertension history 5 (8.9%) COPD history 2 (3.6%) Renal failure history 1 (1.8%) 	<ul style="list-style-type: none"> Age (years) 44.3 (34–53.7) Male 10 (35.7%) Ischemic heart disease 3 (10.7%) Diabetes mellitus history 4 (7.1%) Hypertension history 3 (5.4%) COPD history 0 (0%) Renal failure history 1 (1.8%)
Wang et al. 2020	China, single-center RCT	361 SVM: 181 MVM: 180	<ul style="list-style-type: none"> Men [n (%)]74 (40.88) Age (yr) 49.29 ± 13.59 Weight (kg) 68.22 ± 13.27 Duration of PSVT (yr) 8.60 ± 8.10 Coronary heart disease [n (%)] 8 (4.42) Hypertension [n (%)] 44 (24.31) Diabetes [n (%)]10 (5.52) Pneumonia [n (%)] 0 (0.00) 	<ul style="list-style-type: none"> Men [n (%)] 84 (46.7) Age (yr) 51.76 ± 12.02 Weight (kg) 64.89 ± 20.82 Duration of PSVT (yr) 7.27 ± 7.38 Coronary heart disease [n (%)] 2 (1.11) Hypertension [n (%)] 36 (2.00) Diabetes [n (%)] 10 (5.56) Pneumonia [n (%)] 2 (1.11)

Table 2 Study risk of bias assessment





















	Randomisation process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Appelboom et al. 2015						
Ceylan et al. 2019						
Chen et al. 2020						
Corbacioglu et al. 2017						
Wang et al. 2020						

Table 3 Results of individual studies

Study	Reconversion success			Medication use (adenosine)			Adverse event			ED Length of stay		
	SVM n (%)	MVM n (%)	P	SVM n (%)	MVM n (%)	P	SVM n (%)	MVM n (%)	P	SVM (median, IQR)	MVM (median, IQR)	P
Appelboom et al. 2015	37 (17%)	93 (43%)	< .001	171 (80%)	121 (57%)	< .001	8 (4%)	13 (6%)	0.32	2.83 (1.95– 3.62)	2.82 (1.95– 3.77)	0.31
Ceylan et al. 2019	4 (12.1%)	12 (37.5%)	< .001	-	-	-	-	-	-	-	-	-
Chen et al. 2020	19 (16%)	55 (46%)	NA	84 (71%)	54 (45%)	NA	1 (0.8%)	2 (1.6%)	N/S	2.88 (1.96 - 3.78)	2.79 (1.94 - 3.82)	NA
Corbacioglu et al. 2017	3 (10.7%)	12 (42.9%)	0.007	26 (62.5%)	15 (33.9%)	NA	2 (7.1%)	2 (7.1%)	N/S	-	-	-
Wang et al. 2020	28 (15.47)	36 (19.89)	< .001	-	-	-	14 (7.78%)	20 (11.12%)	NA	-	-	-

SVM: standard Valsalva maneuver, MVM: modified Valsalva maneuver, N/S: not statistically significant; NA: Not

Available; ED: emergency department

Supporting information

S1 search strategy

#1 Tachycardia [Mesh]

#2 tachycard*[tiab]

#3 supraventricular tachycard*[tiab]

#4 Valsalva Maneuver [Mesh]

#5 valsalva* [tiab]

(#1 OR #2 OR #3) AND (#4 OR #5)

S2 review protocol

Effectiveness of the modified valsalva maneuver in adults with a supraventricular tachycardia: a meta-analysis

Lodewyckx E., Bergs J.

Review question.

Next items were derived using the PICO model:

- P (patients) adults with a supraventricular tachycardia
- I (intervention) modified valsalva maneuver
- C (comparison) standard valsalva maneuver
- O (outcome) presence of sinus rhythm

The next research question was used:

“What is the effect of a modified valsalva maneuver with patients in supraventricular tachycardia on reversion to a sinus rhythm compared to a standard valsalva maneuver?”

Searches.

- Sources: Medline, EMBASE, Web of Science, Central
- Search dates: from 1/02/2021 to 07/02/2021
- Restrictions: non-English publications, no restriction in publication date, grey literature
- The search will be re-run prior to the final analysis, as it is considered good practice

URL to search strategy.

#1 Tachycardia [Mesh]

#2 tachycard*[tiab]

#3 supraventricular tachycard*[tiab]

#4 Valsalva Maneuver [Mesh]

#5 valsalva [tiab]

(#1 OR #2 OR #3) AND (#4 OR #5)

Condition or domain being studied.

The domain that is being studied is Cardiology, more specifically adults with a supraventricular tachycardia.

Participants/population.

- Inclusion:
 - adults with a supraventricular tachycardia (QRS duration less than 120ms and a rate more than 100 bpm)
- Exclusion:
 - patients with a sinus tachycardia, atrial flutter, or atrial fibrillation
 - patients under 18 years of age, there are no further restrictions on the population

Intervention(s), exposure(s).

The modified valsalva maneuver involves having the patient sit up straight and perform a forced expiration for about 15 seconds. Immediately after the expiration, the patient is brought into a supine position with the legs raised (45°) for another 15 seconds.

This modification to the standard valsalva maneuver should increase relaxation, phase venous return, and vagal stimulation.

Comparator(s)/control.

The standard valsalva maneuver is performed when the patient is in a sitting position (45° - 90°).

Types of study to be included.

We will include all randomised controlled trials and controlled clinical trials to compare the different interventions.

Context

Studies performed in hospitals (emergency departments) and out of hospital settings will be included.

Main outcome(s).

Primary outcome: presence of sinus rhythm

- A 12-lead ECG will be recorded after the valsalva maneuver. The rhythm will be checked for return of sinus rhythm.
- Check for return to sinus rhythm after 1 min.

Additional outcome(s).

Secondary outcomes

- the use of adenosine
- time spent in the emergency department or out of hospital treatment
- adverse events
- admission to hospital
- 30-day mortality?

Data extraction (selection and coding).

Study selection

2 reviewers will be selecting studies for inclusion in the systematic review. One reviewer will screen the records while the other one will check the decisions.

A third reviewer will be consulted in case of disagreements until consensus is reached.

Data extraction

Data will be extracted by one researcher. Another researcher will check the extracted data. The following data will be extracted:

- study characteristics (authors, publication date, country, study design)
- number of participants
- characteristics of participants (age, gender)
- numbers of interventions
- effect of interventions (sinus presence)
- other outcomes

A third reviewer will be consulted in case of disagreements until consensus is reached.

R Statistics will be used to process the data. Study investigators will be contacted in case of missing data.

Risk of bias (quality) assessment.

For assessing the risk of bias, the Cochrane Risk of Bias tool (1) will be used. The quality assessment will be performed by two reviewers. A third reviewer will be consulted in case of disagreements until consensus is reached. The different domains that are tested are

- selection bias: random sequence generation, allocation concealment
- performance bias: blinding of participants and personnel
- detection bias: blinding of outcome assessment
- attrition bias: incomplete outcome
- reporting bias: selective reporting
- other bias: important concerns not found in other domains

The results of the quality assessment will be presented in a risk of bias table. Each domain will be scored for low risk of bias, unclear risk of bias or high risk of bias.

Strategy for data synthesis.

Primary or secondary outcomes discussed in at least two studies will be included in the narrative synthesis. Meta-analysis will be performed when at least 3 main patient outcome are discussed.

A random-effects meta-analysis using the DerSimonian-Laird estimator obtained odds ratios (ORs) and 95 per cent confidence intervals (CIs) will be used. Risk ratios (RRs) with 95 per cent CIs will be calculated as summary.

Heterogeneity of the study results will be assessed by using the Cochran Q test and the Higgins I2 test. The following thresholds will be used to quantify heterogeneity: $P < 0.10$ in Cochran's Q test and an I2 value exceeding 50 per cent will be considered to show significant heterogeneity ($I^2 \leq 25\%$ for low, $25\% < I^2 < 50\%$ for moderate, and $I^2 \geq 50\%$ for high heterogeneity). Funnel plots will assess publication bias. Sensitivity analysis will identify heterogeneous studies that influenced the meta-analysis.

Data will be analyzed by using R (a language and environment for statistical computing), more specifically the MetaR package will be used. All reported P values will be two-sided; $P < 0.05$ is considered to indicate statistical significance.

Type and method of review.

Systematic review, meta-analysis

Keywords.

Systematic review
meta-analysis
modified valsalva maneuver
supraventricular tachycardia
standard valsalva maneuver
Tachycardia [Mesh]
Valsalva Maneuver [Mesh]

Details of any existing review of the same topic by the same authors.

There are no earlier versions of this systematic review.

Language.

English

Country.

Belgium

Anticipated or actual start date.

01/02/2021

Anticipated completion date.

31/03/2021

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Funding sources/sponsors.

No funding

Conflicts of interest.

There are no known conflicts of interest

08 January 2021

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S3 study selection

See *excel® tool*

S4 Data extraction

See excel® tool

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