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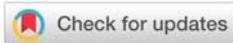
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Keywords: VM: Valsalva maneuver; BNP: Brain natriuretic peptide; HR: Heart rate; BP: Blood pressure; EF: Ejection fraction; NYHA: New York heart association; RV: Right ventricle; LV: Left ventricle; SBP: Systolic blood pressure; CAD: Coronary artery disease; DD: Diastolic dysfunction; DHF: Diastolic heart failure; SHF: Systolic heart failure

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Research Article

Valsalva Maneuver in diastolic heart failure, diastolic dysfunction and systolic heart failure clinically BNP and echocardiography

Abstract

Background: Valsalva maneuver one of the oldest method to diagnose heart failure, it's cheap ,non-invasive ,bedside tool. Its well-studied in systolic heart failure patients which showed abnormal response either square wave or absent phase IV ,however in diastolic heart failure and diastolic dysfunction were not investigated .

Methods: 70 patients were included in our study they were divided into three groups group 1 diastolic heart failure based on echocardiography and BNP above 100pg/L/ml , group 2 diastolic dysfunction based on echocardiography and BNP less than 100 pg/ml and group 3 systolic heart failure ,they went all clinical examination ,BNP were taken ,Valsalva maneuver at 30 mmHg for at least 15 sec using two sphygmomanometers first connected to mouth piece and the other to monitor blood pressure while the physician auscultates brachial artery patient is asked to perform forced expiratory effort against closed airway for at least 15 second and then asked to release and absence or presence of Korotkoff sounds assessed and heart rate is recorded baseline and after strain and full study echocardiography and using in apical 4 chamber view Simpson method to measure right and left ventricle area at baseline , peak strain and after release .

Results: Group 2 showed overshooting of systolic blood pressure by a mean of 11 ± 6.41 mmHg (p value = 0.001), 95% confidence interval (CI): [3.2-15.14] compared to baseline. Moreover, group 3 showed minimal overshooting with a mean of 3.34 ± 4.17 mmHg (p value = 0.002), 95% confidence interval (CI): [2.2-8.2], On the other hand, group 1 showed no overshooting, with a mean change of -3.6 ± 0.63 mmHg (p value = 0.001), 95% confidence interval (CI): [9.34-2.5].

We demonstrated that Valsalva maneuver could differentiate patients with diastolic heart failure from those with diastolic dysfunction, with a sensitivity of 68%, specificity 75%, positive predictive value 71.4%, and negative predictive value 72%. Only group 2 in our study showed a clinically significant decrease in RV end-diastolic area during strain as compared to the baseline, with a mean value of 4.5 ± 0.14 cm² ($23.5 \pm 0.4\%$; p value = 0.001),95% confidence interval (CI):[6.65+2.25]. On the other hand, group 1 showed a minimal decrease (0.9 ± 0.25 cm²; $5.3 \pm 0.6\%$) and group 3 showed a minimal increase (1 ± 2.23 cm²; $5.6 \pm 5\%$). Group 2 showed a clinically significant decrease in LV end-diastolic area during strain as compared to the baseline, with a mean value of 6.1 ± 1.01 cm² ($19.3 \pm 2\%$; p value = 0.001) 95% confidence interval (CI) :[8.2+3.96]. Moreover, group 3 showed a smaller, but significant decrease (4.6 ± 0.98 cm²; $12.6 \pm 0.7\%$), while group 1 demonstrated insignificant change.

Conclusion: VM showed significant overshooting in group 2 compared to other two groups ,not all heart failure patients had abnormal response based as risk factors as NYHA class and diuretics ,stiffness in myocardium affected the Valsalva response in diastolic heart failure group followed by systolic heart failure and finally diastolic dysfunction one ,There is decrease in left and right ventricle area during strain and gradually increase after release during normal Valsalva response which is greatly affected in HF patients .

Introduction

The Valsalva maneuver is a well-known and widely accepted test of cardiac parasympathetic function. This test, which has been used in multicenter trials to evaluate autonomic function, as it is reliable, consistent and operator-independent. The heart

rate changes provoked during the maneuver and expressed as the Valsalva ratio are mostly dependent on cardio vagal integrity [1]. The concomitant variations in HR and arterial BP of Valsalva Maneuver can be divided into four physiological phases [2].

(I) onset of strain with a rise of arterial pressure and a decrease of HR, (II) continued strain with a drop of arterial pressure and its later partial recovery due to the reflex tachycardia and the progressing vasoconstriction, (III) strain release with a sudden drop of arterial pressure and a further heart acceleration, (IV) system recovery with arterial pressure overshoot and the resulting bradycardia, until the BP and HR normalize. The inspiration of various grade preceding the maneuver can be treated as phase 0 [3].

Patients with severely depressed ejection fractions, unlike those with normal ventricular function, are unable to alter stroke output in response to acutely increased intra thoracic pressure. A square wave pressure response is a likely consequence of a fixed stroke output during the strain maneuver, it is worth to mention that the effect of Valsalva maneuver in patients with either diastolic dysfunction or diastolic heart failure is not sufficiently studied yet.

Methods

Settings

Our study included 70 patients who were eligible for study presented to Kasr Al Ainy hospital Cairo University inpatient ward from June 2016 to October 2016 admitted to cardiology unit.

Study design

The study protocol was approved by the ethics committee of the faculty of Medicine, Cairo University .it was a prospective observational study on diastolic heart failure, diastolic dysfunction and systolic heart failure patients.

Inclusion and exclusion criteria

Patients diagnosed as having systolic heart failure with ejection fraction less than 40%. Patients with diastolic heart failure : defined as heart failure with preserved EF with symptoms of Heart failure NYHA II to IV by American heart association 2013 guidelines and BNP positive (BNP > 100 pg / ml) [4]. Patients with diastolic dysfunction defined as BNP<100 pg/ml and echocardiography showed diastolic dysfunction. Patients severe dyspnea unable to do Valsalva Maneuver, Aortic stenosis and those with poor echogenic window were excluded

Collection of data

History were taken from Patients and they underwent full clinical examination ,BNP was withdrawn ,They all did ECG , Valsalva maneuver at parameters 30 mmHg for at least 15 seconds and full study echocardiography particularly areas of left and right ventricle at baseline , peak strain and after release .

Study outcome

Primary outcome was to study the Effect of Valsalva maneuver in systolic versus diastolic heart failure in BNP positive and BNP negative patients regarding blood pressure response and heart rate. While the secondary outcome was

to find the Correlation of systolic heart failure and Valsalva maneuver ,Correlation of diastolic heart failure and Valsalva maneuver.,Correlation of diastolic dysfunction and Valsalva maneuver, Correlation of BNP level and diastolic heart failure and Correlation between BNP level and diastolic dysfunction

Statistical analysis

Data were coded and entered using the statistical package SPSS version 23. Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while non-parametrical Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables (Chan, 2003a). For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b) values less than 0.05 were considered as statistically significant.

Results

Patient related variables

Male gender predominate (n=55) 78.6% in our study groups, Mean age of patients were (57± 13.92), (56± 9.48) and (54±12.68) in the three study groups (diastolic heart failure, diastolic dysfunction and systolic heart failure respectively). Smokers were (n=33) 48%, Most of our patients (n=49)70% were in NYHA II, Diabetic patients were (n=20) 28.6%, Hypertensive patients were (n=31)44.3% and Patients diagnosed as having coronary artery disease were (n=40) 57.1% in our study population (Table 1).

Event related variables

Valsalva response was shown to have sensitivity 68.2% and specificity 75% in detecting diastolic heart failure, It has positive predictive value 71.4% and negative predictive value 72%, The changes among blood pressure changes and heart rate from baseline to after strain was statistically significant among three groups with (p value 0.001), while blood pressure changes was statistically significant among each group respectively with (p value 0.001, 0.001,0.002) (Tables 2,3).

Group 2 (DD) showed mean value in group 2 in RV area (18.87±5.56, 14.42±5.42, 16.39±4.87) decreased in RV area during baseline strain and increased after release with P value of 0.002, The change in RV area in group 1 showed decrease but to a lesser value compared to group 2 with (p value= 0.001) ,while group 3 revealed an increase in RV area with p value 0.002 (Tables 4,5).

Group 2 (DD) patients showed a decrease in LV area with mean value of (31.5±6.8, 25.42±7.81, 30.25±7.13) at baseline study, during strain and at release respectively with P value 0.001, Group 3 (SHF) showed decrease in LV area mean value of (36.57±11.13, 31.95±12.11, 36.42±11.13) during strain phase with P value 0.003, The change in areas from baseline to strain was

Table 1: Demographic and clinical characteristics of our study population.

	Group 1		Group 2		Group 3		P value	
	No	Percentage	No	Percentage	No	Percentage		
Age (years)	57±13.9	56.5%	56±9.4	65%	54±12.6	68%	0.770	
Male	15	68%	18	75%	22	91.6%	0.022	
Smokers	13	59%	16	66%	11	45.8%	0.360	
Clinical presentation	SOB	11	50%	8	33.3%	14	58.3%	0.170
	dizziness	1	4.5%	0	0%	0	0%	
	Chest pain	9	40.9%	14	58.3%	9	37.5%	
	None	1	4.5%	2	8.3%	1	4.2%	
NYHA Class	I	1	4.5%	6	25%	2	8.3%	0.085
	II	15	68.2%	17	70.8%	17	70.8%	
	III	4	18.2%	1	4.2%	5	20.8%	
	IV	2	9.1%	0	0%	0	0%	
Diabetes mellitus	7	31.8%	7	29%	6	25%	0.873	
Hypertension	12	54.5%	12	50%	7	29.2%	0.155	
Renal dysfunction	11	50%	7	29.1%	4	16.6%	0.415	
CAD	13	59%	15	62.5%	12	50%	0.277	
Obesity	4	18.1%	1	4.2%	0	0	0.082	

CAD coronary artery disease.

Table 2: Hemodynamic responses to Valsalva maneuver in the three study groups mean and SD.

Manometry pressure on strain (mmHg)	42.38±9.44	44.50±8.26	49.75±15.60	0.119
Duration on strain seconds(sec)	24.05±7.52	27.33±5.29	26.71±4.82	0.177
Baseline SBP(mmHg)	129.52±32.32	115.71±16.90	104.76±25.22	0.010
SBP on strain (mmHg)	125.95±31.69	126.67±23.31	108.10±29.39	0.063
Baseline HR(beats)	76.67±17.44	75.14±14.09	76.48±16.82	0.946
HR response Afterstrain (beats)	72.38±13.84	74.00±14.52	72.10±15.55	0.902
ΔSBP	3.57±0.63	10.96±6.41	3.34±4.17	0.001
ΔHR	4.29±3.6	1.14±0.43	4.38±1.27	0.001

ΔSBP equals changes of blood pressure from baseline to after strain, ΔHR equals changes in heart rate from baseline to after strain.

Table 3: Valsalva Response in the three Groups

Response	Group			p-value
	group 1 DHF	group 2 DD	group 3 SHF	
Abnormal response	15 (68%)	6 (25%)	13 (54.2%)	0.007
Absent phase IV	8 (36.3%)	3 (12.5%)	6 (25%)	
Square	7(31.8%)	3 (12.5%)	7 (29.2%)	

significant with p value 0.001 and 0.001 in group 2 and 3 with mean value 6.08 ±1.01 and 4.62±0.98 respectively.

Study outcome

Primary outcome: Patients with group 3 [systolic heart failure] as well as group 1 [diastolic heart failure] had abnormal Valsalva response either square wave or absent phase IV, compared to group 2 [diastolic dysfunction] had normal response

Secondary outcome: Not all patients with group 3 [systolic

Table 4: Changes in RV area in our study population

	Group		
	Group 1 (DHF)	Group 2 (DD)	Group 3 (SHF)
	mean±SD	mean±SD	mean±SD
RV baseline	16.80±6.03	18.87±5.56	17.8±6.61
Strain	15.86±6.28	14.42±5.42	18.93±8.84
Release	18.25±7.08	16.39±4.87	18.93±8.00
ΔRV area (B-S)%	0.9±0.25 (5.3±0.6%)	4.45±0.14 (23.5±0.4%)	-1±2.23 (5.6±5%)
P value	0.001	0.001	0.004
sssΔRV(S-R)%	-2.39±0.8 (14.8±13%)	-1.97±0.55 (13.5±9%)	0±0.84 (4.7±12%)
P value	0.019	0.042	0.134
ΔRV(B-R)%	-1.45±1.05 (9±17%)	2.48±0.69 (13.14±12%)	-1.13±1.39 (6.3±21%)
P value	0.017	0.001	0.062

ΔRV area (B-S) % means changes in right ventricle area from baseline area to straining area and its percentage, ΔRV (S-R) % means changes in right ventricle area from straining area to release area and its percentage, ΔRV (B-R) % means changes in right ventricle area from baseline area to release area and its percentage

heart failure] had abnormal response, few patients with group 2 [diastolic dysfunction] showed abnormal response, there is decrease in RV and LV area during strain and gradually increased after release these changes were evident in group 2 compared to the other two groups.

Discussion

We standardized Valsalva maneuver by asking patients to achieve a minimum manometric pressure of 40 mmHg for at least 15 seconds. We recorded the systolic blood pressure and heart rate at baseline and after strain release (phase IV).

Group 2 showed overshooting of systolic blood pressure by a mean of 11 ± 6.41mmHg (p value = 0.001) compared to

baseline. Moreover, group 3 showed minimal overshooting with a mean of 3.34 ± 4.17 mmHg (p value = 0.002). On the other hand, group 1 showed no overshooting, with a mean change of -3.6 ± 0.63 mmHg (p value = 0.001).

Two of our patients—one with systolic and the other with diastolic heart failure – underwent invasive hemodynamic monitoring. There were no significant differences in SBP and heart changes between the clinical and invasive methods as shown in figures 1, 2.

Previous studies have demonstrated that patients with heart failure and elevated left-sided filling pressures have a distinctly different SBP response during the Valsalva maneuver compared to normal individuals. Because the fall in SBP during the strain phase is largely due to a decrease of LV filling, in patients with elevated left-sided filling pressures, SBP remains elevated throughout the strain phase as LV filling remains adequate [5,6]. Furthermore, release of the strain is not followed by an overshoot of the blood pressure. The blood pressure response in patients with elevated left-sided filling pressures has thus been termed a “square wave” response—an increase in SBP that persists throughout the strain phase and then returns to baseline levels when the strain is released [7,8]. These changes in the blood pressure response to the

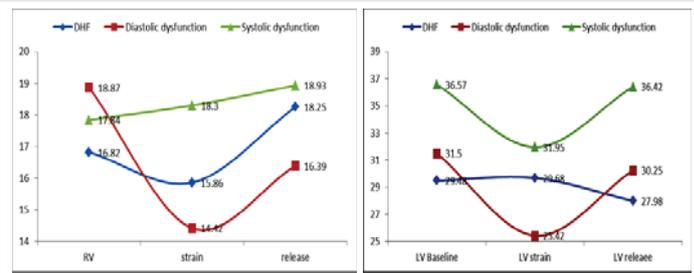


Figure 2: Changes of RV AREA in three groups and LV area in three groups.

Valsalva maneuver have been shown to be useful for detection of elevated left-sided filling pressures [6, 7].

We demonstrated that Valsalva maneuver could differentiate patients with diastolic heart failure from those with diastolic dysfunction, with a sensitivity of 68%, specificity 75%, positive predictive value 71.4%, and negative predictive value 72%.

Roger et al. reported a sensitivity and specificity of 91% and 69%, respectively for Valsalva maneuver in detecting heart failure [9]. They included patients with systolic and diastolic heart failure which explains the difference in sensitivity and specificity compared to our study.

Compared to BNP, Valsalva maneuver is a simple, cheap, and readily available bedside tool that can differentiate between diastolic dysfunction and diastolic heart failure with a reasonable accuracy. We determined BNP levels for all our patients. Group 1 had the highest level (688.3 ± 909.9 pg/ml), followed by group 3 (473.1 ± 511.59 pg/ml), while group 2 had the lowest level (32.08 ± 21.66 pg/ml) (p value < 0.001).

Echocardiography

RV and LV area changes: Only group 2 in our study showed a clinically significant decrease in RV end-diastolic area during strain as compared to the baseline, with a mean value of 4.5 ± 0.14 cm² ($23.5 \pm 0.4\%$; p value = 0.001). On the other hand, group 1 showed a minimal decrease (0.9 ± 0.25 cm²; $5.3 \pm 0.6\%$) and group 3 showed a minimal increase (1 ± 2.23 cm²; $5.6 \pm 5\%$).

Group 2 showed a clinically significant decrease in LV end-diastolic area during strain as compared to the baseline, with a mean value of 6.1 ± 1.01 cm² ($19.3 \pm 2\%$; p value = 0.001). Moreover, group 3 showed a smaller, but significant decrease (4.6 ± 0.98 cm²; $12.6 \pm 0.7\%$), while group 1 demonstrated insignificant change.

Aebischer et al. studied the effects of Valsalva on LV and RV end-diastolic areas in 15 volunteers at multiple time points during and after strain. During the strain phase, LV and RV areas decreased progressively, the RV area (minimum $51.0\% \pm 5.5\%$ of its initial value) decreasing more than the LV area (minimum $61.2\% \pm 3.9\%$ of its initial value). Immediately after strain release, the RV end-diastolic area increased suddenly and dramatically to $143.3\% \pm 9.4\%$ of its baseline value, whereas the LV end-diastolic area decreased further [10].

Table 5: Changes in LV area in our study population

	Group		
	Group 1 (DHF)	Group 2 (DD)	Group 3 (SHF)
	mean±SD	mean±SD	mean±SD
LV baseline (cm ²)	29.68±6.92	31.5 ±6.8	36.57 ±11.13
Strain (cm ²)	29.68±10.75	25.42 ±7.81	31.95 ±12.11
Release (cm ²)	27.98±8.38	30.25 ±7.13	36.42 ±11.13
ΔLV (B-S) (%)	-0±3.83 (0±5%)	6.08±1.01 (19.3±2%)	4.62±0.98 (12.6±0.7%)
P value	0.361	0.001	0.001
ΔLV(S-R) (%)	1.7±2.37 (5.7±4%)	-4.83±0.68 (15.3±1.4%)	-4.47±0.98 (12.2±0.7%)
P value	0.231	0.001	0.001
ΔLV (B-R) (%)	1.7±1.46 (5.7±3%)	1.25±0.33 (3.9±0.7%)	0.15±0 (0.4±0%)
P value	0.061	0.001	0.001

ΔLV area (B-S) % means changes in left ventricle area from baseline area to straining area and its percentage, ΔLV(S-R) % means changes in left ventricle area from straining area to release area and its percentage, ΔLV(B-R) % means changes in left ventricle area from baseline area to release area and its percentage

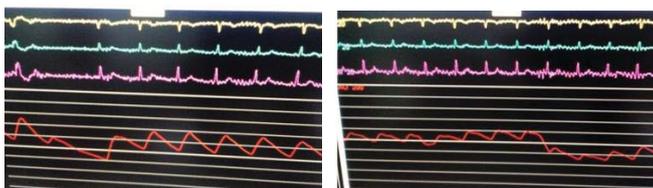


Figure 1: Hemodynamic tracing of catheter introduced to aorta while systolic heart failure patient with mouth piece attached to manometry at 40 mmHg for 30 seconds with abnormal Valsalva response and reflex bradycardia noted (square wave response) and Fig. (2) showed Hemodynamic tracing with mouth piece attached to manometry recording at 40 mmHg for 30 seconds to diastolic heart failure (absent phase IV) blood pressure is much lower the baseline after Valsalva maneuver.

Little et al. studied the effect of the Valsalva maneuver on RV end-diastolic area and LV volume in 12 normal subjects and in 8 patients with non-ischemic cardiomyopathy, evidence of pulmonary congestion, and a mean LV ejection fraction of $23 \pm 9\%$. In both groups the RV area decreased during the late strain phase of the Valsalva maneuver. In normal subjects it decreased from 9.3 ± 1.5 to 5.6 ± 1.6 cm² ($p < 0.001$) and in patients it decreased from 13 ± 2.2 to 10 ± 2.9 cm² ($p < 0.001$). In normal subjects, LV end-diastolic volume decreased from the baseline level during the Valsalva maneuver, and this was apparent in both the four-chamber (96 ± 21 to 68 ± 18 ml, $p < 0.01$) and two-chamber views (97 ± 15 to 56 ± 20 ml, $p < 0.01$). In the patients, LV end-diastolic volume was not significantly different from the baseline in either view [11,12].

We demonstrated that patients with diastolic dysfunction mimic normal individuals in the decrease in LV and RV size in response to Valsalva, although with a significantly lesser degree. On the other hand, our patients with systolic heart failure showed decrease in LV size but not the RV, while patients with diastolic heart failure show insignificant changes. Our findings highlight the fact patients with diastolic heart failure have the “stiffest” ventricles, followed by patients with systolic heart failure, while patients with diastolic dysfunction have the “least stiff” ventricles. Moreover, the significant RV involvement in our 3 groups carries important prognostic consequences, even though we might assume that LV involvement is our primary concern in these patients.

Study limitations: Not all of our patients with systolic / diastolic heart failure showed abnormal response to Valsalva maneuver. This could be explained by milder degrees of heart failure or adequate diuresis in some patients; such patients showed normal response in other studies [1], our sample size was relatively small.

Conclusion

Valsalva response shows overshooting in diastolic dysfunction significantly compared to heart failure patients, Not all patients with systolic heart failure showed abnormal response some showed normal response depending on compliance to treatment, NYHA class and functional capacity of the patient, Right ventricle area decrease during straining in heart failure patients and diastolic dysfunction, Stiffness in the myocardium affects the response to Valsalva response in diastolic heart failure followed by systolic heart failure and finally diastolic dysfunction. the more stiffness the more blunt response to Valsalva and absent overshooting, the change in stroke volume and cardiac output shows mild reduction from baseline.

Recommendation

More studies are needed to reveal the impact of Valsalva hemodynamic on area and volumes of right and left ventricle in normal and diseased individuals and can be a prognostic factor to heart failure patients in further studies.

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