

Evaluation of arterial pulse amplitude ratio and Valsalva ratio in different age groups

Yesar MH AL-Shamma^{1*}, Amir S AL-Mu'min^{2*}, Ahlam KA AL-Hamdany^{3*}.

1.PhD physiology(UK). Department of physiology ,college of medicine, Kufa university.

2.Interventional cardiology ,F.I.C.M.S. Department of Medicine, college of medicine, Babylon university.

3.PhD physiology. Department of physiology ,college of medicine, Babylon university

^{1*}yesarmh47@yahoo.com .,phone number-07801182667

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^{2*}Dr_amir_sahib@yahoo.com , phone number-07801145752

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^{3*}udayanabiah@yahoo.com

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ABSTRACT

Abstract

Aims: To construct normal values of Valsalva ratio for heart rate responses during Valsalva maneuver (VM) and arterial pulse amplitude ratio as reference values of different age groups ,and to investigate effect of aging alone without presence of risk factors on autonomic nervous system.

Study design: case control study.

Place and duration of study: This study was performed in Marjan teaching hospital ,in Hilla city, during the period February ,2012 to June,2012.

Methodology: 40 subjects were included in this study, all were healthy male, group1 (G1) with mean age (28.3± 9.7) years old, group2 (G2) with mean age (48.4 ± 7.1) years old. Strips of leadII of ECG were recorded during performing VM for calculation R-R intervals and measurement of blood pressure during phasel and phasell by mercury sphygmomanometer. Calculation of Valsalva ratio for heart rate and arterial pulse amplitude ratio for both groups were done.

Results: The systolic and diastolic blood pressure of G2 were significantly higher than values of systolic and diastolic blood pressure of G1 at phasel and phasell of VM ($P=0.05$) but pulse pressure for the two groups at phasel (G1: 51± 11, G2: 53±13 mmHg) and phasell (G1: 41±5, G2:41±3.99) of VM were with no significant differences ($P> 0.05$). Valsalva ratio for G1 was (1.5± 0.3) and for G2 was (1.39±0.29), pulse amplitude ratio for G1 was (0.80±

0.19) and for G2 was (0.77 ± 0.19) and there were no significant differences between two groups ($P > 0.05$). All values were expressed as mean $\pm$ SD.
Conclusions: The results showed that autonomic nervous system still intact in older group, this may conclude that aging process without the presence of risk factors not effect autonomic nervous system.

Key wards : Valsalva maneuver, Valsalva ratio, pulse amplitude ratio, autonomic function tests.

1. INTRODUCTION

The Valsalva maneuver (VM) is performed by attempting to forcibly exhale while keeping the mouth and nose closed. eliciting a complex series of changes in heart rate and blood pressure involving both vagal and sympathetic responses. It is used as a diagnostic tool to evaluate the condition of the heart and is sometimes done as a treatment to correct abnormal heart rhythms or relieve chest pain [1]. There are four phases during the Valsalva maneuver [2,3]. Phase one is the onset of straining with increased intrathoracic pressure. The heart rate does not change but blood pressure rises. phase II may be divided into early and late phases. In early phase II, reduced preload and stroke volume lead to a fall in cardiac output despite the tachycardia caused by decreased vagal activity. Total peripheral resistance increases due to increased sympathetic discharge (nucleus tractus solitarius) and an increase in plasma epinephrine concentration. The fall in blood pressure is thus arrested, and is termed "late phase II"; in normal patients there is actually a rise in blood pressure just before release [4]. Phase three is the release of straining with decreased intrathoracic pressure and normalization of pulmonary blood flow. Phase four marks the blood pressure overshoot (in the normal heart) with reflex bradycardia.

Valsalva ratio: The Valsalva ratio is calculated as the ratio of the maximum R-R interval after the strain of VM to that of the shortest R-R interval during the strain of VM. The normal response is an increase in heart rate during phase II in response to the fall in blood pressure, and the baroreflex response to the blood pressure overshoot in phase IV is transient bradycardia. A ratio of greater than 1.45 is considered normal, 1.20 to 1.45 as border line, and less than 1.20 as abnormal (autonomic dysfunction) [5]. According to Ewing et al [6] a Valsalva ratio >1.21 is considered normal.

Arterial pulse amplitude ratio is the ratio of the lowest pulse pressure during active straining (phase II) to the greatest pulse pressure at onset of the strain. In dysautonomic patients, there is typically a loss of both the blood pressure overshoot and the reflex bradycardia [4].

Hébert et al [7] measured the pulse amplitude ratio (i.e., minimum/maximum pulse pressure) during the strain phase of the Valsalva maneuver in 20 adults (42 ± 14 yr) as part of their study and found pulse amplitude ratio ranging from 0.19 to 0.85 (0.45 ± 0.19) and The Valsalva ratio ranged from 1.09 to 2.33 (1.56 ± 0.34).

Precaution of VM : should not be performed by patients who have severe coronary artery disease, have experienced recent heart attack, or have a moderate to severe reduction in blood volume. Risks of VM that the patient may feel dizzy or faint during the procedure, but serious consequences are rare. There is a risk that the VM can cause blood clots to detach, bleeding, and abnormal rhythms originating in the ventricle. It can also cause cardiac arrest. Consequently, the procedure is usually performed in a setting where emergency equipment is accessible.

In our study we had assessed the autonomic status in males of different age groups by measuring Valsalva ratio and arterial pulse amplitude ratio so as to construct normal values of these ratios so can continue this study in future in comparison of disease state, beside that we tried in this study to find if aging by itself without the presence of risk factors or cardiovascular disease can effect autonomic nervous system function.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

- Subjects : 40 healthy male subjects were enrolled in this study , they were divided in to two age groups, group1(G1) : 25 subjects with mean age 28.3 ± 9.7 years, mean body mass index (BMI) $22.8 \pm 0.2 \text{ Kg/m}^2$. Group2(G2) :15 subjects with mean age 48.4 ± 7.1 years, mean BMI $23.1 \pm 0.01 \text{ kg/m}^2$. All subjects gave their consent for the study approved and approval of the ethical committee at Kufa faculty of medicine. The subjects were from medical staff and relatives of patients. The subjects were thoroughly examined clinically by cardiologist to confirm the inclusion criteria. Exclusion criteria include hypertension, diabetes mellitus, coronary heart disease and other cardiac problems, renal disease,, and exclude any risk factors (e.g) smoking, hyperlipidemia. No subject was on any medication.

-Mercury sphygmomanometer: Two devises were needed. One for measuring blood pressure by auscultatory method and one for performing strain part of VM.

-Electrocardiography (ECG) : to record strip of lead II during VM for calculation of R-R intervals at different phases of VM.

Methods: subject put in supine position ,limb leads electrodes were connected to the subject. Mercury Sphygmomanometer was used for measuring blood pressure . after reaching the steady state which means that heart rate in consecutive minutes changes by less than 3beats/min [8] ,the subject should exhale forcefully after a normal inspiration into tube that was connected to another sphygmomanometer .A tiny air leak was placed in the tube to ensure that airway pressure was produced from the thoracic cavity and not pharynx [9]. Valsalva maneuver was performed at a pressure of 40 mmHg for 15 seconds [10].measurement of blood pressure at the beginning of straining-phasel, then repeated the VM after reaching the steady state to measure the blood pressure during phaselII which is occur after 5 seconds of beginning of straining [7]. A continuous ECG was recorded starting 1 min before the maneuver (resting period), during the maneuver (strain period, 15 sec.) and 60 seconds subsequent to the strain period [11]. After that measurement of pulse pressure of phasel and phaselII according to equation: pulse pressure =systolic blood pressure-diastolic blood pressure. Then pulse amplitude ratio=minimum/maximum pulse pressure. Valsalva ratio calculated from longest R-R interval(during phaselV)/shortest R-R interval(during phaselII) [5].

Statistical analysis: All values expressed as mean $\pm$ SD, comparison between G1 and G2 were done by unpaired student t-test , P -value <0.05 considered statistically significant

2. RESULTS AND DISCUSSION

In G1: the systolic and diastolic blood pressure at phasel of VM were 150 ± 11.1 and 99 ± 7.2 mmHg respectively , so maximum pulse pressure at phasel of VM was (mean $\pm$ SD = 51 ± 11 mmHg) which was a result of systolic blood pressure-diastolic blood pressure during phasel of VM . the systolic and diastolic blood pressure at phaselII of VM were 136 ± 9 and 95 ± 7 mmHg respectively ,so minimum pulse pressure at (phase II) (41 ± 5 mmHg). This resulted in pulse amplitude ratio (minimum/maximum pulse pressure)=(0.80 ± 0.19).

118 R-R interval during phaseII is 0.64 ± 0.1 mS and during phaseIV is 0.96 ± 1.2 mS so The
 119 Valsalva ratio was 1.5 ± 0.3 .

120 In G2: maximum (phase I) pulse pressure (mean $\pm$ SD = 53 ± 13 mmHg) from (160mmHg-
 121 107mmHg), and minimum (phase II) pulse pressure (41 ± 3.99 mmHg) from(146mmHg-
 122 105mmHg). This resulted in pulse amplitude ratio (minimum/maximum arterial pulse
 123 pressure)= (0.77 ± 0.19).

124 R-R interval during phaseII is $0.68 \pm 0.01.2$ mS and during phaseIV is 0.95 ± 0.01 mS, so The
 125 Valsalva ratio was 1.39 ± 0.29 .

126 The systolic and diastolic blood pressure of G2 were significantly higher than values of
 127 systolic and diastolic blood pressure of G1 at phaseI and phaseII of VM ($P=0.05$), but There
 128 were no significant differences between pulse pressure at phaseI and phaseII of VM of the
 129 two groups ($P>0.05$), and there were no significant differences between pulse amplitude
 130 ratio and Valsalva ratio of both groups ($P>0.05$).Table-1, figure-1.

131 Table-1 Hemodynamic parameters during phaseI and phaseII of VM of G1 and G2. Values
 132 were expressed as mean $\pm$ SD.

Parameters	G1 28.3 $\pm$ 9.7 years	G2 48.4 $\pm$ 7.1years	P value	Significance
Systolic blood pressure at phaseI of VM*** (mmHg)	150 $\pm$ 11.1	160 $\pm$ 9.1	S*	$P = 0.05$
Diastolic blood pressure at phaseI of VM (mmHg)	99 $\pm$ 7.2	107 $\pm$ 8.2	S	$P = 0.05$
Systolic blood pressure at phaseII of VM (mmHg)	136 $\pm$ 9	146 $\pm$ 7	S	$P = 0.05$
Diastolic blood pressure at phaseII of VM (mmHg)	95 $\pm$ 7	105 $\pm$ 4	S	$P = 0.05$
Pulse pressure at phaseI of VM (mmHg)	51 $\pm$ 11	53 $\pm$ 13	NS**	$P > 0.05$
Pulse pressure) at phase II of VM (mmHg)	41 $\pm$ 5	41 $\pm$ 3.99	NS	$P > 0.05$

133 S* significant difference. ,NS** no significant difference., VM***-Valsalva maneuver

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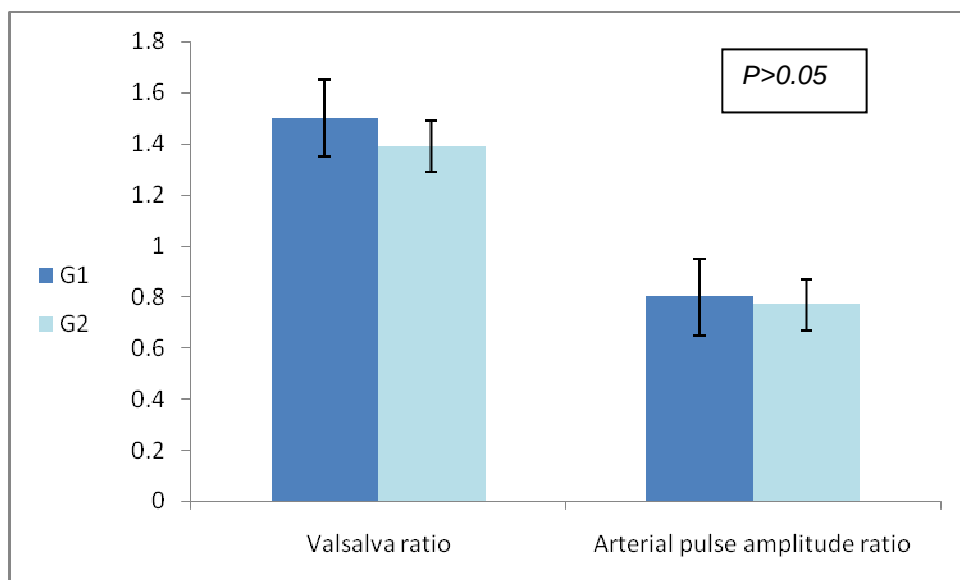


Figure-1: Comparison between Valsalva ratio and pulse amplitude ratio of G1 and G2.(G1:group1(28.3±9.7)years old,G2:group2(48.4±7.1)years old. $P > 0.05$).

Discussion : Beside that VM is usually used to assess autonomic function [12,13], as from changes of heart rate responses during different phases of VM and the changes of systolic and diastolic blood pressure which reflect the integrity of autonomic function, arterial pressure response during the strain phase of the VM might reflect either LV function [14,15], or right-sided pressures [16], or both [17,18,19]. Some authors have suggested that the pulse amplitude ratio may improve the assessment of cardiac status [19,20] and may furnish a noninvasive scale of myocardial dysfunction.. So it seems of physiological interest to clarify this issue and measure values of different age groups which are normal and then to continue this study in the future with different disease states. This study show that systolic and diastolic blood pressure of older group during phasel and phaselI of VM were higher than the younger age and this is due to fact that Increasing age is associated with increased intimal thickness, vascular smooth muscle hypertrophy, fragmentation of the internal elastic membrane and an increase in the amount of collagen and collagen cross-linking in arterial walls [21], intimal thickening occur even in population of low incidence of atherosclerosis [22]. But there were no significant differences between pulse pressure at phasel and phaselI of VM of the two groups , as pulse pressure depends on the compliance of blood vessel , this mean that the compliance of blood vessels of the two groups were not different and give idea about the healthiness of blood vessels of G2 .There were no significant differences of pulse amplitude ratio of VM and Valsalva ratio of heart rate responses to VM of the two groups .This may reflect that the autonomic nervous system still intact and not affected yet by the vascular wall changes that occur during aging as the compliance of blood vessels not changed yet . Gandhi et al [23] studied the association of autonomic functions with gender by taking different age groups of both sex and the result of Valsalva ratio of (15-30) years old group was 1.51 ± 0.27 while (46-60)years old group was 1.26 ± 0.10 , which are nearly the same of our results. We recommend to take other autonomic tests to evaluate this issue about healthy aging people .

4. CONCLUSION

Aging process by itself may not influence the autonomic function unless the presence of other risk factors or cardiovascular disease.

ACKNOWLEDGEMENTS

We would like to express our deepest thanks to the staff members of Marjan Hospital for their cooperation.

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AUTHORS' CONTRIBUTIONS

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" 'Author A' designed the study, , wrote the protocol. 'Author B' and 'Author C' managed the analyses of the study. 'Author C' managed the literature searches, performed the statistical analysis and wrote the first draft of the manuscript All authors read and approved the final manuscript."

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CONSENT (WHERE EVER APPLICABLE)

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"All authors declare that 'written informed consent was obtained from the subjects (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

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ETHICAL APPROVAL (WHERE EVER APPLICABLE)

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UNIVERSITY OF KUFA COLLEGE OF MEDICINE ETHICS COMMITTEE

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APPLICATION FORM FOR HEALTH - RELATED RESEARCH STUDIES

A1 Title of the research Study: Evaluation of arterial pulse amplitude ratio and Valsalva ratio in different age groups

207

A2 Principal Investigator:

211 **Title:** Mr **Name:** Yesar MH al-Shamaa.
212 **Qualifications:** PhD Physiology (UK).
213 **Dept.:** physiology
214 **Organisation:** college of medicine
215 **Tel:** 07801182667
216 **E-mail:** yesarmh47@yahoo.com
217

218 **A3 (a) Is this a multi-site study?**
219 No.
220

221 **A3 (b) Please name each site where this study is proposed to take place and state the**
222 **lead investigator for each site:**

Site:	Lead Investigator:
Merjan medical city-Babylon	Dr. Amir S AL-Mumin

223
224 **A3 (c) For any of the sites listed above, have you got an outcome from the research**
225 **ethics committee (where applicable)?**
226

227 **A4. Co-Investigator:**
228 No.

229 **Name of site:**
230 **Title:** Dr. - Ms. – Mr. – Prof. **Name:**
231 **Qualifications:**
232 **Position:**
233 **Organisation:**
234 **Role in Research:**
235

236 **A5. Overall contact person who is to receive correspondence in relation to this**
237 **application / who is to be contacted if a query arises in relation to this application.**

238 **Title:** Lecturer **Name:** Dr. Ahlam KA AL-Hamdany
239 **Address:** Department of physiology-college of medicine-Babylon University.
240 **Tel (work):** **Tel (mobile):**
241 **E-mail:** udayjanabia@yahoo.com
242

243 **A6. Please provide a lay description of this study.**
244 It involves studying hemodynamic responses during Valsalva maneuver at different age
245 groups by measuring Valsalva ratio and pulse amplitude ratio.
246

247 **A7 (a) Is this study being undertaken as part of an academic qualification?**
248 No.
249

250 **A7 (b) If yes, please complete the following:**

251 **Student Name:** **Course:**
252 **Institution:** **Academic Supervisor:**
253

254	SECTION B	STUDY DESCRIPTORS
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256 **B1. Provide information on the study background.**

257 The study provide some information about the autonomic nervous system at different age
258 groups which is evaluated by Valsalva maneuver.
259

260 **B2. List the study aims and objectives.**

261 1- To construct normal values of Valsalva ratio and pulse amplitude ratio.

262 2- To study effect of aging on autonomic nervous system.

263

264 **B3. List the study endpoints (if applicable).**

265 1- If aging without presence of risk factors effect on autonomic system

266

267 **B4. Provide information on the study design.**

268 Case control study.

269

270 **B5. Provide information on the study methodology.**

271 Measurement of blood pressure changes at phase1 and phaseII of Valsalva
272 maneuver by using sphygmomanometer and calculation of R-R intervals of ECG at
273 phaseII and phaseIV of Valsalva maneuver by using strip of leadII of ECG.then
274 calculate pulse amplitude ratio and Valsalva ratio .

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283 **C1. 1 How many research participants are to be recruited? At each site (if applicable)**

284 **? And in each arm of the study (if applicable)?**

285

Name of site:	Names of arms (if applicable)		
	Insert name of arm (if applicable):	Insert name of arm (if applicable):	Insert name of arm (if applicable):

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SECTION C2 PARTICIPANTS - INFORMED CONSENT

C2.1 (a) Will informed consent be obtained?

Yes.

C2.1 (b) If no, please justify.

C2.1 (c) If yes, how will informed consent be obtained and by whom?

Directly from the participant after explanation of the study, in brief, by the investigator.

C2.1 (d) If yes, will participants be informed of their right to refuse to participate and their right to withdraw from this research study? Please elaborate.

Yes.

C2.1 (e) Will there be a time interval between giving information and seeking consent?

Yes if needed.

C2.1 (f) If yes, please elaborate.

If the participant needs time to think about it, a reasonable time will be allowed.

C2.1 (g) If no, please justify.

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SECTION C3 ADULT PARTICIPANTS - CAPACITY

C3.1 (a) Will all adult research participants have the capacity to give informed consent?
Yes.

C3.1 (b) If no, please elaborate.
C3.1 (c) If no, is this research of such a nature that it can only be carried out on adults without capacity? Yes - No

SECTION C4 PARTICIPANTS UNDER THE AGE OF 18

C4.1 (a) Will any research participants be under the age of 18 i.e. Children?
yes.
C4.1 (b) If yes, please justify:
Persons < 16 No
Persons aged 16 -18 Yes
Children in care No
C4.2. Is this research of such a nature that it can only be carried out on children?No
C4.3. Please comment on what will occur if the researcher discovers that a child is at risk during the course of this study? Will stop the study and assess his health state.
C4.4. Will each child receive information according to his/her capacity of understanding regarding the risks and benefits of the study? Please elaborate- Yes we explain everything for them.
C4.5. Will the explicit wish of the child who is capable of forming an opinion and assessing information to refuse to participate or to be withdrawn from the study be considered by the lead investigators, co-investigators and principal investigator? Please elaborate. Any one refuse to participate or to be withdrawn from the study, his wish will respected.
C4.6. Please comment on the involvement (if any) of parents / legal guardians of the child in the consent process.

SECTION C5 PARTICIPANTS - CHECKLIST

Please confirm if any of the following groups will participate in this study. This is a quick checklist for research ethics committee members and it is recognized that not all groups in this listing will automatically be vulnerable or lacking in capacity.
C5.1 Patients No
C5.2 Unconscious patients No
C5.3 Current psychiatric in-patients No
C5.4 Patients in an emergency medical setting No
C5.5 Relatives / Career of patients Yes
C5.6 Healthy Volunteers Yes
C5.7 Students Yes
C5.8 Employees / staff members Yes
C5.9 Prisoners No
C5.10 residents of nursing homes No
C5.11 Pregnant women No
C5.12 Women of child bearing potential No
C5.13 Breastfeeding mothers No
C5.14 Persons with an acquired brain injury No
C5.15 Intellectually impaired persons No
C5.16 Elderly / aged persons > 65 No

364 **C5.17 If yes to any of the above, what special arrangements have been made to deal**
365 **with issues of consent and assent (if any)?**
366
367
368

369 **SECTION D RESEARCH PROCEDURES**
370

371 **D1. What research procedures or interventions (over and above those clinically**
372 **indicated and/or over and above those which are part of routine care) will research**
373 **participants undergo whilst participating in this study?**

- 374 1- ECG, blood pressure measurement by mercury sphygmomanometer.
375 2- Blood sample for biochemical assessment (e.g) total lipid profile, RBS.
376

377 **D2. If there are any potential harms resulting from any of the above listed procedures,**
378 **provide details below:**

379 Risk of infection due to blood sampling which is minimized by careful skin cleaning &
380 avoiding the infected skin areas. Risk of complication of VM .
381

382 **D3. What is the potential benefit that may occur as a result of this study?**

383 Construct normal values of Valsalva ratio and pulse amplitude ratio in normal subjects to be
384 used later in evaluation of diseased condition.
385

386 **D4 (a) Will the study involve the withholding of treatment? Yes –No–Non Applicable**
387 **No.**
388

389 **D4 (b) Will there be any harms that could result from withholding treatment? Yes- No**
390 **D4 (c) If yes, please elaborate**
391

392 **D5. How will the health of participants be monitored during and after the study?**

393 No need for monitoring as we are not interfering with their ongoing daily regimes.
394

395 **D6 (a) Will the intervention provided during the study be available if needed after the**
396 **termination of the study?**

397 Yes.
398

399 **D6 (b) If yes, please state the intervention you are referring to and state who will bear**
400 **the cost of provision of this intervention?**

401 Merjan medical city
402

403 **D7. Please comment on how individual results will be managed.**

404 Statistically.
405

406 **D8. Please comment on how aggregated study results will be made available.**

407 By publishing the paper in one of the impact journals.
408

409 **SECTION E1 DATA PROCESSING - CONSENT**
410

411 **E1.1 (a) Will consent be sought for the processing of data?**

412 Yes.
413

414 **E1.1 (b) If no, please elaborate.**
415

416 **SECTION E2 DATA PROCESSING - GENERAL**

417 **E2.1 Who will have access to the data which is collected?**
418 The investigators.
419
420 **E2.2 What media of data will be collected?**
421 Paper based.
422
423 **E2.3 Where will data analysis take place and who will perform data analysis (if known)?**
424
425 Using statistical maneuvers.
426
427 **E2.4 (a) After data analysis has taken place, will data be destroyed or retained?**
428 Retained in secure place.
429
430 **E2.4 (b) Please elaborate.**
431 for being as reference if needed again.
432
433 **E2.4 (c) If destroyed, how, when and by whom will it be destroyed?**
434 **E2.4 (d) If retained, for how long, for what purpose, and where will it be retained?**
435 Retained in secure place by the researcher for being as reference if needed again.
436
437 **E2.5 Please comment on the confidentiality of collected data.**
438 Only the investigators will have full access to all data.
439
440 **E2.6 (a) Will any of the data collected consist of audio recordings / video recordings?**
441 No.
442
443 **E2.6 (b) If yes, will participants be given the opportunity to review and amend transcripts of the tapes?**
444
445
446 **E2.7 (a) Will any of the data collected consist of photographs / video recordings?**
447 No.
448
449 **E2.7 (b) If yes, please elaborate.**
450

SECTION E3 ACCESS TO HEALTH CARE RECORDS

453 **E3.1 (a) Does the study involve access to healthcare records (hard copy / electronic)?**
454 No.
455
456 **E3.1 (b) If yes, please elaborate.**
457
458 **E3.1 (c) Who will access these healthcare records?**
459
460 **E3.1 (d) Will consent be sought from patients for research team members to access their healthcare records? Yes - No**
461
462

SECTION F HUMAN BIOLOGICAL MATERIAL

465 Section F is optional. Please delete it if this section does not apply.
466

SECTION F1 BODILY TISSUE / BODILY FLUID SAMPLES - GENERAL

467
468 **F1.1 (a) Does this study involve human biological material?**
469

470 Yes.

471

472

473

SECTION F2

BODILY TISSUE / BODILY FLUID SAMPLES PROSPECTIVELY COLLECTED

474 **F2.1 Does this study involve the prospective collection of human biological material?**

475 Yes.

476

477 **F2.2 Please state the type of human biological material which is being prospectively**
478 **collected?**

479 Blood sample.

480

481 **F2.3 Who or what institution will be the custodian of the prospectively collected**
482 **human biological material?**

483 Merjan medical city.

484

485 **F2.4 (a) Will the human biological material be collected as part of routine clinical**
486 **care?**

487 Yes.

488

489 **F2.4 (b) Will the human biological material be collected specifically for the purpose**
490 **this research study?**

491 Yes.

492

493 **F2.4 (c) With reference to your responses to question F2.4 (a), F2.4 (b), please provide**
494 **more detail, in particular, in relation to whether participants will be consented to the**
495 **taking of a sample or to the use of a sample (or part of a sample) which will be taken**
496 **anyway for clinical reasons.**

497 The participants agree to take blood sample from them because we illustrate the benefit of
498 this research and it is a chance for evaluating their health, for that reason we involved male
499 volunteers only.

500

501 **F2.5 (a) With respect of human biological material which it is proposed to**
502 **prospectively collect for the purpose of this research study, after the laboratory**
503 **analysis which this research study involve, will any human biological material**
504 **remain?**

505 No.

506

507 **F2.5 (b) If yes, will this remaining human biological material be retained? Yes - No**

508 **F2.5 (c) If yes, for how long and where will samples be retained?**

509 **F2.5 (d) If yes, for what purpose will samples be retained?**

510 **F2.5 (e) If yes, please comment on consent for retention of biological material**

511 **F2.5 (f) If yes, will this human biological material and/or data derived from it be used**
512 **for any other purpose (including future research projects)? Yes - No**

513 **F2.5 (g) If yes, please comment on consent for future use of human biological**
514 **material.**

515

516 **F2.6 (a) Will the human biological material be collected specifically for the purposes**
517 **of depositing this human biological material in a biobank? No**

518 **F2.6 (b) If yes, please provide specific information in relation to this proposed biobank**

519 **F2.6 (c) If yes, will research participants be informed in all information leaflets and**
520 **consent forms that this is a biobank?**

521

522

SECTION F3

BODILY TISSUE / BODILY FLUID SAMPLES RETROSPECTIVELY COLLECTED

523
524 **F3.1 Does this study involve accessing retrospectively collected human biological**
525 **material?**
526 No.

527
528 **F3.2 Please state the type of human biological material which is being accessed.**
529 **F3.3 Who will access the material?**

530 **F3.4 Who (or which institution) is the current custodian of the material?**
531

532 **F3.5 Please state for what purpose the human biological material was originally**
533 **collected and please comment on the nature of consent for the collection of this**
534 **material?**
535

536 **F3.6 (a) Do you intend to contact patients to seek their consent to use stored human**
537 **biological material? Yes - No**

538 **F3.6 (b) If no, please justify why you consider existing consent to cover this project,**
539 **or that a waiver of consent from the research ethics committee is warranted.**

540
541 **SECTION F4 BODILY TISSUE / BODILY FLUID SAMPLES – SAMPLE MOVEMENT**

542
543 **F4.1 (a) Will human biological material at any stage leave the institution of origin?**
544 No.

545
546 **F4.1 (b) If yes, for what purpose?**

547 **F4.1 (c) If yes, please state where samples will be sent.**

548 **F4.1 (d) If yes, please state if the samples leaving the institution of origin will be**
549 **anonymous, irreversibly anonymised, pseudonymised, coded, identifiable etc?**

550 **F4.1 (e) If 'coded' , please confirm who will retain the 'key' to re-identify the samples?**

551 **F4.1 (f) Does a memorandum of understanding (or agreement / contract) exist**
552 **between the institution of origin and the institution to which the samples will be sent?**
553 **Please elaborate.**

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555
556 **SECTION F5 GENETIC SETTING**
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558 **F5.1 (a) Does this research study involve 'genetic testing'? Yes – No**
559 No.

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561 **F5.1 (b) If yes, please specify the nature of the genetic testing.**
562

563 **Signature** **Date**
564 **Please print name Ahlam K Abood**

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REFERENCES

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572

1-.Jancin, Bruce. "New Mortality Predictor Found for Heart Failure." Family Practice News .
2004; 15: 48-49 .

- 573 2-Hamilton W F, Woodbury R A, Haper H T. Arterial cerebrospinal and venous pressures in
574 man during cough and strain. *Am. J. Physiol.* 1944; 141:42–45.
- 575 3- Korner PI , Tonkin A M, Uther JB.(Reflex and mechanical circulatory effects of graded
576 Valsalva maneuvers in normal man. *J. Appl. Physiol.* 1976 ; 40:434–440.
- 577 4- [Bradley C, Hiner](#) . Clinic Valsalva Maneuver MD. *Clinical Medicine & Research* . 2005;
578 3(255).
- 579 5- Kubba S, Agarwal SSK, Prakash A et al. Effect of losartan on albuminuria, peripheral and
580 autonomic neuropathy in normotensive microalbuminuric type 2 diabetics. *Neurology*
581 *India*.2003; 51: 355-358.
- 582 6- Ewing D J, Martyn C N, Young R J, Clarke B F. The value of cardiovascular autonomic
583 function tests: 10 years experience in diabetes. *Diabetes Care*.1985; 8:491–498.
- 584 7-Hebert CER, Coirault C, Zamani K, Fontaine et al. Pulse pressure response to the strain of
585 VM in human with preserved systolic function.*J.App.Physiol.* 1998; 85(3):817-823
- 586 8-Hainsworth R and AL-Shamma YMH. Cardiovascular responses to stimulation of carotid
587 receptor in healthy subjects. *Clinical science* .1988;75:159-165.
- 588 9- Weilenmann D, Rickli F, Follath F, Kiowski W, and Peter H. Noninvasive evaluation of
589 pulmonary capillary wedge pressure by blood pressure response to Valsalva
590 maneuver. *Chest the cardiopulmonary and critical care J.* 2002;122:140-145.
- 591 10-Hébert JL, Lecarpentier Y, Zamani K , Coirault C, Daccache G, Chemla D. Relation
592 between aortic dirotic notch pressure and mean aortic pressure in adults. *Am. J. Cardiol.*
593 1995; 76:301–306.
- 594 11. [Sharma R , kumari P, Malhotra AS.](#) Evaluation and correlation of systolic time intervals
595 (STI) with autonomic functions in young adults *Int J Biol Med Res.* 2012; 3(4): 2588-2592
- 596 12- Ewing DJ , Campbell IW , Burt A A , Clarke BF. Vascular reflexes in diabetic autonomic
597 neuropathy. *Lancet.* 1973; 2:1354–1356.
- 598 13-Ewing D J , Martyn CN , Young RJ , Clarke B F. The value of cardiovascular autonomic
599 function tests: 10 years experience in diabetes. *Diabetes Care*.1985; 8:491–498.
- 600 14- Braunwald E , Colucci WS , Grossman W. Clinical aspects of heart failure: high output
601 heart failure; pulmonary edema. *Heart Disease. A Textbook of Cardiovascular*
602 *Medicine*Braunwald E. SaundersPhiladelphia, PA; 1997. *chapt. 15, p. 445–470.*
- 603 15- Hamilton W F, Woodbury R A, Haper HT. Arterial cerebrospinal and venous pressures in
604 man during cough and strain. *Am. J. Physiol.* 1944; 141:42–45.
- 605 16-Judson WE , Hatcher JD , Wilkins RW. Blood pressure responses to the Valsalva
606 maneuver in cardiac patients with and without congestive failure. *Circulation.* 1955;70:889–
607 899.

608 17- Bernardi L, Saviolo R, Spodick DH. Do hemodynamic response to the Valsalva
609 maneuver reflect myocardial dysfunction? *Chest*. 1989; 95:986–989.

610 18- Gorlin R , Knowles JH , Storey C F. The Valsalva maneuver as a test of cardiac function:
611 pathologic physiology and clinical significance. *Am. J. Med*. 1957; 22:197–212.

612 19- Schmidt DE , Shah PK. Accurate detection of elevated left ventricular filling pressure by
613 a simplified bedside application of the Valsalva maneuver. *Am. J. Cardiol*. 1993; 71:462–
614 465.

615 20- Zema M J, Masters AP, Margouleff D. Dyspnea: the heart or the lung? Differentiation at
616 bedside by use of the simple Valsalva maneuver. *Chest*. 1984;85:59–66.

617 21-Joyner MJ. Effect of exercise on arterial compliance. *Circulation*. 2000 ;102:1214-1215.

618 22-Virmani R, Avolio AP, and Mergner WJ. Effect of aging on aortic morphology in
619 population with high and low prevalence of hypertension and atherosclerosis. Comparison
620 between accidental and Chinese communities. *American J of pathology*. 1991;139(5):1119-
621 29.

622 23 - Gandhi DK, Singh J and Kiran. Gender and autonomic nervous system. *Indian Journal*
623 *of Fundamental and Applied Life Sciences*. 2011; Vol. 1 (4): 172-179.

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635 **ABBREVIATION BMI-Body mass index, G1-Group1, Group2-G2, mS-milli second , NS-**

636 **Non significant, S- Significant , VM-Valsalva maneuver.**

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639 **APPENDIX**