Original Research Article

PILOT STUDY: ESTIMATING SAMPLE SIZE FORTHE PREVALENCE OF PRE-CLINICAL LEFT VENTRICULAR DIASTOLIC DYSFUNCTION USING TWO AMERICAN COLLEGE OF ECHOCARDIOGRAPHY GUIDELINES IN A SEMI-URBAN NIGERIAN POPULATION.

ABSTRACT

Aim: To estimate the sample size for the prevalence of pre-clinical left ventricular diastolic dysfunction using two American college of echocardiography guidelines in a semi-urban Nigerian population.
Study design: Cross sectional, population based
Place and Durationof Study: Neni, Anambra State, Nigeria on the 18th and 19th December 2023.
Methodology: Fifty subjects with age range of 18—70 years were consecutively recruited after a community awareness creation. Subjects gave informed oral and/or written consent before proceeding for an interviewer administered questioning of their biodata and clinical history. Anthropometric measurements were obtained followed by clinical examination and electrocardiography. Echocardiography was done using the American Society of Echocardiography (ASE) guideline with the left ventricular diastolic function assessed using the 2009 and 2016 guidelines.
Results: Mean age of participants was 54.3±14.0 years consisting of 15 males and 35 females. The prevalence of pre-clinical left ventricular diastolic dysfunction was 16% and 14% using the ASE 2009 and 2016 guidelines respectively.
Conclusion: Prevalence enabling accurate sample size calculation for the main study was obtained. Modifications were made to the research proposal based on lessons learnt.

Keywords: [prevalence, pre-clinical, diastolic dysfunction,left ventricular, population, Nigeria]

1.INTRODUCTION

Sample size is the minimum number of subjects needed to answer a research question and it is crucial in the planning and designing of a study. Key components to appropriately estimate sample size are an acceptable level of significance (P value) dependent on alpha, power of the study- complement of beta (1 – β), effect size defined as the minimum difference that is clinically and biologically credible and population variability of an outcome which is usually unknown but can be estimated from a pilot or previous studies. [1,2] Others include 1-tailed or 2-tailed testing, outcome of interest, study design and allocation ratio.[3]

Racial, gender and age differences exist in cardiovascular structure and function, risks of heart failure as well as cardiac response to these risks. [4,5] Black populations have been shown to have a higher arterial afterload, left ventricular (LV) dimension, mass and concentricity. [6,7] Significant differences also exist in the left atrial (LA) dimension, LV ejection fraction (EF), mitral annular velocity, tricuspid regurgitant jet pressure gradient and right ventricular dimension. [4,6,8]

High-quality data is insufficient in Africa. [9,10] Evidence based medicine has become patient centered considering individual differences. Therefore, data from the White population may not be applied completely to native black Africans. To the best of our knowledge, population prevalence on the subject matter is lacking in the African continent. Hence, aim of this pilot

study to estimate the sample size for the prevalence of pre-clinical LV diastolic dysfunction (LVDD) in a semi-urban Nigerian population with normal ejection fraction.

2. MATERIAL AND METHODS

2.1SETTINGS

Neni, a semi-urban population with about 30,000 indigenes and non-indigenes according to a written data from the administrative office of Neni town union in April 2023. It is located in Anaocha Local Government Area (LGA) of Anambra state,Southeastern, Nigeria.[11] The town hosts the headquarters of the LGA, a diagnostic centre of a Federal Teaching Hospital and three primary health care centres.

2.2 SUBJECTS

Fifty persons were recruited consecutively over two days on the 18th and 19th December 2023 at agovernment primary health care centre after awareness was created in churches and by the town crier.

2.2.1 Inclusion criteriaare participants who gave consent for the study and aged between 18 – 70 years.

2.2.2 Exclusion criteria included history of pulmonary vascular, parenchymal or obstructive airway disease, history or evidence of any terminal illness e.g. malignancy, symptoms and signs of heart failure, atrial fibrillation, artificial pacemaker, poor echocardiographic window, ejection fraction less than 52% for males and 54% for females, unreliable determination of diastolic dysfunction, moderate or severe valvular heart disease and cardiomyopathy.

2.3 DATA COLLECTION

2.3.1 Clinical history

An interviewer-based questionnaire was administered to obtain the biodata, history of traditional cardiovascular disease risk factors, obstructive airway and heart failure symptoms.

2.3.2 Blood pressure

Blood pressure (BP) was checked using the oscilliometric method (Omron M3 HEM-RML31 sphygmomanometer was used) on both arms and the arm with the higher reading was used for a recheck after 30mins.

2.3.3 Anthropometry

Weight and height measurements were taken with the subjects standing on a standard weighing scale and stadiometer with no shoes, heavy clothing, or head gear. Both readings were reported to the nearest kilogram and centimetre. Body mass index (BMI) and body surface area (BSA) were calculated using the Du bois formula.

2.3.4 Electrocardiography

A 12-lead electrocardiography (ECG) was performed by a trained technician using Cardiovit AT-1 Schillers(Switzerland) ECG machine.

2.3.5 Echocardiography

Echocardiography was performed using GE healthcare Vivid iq (China) echocardiography machine with a 3SC transducer. One cardiologist with experience in both Asian and Black populations performed the echocardiography using the American Society of Echocardiography (ASE) guideline,[12] in the standard parasternal long (PLAX), apical five (A5C), four(A4C) and two(A2C) chamber views. [13] A two-dimensional (2D)-guided direct measurement of the interventricular septal wall thickness at end diastole (IVSd), LV internal diameter at end diastole (LVIDd), and the posterior wall thickness (PWTd) at end diastole measurements were obtained according to ASE guideline. [12] The machine automatically calculated the EF using the Teichholz's formula. [13]EFgreater than or equal to 54% and 52% wereconsidered normal for females and males respectively. [14] From the A4C view, using the pulse wave doppler (PWD), the sample volume was placed at the tip of the mitral leaflets. The mitral inflow E and A wave velocities were obtained. The machine automatically gave the E/A ratio and deceleration time (DT) on tracing the slope of the E wave. The A wave duration was taken in millisecs. Subjects were asked to bear down to assess changes on the mitral E/A ratio during valsalva manoeuvre. Tissue doppler imaging (TDI) was used to obtain the mitral annular velocities with the sample volume placed at the septal and lateral annulus respectively to obtain the septal and lateral e^{l} velocities. Average of the septal and lateral $e^{l}$was calculated manually. Average E/$e^{l}$was obtained by diving the E velocity with the averagesum of the septal and lateral e^{l} velocities. Continuous wave doppler (CWD) with sample volume placed at the vena contracta of the tricuspid regurgitant jet gave the maximum tricuspid regurgitation velocity (TRVmax) from the spectral envelope. Isovolumic relaxation time (IVRT) was obtained from the A5C view with the PWD, sample volume was placed in the LV cavity to obtain both the left ventricular outflow and mitral inflow spectral profiles.Due to technical challenges encountered in the field the pulmonary venous waves were not used for assessment. Left atrial maximum volume index (LAVI) was obtained in the A4C and A2C views at ventricular end systole using the formula: [15]$LAVI = \frac{8/3 \prod (A1 \times A2)/ L}{BSA} = \frac{8.5(A1XA2)/L}{BSA}$.

after the left atrial areawas traced in both views and assigned A1 and A2 respectively. Length of left atrium (L) was assigned L1 and L2 respectivelyand was measured as a line drawn from the midpoint (of another line, drawn from the mitral septal and lateral annulus) to the roof of the left atrium (LA). The shorter of L1 and L2 was used in the formula.

2.3.5.1*ASE (2009) guideline for diagnosing diastolic dysfunction.* [16,17]

Diagnosis of diastolic dysfunction in the presence of normal EF was made when average e^{l}< 9 cm/sand LAVI≥34ml/m^2.

2.3.5.2*ASE (2016) guideline for diagnosing diastolic dysfunction.* [18]

Diagnosis of diastolic dysfunction in the presence of normal EF was made whenthree out of the four following parameters are present; septal e^{l}< 7cm/s or lateral e^{l}< 10cm/s; Ave E/e^{l}>14; LAVI >34 ml/m^2; TRVmax > 280cm/s

2.4 STATISTICAL ANALYSIS

IBM-SPSS version 25.0 (Chicago Illinois, USA) was used for analysis.Frequency tables, percentages, mean, and standard deviation were used to provide a descriptive summary of the study participants. Prevalence was calculated as the total number of subjects with diastolic dysfunction divided by the sample population.

3. RESULTS

Table 1 shows the socio-demographic profile of the respondents. Table 2 shows history of participants' cardiovascular disease risks and symptoms.

Table 1: Socio-demographic characteristics of respondents.

Variable	Frequency (n=50)	Percent (%)
Age of respondents in years		
Mean±SD	54.3±14.0	
Age of respondents in groups		
<40 years	7	14.0
40-49 years	7	14.0
50-59 years	17	34.0
≥60 years	19	38.0
Gender		
Male	15	30.0
Female	35	70.0
Marital status		
Single	5	10.0
Married	30	60.0
Divorced	13	26.0
Widowed	2	4.0
Educational attainment of respondent		
No formal education	3	6.0
Primary education	12	24.0
Secondary education	16	32.0
Tertiary education	19	38.0
Employment status		
Unemployed	9	18.0
Self-employed	33	66.0
Paid employment	8	16.0

SD- standard deviation

Table 2: Cardiovascular risk factors and symptoms of participants.

Variable	Frequency (n=50)	Percent (%)
History of hypertension		
Yes	24	48
No	26	52
History of diabetes mellitus		
Yes	7	14
No	43	86
History of alcohol use		
Yes	17	34
No	33	66
History of smoking		
Yes	0	0
No	50	100
History of cough		
Yes	1	2.0
No	49	98.0
History of breathlessness		
Yes	12	24
No	38	76
History of leg swelling		
Yes	1	2.0
No	49	98.0

Prevalence of left ventricular diastolic dysfunction using the 2009 ASE guideline was 16% as shown in table 3.

Table 3: Left ventricular diastolic dysfunction using the 2009 ASE guideline.

Variable	Frequency (n=50)	Percent (%)
Ave e^{I}< 9cm/s		
Yes	20	40.0
No	30	60.0
LAVI ≥34ml/m^2		
Yes	29	58.0
No	21	42.0
Diastolic dysfunction (2009)		
Present	8	16.0
Absent	42	84.0

LAVI- left atrial maximum volume index; Ave eI – average sum of the mitral annular septal and lateral velocities

Prevalence of left ventricular diastolic dysfunction using the 2016 ASE guideline was 14% as shown in table 4.

Table 4: Left ventricular diastolic dysfunction using the 2016 ASE guideline.

Variable	Frequency (n=50)	Percent (%)
Septal e^I< 7cm/s or Lateral e^I< 10cm/s		
Yes	28	72.0
No	14	28.0
Ave E/ e^I>14		
Yes	1	2.0
No	49	98.0
LAVI >34 ml/m^2		
Yes	36	56.0
No	22	44.0
TRVmax > 280cm/s		
Yes	14	28.0
No	36	72.0
Diastolic dysfunction (2016)		
Present	7	14.0
Absent	43	86.0

eI – mitral annular velocity; LAVI- left atrial maximum volume index; Ave E/ eI – left ventricular filling pressure; TRVmax- tricuspid regurgitation velocity maximum.

4. DISCUSSION

Prevalence of LVDD in a general population from previous studies [19,20,21,22] outside the African continent varied from 11.1 – 67.4% depending on the population characteristics and diagnostic criteria. The prevalence in a German study [19] dropped to 3.1% when left atrial enlargement was considered. This may explain the low prevalences in our study, as LAVI was a parameter used in both diagnostic guidelines. All [18,21,22] previous but the German study [19] did not consider the left atrial volume in their diagnostic criteria. A dilated LAVI is a marker of chronically elevated left ventricular filling pressure in the presence of other diastolic parameters and also has prognostic implications. A Tibetan study [21] had a prevalence of 34.39% using the 2009 ASE guideline in a population living at a higher altitude than our study participants. Higher altitude is an independent risk factor for LVDD [21,23] and may have contributed to the higher prevalence. Our study excluded subjects with renal dysfunction, coronary artery disease, significant valvular heart disease and cardiomyopathy which a Hispanic study [22] with a high prevalence of 67.4% included.

Limitations of this study are that the sample size calculation is dependent on the value chosen by the investigator(s) which is small therefore, results may differ from large scale studies. Also, causality cannot be established since it is an observational study.

Study is however, feasible with the following recommendations;

1.Data collection should be carried out for nine days with three consecutive days dedicated to each of the three primary health care centres located in the town.

2.Pulmonary venous waveform will not be used in grading diastolic dysfunction as there may be difficulty getting reliable waveforms in the field.

3.Training rehearsals for the data collectors/ interviewers every morning of each study day.

5. CONCLUSION

This pilot study achieved its aim in calculating the sample size for the main study and also proves study's feasibility.

AUTHORS' CONTRIBUTIONS

Udora NC designed the study,wrote the protocol and thefirst draft of the manuscript. Ajulufo IJ managed the literature searches and data collection process. Ossai EN managed the statistical analyses of the study. Ejim EC developed the conceptand design of the study. All authors read and approved the final manuscript.

CONSENT

Informed oral and/or written consent were obtained from all participants after the Traditional Ruler and President General of the town union gave their permissions.

ETHICAL APPROVAL

Ethical approval was obtained from the Health Research Ethics Committee of the University of Nigeria Teaching Hospital Enugu, Nigeria with reference no NHREC/05/01/2008B-FWA00002458-1RB00002323.

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