Fast Assessment of Left Ventricular Systolic Function in Obstructive Sleep Apnea Patients with Automated Function Imaging: Comparison with Mitral Annular Plane Systolic Excursion

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Abstract

Background: Early cardiovascular impairment in obstructive sleep apnea (OSA) patients is often overlooked, leading to irreversible outcome. Left ventricular (LV) global longitudinal strain (GLS) derived from automated function imaging (AFI) echocardiography provides a fast tool to assess global longitudinal function. We therefore aimed to compare the feasibility and reproducibility of AFI with mitral annulus plane systolic excursion (MAPSE) as obesity is common in OSA. Methods: A comprehensive echocardiographic examination was done in 186 consecutive patients having polysomnography for suspected OSA in this prospective study. MAPSE was measured by using M-mode. AFI was derived by offline analysis of three long-axis views that semi-automatically detects LV endocardial boundary, which is adjusted manually as necessary. Variability of AFI and MAPSE were compared among the different subgroups and further tested in BMI subgroups. Results: Despite a relatively high obesity rate (42.9%), AFI was feasible in 94% (175/186) patients and MAPSE could be recorded in all patients. Although more segments were measured with AFI it showed excellent correlation (r=0.882) superior to MAPSE (r=0.819) between the expert and beginner. Intra- and inter- observer variability of AFI were comparable with MAPSE in Bland-Altman analysis, 5.5% and 6.5% for AFI, 6.2% and 8.8% for MAPSE, respectively. In repeated measurements, AFI showed higher intra-class correlation (ICC=0.95) than MAPSE (ICC=0.87). Furthermore, analysis showed that AFI was feasible even in more obese patients (BMI[?]28kg/m2). Conclusions: Even in obese patients with OSA, AFI-GLS is feasible and more reliable for less expert operators than MAPSE for detecting LV longitudinal dysfunction.

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Background : Early cardiovascular impairment in obstructive sleep apnea (OSA) patients is often overlooked, leading to irreversible outcome. Left ventricular (LV) global longitudinal strain (GLS) derived from automated function imaging (AFI) echocardiography provides a fast tool to assess global longitudinal function. We therefore aimed to compare the feasibility and reproducibility of AFI with mitral annulus plane systolic excursion (MAPSE) as obesity is common in OSA.

Methods : A comprehensive echocardiographic examination was done in 186 consecutive patients having polysomnography for suspected OSA in this prospective study. MAPSE was measured by using M-mode. AFI was derived by offline analysis of three long-axis views that semi-automatically detects LV endocardial boundary, which is adjusted manually as necessary. Variability of AFI and MAPSE were compared among the different subgroups and further tested in BMI subgroups.

Results: Despite a relatively high obesity rate (42.9%), AFI was feasible in 94% (175/186) patients and MAPSE could be recorded in all patients. Although more segments were measured with AFI it showed excellent correlation (r=0.882) superior to MAPSE (r=0.819) between the expert and beginner. Intra- and inter- observer variability of AFI were comparable with MAPSE in Bland-Altman analysis, 5.5% and 6.5% for AFI, 6.2% and 8.8% for MAPSE, respectively. In repeated measurements, AFI showed higher intra-class correlation (ICC=0.95) than MAPSE (ICC=0.87). Furthermore, analysis showed that AFI was feasible even in more obese patients (BMI[?]28kg/m^2).

Conclusions: Even in obese patients with OSA, AFI-GLS is feasible and more reliable for less expert operators than MAPSE for detecting LV longitudinal dysfunction.

Running Title: Comparison of AFI and MAPSE in OSA

Key words: Automated function imaging, Mitral annular plane systolic excursion, Global longitudinal strain; Obstructive sleep apnea Words Count: 2,914

The abbreviation list:

AFI = automated function imaging

BMI = body mass index

GLS = global longitudinal strain

ICC = intra-class correlation

LV = left ventricular

MAPSE = mitral annular plane systolic excursion

OSA = obstructive sleep apnea

Introduction

Subclinical left ventricular (LV) dysfunction is common in many systemic diseases and in normal subjects with risk factors for cardiovascular diseases such as hypertension, diabetes, obesity and aging[1-4]. It has been noted the close relationship between obstructive sleep apnea (OSA) and cardiovascular diseases[5-6]. However, detecting subclinical cardiac dysfunction is often difficult with conventional echocardiography in obese subjects and this is common in OSA, with a prevalence of about 70%[7-9]. A simple and precise screening method to detect early changes of subclinical cardiac dysfunction would be useful. Automated function imaging (AFI), based on 2-dimensional speckle tracking echocardiography with angle-independence, has been introduced to measure LV systolic function by calculating the regional and global longitudinal strain (GLS)[10,11]. AFI uses semi-automated algorithms for endocardial tracking with manual adjustments when needed. As a semi-automated measurement, it is less time consuming and less experience dependent. A previous study showed that GLS was a major predictor of cardiac events in a low risk general population[12]. However, many patients may have relatively inadequate echocardiographic windows, which may reduce the general applicability of AFI. And it needs dedicated software which may not be accessible in every echocardiographic laboratory. An older M-mode method of mitral annular plane systolic excursion (MAPSE) is often used in patient with a poor acoustic window for a simple and rapid assessment of LV function[13,14]. No comparison of these two methods has been reported.

Accordingly, the present study was designed to evaluate the feasibility and reliability of LV longitudinal strain calculated by advanced AFI, based on 2-dimensional echocardiography compared with another simple and fast method, i.e., MAPSE.

Methods

Enrollment

This prospective study consecutively recruited 186 patients from Aug 2017 to Jun 2018 with overnight polysomnography monitoring and comprehensive transthoracic echocardiography. Inclusion criteria was : 2-dimension images were able to fully display the entire LV in any apical orientation. Exclusion criteria were as follows : (1) history of valve replacement; (2) arrhythmia during acquisition; and (3) mitral annular calcification. This study was registered in Chinese Clinical Trial Registry ***(http://chictr.org.cn:Clinical Trial: ChiCTR-ROC-17011027)*** and was approved by Anzhen Hospital Ethics Committee. Consent forms were obtained from all patients.

Polysomnography

All participants underwent an overnight PSG (Compumedics, Grael, Australia) under continuous sleep technician monitoring, which confirmed the diagnosis of OSA according to the recommendations of the American Academy of Sleep Medicine[15]. The recording included 6 channels for electroencephalography, 2 channels for electro-oculography, 2 channels for reference electrodes, submental electromyography, oral and nasal airflow (heat sensitive and pressure can be monitored at the same time), chest and abdominal excursions, blood oxygen saturation, tibial electromyogram, body position detector, electrocardiogram and tracheal sound.

Two-dimensional Transthoracic

echocardiography

Echocardiographic images were acquired by an experienced operator. All patients underwent complete transthoracic echocardiography studies (Vivid E9, GE-Vingmed Ultrasound AS) using a 2.5-3.5 MHz transducer. Echocardiographic images were taken with patients in the left lateral decubitus position and acquired three consecutive cardiac cycles with frame rate [?] 60Hz for offline analysis on the EchoPAC (GE Healtcare, version 201, Norway).

MAPSE was measured by using the apical-4 chamber view focused on left ventricle and placing cursor at mitral annulus near to the lateral wall (Figure 1) . LV longitudinal strain was assessed by 2- dimensional based AFI. Off-line analysis of apical, 4- and 2-chamber images were completed by semi-autotracing the endocardium[16](Figure 2) . AFI tracked a small region of gray-scale echocardiographic pattern of myocardial regions over the cardiac cycle. The width of the region of interest was automatically adjusted by the software, including the entire myocardium. The end of systole point was defined on the apical long-axis view and the timing of the aortic valve closure was automatically defined with the software. GLS was derived when at least 16 of 17 LV segments were analyzable with automated detection or acceptable after manual adjustment. Off-line measurements were performed by the same individual.

Reproducibility analysis

To test the intra-observer reproducibility of AFI and MAPSE, the measurements were repeated by the same operator at least a week later (Expert 1A and 1B) and the correlation of AFI measurement with or without manual adjustment was compared. We spent a few minutes to teach a novice operator (Beginner) these two methods of measurement. Then,32 randomly selected patients were repeated by the Beginner to test the inter-observer variability, who was blinded to the measurement of the Expert. The reproducibility of AFI and MAPSE was evaluated by Beginner and Expert in 16 patients with relatively poor image quality. Further analysis was in different body mass index (BMI) subgroups (normal: BMI<24kg/m^2; overweight: 24kg/m^2[?]BMI<28kg/m^2; obesity: BMI[?]28kg/m^2)[17]. Randomly selected 10 patients in every BMI subgroup and the variability of AFI and MAPSE was analyzed.

Statistical analysis

All continuous variables were expressed as mean ± SD, and categorical variables were shown as numbers and percentages. For each technique, the measured parameter (AFI and MAPSE) was compared between the expert and the beginner using linear regression with Pearson correlation coefficients. Bland-Altman analysis was used to assess the bias and limits of agreement and measurement variability, and was expressed as the absolute difference of the corresponding pair of repeated measurements in percentage of their mean in each patient and then averaged over the entire study group. Intra-observer variability was quantified by calculating intra-class correlation (ICC) coefficients. A significant difference was defined as $p< 0.05$ (2-tailed). Statistical software of SPSS version 17 (SPSS Inc., Chicago, Illinois, USA) was used.

Results

Demographic Data

A total of 186 patients were screened, and 175 subjects (46±12 years) were finally analyzed after excluding 11 patients (6%) in whom AFI could not be obtained due to unsatisfactory tracking. Clinical characteristics of the study population were presented in **Table 1** .

Feasibility of AFI and MAPSE

Overall, AFI was feasible in 94% patients (n=175 in 186 patients) despite relatively high obesity rate of 42.9% (defined as BMI [?] 28kg/m^2), Region of interest was quickly manually adjusted during AFI curve processing in 73 patients (42%) to optimize the assessment. MAPSE could be acquired in all patients.

Variability of AFI and MAPSE

The result showed that with or without manual adjustment the correlation of AFI between the expert and beginner were similar (r=0.896, r=0.874 respectively). Of the randomly selected 32 patients (male 94%, 48+-10 years, BMI 29.9+-4.0 kg/m^2) AFI showed excellent correlation (r=0.882) superior to MAPSE (r=0.819) between the expert and beginner (Figure 3) . The intra- and inter-operator variability was 5.5% and 6.5% for AFI; 6.2% and 8.8% for MAPSE, respectively (Table 2) . The intra- and inter-operator repeatability for AFI were 2.6% and 3.1%, while 2.3% and 3.7% for MAPSE(***Figure 4 & Table 2***) . Regarding those with relatively poor image quality, the variability parameters were 5.7% and 7.1% for AFI, and 6.8% and 8.2%

for MAPSE (Figure 5 & Table 3) . Intraclass Correlation analysis were 0.95 and 0.87 for AFI and MAPSE, respectively (both $p<0.001$).

Stratification by Body Weight

To further assess the feasibility of AFI in obese patients, we randomly selected 10 patients in every BMI group (Normal: BMI<24kg/m^2, n=25; Overweight: 24[?]BMI<28kg/m^2, n=75; Obese: BMI[?]28kg/m^2, n=75). Bland-Altman analysis showed that intra-operator variability in each BMI group were 3.8%,4.3% and 4.1% for AFI, and 9.4%,7.9% and 9.9% for MAPSE; and inter-operator variability was 3.8%,6.3% and 6.6% for AFI, and 6.7%,8.6% and 9.0% for MAPSE (Table 4) . Intraclass Correlation analysis was done for both AFI and MAPSE in every subgroup, the corresponding values were 0.963,0.951,0.897 and 0.942,0.792,0.872 respectively (all $p<0.001$).

Discussion

To our best knowledge, the present study was the first to compare MAPSE with AFI in evaluating LV longitudinal contractile function in patients with OSA. In our study, the feasibility of AFI was acceptable even superior to MAPSE in OSA, a population predominantly obese. AFI-GLS is more reliable for less expert operators than MAPSE for detecting LV longitudinal dysfunction.

LV longitudinal function is a sensitive marker of LV subclinical dysfunction due to pathologic diseases or aging. Both GLS derived from AFI and MAPSE measured with M-mode are simple and fast methods to assess LV longitudinal contraction. Despite the two methods being fast, AFI is more comprehensive with global and regional assessment, and has been validated in normal subjects[1,2,4]. We demonstrated firstly its good performance even in difficult cases with satisfactory results. A possible reason for the improved reproducibility and accuracy compared to MAPSE may be related to the semi-automated speckle tracking algorithm. This is because manual measurement of MAPSE starts with no predetermined profile of mitral annulus displacement throughout the cardiac cycle. And the users determine the border position according to their personal preferences.

Advantage of Automated Function Imaging over MAPSE

In clinical practice, manual acquisition of 2-dimensional speckle tracking measurement can be cumbersome and off-line data analysis time consuming. With the introduction of AFI, the widespread usage of 2-dimensional speckle tracking method becomes more feasible[18]. The simple manual adjustment of automatic endocardial border recognition is also efficient to improve the accuracy of LV quantification analysis. Our results showed that both the feasibility and reproducibility of AFI measurement was good even without manual adjustment, and AFI showed comparable and was even better than MAPSE, which has been recognized to be a robust and simple method to measure LV longitudinal function. Another advantage of AFI over MAPSE is angle independence as the myocardial speckles are tracked to calculate strain from 17 LV segments.

Advantage of MAPSE over Automated Function Imaging

Overweight is common in China, with a prevalence of about 33.8%[19] and creates difficulties in obtaining good images. For those who have inadequate images for AFI, the simple M-mode based MAPSE could be an alternative[20], but it is limited by incomplete assessment of LV longitudinal function even though the movement of the mitral annulus integrates regional motion. Previously, some studies have shown that MAPSE can be an indicator of disease prognosis[13,14,21]. MAPSE does not require a good acoustic window, and thus can be applied when visualization of the endocardial border is not obtainable. In our study, although obese patients accounted for nearly half, AFI showed comparable intra- and inter-observer variability to MAPSE. But the successful measurement was higher with MAPSE than AFI since in some difficult case, the endocardial border was not delineated. Further innovation with higher frame rate and penetration ability may resolve the problem.

Clinical Implication

LV function assessment is useful to guide clinical management and in clinical trials. But the most frequently utilized parameter LV ejection fraction can be normal despite abnormalities of LV diastolic and longitudinal systolic function[22,23]. Impaired longitudinal ventricular function is one of the earliest signs of myocardium dysfunction. GLS has been shown to predict major cardiac events and long-term mortality in several cardiac diseases[24-26]. Furthermore, GLS appears to have superior prognostic value to ejection fraction for predicting major adverse cardiac events[27]. The early awareness and detection of cardiac dysfunction is crucial in OSA patients due to its close relationship with cardiovascular diseases. Our study reveals that GLS based on automated imaging allows rapid acquisition and analysis even in relatively overweight patients. Meanwhile, non-cardiologists can quickly evaluate cardiac function of OSA patients by AFI. Compared with MAPSE, it is a convenient method to be applied clinically with more comprehensive information.

Studies Limitations:

There are several limitations for this study. First, AFI tracked 16 segments instead of 17 segments of the LV myocardium in 10 patients, but it is allowed according to the standard of procedure in AFI analysis. Second, MAPSE was assessed in LV lateral wall instead of both annuli.

Conclusion

The present study suggests that AFI, which is based on 2-dimensional speckle tracking, is much easier and faster to assess LV function. There is some limitation in that about 6% of patients' images could not be produced. In these cases, MAPSE can still be used to assess LV systolic longitudinal function especially if dedicated software for speckle tracking is not available.

Authors' Note

F Fang contributed to the study conception and design. Material preparation, data collection and analysis were performed by CY Ma, Q Chen, XJ Zhan, C Wu, H Liu and L Xiao. The first draft of the manuscript was written by CY Ma. F Fang, J E Sanderson and YX Wei supervised the research and revised the manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The authors declare that they have no conflict of interest.

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FIGURE LENGENDS

Figure 1. The measurement of MAPSE.

Figure 2. The measurement of AFI**.**

Figure 3. Results of linear regression analyses for AFI (left) and MAPSE (right) between the expert and beginner.

Figure 4. Results of Bland-Altman analysis for AFI and MAPSE measurements by Expert 1A versus Expert 1B (**Fig. 1A**) (**Fig. 1B**), Beginner versus Expert 1A (**Fig. 1C**) (**Fig. 1D**).

Figure 5. Results of Bland-Altman analysis for AFI and MAPSE measurements in patients with relatively poor image quality by Expert 1A versus Expert 1B (**Fig. 2A**) (**Fig.2B**), Beginner versus Expert 1A (**Fig.2C**) (**Fig.2D**).

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