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Evaluating the Relationship Between Measures of Diastolic Function and Exercise Capacity in Young and Healthy Adults: A Retrospective Analysis

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Abstract

Background: Diastolic function during exercise is typically assessed via relationships between the early mitral inflow velocity (E) and early mitral annular tissue wave velocities (e'). Data involving patients over 50 years old suggests an increase in E/e' with exercise indicates diastolic dysfunction. Limited data in young and healthy patients however suggests increases in E/e' may actually be indicative of increased exercise capacity within this patient population, rather than diastolic dysfunction.

Objectives: To determine correlation between changes in E/e' and exercise capacity in a population of young and healthy adults.

Methods: This retrospective study included 19 (12 men, 7 women) patients between the ages of 18-40 years that did not have a diagnosis of any cardiac or pulmonary disease who underwent exercise stress echocardiography. The primary outcome was the relationship between change in E/e' and maximum METs achieved during testing. Secondary outcomes included sex-specific relationships between changes in E/e' and overall performance on exercise stress testing.

Results: Statistical analysis showed that increases in E/e' values correlated with improved stress test performance (r = 0.65). The secondary outcome of sex-related changes in E/e' from pre- to post-stress was significant in that the E/e' in males increased by an average of 0.59 (SD 0.69) while female E/e' had a non-statistically significant decrease with a mean change of -0.02 (SD 1.15). Overall, there was no significant change in E/e' when comparing pre-and post-stress imaging.

Conclusions: The study observed that while there was no significant change in E/e' from pre- to post-stress, an overall increase in E/e' value was positively correlated with maximum METs achieved during exercise stress testing, particularly in males.

Keywords: Diastology; Stress Echocardiography; Transmitral velocity; Mitral annular tissue wave velocity.

Introduction

Diastology is an inherently complicated process, and its dysfunction is the cause of heart failure with preserved ejection fraction. Standard assessment of diastolic function via echocardiography involves several variables, most important of which being early diastolic transmitral velocity (E), early diastolic mitral annular tissue velocity (e'), and late diastolic transmitral velocity (A).

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Prior studies have shown that E/e' values above normal limits (>14) both at rest and during exercise are due to high left ventricular filling pressures and are therefore suggestive of diastolic dysfunction [1,2]. In particular, when E/e' increases with exercise, this has been thought to be due to an increase in left ventricular filling pressures which suggests exercise-induced diastolic dysfunction. Notably, all of the patients analyzed in these past studies were greater than 45 years of age at time of testing. To date, there have been very few studies that analyze the relationship between diastolic measurements in stress echocardiography and exercise stress test performance in a young and healthy population. Interestingly, the limited data that does exist has found that athletes have a higher left ventricular filling velocity at rest, and that with higher increases in E/e' during exercise, individuals were able to achieve a greater exercise performance [3,4]. These findings contradict the commonly accepted notion that increases in E/e' with activity always suggest diastolic dysfunction.

Given that most guidelines surrounding the stress echocardiography-based diagnosis of diastolic dysfunction are based on data that has been extrapolated from older populations [2,5], the interpretation of diastolic parameters in stress echocardiography involving healthy patients less than 40 years of age remains unclear. In order to shed light on the theory that traditional measures of diastolic dysfunction may be inaccurate in this population, this study aims to further clarify the relationship between traditional echocardiographic measures of diastology and maximal exercise performance in young, healthy adults.

Materials and Methods

This investigation was a retrospective cohort study that utilized patient EMRs at a large, urban academic medical center. Inclusion criteria consisted of patients between the age of 18-40 years that had undergone exercise stress TTE between 2019-2024. Exclusion criteria included a diagnosis of atrial fibrillation, hypertension, coronary artery disease, peripheral vascular disease, COPD, asthma, valvular heart disease, and use of any cardiac-related medications including anti-hypertensives, beta blockers and calcium channel blockers. All patients underwent treadmill exercise stress testing via standardized Bruce protocol.

Data that was recorded included demographic information (sex and age) in addition to BMI, medial and lateral E and e' at rest and immediately post-exercise, and maximal METs achieved during stress testing. After all records were reviewed, a total of 19 patients (12M, 7W) met inclusion criteria.

Statistical relationships between variables were analyzed using linear regression analysis and student's T-test to determine significance. These relationships are outlined in table 1. Primary outcomes consisted of relationships between changes in E/e' (averaged medial and lateral ratios) and maximal METs achieved, while secondary outcomes involved relationships between E/e' and sex, as well as sex and maximal METs achieved.

Results

Analysis indicated that overall, there was no significant increase in E/e' values immediately after completing exercise stress testing when compared to baseline measurements, and all post-exercise E/e' measurements were found to be within normal limits (<14) for young, healthy adults. However, there was a significant linear relationship between overall increase in E/e' from pre to post stress and maximum METs achieved during stress as illustrated in figure 1 (r=0.649). In addition, significant secondary outcomes surrounding male vs. female comparisons were found. Most notably, men achieved both higher maximal METs (p=0.003) while also having a positive change in E/e' between rest and stress when compared to females, as seen in figure 2.

Table 1: Demographics and Intersex Comparison of Data

Characteristic	Overall N = 19	Female N = 7	Male N = 12	p-value
Average Age in Years (mean ± SD)	30.53 (6.40)	33.4 (5.91)	28.83 (6.28)	0.13
Average Baseline E/E' (mean ± SD)	6.36 (2.37)	8.1 (3.04)	5.34 (1.02)	0.053
Average Peak exercise E/E' (mean ± SD)	6.33 (1.68)	7.03 (2.39)	5.93 (1.01)	0.28
Average Maximum METs Achieved (mean ± SD)	13.72 (4.26)	9.86 (3.54)	15.98 (2.79)	**0.003**
Average BMI (mean ± SD)	28.91 (8.15)	32.5 (7.11)	26.81 (8.25)	0.13
Average Change in *lateral* E/E' (mean ± SD)	0.26 (0.76)	-0.17 (0.83)	0.51 (0.63)	0.090
Average Change in *septal* E/E' (mean ± SD)	-0.08 (1.72)	-1.59 (1.82)	0.67 (1.10)	0.027
Change in E/E' from pre to post stress (mean)	-0.02 (1.15)	-1.07 (1.03)	0.59 (0.69)	**0.004**

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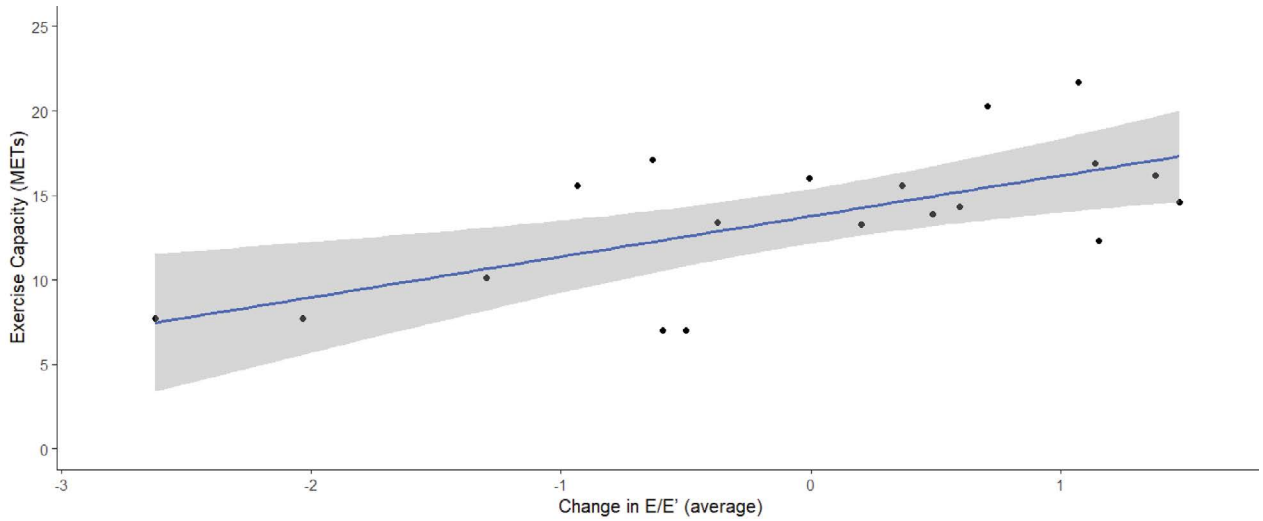

Figure 1: Relationship Between Exercise Capacity and Change in E/e' (average of lateral and septal values) from pre-to-post stress (r=.649).

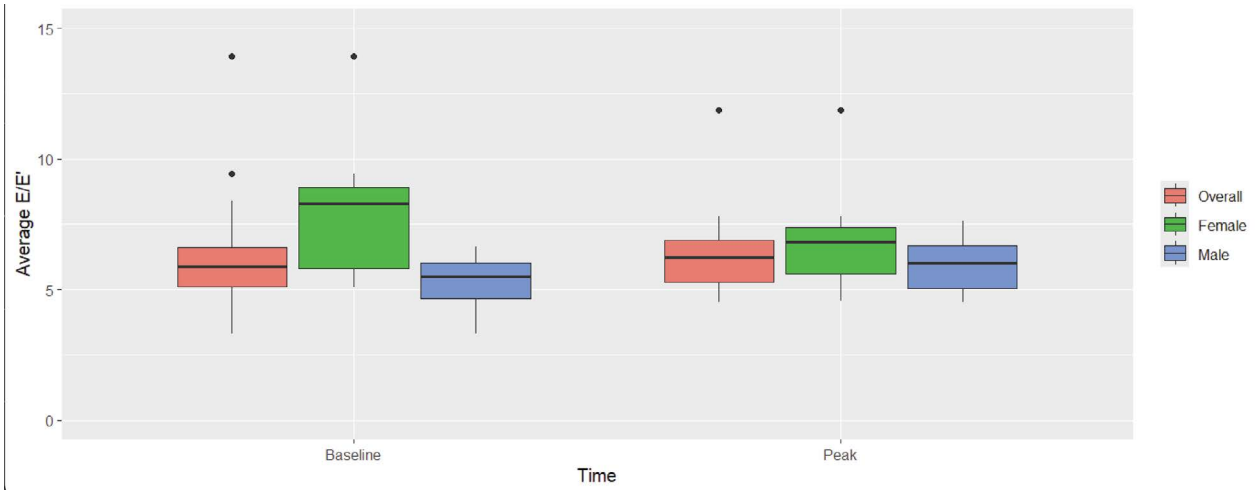

Figure 2: Relationship Between Male and Female Changes in E/e' from Baseline to Peak Exercise

Discussion

The findings of this study highlight the fact that the same echocardiographic changes that are observed during stress echocardiography can mean significantly different things depending on the patient population being tested. Myocardial relaxation and elastic recoil have been shown to decline significantly with age, thus in a middle aged to older patient population, an increase in early diastolic filling velocity (E) is likely due to an increase in pressure of the left atrium as a result of inefficient left ventricular relaxation during stress [6]. However, in a young and otherwise healthy population, the increase in filling velocity is more likely to be due to increased myocardial relaxation as well as more efficient systolic emptying [7]. As the heart continues to squeeze more vigorously and relax more efficiently during stress, the left ventricular inflow velocity will continue to increase. Although the mitral annular tissue velocities continue to increase as well, it can be expected that the increase in inflow velocity will exceed the increase in tissue wave velocity in this population during exertional activity. This was previously shown to occur during or immediately after exercise on a stationary bicycle, and our investigation shows that this process continues to occur more robustly with increasing time and exercise intensity on a treadmill [3].

Given that larger increases in E/e' values were seen with increased exercise capacity, this strongly suggests a physiologic relationship between these variables in the young and healthy patient population. Separating exercise-induced diastolic dysfunction from normal physiology has significant clinical implications, as the diagnosis of stress-induced diastolic dysfunction can suggest the presence of significant cardiac pathology in an individual who does not truly have cardiac disease. This type of misdiagnosis can lead to inappropriate false positives in TTE-based screenings, such as those utilized to assess fitness for athletic activity. Fortunately, some differentiation can be made by using

absolute values of E/e'. According to latest guidelines, stress-induced E/e' ratios above 14 are indicative of stress-induced diastolic dysfunction [8]. Given that the absolute E/e' values in the current and prior studies are much below 14, using established guidelines within this population should prevent any inappropriate diagnosis of stress-induced diastolic dysfunction.

Finally, this study demonstrates an interesting sex discrepancy in the E/E' changes with exercise. Although there was a small sample size of females, this cohort showed a slight decrease in E/e', whereas males showed an increase in E/e' with exercise. Given the small sample sizes of the individual groups, neither finding was statistically significant, but the trend does bring up a discussion worth investigating. Prior data shows that vigorous cardiovascular exercise has significantly different effects on males vs. females in several ways. Specifically, men who engage in regular high intensity activity are at a higher risk for atrial fibrillation, development of coronary artery calcification, and overall risk for sudden cardiac death with exercise when compared to women [9,10,11]. The fact that men achieved a significantly higher amount of METs with activity is certainly a possible confounding factor, and further assessment of this relationship could be assessed with a larger patient population.

Conclusion

The study observed that while there was no significant change in E/e' from pre to post stress, a larger increase in E/e' value was significantly and positively correlated with maximum METs achieved during exercise stress testing, particularly in young and healthy males. While a magnitude of data exists surrounding measures of diastolic function in older patients with various comorbidities, this study supports the theory that typical measures of diastolic function, particularly those employed in stress echocardiography, are not as straightforward in young and healthy patients. Future research regarding this phenomenon should both involve a larger number of subjects, in addition to focusing on well-trained athletes and measures of their diastolic function via echocardiography.

Limitations

Although there was a positive correlation between increase in E/e' and functional capacity, there were limitations which likely prevented the findings from being more robust. To begin with, this was a retrospective study, and the stress echoes performed were not primarily focused on diastology. As a result, the diastolic assessment was performed after the wall motion assessment, meaning that the diastology assessment was not truly immediately post exercise. Because of this, the increase in E/e' values were likely not as robust, and this may be why there was not a statistically significant difference between pre and post exercise E/e' values. Additionally, the small sample size of individuals from the general population minimized the ability to generate a stronger correlation. Although the data allows us to generalize the results to a broader population, a larger group of more active individuals likely would have shown a more significant increase between pre and post E/e' values. Future studies should direct their attention towards a larger group of young elite athletes, as the effects of vigorous aerobic physical activity are known to drastically change the heart's form and diastolic function [12].

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Conflicts of Interest: None to report

Ethics approval and consent to participate

This study was approved by the institutional review board of Rush University Medical Center.

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