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Left Atrium Measurements via Computed Tomography Pulmonary Angiogram as a Predictor of Diastolic Dysfunction

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Abstract

PURPOSE—Left atrium (LA) enlargement on echocardiography may be an indicator of diastolic dysfunction (DD). It is not well known if computed tomography pulmonary angiography (CTPA) can detect DD.

METHODS—127 patients who underwent both CTPA and echo within 48 hours were analyzed retrospectively. LA diameters from CTPA were correlated with echo and evaluated against degrees of DD. CTPA pulmonary artery (PA)/Aorta ratio was analyzed as a tool to detect pulmonary hypertension.

RESULTS—42% of patients had DD. There was a strong correlation between LA size on CTPA and echo ($r=0.78$). A LA>4.0 cm gave a sensitivity of 68.1% and specificity of 73.9% for DD detection. A PA/Aorta cutoff >0.84 yielded a sensitivity of 84% and specificity of 33% for pulmonary hypertension.

CONCLUSIONS—CTPA measurements of LA and PA/Aorta ratio correlate strongly with equivalent findings on echo. We suggest that LA and PA/Aorta measurements be included on chest CTPA reports.

Keywords

Diastolic Dysfunction; Pulmonary Hypertension; Left Atrium; Computed Tomography (CT); Echocardiography

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Introduction

Diastolic dysfunction refers to the pathophysiologic phenomenon characterized by abnormal filling and relaxation of the left ventricle.(1) It often leads to a diagnosis of heart failure with a preserved ejection fraction (HFpEF), but it can occur whether the ejection fraction is preserved or reduced.(1) Previous studies have shown that a new or worsening diagnosis of diastolic dysfunction is associated with an increased risk of heart failure.(2) In addition, Gerber et al demonstrated that the proportion of heart failure patients with HFpEF has increased over the last decade.(3) The mortality, morbidity and health care costs of HFpEF are exceptionally high, with hospitalization rates similar to patients with heart failure with reduced ejection fraction.(4–6) Therefore, it is essential to identify diastolic dysfunction using all available data sources.

Diastolic dysfunction is routinely evaluated with echocardiography (echo) and is one of the key criteria for the diagnosis of HFpEF.(7) Enlargement of the left atrium (LA) and increased pulmonary artery (PA) pressures are often associated with HFpEF.(8) Left atrial size can be quantified on echo either by LA diameter measurement, which when enlarged is highly specific for LA dilation, or by using the preferred method of left atrial volume index estimation.(9) Since the LA is a good indicator of diastolic dysfunction, as well as overall function of the heart, clinicians sometimes refer to it as the “hemoglobin A1C of the heart”. (10–12)

In a recent article, the authors demonstrated that between 1996 and 2010 the number of chest CT scans has continued to increase, with an annual rate of approximately 23 per 1000. (13) This increase in scans has led to a wide array of CT measurements available to clinicians, including LA size. For instance, a study by Al-Mohaissen *et al* compared ECG-gated cardiac CT-calculated LA volumes against echo LA volumes and found that while there was good correlation, echo derived volumes often underestimated those calculated using CT modalities.(14) While these studies have validated equations that calculate LA volumes using CT, it has not yet been established if LA diameter measured on standard CT pulmonary angiography (CTPA) correlates with echo derived LA dimensions. Here we have demonstrated a quick and simple method to evaluate LA sizes in patients who have underwent CT examination that correlates well with echo LA measurements. We undertook this study to provide clinicians with a method for detection of diastolic dysfunction, as well as to corroborate the correlation between pulmonary artery size on CTPA and presence of elevated estimated PA pressure.

Methods

This was a single center, retrospective cross-sectional analysis of patients presenting to University Hospital in New Orleans, Louisiana with a chief complaint of either dyspnea, syncope or chest pain, who had undergone both CTPA and echo within 48 hours of each other. This study was conducted in accordance with the amended Declaration of Helsinki. Local institutional review boards or independent ethics committees approved the protocol, Louisiana State University Health New Orleans Institutional Review Board #8358.

Patient Selection

200 consecutive patients between 1/1/2008 and 6/14/2013 were originally identified for this study by searching for patients who had undergone both CTPA and echo after presenting to University Hospital for dyspnea, syncope or chest pain. Manual data acquisition from patient charts was done on those that met the inclusion criteria of: age ≥ 18 years and CTPA and echo within 48 hours of each other. Patients were excluded due to uninterpretable CTPA or incomplete chart data (figure 1).

Data Acquisition

Left atrial size was determined on non-ECG gated CTPA using the maximum anterior-posterior diameter of the midline in its middle 50% (figure 2, panel A). Pulmonary artery sizes were measured using the widest diameter perpendicular to the long axis at the level of pulmonary artery bifurcation.(15) Ascending aorta diameter was measured at the same level, and was used to calculate the PA/Aorta ratio in order to standardize PA sizes (figure 2, panel B). A value of >0.84 was considered enlarged.(16) All CTPA measurements were determined by two independent, board-certified chest radiologists who were blinded to echo measurements or clinical parameters; values from both radiologists were averaged. LA size, PA pressure, left ventricular function and diastolic function were taken from echo reports. LA enlargement was defined as a LA >3.8 cm in female patients and >4.2 cm for males.(17) Left ventricular ejection fraction (LVEF) was measured according to guidelines and a decreased LVEF was defined as being $<55\%$. All mild, moderate and severe values for mitral and tricuspid regurgitation were included in the echo findings. Severity of diastolic dysfunction was graded based on consensus guidelines.(8) An estimated systolic PA pressure on echo of >35 mmHg was defined as being elevated.(18,19)

Statistical Analysis

CTPA measurements for LA and PA sizes were compared against sizes and pressures gleaned from echo reports. CTPA LA and PA/Aorta measurements made by both radiologists were compared against each other using linear regression with a Pearson correlation coefficient. Correlations between LA size on CTPA and echo were measured using linear regression again using Pearson correlation coefficients, as well as Bland-Altman plots. CTPA-determined PA size was compared to echo PA pressures using unpaired, two-tailed t-tests. CTPA LA sizes were analyzed in patients with normal or abnormal diastolic function using unpaired, two-tailed t-tests and analysis of variance (ANOVA); a receiver operating curve was used to evaluate a cut off for LA sizes with abnormal diastolic function. A p value of <0.05 was considered significant. Statistical analyses were performed using Graphpad Prism 6 software (Graphpad software Inc.).

Results

A convenience sample of 200 consecutive patients from University Hospital in New Orleans was selected for this study. Of those, 127 met eligibility criteria (figure 1) with exclusions resulting from either incomplete CTPA data (n=45), a greater than 48-hour time frame between scans (n=13), or echo reports lacking LA measurements (n=15). The average age of the study group was 54.5 ± 12.1 years, with a body mass index of 30.4 ± 9.6 kg/m² and 51%

were female (table 1). The average time between CTPA and echo studies was 15.5 ± 11.8 hours. Not surprisingly, the two major comorbidities in this study were hypertension (72%) and diabetes (38%). In addition, there was a strong inter-reader correlation between measurements of LA ($r=0.94$, 95% CI 0.91–0.95, $n=127$) and PA/Aorta ratio ($r=0.77$, 95% CI 0.69–0.83, $n=127$) made by both radiologists.

Left atrium size and diastolic dysfunction

In order to assess the ability of an enlarged LA measured on CTPA to serve as an indicator for diastolic dysfunction, we first evaluated the reliability of CTPA when measuring LA sizes. To do this, we plotted LA sizes measured on CTPA against those obtained from echo reports (figure 3A). There was a strong correlation of between LA sizes measured on CTPA and those obtained from echo reports, ($r=0.78$, 95% CI 0.70–0.84, $n=127$). This was further supported when LA measurements from both modalities were analyzed for variance using a Bland-Altman plot (figure 3B). There was a minimal average discrepancy in LA sizes between CTPA and echo imaging (bias=0.07, 95% limit of agreement= -0.56 to 0.71 , $n=127$).

Patients were divided into four groups (normal, mild, moderate or severe) based on classification of their diastolic function from echo reports. CTPA left atrial sizes were then compared for each of the four groups (figure 4A). There was a significant difference in CTPA left atrial size between patients with normal diastolic dysfunction on echo (3.59 ± 0.80 cm, 95% CI 3.39–3.79 cm, $n=65$) and those with moderate (4.25 ± 0.66 cm, 95% CI 3.99–4.51 cm, $n=27$) or severe dysfunction (4.56 ± 0.42 cm, 95% CI 4.25–4.87 cm, $n=10$) ($n=112$, $p<0.0001$). There was no significant difference between the normal and mild dysfunction groups (4.12 ± 0.62 cm, 95% CI 3.68–4.56 cm, $n=10$). A receiver operating curve, with an area under the curve of 0.75 ($n=112$, 95% CI 0.66–0.84), was used to calculate sensitivity and specificities for several LA sizes (figure 4B). Using a LA size of 4.0 cm, a value between the previously reported cutoffs of 3.8 cm for women and 4.2 cm for men (17), gave a sensitivity of 68.1% (95% CI 52.9–80.9%) and specificity of 73.9% (95% CI 61.5–84.0%), with a likelihood ratio that a patient would have diastolic dysfunction of 2.6. To further assess the validity of using CTPA LA sizes to comment on diastolic dysfunction we correlated them to a known measurement of diastolic function, E/E' (20) (Figure 4C). There was a moderate, positive correlation of 0.45 between CTPA LA size and echo E/E' (95% CI 0.24–0.61, $n=76$).

PA/Aorta ratio and pulmonary pressures

Next, we looked at PA/Aorta ratios measured on CTPA for patients with elevated estimated pulmonary pressures on echo against those with normal pressures (figure 5). Our data confirmed the previous assessments that PA/Aorta ratios measured on CTPA were significantly larger in the group with elevated pulmonary pressures on echo (0.98 ± 0.16 , 95% CI 0.93–1.04, $n=38$), when compared to those with normal pressures (0.89 ± 0.12 , 95% CI 0.86–0.93, $n=49$). Using a cutoff ratio of >0.84 yielded 65 patients (75%) with an abnormal PA/Aorta ratio. Of these 65 individuals, 32 (49%) had an elevated estimated pulmonary pressure on echo. The sensitivity of this cutoff value was 84% and the specificity was 33%. Using a PA/Aorta ratio >1.0 yielded a sensitivity of 29% and specificity of 88%.

Discussion

The mortality and morbidity as well as health care costs are exceptionally high for HFpEF and are comparable to heart failure patients with reduced ejection fraction.(4–6) The initial symptoms can be silent and the disease is often unrecognized until its later stages.(21) These reasons offer a compelling argument for the increased detection of diastolic dysfunction.

This paper, focusing on the reliability of CTPA based LA and PA measurements, has several key findings. To our knowledge, this is the first study that has compared LA diameters using both standard CTPA and echo modalities. Previous studies have used advanced formulaic calculations to compare LA volumes from CT and echo.(14) However, we were interested in validating a quick and simple technique that all radiologists/clinicians could use as an initial guide in the evaluation of diastolic dysfunction or pulmonary hypertension.

First we have demonstrated that there exists a strong correlation between LA sizes measured on CTPA and echo. Second, the data suggest that LA measurements via CTPA could be used to identify patients with moderate to severe diastolic dysfunction. In fact, if a cutoff of 4.0 cm was used as a standard for LA enlargement on CTPA, the test would have a sensitivity of 68% and a specificity of 74%. This number is the median size for LA enlargement for both men and women as previously reported.(17) Clinicians using this cutoff value could indicate that a patient is over 2.5 times more likely to have diastolic dysfunction than not.

Furthermore, one of the most efficient tools for estimating filling pressures on echo is the early mitral inflow velocity to mitral annular early diastolic velocity, otherwise known as the E/E' ratio.(20,22) An E/E' between 8 and 15 is suggestive of diastolic dysfunction.(7) Here we have demonstrated that CTPA LA measurements have a moderate correlation with E/E' ratios, thus further substantiating the ability of CTPA to identify cases of diastolic dysfunction. These findings are important as only 2% of our sample population had a definitive diagnosis of HFpEF, while ultimately 42% had evidence of diastolic dysfunction after undergoing evaluation by echo.

Diastolic dysfunction can be associated with a number of other co-morbidities, including pulmonary hypertension.(21,23) Previous trials had examined the role of CTPA measurements of the PA and aorta in diagnosing pulmonary hypertension by comparing them to pressure readings from right heart catheterization.(24,15) Ng et al reported that a PA/Aorta ratio >1.0 should alert clinicians to the possibility of pulmonary hypertension.(15) This was further evaluated by Leg et al, who suggested the cutoff be lowered to >0.84 .(16) Here we have shown in our population that the PA/Aorta ratio can be predictive of increased filling pressures found on echo. We would endorse that a PA/aorta ratio be calculated on all chest CT scans, and that a ratio <0.84 would be reassuring of the absence of pulmonary hypertension.

In a recent publication, Smith-Bindman et al found that the number of CT scans has increased on an annual basis since 1996.(13) There remains a wealth of untapped information that can be gleaned from this abundance of scans. Throughout this manuscript we have substantiated the ability of CTPA-guided measurements to potentially identify two late presenting diseases. As the number of patients undergoing diagnostic imaging will most

likely increase over the future, it is imperative that clinicians use every available aspect of each scan. We suggest that quick and simple measurements of LA, PA, aorta and PA/Aorta ratio are included in all CTPA reports. These included data could allow for the early detection of diastolic dysfunction or pulmonary hypertension and allow practicing clinicians to refer suspected patients for earlier definitive testing and treatment. A recent study by Katikireddy et al established that LA areas calculated on CT could be predictive of pulmonary hypertension due to left heart disease when used in conjunction with pulmonary artery and right ventricle measurements.(25) Their work further substantiates our suggestion that LA, PA and aorta dimensions be included in CT chest studies.

This study does have several limitations that must be acknowledged. It is a retrospective chart review, and therefore has limitations based on non-standardized reporting of clinical data. Second, we used LA diameter on both CT and echo. Previous reports have indicated that a more accurate representation of LA size is by volume.(9,26) However, we argue that the purpose of this study was to find a quick and efficient measurement that did not involve complex, multifactorial calculations, as is required for left atrial area measurements.(26) Furthermore, the study used information gleaned from echo reports including elevated PA pressures and evaluation of diastolic dysfunction and not from the gold standard measurement of filling pressures via heart catheterization. Echocardiograms and CTPAs were not obtained simultaneously and treatments such as diuretics could have affected measurements if there was a lag between the two tests. However, despite this we still were able to show a strong correlation between measurements on CTPA and echo. Lastly, for feasibility reasons the echocardiograms were interpreted by different readers; however, they all followed standard guideline practices for interpretation. Despite these limitations, we suggest that measurements of LA and PA/Aorta ratio be included on CTPA reports. This paper could lead to future studies that perhaps include echo LA volumes as well as filling pressures from heart catheterization studies.

In summary, we have shown that CTPA measurements of LA and PA/Aorta ratio correlate strongly with equivalent findings on echo. We would suggest that LA, PA and ascending aorta measurements be included on all reports of chest CTPAs. This invaluable data could alert clinicians to catch a diagnosis of diastolic dysfunction or pulmonary hypertension, thus allowing patients to be referred for definitive testing.

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Abbreviations

ANOVA	analysis of variance
BMI	body mass index
CTPA	computed tomography pulmonary angiogram

DD	diastolic dysfunction
ECG	electrocardiogram
HFpEF	heart failure with preserved ejection fraction
HFrfEF	heart failure with reduced ejection fraction
LA	left atrium
LV	left ventricle
LVEF	left ventricular ejection fraction
PA	pulmonary artery
RV	right ventricle

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Fig. 1. Inclusion and Exclusion Criteria

200 charts were originally selected for study based on inclusion criteria. 13 were eliminated as they were just outside of the 48-hour restriction, 45 had incomplete CTPA data. 15 of the remaining 142 charts were not included as they lacked LA measurements in their echo reports, leaving a total of 127 charts in the final analysis

A **B**

Fig. 2. Left atrium and pulmonary artery measurements using CTPA

Panel A: CTPA left atrial measurement using the maximum anterior-posterior diameter of the midline in its middle 50%; **Panel B:** CTPA pulmonary artery measurement using the widest diameter perpendicular to the long axis at the pulmonary artery bifurcation. Ascending aorta measurement was taken at the same level.

Fig. 3. Left atrial sizes measured using CTPA correlated strongly with left atrial sizes measured with echo

Panel A: Left atrial sizes from CTPA were correlated against left atrial sizes gleaned from echo reports. There was a strong correlation between left atrial sizes using both methods, ($r=0.78$, $n=127$, 95% CI 0.70–0.84); **Panel B:** Further analysis with a Bland-Altman plot revealed a minimal average discrepancy between both modalities ($n=127$, bias=0.07, 95% limit of agreement= −0.56 to 0.71).

Fig. 4. Left atrial sizes measured on CTPA are significantly larger in patients with moderate or severe diastolic dysfunction

Panel A: LA sizes measured on CTPA were analyzed against diastolic dysfunction grades gleaned from echo reports; **Panel B:** Receiver operating curve of CTPA LA size and diastolic dysfunction on echo; **Panel C:** LA sizes measured on CTPA were correlated with estimation of filling pressures using E/E' from echo reports.

Fig. 5. CTPA pulmonary artery to aorta ratios were significantly larger in patients with elevated pulmonary artery pressures determined by echo

Pulmonary artery size was measured on CTPA and standardized using the ascending aorta measurement for each patient. An estimated systolic pressure of >35 mmHg on echo was defined as elevated. There was a significant difference in the CTPA determined PA/Aorta ratio for patients with normal pressures, 0.89 (n=38, 95% CI 0.93–1.04), and those with elevated pressures, 0.98 (n=49, 95% CI 0.86–0.93).

Table

Baseline characteristics of included patients

Characteristic	N=127	Characteristic	N=127
Clinical		Echocardiogram Findings	
Age (years)	54.5 ± 12.1	Left Atrium Enlargement N=83	33 (40%)
Sex (% female)	51%	Impaired RV Systolic Function N=92	14 (15%)
BMI (kg/m ²) N=104	30.4 ± 9.6	LV Hypertrophy N=68	13 (19%)
Median time between CTPA and Echo (hours)	12.7	LV Ejection Fraction N=103	
Comorbidities N=104		Preserved	76 (74%)
Diabetes	40 (38%)	Reduced	27 (26%)
Pulmonary Hypertension	5 (5%)	Mitral Regurgitation N=102	34 (33%)
Coronary Heart Disease	18 (17%)	Tricuspid Regurgitation N=102	64 (63%)
Myocardial Infarction	6 (6%)	Diastolic Dysfunction N=112	47 (42%)
Systemic Hypertension	75 (72%)		
Renal Disease	14 (13%)		
HFrEF	6 (6%)		
HFpEF	2 (2%)		
Atrial Fibrillation	5 (5%)		

^a Abbreviations: BMI: Body Mass Index, CTPA: Computed Tomography Pulmonary Angiogram, Echo: Echocardiography, HFpEF: Heart Failure Preserved Ejection Fraction, HFrEF: Heart Failure Reduced Ejection Fraction, RV: Right Ventricle, LV: Left Ventricle