International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print), 2222-5234 (Online)
http://www.innspub.net
Vol. 13, No. 4, p. 92-101, 2018

INNSPUB

RESEARCH PAPER OPEN ACCESS

Impact of chronic organic Mitral Regurgitation on Right Ventricular Diastolic Function using Doppler echocardiographic study in multi cardiac center in Baghdad

Attaa K. Taha[1], Ghazi F. Al-haji[2], Ghassan Thabet Saeed[3]

[1]*Baghdad College of Medicine, University of Baghdad, Iraq*

[2]*Al Numan Hospital, Baghdad, Iraq*

[3]*Baghdad Teaching Hospital, Baghdad, Iraq*

Key words: Right ventricular function, compensated mitral regurgitation, Doppler Echocardiography.

http://dx.doi.org/10.12692/ijb/13.4.92-101 Article published on October 14, 2018

Abstract

To study the effect of left ventricular volume overload on right ventricular diastolic function by Doppler echocardiography in patients with chronic organic compensated mitral regurgitation. A cross-sectional study held in multi cardiac center in Baghdad from April 2015 to June 2016. Patients categorized in to two groups; Thirty-one were without pulmonary hypertension (group I, mean age 32±7.1 years) and thirty of patients were with pulmonary hypertension (group II, mean age 36.1±5.7years). All of them compared with sixty-one healthy individuals serving as a control group (group III, mean age 32.1±6.6 years). Transthoracic echocardiography (multiple views) M-mode, Two-dimensional and Doppler were done for all groups of study. Conventional and tissue Doppler echocardiographic assessment of right ventricular diastolic function revealed impairment in up to 44.3% of patients, (19.4% in group I vs 70% in group II, P<0.001). Patients had lower right ventricular E-wave velocity, lower E/A ratio, and prolonged right ventricular isovolumic relaxation time compared to control. Tissue Doppler analysis showed lower E', and lower E'/A' ratio. All changes were statistically significant at P < 0.001. Patients with pulmonary hypertension were older with higher E/E' ratio in comparison to the other two groups (5.79±1.75 in group II vs 3.91±0.41, 4.08±0.93 in group III and I, respectively, P <0.001). Right ventricular diastolic function is frequently impaired in patients with chronic organic compensated mitral regurgitation. Early identification of such changes by Doppler echocardiography might help in identifying patients who need more aggressive therapy early on in the disease process.

* **Corresponding Author:** Attaa K. Taha ✉ dr.alkarkhi@gmail.com

Introduction

The most frequently encountered causes of right-sided diastolic dysfunction are pulmonary hypertension (PH), pulmonary embolism, myocardial ischemia, and congenital heart disease.

The presence of RV diastolic dysfunction is associated with worse functional class and is an independent predictor of mortality (Enger *et al.,* 1982). Identifying the most sensitive markers of RV dysfunction is of immense importance in daily clinical practice (Baker *et al.,* 1984).

It has been shown that Right Ventricular (RV) function is a major determinant of the cardiac symptoms and exercise capacity in chronic heart failure as well as peri-operative and postoperative survival outcome (Wranne *et al.,* 1991). RV diastolic dysfunction has been proposed as an early sign of subclinical RV dysfunction (Leonardo *et al.,* 2002). Other causes include primary lung disease, hypoxic states, cardiomyopathies, both pressure and volume overload pathologies and a number of systemic diseases (Meluzı´n *et al.,* 2003).

Right ventricular function is a well known predictor of mortality after acute myocardial infarction or CABG, in chronic heart failure or primary PH (Rosen *et al.,* 1994). Limited data raised the question of whether RV function influences the prognosis of patients with chronic organic MR (Borer *et al.,* 2002). In patients with a symptomatic severe organic mitral regurgitation (MR), Ventricular function is an important determinant of preoperative and postoperative outcome. This is well known in regard to left ventricular (LV) function, which figures prominently in the clinical guidelines for surgical indications but it is less well known in regard to right ventricular (RV) function (Lang *et al.,* 2010). There is a dilemma with regard to the type of treatment that should be used: i.e. watchful waiting versus early prophylactic surgery (Vahanian *et al.,* 2012).

To date, little is known regarding the effect of left ventricular volume overload on right ventricular diastolic function. We hypothesized that patients with chronic organic mitral regurgitation and preserved left ventricular systolic function might have subclinical right ventricular dysfunction, and related to pulmonary artery systolic pressure

Materials and methods

Those MR patients without PH (31) (group I), and MR with PH (30) patients (group II). All of them compared with sixty-one healthy individuals matched for age and sex, serving as control (group III). Inclusion criteria: All diagnosed male and female with chronic organic mitral regurgitation grade 3 or grade 4, (LV EF >60%). The main etiology is myxomatous (mitral valve prolapse), age less than 50 years old, clinically stable, free of symptoms with sinus rhythm.

Characteristics of patients

Individuals with the following characteristics were excluded, Hypertensive, diabetic , rheumatic heart disease, ischemic heart disease, echocardiographic evidence of concentric LV hypertrophy, systolic dysfunction, wall motion abnormalities, infiltrative diseases or pericardial disease and alcoholics. Heavy smokers, patients with any concomitant significant valvular heart disease, previous valvular surgery, CABG, congenital heart disease, patients for whom good quality echocardiographic images could not be obtained were also excluded. Institutional ethics committee approval and informed consent, full history data included age, gender, predominant symptoms and their duration, complete clinical examination included (Heart rate, Blood pressure), electrocardiography (ECG), and echocardiographic (include 2D/ M-mode ,Conventional Doppler and Pulsed wave tissue Doppler imaging(TDI))data were recorded for all individual in all groups.

Transthoracic echocardiographic

This examination using the General Electric Vivid E9 equipped with a phase array transducer of 3.5 MHZ frequency with TDI capabilities and the subject in the left lateral decubitus postion without breathing holding. Echocardiographic parameters were obtained from the mean of 3 to 6 cardiac cycles from multiple views by three observers to avoid bias in results ,all measurements were performed according to the recommendation of the American Society of Echocardiography and European Society of Cardiology LV ejection fraction was determined by the formula of Teichholz *et al.* EF= measure of how much end-diastolic value is ejected from LV with each contraction (≥ 52% for male, ≥ 54%for female) (Teichholz *et al.,* 1978).

Enlargement of RV and RA

Right ventricular end-systolic and diastolic diameters were measured from a right ventricle-focused apical 4-chamber view demonstrating the maximum diameter of the right ventricle without foreshortening (Weber *et al.,* 1981). Diameter > 41 mm at the base and > 35 mm at the mid level indicates RV dilatation. Similarly, longitudinal dimension > 86 mm indicates RV enlargement. RA area > 18 cm at ventricular end-systole from the same view indicate RA enlargement (Roberto *et al.,* 2015). RV long axis motion using M-mode technique with the cursor positioned at the lateral angle of the tricuspid annulus, from which TAPSE was measured in millimeters, a TAPSE cutoff value < 17 mm yielded high specificity to distinguish abnormal from normal subject RV out-flow acceleration time and tricuspid regurgitation velocity were measured to determine if there was any evidence of PH (Roberto *et al.,* 2015).

Bernoulli's equation

Result were considered to be suggestive of PH when the tricuspid regurgitation velocity was > 2.8 m/s without pulmonary valve stenosis (Chuwa-Tei *et al.,* 1996), when PA acceleration time was <90 ms, or when PA acceleration time/PA ejection time was <0.3 (Schiller *et al.,* 1989; Grifoni *et al.,* 2000). As pulmonary stenosis was excluded in all patients, it was agreed that the RVSP value obtained, relates to the pulmonary artery pressure. The modified Bernoulli's equation was used to calculate PASP (mmHg) = 4× (tricuspid systolic jet velocity)^2 + right atrial pressure (Serra *et al.,* 2010). A peak pulmonary artery pressure > 35 mmHg at rest was defined as pulmonary hypertension, mild PH (36-49), moderate PH (50-59), severe PH≥60 mmHg (Roberto *et al.,* 2015).

Dopper Calculation

In Pulsed wave tissue Doppler imaging, the following parameters were taken; peak systolic velocity (S'), peak early diastolic (E'), peak late diastole (A'), and E'/A' ratio. S' <9.5 cm/s raise the suspicion for abnormal RV function, Further pulsed doppler and TDI data were combined in the calculator of the E/E'. All measurements were obtained on 3 to 6 consecuitive heart cycles, and the mean value was calculated (Mangion 2010).

Right-sided diastolic function may be divided in to normal filling, impaired relaxation (mild diastolic dysfunction), pseudo normal filling (moderate diastolic dysfunction), and restrictive filling (severe diastolic dysfunction). E/A ratio less than 0.8 or E' less than 7.5 cm/s, E'/A' ratio less than 0.5 with deceleration time greater than 242 msec are consistent with impaired relaxation. E/A ratio of 0.8 to 2.1 is associated with plethoric or non collapsing IVC, E/E' ratio greater than 6 or diastolic flow predominance in the hepatic veins is consistent with pseudo normal filling (Sade *et al.,* 2007). E/A ratio greater than 2.1 with deceleration time less than 120 msec or late diastolic antegrade flow in the pulmonary artery is consistent with restrictive filling (Willis *et al.,* 2012).

Each patient assigned a serial identification number. The data were analyzed using STATA software for windows (version 13).The categorical data presented as frequency and percentage tables. The Chi-square test was used to assess the association between variables. The continuous data were represented by mean, and standard deviation. Analysis of variances (ANOVA) and Student's t-test were used for analysis of continuous data comparison.

Results and discussion

In the current study the comparison of the clinical demographic findings in MR patients (with and without pulmonary hypertension) and control group.

A 61 patients with chronic organic compensated MR (46% male, 54% female). They formed three groups: Thirty-one of MR patients were without PH (group I, mean age 32±7.1 years) and thirty patients were MR with PH (group II, mean age 36.1±5.7years). All of them compared with another sixty-one healthy individuals as control (group III, mean age 32.1±6.6 years). The average range of the age is (21- 44 years).

Table 1. Clinical characteristics and PASP, LA pressure in studied group.

Variables	MR without PH	MR with PH	Control	p-value
	Mean±SD	Mean±SD	Mean±SD	
	(N=31)Group I	(N=30)Group II	(N=61)GroupIII	
Age (years)	32±7.1	36.1±5.7	32.1±6.6	0.012*
p-value	1&3= 0.005*	2&3= 0.015*	1&2= 0.947	
Gender, No. (%)				
Male (N=42)	16 (38.1)	12 (31)	14 (33.3)	0.018*
Female (N=80)	15 (18.8)	18 (22.5)	47 (58.8)	
HR (beat/min.)	91±4.6	91.8±4.6	82.6±3.8	<0.001*
p-value	1&3<0.001*	2&3= 0.432	1&2<0.001*	
SBP (mmHg)	110.5±10.6	112±7.9	107.9±7.6	0.067
DBP (mmHg)	71.2±7.9	73.1±6.4	72±5.1	0.474
PASP (mmHg)	20.7±3.3	50.1±10.6	18±3.3	<0.001*
p-value	1&3<0.001*	2&3<0.001*	1&2= 0.102	
LAP (mmHg)	12.6±2.7	21.1±6.6	-	<0.001*
p-value	1&3<0.001*	2&3<0.001*	1&2= 0.237	
TRV (m/s)	2±0.3	3.4±0.4	2.1±0.1	<0.001*
p-value	1&3<0.001*	2&3<0.001*	1&2= 0.566	

SD= Standard deviation, ANOVA test, $^{\chi}$ chi-square *Significant at 0.05 level.

Clinical characteristics

The impairment of RV systolic function in chronic organic MR had been demonstrated in few studies. While, the effect of MR on RV diastolic function till recent years, had not been adequately studied. There was statistical significant difference with respect to age, gender values between MR patients and control group.

Table 2. Distribution of patients, according to MR severity and prevalence of pulmonary hypertension.

Variable	MR grade		Total
	Moderate	Severe	
Patients without PH No(%)	16(51,6)	15(48.4)	31(100)
Patients with PH No(%)	5(16.7)	25(83,3)	30(100)
Total	21(34.4)	40(65.6)	61(100)

p-value= 0.004* Significant at 0.05 by Pearson's chi-square test.

In the present study, there was a highly statistically significant difference in heart rate between MR patients compared with control. We found that patients with MR had significant highest heart rate. PASP was higher for group II compared with group I and III, and this was statistically significant, no important statistical differences were found with respect to systolic and diastolic blood pressure between MR patients and in control group, groups (82.6±3.8 in group I vs 91±4.6, 91.8±4.6 in group II and III respectively, P value <0.001*). LA pressure was higher in group II compared to group I and this was statistically significant as shown in table 1, this could be explained by the hyperdynamic state of LV to compensate the effect of regurgitant volume overload with each heart beat in MR patients.

Table 3. Echocardiographic parameters assessing the RV dimensions and systolic function in each group.

Parameters	Mean±SD	Mean±SD	Mean±SD	p-value
	(N=31)	(N=30)	(N=61)	
RVESD (cm)	2.35±0.18	2.70±0.32	2.18±0.07	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2<0.001*	
RVEDD (cm)	3.08±0.18	4.53±5.58	2.92±0.08	0.032*
P-value	1&3= 0.011*	2&3= 0.049*	1&2= 0.810	
RA area(cm^2)	15.37±0.96	19.38±4.15	13.57±1.04	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2= 0.001*	
TAPSE (mm)	23.34±2.68	20.53±2.83	25.80±0.75	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2<0.001*	
S´ (cm/s)	12.19±1.45	9.97±1.34	12.61±1.02	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2= 0.133	

SD= Standard deviation, ANOVA test

*Significant at 0.05 level.

This might be related to increase the duration of disease that become more severe with age. Davidson (Davidson *et al.,* 1990) and Dib (Dib *et al.*, 1997) have also reported an association between age and PASP. This has been attributed to an increase in pulmonary vascular resistance and decreased LV compliance with age. Females were more predominant in the population study and more prevalent in MR patients with PH. However, PASP was higher in male than in female. This is similar to that found by Alexopoulos, (Alexopoulos *et al.*, 1989).

Table 4. Echocardiographic parameters assessing the RV diastolic function in studied group.

Parameters	MR without PH	MR with PH	Control	
	Mean±SD	Mean±SD	Mean±SD	p-value
	(N=31)	(N=30)	(N=61)	
E (cm/s)	47.1±6.66	44.78±7.46	52.67±4.64	<0.001*
P-value	1&3<0.001*	2&3= 0.133*	1&2<0.001*	
A (cm/s)	49.07±6.87	48.19±4.87	47.61±8.25	0.664
E/A	0.96±0.19	0.92±0.16	1.13±0.11	<0.001*
P-value	1&3<0.001*	2&3= 0.206	1&2<0.001*	
IVRT(ms)	73.5±9.54	77.79±11.83	61.5±6.31	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2<0.001*	
DT(ms)	198.45±21.15	223.84±23.17	190.7±11.29	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2= 0.053	
E´(cm/s)	12.03±3.01	8.22±2.59	13.39±1.36	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2<0.001*	
A´	13.31±2.44	13±1.88	13.64±1.77	0.325
E´/A´	0.92±0.28	0.64±0.18	1±0.18	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2<0.001*	
E/E´	4.08±0.93	5.79±1.75	3.91±0.41	<0.001*
P-value	1&3<0.001*	2&3<0.001*	1&2= 0.488	

SD= Standard deviation, ANOVA test

*Significant at 0.05 level.

Patient's distribution

Distribution of patients according to MR severity and prevalence of pulmonary hypertension is illustrated in (table 2). 25 (83.3%) of MR patients with PH and15 (48.4%) without PH had severe MR. while, 5(16.7%) MR patients with PH and 16 (51.6%) patients without PH had moderate MR, (p value=0.004). Pulmonary hypertension in chronic organic mitral regurgitation was observed in the presence of preserved systolic left ventricular function particularly in severe MR. A high proportion of patients had increased pulmonary artery pressure and 5 of 61 patients exhibited significant elevation (>60 mm Hg). Differences in the dispensability of the pulmonary vascular bed may also lead to the development of severe pulmonary hypertension (Hirakawa *et al.,* 1981).

Table 5. Comparison of Echocardiographic parameters between moderate & severe grades in MR patients.

Parameters	Moderate MR	Severe MR	p-value
	Mean±SD (N=21)	Mean±SD (N=40)	
LVESD (cm)	3.17±0.28	3.58±0.39	<0.001*
LVEDD (cm)	4.77±0.34	5.20±0.45	<0.001*
LV EF %	70.4±2.7	66.3±4.7	<0.001*
LAD (cm)	4.18±0.15	4.55±0.81	0.008*
IVSD (cm)	1.02±0.07	1.03±0.08	0.117
RVESD (cm)	2.34±0.18	2.63±0.32	<0.001*
RVEDD (cm)	3.03±0.17	4.26±5.00	0.127
RA area	15.64±1.34	18.45±4.11	0.003*
TAPSE (mm)	23.76±2.23	20.88±3.01	<0.001*
S´ (cm/s)	12.40±1.39	10.3±1.51826	<0.001*
E (cm/s)	47.71±5.99	44.90±7.55	0.122
A (cm/s)	46.38±4.31	49.78±6.28	0.016*
E/A	1.03±0.15	0.89±0.16	0.002*
IVRT(ms)	70.33±8.52	77.80±10.86	0.016*
DT (ms)	194.10±14.25	221.05±25.28	<0.001*
E´ (cm/s)	12.62±2.62	8.68±2.91	<0.001*
A´(cm/s)	13.00±2.39	13.23±2.04	0.716
E´/A´	0.98±0.21	0.67±0.24	<0.001*
E/E*	3.83±0.70	5.58±1.70	<0.001

SD= Standard deviation, Student's t-test &

*Significant at 0.05 level.

Table 2 shows the pulmonary hypertension. Also, it is possible that the development of pulmonary hypertension was simply related to more severe mitral regurgitation than is found in patients with normal pulmonary artery pressures. However, this possibility as quantitative techniques was not applied in assessing the mitral regurgitation. The compliance of the venous tissue varies widely from patient to patient. Recently, Peyman (Peyman *et al.*, 2015), who studied the impact of duration of mitral regurgitation on outcomes in asymptomatic patients with myxomatous mitral valve related the higher right ventricular systolic pressure at rest to the duration of mitral regurgitation in systole not only to its severity.

Echocardiographic parameters (RV dimensions and systolic function)

Systolic function parameters of RV including RV dimensions, right ventricular tricuspid valve annular velocity (S') and TAPSE in studied groups are shown in table 3. Systolic and diastolic RV diameters were higher for group II compared to other two groups, and this was statistically significant. TAPSE was significantly lower in MR patients compared with control, and lower in group II compared to group I and the difference was statistically significant, P value <0.001). In the present study comparison of conventional 2-D, M-mode echocardiography measurements of LA and LV diameters in both patients groups and control shows that all these measurement were higher in MR patients.

Table 6. Patients classification, according to diastolic dysfunction of RV and prevalence of pulmonary hypertension.

Diastolic dysfunction	Without PH	With PH	Total
No	25 (80.6)	9 (30)	34 (55.7)
Yes	6 (19.4)	21 (70)	27 (44.3)
Total	31 (100)	30 (100)	61 (100)

p-value< 0.001

*Significant at 0.05 by Pearson's chi-square test.

That could be explained by the adaptive changes that occurs during the development of a chronic volume overload in MR patients. TAPSE and right ventricular S' showed a good correlation with the right ventricular ejection fraction (Ueti *et al.,* 2002; Miller *et al.,* 2004; De-Castro *et al.,* 2008). Di Mauro *et al.* demonstrated that in patients with heart failure and MR, preoperative TAPSE and S' predict survival after mitral valve repair (Di-Mauro *et al.,* 2007). In the current study TAPSE shown to be decreased. Significant TAPSE difference was observed between MR group and the control group, nevertheless, TAPSE was significantly lower in the presence of PH than patients with MR alone. Table 3.

Echocardiographic parameters (RV diastolic function)

The right ventricular diastolic function parameters in studied groups are shown in table 4. Conventional RV diastolic function parameters (E, E/A, and deceleration time of E) were impaired for groups I and II compared with group III,E/A ratio was higher in the control group compared with the other patients groups table 4 shows the data. The Iso Volumic Relaxation Time (IVRT) was significantly longer in group II and group I in relation to control. Tricuspid early diastolic annular velocity (E') and early diastolic to late diastolic annular velocities ratio (E'/A'), was significantly lowest in MR patients. The tricuspid annular velocities ratio (E'/A') was significantly lowest in MR patients with PH and The ratio of early tricuspid diastolic velocity to early diastolic annular velocity (E/E') was significantly higher in group II compared with group I and III, patients with PH had larger RA area, RV diameters than patients without PH and control subjects.

These findings suggest that the development of impaired RV dysfunction is more likely to be the consequence of higher level of PH, rather than the result of MR alone.

Long-standing passive PH resulting from venous congestion can lead to structural changes in the distal pulmonary arterioles and endothelial injury with vascular functional abnormalities, which can result in reactive precapillary pulmonary arterial hypertension (PAH). Small increase in pulmonary artery pressure may result in large increase in RV work because RV is thin- walled and eccentric .PH overload the RV, enlarges right heart chambers, and ultimately causes RV failure (Bristow *et al.,* 1966). Table 4.

Comparison of Echocardiographic parameters

Comparison between moderate and severe MR show significant difference regarding LV systolic (EF %), LA diameter and LV dimensions (LVESD, LVEDD). There was no significant difference regarding IVSD.

There was statistical significant difference regarding RV systolic (TAPSE, S') and RV diastolic parameters (E/A, E', E'/A', E/E', IVRT, DT), also statistically significant difference in RV dimensions RVESD, RA area.

These are illustrated in table 5. it has systematically assessed RV diastolic function in patients with chronic organic MR in those with preserved LV systolic function using conventional Doppler echocardiography and Pulsed wave TDI. Second, this is the first study assessing the relation between pulmonary artery pressure and RV systolic and diastolic function. According to data in this study, right ventricular diastolic function seems to be impaired in up to 44.3% of patients with chronic organic mitral regurgitation with preserved LV systolic function. (19.4 % in group II vs 70% group III, P<0.001), clearly suggesting that PASP is the main determinant of RV diastolic function in chronic organic MR. Recently, Celik, (Celik *et al.*, 2015) studied the effect of age on right ventricular diastolic function in healthy subjects and showed that patients >45 years are at greater risk of complications probably because of decreased contractile reverse associated with age. Table 5.

Patients classification

Patient's classification according to diastolic dysfunction is illustrated in table 6. The prevalence of RV diastolic dysfunction is higher in MR patients with PH compared with MR patients without PH and this was statistically significant (P <0.001).

RV diastolic function is impaired in MR patients with PHT. Marangoni (Marangoni *et al.*, 1992; Rudski *et al.,* 2010) similarly found in sixty-seven patients with chronic obstructive lung disease a good correlation between PASP and indexes of diastolic function. Obviously, the mechanism for impaired RV diastolic function in MR patients is PHT secondary to increased left atrial pressure. However, RV diastolic function abnormalities were still common in patients with MR and normal PASP in the present study. It would appear that there is a separate mechanism independent of PASP. Table 6.

Conclusion

Right ventricular diastolic function is frequently impaired in patients with chronic organic mitral regurgitation in those with preserved left ventricular systolic function.

Right ventricular diastolic impairment is more prevalent among patients with mitral regurgitation and elevated pulmonary artery systolic pressure compared to those patients with mitral regurgitated alone.

References

Alexopoulos D, Lazam C, Borrico S, Fiedler L, Ambrose J. 1989. Isolated chronic mitral regurgitation with preserved systolic left ventricular function and severe pulmonary hypertension. JACC, **14,** 319-322.

Baker BJ, Wilen MM, Boyd CM, Dinh H, Francisa JA. 1984. Relation of right ventricular ejection fraction to exercise capacity of patients with chronic left ventricular failure, American Journal of Cardiology **54,** 596-599.

Borer JS, Hochreiter CA, Supino PG, Herrold EM, Krieger KH, Isom OW. 2002. Importance of right ventricular performance measurement in selecting asymptomatic patients with mitral regurgitation for valve surgery, Advances in Cardiology **39,** 144-152.

Bristow JD, Morris JF, Kloster FE. 1966. Hemodynamics of cor pulmonale. Progress in Cardiovascular Diseases **9,** 239-258.

Celik M, Yalcinkaya E, Yuksel UC. 2015. The effect of age on right ventricular diastolic function in healthy subjects undergoing treadmill exercise test, Echocardiography, **32(3),** 436-442.

Chuwa-Tei MD, Karl S, Dujardin MD, David O, Hodge MS, Kent RB, Michael D, McGoon MDA, Jamil-Tajik MD, James B, Seward MD. 1996. Doppler echocardiographic index for assessment of global right ventricular function, Journal of the American Society of Echocardiography, **9(6),** 838-847.

Davidson WRJR, Fee EC. 1990. Influence of aging on pulmonary hemodynamic in a population free of coronary artery disease. American Journal of Cardiology **65,** 1454–1458.

De-Castro S, Cavarretta E, Milan A. 2008. Usefulness of tricuspid annular velocity in identifying global RV dysfunction in patients with primary pulmonary hypertension: A comparison with 3D echo-derived right ventricular ejection fraction. Echocardiography **25(3),** 289–293.

Dib JC, Abergel E, Rovani C. 1997. The age of the patient should be taken into account when interpreting Doppler assessed pulmonary artery pressures. Journal of American Society, Echocardiography **10,** 72–73.

Di-Mauro M, Calafiore AM, Penco M. 2007. Mitral valve repair for dilated cardiomyopathy: Predictive role of right ventricular dysfunction. European Heart Journal, **28,** 2510–2516.

Enger R, Ray R, Higgins CB. 1982. Clinical assessment and follow up of functional capacity in patients with chronic congestive cardiomyopathy. American Journal of Cardiology, **49,** 1832-1837.

Grifoni S, Iacopo O, Cecchini P, Berni G. 2000. Short term clinical outcome of patients with acute pulmonary embolism, normal blood pressure, and echocardiographic right ventricular dysfunction, Circulation **101(24),** 2817-2822. http://dx.doi.org/10.1161/01.CIR.101.24.2817

Hirakawa S, Ito H, Sakai A, Wakabayashi A. 1981. Estimation of the compliance of the human pulmonary "venous" system from pulmonary artery wedge pressure tracings. Japanese Circulation Journal **45(1),** 15- 23.

Lang IM, Plank C, Sadushi-Kolici R, Jakowitsch J, Klepetko W, Maurer G. 2010. Imaging in pulmonary hypertension. JACC Cardiovasc Imaging **3,** 1287-1295.

Leonardo AM, Zornoff MD, Hicham SMD, Marc A, Pfeffer MD. 2002. Right ventricular dysfunction and risk of heart failure and mortality after myocardial infarction, Journal of the American College of Cardiology, **39**, 1450–1455.

Mangion JR. 2010. Right ventricular imaging by two-dimensional and three dimensional echocardiography, Current Opinion in Cardiology, **22,** 423–429.

Marangoni S, Scalvini S, Schena M, Vitacca M, Quadri A, Levi G. 1992. Right ventricular diastolic function in chronic obstructive lung disease. European Respiration Journal **5,** 438-443.

Miller D, Farah MG, Liner A. 2004. The relation between quantitative right ventricular ejection fraction and indices of tricuspid annular motion and myocardial performance, Journal of American Society Echocardiography **17,** 443–447.

Meluzı´n L, Špinarová L, Dušek L, Toman J, Hude P, Krejčı´ J. 2003. Prognostic importance of the right ventricular function assessed by Doppler tissue imaging. European Journal of Echocardiography, **4(4),** 262–271, https://doi.org/10.1016/S1525-2167(02)00171-3

Peyman N, Fadi A, Tyler B, Milind YD. 2015. Impact of Duration of Mitral Regurgitation on Outcomes in Asymptomatic Patients With Myxomatous Mitral Valve Undergoing Exercise Stress Echocardiography. Journal of the American Heart Association **4(2),** 1-9. http://dx.doi.org/10.1161/JAHA.114.001348.

Roberto M, Lang MD, Luigi P, Badano MD, Victor MA, Jonathan A. 2015. Recommendations for cardiac chamber Quantification by Echocardiography and the European Association of Cardiovascular Imaging, Journal of the American Society of Echocardiography, **28,** 1-39.

Rosen SE, Borer JS, Hochreiter C, Supino P, Roman MJ. 1994. Natural history of the asymptomatic/minimally symptomatic patient with severe mitral regurgitation secondary to mitral valve prolapse and normal right and left ventricular performance. American Journal of Cardiology, **74,** 374-380.

Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD. Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. 2010. Guidelines for the Echocardiographic assessment Assessment of the right heart in adults: Areport from the American Society of Echocardiography, endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography, Journal of the American Society of Echocardiography **23,** 685-713. http://dx.doi.org/10.1016/j.echo.2010.05.010.

Sade LE, Gulmez O, Eroglu S. 2007. Noninvasive estimation of right ventricular filling pressure by ratio of early tricuspid inflow to annular diastolic velocity in patients with and without recent cardiac surgery, Journal of American Society, Echocardiography **20,** 982–988.

Serra W, Chetta A, Santilli D, Mozzani F, Dall Aglio PP, Olivieri D. 2010. Echoardiography may help detect pulmonary vasculopathy in the early stages of pulmonary artery hypertension associated with systemic sclerosis. Cardiovascular Ultrasound **8,** 25. http://dx.doi.org/10.1186/1476-7120-8-25.

Schiller NB, Shah PM, Crawford M. 1989. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of echocardiography Committee on standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms, Journal of American Society Echocardiography **2,** 358-367.

Teichholz LE, kreulen T, Herman MV, Gorlin R. 1976. Problems in echocardiogrphic volume determinations: echocardiographic- angiographic correlations in the presence of absence of asynergy, American Journal of Cardiology **37,** 7-11.

Ueti O, Camargo E, Ueti A. 2002. Assessment of right ventricular function with Doppler echocardiographic indices derived from tricuspid annular motion: Comparison with radionuclide angiography. Heart, **88,** 244–248.

Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, Borger MA. 2012. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), European Heart Journal **33,** 2451-2496.

Willis J, Augustine D, Shah R. 2012. Right ventricular normal measurements: time to index?, Journal of American Society Echocardiography **25,** 1259–1267.

Wranne B, Pinto FJ, Hammarstrom E, St-Goar FG, Puryear J, Popp RL. 1991. Abnormal right heart filling after cardiac surgery: time course and mechanisms. British Heart Journal **66,** 435-442.