

Using TAPSE Versus Speckle Tracking in Assessment of Right Ventricular Function in Healthy Heavy Chronic Cigarette Smokers

Mohamed Mosa Abdo,¹ MBBCH, Ali Mohammed El Amin Abdelmeguid,¹ MD, Ahmed Ali Faheem Abdo,¹ MD

** Corresponding Author:*

Mohamed Mosa Abdo

Mosamohamed449@gmail.com

Received for publication October 23, 2021; Accepted February 9, 2022; Published online February 9, 2022.

Copyright The Authors published by Al-Azhar University, Faculty of Medicine, Cairo, Egypt. Users have the right to read, download, copy, distribute, print, search, or link to the full texts of articles under the following conditions: Creative Commons Attribution-Share Alike 4.0 International Public License (CC BY-SA 4.0).

doi: 10.21608/aimj.2022.100605.1623.

¹Cardiovascular Medicine Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

ABSTRACT

Background: Smoking increases risks of cardiovascular mortality and morbidity by multiple potential mechanisms. The right ventricle hasn't been well studied in the healthy heavy smokers' population in which chest causes of right ventricle dysfunction hasn't progressed yet.

Aim of the study: to evaluate right ventricular functions in healthy heavy chronic cigarette smokers using conventional echocardiography (measuring TAPSE) and speckle tracking echocardiography as a non-invasive method of assessment.

Patients and Methods: All participants were subjected to clinical examination, spirometry and oxygen saturation analysis, ECG, a full echocardiographic study focusing on the right ventricle, right atrium parameters and speckle tracking.

Results: The enrolled population were 300 cases, divided into 200 healthy heavy smokers and 100 nonsmokers. There was a significantly lower RV function in the heavy smokers' group by TAPSE, FAC and RV GLS. Moreover, there were also higher pulse, blood pressure and PASP in the same group. Right atrial area and function by speckle tracking were also affected in heavy smokers.

Conclusion Heavy chronic cigarette smoking among healthy individuals is associated with decreased function of RV that can be analysed by different echocardiographic modalities e.g., TAPSE, RV FAC and RV GLS using speckle tracking.

Keywords: TAPSE; speckle; right ventricle; cigarette; smokers.

Disclosure: The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.

Authorship: All authors have a substantial contribution to the article.

INTRODUCTION

Smoking increases risks of cardiovascular mortality and morbidity by multiple potential mechanisms including: vascular dysfunction, increased inflammation, progression of atherosclerosis, development of thrombi, oxidative stress and mitochondrial damage to myocytes.¹

The right ventricle (RV) was considered the heart's neglected side, with little attention devoted to its assessment.²

Speckle tracking, a relatively recent method, indicated that chronic heavy smokers with chronic obstructive pulmonary disease (COPD) had echocardiographic indications of right ventricular dysfunction even before the onset of pulmonary hypertension and cor pulmonale. Strain rate imaging parameters can detect

right ventricular dysfunction in addition to traditional echocardiographic indices and are correlated with pulmonary hypertension and respiratory function testing.³ Reduced RV systolic function was present

(sub-clinically) even in patients with COPD who did not have pulmonary hypertension compared with controls.^{4,5}

However, the few studies that have focused on the smoking impact on right ventricular function, independent of coronary artery disease and COPD, have shown conflicting results.

Right ventricular functions may be appreciated with different techniques such as catheterization, nuclear magnetic resonance imaging and echocardiography.

Several echocardiography parameters such as fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), tricuspid annular systolic velocities, myocardial performance index (MPI) derived by tissue Doppler imaging have been thoroughly described in the evaluation of RV functions.⁶

Several studies have shown that 2D speckle tracking of the RV and RA can be utilised to assess the physio-mechanics of the right heart. Furthermore, it may offer parameters of load status, that is

particularly significant in patients with right heart diseases.⁷

We aimed by this work to evaluate right ventricular functions in healthy heavy chronic cigarette smokers using conventional echocardiography (measuring TAPSE) and speckle tracking echocardiography as a non-invasive method of assessment.

PATIENTS AND METHODS

This study is a Multicenter, cross-sectional, comparative study was conducted in Sayed Galal University Hospital and General Air force hospital from November 2020 to September 2021.

The final study population were 300 males; 200 of them were apparently healthy heavy chronic cigarette smokers (Group I) and 100 apparently healthy non-smokers (Group II) of matched age, gender and risk factors.

Inclusion criteria include apparently healthy current cigarette smokers with at least 5 pack-years of smoking history and a daily cigarette consumption of at least 1 pack per day (20 cigarettes). Pack-years are determined by dividing the average number of cigarettes smoked each day by 20 and multiplying by the number of years of smoking.⁸

Exclusion criteria include patients who have one or more of the following: suboptimal echocardiographic image, more than one of the six RV segments lacking clearly defined boundaries, substance abuse, obese patients with BMI more than 30 kg/m², COPD, elevated Pulmonary artery systolic pressure (PASP) ≥ 35 mmHg⁶, valvular heart disease, myocardial heart disease, patient with EF < 50%, coronary artery disease, moderate to severe pericardial disease, congenital heart disease, significant valvular heart disease, non-sinus rhythm or patient refusal.

All population were subjected to: full history taking (including age, sex, DM, HTN and smoking), full clinical examination (including pulse, blood pressure measurement and cardiac auscultation), pulse oximetry (to measure the oxygen saturation of blood), chest x-ray (to evaluate heart and lung condition), spirometry (to detect FEV1, FVC and FEV1/FVC ratio). The smokers were instructed to avoid smoking for at least 30 minutes before spirometry.

Electrocardiography (ECG):

Twelve lead surface ECG was done to assess patients' heart rate and rhythm with the exclusion of ischemic changes or other ECG changes.

Echocardiography:

All images of the RA and RV were performed with the patients in the standard left lateral position in the apical-four chamber view with stable ECG reading using GE vivid 7 with 3S transducer (1.5-3.6 MHz).

The smokers were advised to avoid smoking for at least 30 minutes and all the population not to consume coffee for at least 3 hours before the echocardiographic examination. All measurements were taken according to the last ASE guideline for chamber size assessment.⁹ Apical four-chamber view was done to evaluate the right side of the heart to assess:

Right ventricular dimensions:

The basal diameter was measured in basal 1/3 of the right ventricle, the mid-cavity diameter in the middle 1/3 of RV at the level of LV papillary muscles, and the longitudinal diameter was assessed by drawing a line from the plane of the tricuspid annulus to RV apex from an apical four-chamber view.

Right ventricular areas and fractional area change (FAC):

FAC was traced from a four-chamber image by the right ventricular endocardial from the annulus, down the free wall to the apex, and then back to the annulus, along the interventricular septum, in both systole and diastole.

Pulmonary artery systolic pressure (PASP):

PASP was calculated by using the tricuspid regurge jet's CW Doppler to calculate the systolic pressure gradient between RV and RA. The RVSP was calculated from the peak TR jet velocity using simplified Bernoulli equation then combining this result with RA pressure estimation: $RVSP = 4(V)^2 + RA$ pressure, where V is the tricuspid valve regurge jet's peak velocity (in m/sec) and RA pressure is calculated from IVC diameter, collapsibility, and respiratory variations.

Tricuspid annular plane systolic excursion (TAPSE):

TAPSE was calculated by measuring the distance of the RV annular segment's systolic excursion along its longitudinal plane from a conventional apical 4-chamber window.

Assessment of left ventricular ejection fraction (LVEF):

The following formula was used to determine LVEF from left ventricular end-diastolic volume (EDV) and left ventricular end-systolic volume (ESV): $(EDV - ESV)/EDV = EF$ This was accomplished by the use of a modified Simpson's rule.

Speckle tracking echocardiography:

Right atrial global longitudinal strain:

The RA longitudinal strain (RALS) was assessed by manual tracing the right atrium endocardium in 4 chamber images, defining six-segment zones. The software generated longitudinal strain curves for each atrial segment after analysing segmental tracking

quality. RALS was evaluated in six RA segments. Peak RALS was determined at the end of the RA reservoir phase as the average of all RA segments to give the global RALS.¹⁰

Right ventricular global longitudinal strain (RV GLS):

At end-systole, by right ventricular tracing along the endocardium manually and automatic modification to accommodate the whole myocardium and to guarantee adequate tracking. The thickness of the myocardium was adjusted manually to the region of interest.¹¹

Right ventricular strain and strain rate are useful parameters for calculating the RV global and regional systolic functions. Longitudinal strain is measured as the proportion of systolic shortening of the RV free wall from base to apex, and longitudinal strain rate is the pace at which this shortening occurs.¹²

Statistical analysis:

The Statistical Package for Social Sciences was used for statistical analysis (version 26.0; SPSS Inc., Chicago, Illinois, USA). The mean and standard deviation were used to express the data. The independent t-test or one-way ANOVA was used to examine differences between groups. Pearson and Spearman coefficients of correlation were used to identify possible correlations. A P value < 0.05 was considered significant.¹³

RESULTS

Demographic data and smoking status:

The study included 300 males; 200 of them were healthy heavy chronic cigarette smokers (Group I) and 100 apparently healthy non-smokers (Group II). The age in both groups and indexes for the severity of smoking was reported in (Table 1 and Figure 1).

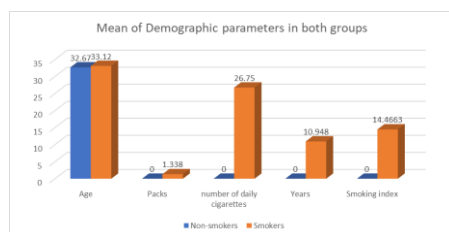


Fig 1: Comparing demographic parameters in both groups.

Blood pressure, pulse and smoking:

Pulse is lower in non-smokers than smokers with significant difference despite being within normal values in both groups.

Blood pressure measurements (either systolic, diastolic or calculated mean) were lower in non-smokers than smokers' group but with minor differences that are statistically significant more in

systolic and mean blood pressure than diastolic blood pressure. SBP was 120 ± 7.521 in non-smokers' group versus 122.5 ± 7.878 in smokers' group. DBP was 75.35 ± 6.327 in non-smokers' group versus 77.55 ± 6.340 in smokers' group.

Oxygen saturation, spirometry and Smoking:

Oxygen saturation is higher in non-smokers than smokers with significant difference despite being within normal values in both groups.

Spirometry results didn't signify any statistical difference between the 2 groups which may be due to the presence of other factors that affect FEV1 and FVC e.g., Body surface area. Yet, they had an important value to exclude chest diseases that may affect the right side of the heart. (Table 1 and Figure 2).

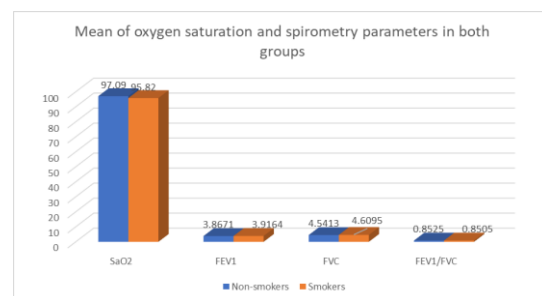


Fig 2: Comparing oxygen saturation and spirometry in both groups.

Left ventricular systolic function and smoking:

Smokers had a lower ejection fraction than non-smokers and the difference is statistically significant. The mean EF in smoker group was $61.11 \pm 4.69\%$, while it was $68.29 \pm 4.82\%$ in non-smoker group ($P < 0.001$).

Conventional parameters of RV parameters and smoking:

There is no statistically significant difference in right ventricular basal and middle diameters among the two groups. Right ventricular longitudinal diameter is otherwise more in smokers than non-smokers with a statistically significant difference.

TAPSE was more in non-smokers than smokers with a statistically significant difference.

Right ventricular end-diastolic and end-systolic areas were larger in smokers than non-smokers with subsequent better fractional area change in non-smokers than smokers with a statistically significant difference.

PASP is higher in heavy smokers than non-smokers with statistically significant difference (Table 2 and Figure 3).

RV speckle tracking and smoking:

Right ventricular global longitudinal strain was lower in non-smokers than smokers with statistically significant difference (Table 2 and Figure 4).

Right atrial end-systolic area and smoking:

Right atrial end-systolic area is higher in heavy smokers than non-smokers with a statistically significant difference.

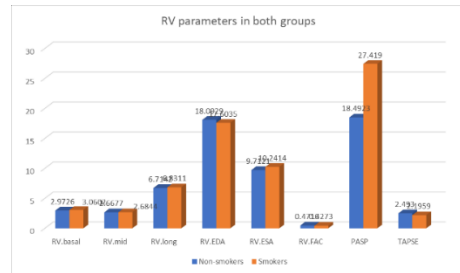


Fig 3: Comparing RV parameters in both groups.

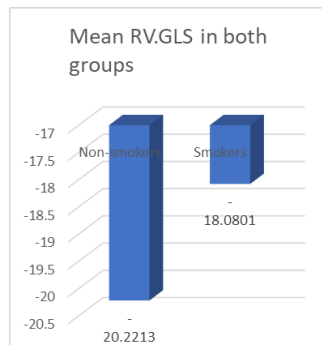


Fig 4: Comparing RV-GLS in both groups.

RA speckle tracking and smoking:

Right atrial global longitudinal strain is more in non-smokers than smokers with a statistically significant difference. (Table 2 and Figure 5).

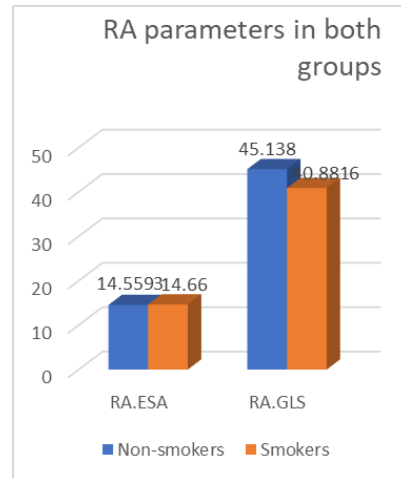


Fig 5: Comparing RA parameters in both groups.

Correlation between RV indices:

By comparing different echo modalities of right ventricular function assessment i.e., TAPSE, FAC and RV GLS, using R coefficient, all methods have correlation being higher in TAPSE and FAC and moderate in GLS.

Parameter	Heavy smokers (group 1) n=200		Non-smokers (group 2) n=100		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Age	33.12	4.748	32.67	3.646	0.370
Packs	1.338	.4101	0	0	<0.001
Number of daily cigarettes	26.7500	8.20206	0	0	<0.001
Smoking years	10.948	4.1466	0	0	<0.001
Smoking index	14.4663	6.37681	0	0	<0.001
Pulse	74.32	8.395	69.19	7.949	<0.001
SBP	122.50	7.878	120.00	7.521	0.009
DBP	77.55	6.340	75.35	6.327	0.05
MABP	92.53	5.6097	90.23	5.217	0.001
SaO2	95.82	1.052	97.09	.922	<0.001
FEV1	3.9164	.41172	3.8671	.41762	0.332
FVC	4.6095	.43049	4.5413	.39911	0.187
FEV1/FVC	0.8505	0.05637	0.8525	0.06809	0.798

Table 1: Baseline demographic and clinical characteristics of the study population.

Parameter	Heavy smokers (group 1) n=200		Non-smokers (group 2) n=100		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
LVEF	61.1115	4.69393	68.2954	4.82549	<0.001
RV basal diameter	3.0602	.83215	2.9726	.83510	0.391
RV mid diameter	2.6844	.83555	2.6677	.81942	0.870
RV long diameter	6.8311	1.17486	6.7142	1.22389	0.424
TAPSE	2.1959	.47048	2.4930	.45103	<0.001
RV.EDA	17.6035	3.40827	18.0929	2.50629	0.160
RV.ESA	10.2414	3.10280	9.7121	2.54586	0.004
RV.FAC	.4273	0.07090	0.4716	0.07174	<0.001
PASP	27.4190	10.47842	18.4923	9.63394	<0.001
RV.GLS	-18.0801	4.30885	-20.2213	3.48077	<0.001
RA.ESA	14.6600	3.93709	14.5593	4.71254	<0.001
RA.GLS	40.8816	8.95103	45.1380	7.64829	<0.001

Table 2: Echocardiographic parameters of the study population.

		Smoking index
RV.FAC	r value	- 0.501
	P value	<0.001
TAPSE	r value	-0.531
	P value	<0.001
RV.GLS	r value	0.476
	P value	<0.001

Table 3: Demonstrating different correlations of coefficients between different methods to assess right ventricular functions.

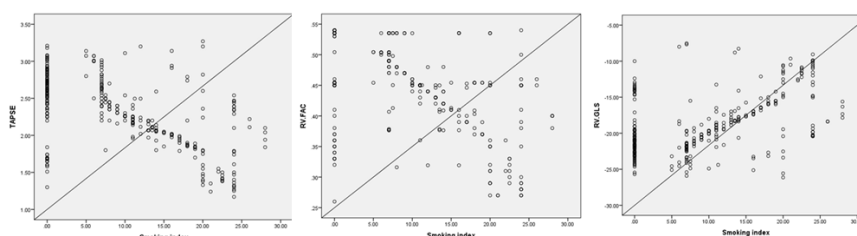


Fig 6: Three simple scatters with fit line demonstrating different correlations of coefficients between different methods to assess right ventricular function.

DISCUSSION

Cigarette smoking is a significant preventable source of morbidity and mortality that is expected to kill 450 million people over the next fifty years. According to WHO data, smoking is currently responsible for 6 million premature deaths yearly, with 600,000 people dying as a result of passive smoking. Given a combination of low resources and smoking's health and financial implications, developing countries must combat smoking and its risk factors. In 2010, the prevalence of smoking was 22%, and it is quickly growing in Egypt.¹⁴

Several studies show that excessive smoking has an immediate and long-term effect on LV function. Using traditional 2d echocardiography, tissue doppler, and speckle tracking, healthy young heavy smokers had considerably worse LV diastolic performance than nonsmokers.⁸

The relatively new technology of speckle tracking found that chronic heavy smokers with COPD had echocardiographic signs of RV dysfunction even before the onset of pulmonary hypertension and Cor Pulmonale. Vitarelli et al. found that strain rate imaging measures can detect RV dysfunction in addition to standard echocardiographic parameters and are associated with pulmonary hypertension and respiratory function tests.³ More recently, Hilde et al. showed that reduced RV systolic function was present even in patients with COPD who did not have pulmonary hypertension compared with controls.⁴ Sabit et al. also demonstrated subclinical RV dysfunction in patients with COPD.⁵

The present study aims to find out the best method of right ventricular functional assessment using echocardiographic three different modalities i.e TAPSE, FAC and RV GLS to detect early functional affection of right ventricular function in healthy heavy chronic cigarette smokers.

200 healthy asymptomatic chronic heavy cigarette smokers (Group 1) and 100 healthy asymptomatic non-smoking controls (Group 2), aged 45 years or younger, participated voluntarily after informed verbal consent. 'Heavy chronic smokers' were defined as those who smoked at least 20 cigarettes daily for at least 5 years.

The smokers were asked not to smoke for at least 30 minutes and all the population to avoid coffee for at least 3 hours before the echocardiographic examination. They were also asked not to smoke for at least 30 minutes before spirometry. Age, gender, and risk factors were all matched between the two groups.

Chronic heavy cigarette smokers had a higher pulse rate than non- smokers (despite being both groups within normal ranges). The result found was in accordance with the results of Janhangeer, Mohammad Iqbal, et al.¹⁵

Chronic heavy cigarette smokers also have higher blood pressure either systolic, diastolic or calculated mean arterial blood pressure with statistically significant difference. These data were found to be similar to the results of Abtahi, Kianpour et al.¹⁶ Yet, the result was contradictory to the results of Eroglu, Aydin et al.¹⁷

In the study of Lichodziejewska, Kurnicka et al. despite that have smokers have higher means of pulse and blood pressure, yet with no statistical significance except in pulse if chronic smokers have one cigarette just before the study to demonstrate acute effect of smoking.¹⁸

Heavy smokers also have lower SaO₂ than non-smokers with a statistically significant difference (p value = 0.001). Spirometry data didn't have statistical difference being population had different

body surface areas, yet they were an important tool in excluding respiratory conditions affecting the lungs which may bias right ventricular functions.

This result was contradictory to Witting and Scharf that mentioned that smoking has no effect on pulse oximetry results¹⁹, yet in accordance with results of Pezzuto, Aldo et al. and Vold, Aasebø et al.^{20, 21}

Spirometry results were contradictory to the results of Vold, Aasebø et al. that mentioned that spirometry results were regressed in heavy smokers than normal population.²¹ It is worthy to notice that in the mentioned study there was a good correlation of spirometry results with BMI while in our study, the population with below normal spirometry indices were excluded from the study to allow right ventricular functional assessment that is not affected by chest causes e.g., COPD.

Heavy smokers tend to have lower ejection fraction (but still within normal EF) than non-smokers and the difference is statistically significant (p value = 0.001) which is consistent with data from Farsalinos, Tsiapras et al. that was performed on 83 healthy population (42 of them were heavy smokers)⁸ but contradictory to results of Eroglu, Aydin et al.¹⁷

There was no statistical difference in RV dimensions between the two groups including the basal, mid or longitudinal diameters. Yet, there was no statistical difference in the absolute values of RV end-diastolic area although RV end-systolic area was lower in non-smokers (with statistically significant difference) with subsequent statistically significant RV FAC being less in heavy smokers than nonsmokers with significant p value (p value = 0.001).

TAPSE also was lower in non-smokers than heavy smokers with statistically significant difference (p value = 0.001).

PASP was estimated as mentioned previously for excluding pulmonary hypertension in all population of both groups. Despite all population had normal PASP but the mean was higher in heavy smokers than non-smokers with statistically significant difference (p value = 0.001).

Speckle tracking of RV to estimate RV GLS revealed that non-smokers have better RV function than heavy smokers with statistically significant difference (p value = 0.001).

In order to detect the effect of heavy smoking on right atrium either directly or indirectly in healthy individuals, RA End systolic area wasn't statistically significant meanwhile RA GLS was higher in non-smokers than heavy smokers with statistically significant difference (p value = 0.001).

In our study three different modalities were used to assess RV function i.e., TAPSE, RV FAC and RV GLS. All methods were accurate and comparable in assessing RV function either in heavy smokers or non-smokers using p value and R correlation.

These findings aren't in controversy with previous studies despite that studies on the acute effect of smoking on right ventricle mentioned that there is no effect of smoking in right ventricle (which was on forty smokers and forty non-smokers).¹⁷

In other study on the acute effect of smoking on right ventricular function, there was an effect on diastolic function of right ventricle rather than systolic function on only 20 population using tissue doppler.²²

According to previous studies, the effect of acute smoking was abolished after 30 minutes during which we advised our population not to smoke within before echocardiography.

The suggested affection of right ventricular function in heavy smokers correlate with smoking index that include packs number (cigarettes/day) and smoking years.

The mechanism suggested of this affection may include the cellular and biochemical effect of many toxins and chemicals in the cigarettes which may need further biochemical and physiological investigations to understand the exact mechanism the heavy smoking may over years affect right ventricular function although respiratory system hasn't been affected causing pulmonary hypertension.

CONCLUSION

Heavy chronic cigarette smoking among healthy individuals is associated with decreased function of RV that can be analysed by different echocardiographic modalities e.g., TAPSE, RV FAC and RV GLS using speckle tracking.

REFERENCES

1. Steven S, Frenis K, Oelze M, et al. Vascular inflammation and oxidative stress: major triggers for cardiovascular disease. *Oxidative medicine and cellular longevity*. 2019; 23:2019.
2. Kossaify A. Echocardiographic assessment of the right ventricle, from the conventional approach to speckle tracking and three-dimensional imaging, and insights into the "right way" to explore the forgotten chamber. *Clinical Medicine Insights: Cardiology*. 2015; 9:27462.
3. Vitarelli A, Conde Y, Cimino E, et al. Assessment of right ventricular function by strain rate imaging in chronic obstructive pulmonary disease. *European Respiratory Journal*. 2006; 27(2):268-75.
4. Hilde JM, Skjørten I, Grøtta OJ, et al. Right ventricular dysfunction and remodeling in chronic obstructive pulmonary disease without pulmonary hypertension. *Journal of the American College of Cardiology*. 2013 Sep 17;62(12):1103-11.

5. Sabit R, Bolton CE, Fraser AG, et al. Sub-clinical left and right ventricular dysfunction in patients with COPD. *Respiratory medicine*. 2010; 104(8):1171-8.
6. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report 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*. 2010;23(7):685-713.
7. Ünlü S, Şahinarslan A, Gökalp G, et al. The impact of volume overload on right heart function in end-stage renal disease patients on hemodialysis. *Echocardiography*. 2018; 35(3):314-21.
8. Farsalinos K, Tsiapras D, Kyrzopoulos S, et al. Acute and Chronic Effects of Smoking on Myocardial Function in Healthy Heavy Smokers: A Study of Doppler Flow, Doppler Tissue Velocity, and Two-Dimensional Speckle Tracking Echocardiography. *Echocardiography*. 2013;30(3):285-92.
9. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal-Cardiovascular Imaging*. 2015;16(3):233-71.
10. Mondillo S, Galderisi M, Mele D, et al. Speckle-tracking echocardiography: a new technique for assessing myocardial function. *Journal of Ultrasound in Medicine*. 2011; (1):71-83.
11. Amundsen BH, Helle-Valle T, Edvardsen T, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. *Journal of the American College of Cardiology*. 2006;47(4):789-93.
12. Guendouz S, Rappeneau S, Nahum J, et al. Prognostic significance and normal values of 2D strain to assess right ventricular systolic function in chronic heart failure. *Circulation Journal*. 2012;76(1):127-36.
13. McLeod, S. What a p-value tells you about statistical significance. *Simply psychology*. 2019: 1-4.
14. Fouda, S., et al., Tobacco smoking in Egypt: a scoping literature review of its epidemiology and control measures. 2018; 24(02): p. 198-215.
15. Fouda S, Kelany M, Moustafa N, et al. Tobacco smoking in Egypt: a scoping literature review of its epidemiology and control measures. *EMHJ-Eastern Mediterranean Health Journal*. 2018;24(02):198-215.
16. Abtahi F, Kianpour Z, Zibaenezhad MJ, et al. Correlation between cigarette smoking and blood pressure and pulse pressure among teachers residing in Shiraz, Southern Iran. 2011.
17. Eroglu E, Aydin S, Yalniz F, et al. Chronic cigarette smoking affects left and right ventricular long-axis function in healthy young subjects: a Doppler myocardial imaging study. *Echocardiography*. 2009; 26(9):1019-25.
18. Lichodziejewska B, Kurnicka K, Grudzka K, et al. Chronic and acute effects of smoking on left and right ventricular relaxation in young healthy smokers. *Chest*. 2007;131(4):1142-8.
19. Witting MD and Scharf SM. Diagnostic room-air pulse oximetry: effects of smoking, race, and sex. 2008; 26(2):131-6.
20. Pezzuto A and Carico E. Effectiveness of smoking cessation in smokers with COPD and nocturnal oxygen desaturation: functional analysis. *The Clinical Respiratory Journal*. 2020;14(1):29-34.
21. Vold ML, Aasebø U, Hjalmarsen A, et al. Predictors of oxygen saturation \leq 95% in a cross-sectional population based survey. *Respiratory medicine*. 2012; 106(11):1551-8.
22. Ilgenli TF and Akpinar O. Acute effects of smoking on right ventricular function. *Swiss Medical Weekly*. 2007;137(0506).