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Which Echocardiophic Parameters Allow to Predict Systolic Disfunction in Asymptomatic Subjects Who Take Alcohol Plus Other Drugs?

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Abstract

Background: It is known that alcohol plus other recreational drugs abuse may cause a dilated hypokinetic cardiomyopathy which is highlighted only at the end-stages of the disease, conversely most of these subjects remain asymptomatic for long periods. Nowadays Transthoracic echocardiography (TTE) represents the most available diagnostic tool to identify early cardiac dysfunction. This study is finalized to investigate which echocardiographic parameters either derived from standard TTE or from the newest echocardiographic approach such as speckle tracking (ST) may allow to identify early cardiac damage in asymptomatic patients (pts).

Methods: 26 consecutive asymptomatic pts assuming alcohol and other drugs were enrolled, mean age was 43±11 years, 73% were male. All pts underwent standard TTE plus ST analysis for the evaluation of global longitudinal strain (GLS).

Results: all pts did not present systolic dysfunction, nor other echocardiographic abnormalities at TTE, while lower values of GLS were displayed. A modest, yet significant correlation between average GLS and E/A was found, whereas a correlation with E/e' was not displayed.

Conclusions: our pts presented low GLS thus suggesting the presence of subclinical involvement. The positive correlation between E-A ratio and GLS may be ascribed to the hemodynamic overload due to alcohol abuse, while no correlation was found between GLS and E/e', this may be due to the fact that these pts are asymptomatic and don't present structural cardiac abnormalities. Further studies involving a larger population of asymptomatic pts are needed to confirm such results and to investigate whether sex-differences exist

keywords: Alcohol Plus Other Drugs-Echocardiography-Global Longitudinal Strain.

Introduction

Long lasting alcohol intake has been progressively recognized as a leading cause of non-ischemic dilated cardiomyopathy, affecting near 10% of all alcoholic people [1]. Nowadays chronic alcohol intake and abuse are more and more frequently associated with the assumption of other drugs such as cannabinoids, cocaine and others, and undoubtedly these associations may amplify the cardiac damage [2]. While Left ventricular (LV) dilatation, together with severely impaired systolic function and increased LV mass, represent the symptomatic end-stage of the disease, a great number of subjects are asymptomatic for a long time and in these patients, it is of huge importance to succeed in identifying earlier markers of cardiac impairment in order to stop the intake of harmful substances and to undertake the appropriate therapeutic strategies thus improving prognosis [2-4]. Due to the fact that Echocardiography represents the most widely-available and easy to perform non-invasive diagnostic test to evaluate cardiac function this study was undertaken to determine which echocardiographic parameters, either derived from traditional echocardiographic exam or derived from the newest echocardiographic approach based on strain analysis, allow to predict better LV dysfunction even in subclinical stages in asymptomatic subjects who take alcohol plus other drugs.

Alcohol plus other drugs

It has been demonstrated that long-lasting alcohol intake is associated with important effects on cardiovascular system. Chronic abuse of alcohol is often associated with abuse of other substances including Cannabinoids. In this regard various studies conducted both on animal models [5-6] and on humans [7-8] have shown that cannabinoids exert many cardiovascular effects through the interaction with CB1 receptors which are located in the myocardium, aorta, vascular endothelium, in platelets, central and peripheral nervous system. Main cardiovascular effects of cannabinoids could be summarized as enhanced sympathetic tone, increased catecholamine levels and increased heart rate at lower doses, and bradycardia/hypotension at higher doses due to parasympathetic stimulation occurring at these doses [9]. Other cardiovascular effects which may be identified are platelet activation, endothelial dysfunction and oxidative stress [10].

In addition, smoking marijuana may cause an increase in the amount of carboxyhemoglobin due to combustion, so causing an additional decrease in oxygen supply [11]. Furthermore, multiple case reports have linked marijuana use to procoagulant effect so causing thrombus formation leading to acute myocardial infarction in young adults [12-13]. On the other hand, in many reported cases of cannabis induced AMI coronary angiography showed clean coronaries and documentation of coronary spasm [14].

Although the evidence is weaker, there are also links to a higher risk of atrial fibrillation or ischemic stroke immediately following marijuana use [15-16].

Alcohol intake may be also associated to the assumption of cocaine which presents important cardiovascular effects [17]. Long-term cocaine use, as well as acute cocaine use, is associated with adverse cardiovascular consequences, including arrhythmias, angina, myocardial infarction, heart failure, and other conditions [18]. Over the long term, cocaine can result in structural changes to the heart such as increased left- ventricular mass and decreased left-ventricular end-diastolic volume. Cocaine, ecstasy, and amphetamines share similar adverse effects on the cardiovascular system, related predominantly to activation of the sympathetic nervous system [19].

Finally, Morphine and its semisynthetic analogue heroin may cause cardiovascular damage by determining the occurrence of various bradyarrhythmia's and tachyarrhythmias [20]. Their main effects are due to the fact that they act centrally to increase parasympathetic and reduce sympathetic activity, resulting in bradycardia and hypotension. On the other side the intake of hallucinogens lysergic acid (LSD) and psichedelics is instead characterized by both sympathomimetic effects and serotonergic hyperactivity thus determining the occurrence of supraventricular tachiarrhythmias and of acute coronary syndromes and pulmary hypertension [21].

Echocardiography

As we have already underlined in the introduction a cardiomyopathy characterized from the echocardiographic point of view by Left ventricular (LV) dilatation, together with severely impaired systolic function and increased LV mass, represents the symptomatic end-stage of the disease which may occur in subjects assuming alcohol and other drugs. Echocardiographic evaluation of left ventricular ejection fraction (LVEF), in addition to the evaluation of the volumes, of the thicknesses of the cardiac chambers, of the morphology and functionality of the valve systems and of the estimation of pressures provides important information regarding myocardial function. In particular LVEF offers important information regarding both myocardial function and prognosis. However, this parameter presents various limitations; LVEF may influenced by hemodynamic load, by geometric assumptions and image quality and it does not reflect myocardial contractility, and in particular it does not allow early detection of myocardial dysfunction [22]. In this regard an important aid may be offered by the evaluation of diastolic function since alterations in LV diastolic function are considered markers of early cardiotoxicity and precede

alterations in systolic function [23]. To assess diastolic function Pulsed-wave Doppler mitral velocity curves must be obtained.

Accordingly, to the definition proposed by the European Association of Cardiovascular Imaging [24], in normal conditions, the majority of filling pressures occur during the early LV diastolic phase, then during atrial systole (the ratio between E and A velocities is greater than 1. In case of early reduction of myocardial relaxation (grade I of diastolic dysfunction), the early transmittal pressure gradient is reduced, and increased portion of diastolic filling pressure due to atrial contraction takes place. So, the E/A ratio is less than 1, together with a longer deceleration time (DT) of mitral inflow (normal ranges between 160–240 ms), because of a longer time to equilibrate left-sided chamber pressures. Along with the progression of worsening diastolic dysfunction (grade II of diastolic dysfunction), LA pressure increases with consequent LA sizes enlargement; the rise of early LV diastolic filling pressure is steeper, so the mitral inflow pattern of moderate diastolic dysfunction seems to be similar to that of the true normal diastolic filling pattern of E/A greater than 1 with DT equal or greater than 160 ms (leading to a pseudo-normalized pattern). In case of grade III of diastolic dysfunction (restrictive diastolic dysfunction), early LV diastolic filling is predominant, with a faster rise in filling pressures and very short DT (E/A > 1.5 and DT < 160 ms) [23]. Diastolic function evaluation may be improved recurring to Tissue doppler which has additionally the advantage to be load independent (while the assessment of Pulsed- wave Doppler mitral velocity curves is load-dependent) [25]. Furthermore, through integrated use of echo-Doppler and tissue Doppler imaging (TDI), it is possible to obtain a comprehensive evaluation of both left ventricular (LV) diastolic and longitudinal function indeed the combination of standard Doppler mitral inflow peak early (E) velocity with TDI annular early (e′) velocity (E/e′) is useful to noninvasively estimate the degree of LV filling pressure (LVFP). By averaging e′ velocity of septal and lateral mitral annulus, an E/e′ ≥ 13 accurately predicts elevated LVFP as a result of advanced LVDD [26].

Thus, in asymptomatic subjects, by recurring to the evaluation of these parameters, during standard basal echocardiography, earlier markers of cardiac dysfunction may be detected. A further aid in the evaluation of myocardial function may be given by the newest echocardiographic technique such as strain analysis.

Speckle tracking echocardiography (STE), through the measurement of strain and strain rate, which detect myocardial deformation, allows an even earlier identification of myocardial dysfunction [27]. STE is particularly useful in all conditions in which cardiac dysfunction is not still overt, but a subclinical involvement is undoubtedly present such as in presence of cardiovascular risk factors, in the early stages of chemotherapy induced cardiotoxicity, in asymptomatic subjects with chronic kidney disease [28].

In particular Global longitudinal strain (GLS) represents s probably the most frequent type of strain used to characterize LV systolic function in clinical practice [27]. It is the negative ratio of the maximal change in LV longitudinal length in systole to the original length as assessed by speckle tracking echocardiography. For what regards its prognostic role, previous studies have demonstrated that it proved to be superior to standard LV ejection fraction (EF) in predicting cardiac events and all-cause mortality in the general population [29, 30].

Accordingly, our investigation sought to assess which echocardiographic parameters derived from both standard basal echocardiography and strain analysis could allow to predict cardiac dysfunction in a subset population of chronic, asymptomatic subjects who take alcohol plus other drugs, with no known cardiovascular disease and no comorbidity known to affect cardiovascular function.

Methods

A total of 26 consecutive asymptomatic subjects assuming alcohol and other drugs were enrolled from the Unit of Addiction and Hepatology, Alcohological Regional Centre of our Policlinic. Among the patients, 12 (46%) were suffering from hypertension and all of them were on anti-hypertensive therapy, one patient was previously studied by echography for positive blood cultures without finding any significant alteration. Exclusion criteria were: known coronary arterial disease, severe valve disease, surgical correction of valve diseases, atrial fibrillation, congenital heart disease, chronic renal and liver dysfunction. After a complete physical examination, demographic data and anthropometric measurements of height and weight were provided, in order to calculate the body mass index (BMI, kg/m2) and body surface area (BSA, m2). Details of alcohol and other drugs consumption were obtained from the predefined questionnaires, involving information regarding the pattern, frequency and amount of daily intake of alcohol plus other drugs. Based on the assumption that one standard drink contains 12 g alcohol, the conversion of total alcohol consumption into number of standard drinks on a daily basis was then derived. Conventional transthoracic echocardiography was uniformly performed by an ultrasound device GE- Vingmed vivid 7system (GE-Vingmed Ultrasound AS, Horten, Norway), equipped with a 2-to 4-MHz transducer. The standard echocardiographic imaging protocol included measurements of LV end-diastolic and end-systolic diameters, wall thickness, LV mass (per European Association of Cardiovascular Imaging criteria), left atrial (LA) and LV volumes (using the biplane Simpson method for volume calculation), right ventricular basal and middle diameter. Complete pulsed-wave (PW) Doppler derived mitral inflow echocardiographic parameters of LV

diastolic function included the early (E) and late (A) diastolic filling velocities at the tip of the mitral leaflets from the apical four-chamber view, DT of early filling velocity and isovolumetric relaxation time (IVRT), corresponding to the time from aortic valve closure to onset of mitral inflow. The ratio between peak systolic (S) and diastolic (D) flow velocity was obtained by PW Doppler interrogation of pulmonary venous flow from the apical four-chamber view. Furthermore, Doppler tissue imaging-based mitral annular relaxation velocity (e') was assessed at the lateral mitral annulus using spectral Doppler techniques with LV filling pressure estimated using the E/e' ratio. Tricuspid annular plane systolic excursion (TAPSE) was measured by pointing the motion-mode (M-mode) cursor on the tricuspid lateral annulus in the apical 4-chamber view, as the height difference of the valve annulus excursion (in millimetres). The peak tricuspid regurgitation (TR) gradient was calculated by the simplified Bernoulli equation on the basis of the peak TR velocity, by using the continuous-wave Doppler of the TR trace in apical 4-chamber view. Right atrial pressure (RAP) was estimated by the basal diameter of inferior vena cava and its respiratory excursions. Systolic pulmonary artery pressure (sPAP) was calculated by adding the TR peak systolic gradient to the RAP estimate Finally Speckle tracking analysis was executed.

Speckled tracking echocardiography was performed on three consecutive cardiac cycles of two-dimensional LV images from the three standard apical views. Custom acoustic tracking software allowing semi-automated, two-dimensionally derived strain analysis (Echo PAC Advanced Analysis Technologies; GE Healthcare) was applied to two-dimensional grayscale images by tracking movements of "speckles" in myocardial tissue, frame by frame, throughout the cardiac cycle. The software automatically divides each image into six myocardial segments and accepts segments of good tracking quality while rejecting poorly tracked segments, allowing the observer to manually override its decision at the same time using visual assessment. The peak negative systolic longitudinal strain was assessed from six segments in apical long- axis, four-chamber, and two-chamber view. GLS was calculated by averaging each value of regional peak longitudinal strain obtained in each apical view before aortic valve closure, which was defined in the apical long-axis view. Longitudinal strain was calculated by average of six basal, six middle, and six apical LV segments.

Peak systolic dispersion (PSD) was estimated directly by the machine, by comparing the difference between the earliest systolic peak and the latest amongst all the segments. Less negative values reflect progressive impairment in GLS and therefore in LV systolic function.

Statistical analyses

Continuous variables distribution was checked for normality using the Shapiro- Wilkinson test, and reported accordingly as mean ± standard deviation or median (quartile 1 – quartile 3). Categorical variables were reported as count and percentage. Univariate association between global longitudinal strain and echocardiographic variables was tested using Spearman's correlation. Two-tailed p values <0.05 were considered statistically significant. Statistical analysis was conducted using R (R Foundation for Statistical Computing).

Results

Between march and august 2022, twenty-six patients were enrolled. Table 1 summarizes the main baseline characteristics of the enrolled population. 73% were male and mean age was 43±11 years. Most patients were male (73%), smokers, with an average consumption of 1 (0.81-1.88) pack/die, and the totality were alcoholics. Among the patients, 12 (46%) were suffering from hypertension and all of them were on anti-hypertensive therapy, psychotropic drugs were assumed by almost 31%. Up to 1/3rd of patients were multi-drug users, with an average consumption of 1.50±0.91 drugs, in particular, half of the population took cocaine and marijuana, whereas roughly 12% used heroin, methadone or hashish.

Echocardiographic features are summarized in Table 2. Mean ejection fraction was 57% (53%–63%), with regional wall motion abnormalities being reported in only one patient, sent for further evaluations. Valvopathies were reported in a minority of individuals, of whom 11.5% had aortic regurgitation and 15.4% mitral regurgitation both trivial. Mean average global longitudinal strain value was -18.3% (-%17 – - 20,1%). Mean E/A was 1.1 (0.9-1.2) and mean e/e' average 6.7 (6.2-7.2). Right ventricular function estimated by TAPSE ad S' wave evaluation was preserved.

Scatter plots depicting the correlations between average global longitudinal strain and echocardiographic parameters are shown in the Figure 1(correlation between average GLS and E/A and e/e', DTD, systolic PAP). In particular, we found a modest, yet significant correlation between average GLS and E/A (Spearman's $r = 0.43$, $p = 0.03$), whereas other parameters did not correlate significantly with GLS.

	Overall (N=26)
Demographic and anamnestic information	
Age	43 ± 11
BSA, kg/m2	1.91 ± 0.24
Hypertension	12 (46.2)
Diabetes	1 (3.8)
Smoking	26 (100)
Pack/day, units	1 (0.81-1.88)
Alcohol use	26 (100)
Male sex	19 (0.73)
Other cardiovascular comorbidities	2 (7.7)
Medication	
Aspirin	2 (7.7)
Psychotropic	8 (30.8)
Statins	1 (3.8)
ACEI/ARBs	5 (19.2)
Beta blocker	2 (7.7)
Diuretics	4 (15.4)
Alfa antagonists	1 (3.8)
Drug use	
Number of used drugs	1.50 ± 0.91
Multi-drug user	9 (34.6)
Cocaine	13 (50)
Heroin	3 (11.5)
Methadone	3 (11.5)
Marijuana	13 (50)
Hashish	3 (11.5)
Amphetamine	1 (3.8)
LSD	1 (3.8)
Acid	1 (3.8)
Crack	1 (3.8)

BSA stands for body surface area; ACEI: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers; LSD: lysergic acid diethylamide.

Table 1: Baseline features.

	Overall (N=26)
Interventricular septum diameter (diastolic), mm	9.69 ± 2.04
Interventricular septum diameter (systolic), mm	13 (12 - 15)
End-diastolic diameter, mm	46.31 ± 4.07
Posterior wall, mm	13 (10 -14)
WT.IVS, mm	41 (32 - 68)
Aortic root diameter, mm	32 ± 3
Ascending aorta diameter, mm	29 (22 - 32)
Pulmonary acceleration time, ms	142 (127 - 164)
Ejection fraction (Simpson method), %	57 (53 - 63)
Regional wall motion abnormalities	1 (3.8)
Aortic regurgitation	
0	23 (88.5)
1	2 (7.7)
2	1 (3.8)
Mitral regurgitation	4 (15.4)
GLS	
4-chambers	18.10 (16.35 - 20.25)
2-chambers	19.30 (15.98 - 20.17)
3-chambers	17.70 (15.20 - 19.98)
GLS average	18.34 ± 2.51
PSD, ms	35.36 (22 - 43.58)
E velocity, cm/s	0.77 ± 0.17
Deceleration time, ms	220 (185 - 250)
A velocity, cm/s	0.72 ± 0.13
E/A	1.06 (0.88 - 1.21)
E septal cm/s	0.11 (0.09 - 0.12)
E lateral cm/s	0.13 (0.10 - 0.14)
E/e' average	6.69 (6.16 - 7.23)
Left atrial anteroposterior diameter, mm	34 (30.25 - 39.75)
Left atrial area 4-chamber, mm2	16.05 (14.03 - 17.95)
Left atrial volume index, ml/m2	22.68 ± 7.50
Left atrial volume, ml	43.15 ± 15.09
Right atrial area mm2	15 (13.40 - 17)
Right atrial volume, ml	39.71 ± 17.2
Basal RVEDD, mm	34 (31.25 - 37)
Medium RVEDD, mm	24 (20.25 - 26)
TAPSE, mm	23.50 (21 - 27.75)
TV S', cm/s	14 (12.25 - 16)
Pulmonary arterial systolic pressure, mmHg	22.11 ± 9.87
RVTDD stands for right ventricular end-diastolic diameter, TAPSE: tricuspid annular plane systolic excursion – other abbreviations GLS stands for Global longitudinal strain, PDS stands for Peak systolic dispersion, TV S' stands tricuspid annulus S' wave velocity.	

Table 2: Echocardiographic features

Discussion

Our investigation, involving a study-population of asymptomatic European subjects, who took alcohol and other drugs and who underwent echocardiographic exam, showed that, in these patients, who did not present a significant rate of systolic dysfunction, nor echocardiographic findings of increased LV sizes, mass or relative wall thickness (which could suggest a LV structural abnormality), the median values of average GLS were closer to the lower range of normal. This finding, despite the absence of a healthy control group for comparison, might indicate a subclinical alteration in these subjects thus confirming that GLS may be considered the earliest and more reliable index of future impairment of systolic function in asymptomatic individuals with high cardiovascular risk (indeed all were smokers, alcoholics and in large part hypertensive although the age was not advanced).

Statistical analysis displayed a significant positive correlation between E/A and GLS average. Concerning E/e' no relationship was found, hence suggesting that left ventricular filling pressures are still normal if patients are asymptomatic, or that the effect is too small to be observed by standard echocardiographic methods. For what regards the fact that the only existing positive correlation was between GLS and E- A this may be ascribed to the fact that while e/e' (evaluated through tissue-doppler) is load-independent, E-A ratio is markedly load-dependent and these patients who assume alcohol plus other drugs are subject to marked variations in the hemodynamic load (alcohol is a vasodilator and the other drugs often act by modulating the sympathetic nervous system activity thus influencing hemodynamic status).

These results must be confirmed by further studies involving a larger population of patients with an adequate percentage of both male and female subjects so as to evaluate whether sex- differences exist for what regards echocardiographic parameters which allow to predict cardiac dysfunction (in this regard sex-differences were found in our previous study involving asymptomatic patients who assumed alcohol [31]).

Conclusions

It is known that long-lasting alcohol plus other drugs intake may be associated to the development of a form of non-ischemic cardiomyopathy, conversely echocardiography is a useful non-invasive diagnostic tool to demonstrate the presence of both systolic and diastolic dysfunction in presence of cardiomyopathy. In this study we have examined asymptomatic subjects who assumed alcohol plus other drugs who have undergone echocardiographic exam with the aim to demonstrate the presence of early markers of subclinical dysfunction. Our patients displayed lower values of average GLS. No correlations were found between GLS and e/e', thus suggesting that left ventricular filling pressures are still normal if patients are asymptomatic and don't display structural abnormalities of the heart. Furthermore, statistical analysis demonstrated only a positive correlation between E-A ratio and GLS this may be ascribed to the state of hemodynamic overload of these subjects, who present alcohol plus other drugs abuse, and will undergo systolic dysfunction as predicted by a pathological GLS. These data may be considered interesting but must be confirmed by further studies involving a larger population of asymptomatic patients, with an adequate percentage of both male and female to investigate whether sex-differences exist.

References

1. Alcoholic cardiomyopathy: incidence characteristics, and, clinical pathophysiology. Chest. 121:1638-50.
2. Ghuran A, van der Wieken LR and Nolan J (2001) Cardiovascular Complications of Recreational Drugs: Are An Important Cause Of Morbidity And Mortality, BMJ. 323: 464–466.
3. Iacovoni A, De Maria R, Gavazzi A. (2010) Alcoholic cardiomyopathy. J Cardiovasc Med (Hagerstown). 11:884-92.
4. Demakis JG, Proskey A, Rahimtoola SH, Jamil M, Sutton GC, et al. (1974) The natural course of alcoholic cardiomyopathy. Ann Intern Med. 80:293.
5. Lépicier P, Bouchard J-F, Lagneux C, Lamontagne D. (2003) Endocannabinoids protect the rat isolated heart against ischaemia. Br J Pharmacol. 139:805–15.
6. Lake KD, Compton DR, Varga K, Martin BR, Kunos G. (1997) Cannabinoid-induced hypotension and bradycardia in rats mediated by CB1-like cannabinoid receptors. J Pharmacol Exp Ther. 281:1030–7.
7. Liu J, Gao B, Mirshahi F, Sanyal AJ, Khanolkar AD, et al. (2000) Functional CB1 cannabinoid receptors in human vascular endothelial cells. Biochem J. 346:835–4.
8. Rosa GM, Puce L, Mori L, Currà A, Fattapposta F, et al (2022) Nabiximols effect on blood pressure and heart rate in post-stroke patients of a randomized controlled study. Front Cardiovasc Med. 9:990188.
9. Iannaccone G, Porto I. (2021) Marijuana influence on cardiac modulation and heart rate: novel hypotheses and gaps in evidence. Minerva Cardiol Angiol. 69:466–8.
10. Han KH, Lim S, Ryu J, Lee C-W, Kim Y, et al. (2009) CB1 and CB2 cannabinoid receptors differentially regulate the production of reactive oxygen species by macrophages. Cardiovasc Res. 84:378–86.
11. Jones RT. (2002) Cardiovascular system effects of marijuana. J Clin Pharmacol. 42:58S–63S.
12. Marchetti D, Spagnolo A, De Matteis V, Filograna L, De Giovanni N. (2016) Coronary thrombosis and marijuana smoking: a case report and narrative review of the literature. Drug Test Anal. 8:56–62.
13. Richards JR, Bing ML, Moulin AK, Elder JW, Rominski RT, et al. (2019) Cannabis use and acute coronary syndrome. Clin Toxicol. 57:831–41.
14. Patel R, Kamil S, Bachu R, Adikey A, Ravat V., et al (2019) Marijuana use and acute myocardial infarction: A systemic review of published cases in the literature. Trends Cardiovasc. Med. 30:298–307.
15. Chouairi F. Miller PE, Guha A, Clarke JR, Reinhardt S,et al (2021) Cannabis use disorder among atrial fibrillation admissions, 2008–2018. Pacing Clin Electrophysiol. 44: 1934-1938.

16. Dutta T, Ryan KA, Thompson O, Lopez H, Fecteau N, et al (2025) Marijuana Use and the Risk of Early Ischemic Stroke: The Stroke Prevention in Young Adults Study. Stroke. 52:3184-3190.

17. Kim ST, Park T (2019) Acute and chronic effects of cocaine on cardiovascular health. Int J Mol Sci. 20:584.

18. Mouhaffet A, Madu E, Satmary W, Fraker T. (1995) Cardiovascular complications of cocaine. Chest.107: 1426-1434.

19. Ghuran A, Nolan J. (2000) Recreational drug misuse: issues for the cardiologist. Heart. 83:627–633.

20. Osterwalder JJ. (1995) Patients intoxicated with heroin or heroin mixtures: how long should they be monitored? Eur J Emerg Med. 2: 97-101.

21. Borowiak KS, Ciechanowski K, Waloszczyk P. (1998) Psilocybin mushroom (Psilocybe semlanceata) intoxication with myocardial infarction. Clin Toxicol. 36: 47-49.

22. Stokke TM, Hasselberg NE, Smedsrud MK, Sarvari SI, Haugaa KH, et al. (2017) Geometry as a Confounder when assessing ventricular systolic function: comparison between ejection fraction and strain. J Am Coll Cardiol 70:942–54.

23. V. Mor-Avi, K.A. Collins, C.E. Korcarz, M. Shah, K.T. Spencer, R.M. (2010) Lang Detection of regional temporal abnormalities in left ventricular function during acute myocardial ischemia Am. J. Physiol. Heart Circ. Physiol., 280: pp. H1770-H1781.

24. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al (2016) Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 29:277-314.

25. Dini FL, Lattanzi F, Fontanive P, Rosa GM, De Tommasi SM (2009) Value of tissue Doppler imaging for risk stratification of patients with chronic systolic heart failure with or without restrictive mitral flow. Eur J Echocardiogr. 10:562-6.

26. Dini, F.l, Galderisi, M, Nistri, S, Buralli, S, Ballo, P, et al. (2013). Abnormal left ventricular longitudinal function assessed by echocardiographic and tissue Doppler imaging is a powerful predictor of diastolic dysfunction in hypertensive patients: The SPHERE study. Internationational Journal of Cardiology. 168: 3351-3358.

27. Lotti R, DE Marzo V, Della Bona R, Porto I, Rosa GM (2023) Speckle-tracking echocardiography: state of art and its applications. Minerva Med. 114:500-515.

28. Ravera M, Rosa GM, Fontanive P, Bussalino E, Dorighi U, et al (2019) Impaired Left Ventricular Global Longitudinal Strain among Patients with Chronic Kidney Disease and End-Stage Renal Disease and Renal Transplant Recipients Cardiorenal Med. 9:61-68.

29. Stanton T, Leano R, Marwick TH. (2009) Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. Circ Cardiovasc Imaging. 2:356–64.

30. Takahashi, T., Kusunose, K., Zheng, R. Yamaguchi N, Hirata Y, et al. (2022) Association between cardiovascular risk factors and left ventricular strain distribution in patients without previous cardiovascular disease. J Echocardiogr 20: 208–215.

31. Rosa GM, Scagliola R, Zoppoli G, Perna V, Buscaglia A, et al (2021) May standard basal echocardiogram allow to obtain predictors of asymptomatic cardiac dysfunction in alcoholics? Minerva Medica, 112:786-91.