Correlation of echocardiography with right heart catheterization for the diagnosis of pulmonary hypertension

Correlación de la ecocardiografía con el cateterismo del corazón derecho para el diagnóstico de hipertensión pulmonar

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Abstract

Background: Pulmonary hypertension is a fatal disease of multiple etiologies that is estimated to affect over 100 million people worldwide, therefore earlier diagnosis of pulmonary hypertension would be of great benefit for the estimation and treatment of the condition and underlying causes. Aim of study: The purpose of this analysis is to study the reliability and accuracy of echocardiography in the measurement of pulmonary artery pressures in comparison with right heart catheterization for patients with pulmonary hypertension. Patients and Methods: In a prospective study 150 patients evaluated for suspected pulmonary hypertension. Echocardiography was performed and systolic and mean pulmonary artery pressure estimated. Subsequently, pulmonary hemodynamic parameters measured by right heart catheterization for definitive diagnosis of pulmonary hypertension. Results: The echocardiographic parameters showed high sensitivity (87.5%), specificity (94%), with significant p-value (< 0.001) for systolic pulmonary artery pressure and high sensitivity (79%), specificity (82.5%) with significant p-value (< 0.001) for mean pulmonary artery pressure . There is strong correlation between the Systolic pulmonary artery pressure (67.13±26.53) mm Hg measured by echocardiography and (71.43±30.89) mm Hg measured by right heart catheterization (r = 0.91, p < 0.001). Correlation also observed between mean pulmonary artery pressure (43.23±18.8) mm Hg by echocardiography and (49.31±22.7) mm Hg by right heart catheterization (r = 0.80, p < 0.001). Conclusion: Echocardiographic parameters have high sensitivity for detecting pulmonary hypertension. Estimation of systolic pulmonary artery pressure has the highest correlation with right heart catheterization. Invasive measurement of pulmonary pressure is required among patients with possible pulmonary hypertension on echocardiogram for further evaluation and stratification.

Keywords: Correlation, Echocardiography, Right, Heart, Catheterization, Diagnosis, Pulmonary, Hypertension.

Resumen

Antecedentes: La hipertensión pulmonar es una enfermedad mortal de múltiples etiologías que se estima que afecta a más de 100 millones de personas en todo el mundo, por lo que un diagnóstico más temprano de la hipertensión pulmonar sería de gran beneficio para la estimación y el tratamiento de la afección y las causas subyacentes. Objetivo del estudio: El propósito de este análisis es estudiar la confiabilidad y precisión de la ecocardiografía en la medición de las presiones de la arteria pulmonar en comparación con el cateterismo del corazón derecho para pacientes con hipertensión pulmonar. Pacientes y Métodos: En un estudio prospectivo se evaluaron 150 pacientes por sospecha de hipertensión pulmonar. Se realizó una ecocardiografía y se estimó la presión sistólica y media de la arteria pulmonar. Posteriormente se midieron los parámetros hemodinámicos pulmonares mediante cateterismo cardíaco derecho para el diagnóstico definitivo de hipertensión pulmonar. Resultados: Los parámetros ecocardiográficos mostraron alta sensibilidad (87,5%), especificidad (94%), con valor de p significativo (< 0,001) para la presión de la arteria pulmonar sistólica y alta sensibilidad (79%), especificidad (82,5%) con p-significativo. valor (< 0,001) para la presión media de la arteria pulmonar. Existe una fuerte correlación entre la presión de la arteria pulmonar sistólica (67,13±26,53) mm Hg medida por ecocardiografía y (71,43±30,89) mm Hg medida por cateterismo cardíaco derecho (r = 0,91, p < 0,001). También se observó correlación entre la presión media de la arteria pulmonar (43,23±18,8) mm Hg por ecocardiografía y (49,31±22,7) mm Hg por cateterismo cardíaco derecho (r = 0,80, p < 0,001). Conclusión: Los parámetros ecocardiográficos tienen alta sensibilidad para detectar hipertensión pulmonar. La estimación de la presión sistólica de la arteria pulmonar tiene la mayor correlación con el cateterismo del corazón derecho. Se requiere una medición invasiva de la presión pulmonar en pacientes con posible hipertensión pulmonar en un ecocardiograma para una evaluación y estratificación adicionales.

Palabras clave: Correlación, Ecocardiografía, Derecho, Corazón, Cateterismo, Diagnóstico, Pulmonar, Hipertensión.

Introduction

Pulmonary hypertension (PH) is a significant global health issue, affecting an estimated 100 million people worldwide, with a prevalence of about 1% globally and up to 10% in individuals over 65 years of age1,2. Characterized by increased pulmonary vascular resistance leading to elevated pulmonary artery pressure, right ventricular hypertrophy, and heart failure, PH presents non-specific symptoms such as dyspnea on exertion, fatigue, chest pain, and syncope3-6. The pathogenic features of PH include sustained pulmonary vasoconstriction, vascular remodeling, in situ thrombosis, and increased vascular stiffness3,4. PH is defined by a mean pulmonary arterial pressure (mPAP) over 20 mmHg, with the diagnostic criteria also including pulmonary vascular resistance (PVR) and pulmonary arterial wedge pressure (PAWP) to differentiate pre-capillary PH from other types7-9. The life expectancy of PH patients has notably improved, with a current 3-year survival rate of 70-80%, compared to 40% in the 1980s10,11. Epidemiologically, PH has different incidences and prevalences across regions. In Europe, the prevalence of pulmonary arterial hypertension (PAH) is 15–60 patients per million adult populations, with an incidence of 5–10 cases per million per year. In Germany, the incidence of chronic thromboembolic pulmonary hypertension is 4 per 1 million adults per year10. Pediatric PH incidence ranges from 4–10 cases per million children per year in Europe and 5–8 cases per million in the USA12-14. A Dutch study reported an annual incidence rate of 63.7 per million children15. The clinical classification of PH has evolved to better categorize conditions based on pathophysiological mechanisms, clinical presentation, hemodynamics, and management16. Notable changes include additions to idiopathic pulmonary artery hypertension (IPAH) subgroups and the inclusion of conditions like pulmonary veno-occlusive disease/pulmonary capillary haemangiomatosis (PVOD/PCH) and persistent PH of the newborn (PPHN) in group 1 PAH17-19. Bedside cardiovascular findings in PH patients are crucial for assessing the severity of right heart failure. Key indicators include blood pressure, resting heart rate, jugular venous pressure (JVP), presence of right ventricular heave, and palpable P220-22. Transthoracic echocardiography is used for PH estimation, with challenges in measuring right ventricular ejection fraction due to its unique geometry23-25. Surrogate measures of right ventricular function are used, with peak tricuspid regurgitation velocity measured by continuous-wave Doppler echocardiography being a key indicator. Despite advancements in understanding and managing PH, the condition remains incurable, and its complex nature necessitates detailed clinical evaluation for accurate diagnosis and treatment26-28. The purpose of this analysis is to study the reliability and accuracy of echocardiography in the measurement of pulmonary artery pressures in comparison with right heart catheterization for patients with pulmonary hypertension.

Methods

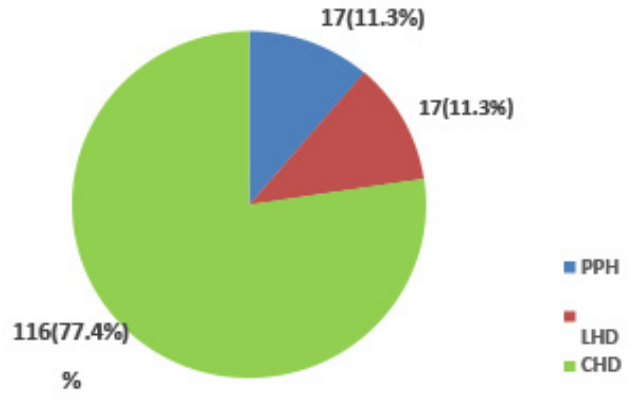
In this prospective study conducted at Ibn-Albitar specialty center for cardiac surgery in Baghdad from June 2022 to May 2023, 150 patients were evaluated for pulmonary hypertension (PH). Pre-capillary PH was defined as a mean pulmonary artery pressure (mPAP) > 20 mmHg and pulmonary vascular resistance (PVR) ≥ 3 woods units (WU) as per the European Society of Cardiology (ESC) and World Symposium for Pulmonary Hypertension-6 (WSPH-6) guidelines. Post-capillary PH was characterized by mPAP > 20 mmHg and pulmonary capillary wedge pressure (PCWP) > 15 mmHg. Data were collected through direct interviews and questionnaires after obtaining consent. Demographic characteristics detailed medical history, and family history of PH were recorded. EchoCardiography (TTE) was performed using the G.E Vivid E9 echocardiography machine, estimating right ventricular systolic pressure (RVSP) by adding mean right atrial pressure (RAP) to the transtricuspid pressure gradient (TPG), calculated using the modified Bernoulli equation. TTE also assessed anatomical and functional abnormalities indicative of PH. Right heart catheterization (RHC) was performed under general or local anesthesia through femoral access, measuring various hemodynamic parameters. RHC was reserved for patients with strong clinical suspicion of PH or those with low probability PH by TTE but with consistent symptoms or risk factors. The study included patients of any age who voluntarily consented and had risk factors for PH. Exclusions included patients refusing RHC, those where tricuspid regurgitation couldn't be measured, and patients with complex heart anatomical abnormalities. Statistical analysis was performed using SPSS 29.0, with continuous data presented as mean and standard deviation, and categorical data as frequency and percent. The relationship between estimated RVSP by TTE and RHC measurements was assessed using Pearson correlation analyses. The sensitivity, specificity, positive, and negative predictive values of TTE in diagnosing PH were calculated using RHC as the gold standard. A value of $p < 0.05$ was considered statistically significant.

A 150 patients in whom PH is suspected underwent TTE and RHC. They include 70 (46.7%) males and 80 (53.3%) females. The mean age (14.03±13.406), the patients divided into three age groups including those with age less than 6 years are 52(34%) patients in which 24 (46.2%) males and 28 (53.8%) females, and those ages between 6-18 years are 54 (36%) patients in which 27 (50%) males and 27 (50%) females and those more than 18 years are 44 (30%) patients in which 19 (43.2%) males and 25 (56.8%) females All these data showing in table 1.

Table 1: Age and gender distribution of the study population.			
Characteristics	(mean ± SD)		
Mean age (years)	14.03 ± 13.406		
< 6 years	24 (46.2)	28 (53.8)	52 (34%)
6 – 18 years	27 (50.0)	27 (50.0)	54(36%)
> 18 years	19 (43.2)	25 (56.8)	44(30%)
Total	70 (46.7)	80 (53.3)	150(100%)
Gender	Male (n. %)	Female (n. %)	Total
	70 (46.7%)	80 (53.3%)	150 (100%)

The causes of PH in patients enrolled in this study were CHD in 116 (77.4%) of cases, LHD in 17 (11.3%) of cases and primary pulmonary hypertension in 17 (11.3%) of cases as seen figure 1.

Figure 1 causes of PH in patients



The parameters measured by TTE and RHC were evaluated and showed in means and standard deviations including sPAP by TTE (67.13 ±26.53) mmHg, mean pulmonary artery pressure using early pulmonary valve regurgitation (mPAP using PR) by TTE was (43.23 ±18.8) mmHg, mean pulmonary artery pressure using tricuspid valve regurgitation velocity (mPAP using TR) by TTE was (39.67±16.44) mmHg, mean pulmonary artery pressure using pulmonary artery acceleration time (mPAP using PAAT) by TTE (39.75±15.79) mmHg, mean right atrial pressure (mRAP) by TTE was (6.45±3.16) mmHg, mean pulmonary vascular resistance (mPVR) by TTE was (4.53±2.69) WU, mean tricuspid regurgitation jet velocity (mTRV) by TTE (2.47±0.739) m/s, mean pulmonary artery acceleration time (mPAAT) by TTE was (86.63±34.87) m/s, mean tricuspid annulus plane systolic excursion (mTAPSE) was (17.81±2.799) mm, mean left ventricular ejection fraction (mLVEF) was 53.5% (±6.48), as shown in table 2.

Table 2: Mean values and standard deviations of TTE parameters.	
Echocardiography parameters	Mean (SD)
sPAP using TR (mmHg)	67.13 (±26.53)
mPAP using PR (mmHg)	43.23 (±18.8)
mPAP using TR (mmHg)	39.67 (±16.44)
mPAP using PAAT (mmHg)	39.75 (±15.79)
mRAP (mmHg)	6.45 (±3.16)
PVR (WU)	4.53 (±2.69)
TRV (m/s)	2.47 (±0.739)
PAAT (m/s)	86.63 (±34.87)
TAPSE (mm)	17.81 (±2.799)
LVEF (%)	53.5 (±6.48)

The RHC parameters including systolic pulmonary artery pressure (sPAP) was (71.43±30.89) mmHg, mean pulmonary artery pressure (mPAP) was (49.31±22.7) and mean pulmonary vascular resistance (mPVR) was (8.74 ±6.61) WU, these data demonstrated in table 3.

Table 3: Mean values and standard deviations of RHC parameters.	
RHC parameters	Mean (SD)
sPAP (mmHg)	71.43 (±30.89)
mPAP (mmHg)	49.31 (±22.7)
PVR (WU)	8.74 (±6.61)

In this study we have shown that when compared to sPAP by RHC; (98.91%) of those with a high probability of PH by TTE had PH by RHC and (1.09%) no PH by RHC, (97.2%) of those with an intermediate probability of PH by TTE had PH by RHC and (2.8%) with no PH. Strikingly, (36.36%) of patients with low probability of PH by TTE had PH by RHC and (63.63%) with no PH with significant P-value($P < 0.001$) and when compared to mPAP by RHC; (100%) of those with a high probability of PH by TTE had PH by RHC and (0.0%) no PH by RHC, (93.1%) of those with an intermediate probability of PH by TTE had PH by RHC and (6.9%) with no PH, (5.9%) of patients with low probability of PH by TTE had PH by RHC (94.1%) with no PH with significant P-value($P < 0.001$) as seen in table 4.

Table 4: Number and percentage of patients with and without PH by RHC according to low, intermediate and high probabilities of PH by TTE.

	Probability of PH based on TRV			
Parameter	Low No. (%)		High No. (%)	p-value
sPAP by RHC				< 0.001**
No PH	14 (63.63)	1 (2.78)	1 (1.08)	
PH	8 (36.36)	35 (97.2)	91 (98.91)	
mPAP by RHC				< 0.001**
No PH	16 (94.1)	1 (6.9)	0 (0.0)	
PH	6 (5.9)	35 (93.1)	92 (100)	

The validity of the diagnosis of PH by echocardiography was assessed compared to right heart catheterization as a gold standard. The validity was assessed by measuring the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. The echocardiographic measurement of sPAP showed (87.5%) sensitivity, (94%) specificity, (63.6%) PPV, (98.4%) NPV, (93.3%) accuracy and correlation (0.91) with significant p-value (< 0.001), the echocardiographic measurement of mPAP (via PR) showed (79%) sensitivity, (82.5%) specificity, (63%) PPV, (78%) NPV, (83.3%) accuracy and correlation (0.81) with significant p-value (< 0.001), the echocardiographic measurement of mPAP(using sPAP) showed (84.1%) sensitivity, (82.5%) specificity, (61.5%) PPV, (89.2%) NPV, (82.7%) accuracy and correlation (0.82) with significant p-value (< 0.001), the echocardiographic measurement of mPAP(using PAAT) showed (74.1%) sensitivity, (71%) specificity, (57.1%) PPV, (79.2%) NPV, (71.3%) accuracy and correlation (0.77) with significant p-value (< 0.001) as shown in table 5.

Table 5. Validity and correlation of echocardiographic parameters with parameters in right heart catheterization.

	Comparison with parameters of RHC					
Echocardiography parameters	Sensitivity	Specificity	PPV	NPV	Accuracy	Correlation r (p value)
Estimation of Spap	87.5%	94%	63.6%	98.4%	93.3%	0.91 (< 0.001)
Estimation of mPAP (using PR)	79%	82.5%	63%	78%	83.3%	0.81 (< 0.001)
Estimation of mPAP (sPAP)	84.1%	82.5%	61.5%	89.2%	82.7%	0.82 (< 0.001)
Estimation of mPAP (using PAAT)	74.1%	71%	57.1%	79.2%	71.3%	0.77 (< 0.001)

In this study, we found correlation between the sPAP (67.13±26.53 mm Hg) measured by TTE and sPAP (71.43±30.89 mm Hg) measured by right-heart catheterization. A strong correlation was found ($r = 0.91$, $p < 0.001$). Also, correlation was observed between mPAP (43.23±18.8 mm Hg) by TTE and mPAP (49.31±22.7 mm Hg) by RHC ($r = 0.80$, $p < 0.001$) as seen in table 6.

Table 6. Correlation of invasive and noninvasive methods in the measurement of both sPAP and mPAP.

TTE		RHC	Correlation	P-vlue
mPAP (mmHg)	43.23 (±18.8)	49.31 (±22.7)	0.80	0.001
sPAP (mmHg)	67.13 (±26.53)	71.43 (±30.89)	0.91	0.001

Discussion

This study examines the role of echocardiography in assessing pulmonary hypertension (PH) and its correlation with right heart catheterization (RHC) measurements. The study involved 150 patients diagnosed with PH using both transthoracic echocardiography (TTE) and RHC. It was observed that the majority of the cases were females, aligning with findings from studies by Sohail et al.4 in Pakistan and Griener et al.28 in America. The mean age of the patients was 14.03±13.406 years, with the most common age group being between 6-18 years. This contrasts with the findings of Sohail et al.4 and Griener et al.28, who reported different predominant age groups in their respective studies. In terms of echocardiographic parameters, the study recorded systolic pulmonary artery pressure (sPAP) at 67.13±26.53 mmHg, mean pulmonary artery pressure (mPAP) using tricuspid regurgitation (TR) at 39.67±16.44 mmHg, and mPAP using pulmonary artery acceleration time (PAAT) at 39.75±15.79 mmHg. These results are closely related to those found in a study conducted in the Kingdom of Saudi Arabia by Soofi et al.29. Regarding RHC parameters, sPAP was measured at 71.43±30.89 mmHg and mPAP at 49.31±22.7 mmHg. These results are similar to those from a study in China by Wang et al.30 but differ from a German study by Hammerstingl C. et al.16, possibly due to differences in sample sizes. The study also found that a significant percentage of patients with high and intermediate probabilities of PH by TTE were confirmed to have PH by RHC, supporting findings from a UK study by Slegg et al.31. Non-invasive sPAP measurement by TTE showed good correlation with RHC, with sensitivity, specificity, and accuracy aligning closely with findings from an American study by Griener et al.28. In terms of mPAP measurement by TTE, using PR showed 79% sensitivity, 82.5% specificity, and 83.3% accuracy, similar to results from a Canadian study by Janda et al.32. Measurement of mPAP using sPAP showed 84.1% sensitivity, 82.5% specificity, and 82.7% accuracy, closely related to the findings of Swift et al. (33) in the UK. However, measurement of mPAP using PAAT showed lower sensitivity, specificity, and accuracy, which is consistent with findings by Sohail et al.4.

The study concluded a strong correlation between sPAP measured by TTE and RHC, with a correlation coefficient ($r = 0.91$, $p < 0.001$). Similar findings were observed for mPAP, with a correlation coefficient ($r = 0.80$, $p < 0.001$), aligning closely with results from studies in Germany (Hammerstingl et al.16) and China (Wang et al.30). The study emphasizes the importance of TTE as a non-invasive tool in assessing PH but also highlights the need for confirmatory RHC in certain cases. The study's findings contribute to a better understanding of PH assessment and management, especially in pediatric patients from congenital heart disease consultation clinics.

Conclusions

Echocardiographic methods are highly sensitive for detecting pulmonary hypertension. Pulmonary artery systolic pressure estimation via echocardiography correlates best with right heart catheterization. Mean pulmonary artery pressure estimation using tricuspid valve regurgitation in TTE aligns more closely with invasive measurements than pulmonary artery acceleration time, except in cases of moderate to severe tricuspid regurgitation. Patients showing potential or definite pulmonary hypertension on an echocardiogram require invasive pulmonary pressure assessment for further evaluation and stratification. The diagnostic accuracy of echocardiography for pulmonary hypertension using a systolic pulmonary artery pressure (sPAP) threshold of 37 mmHg is moderately effective.

References

1. Galie N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019;53:1802148.

2. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J 2019;53:1801913.

3. Hemnes, AR, and HC Champion. 2008. Right heart function and haemodynamics in pulmonary hypertension. Int. J. Clin. Pract. Suppl. 160:11–19.

4. Sohail A, Korejo HB, Shaikh AS, Ahsan A, Chand R, Patel N, Karim M, Korejo H. Correlation between echocardiography and cardiac catheterization for the assessment of pulmonary hypertension in pediatric patients. Cureus. 2019 Aug 29;11(8).

5. Rich S. Pulmonary hypertension. In: Bonow R, Mann D, Zipes D, Libby P, eds. Braunwald's heart disease: A textbook of cardiovascular medicine. 2012:1696–1718.

6. van Wolferen SA, Marcus JT, Westerhof N, Spreeuwenberg MD, Marques KM, Bronzwaer JG, Henkens IR, Gan CT, Boonstra A, Postmus PE, Vonk- Noordegraaf A. Right coronary artery flow impairment in patients with pulmonary hypertension. Eur Heart J. 2008;29:120–127.

7. Xanthouli P, Jordan S, Milde N, Marra A, Blank N, Egenlauf B, et al. Haemodynamic phenotypes and survival in patients with systemic sclerosis: the impact of the new definition of pulmonary arterial hypertension. Ann Rheum Dis 2020;79:370–378.

8. Paulus WJ, Tschope C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J 2007;28:2539–2550.

9. Pieske B, Tschope C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J 2019;40:3297–3317

10. Peacock AJ, Murphy NF, McMurray JJ, Caballero L, Stewart S. An epidemiological study of pulmonary arterial hypertension. Eur Respir J 2007;30:104-9. JH Park et al. 10 Tuberc Respir Dis 2022;85:1-10 www.e-trd.org

11. Sitbon O, Humbert M, Jais X, Ioos V, Hamid AM, Provencher S, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. Circulation 2005;111:3105-11.9.

12. Song S, Lee SE, Oh SK, Jeon SA, Sung JM, Park JH, et al. Demographics, treatment trends, and survival rate in incident pulmonary artery hypertension in Korea: a nationwide study based on the health insurance review and assessment service database. PLoS One 2018;13:e0209148.

13. Chung WJ, Park YB, Jeon CH, Jung JW, Ko KP, Choi SJ, et al. Baseline characteristics of the Korean Registry of Pulmonary Arterial Hypertension. J Korean Med Sci 2015;30:1429-38.

14. Shariati, A., Azaribeni, A., Hajighahramanzadeh, P., & Loghmani, Z. (2013). Liquid–liquid equilibria of systems containingsunflower oil, ethanol and water. APCBEE procedia, 5, 486-490.

15. Nodar, S. R., Salazar, S., Cárdenas, C., & Yllán, V. G. (2022). Testicular Tumor in Children: A Rare Case Report. Current Practice in Medical Science Vol. 9, 25-34.

16. Hammerstingl C, Schueler R, Bors L, Momcilovic D, Pabst S, Nickenig G, Skowasch D. Diagnostic value of echocardiography in the diagnosis of pulmonary hypertension. PLoS One. 2012 Jun 7;7(6):e38519.

17. Gibbs S, Lang I, Torbicki A, et al. 2015 . diagnosis of pulmonary hypertension. Eur Heart J 2016;37:67–119.

18. Asadipour, A., Mehrabani, M., & Najafi, M. L. (2005). Volatile oil composition of Centaurea aucheri (DC.) Wagenitz. DARU Journal of Pharmaceutical Sciences, 13(4), 160-164.

19. Swietlik EM, Ruggiero A, Fletcher AJ, Taboada D, Knightbridge E, Harlow L, et al. Limitations of resting haemodynamics in chronic thromboembolic disease without pulmonary hypertension. Eur Respir J 2019;53:1801787.

20. Kalantari S, Gomberg M, Maitland M. Group 5 pulmonary hypertension: the orphan's orphan disease. Cardiol Clin 2016;34:443–449.

21. Najafi, M. L., & Nasiri, M. (2019). Review of drug abuse patterns and their association with some individual and social variables among addicts. J. Adv. Pharm. Educ. Resl Apr-Jun, 9(2), 99-101.

22. Donoso, P. C., Pérez, M. P. S., Aguirre, C. C., Barbosa, A. O., Gómez, C. M. G., Jimenez, A. M., & Nodar, S. R. (2022). Angiosarcoma suprarrenal primario. Reporte de caso. Archivos de Patologia, 3(3), 96-103.

23. Jamalpour, H., & Derabi, J. Y. (2023). Aesthetic Experience, Neurology and Cultural Memory. Passagens: Revista Internacional de História Política e Cultura Jurídica, vol. `5, no. 2, pp. 340-348, https://doi.org/10.15175/1984-2503-202315208

24. Farhud, D., & Mojahed, N. (2022). SARS-COV-2 Notable Mutations and Variants: A Review Article. Iranian Journal of Public Health, 51(7), 1494.

25. McLaughlin VV, Archer SL, Badesch DB, Barst RJ, Farber HW, Lindner JR, Mathier MA, McGoon MD, Park MH, Rosenson RS, Rubin LJ, Tapson VF, Varga J; American College of Cardiology Foundation Task Force on Expert Consensus J Am Coll Cardiol. 2009;53:1573–1619.

26. Mojahed, N., Mohamadkhani, M. A., & Mohamadkhani, A. (2022). Climate Crises and Developing Vector-Borne Diseases: A Narrative Review. Iranian Journal of Public Health, 51(12), 2664-2673.

27. Bastian Bonhoeffer, Andreas Kordikowski, Edgar John, Michael Juhnke. Numerical modelling of the dissolution of drug nanocrystals and its application to industrial product development, ADMET and DMPK, Vol. 10 No. 4 (2022), 253-287. https://doi.org/10.5599/admet.1437

28. Greiner S, Jud A, Aurich M, Hess A, Hilbel T, Hardt S, Katus HA, Mereles D. Reliability of noninvasive assessment of systolic pulmonary artery pressure by Doppler echocardiography compared to right heart catheterization: analysis in a large patient population. Journal of the American Heart Association. 2014 Aug 21;3(4):e001103.

29. Soofi MA, Shah MA, AlQadhi AM, AlAnazi AM, Alshehri WM, Umair A. Sensitivity and Specificity of Pulmonary Artery Pressure Measurement in Echocardiography and Correlation with Right Heart Catheterization. Journal of the Saudi Heart Association. 2021;33(3):228.

30. Wang B, Feng Y, Jia LQ, Wu XL, Li DD, Zhou HX, Yang J, Liang BM, Wang L, Cui KJ, Huang H. Accuracy of Doppler echocardiography in the assessment of pulmonary arterial hypertension in patients with congenital heart disease. Eur Rev Med Pharmacol Sci. 2013 Apr 1;17(7):923-8.

31. Slegg OG, Willis JA, Wilkinson F, Sparey J, Wild CB, Rossdale J, Ross RM, Pauling JD, Carson K, Kandan SR, Oxborough D. IMproving PULmonary hypertension Screening by Echocardiography: IMPULSE. Echo Research & Practice. 2022 Dec;9(1):1-3.

32. Janda S, Shahidi N, Gin K, Swiston J. Diagnostic accuracy of echocardiography for pulmonary hypertension: a systematic review and meta-analysis. Heart. 2011 Apr 15;97(8):612-22

33. Swift AJ, Dwivedi K, Johns C, Garg P, Chin M, Currie BJ, et al. Diagnostic accuracy of CT pulmonary angiography in suspected pulmonary hypertension. Eur Radiol 2020; 30:4918–4929.