

ARTIFICIAL INTELLIGENCE IN PULMONARY HYPERTENSION AND ANESTHESIA: INNOVATIONS IN RISK STRATIFICATION, PERIOPERATIVE MANAGEMENT, AND PROGNOSTIC MODELING

V. Prathima¹, S. D. Divyaprakash², G. Keerthana³, K. Naga Tejaswini⁴, C. Charan
Kumar Reddy⁵ and Yamini Kosaraju^{6*}, Tirumerlla Karuna⁷

^{1,2,3,5}Pharm D, Department of Pharmacy Practice, Sri Venkateswara College of Pharmacy,
India.

^{4,6}Pharm D, Acharya Nagarjuna University, Chalapathi Institute of Pharmaceutical Science,
India.

⁷Narayana Pharmacy College, Chinthareddypalem, Nellore.

Article Received on
22 December 2024,

Revised on 12 Jan. 2025,
Accepted on 02 Feb. 2025

DOI: 10.20959/wjpr202504-35530



***Corresponding Author**

Yamini Kosaraju

Pharm D, Acharya
Nagarjuna University,
Chalapathi Institute of
Pharmaceutical Science,
India.

ABSTRACT

Pulmonary hypertension (PH) presents a significant challenge in perioperative management due to its complex hemodynamic alterations and increased perioperative risks, necessitating precise anesthetic and therapeutic strategies. This review explores the pathophysiological mechanisms underlying PH, emphasizing the critical role of vascular remodeling, hemodynamic perturbations, and right ventricular dysfunction. Advanced monitoring techniques, including echocardiography and biomarker analysis, are essential for perioperative risk assessment and optimization. Artificial intelligence (AI) has emerged as a transformative tool in PH management, enabling predictive analytics, patient-specific anesthetic planning, and continuous postoperative surveillance. AI-driven algorithms integrate multi-omics data, hemodynamic parameters, and clinical biomarkers to enhance early diagnosis, prognostication, and individualized therapeutic interventions. Moreover, AI-facilitated pharmacotherapy

and drug repurposing strategies offer promising avenues for optimizing PH treatment. This review highlights the evolving role of AI in anesthetic precision, perioperative decision-making, and long-term management, underscoring the necessity for multidisciplinary

collaboration and AI-enabled innovations to improve outcomes in PH patients undergoing surgical procedures.

1. INTRODUCTION

A complicated clinical state known as pulmonary hypertension (PH) is characterized by increased pulmonary arterial pressure resulting from a variety of etiologies, such as lung illnesses, chronic thromboembolic PH, idiopathic forms, or left heart disease (LHD) (Nathan et al., 2019). Pathophysiological insights reveal the complex hemodynamics of pulmonary hypertension, affecting heart function and pulmonary vasculature, common in left ventricular heart failure patients, significantly impacting morbidity and death (Rosenkranz et al., 2016). This illness is often caused by increased left ventricular filling pressures, which can result from passive elevation in pulmonary pressures (post-capillary PH), or pre-capillary components from pulmonary vascular remodeling (Pokharel et al., 2023). Mitochondrial dysfunction is a significant factor in cardiovascular illnesses like pulmonary artery disease (PH), affecting endothelial dysfunction and smooth muscle cell proliferation (Klionsky et al., 2021). The Warburg effect, decreased fatty acid oxidation, and metabolic modifications also contribute to cellular proliferation and resistance to apoptosis (Xu, Janocha, & Erzurum, 2021).

The relationship between pulmonary vascular load and right ventricular (RV) function is one important feature. The article emphasizes the importance of considering ventricles' functioning when assessing patients with pulmonary vascular load (PH), as RV failure often results from higher afterload (Chatterjee, Ing, & Gien, 2020). Genetic variants in potassium channels and transcription factors contribute to PAH susceptibility, revealing its complexity as a Mendelian disorder (Southgate, Machado, Gräf, & Morrell, 2020). Therapeutic tactics remain palliative, necessitating innovative targets (Harjola et al., 2016).

1.1. Imperatives of anesthetic precision: Mitigating perioperative risks in pulmonary hypertension

Pulmonary hypertension, characterized by elevated blood pressure in pulmonary arteries, can lead to right heart failure and increased ventricle strain during surgery due to anesthesia and operation stress.

Aesthetic points to remember

1. **Hemodynamic monitoring:** The treatment of anesthesia is greatly aided by the continuous monitoring of hemodynamic parameters such as cardiac output, central venous pressure, and pulmonary artery pressure.
2. **Selection of anesthesia drugs:** In order to prevent patients with pulmonary hypertension from experiencing worsening right heart failure, it is essential to use anesthetics with low adverse inotropic effects.
3. **Optimal fluid management:** To keep right heart strain and pulmonary hypertension from getting worse, it's important to maintain euvolemia and avoid volume overload.
4. **Ventilation techniques:** Low tidal volumes and positive end-expiratory pressure are two lung-protective ventilation techniques that can aid maximize oxygenation and reduce pulmonary vascular resistance (Chatterjee et al., 2020).

Minimizing perioperative risk

1. **Preoperative optimization:** To lower perioperative risks, a thorough preoperative evaluation and optimal pulmonary hypertension care are crucial.
2. **Multidisciplinary method:** In order to create a comprehensive perioperative strategy that is customized to each patient's needs with pulmonary hypertension, anesthesiologists, cardiologists, and surgeons must work together.
3. **Following surgery:** For patients with pulmonary hypertension, close observation during the recovery phase is essential for the early identification and treatment of problems, including measurements of oxygenation and hemodynamics.

2. Pulmonary vascular dynamics: Understanding the pathophysiological landscape**2.1. Vascular remodeling phenomena: Hemodynamic Repercussions and Structural Alterations**

The complex process of vascular remodeling involves changes in the vasculature's structure as well as functional adjustments in response to a variety of physiological and pathological stimuli. (Burton & Jauniaux, 2018). The understanding of hemodynamic consequences contributing to cardiovascular disorders like hypertension, atherosclerosis, and heart failure relies on understanding vascular remodeling, including endothelial dysfunction, smooth muscle cell proliferation, inflammation, and extracellular matrix changes (Ghali, Butler, Tepper, & Gurtner, 2007). Insufficient remodeling of the uterine spiral arteries during pregnancy, for example, may result in placental malperfusion, which can have serious

consequences, including fetal growth restriction (Burton & Jauniaux, 2018). Similar to this, it has been demonstrated that training with blood flow restrictions causes advantageous vascular changes that increase muscular strength through molecular reactions like hypoxia-regulated gene expression (Kacin et al., 2021).

The initiation of vascular remodeling processes is significantly influenced by mechanical stresses. Shear stress is one of the hemodynamic forces that affects endothelial function and stimulates structural alterations in the arterial wall (Rizzoni, Agabiti-Rosei, & Agabiti-Rosei, 2017). A higher media-to-lumen ratio, which is one of the microvascular structural changes brought on by chronic hypertension, is a major factor in increased vascular resistance and target organ damage (Gonzalez-Marrero, Hernández-Abad, Castañeyra-Ruiz, Carmona-Calero, & Castañeyra-Perdomo, 2022).

Aging impacts vascular architecture, leading to changes in brain barriers due to choroid plexus dysfunction and high blood pressure, affecting the blood-CSF barrier more than the blood-brain barrier. This demonstrates how localized effects of systemic diseases such as hypertension on particular arterial beds can affect the overall function of an organ (Luther, 2016). Aldosterone significantly influences microcirculation by affecting small resistance arteries' morphology, which in turn affects macrovascular function, large vessel structure, and cardiovascular risk factors (Rizzoni et al., 2015). The circulatory system's interdependence is exemplified by macro- and micro-circulation interactions, where changes at one level impact functionality at another (Thornburg & Louey, 2013). Carboxytherapy, a new therapeutic approach targeting vascular remodeling patterns, has shown promise in treating various scar types by improving local circulation and promoting tissue healing through increased collagen production (Stolecka-Warzecha et al., 2022).

2.2. Hemodynamic perturbations in pulmonary hypertension: Deciphering the intricacies of pressure-flow relationships

The hemodynamic disturbances associated with PH are complex, affecting not only the pulmonary vasculature but also the functioning of the respiratory system and how it interacts with mechanical ventilation (MV). By altering transpulmonary pressure (TP) and pleural pressure (Ppl), MV can have a substantial impact on RV afterload, which in turn affects venous return and pulmonary vascular resistance (PVR) (Vieillard-Baron et al., 2016). The management of patients with acute respiratory distress syndrome (ARDS) who develop secondary pulmonary hypertension (PH) can become more complex due to these ventilatory-

induced shifts, since they can exacerbate PH by raising PVR in a direct proportion to their impact on mean airway pressure (mPaw).

Left ventricular failure can lead to RV failure due to septal wall motion abnormalities, decreased LV filling, and increased PVR. Inhaled nitric oxide (NO), a selective pulmonary vasodilator, can improve these abnormalities and increase LVAD capacity (Lovich et al., 2015). It can be advantageous to focus on decreasing PVR while treating biventricular illness conditions that are made worse by mechanical circulatory support devices. Maintaining RV function during ARDS therapy is crucial for patient outcomes, including low driving pressures, positive end-expiratory pressure, avoiding hypercapnia, prone positioning, and prudent fluid therapy with vasoactive agents (Vieillard-Baron et al., 2016).

These factors make it clear how important it is to comprehend the dynamic interactions between intrathoracic pressures caused by MV or LVAD support systems and how they affect pulmonary circulation. The main objective of managing treatment for patients with underlying cardiac dysfunction or those requiring mechanical circulatory support is to minimize adverse hemodynamic effects while maintaining adequate oxygenation.

Table 1: *Quantitative metrics in pulmonary hypertension severity assessment: implications for perioperative management.*

Metric	Clinical significance
Mean Pulmonary Arterial Pressure (mPAP) (McLaughlin et al., 2009)	Elevated mPAP indicates increased pulmonary vascular resistance and PH severity. Thresholds for defining PH vary but commonly mPAP >25 mmHg at rest is considered elevated. Elevated mPAP may necessitate closer perioperative monitoring and tailored anesthetic management.
Pulmonary Vascular Resistance (PVR) (Galiè et al., 2016)	Elevated PVR reflects increased vascular remodeling and PH severity. PVR >3 Wood units is generally considered elevated. High PVR indicates increased risk of perioperative complications, including right heart failure and hemodynamic instability.
Cardiac Output (CO) (Stout et al., 2019)	Reduced CO in PH patients indicates impaired right ventricular function and increased perioperative complications, necessitating fluid management and inotropic support to optimize cardiac function.
Right Atrial Pressure (RAP) (Stout et al., 2019)	Elevated RAP indicates right heart dysfunction and can occur in PH. Elevated RAP may necessitate cautious fluid management to avoid exacerbating right heart failure perioperatively.
Echocardiographic Parameters (Hooper et al.,	Abnormal echocardiographic findings suggest underlying PH and may guide perioperative risk stratification. Assessing

2013)	right ventricular function is particularly important in predicting perioperative outcomes.
Functional Capacity Assessment(Rudski et al., 2010)	Impaired functional capacity is associated with increased perioperative risk. Patients with poor exercise tolerance may require more vigilant monitoring and advanced perioperative care strategies.
Biomarkers (e.g., BNP, NT-proBNP)(Galiè et al., 2015)	Biomarkers like BNP or NT-proBNP can indicate cardiac stress and worsening PH severity, aiding in perioperative risk assessment and identifying patients at higher risk of complications.

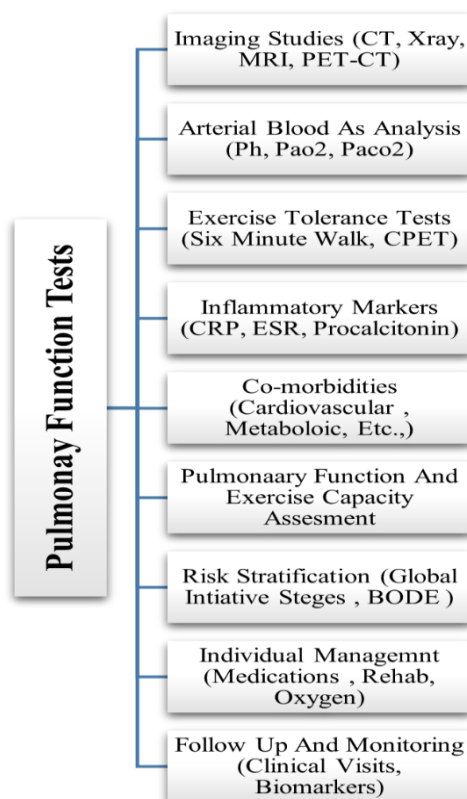


Figure 1: Risk stratification paradigms: Integrating clinical parameters for prognostic precision.

3. Hemodynamic monitoring modalities: Tools for precise navigation

Hemodynamic monitoring techniques, combined with precision medicine, are crucial in critical care for diagnosing, staging, early treatment, and managing patients experiencing cardiogenic shock (VanDyck & Pinsky, 2021). Targeted hemodynamic parameters can inform prognostication and therapy selection, and understanding each patient's unique needs is essential for effective symptomatic management (Gottlieb, Long, & Koyfman, 2018).

Nevertheless, there are still issues with accuracy and dependability across many technologies, even with these advancements (Tabi et al., 2019). For example, de Waal et al. pointed out that

there are still disagreements on whether noncalibrated pulse-contour analysis is more accurate than conventional thermodilution techniques (Burmester, Bijlsma, Cutolo, & McInnes, 2017). These disparities highlight the necessity of conducting thorough validation studies to determine the effectiveness of each modality in certain clinical settings (Criner et al., 2018; Hobson & McDermott, 2016; de Waal, Wappler, & Buhre, 2009). Moreover, even when technological advancements improve patient care by delivering complex physiological insights—as shown by A critical analysis of these advancements reveals a complex environment in which the practical limitations of evidence-based application within global healthcare systems must be weighed against it (Bronicki, 2016; Burmester et al., 2017; Leite et al., 2020; Nohria et al., 2003).

3.1.Surgical Planning and Execution: Mapping safe passage

Pneumonia treatment for patients with pulmonary hypertension (PH) requires careful consideration of anesthetic methods and timing. Factors like severity of PH, comorbidities like diabetes, heart failure, COPD, and cardiac arrest significantly impact perioperative risks. Severe COPD and CHF are significant contributors to adverse postoperative outcomes. Preoperative management can improve functional status and reduce perioperative death risk. Machine learning advancements can identify high-risk patients more accurately, leading to better surgical decisions. Data supports specific anesthetic procedures, such as mechanical ventilation and real-time hemodynamic monitoring (Tabi et al., 2019; VanDyck & Pinsky, 2021).

4. Postoperative recovery: Safeguarding hemodynamic integrity

Postoperative pain management is crucial for patient care, aiming to improve recovery while maintaining hemodynamic stability. A multidisciplinary approach is necessary to achieve this balance (Allegranzi et al., 2016). Opioids are crucial for pain relief but can cause hemodynamic disturbances. Adjunctive non-opioid analgesics, regional anesthesia techniques, and non-pharmacological approaches like cognitive-behavioral therapy, acupuncture, and music therapy can reduce opioid requirements and maintain hemodynamic stability (Jaber et al., 2012; Swathi & Kumar, 2024; Vieillard-Baron et al., 2016).

Postoperative complications pose significant threats to hemodynamic stability and overall patient outcomes. Proactive identification, prevention, and prompt management of these complications are essential to safeguard hemodynamic integrity (Cecconi et al., 2013; Pyati & Gan, 2007). Key complications include surgical site infections, fluid and electrolyte

imbalances, venous thromboembolism, and respiratory complications. Strict adherence to aseptic techniques, perioperative antimicrobial prophylaxis, and early mobilization protocols are essential. Fluid management strategies tailored to individual patient needs are crucial for maintaining euvolemia and preventing hemodynamic instability (Samama et al., 1999; Wilson, Hellman, James, Adler, & Chandrakantan, n.d.). Vascular thromboembolism prophylaxis, including mechanical compression devices and pharmacological agents like low molecular weight heparin, mitigate the risk of thromboembolic events that can compromise hemodynamic function. Proactive respiratory care, including incentive spirometry, early ambulation, and pulmonary hygiene measures, attenuates the incidence of postoperative atelectasis and respiratory compromise, preserving pulmonary function and hemodynamic stability (Stamer et al., 2021; Ye, Miao, Chen, Huang, & Jiang, 2024).

4.1. Outcome Assessment and Prognostic Indicators, Role of AI

In pulmonary hypertension (PH), artificial intelligence (AI) technologies such as machine learning algorithms and predictive analytics are essential for measuring perioperative success and determining prognostic markers. Artificial intelligence (AI) systems are able to analyze enormous volumes of patient data in order to spot trends, forecast results, and enhance treatment plans that are customized for each patient (Kwon et al., 2020).

Artificial intelligence (AI) predictive models use information from imaging investigations, hemodynamic monitoring systems, and electronic health records (EHRs) to estimate perioperative risk and forecast postoperative outcomes in patients with Parkinson's disease (PH). To produce individualized risk scores and prognosis assessments, these models incorporate variables such as hemodynamic measurements, functional assessments, comorbidities, and treatment responses (Dwivedi et al., 2021).

4.2. Long-term prognosis: Managing the transition past the perioperative era: The Function of AI

In terms of long-term prognosis for PH patients, AI enables continuous monitoring, risk assessment, and individualized care options outside of the perioperative time. AI algorithms use longitudinal data from many sources, such as EHRs, wearable devices, and remote monitoring platforms, to follow illness progression, forecast exacerbations, and optimize treatment regimens (Tchuente Foguem & Teguede Keleko, 2023). AI-powered predictive models combine clinical, laboratory, and imaging data to detect early disease worsening and predict long-term prognosis in PH patients. By examining trends and patterns over time, these

models enable proactive intervention methods such as medication adjustments, lifestyle changes, and referral to specialist care facilities to improve outcomes and quality of life (Liu et al., 2022).

4.2.1. Innovations in PH Therapy

Exploring Emerging Pharmacotherapeutic Modalities, and the Role of AI. AI-driven medication development, drug repurposing, and therapeutic optimization methodologies complement PH therapy innovations. AI algorithms examine molecular structures, biological processes, and clinical trial data to identify new drug targets, forecast medication efficacy, and speed up the development of new pharmacotherapeutic modalities for PH (Winter & Carusi, 2022). AI-powered drug repurposing tools use current drug databases, omics data, and clinical evidence to discover prospective PH therapy options among licensed drugs in other therapeutic domains. By studying drug-target interactions and disease processes, these platforms allow for the quick identification of promising repurposed medications that have the potential to enhance outcomes in PH patients (Singh & Mehta, 2024). Likewise, AI-driven precision medicine approaches customize medication to specific patient profiles, improving treatment efficacy while minimizing side effects. AI algorithms provide patient-specific treatment recommendations by combining multi-omics data, genetic markers, and clinical phenotypes, aiding doctors in picking the best medicines for PH patients based on their individual characteristics and illness trajectory (Nikkho et al., 2022).

4.3. Evolving strategies in anesthetic management: Anticipating Future Challenges and Opportunities

In the field of anesthesia management, AI-driven decision support systems improve perioperative safety, optimize resource use, and improve patient outcomes in PH patients undergoing surgery. AI algorithms examine perioperative data, such as vital signs, hemodynamic parameters, and intraoperative events, to detect patterns of physiological response and anticipate perioperative complications in real time. AI-powered anesthesia monitoring systems combine data from several sources, including anesthetic equipment, patient monitors, and electronic health records, to enable continuous monitoring and early warning alerts for adverse events in PH patients (Teo & Greenhalgh, 2010). These devices assist anesthesiologists in rapid intervention, optimization of anesthetic depth, and adjustment of hemodynamic support, thus reducing perioperative risks and enhancing patient safety. On top of that, AI-powered simulation platforms provide virtual training, scenario-based

learning, and competency assessment for anesthesiologists and perioperative teams treating PH patients. These platforms improve team readiness, decision-making skills, and crisis management abilities by modeling complex surgical scenarios, emergency situations, and unusual complications, resulting in better perioperative outcomes and fewer adverse events. Incorporating AI technologies into perioperative treatment techniques for pulmonary hypertension improves decision-making, patient outcomes, and surgical care quality. Clinicians can improve perioperative management, reduce risks, and improve patient safety in PH patients having surgery by utilizing AI-driven predictive analytics, precision medicine techniques, and decision support systems (Roessler & Lambert, 1986; Teo & Greenhalgh, 2010).

5. CONCLUSION

Pulmonary hypertension (PH) presents complex perioperative management challenges, requiring evaluation of outcomes, prognostic indications, and pharmacological and anesthetic methods. Multidisciplinary teamwork, tailored treatment techniques, and close monitoring are essential for maintaining good surgical outcomes. Advanced hemodynamic monitoring techniques can improve patient outcomes, but standardized validation protocols are needed. Barriers like training, cost, and infrastructure support must be addressed for widespread clinical adoption.

REFERENCES

1. Allegranzi, B., Zayed, B., Bischoff, P., Kubilay, N. Z., de Jonge, S., de Vries, F., Gomes, S. M., et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: An evidence-based global perspective. *The Lancet. Infectious Diseases*, 2016; 16(12): e288–e303.
2. Bronicki, R. A. Hemodynamic Monitoring. *Pediatric Critical Care Medicine: A Journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*, 2016; 17(8, 1): S207-214.
3. Burmester, G. R., Bijlsma, J. W. J., Cutolo, M., & McInnes, I. B. Managing rheumatic and musculoskeletal diseases—Past, present and future. *Nature Reviews. Rheumatology*, 2017; 13(7): 443–448.
4. Burton, G. J., & Jauniaux, E. Pathophysiology of placental-derived fetal growth restriction. *American Journal of Obstetrics and Gynecology*, 2018; 218(2S): S745–S761.

5. Cecconi, M., Corredor, C., Arulkumaran, N., Abuella, G., Ball, J., Grounds, R. M., Hamilton, M., et al. Clinical review: Goal-directed therapy-what is the evidence in surgical patients? The effect on different risk groups. *Critical Care (London, England)*, 2013; 17(2): 209.
6. Chatterjee, D., Ing, R. J., & Gien, J. Update on Congenital Diaphragmatic Hernia. *Anesthesia and Analgesia*, 2020; 131(3): 808–821.
7. Criner, G. J., Dreher, M., D'Ambrosio, C. M., Zuwallack, R., Geiseler, J., & Pépin, J. L. COPD Advanced Patient Management. *Chest*, 2018; 153(6): 1497–1498.
8. Dwivedi, K., Sharkey, M., Condliffe, R., Uthoff, J. M., Alabed, S., Metherrall, P., Lu, H., et al. Pulmonary Hypertension in Association with Lung Disease: Quantitative CT and Artificial Intelligence to the Rescue? State-of-the-Art Review. *Diagnostics*, 2021; 11(4): 679. Multidisciplinary Digital Publishing Institute.
9. Galiè, N., Barberà, J. A., Frost, A. E., Ghofrani, H.-A., Hoeper, M. M., McLaughlin, V. V., Peacock, A. J., et al. Initial Use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension. *The New England Journal of Medicine*, 2015; 373(9): 834–844.
10. Galiè, N., Humbert, M., Vachiery, J.-L., Gibbs, S., Lang, I., Torbicki, A., Simonneau, G., et al. (2016). ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *European Heart Journal*, 2015; 37(1): 67–119.
11. Ghali, S., Butler, P. E. M., Tepper, O. M., & Gurtner, G. C. Vascular delay revisited. *Plastic and Reconstructive Surgery*, 2007; 119(6): 1735–1744.
12. Gonzalez-Marrero, I., Hernández-Abad, L. G., Castañeyra-Ruiz, L., Carmona-Calero, E. M., & Castañeyra-Perdomo, A. Changes in the choroid plexuses and brain barriers associated with high blood pressure and ageing. *Neurologia*, 2022; 37(5): 371–382.
13. Gottlieb, M., Long, B., & Koyfman, A. Approach to the Agitated Emergency Department Patient. *The Journal of Emergency Medicine*, 2018; 54(4): 447–457.
14. Harjola, V.-P., Mebazaa, A., Čelutkienė, J., Bettex, D., Bueno, H., Chioncel, O., Crespo-Leiro, M. G., et al. Contemporary management of acute right ventricular failure: A statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology. *European Journal of Heart Failure*, 2016; 18(3): 226–241.

15. Hobson, E. V., & McDermott, C. J. Supportive and symptomatic management of amyotrophic lateral sclerosis. *Nature Reviews. Neurology*, 2016; 12(9): 526–538.
16. Hoeper, M. M., Bogaard, H. J., Condliffe, R., Frantz, R., Khanna, D., Kurzyna, M., Langleben, D., et al. Definitions and diagnosis of pulmonary hypertension. *Journal of the American College of Cardiology*, 2013; 62(25): D42-50.
17. Jaber, S., Coisel, Y., Chanques, G., Futier, E., Constantin, J.-M., Michelet, P., Beaussier, M., et al. A multicentre observational study of intra-operative ventilatory management during general anaesthesia: Tidal volumes and relation to body weight. *Anaesthesia*, 2012; 67(9): 999–1008.
18. Kacin, A., Drobnič, M., Marš, T., Miš, K., Petrič, M., Weber, D., Tomc Žargi, T., et al. Functional and molecular adaptations of quadriceps and hamstring muscles to blood flow restricted training in patients with ACL rupture. *Scandinavian Journal of Medicine & Science in Sports*, 2021; 31(8): 1636–1646.
19. Klionsky, D. J., Abdel-Aziz, A. K., Abdelfatah, S., Abdellatif, M., Abdoli, A., Abel, S., Abeliovich, H., et al. Guidelines for the use and interpretation of assays for monitoring autophagy, 2021; (4)1, 17(1): 1–382.
20. Kwon, J., Kim, K.-H., Medina-Inojosa, J., Jeon, K.-H., Park, J., & Oh, B.-H. Artificial intelligence for early prediction of pulmonary hypertension using electrocardiography. *The Journal of Heart and Lung Transplantation*, 2020; 39(8): 805–814.
21. Leite, R. G. O. F., Banzato, L. R., Galendi, J. S. C., Mendes, A. L., Bolfi, F., Veroniki, A. A., Thabane, L., et al. Effectiveness of non-pharmacological strategies in the management of type 2 diabetes in primary care: A protocol for a systematic review and network meta-analysis. *BMJ open*, 2020; 10(1): e034481.
22. Liu, C.-M., Shih, E. S. C., Chen, J.-Y., Huang, C.-H., Wu, I.-C., Chen, P.-F., Higa, S., et al. Artificial Intelligence-Enabled Electrocardiogram Improves the Diagnosis and Prediction of Mortality in Patients With Pulmonary Hypertension. *JACC: Asia*, 2022; 2(3_Part_1): 258–270. American College of Cardiology Foundation.
23. Lovich, M. A., Pezone, M. J., Wakim, M. G., Denton, R. J., Maslov, M. Y., Murray, M. R., Tsukada, H., et al. Inhaled Nitric Oxide Augments Left Ventricular Assist Device Capacity by Ameliorating Secondary Right Ventricular Failure. *ASAIO journal (American Society for Artificial Internal Organs)*, 2015; 1992: 61(4): 379–385.
24. Luther, J. M. Aldosterone in vascular and metabolic dysfunction. *Current Opinion in Nephrology and Hypertension*, 2016; 25(1): 16–21.

25. McLaughlin, V. V., Archer, S. L., Badesch, D. B., Barst, R. J., Farber, H. W., Lindner, J. R., Mathier, M. A., et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association: developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *Circulation*, 2009; 119(16): 2250–2294.
26. Nathan, S. D., Barbera, J. A., Gaine, S. P., Harari, S., Martinez, F. J., Olschewski, H., Olsson, K. M., et al. Pulmonary hypertension in chronic lung disease and hypoxia. *The European Respiratory Journal*, 2019; 53(1): 1801914.
27. Nikkho, S. M., Richter, M. J., Shen, E., Abman, S. H., Antoniou, K., Chung, J., Fernandes, P., et al. Clinical significance of pulmonary hypertension in interstitial lung disease: A consensus statement from the Pulmonary Vascular Research Institute's innovative drug development initiative—Group 3 pulmonary hypertension. *Pulmonary Circulation*, 2022; 12(3): e12127.
28. Nohria, A., Tsang, S. W., Fang, J. C., Lewis, E. F., Jarcho, J. A., Mudge, G. H., & Stevenson, L. W. Clinical assessment identifies hemodynamic profiles that predict outcomes in patients admitted with heart failure. *Journal of the American College of Cardiology*, 2003; 41(10): 1797–1804.
29. Pokharel, M. D., Marciano, D. P., Fu, P., Franco, M. C., Unwalla, H., Tieu, K., Fineman, J. R., et al. Metabolic reprogramming, oxidative stress, and pulmonary hypertension. *Redox Biology*, 2023; 64: 102797.
30. Pyati, S., & Gan, T. J. Perioperative pain management. *CNS drugs*, 2007; 21(3): 185–211.
31. Rizzoni, D., Agabiti-Rosei, C., & Agabiti-Rosei, E. Hemodynamic Consequences of Changes in Microvascular Structure. *American Journal of Hypertension*, 2017; 30(10): 939–946.
32. Rizzoni, D., De Ciuceis, C., Salvetti, M., Painsi, A., Rossini, C., Agabiti-Rosei, C., & Muiesan, M. L. Interactions between macro- and micro-circulation: Are they relevant? *High Blood Pressure & Cardiovascular Prevention: The Official Journal of the Italian Society of Hypertension*, 2015; 22(2): 119–128.
33. Roessler, P., & Lambert, T. F. Anaesthesia for Caesarean Section in the Presence of Primary Pulmonary Hypertension. *Anaesthesia and Intensive Care*, 1986; 14(3): 317–320. SAGE Publications Ltd.

34. Rosenkranz, S., Gibbs, J. S. R., Wachter, R., De Marco, T., Vonk-Noordegraaf, A., & Vachiéry, J.-L. Left ventricular heart failure and pulmonary hypertension. *European Heart Journal*, 2016; 37(12): 942–954.
35. Rudski, L. G., Lai, W. W., Afilalo, J., Hua, L., Handschumacher, M. D., Chandrasekaran, K., Solomon, S. D., 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: Official Publication of the American Society of Echocardiography*, 2010; 23(7): 685–713; quiz 786–788.
36. Samama, M. M., Cohen, A. T., Darmon, J. Y., Desjardins, L., Eldor, A., Janbon, C., Leizorovicz, A., et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. *The New England Journal of Medicine*, 1999; 341(11): 793–800.
37. Singh, N., & Mehta, S. Artificial intelligence to improve the diagnosis of pulmonary hypertension: Promises and pitfalls. *Heart*, 2024; 110(8): 541–542. BMJ Publishing Group Ltd and British Cardiovascular Society.
38. Southgate, L., Machado, R. D., Gräf, S., & Morrell, N. W. Molecular genetic framework underlying pulmonary arterial hypertension. *Nature Reviews. Cardiology*, 2020; 17(2): 85–95.
39. Stamer, U. M., Erlenwein, J., Freys, S. M., Stammschulte, T., Stichtenoth, D., & Wirz, S. [Perioperative analgesia with nonopioid analgesics: Joint interdisciplinary consensus-based recommendations of the German Pain Society, the German Society of Anaesthesiology and Intensive Care Medicine and the German Society of Surgery]. *Der Anaesthetist*, 2021; 70(8): 689–705.
40. Stolecka-Warzecha, A., Chmielewski, Ł., Deda, A., Śmich, A., Lebiedowska, A., & Wilczyński, S. The Influence of Carboxytherapy on Scar Reduction. *Clinical, Cosmetic and Investigational Dermatology*, 2022; 15: 2855–2872.
41. Stout, K. K., Daniels, C. J., Aboulhosn, J. A., Bozkurt, B., Broberg, C. S., Colman, J. M., Crumb, S. R., et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, 2019; 73(12): 1494–1563.

42. Swathi, N. L., & Kumar, A. Advanced Technologies in Clinical Research and Drug Development. *The Ethical Frontier of AI and Data Analysis*, 2024; 1–17. IGI Global. Retrieved March 6, 2024, from <https://www.igi-global.com/chapter/advanced-technologies-in-clinical-research-and-drug-development/www.igi-global.com/chapter/advanced-technologies-in-clinical-research-and-drug-development/341183>
43. Tabi, K., Randhawa, A. S., Choi, F., Mithani, Z., Albers, F., Schnieder, M., Nikoo, M., et al. Mobile Apps for Medication Management: Review and Analysis. *JMIR mHealth and uHealth*, 2019; 7(9): e13608.
44. Tchuente Foguem, G., & Teguede Keleko, A. Artificial intelligence applied in pulmonary hypertension: A bibliometric analysis. *AI and Ethics*, 2023; 3(4): 1063–1093.
45. Teo, Y. W., & Greenhalgh, D. L. Update on anaesthetic approach to pulmonary hypertension. *European Journal of Anaesthesiology / EJA*, 2010; 27(4): 317.
46. Thornburg, K. L., & Louey, S. Uteroplacental circulation and fetal vascular function and development. *Current Vascular Pharmacology*, 2013; 11(5): 748–757.
47. VanDyck, T. J., & Pinsky, M. R. Hemodynamic monitoring in cardiogenic shock. *Current Opinion in Critical Care*, 2021; 27(4): 454–459.
48. Vieillard-Baron, A., Matthay, M., Teboul, J. L., Bein, T., Schultz, M., Magder, S., & Marini, J. J. Experts' opinion on management of hemodynamics in ARDS patients: Focus on the effects of mechanical ventilation. *Intensive Care Medicine*, 2016; 42(5): 739–749.
49. de Waal, E. E. C., Wappler, F., & Buhre, W. F. Cardiac output monitoring. *Current Opinion in Anaesthesiology*, 2009; 22(1): 71–77.
50. Wilson, S. H., Hellman, K. M., James, D., Adler, A. C., & Chandrakantan, A. (n.d.). Mechanisms, diagnosis, prevention and management of perioperative opioid-induced hyperalgesia. *Pain Management*, 11(4): 405–417.
51. Winter, P., & Carusi, A. Professional expectations and patient expectations concerning the development of Artificial Intelligence (AI) for the early diagnosis of Pulmonary Hypertension (PH). *Journal of Responsible Technology*, 2022; 12: 100052.
52. Xu, W., Janocha, A. J., & Erzurum, S. C. Metabolism in Pulmonary Hypertension. *Annual Review of Physiology*, 2021; 83: 551–576.
53. Ye, G., Miao, R., Chen, J., Huang, J., & Jiang, M. Effectiveness of Complementary and Alternative Medicine in Fibromyalgia Syndrome: A Network Meta-Analysis. *Journal of Pain Research*, 2024; 17: 305–319.