Critical Rounds

Vol 3 | Issue 37 | 2022

Critical Rounds Newsletter
VOL 3 | Issue 37 | 2022

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care .

This issue contains :

1. **Analysis of the lung microbiome's composition and diversity in patients with suspected ventilator-associated pneumonia**
2. **Dyspnea and the electromyographic activity of the inspiratory muscles while transitioning off mechanical ventilation.**
3. **Red blood cell distribution width as a predictive marker in sepsis.**
4. **A case report on the identification of vascular anomalies using a misplaced central venous catheter**

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in
free to contact us at medicalservices@microlabs.in
Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

Critical Rounds

Vol 3 | Issue 37 | 2022

1. Analysis of the lung microbiome's composition and diversity in patients with suspected ventilator-associated pneumonia

Introduction:

When pneumonia (lung infection) manifests in a patient who has been receiving mechanical ventilation for more than 48 hours, the condition is known as ventilator-associated pneumonia (VAP).[1]Although detection of ventilator-associated pneumonia (VAP) remains difficult, it is linked to significant morbidity and medical expenses. Since pneumonia is characterised by a disturbance of the microbiome, analysis of the airway microbiota by amplicon sequencing offers a potential remedy. There aren't many studies examining the diagnostic potential of microbiome analysis, and there isn't clarity on potential biomarkers.[2] Researchers used bronchoalveolar lavage fluid (BALF) from ventilated adult patients suspected of VAP to investigate whether there were any differences in the microbiomes of patients who had positive and negative BALF cultures, and whether those differences might have any impact on the clinical management of the patients.

In patients with a positive BALF culture, dysbiosis and genus dominance were more prevalent.

Methods:

This is a post hoc analysis of the BreathDx research by van Oort et al., entitled "Molecular Analysis of Exhaled Breath as Diagnostic Test for Ventilator-Associated Pneumonia."[3] In order to: (1) distinguish between patients with and without a positive culture; (2) assess whether there was any association between microbiome diversity and local inflammatory response; and (3) correctly identify pathogens detected by conventional culture, BALF from patients suspected of having VAP was examined using 16s rRNA sequencing.

Results:

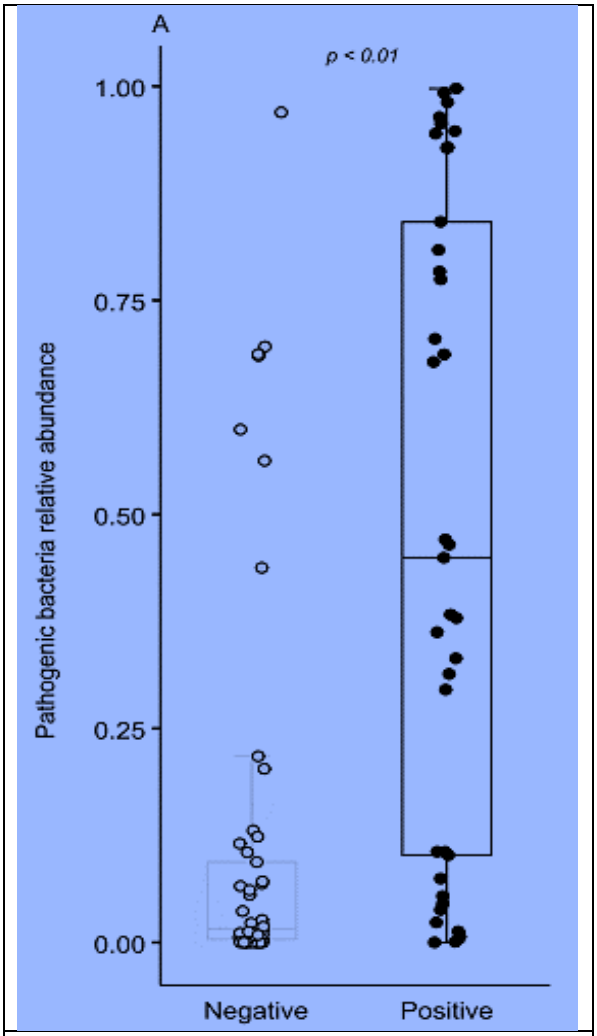
In a total of 90 ICU patients with potential VAP had 37 patients with positive cultures. Patients who had a favourable culture had a large dysbiosis of the microbiome and less alpha diversity. Gross compositional variation, however (AUROCC range 0.66-0.71), was not significantly related to culture positive. Patients who had a positive culture had a significantly higher relative abundance of pathogenic bacteria than those who did not [0.45 (IQR 0.10-0.84), 0.02 (IQR 0.004-0.09, respectively], and an increased level of interleukin (IL)-1 was linked to decreased species evenness ($rs = 0.33$, $p<0.01$) and a higher presence of pathogenic bacteria ($rs = 0.28$, $p = 0.013$). False positives were a limitation of untargeted 16s rRNA pathogen detection, whereas pathogen-specific relative abundance limits demonstrated improved diagnostic accuracy (AUROCC range 0.89-0.998).

Discussion:

In this investigation, compared to patients with suspected VAP but negative cultures, those with suspected VAP with a positive culture exhibited greater lower airway microbiome dysbiosis and a higher prevalence of pathogenic microorganisms. Additionally, a lesser species evenness and a higher abundance of pathogenic bacteria were linked to an enhanced local inflammatory response, as seen by a rise in IL-1b concentration, according to the study's

Critical Rounds
Vol 3 | Issue 37 | 2022

culture-independent bacterial analysis. Higher amounts of IL-1b were detected in BAL fluid in patients who had increased dysbiosis and loss of diversity. According to Trachalaki et al research,the elevated inflammasome complex activity may be responsible for this favourable association.[4] Researchers discovered a different strategy that was assessed using relative abundance thresholds specific to the pathogens.16s sequencing was more suitable to rule out the presence of Pseudomonas and Klebsiella. This is consistent with findings from a comparable study in individuals with COVID-19 who were invasively ventilated conducted by Kullberg et al.[5]



Pathogenic bacteria relative abundance per patient sample (N = 90) is altered in patients suspected of VAP with positive BALF cultures compared to those with negative cultures.

Conclusion:

In patients with a positive BALF culture, dysbiosis and genus dominance were more prevalent. An association between reduced species evenness and increased pathogenic bacterial presence and an increase in caspase-1-dependent IL-1b expression suggests a possible causal relationship between lung injury development in VAP and microbiome dysbiosis. Measures of diversity, however, proved to be not a reliable predictor of culture positive, and infections could not be effectively identified by 16S sequencing when employed empirically. This problem might be solved by using relative abundance criteria that are unique to a certain pathogen.

References:

1. Kohbodi GNA, Rajasurya V, Noor A. Ventilator-associated Pneumonia. [Updated 2022 May 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022.
2. Fenn D et al. +BreathDx Consortium. Composition and diversity analysis of the lung microbiome in patients with suspected ventilator-associated pneumonia. Crit Care. 2022 Jul 6;26(1):203.
3. van Oort P Met al Untargeted Molecular Analysis of Exhaled Breath as a Diagnostic Test for Ventilator-Associated Lower Respiratory Tract Infections (BreathDx). Thorax. 2022 Jan;77(1):79-81.
4. Kullberg RFJ et al. ArtDECO consortium and the Amsterdam UMC COVID-19 Biobank Study Group. Lung Microbiota of Critically Ill COVID-19 Patients are Associated with Non-Resolving Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2022 May 26.
5. Trachalaki A et al. Enhanced IL-1β Release Following NLRP3 and AIM2 Inflammasome Stimulation Is Linked to mtROS in Airway Macrophages in Pulmonary Fibrosis. Front Immunol. 2021 Jun 15;12:661811.

Critical Rounds

Vol 3 | Issue 37 | 2022

2. Dyspnea and the electromyographic activity of the inspiratory muscles while transitioning off mechanical ventilation.

Introduction:

The subjective experience of difficult breathing of varied intensity is known as dyspnea, or shortness of breath. Millions of individuals experience it frequently, and it may be the main symptom of a respiratory, cardiac, neuromuscular, psychogenic, or systemic ailment, or a combination of these.[1] One of the main indicators of acute respiratory failure, dyspnea, is not one of the spontaneous breathing trial(SBT) failure criteria.[2] Here, the aims were to: (1) identify if dyspnea is a valid indicator of SBT failure; (2) evaluate the relationship between dyspnea and the electromyographic activity(EMG) of the diaphragm (EMGdi), parasternal (EMGpa), and Alae nasi (EMGan)

Dyspnea is a reliable criterion of spontaneous breathing trial (SBT) failure, suggesting that Dyspnea-Visual Analogic Scale could be used as a monitoring tool of the SBT

Methods:

Patients receiving an SBT who were mechanically ventilated were included in the study At the beginning and end of the SBT, data on dyspnea, heart rate, and systemic blood pressure were recorded. The MRC score 48, which indicates the presence of neuromuscular weakness, was obtained. During the closest SBT evaluation, data on the Richmond Agitation Sedation Scale and Pain-Visual Analogue Scale (from 1 to 100 mm) were obtained. Researchers collected the patient's medications from both before and after the SBT. The Dyspnea-Visual Analogic Scale (Dyspnea-VAS) was used to assess the severity of dyspnea. The EMGdi was constantly monitored with a multi-electrode nasogastric catheter during the 30-min SBT or until SBT failure, and the EMGan and EMGpa with surface electrodes.

Results:

A Total of thirty-one patients, SAPS 2 (median [interquartile range]) 53 (37–74), were enrolled. They required mechanical ventilation for six (3–10) days. 17 patients (or 45% of them) failed the SBT. Patients who failed had an increase in Dyspnea-VAS along the SBT of 6 [48] cm compared to those who passed (0 [01] cm, $p = 0.01$). Dyspnea-VAS has an area under the receiver operating characteristic curve of 0.909 (0.786-1.032). However, there was no significant correlation between the rise in EMGpa (Rho = 0.121 [0.495 to 0.290], $p = 0.555$) or EMGdi (Rho = 0.26 [0.68 to 0.28], $p = 0.289$) and The Dyspnea-VAS was significantly correlated to the increase in EMGan (Rho = 0.42 [0.040.70], $p<0.05$).

Discussion:

The following sentences serve as a summary of the findings. Dyspnea can be used as a clinical decision-making tool for SBT since it is a reliable predictor of weaning success and failure throughout the procedure. Furthermore, dyspnea seems to be more closely associated correlated with the extradiaphragmatic inspiratory muscles' EMG activity than the diaphragm. The

correlation between dyspnea and an increase in respiratory drive is supported by these findings.[2] Rapid increases in respiratory loading brought on by the SBT improve the central respiratory drive to the inspiratory muscles.[3] According to earlier research, this increase in drive also involves the extradiaphragmatic and diaphragmatic inspiratory muscles. In this study, researchers discovered that there was no difference between the increase in EMG activity of the diaphragm and the Alae nasi, which is consistent with a recent study that revealed a similar increase in the EMG of various inspiratory muscles during a substantial decline in pressure support in patients who were being mechanically ventilated.[4]

	Total ($n=31$)	Success ($n=17$)	Failure ($n=14$)	p
Alae nasi				
EMGmax	1.02 (0.94–1.25)	0.98 (0.77–1.10)	1.24 (0.94–1.60)	0.010
EMGauc	1.07 (0.66–1.44)	0.93 (0.60–1.11)	1.44 (0.91–2.40)	0.015
Parasternal intercostal muscles				
EMGmax	0.99 (0.87–1.01)	1.00 (0.98–1.01)	0.97 (0.83–1.01)	0.426
EMGauc	1.12 (0.90–1.69)	1.12 (1.04–1.25)	1.03 (0.71–1.78)	0.855
Diaphragm				
EMGmax	1.24 (0.80–2.06)	0.84 (0.60–1.57)	1.87 (1.19–2.92)	0.008
EMGauc	1.28 (0.98–1.81)	1.12 (0.79–1.70)	1.65 (1.47–2.93)	0.125
Alae nasi/diaphragm ratio				
EMGmax	0.79 (0.54–1.22)	0.87 (0.58–1.52)	0.55 (0.45–0.99)	0.039
EMGauc	0.76 (0.49–1.04)	0.72 (0.43–0.93)	0.68 (0.23–0.96)	0.812

Changes in the electromyographic activity (EMG) of the *Alae nasi*, the parasternal intercostal muscles and the diaphragm between the initiation and end of spontaneous breathing trial
The EMG activity is described by peak EMG (EMGmax) and area under the curve (EMGauc). Values are normalized to EMG activity at initiation of the SBT and are expressed as the ratio of the EMG activity and the end of the SBT to the EMG activity at the initiation of the SBT

Conclusion:

In conclusion, the Alae Nasi's EMG activity during an SBT is more directly linked to alterations in dyspnea than the diaphragm. In addition, the intensity of dyspnea seems to be a reliable predictor of weaning success or failure. This suggests that alteration in dyspnea may be used as a fundamental SBT monitoring technique.

References:

1. Hashmi MF, Modi P, Sharma S. Dyspnea. [Updated 2022 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022
2. Bureau C et al. Dyspnea and the electromyographic activity of inspiratory muscles during weaning from mechanical ventilation. Ann Intensive Care. 2022 Jun 10;12(1):50.
3. Dres M et al.Dyspnoea and respiratory muscle ultrasound to predict extubation failure. Eur Respir J. 2021 Nov 11;58(5):2100002.
4. Roesthuis LH et al. Recruitment pattern of the diaphragm and extradiaphragmatic inspiratory muscles in response to different levels of pressure support. Ann Intensive Care. 2020 May 29;10(1):67.

Critical Rounds
Vol 3 | Issue 37 | 2022

3. Red blood cell distribution width as a predictive marker in sepsis.

Introduction:

Sepsis is a life-threatening illness characterised by several physiological and metabolic abnormalities. For the first time, the Third International Consensus (Sepsis-3) defines sepsis as "organ dysfunction induced by a dysregulated host response to infection," highlighting the critical involvement of the innate and adaptive immune responses in the development of the clinical condition.[1] Changes in the physiology of red blood cells are more prevalent in patients with critical illnesses, those hospitalised to the intensive care unit, and those with hyperinflammatory conditions. According to prior studies, red blood cell distribution width (RDW) is an inflammatory predictor of mortality in a variety of clinical contexts, including acute respiratory distress syndrome (ARDS), cardiovascular illness, infections, and chronic inflammatory disorders.[2] The aim of this study was to better understand RDW dynamics and its predictive role in sepsis, as compared to other biomarkers.

Red blood cell distribution width is an independent prognostic marker of death in septic patients admitted in the ICU that improves SOFA, LODS, APACHE-II and SAPS-II discrimination ability

Methods:

A retrospective cohort of patients who had previously been hospitalised to the intensive care unit (ICU) at a 620-bed tertiary University Hospital formed the research cohort. If sepsis was the cause of admission or if sepsis criteria were fulfilled during ICU admission, patients were included. physiological, laboratory, and microbiological characteristics, supportive therapy received, time spent in the intensive care unit, and baseline conditions and comorbidities. Additionally, RDW, CRP, and procalcitonin (PCT) values were examined upon ICU admission as well as 24, 48, 72, and 7 days later. The highest values found during ICU and hospital admission were taken into account if the patient was discharged from the ICU. Using the AUC-ROC, RDWdynamics, hospital mortality discrimination ability, and the value added when SOFA, LODS, SAPS-II, and APACHE-II scores were included were analysed.

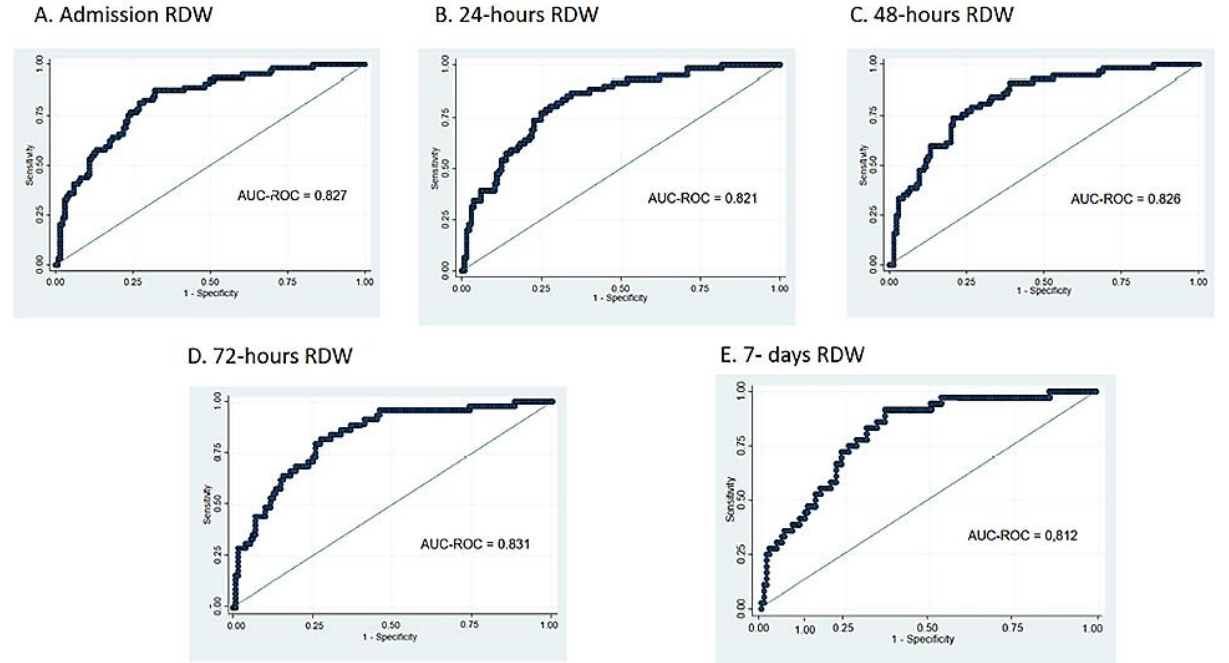
Results:

In the first week following ICU admission, non-survivors had higher RDWvalues (p=0.048). When adjusted for Charlson, immunosuppression, nosocomial infection, NEWS2, SAPS-II, septic shock, and haemoglobin, only SOFA and RDW remained independently related with mortality ($p < 0.05$). After adjustment, the AUC-ROC values for each model, comprising admission, 24, 48, and 72-h and 7-days RDW, were 0.827, 0.822, 0.824, 0.834, and 0.812, respectively. 24-h RDW plus admission RDW increased the scores' capacity to discriminate across groups (SOFA AUC-ROC = 0.772 vs. 0.812 SOFA + admission RDW, p = 0.041; LODS AUC-ROC = 0.687 vs. 0.710, p = 0.002; SAPS-II AUC-ROC = 0.734 vs. 0.785, p = 0.021; APACHE-II AUC--ROC = 0.672 vs 0.755, p = 0.003) Admission RDW with SOFA shown the superior ability to discriminate for mortality.

Discussion:

Given that RDW was consistently and independently linked with mortality over time, the current study demonstrates that RDW is a predictive biomarker of hospital mortality in septic

patients admitted to the ICU. Additionally, RDW enhanced the capacity of SOFA, LODS, APACHE-II, and SAPS-II to discriminate, making it a prospective criterion to be added to these prognostic scores.[2] RDW independently predicts mortality in septic patients in the emergency room and in intensive care units, according to prior studies.[3,4] APACHE-II and SAPS-II scores, which are predictors of hospital and ICU mortality, were also taken into account of RDW's role in the current study. These prognostic scores characterise and quantify organ failure. The findings show that RDW enhances the SOFA, LODS, and SAPS-II scores' ability for mortality discrimination. Because they indicate that RDW is a strong marker of the dysregulated inflammatory response that transmits systemic organ failure, researchers think these unique findings are both promising and significant.[2]



Discrimination ability for the hospital mortality adjusted models. The figure shows the Area Under the Receiver Operating Characteristic Curve (AUC-ROC) for themodels including admission Red blood cell distributionwidth (RDW) (A), 24-hRDW(B), 48-hRDW, 72-hRDW(D) and7-daysRDW(E).All theanalyseswere adjusted by the Charlson Comorbidity Index, immunosuppression, nosocomial infection,National EarlyWarning Score 2, SequentialOrgan Failure Assessment, Simplified Acute Physiology Score-II and haemoglobin.

Conclusion:

The study's findings suggest that RDW values and their variations over time are a distinct prognostic marker of death in septic patients admitted to the ICU, and that when combined with SOFA, LODS, APACHE-II, and SAPS-II scores, they may improve these tests' ability to differentiate between various cases. The RDW is an easily measurable and easily obtainable marker that reflects the dysregulated inflammatory response and systemic dysfunction in septic patients.

References:

1. Jarczak D, Kluge S, Nierhaus A. Sepsis—Pathophysiology and Therapeutic Concepts. Frontiers in Medicine. 2021 May 14; 8:628302
2. Moreno-Torres et al. Red blood cell distribution width as prognostic factor in sepsis: A new use for a classical parameter. J Crit Care. 2022 Jun 2;71:154069.
3. Hu ZD, Lippi G, Montagnana M. Diagnostic and prognostic value of red blood cell distribution width in sepsis: A narrative review. Clin Biochem. 2020 Mar;77:1-6.

4. Zhao C, Wei Y, Chen D, Jin J, Chen H. Prognostic value of an inflammatory biomarker-based clinical algorithm in septic patients in the emergency department: An observational study. Int Immunopharmacol. 2020 Mar;80:106145.

4. A case report on the identification of vascular anomalies using a misplaced central venous catheter

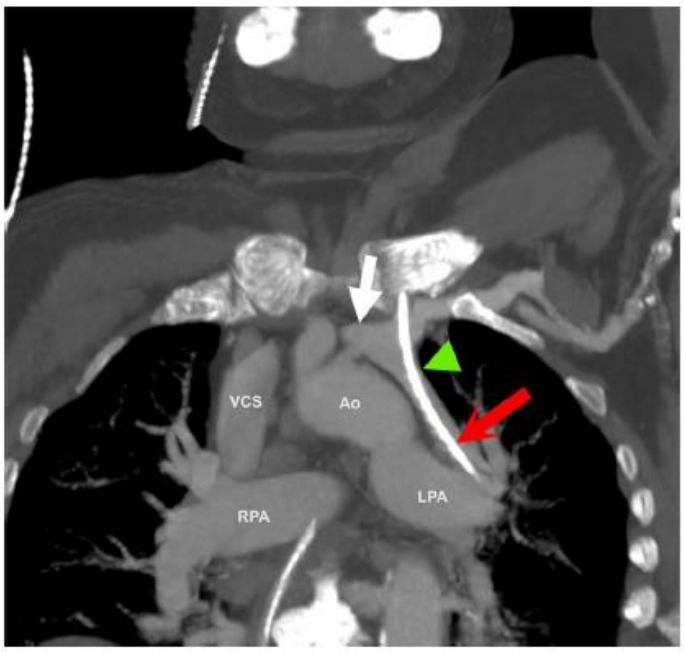
Introduction:

Congenital heart disease comprises structural abnormalities of the heart that develop before to birth. While the foetus is growing in the uterus during pregnancy, several abnormalities might appear.[1] Congenital cardiac disease rarely manifests in adults. Adult pulmonary hypertension is rarely brought on by congenital cardiac conditions.[2] Researchers present a concomitant finding of pulmonary hypertension and partial anomalous pulmonary venous return (PAPVR) in the critical care unit (ICU). This disorder is frequently asymptomatic. However, researchers anticipate a rise in the number of reported patients given the present trend toward more medical imaging. The question of whether and when to treat such patients is raised by this.[2]

Partial anomalous pulmonary venous return is a potentially treatable cause of pulmonary hypertension.

Case Presentation:

A left-sided stroke inflicted 70-year-old female patient arrived at the emergency department. She was obese, had high blood pressure, atrial fibrillation, insulin-dependent diabetes, chronic renal failure, heart failure with maintained ejection fraction, and moderate pulmonary hypertension in her medical history. The stroke could not have been treated with interventions, thus it was treated conservatively. The patient experienced worsening melena and stomach pain a week after being admitted. A computed tomography (CT) scan revealed superior mesenteric vein thrombosis-related small intestinal ischemia. 60 cm of ischemic bowel was surgically resected by a laparotomy. In the right internal jugular vein, the attending anesthesiologist inserted a central venous catheter (CVC). The patient was admitted to the ICU following surgery.Two days following surgery, her vital signs improved, and she was sent back to the ward. After experiencing a stroke and mesenteric thrombosis while on direct oral anticoagulation, further diagnostics for coagulation abnormalities were started.Blood was



Multiplanar reconstruction image from the chest computed tomography examination. The intravenous catheter (red arrow) travels through the left jugular vein and would be expected to continue in the left brachiocephalic vein (white arrow). In this case, however, the route of least resistance was in the retrograde direction through the anomalous left superior pulmonary vein (green arrow head). Also visible are the superior vena cava (VCS), the aortic arch (Ao), and the left and right pulmonary artery (LPA, RPA)

collected to measure homocysteine, calreticulin, Janus kinase (JAK2), myeloproliferative leukaemia (MPL), and anti-cardiolipin antibodies. Dalteparin and clopidogrel were added to the anticoagulation regimen in therapeutic dosages. Six days following the laparotomy, the patient had worsening stomach pain once more. An urgent abdominal CT scan showed distal superior mesenteric artery blockage. A second laparotomy was done, and thrombectomy of the superior mesenteric artery along with a revision of the bowel anastomosis. Unfortunately, the CVC that had been put earlier had already been removed . A CVC was placed into the left internal jugular vein during surgery, and the patient was again admitted to the intensive care unit. The CVC positioned abnormally was seen in postoperative routine radiographic imaging for catheter insertion. A later contrast-enhanced CT scan revealed a partial abnormal pulmonary venous return on the left side. The left lung's venous drainage is where the CVC's tip was discovered. It was demonstrated that this vein empties into the left brachiocephalic vein. The scan also revealed a small level of parenchymal damage at the catheter tip. A new CVC was implanted in the right internal jugular vein after the old one was removed. The patient was brought back to the surgical ward three days following the second laparotomy. The patient was sent to a rehabilitation facility once her clinical state improved. The results of the laboratory tests on coagulation disorders were normal.

Discussion:

The prevalence of PAPVR, an uncommon congenital cardiac condition, is around 0.2% on thoracic CT scans. Most PAPVR patients are asymptomatic.[2] Typically, the diagnosis occurs by coincidence. MRI or CT scans are more sensitive for establishing the diagnosis. Adults are undergoing CT and MRI scans more often for a variety of purposes, which is a noticeable trend.[3] The onset of pulmonary arterial hypertension may be significantly influenced by PAPVR. With an increase in anomalous venous return, this risk increases. Pulmonary hypertension may be reduced as a result of surgical PAPVR therapy. PAPVR is a very infrequent cause of treatable pulmonary arterial hypertension.[4]

Conclusion:

A potentially treatable cause of pulmonary hypertension is partial anomalous pulmonary venous return. As CT rates increase, it is anticipated that incidental diagnoses of this congenital abnormality in adults would increase.

References:

1. Sun R, Liu M, Lu L, Zheng Y, Zhang P. Congenital Heart Disease: Causes, Diagnosis, Symptoms, and Treatments. Cell Biochem Biophys. 2015 Jul;72(3):857-60.
2. de Smalen PP, Stoutjesdijk MJ. Vascular anomaly diagnosis by central venous catheter misplacement: a case report. J Med Case Rep. 2022 Jun 22;16(1):259.
3. Smith-Bindman R et al. Trends in Use of Medical Imaging in US Health Care Systems and in Ontario, Canada, 2000-2016. JAMA. 2019 Sep 3;322(9):843-856.
4. Hegde M, Manjunath SC, Usha MK. Isolated Partial Anomalous Pulmonary Venous Connection: Development of Volume Overload and Elevated Estimated Pulmonary Pressure in Adults. J Clin Imaging Sci. 2019 Jun 14;9:29.