MediPines AGM100 Use Case:
Pulmonary Embolism and Impaired Gas Exchange

Summary

Pulmonary embolism is a common problem in hospitalized patients that is difficult to diagnose, making it a leading cause of death. PE causes a substantial negative impact on pulmonary gas exchange and typically presents with severely elevated Oxygen Deficit. Implementing gas exchange analysis with the MediPines AGM100 in targeted patient care areas will quickly identify PE that could otherwise be missed. Earlier and more comprehensive identification of PE can lead to shorter hospital stays, better patient outcomes, and less downstream costs.

Gas Exchange Analysis to Detect Pulmonary Embolism

Pulmonary embolism (PE) is a type of venous thromboembolism (VTE) in which a clot or other obstruction breaks off and moves to the pulmonary vasculature and results in reduced pulmonary gas exchange. The impaired transfer of oxygen and carbon dioxide across the affected region of the lung is due to ventilation and perfusion mismatch caused by reduced perfusion.[1] PE is a common problem and can be fatal as it is one of the leading causes of death in the US and the third leading cause of death in hospitalized patients.[2] It is difficult to know the true incidence and mortality associated with PE because deaths due to PE are often misattributed to cardiac causes. However, it is estimated that approximately 10 million people worldwide suffer from thromboembolism. Within the United States, the number of patients diagnosed with PE more than tripled between 1993 (60,000) and 2012 (202,000).[5] By 2050 it is projected that factors such as an aging demographic with increased comorbidities will drive VTE cases to more than 1.8 million in the US.[6] The growing incidence of patients with PE coming though Emergency Departments and in admitted hospitalized patients necessitates an effective diagnostic tool to help

Figure 1: Summary of case report where the AGM100 was used for diagnostic support. The Emergency Department physician utilized gas exchange analysis to quickly push the patient for a diagnostic chest CT scan for PE diagnosis, which could have otherwise been missed due to low PE risk analysis.

recognize and treat PE before the patient's status turns critical.

PE is difficult to diagnose due to a wide spectrum of medical presentations and does not have a defining historical feature, physical examination finding, laboratory test, or diagnostic modality that can independently and confidently exclude its possibility.[3] Given the possibility of asymptomatic and atypical presentation, it is generally accepted that many cases go undiagnosed.[2] Due to the diagnostic difficulty of PE, clinical prediction criteria such as the Wells Score is commonly used to determine the probability of a patient suffering from PE. The Wells Criteria for PE is not sensitive as a standalone test and typically used in conjunction with other diagnostic tests like blood analysis of clot fragmentation, D-Dimer testing, or ECG and echocardiogram analysis of cardiac function. Taken together, a negative D-Dimer in the setting of a low Well's Score has good sensitivity and negative predictive value to appropriately rule out PE. However, there are numerous causes to have a positive D-Dimer test, including advanced age, obesity, pregnancy, trauma, infections, and heart disease. Given the risk of a "false" positive, it is common practice to order D-Dimer tests judiciously in certain patient populations to avoid non-essential expensive and invasive investigations including Computed Tomography (CT). Therefore, there is a need for non-invasive adjunct tools to enhance recognition of PE.

The MediPines AGM100 Gas Exchange Analyzer fills this need as the world's first non-invasive pulmonary gas exchange analyzer. Implementing gas exchange analysis on patients presenting with a wide range of cardiac and respiratory complaints will help identify PE in patients that would otherwise be missed. The following case is an example of a patient that had shortness of breath and the physicians suspected he was suffering from a heart attack. Luckily, a gas exchange analysis was performed which helped identify the actual cause of his symptoms, impaired gas exchange, and allowed the physician to quickly administer the correct life-saving treatment.

Pulmonary Embolism Case

An 81-year-old male presented to a rural hospital emergency department with shortness of breath, which had been persisting for the previous four weeks with

Figure 2: MediPines AGM100 results screen from a Pulmonary Embolism patient indicating a severe gas exchange impairment.[7]

exertion and had started the previous week at rest. The patient denied having chest pain, cough, loss of consciousness, leg swelling, and shortness of breath did not change while supine and was not noticed at night. The patient had no blood in his stool or melena and his review of symptoms was otherwise unremarkable.

During triage, vitals were blood pressure of 132/80 mmHg, body core temperature of 36.2 degrees Celsius, a pulse rate of 90 beats per minute, and a respiratory rate of 18 breaths per minute with no distressed breathing noted. Hemoglobin oxygen saturation (SpO_2) on room air was 97%. The patient appeared to be fatigued but in no apparent distress. He was alert and oriented with a normal Glasgow Coma Scale of 15. The patient had a medical history that included myocardial infarction with placement of a cardiac stent, hypertension, depression, type 2 Diabetes Mellitus, gastroesophageal reflux disease, and a smoking 50 pack per year history, however he had quit smoking 20 years ago with no diagnosis of COPD.

A chest exam revealed good air entry bilaterally and clear air flow with no crackles or wheezes. A cardiovascular exam revealed normal Korotkoff heart sounds, normal apex heart sounds, the pedal pulse was palpable, no leg edema detected, and no carotid bruit. A neurological exam was completed with normal results.

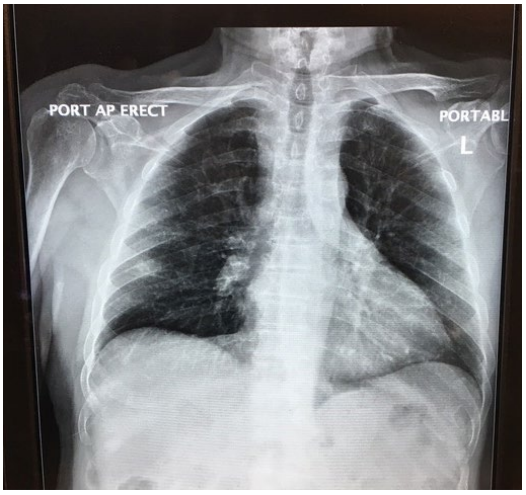

Figure 3: Chest X-ray reviewed as normal.

Given this patient's presentation and past medical history an Acute Coronary Syndrome (ACS) / non-ST Elevation Myocardial Infarction (NSTEMI) or possible missed "silent MI" would certainly need to be considered among other diagnosis including, but not limited to, anemia, upper respiratory tract infection (including COVID-19 infection), malignancy, and pulmonary embolism.

A cardiac panel was ordered that included a 12 lead ECG, chest x-ray (Figure 2), and routine bloodwork including cardiac enzymes (Troponin I). Initial 12 lead ECG revealed some T-wave inversion in anterior leads V1-V5 (Figure 3), which were not present in an ECG from a year previously. The T-wave inversion was suspicious for cardiac ischemia but not infarction. Despite the fact he had not had any chest pain at the time and given his cardiac history an Acute Coronary Syndrome diagnosis still needed to be considered. Subsequent positive cardiac troponin enzymes of 0.169 ug/l, a chest x-ray, and a normal hemoglobin supported the diagnosis of ACS / NSTEMI.

With respect to PE as a differential diagnosis one must consider the clinical picture and incorporate probability assessment scores such as the Well's Criteria for PE. After assessment, it was found that the patients Well's score was 0. A negative D-Dimer in the setting of Well's Score of 0-1.5 has good sensitivity and negative predictive value to rule out PE. However, there are numerous causes to have a positive D-Dimer, including advanced age, among others. Given the risk of a "false" positive, it is common practice to order D-Dimer tests judiciously to avoid more invasive investigations including Computed Tomography (CT) scans that include intravenous contrast and may be harmful to the patient.

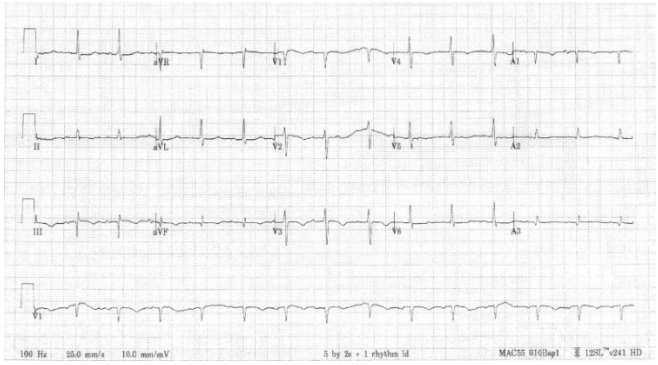

Figure 3: 12-Lead ECG demonstrating slight T-wave inversion.

An alveolar gas-exchange monitor (MediPines AGM100) was used to administer a non-invasive pulmonary gas-exchange analysis while waiting for the patient's bloodwork results to be available (Figure 1). The readings on the monitor showed an SpO_2 of 94% with an $ETCO_2$ of 19 mmHg. The respiratory rate was 29 breaths per minute and pulse rate was 85 beats per minute. The most important and concerning data that was obtained from the AGM100 was the O_2 Deficit of 65 mmHg, which is the difference of the alveolar PO_2 (PAO_2) in the lungs and the calculated arterial blood level PO_2 ($gPaO_2$) (Figure 1). O_2 Deficit measures the

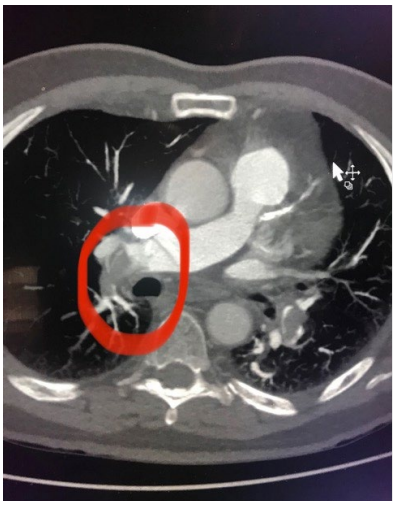

Figure 4: Chest CT scan with PE identification circled in red.

degree of respiratory impairment (i.e., impaired pulmonary gas exchange efficiency). A higher O_2 Deficit is indicative of a higher degree of impaired gas exchange within the lungs.[4]

It is unlikely that an ACS / NSTEMI diagnosis would account for an O_2 Deficit this high. Even though the patient had no chest pain, no tachycardia, no cough, a Well's score of 0, and a plausible diagnosis of ACS / NSTEMI, it was decided that a chest CT scan was needed for a possible PE. The CT exam revealed a prominent thrombotic load with the lobar and segmental pulmonary arteries affecting most significantly the lower lobes which was worse on the right side (Figure 4). The patient was admitted to the Medical / Surgical Unit and treated appropriately for PE, had an uneventful stay, and was discharged 3 days later.

Discussion

O_2 Deficit has been shown to be a sensitive indicator of pulmonary gas exchange impairment.[4] This patient presented with an O_2 Deficit of 65 mmHg, which from previous experience, gave evidence that the diagnosis of ACS / NSTEMI was not as plausible and further investigation was needed to determine the cause of gas exchange impairment and shortness of breath. In this case, O_2 Deficit was used as a respiratory marker in conjunction with the clinical presentation and physical judgement. The AGM100 samples spontaneous expired gas by having the patient breathe through a single patient use mouthpiece that is connected to a sample line and connected to the monitor. The patients' saturation data is collected by an integrated finger pulse oximeter. The AGM100 displays various respiratory measurements in real time. Typically, gas sampling takes about 90 seconds to reach a steady state, and the results are displayed on the device screen in real time. In this case, the AGM100 took about 90 seconds (1 minute 38 seconds) to display the result (Figure 1).

Having an objective measure of pulmonary gas exchange impairment can factor into the diagnosis and treatment decisions that must be made in a time sensitive manner. Traditional methods of obtaining information on pulmonary gas exchange requires the use of invasive arterial blood gas sampling and estimations of alveolar oxygen levels to calculate an Alveolar-arterial gradient. However, due to the estimation of alveolar oxygen levels requiring multiple static value assumptions (such as assuming 0.8 for the respiratory quotient and 760 mmHg for barometric pressure), which do not reflect the real time values of the dynamic physiology of the patient, traditional A-a gradients may not be adequate for acute cases.

This patient presented with an O_2 Deficit of 65 mmHg in the setting of a normal ECG and no previous lung history. Two different strategies to D-dimer testing in low-risk patients includes the use of blanket testing or the use of the PE Rule Out Criteria (PERC) rule to prevent unnecessary testing. In this case, O_2 Deficit, the difference of the alveolar PO_2 and the calculated arterial blood PO_2 was used as a respiratory marker in conjunction with the clinical presentation and physical judgement to help determine if a CT scan with contrast was warranted. Having an objective measure of pulmonary gas exchange impairment can factor into the diagnosis and treatment decisions that must be made in a time sensitive manner.

Conclusion

PE is difficult to diagnose because it presents with a wide spectrum of medical presentations and does not have a defining historical feature, physical examination finding, laboratory test, or diagnostic modality that can independently and confidently exclude its possibility. Given the possibility of asymptomatic and atypical presentation, it is generally accepted that many cases of PE go undiagnosed. Therefore, there is a need for adjunct tools to enhance recognition of PE. The MediPines AGM100 can be a helpful adjunct tool in the diagnosis of PE and is ideally suited because if the quick precise measurements it provides will being non-invasive and easy to use. The O_2 Deficit measurement can be highly informative in scenarios similar to this case and will improve identification of PE in patients thought to be at low risk.

Key Terms

SpO_2 – Oxygen saturation of hemoglobin obtained non-invasively from a pulse oximeter. A pulse oximeter utilizes a validated light-based method that relates light absorption to empirical oxygen saturation using the co-oximetry method.

PaO_2 – Partial pressure of arterial oxygen; the oxygen level in the blood, measured in mmHg, obtained from arterial blood gas (ABG) method.

$gPaO_2$ – Partial pressure of arterial oxygen obtained non-invasively from calculations and breathing gas sampling methods. Measured in mmHg. Exclusively provided by MediPines AGM100.

$PETCO_2$ – End-tidal carbon dioxide, commonly denoted as $etCO_2$, a measure of ventilation; the partial pressure of carbon dioxide at the end of an exhaled breath, measured in mmHg.

Oxygen Deficit – A-a gradient ($AaDO_2$) equivalent measured non-invasively. The difference between the alveolar (lung) and arterial (blood) levels of oxygen that represents the degree of respiratory gas exchange inefficiency, a measurement of respiratory impairment, measured in mmHg.

Ventilation/Perfusion matching – arterial oxygenation is affected by ventilation/perfusion (V/Q) matching in the lungs, which determines the degree of contact between fresh gas in the airspaces and pulmonary capillary blood. V/Q mismatch generates hypoxemia when airspaces do not receive sufficient oxygen in fresh gas to fully saturate the hemoglobin. Perfused regions that receive no ventilation at all send blood with the systemic mixed venous partial pressure of oxygen to the left heart, generating a true shunt across the lung. Admixture of blood containing unsaturated hemoglobin in the pulmonary veins and left atrium results in equilibration of oxygen among red blood cells, decreasing PaO_2 and hemoglobin saturation.

Abbreviations

ECG = Electrocardiogram

D-Dimer = fibrin degradation product

ETCO2 = end-tidal carbon dioxide

FiO2 = fraction of inspired oxygen

ug/l = micrograms per liter

ACS = Acute coronary syndrome

NSTEMI = ST-elevation myocardial infarction

References

1. D'Angelo, E. (1997). Lung mechanics and gas exchange in pulmonary embolism. Haematologica, 82(3), 371–374.
2. Ouellette, D. W., & Patocka, C. (2012). Pulmonary Embolism. Emergency Medicine Clinics of North America, 30(2), 329–375. https://doi.org/10.1016/j.emc.2011.12.004
3. Stein, P. D., Beemath, A., Matta, F., Weg, J. G., Roger, D., Hales, C. A., Hull, R. D., Jr, K. V. L., Sostman, H. D., Tapson, V. F., Buckley, J. D., Gottschalk, A., Goodman, L. J., Wakefield, T. W., & Woodard, P. K. (2007). Clinical Characteristics of Patients with Acute Pulmonary Embolism. Am J Med, 120(10), 871–879.
4. West, J. B., Crouch, D. R., Fine, J. M., Makadia, D., Wang, D. L., & Prisk, G. K. (2018). A New, Noninvasive Method of Measuring Impaired Pulmonary Gas Exchange in Lung Disease: An Outpatient Study. Chest, 154(2), 363–369. https://doi.org/10.1016/j.chest.2018.02.001
5. Girard, P. et al., 2001. Diagnosis of pulmonalry embolism in patients with proximal deep vein thrombosis: specificity of symptoms and perfusion defects at baseline and during anticoagulatn therapy. *Am J Respir Crit Care Med,* 164(6), p. 1033.
6. Ryu, J. et al., 2007. Saddle pulmonary embolism diagnosed by CT angiography; frequency, clinical features and outcome. *Respir Med,* 24 Jan, 101(7), p. 1537.
7. McGuire, W.C., Pearce, A. K., Elliott, A.R., Fine, J., West, J.B., Prisk, G., Crouch, D. R., Malhotra, A., Use of the Alveolar Gas Meter to Predict Respiratory Deterioration in COVID-19.

The MediPines AGM100 is US FDA-cleared, Health Canada approved pulmonary gas exchange monitor that exclusively provides Oxygen Deficit, (AaDO2, aka. A-a gradient), as well as blood oxygen level (gPaO2), PETCO2, and other sensitive measurements of pulmonary gas exchange. The respiratory parameters are available from patient breathing gas sampling method typically lasting 2 minutes. Visit www.medipines.com for more information on AGM100.

MediPines.com
info@medipines.com (949) 398-4670