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An Overview of Extended Ventilation Requirements Related to Comorbidities.

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My internship was completed at Mercy Hospital in Rogers, Arkansas. The internship began in May of 2021 and continued for several months following the completion of my allotted hours. I began working in units as a night shift float pool student nurse intern, working wherever my assistance was needed most for the particular shift I was scheduled to work that night. However, towards the end of July of 2021 I began getting scheduled on the Covid-19 Intensive care unit of the hospital. This is when the second large peak in cases developed, in Northwest Arkansas, so with the overload of patients, more nursing staff was needed on the unit. While I did not spend every shift on this unit, I spent a majority of my shifts in July and August of 2021. This resulted in my curiosity about intensive care patients. I wanted to learn why some people were only on a ventilator for a few days, and why some patients were on them for weeks to months. This piqued my interest in learning about the comorbidities of extensive oxygenation requirements for patients on a ventilator. This led to my research question and article search in which I analyzed factors related to patient time on the ventilator. I used specific search criteria to articulate my review research to complete a comprehensive overview.

Reflection of Internship

During my internship at Mercy of Northwest Arkansas I have learned many valuable lessons that I will be able to practice not only in my career but in my daily life as well. As a student nurse intern at Mercy, I worked as a Patient Care Technician, or PCT. My responsibilities as a patient care technician included but were not limited to, obtaining, and monitoring vital signs, providing patient care, ensuring patients' needs were met, and assisting the nurses whenever they needed. This experience provided me with hundreds of hours of uninterrupted learning opportunities. For the internship my mentor and I established goals to

focus on throughout the internship. These goals include improving interpersonal communication and relationships among peers, coworkers, and patients, establishing real life connections between university course work and internship workload, and advocating for safe and high-quality patient care outcomes as a member of the healthcare team.

Communication is an essential part of the healthcare profession especially between the healthcare workers and the patients and their families. This internship has provided me with the ability to answer questions that may arise from patients, family, or coworkers. Questions of "why is this being done" or "how will this benefit my family member?" The experience that I was able to gain at Mercy has allowed me to gain confidence in my ability to speak with patients and family members. Communication amongst coworkers is also an essential aspect of patient care in any healthcare setting. The nurses at Mercy take the time to make sure that I know what is going on at all times and ensure that I am absorbing as much information as I can be during my time on shift. This has prepared me for my future career by allowing me to ask questions, see first-hand the organization of a twelve-hour shift, witness the proper technique of patient care, and become familiar with the responsibilities of a nurse.

My second goal was to be able to make connections between my course work and my shift work. Throughout my role at Mercy, I have been exposed to many new disease processes that I had not previously been familiar with. This is also true for medications. Despite spending so much of my time in nursing school in pharmacology, I feel as though I have been able to retain more information about medications and medication administration in the physical setting of the hospital. This may be attributed to the challenge of Covid-19 and the inability to attend clinicals in the first semester of nursing school. As I reflect on my time I have spent at Mercy, I appreciate all of the time and effort that the nurses have taken to include me in the patient's plan

of care and teach me when/why/how they are doing each task. I hope to carry this on into my career and be there as a supporter and an educator for the future nursing students.

My final goal for the internship was to grow in my role of patient advocate. My primary focus of a student nurse intern was to provide patient care to the best of my abilities. Working as an intern at Mercy required a lot of responsibility on my behalf. My primary obligation was to my patients and providing them the best care that I was capable of. A typical shift for me included taking each patients' vital signs every four hours, providing care such as bathing, toileting, and daily hygiene. An additional responsibility of mine was to obtain and record blood sugars on any patients who may have required monitoring such as patients who have diabetes or have doctor's orders to be nothing by mouth, or NPO. Assisting nurses whenever they needed it was also one of my primary duties. I would help them with tasks that were still in my scope of practice such as collecting urine or stool samples, ambulating, or turning patients, and assisting with patient care.

Mercy has carved a path for my future that I never quite imagined it would. This experience has been so important to my career as a nurse. It has taught me the value of respect, patience, integrity, and so much more. Without this opportunity, I would not have been able to find an area of nursing that I am truly passionate about. It has allowed me to channel my strengths in patient care. I have been able to observe teamwork between PCT, nurses, as well as providers. This experience has been vital in my ability to problem solve when difficult situations arise. Every career has its challenges and that is no different as a patient care technician. Some of the main challenges that I faced each shift included uncooperative patients, disrespectful staff, and overwhelming workload.

Uncooperative patients were common, and I learned how to work with these patients early on. Most commonly the patients who were uncooperative were ones who had been diagnosed with diseases such as Alzheimer's or had memory loss related to previous drug use. The most frequent issue was that they could not remember that they were at the hospital. Sometimes when they do not remember where they are, they become agitated and occasionally combative. I unfortunately had to call security on a patient who had become aggressive with me and the nurse. Learning how to deal with these patients was a significant challenge that was presented during my time Mercy.

While it was rare, staff members were occasionally disrespectful to not only their nurse assistants but their fellow nurses as well. This was a challenge that I had to learn to cope within my first few shifts. I noticed that some of the nurses were rude and unyielding with their assistants and coworkers. There was once a nurse who delegated each possible task to everyone except herself making it an unequal divide in responsibility. This was a challenge because I felt as though it was an abuse of power, and it decreased the morale of the entire floor for that shift. This was a challenge for me to work through, but it made me stronger as tech and taught me the importance of not only comradery but also time management.

Some shifts were better than others, and that is true for any job, I am sure, but occasionally, a shift would be overwhelming and difficult. Learning time management and problem-solving skills was an essential part of this internship. There were shifts when I had time to take all of my allotted breaks, and there were shifts that I took zero breaks and had to stay and hour to be able to get my tasks completed. On the days when I was struggling to complete my duties, it felt overwhelming and difficult to concentrate on the tasks. I was able to overcome this challenge by taking fifteen minutes at the beginning of each shift to write out all of my tasks for

the next twelve hours. I would make a “To Do” list and prioritize each item on the list. This allowed me to visualize what was the most important things that needed to be completed. There were still some days that I was unable to complete everything on my list, but I learned to be okay with that, and know that I am not capable of doing everything on my own. Another challenge that I had to overcome was asking for help. I was scared to be seen as someone who was not capable of doing their work, so I was reluctant to ask for help from my colleagues. When I soon realized that most of the staff are more than willing to assist you when you need it, it allowed me to decrease the stress of the shift when needed.

Learning was a major aspect of this internship. Some of the most important lessons that I learned involved patient care. I was able to learn how to talk to patients, talk to families, and talk with coworkers. I learned that communication is one of, if not, the most important aspects of care. Knowing how to talk to patients allowed patients to remain calm, to trust me as the PCT, and to talk to me respectfully as well. There were many patients who, if you spoke to them rudely, they would speak to you rudely as well. Whereas if you spoke to the patient with respect and dignity, they would reciprocate those feelings. Communicating with patients is extremely important because it facilitates care by allowing myself and the patient to work together.

Talking with families is also a more than valuable lesson that I have learned during my time as an intern. This is vitally important because families are just as important as our patients. Friends and families are our patients’ support systems, who they typically trust more than they trust their healthcare providers. The way we speak to families can have many different effects on the patient. If we talk to the families in a panicked tone, then they will be panicked. This is the same for disrespectful tones and, most importantly, calm tones. Learning to talk to the families was something that I had to learn early on in my time as an intern. However, when I would work

the covid ICU, there was no family or guests on any kind allowed on the floor. I noticed that this caused several issues with the patients such as fear, anxiety, and loneliness. In these times I had to learn how to be the patients confidant during the 12 hours I spent with them. Being able to successfully speak with patients and their family members is arguably one of the most important aspects of being a healthcare worker.

As a nursing student a lot of my coursework relates to my internship at Mercy. We focus on subjects like therapeutic communication, which as I have just mentioned, is extremely important for anyone who works in a hospital. We also focus on medications, which I cannot administer, but it has been extremely beneficial to see these medications be used in practice. A few classes throughout the nursing program focus on the body systems and illnesses that can present in each of those systems, so that has helped prepare me for how to better care for my patients. These classes have allowed me to see what body systems are affected with each disease process, and how they can affect other body systems. I have been able to focus more on the patient as a whole, rather than just their diagnosis.

I have been so grateful to be a part of this internship for the past several months. It has allowed me to focus on the advancement of my future and become more focused on my goals as a future nurse. One of the biggest benefits of the internship is the comradery I have found among the nurses on each floor. Almost every nurse was so welcoming and kind. Each time I told a nurse that I was in nursing school they would give me advise or allow me to visualize them do a task like dressing changes. They always took the time to teach and allowed me to ask questions whenever I needed to. This opportunity also will benefit me when it comes to my confidence. I lacked confidence when I first started working, but now I arrive at each shift ready to work and comfortable with my abilities. It has also caused me to calm my nerves about beginning my

journey as a nurse, specifically the interview process. I had to interview for this internship, and once I was accepted, it helped me grow in my confidence.

Abstract

Mechanical ventilation is a machine that that allows patients to breathe when they are unable to adequately do it themselves. This could be due to illness or injury. Ventilators pump oxygen into the lungs through a tube that travels through the trachea. When a patient is put on a ventilator, they will be placed in the Intensive Care Unit. While ventilation is typically a short-term intervention, some patients require ventilation for extended periods of time, and some may not come off the ventilator, eventually dying. Dozens of patients were ventilated in the ICU at Mercy, and most of them spent months on the ventilators or unfortunately, died. A review of research was conducted on the comorbidities and predisposing risk factors of what increases the risk of long-term ventilation, or not coming off the ventilator at all. Studies conducted of these risk factors focused on the populations that have been affected the most. The majority of the research articles performed retrospective research in order to observe the mortality rates of the comorbidities. Each study focused on a different comorbidity. Some studies were performed in other countries and were included in this study because Covid-19 effected all parts of the world. However, not all of the studies are related to Covid-19, and solely focused on ventilator patients in general.

Literature Review

The most common risk factors of the requirement of long-term mechanical ventilation found in the research include obesity, age, alternate infection, and diabetes. If comorbidities can be determined it may help in the future when patients are being weaned off the ventilator. The

purpose of this review is to improve patient outcomes on the ventilator in the future. The primary goal is to improve patient outcomes and enhance the role of the nurse as the patient advocate. The role of the patient advocate can increase the patients' comfort and care, as well as the families' feeling of support throughout the patients stay in the Intensive care unit.

Methods

In order to obtain the references, CINAHL database was utilized via the University of Arkansas library website. Search words included "mechanical ventilation" "prolonged use" "risk factors" "obesity" "pregnancy" and "diabetes". Fifteen academic and research articles were found to facilitate the research. Each of these contributed to the understanding of ventilation requirements and the contribution of comorbidities on the patient's oxygen needs. Some articles were included because of their direct relation to the research purpose. Some articles were excluded due to the lack of relevance to the research purpose, or only providing small bits of insight to the research purpose.

Of the fifteen articles, seven took place in the United States, two in Brazil, one in Italy, one in Portugal, one in Indonesia, one in the United Kingdom, and two were unspecified. The majority of them performed some form of retrospective study. All of them focusing on ventilation requirements, and comorbidities of ventilation, and subsequently, Covid-19. These were used in combination to articulate a complete overview.

Results

To determine the most common comorbidities of extended ventilation requirements, the following studies were analyzed. Wahyuningsih et al., (2021) created a cumulative study of differing demographics of the patients requiring hospitalization and mechanical ventilation for

Covid-19 patients. This study used the medical records of positive Covid-19 patients to obtain their demographic information and find similarities between those who spent extensive periods of time in the ICU, or those who passed away during their stay. 85% of the patients in the study had a comorbidity, and in this study, 91 of those patients studied had hypertension, and 89 of them had type two diabetes mellitus (Wahyuningsih et al., 2021). Only 3.9% of the patients included in this study were discharged from the hospital, while 66.7% died while in the hospital (Wahyuningsih et al., 2021). This study reveals that male gender was also a significant comorbidity in developing the Covid-19 infection, and attributed this to the female gender's innate, humoral immune response. This allows them to better respond to viral, fungal, parasitic, and bacterial infections. The other comorbidities can exacerbate the manifestations of Covid-19 which is why they contributed to the necessity of extended ventilator requirements for many of the patients. A major contributor to the exacerbation is suspected to the be ACE-2 receptor expression, which is being emphasized in patients who smoke, are hypertensive, and/or have diabetes mellitus. It has been revealed that the ACE-2 receptor is the "entry point" for Covid-19, so with the expression at higher levels in these patients, this makes them much more susceptible to the Covid-19 infections. This study discovered that the mortality rate of patients on mechanical ventilators was extremely higher than those who were ventilated for influenza or other causes of ARDS.

Richardson et al., (2020) studied similar comorbidities as the previous article. The main purpose of the article was to "describe the clinical characteristics and outcomes of patients with Covid-19 hospitalized in a US health care system." (Richardson et al., 2020). The most common comorbidities that this study found were hypertension, obesity, and diabetes. These are all similar to the prior article's findings. A total of 12.2% of the patients in this study were

mechanically ventilated, and 3.2% were placed on kidney replacement therapy. 21% of the patients died due to Covid-19 or Covid-19 related manifestations. The state of New York, where this study took place, had the most cases of Covid-19 compared to any other state due to its high population density. Older age was a noticeable comorbidity as their chart shows how the age range of the highest mortality was greater than or equal to 90 years old at 63.6% mortality rate. For each ten-year interval of age ranges the mortality rate increases. This article facilitates the study by giving numerical percentages and visualization of charts. This article also provides information on averages of laboratory values which not all of the studies provided. This study also provided us with the information that patients who regularly take Angiotensin-converting enzyme (ACE) inhibitors, and Angiotensin II receptor blockers (ARBs) were also at a greater risk of contracting Covid-19. This corresponds with the previous article's findings. Because these two medication therapies are two of the most common treatments for hypertension, this can be a contributing factor as to why hypertension is one of the most common comorbidities in mechanically ventilated patients with Covid-19.

Another significant comorbidity that was studied, and that I noticed frequently during my internship was pregnancy. Qeadan et al., (2021) discusses this comorbidity and the pathophysiology behind why pregnancy can lead to more severe and extended ventilation requirements. One of the reasons is due to a physiological immune suppression during pregnancy. While this study was done fairly early on in the pandemic, it still can conclude that "pregnancy confers substantial additional risk of morbidity" in Covid-19 (Qeadan et al., 2021). The presence of pregnancy in women also correlated to other comorbidities previously mentioned. For example, a significant number of pregnant women in the study also reported obesity and gestational diabetes mellitus. In this study, pregnant women showed higher rates of

hospitalization, moderate ventilation, and length of stay, but this study did not come to any significant conclusions in regard to invasive ventilation and death. This is different findings from other studies, in a way that most studies have concluded that comorbidities have led to longer ventilation requirements and even death in some scenarios. The other studies that classified older age as a comorbidity, (Richardson et al., 2020) can be related to this study because this study reported that the pregnant women with the highest incidence of moderate ventilation was the pregnant women aged 35-44 years. While this age range is not considered older age, it is considered geriatric pregnancies, and that is most likely why the higher incidence of moderate ventilation involves this age range. Geriatric pregnancies already put a significant strain on the women's body, so when these women contract Covid-19 this adds an additional strain on the body, and more specifically the lungs. For example, when I was participating in my internship, we had a pregnant female patient who was on the ventilator. Her oxygen saturation was consistently in the high seventies and low eighties, so they made the decision to do an emergency bedside cesarean section. Once the baby was removed from the mother, almost instantly, her oxygen saturation rose to the mid-nineties. The baby spent approximately two months in the neonatal intensive care unit and is now at home. We had three other pregnant mothers in the intensive care unit at Mercy, and unfortunately none of the mothers survived. These women are actually what inspired me to perform this research. A lot of the news reports would say that the elderly or chronically sick were most at risk of dying from Covid-19, but I wanted to show that those were not the only populations at risk. The study concluded that "access to care for these women" is of the utmost importance, and their "findings provide further justification for the CDC and ACOG's current recommendations regarding the vaccination of pregnant women who are part of recommended priority groups," (Qeadan et al., 2021). People have been skeptical of

pregnant women receiving the vaccination, but this study supports the CDC's recommendation of vaccinating pregnant women against Covid-19.

The fourth study that contributed to this research was related to body mass index and provided more information related to how obesity is a comorbidity of excessive ventilation. Kompaniyets et al., (2021) provided information such as how severe Covid-19 in obese people is related to "chronic inflammation and thrombogenic responses to pathogens as well as to impaired lung function from excess weight, (Kompaniyets et al., 2021). Obesity is a common risk factor for other chronic diseases, that in turn are also other comorbidities for Covid-19 such as Diabetes Mellitus, hypertension, and heart disease. The article states that "overweight and obesity were risk factors for invasive mechanical ventilation, and obesity was a risk factor for hospitalization and death," but alternatively, intensive care unit admissions and deaths were significantly decreased among patients whose BMI was within a normal limit. There was a direct relationship between increasing BMI and increasing ventilation requirements. This is most likely due to the decreased lung function that is caused by the excessive weight put on the lungs in overweight and obese patients. Because Covid-19 is a respiratory illness this is why the pressure on the lungs can cause such a negative impact on the outcome of the illness. The article supports the research that obesity, as well as diabetes mellitus, hypertension, and other obesity related illnesses are all contributing comorbidities to extensive ventilation requirements related to Covid-19.

The remaining articles each touched on similar comorbidities and provided insight others that were not as common as well. Syed et al., 2021, elaborated on the correlation between morbidly obese persons and severe hypoxemia. This article concluded that morbidly obese patients are at a higher risk of lung injury while on the mechanical ventilator because their chest

wall and lung mechanics (Syed et al., 2021). Steinberg et at., (2020), provided insight in younger adults with Covid-19 and some of the adverse outcomes that come from the ventilation requirements with those patients. This study wanted to determine if weight was a primary factor in leading to these adverse outcomes in younger adults. The results show that each of the adverse outcomes were directly associated with a BMI greater than thirty in younger adult patients that required mechanical ventilation and/or died. The study concluded that "obesity appears to be an independent risk factor for poor outcomes in young patients with Covid-19" (Steinberg et at., 2020). Additionally, Silva et al., (2021) focused on obesity as an aggravating factor of Covid-19 patients who had been hospitalized. This study concluded that obesity is a risk factor for worsening to severe Covid-19 cases and reported that 22.2% of their reviewed researched "associated obesity with the development of severe Covid-19…, 33.3% … associated obesity with the need for mechanical ventilation, [and] … 33.3% … associated obesity with mortality due to Covid-19 infection" (Silva et al., 2020). Martins et al., (2021) focused on the common characteristics of the critically ill in Portugal. This study used demographical data to interpret findings of use of mechanical ventilation and/or death related to respiratory failure caused by Covid-19. This study's conclusion led to characteristics of treatment that "can be used to optimize ICU preparedness in the future" (Martins et al., 2021). Grasselli et al., (2020) studied patients in Lombardy, Italy who had been diagnosed with Covid-19, admitted to the ICU. This study measured time to death or hospital discharge, as well comorbidities of these patients. Grasselli et al., (2020) concluded that a significantly high number of patients required mechanical ventilation, and eventually died. This went through several different comorbidities including but not limited to, gender, BMI, heart disease, diabetes, age, and other disease processes. Barrett et al., (2021) studied the correlation between mechanically ventilated patients

with Covid-19 whom of which also had type-1 diabetes. This study was an attempt to determine if the patients experienced different outcomes when not having been diagnosed with type-1 diabetes. This study resulted that 21% higher association of absolute risk of ICU/MV and a 5% higher risk of mortality (Barrett et al., 2021). Mendes (2020) writes a journal article pertaining to the treatments of Covid-19 that had been developed by August 2020. She studied antivirals and immune modulators. This article allowed for studying of the combination of immune modulators and antivirals if on a mechanical ventilator. Kallet (2021) studied mechanical ventilation during the first year of the pandemic. He studied patients' times on ventilators, lung weight, ventilation settings, and inhaled vasodilators. He concluded that based on the PEEP requirements, viral etiology, severity of hypoxemia, etc., are all characteristics of acute respiratory distress syndrome related to Covid-19, "with regard to mortality associated with invasive ventilation in Covid-19" (Kallet, 2021). Obi et al, (2018) studies the process of weaning patients off of the mechanical ventilator and how that process can differ for patients who are morbidly obese. They studied average time on the ventilator, optimal PEEP levels, and the relation to BMI. The study concluded that "optimization of PEEP using esophageal balloon to achieve positive transpulmonary pressure did not change the proportion of patients weaned," (Obi et al., 2018). Because all of the patients in this study were morbidly obese, this study was used more to determine the effectiveness of raising the PEEP during weaning and concluded that there were no consequences of a higher PEEP (Obi et al., 2018). Branco et al., (2020) studied the prevalence of ventilator-associated pneumonia, and how to prevent it. This study reviewed the position of the ventilator filter, oral hygiene maintenance, position of the head of bed, etc. Branco et al., concluded that "the bundle application and education made it possible to increased adherence and decrease infection" levels of ventilator-associated pneumonia (Branco et al., 2020). Ha

(2020) also studied the prevalence of ventilator-associated pneumonia in Covid-19 patients. This article claims that “poor positioning and incorrect tidal volumes can lead to negative outcomes” resulting in longer ventilation requirements and even ventilator-associated pneumonia (Ha, 2020). Each of these studies contributed and facilitated my review of research.

Discussion

The most common comorbidities found throughout all of the studies were obesity, diabetes, hypertension, and geriatric age. An additional comorbidity that was studied was pregnancy. All of these contributed the high morbidity and mortality rates of Covid-19 and ventilator use. While Covid-19 was not the intentional primary subject matter, due to current times, Covid-19 was the most common search result, and therefore became a primary subject matter.

Limitations of the search include the Covid-19 pandemic, which resulted in altered search results. Despite not including “Covid-19” in the search bars, it came up in almost all of the articles that were included in the advanced searches. This most likely skewed the results of the results, in turn skewing the results of the research as a whole. Additional limitations also include the varied locations of the studies. While most of the studies took place in the United States, many of them took place outside of the States. Many of the countries are developed countries, but not all countries have the same technologies as the United States, and the United States do not have the same technologies as other countries. This can result in skewed results due to different countries having different morbidity and mortality rates of ventilator uses. An additional potential issue to the search results is that I began this research shortly after the vaccine was brought to the public. The first group that was offered the vaccine was health care workers and people over the age of sixty-five. Because of this, almost all of the people studied

had not received the Covid-19 vaccine. This may have allowed for a more precise study however, because some of the results may have been different had those studied been vaccinated. I did notice during my internship, which began after the vaccination had been offered to the general public, that almost ninety-seven percent of the patients in the Covid-19 intensive care unit were unvaccinated. Having limited participation in hospitals can result in skewed results because this may not represent the general population. If most of the participating hospitals are in suburban or urban areas, such as the study based in the New York Metropolitan area, then it does not accurately represent the rural population or vice versa. An additional data limitation also mentioned was limited data of patients in the medical records.

This research relates to nursing care on the Intensive Care Unit because it can allow ICU nurses, especially those on the Covid ICU to adjust their patient care for those who have comorbidities included in the study. For those patients who are obese, elderly, or diabetic, the nurses can alter their plan of care to incorporate these patients increased oxygenation needs. With the knowledge of these comorbidities, it may allow healthcare workers to provide better, more focused care to their patients, and support to their families. While the knowledge of these comorbidities may not improve outcomes, it may improve the support and care that nurses and other healthcare workers can offer, in an attempt to improve outcomes to the best of their abilities. This will also improve their roles as patient advocates and standing up for the patients' quality of care.

Additional research can be done now that the vaccine has been out for over a year. This research can facilitate care of patients who have and have not been vaccinated. Because the majority of this research was performed before the vaccine was released the public, it would be beneficial if similar research was done to determine if these comorbidities are still as significant

as they had been prior to these patients being vaccinated. Additional research could also be performed when we have reached a state in which we are in “post-pandemic” era. My results were extremely skewed to Covid-19 related incidence, so there could be a potential difference in comorbidities and risk factors of mechanical ventilation.

Conclusion

Comorbidities of excessive ventilation requirements include high body mass index, diabetes, pregnancy, old age, and coexisting diseases. Each of which effects the body in its own way. The lungs effect so many other body systems, but the reverse is true as well where so many other body systems effect the lungs significantly. With Covid-19 ravaging not only the United States, but the entire world, the number of patients that were being put on machinal ventilators significantly increased. As someone who saw this firsthand, I wanted to learn more about how to better care for these patients, and what could be done by healthcare workers to better advocate for the patients as well. Taken as a whole, knowing about these comorbidities allows healthcare workers to provide the best care possible to each individualized patient as a whole, rather than just a Covid-19 patient. Going from here, the most important thing to be learned from this would be patient education on these comorbidities. Teaching patients who have these comorbidities about vaccine education, attempting to eliminate modifiable risk factors, and protecting themselves from life-threatening viral and bacterial infections.

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