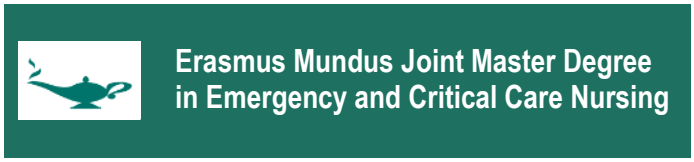

ERASMUS MUNDUS JOINT MASTER'S DEGREE IN EMERGENCY AND CRITICAL CARE NURSING (EMJMD NURSING)

Nursing care in ventilator-associated pneumonia and COVID-19: an informative intervention among nurses

Raquel Rodríguez Fernández

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Master's thesis

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CERTIFY,

That the Master's Thesis submitted by Miss. Raquel Rodríguez Fernández, entitled "Nursing care in ventilator-associated pneumonia and COVID-19: an informative intervention among nurses" carried out under our supervision in the Erasmus Mundus Joint Master Degree in Emergency and Critical Care Nursing, meets the necessary requirements to be approved as a Master´s Thesis.

And for the record, and for the relevant purposes, the present certification is issued in Oviedo, on February 11th, 2021.

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ACRONYMS AND ABBREVIATIOS

-ARDS: Acute Respiratory Distress Syndrome

-BAL: Broncho Alveolar Lavage

-CAP: Community-Acquired Pneumonia

-CDC: Centers for Disease Control and Prevention

-CKD: Chronic Kidney Disease

-COPD: Chronic Obstructive Pulmonary Disease

-CT: Computed Tomography

-DVT: Deep-Vein Thrombosis

-ECDC: European Centre for Disease Prevention and Control

-ECMO: Extracorporeal Membrane Oxygenation

-ETI: Endotracheal Intubation

-ETT: Endotracheal Tube

-GI: Gastrointestinal

-GNB: Gram-Negative Bacteria

-HAP: Hospital-Acquired Pneumonia

-HTN: Hypertension

-HUCA: Central University Hospital of Asturias

-ICU: Intensive Care Unit

-IV: Intravenous

-LUS: Lung Ultrasound

-MDR: Multi-Drug Resistant

-MIC: Minimum Inhibitory Concentration

-MRSA: Methicillin-Resistant Staphylococcus Aureus

-MV: Mechanical Ventilation

-NGT: Nasogastric Tube

-NIV: Non-Invasive Ventilation

-NTI: Nasotracheal Intubation

-PCR: Polymerase Chain Reaction

-PDR: Pandrug Resistant

-PCT: Procalcitonin

-PPI: Personal Protective Equipment

-q: Every

-SSD: Subglottic Secretion Drainage

-VAE: Ventilator-Associated Events

-VAP: Ventilator-Associated Pneumonia

-WHO: World Health Organization

- XDR: Extensively drug resistant

TABLE OF CONTENTS

1. INTRODUCTION

Lower respiratory infections are a group of diseases, generally caused by a virus, that compromise the lungs. It can affect children as well as adults (European Lung Foundation [ELF], 2021). According to the World Health Organization (WHO), 2.6 million of people died of lower respiratory infections in 2019, being the 4th leading cause of death as well as the most fatal transmittable disease (WHO, 2020). These numbers dramatically increased later in 2020 after the COVID-19 pandemic was declared worldwide (Ripa et al., 2021).

Bronchitis, bronchiolitis, influenza or pneumonia are some examples of these type of infections. The latter is the most common infection-related death in European countries as well as in the United States of America (ELF, 2021).

1.1. Defining pneumonia

Pneumonia is an acute infection which causes difficult and painful breathing due to the presence of pus and other fluids in the air sacks inside the lungs known as alveoli (Kaplan et al., 2013). According to European Lung Foundation (ELF) its symptoms can last for up to a month and it is more common in children under 5 and elderly adults (ELF, 2021).

This condition caused the hospitalization of nearly 7 million of older adults (65 years old or over) in 2015, from which one million perished (Shi et al., 2020).

This infection can be contracted during the daily life (community-acquired pneumonia, CAP) (ELF, 2021). However, if a person is admitted to the hospital for 48 hours or more and develops this infection, it would become a nosocomial pneumonia or hospital-acquired pneumonia (HAP) (Vallecoccia et al., 2020). When related to mechanical ventilation (MV), it is diagnosed as ventilator-associated pneumonia (VAP).

2. LITERATURE REVIEW

2.1. Ventilator-associated pneumonia

According to the Centers for Disease Control and Prevention (CDC), "VAP is a lung infection that develops in a person who is on a ventilator" (CDC, 2010). Modi and Kovacs highlight that it appears when the patient has been intubated for at least 48 hours and that the symptoms can emerge even when the tube has already been removed (Modi & Kovacs, 2020).

2.1.1. Epidemiology

Mechanical ventilators are used every day in the intensive care units (ICU). A study performed in the United States about the ICU occupancy and the use of mechanical ventilators concluded that over the period of three years 29% of the beds in those units were occupied by a mechanically ventilated patient. They also found out that in any given hour nearly 40% of patients were connected to a ventilator (Wunsch et al., 2013).

VAP is a frequent complication in the intensive care facilities. It's the second most common nosocomial infection inside those units and also the most lethal (Timsit et al., 2017). Its incidence rate varies from 9 to 67%, with up to more than 15 cases per 1000 mechanically-ventilator days (Ramos Lapa, 2019).

According to Timsit et al., a patient who develops VAP is likely to stay 7 days longer at the hospital, requiring more treatment and increasing hospitalization costs up to a total of $40.000 USD (Timsit et al., 2017).

VAP mortality is variable due to the difficult diagnosis, mixed definitions as well as the varied risk factors associated to the disease (Timsit et al., 2017). Time seems to be a major cornerstone defining the resolution of the infection. The later the infection begins, the higher are the mortality rates (Nguile-Makao et al., 2010). However, a study in 2017 concluded otherwise. There was no difference in mortality rates between an early or a late-onset of the infection (Injac et al., 2017).

2.1.2. Aetiology

Lower respiratory tract is normally a sterile territory in a healthy individual. When MV is in place, the natural sterile barrier that protects our organism is broken. The endotracheal tube keeps the mouth open, serving as a freeway to the lungs for the microorganism (Díaz et al., 2010).

The endotracheal tube is secured in the trachea with an inflated cuff. Mouth secretions and other fluids which contain microorganisms accumulate around this area. If the cuff is not properly filled with air, secretions may leak and be aspirated, carrying the pathogens with them to the lungs (Moghaddam & Zoka, 2020).

The aspiration of gastric fluids as well as contamination caused by health care workers also contributes to the appearance of pneumonia (Pezo Galdea et al., 2018).

In 2017, Injac et al., determined that gram negative bacteria were the predominant microorganism when VAP was developed, especially *Acinetobacter spp.* (XDR strain) (Injac et al., 2017). Later in 2020, another study which investigated VAP rates and the microorganisms causing it found that the most common microorganism present in the endotracheal aspirate samples was *Pseudomona aeruginosa* (25%). The second was *Klebsiella spp.* with nearly a 12%, followed by *Proteus spp.* (10.3%), *Enterobacter spp.* (7.4%) and *Staphylococcus aureus* (1.5%) (Kepekci, 2020).

Díaz et al. points out the presence of different microorganisms in early and late onset of the infection. While *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus* are present in those episodes where the infection sets earlier; *Pseudomonas aerugi-nosa*, *Acinetobacter baumannii*, *Staphylococcus aureus* meticilin-resistant and other gram-negative bacteria predominate in late-onsets. This last ensemble puts the patient in higher risk for recovery as they are multidrug resistant (MDR) pathogens. Thus, treatment tends to be more complex (Diaz et al., 2010). Timsit et al. agrees with the fact that in cases where the infection starts later, it seems that MDR pathogen prevail (Timsit et al., 2017).

2.1.3. Diagnosis

VAP diagnosis has been extensively studied. However, researchers do not seem to find a consensus to this matter. Many investigators and guidelines agree that VAP can be diagnosed in accordance with these three components:

1. Clinical suspicion:

   There are many signs and symptoms which presumably show that the patient has contracted pneumonia:

   -High temperature: >38ºC

   -Leucocytosis: >=12.000/mm3 or leucopoenia: <4.000/mm3

   -An increment in oxygen requirements

   -Purulent secretions

   These are generic indications of a respiratory infection. Thus, further tests are required to support pneumonia diagnosis (Olleta Irisarri, 2021; Papazian et al., 2020).

2. Radiographic studies:

   A chest x-ray will show a clear picture of the actual state of the lungs. To support pneumonia diagnosis it must show new or worse lung infiltrates (Leone et al., 2018; Modi & Kovacs, 2020). However, as x-rays are not precise to determine the presence of VAP, other radiological studies such as computed tomography (CT) or lung ultrasound (LUS) have recently been suggested due to being more sensitive (Papazian et al., 2020).

3. Microbiological tests:

   The objective of these is to isolate and recognize the microorganism causing the infection in order to provide treatment (Modi & Kovacs, 2020). In this case, it is recommended that samples are obtained prior to start or even change of antibiotic therapy to avoid alterations in the results (Agarwal et al., 2020; Papazian et al., 2020; Torres et al., 2017).

There are several tests that can be performed:

-**Respiratory sample**: after the endotracheal tube (ETT) is inserted for MV, the sterile environment of the respiratory tract is breached, thus obtaining an adequate sample might be challenging. Samples from this area may result positive, which does not necessarily represent VAP but only colonization of a pathogen (Fernando et al., 2020; Vallecoccia et al., 2020). Invasive techniques such as bronchoscopy or bronchoalveolar lavage (BAL) appear to be useful in VAP diagnosis, particularly in environments where resources are insufficient (Agarwal et al., 2020). The use of this technique together with quantitave cultures may have higher specificity than the use of qualitative cultures. However, it has some disadvantages such as the cost, the need for specialized personnel to perform the procedure and the possible complications for the patient (hypoxemia, barotrauma, haemorrhage) (Papazian et al., 2020).

-**Blood cultures**: are commonly used in VAP diagnosis. They are especially helpful if respiratory cultures are not decisive. They can also reveal other concomitant infections not related to VAP (Ferreira-Coimbra et al., 2020; Modi & Kovacs, 2020).

-**Polymerase chain reaction (PCR)**: the importance of this test is time-related. Generally, it takes 48 to 72 hours to identify the pathogen causing VAP. When using targeted-PCR test, this time can be reduced to 24-36 hours, which will help avoiding the use of broad-spectrum antibiotic therapy (Papazian et al., 2020). Multiplex PCR should also be taken into account, as results can be obtained within 1 to 2 hours (Ferreira-Coimbra et al., 2020). Further studies are required as it has not been deeply studied yet. In a study performed in 2020, this test was able to identify the source of VAP as well as the resistance mechanism in 73% of cases (Luyt et al., 2020).

-**Gram stain**: although it is not extremely specific in diagnosing VAP, it can be practical in choosing the appropriate route for antibiotic treatment and reducing the use of broad-spectrum antibiotics (Yoshimura et al., 2017).

-**Procalcitonin (PCT)**: is a serum biomarker which levels tend to elevate when there is a bacterial infection, but not during a viral infection. Thus, it is quite

useful to help distinguish between one another (Kamat et al., 2020). It can also be useful to decide when to cease antibiotic treatment (Modi & Kovacs, 2020).

Which sampling method to use, or which one is the most accurate is still controversial nowadays. Papazian et al. claim that further randomized trials and new microbiological tests will shed some light on this matter (Papazian et al., 2020). Most of studies agree on the fact that these tests should not be trusted individually but combined in order to have a suitable VAP diagnosis (Ferreira-Coimbra et al., 2020; Leone et al., 2018; Olleta Irisarri, 2021; Torres et al., 2017).

2.1.4. Risk factors

The most efficient approach to prevent VAP is to elude exposure to the risk factors associated. Thus, placing an ETT should be avoided whenever possible in the first place. The use of non-invasive ventilation (NIV) might be a good alternative in patients where the oxygen requirements are not met (Timsit et al., 2017).

There are many risk factors associated with VAP. Each risk factor is independent from each other, but at the same time they have an impact on the rest. Some of them can be modified or easier to prevent. However, there are others which are intrinsic to the patient or intervention-related. In this case prevention and care bundles play a crucial role to avoid complications (Wu et al., 2019).

Host-related risk factors

- **Age and gender**: most of the bibliography available agree that male patients are more vulnerable to VAP. In terms of age, people over 60 tend to develop VAP easier than younger adults, which may be due to the dysfunctions related to the ageing of the respiratory muscles (Campos et al., 2021; Olleta Irisarri, 2021; Wałaszek et al., 2016).

- **Underlying illnesses**: patients suffering from heart or respiratory diseases as well as immunodeficiency are at a higher risk of acquiring VAP, especially those suffering from chronic obstructive pulmonary disease (COPD). Furthermore, hypertension (HTN), diabetes, arteriosclerosis and obesity are

the most common conditions to develop complications related to MV (Barletta Farías et al., 2019; Olleta Irisarri, 2021).

- **Smoking**: the alveolar macrophague is a type of cell in charge of removing detrimental particles from our lungs (Weinberger, 2019). It's been shown that in smokers this cells malfunction, consequently the lungs are vulnerable to pathogens (Wu et al., 2019).

- **Surgery**: patients who have had prior surgery seem to have higher attributable mortality than those who did not in terms of VAP (Melsen et al., 2013; Nguile-Makao et al., 2010).

- **Burns**: burned patients are more likely to contract pneumonia, with an incidence of 10-65% (Latenser et al., 2007). It is as common in children (Rogers et al., 2014) as in adults (Sen et al., 2016). Severe burns may damage the lung, leaving it unable to perform proper bacterial clearance, what can lead to VAP (Wu et al., 2019).

-**Ulcer disease**: this condition can damage the mucosa and favour the appearance of VAP as well as cause gastrointestinal (GI) bleeding (Lim et al., 2015).

-**Extracorporeal membrane oxygenation** (ECMO): patients in severe conditions such as cardiogenic shock or acute respiratory distress syndrome (ARDS) may require ecmo therapy, which provides and improves gas exchange and blood flow. However, it's been shown that patients undergoing this treatment have higher VAP incidence than those who don't (Franchineau et al., 2018).

Intervention-related factors

- **Ventilation time**: appears to be one of the most determinant risk factors of them all. Many studies have proved that the more time a patient is exposed to MV, the higher is the risk of contracting VAP (Olleta Irisarri, 2021). Moreover, the incidence of VAP development increases a 5% after one day of MV, whereas it raises up to 65% after 30 days of ventilator support (Abdelrazik Othman & Salah Abdelazim, 2017).

- **Intubation and tracheostomy**: after inserting the ETT or performing a tracheostomy the sterility of the airway is breached, thus the natural defence of the organism is put at risk (Diaz et al., 2010). The cuff that maintains the

tube/tracheostomy secure plays a key role in the prevention of VAP. This cuff must be properly inflated (not less than 20cm H20) to seal the respiratory tract, otherwise the secretions gathered around the ETT may leak into the lungs (Moghaddam & Zoka, 2020).

- **Sedation**: patients under MV require of deep sedation. This causes that reflexes such as expectoration or cough are voided, complicating the removal of secretions (Ramirez-Estrada et al., 2020). The longer MV is required, the longer the patient requires deep sedation, which in time can cause immunodeficiency (Olleta Irisarri, 2021).

- **Reintubation**: reintubation is known to put in higher risk patients who are already in critical circumstances. It leads to prolonged MV time, thus longer ICU stay and complications such as hypertension, hypoxia and higher risk of aspirations due to previous intubation (Babu et al., 2019).

- **Blood transfusion**: several studies have shown that blood transfusions on admission increase the risk of VAP, which can be related to an enhanced inflammatory response caused by this procedure (Li et al., 2020).

- **Positive fluid balance**: patients who have received an excess of fluids are more likely to develop ventilator-associated events (VAE). This can be due to the presence of oedema in the lungs, which eventually can lead to congestive heart failure (Liu et al., 2019).

- **Prior antibiotic therapy**: prolonged exposure to antibiotics which may not be necessary will help the pathogens to develop a resistance against the treatment (MDR), making it difficult to provide an adequate therapy (Wu et al., 2019).

- **Replacement of ventilatory circuits**: too many frequent changes in the ventilator circuits is related to a high risk of infection. In a study performed in 2010, patients whose ventilator receive circuits replacements every 48 hours developed higher risk-infection rates than those where the exchange was applied every 7 days (Han & Liu, 2010).

- **Supine position**: it is well known now that in this position the risk of aspiration is higher, either of secretions or enteral nutrition. 30º degree head inclination or semi-recumbent position may help preventing these events. The results of

a study from 2016 declared that from those patients who developed VAP nearly a 32% were in supine position compared to 12.6% that were in semi-recumbent position (Wang et al., 2016).

- **Enteral nutrition**: this procedure is essential for the patient's recovery; however, it brings along various complications. This type of nutrition changes the pH, making it a more alkaline environment which favours the appearance of pathogens. Also the presence of the nasogastric tube (NGT) itself in the GI tract increases the gastric reflux and intra-abdominal pressure which, again, increments the risk of aspiration and VAP development (Olleta Irisarri, 2021).

- **Nasotracheal intubation (NTI)**: this technique has some advantages compared with endotracheal intubation (ETI) such as reduced unplanned extubation or survival to discharge rates. However, this method is less used and the risk for sinusitis and VAP is similar to ETI as pathogens can easily travel from paranasal sinus to oropharynx (Kumar & Kumar Angurana, 2020).

- **Subglottic secretion drainage (SSD)**: it is a common preventive measure for preventing VAP as it reduces its risk and also mortality, although it does not seem to have an impact in reducing ICU stay nor MV time (Pozuelo-Carrascosa et al., 2020).

- **Intrahospital transport**: transferring critically ill patients outside ICU can bring potential complications that can put patient's life in danger. Furthermore, it seems to increment the risk for aspiration, thus the risk for VAP appearance (Rouzé et al., 2018).

2.1.5 Complications

VAP is a complication derived from prolonged MV, but pneumonia itself can cause some extra problems to the patient who has been diagnosed with it. According to Abdelrazik & Abdelazim (2017), the most common complication surrounding this disease is severe septic shock along together with ARDS and atelectasis. Colonizations with MDR pathogens also tend to be present in most of cases of VAP.

Pulmonary abscess, kidney insufficiency or respiratory insufficiency can also endanger the patient's condition or delay his/her recovery (NHLBI, 2022).

2.1.6. Treatment

As for clinical management of VAP, controversy continues. Years ago once VAP was suspected the right approach to follow was to start empiric antibiotic treatment immediately while waiting for the cultures results. However, recent studies argue this fact, as initiating improper antibiotic treatment may result in higher risk of mortality (Timsit et al., 2017; Zahar et al., 2011). MDR pathogens play a key role in the decision of choosing an appropriate antibiotic treatment (Klopmas, 2021).

MDR pathogens

With the modern world the use of antibiotics has become more and more common inside and outside the clinical setting. This has caused the appearance of pathogens resistant to some of these drugs, which are known as MDR agents. Thus, the treatment for some infections has become more difficult (Esposito & De Simone, 2017).

According to the United States' CDC and the European Centre for Disease Prevention and Control (ECDC), the most common antibiotic resistant gram-negative bacili that cause HAP/VAP can be classified within 3 different groups (Klompas, 2021):

- Multidrug resistant (MDR): pathogens resistant to at least one agent in three different antimicrobial categories.
- Extensively drug resistant (XDR): pathogens resistant to at least one agent in all the antimicrobial categories but two.
- Pandrug resistant (PDR): pathogens resistant to all antimicrobial agents that can be used to treat the infection.

In these cases, antibiotic therapy should be administered as soon as possible. The regimen should include a suitable dosage as well as another antibiotic agent in combination. At the beginning, this dose should follow some principles such as the minimum inhibitory concentration (MIC) and the pharmacokinetics and pharmacodynamics theory, to assure the efficacy of the treatment (Shi et al., 2019).

In patients with high risk of infection for XDR pathogens, it is recommended to use polymyxin and tigecycline (Shi et al., 2019).

Empiric antibiotic treatment

After suspecting VAP, blood and sputum samples should be taken. In patients with severe condition such as sepsis or beginning of organ failure it is recommended to start antibiotic treatment as soon as possible (Klompas, 2021).

To choose the antibiotic regimen to commence the treatment it would be appropriate to know the predominant pathogen in the health care setting as well as the patient's risk factors. It is important that this drug acts against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and other gram-negative bacilli, for being the most common pathogens causing VAP. In case the patient has received prior antibiotic treatment, the agent of choice should be from a different class, as the pathogens may have developed a resistance towards the antibiotic used in the first place (Klompas, 2021).

MDR pathogens should be taken into account as well as patient's risk factors. Timsit et al. recommendations to start empiric antibiotic focus on the risk of mortality and presence of risk factors. These suggestions derive from the American guidelines (Kalil et al., 2016; Timsit et al., 2017):

- Not at high risk of mortality AND no risk factors:

  -> Piperacillin-tazobactam 4.5 g intravenous (IV) every (q) 6h

  OR

  ➔ Cefepime 2 g IV q8h + Levofloxacin 750 mg IV daily

- Not at high risk of mortality BUT with factors increasing the possibility of Gram-negative bacteria:

  ➔ Piperacillin-tazobactam 4.5 g IV every 6h

  OR

  ➔ Cefepime or ceftazidime 2 g IV q8h

  OR

➔ Levofloxacin 750 mg IV daily

➔ Ciprofloxacin 400 mg IV q8h

OR

➔ Imipenem 1g IV q8h

➔ Meropenem 1 g IV q6h

➔ Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)

OR

➔ Linezolid 600 mg IV q12h

- High risk of mortality OR prior IV antibiotic treatment in the last 90 days:

➔ Piperacillin-tazobactam 4.5 g IV q6h

OR

➔ Cefepime or ceftazidime 2 g IV q8h

OR

➔ Levofloxacin 750 mg IV daily

➔ Ciprofloxacin 400 mg IV q8h

OR

➔ Imipenem 1g IV q8h

➔ Meropenem 1 g IV q6h

AND

➔ Amikacin 25 (30) mg/kg IV daily

OR

➔ Gentamicin 5–7 mg/kg IV daily

OR

➔ Tobramycin 5–7 mg/kg IV daily

➔ Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)

OR

➔ Linezolid 600 mg IV q12h

Methicillin-resistant Staphylococcus aureus (MRSA) should be covered empirically only in patients where there is respiratory tract colonization or in settings where it has high prevalence (Shi et al., 2019).

According to Klompas (2021), the risk of MDR agents in VAP increases when these factors are present: IV antibiotics in the previous 90 days, at least 5 days of hospital stay prior to the appearance of VAP, septic shock concomitant with VAP, ARDS prior to VAP, and renal replacement therapy before VAP occurrence.

Pathogen-specific treatment

Once the cultures results are available, the pathogen present in the organism is identified and so are its susceptibilities. For this reason, it is also known as tailored treatment (Shi et al., 2019).

Regardless the empiric antibiotic treatment started, this allows to adjust the regimen into a more specific one that will be more effective against the pathogen. If the cause of VAP is thought to be aspiration, oral and enteric flora should also be covered, even if the cultures show only one pathogen, as aspiration events are known to be polymicrobial (Modi & Kovacs, 2020).

Length of treatment

The majority of guidelines agree that the duration of the antibiotic regimen in uncomplicated pneumonias should be 7 days long. Prolonged courses have not shown any benefits nor reduced rates (Modi & Kovacs, 2020).

The American guidelines seem to have a stronger conviction than the European in regards of the duration of the treatment. The American confirm that the regimen should only be extended longer than one week in cases where the infection is still active. However, the European recommend to extend the course in cases where the initial empiric treatment was inappropriate (Martin-Loeches et al., 2018).

It is common for both guidelines the recommendation of de-escalation or discontinuation of the regimen, minimizing unnecessary antibiotic exposure (Martin-Loeches et al., 2018).

Inhaled antibiotic treatment

The Chinese guidelines support the inhaled antibiotic treatment in combination with the systemic or IV one when some conditions apply (Shi et al., 2019):

-MDR gram-negative bacteria (GNB) causing VAP.

-IV therapy on its own has poor efficacy, unable to provide supply an adequate treatment for the infection.

-The inhaled treatment is suitable to act against the identified pathogen

Although further studies are required, in those cases where VAP is cause by agents only susceptible to polymyxins and aminoglycosides inhaled antibiotics can be a good option to avoid the nephrotoxicity produced by the IV administration of this group of antimicrobials (Modi & Kovacs, 2020).

Conversion to oral antibiotics

Moving from IV to oral therapy will be decided upon the patient's status. If the patient is clinically stable and his prognosis is moving towards recovery, oral therapy can be applied. Naturally, oral intake must be tolerated (Klompas, 2021).

The choice of the oral antibiotic should follow the same guidelines as for the IV therapy; based on the identification or not of the pathogen causing the infection.

Special considerations

In patients with a situation of immunodeficiency, the treatment should include antibiotic regimens against fungi, virus, parasites and other bacterial pathogens that are not that common (Klompas, 2021).

In patients with allergies to penicillin, it is important that the severity and the type of the adverse reactions is assessed. In cases where patients have been diagnosed by skin testing cephalosporins can be administered.

In cases where there has been an episode of mild reaction to penicillin, a cephalosporin or an antipseudomonal carbapenem can still be used. However, the first administration should be a small dose (1/10 of the due dose) continued with close observation during the following hour. If no reactions nor symptoms emerged, the full dose can be given.

When there is history of allergic events to cephalosporins, aztreonam can be used instead, unless there is a known allergy to Ceftazidime as these drugs have alike chain groups.

2.2. Prevention and nursing care

Prevention should be the first step towards avoiding VAP. In order to do this, care bundles and guidelines are a set of instructions developed to promote patient's health and avoid complications (Rello et al., 2013). Protocols should be available in every setting or ward to help the health professionals achieve the best practice which will have direct effect on patient's prognosis (Crunden et al., 2005).

Preventive measures should be present in every part of the intubation process, from the decision to choose the type of ventilation to extubation (Peña-López et al., 2016). NIV devices can be a good alternative to reduce the risk of VAP when possible. However in terms of invasive ventilation, orotracheal intubation is preferred rather than the nasotracheal option (Osti et al., 2017).

The main precaution that must be taken in order to prevent VAP is aspiration from both oral secretions and gastric contents (Moghaddam & Zoka, 2020; Pezo Galdea et al., 2018). Thus, it is very important that the ETT has suction ports to facilitate this task. The size of the ETT should be adequate for each patient and also a proper pressure inside the cuff (Moghaddam & Zoka, 2020).

In order to prevent gastric aspiration, it is recommended to maintain the head of the bed between 30 and 40 degrees unless it is contraindicated. Monitor gastric residual

volumes and routinely turn patients every 2 hours can also avoid reflux and aspiration of body fluids (Osti et al., 2017; Wang et al., 2016).

Hand washing is known to play a crucial role in preventing the transmission of infections, especially between contact with different patients (Kolawole Damilare, 2020). Failure to accomplish this low-cost-effective technique as well as wearing gloves (sterile and non-sterile) seems to increase the risk of VAP (Osti et al., 2017).

Oral decontamination and proper mouth hygiene helps to elude the filtration of bacteria into the lungs. The use of chlorhexidine seems to be more efficient than saline solutions in order to prevent nosocomial pneumonia (Chan et al., 2007; Osti et al., 2017; Rabello et al., 2018).

The correct maintenance of the ventilatory device can also help preventing infections. According to Osti et al. (2017), the changes in the ventilator circuits should take place when contaminated. Abiramalatha et al. (2021) found that changing the circuits once a week compared to "once in less than 7 days", may not raise the risk of VAP not mortality prior to discharge, which will imply economic benefits. An adequate humidification together with the application of nebulisers can help mobilise the secretions by providing fluidity so lavage with saline solutions can be avoided (Osti et al., 2017).

The use of different drugs, such as sedatives, is needed so as to mechanically ventilate a patient. However, to prevent risks several care bundles and protocols such as "*Wake up and breath*", recommend to daily interrupt sedations or lower dosages to avoid aspirations and other complications (Khan et al., 2014; Olleta Irisarri, 2021; Osti et al., 2017). As already mentioned, an adequate antibiotic treatment, empiric or targeted, will be key to determine the patient's future (Klompas, 2021; Shi et al., 2019; Timsit et al., 2017). Other drugs are used for prophylaxis to prevent complications including stress ulcer or deep-vein thrombosis (DVP) (Osti et al., 2017).

2.2.1. Nurses' role

Nurses are the main carers for patients in any hospital setting, thus they are the first and main barrier to prevent infection transmissions, especially nosocomial diseases (Osti et al., 2017).

Most of the activities and procedures that take place in critically care units are performed by nurses, particularly ETT maintenance and management of ventilatory devices. For this reason, reducing risk of VAP lies directly on their hands (Abou Zed & Mohammed, 2019).

It is important that nurses follow the nursing process from the beginning when the patient is admitted. This approach is a systematic guideline that comprises 5 steps leading to patient-centred care: assessment, diagnosis, planning, implementation and evaluation. Each one of them is as important as the previous one and help nurses to look after their clients in a holistic manner. This along with more specific care bundles and protocols that should be available in the units are some of the tools that help the nurses to adequately perform all the tasks related to the patients' health (Toney-Butler & Thayer, 2021). Adhesion to care bundles and providing education for nurses are tools that proved to reduce risk of new infections (Branco et al., 2020).

Being close to the patient 24 hours a day gives the nurses the capacity to promptly identify patients who are at higher risk of VAP and other infections and raise and share their concerns with the physicians. Nevertheless, prevention and infection control is something that every individual of the health team should promote (Ramos Lapa, 2019).

Nurses should also protect themselves making use of the personal protective equipment (PPI) and act as a guide to everyone who may be in contact with the patients, from other health care workers to visitors, relatives and health students (Osti et al., 2017).

Although nurses are in first line to stop prevention, it must become a holistic process where all health professionals take part in protecting patients from nosocomial infections and other diseases that can compromise their lives (Osti et al., 2017).

2.3. Ventilator-associated pneumonia in COVID-19 pandemic

On December 31st 2019 COVID-19 disease was notified for the first time in Wuhan, China (WHO, 2021). As of today, this nomenclature can be recognised worldwide and it is known that it is an infection caused by a virus identified as SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) (Póvoa et al., 2020).

A great amount of patients who suffered from this disease developed COVID-19-associated pneumonia and ARDS requiring their admission into ICU with measures such as deep sedation and muscle blockers for several weeks, prone-positioning and especially prolonged MV. All these actions meant to stabilise the patient also put them at high risk of VAP (Luyt et al., 2020).

In a study performed in the height of the outbreak 29% of the participants suffering from COVID-19 developed as well VAP. Fatality after 30 days reached 46% of cases and was associated with ARDS and septic shock at VAP onset. *Pseudomonas aeuroginosa* (35%) and *Staphylococcus aureus* (23%) were the most common microorganisms (Giacobbe et al., 2021).

These facts support those in the study performed by Blonz et al. (2021) where the number of participants was similar (171 versus 188) but the incidence rate of VAP was higher (48,9%). In this case, *Enterobacteria* was the most common pathogen and the complications associated to the pneumonia were thoracic empyema and pulmonary abscess, but just in few cases. It was significant that males appeared to be at higher risk of VAP than women and almost 20% of patients had a relapse.

Recurrence of VAP in COVID-19 appears to be usual, even in cases where the antibiotic treatment is adequate (Luyt et al., 2020).

As previously mentioned, diagnosing VAP is still challenging these days. COVID-19 associated pneumonia presents similar signs and symptoms to VAP which makes it almost impossible to distinguish one infection from the other. Hence, the majority of patients with COVID-19-associated pneumonia and ARDS are treated with empiric antibiotics that cover also for VAP, even undiagnosed (François et al., 2020).

To date (09/02/2022) SARS-CoV-2 has caused 5.784.051 deaths in 222 countries around the world. It is then important to acquire and apply preventive measures and guidelines in order to promote infection control and avoid transmission of infections (WORLDOMETERS, 2021).

3. JUSTIFICATION

COVID-19 disease has affected people's lives for the last two years. Millions of lives were lost worldwide due to this pandemic. The health care systems of every country had to face and are still facing today what can be compared to a war inside their hospitals and especially ICUs, where patients had to go under MV to survive. Many of these patients developed VAP, being this one of the main complications of a prolonged MV.

All health care professionals had to stay together to fight this virus. Nurses, being the backbone of the health care systems had to gather their knowledge and expertise and confront situations of extreme delicacy and difficulty and take positions where they have never been before.

In light of the above, the researcher will develop a series of informative sessions to display among nurses who work in the main COVID-ICU at Central University Hospital of Asturias (HUCA), in Oviedo. These sessions will stress the main points of nursing care that lead VAP prevention and treatment.

Hence, the aim of this study is to determine whether this intervention can improve nursing care by reducing complications of VAP and VAP-associated mortality as well as ICU length of stay in COVID-ICU at HUCA.

4. RESEARCH QUESTIONS, HYPOTHESIS AND OBJECTIVES

4.1. Research question

Can a series of informative sessions among nurses have an impact on VAP-related complications, VAP-associated mortality and length of ICU stay in COVID-19 patients?

4.2. Hypothesis

Null hypothesis (H0):

There is no impact on VAP-related complications, VAP-associated mortality or ICU stay in terms of COVID-19 patients after implementing a series of informative sessions among nurses.

Alternative hypothesis:

H1: VAP-related complications in COVID-19 patients is reduced after implementing a series of informative sessions among nurses

H2: VAP-associated mortality in COVID-19 patients is reduced after implementing a series of informative sessions among nurses

H3: ICU stay is reduced in terms of COVID-19 patients after implementing a series of informative sessions among nurses.

4.3. Objectives

General objective:

- To determine the impact that an informative intervention among nurses has on VAP-related complications, VAP-associated mortality and ICU length of stay in a COVID ICU of HUCA.

Specific objectives:

- To examine the demographic characteristics of patients hospitalized in COVID-19 ICU who developed VAP at HUCA.
- To examine the demographic characteristics and professional information among nurses working in COVID-19 ICU at HUCA.
- To analyse the relation of the nurses' sociodemographic data and professional characteristics and patient's VAP-related complications in COVID-19 ICU at HUCA.
- To analyse the relation of the nurses' sociodemographic data and professional characteristics and patient's mortality in COVID-19 ICU at HUCA.
- To analyse the relation of the nurses' sociodemographic data and professional characteristics and patient's length of ICU stay at COVID-19 ICU at HUCA.

5. METHODS

5.1. Study design

A quasi-experimental prospective study with two cohorts will be performed.

5.2. Time and setting

The study will be conducted in COVID-19 ICUs number 8 and 9 at HUCA.

HUCA is a third level hospital situated in the city of Oviedo (Asturias, Spain). It has 1039 beds and counts on many different specialized medical services. It is also centre of national reference for inherited cardiovascular diseases or brachial plexus surgery among others.

It has a total of 9 ICUs, being number 7, 8 and 9 designated to treat COVID-19 patients. This distribution changes along with the pandemic needs and requirements.

ICUs 8 and 9 receive patients with the same conditions and both of them are alike in terms of equipment, staff and work methodology. Each unit has capacity for up to 15 patients in individual boxes distributed around the nursing station, which is located in the centre.

A total of 7 nurses are allocated in each unit per shift, being each one of them in charge of 2 to 3 patients.

The field work of the study will be conducted from the last week of February 2022 until reaching the number of participants set by the investigator.

After gathering all the data, the statistical analysis will be performed, followed by the examination of the results and discussion until reaching the conclusion.

5.3. Study participants: population and sample

Population

The study will include patients admitted to the ICU number 8 and number 9 from HUCA, who tested positive for COVID-19 and also develop VAP. Both units receive the same type of patients.

Sample

The study will include a total of 100 patients; 50 from each unit, that meet the inclusion criteria selected via convenient quota sampling.

The participants will be selected consecutively after admission and assurance that they meet the inclusion and exclusion criteria.

- **Inclusion criteria for patients**
  - -Admitted to ICU number 8 or 9 from HUCA.
  - -Tested positive for SARS-CoV-2.
  - -ICU stay of at least 3 days.
  - -At least, 2 days of MV therapy.
  - -Diagnosed for VAP after 2 days of MV in this ICU admission.
- **Exclusion criteria for patients**
  - -Use of ventilator devices other than MV.
  - -Death or discharge from ICU during the first 3 days of admission.
  - -Diagnosed only with either COVID-19 or VAP.
  - -Diagnosed with VAP prior to ICU admission.

- **Inclusion criteria for nurses**
  - -Working in ICUs number 8 or 9 at HUCA.
  - -Job experience of at least one year.
  - -Signed off informed consent.
  - -Attended to at least 2 informative sessions.
- **Exclusion criteria for nurses**
  - -In supervisory or managing roles
  - -Refused to participate in the study.

-Whose data collection sheet is unfinished.

-Attended to 1 or noninformative sessions.

5.4. Variables

- **Patient-related variables**
  - Sociodemographic variables

    -Age: in number of years

    -Gender: male, female
  - Past medical history

    -Toxic habits: smoking, alcohol, other drugs

    -Chronic diseases: diabetes, hypertension, heart disease, COPD/asthma, cancer, chronic kidney disease (CKD), others
  - Current disease

    -Initial diagnosis

    -Number of days since admission

    -ICU stay: number of complete days in ICU

    -Ventilator days: number of days requiring MV

    -Nutrition: enteral, parenteral, both

    -Complications (yes/no): septic shock, ARDS, atelectasis, pulmonary abscess, renal insufficiency, others

    -Mortality during ICU stay (yes/no)

    If so:

    -Days in ICU until death

    -Cause of death

- **Nurse-related variables**
  - Sociodemographic variables

    -Age: in number of years

    -Gender: male, female
  - Career-related variables

    -Academic training in years: 3 years (Diplomatura), 4 years (Grado)

    -Job experience in nursing in years

-Academic training in critical care: profile, master, other.

-Job experience in critical care in years

-Current position status: permanent, temporary.

5.5. Instruments

All the information will be collected by using a data collection sheet developed by the researcher that includes all the variables mentioned above (Appendix 4).

5.6. Procedure

Prior to commence with the field work it will be required to obtain the approval of the Research Ethics Committee of the Principality of Asturias as well as the authorization of the HUCA board (Appendix 1).

Both supervisors from ICU number 8 and 9 will be briefed and informed about the procedure so they can grant the researcher the permission to proceed in their units. The staff nurses who are willing to participate will fill out an informed consent (Appendix 2) and then receive instructions regarding the sessions and data collection.

The data collection sheets will be deposited in the nursing stations so the nurses have immediate access when a patient who meets the inclusion criteria is admitted. Once the patient included in the study is discharged from the unit, the sheet report should be completed and deposited in a folder kept in the supervisor's office. The researcher will gather the data collection sheets every two weeks until the number fixed at the beginning is reached.

Each unit will act as an independent cohort. The nurses allocated in ICU number 8 will attend to the informative sessions whereas the nurses allocated in ICU number 9 will not. The data will be collected from both units and later be compared after performing the statistical analysis.

Prior to start with the sessions, a day will be set in accordance with the supervisor of ICU number 8. After that, the following sessions will take place every two weeks at the same time.

The chosen time will be agreed with the supervisor of ICU number 8. The investigator's proposal will be from 15 to 15:20h for the initial session and from 15 to 15:10 for the ones to follow (reminder sessions) so that both morning and afternoon shift staff can be present.

A PowerPoint presentation will be used in every session. For the initial session the presentation will include 12 slides and last 20 minutes divided as follow:

- 5': Study and researcher introduction, sharing facts regarding the epidemiology of VAP and COVID-19.
- 5': Aetiology, risk factors and complications surrounding VAP.
- 7': Latest update stressing the main points of nursing care in patients with VAP diagnosis: oral care, feeding positioning, ventilator maintenance, aspiration of secretions…
- 3': Questions & answers

The reminder sessions will last 10 minutes and the PowerPoint presentation will be shortened to 7 slides:

- 2': Epidemiology of VAP and COVID-19.
- 3': Risk factors and possible complications of VAP.
- 3': Latest update stressing the main points of nursing care in patients with VAP diagnosis: oral care, feeding positioning, ventilator maintenance, aspiration of secretions…
- 2': Questions & answers

All the information displayed in the slides will be supported with bibliographic references.

The informative sessions will take place in a meeting room close to ICU 8 where all the Covid-19 preventive measurements can be applied with a maximum of 40 attendants per session.

5.7. Statistical analysis

Data will be collected and treated with the Statistical Package for the Social Sciences (SPSS) Version 25.

Descriptive and inferential statistical techniques will be used to describe and synthesize the data. The demographic variables will be analysed with frequencies, percentages, ranges, means and standard deviations.

Different tests will be used; Kolmogorov-Smirnov test for the normality and T-test, U Mann-Whitney, ANOVA and Chi Square for comparing and examining the relationship of the variables and VAP-related complications, VAP-associated mortality and ICU length of stay in a COVID ICU.

The value for accepting the statistical significance will be $p \leq .05$.

5.8. Ethical aspects

The study will be performed with the approval of the Research Ethics Committee of the Principality of Asturias.

The study will be conducted in accordance to confidentiality and protection of data present in the Spanish Law "Organic Law 3/2018, of December 5, on Protection of Personal Data and guarantee of digital rights".

The data of every participant, both patients and nurses will remain anonymous.

The researcher will follow the ethical principles of beneficence and benevolence. No one will be harmed during the development of this study.

No economic compensation will be obtained in the development of this study.

6. RESOURCES AND TIMEFRAME

6.1 Resources

6.1.1 Human resources

Besides the nurses which participation will be voluntary, the researcher along with a co-worker will be in charge of all the aspects of the study, from spreading and collecting the sheets to performing the statistical analysis and publication of the results.

6.1.2. Material resources

- **Preparing research proposal and literature review**
  -Laptop with internet access
  -Access to University VPN
  -Microsoft Word software
  -PowerPoint software
- **Field work**
  -500 pieces of A4 size blank paper
  -A printer
  -A folder A4-sized
  -20 black pens
  -Packet of 1000 staples
  -Stapler
  -USB
- **Data analysis**
  -SPSS software

6.1.3 Economical resources

- **Elaboration of project and field work**

-Laptop with internet access……...…Provided by researcher

-Pack of 500 pieces of A4 blank paper……3.50€

-A4-sized folder……...1.50€

-20 black pens…….6.65€

-Packet of 1000 staples……3.24€

-Stapler…….5.82€

-USB……5.99€

-TOTAL…….26.70€

❖ **Data analysis**

-IBM® SPSS® Statistics software license

(one month) …….87.81€

-TOTAL……...87.81€

❖ **Publications**

-Publication in online journals……Free

-Participation in national/international congress…….540€

-Entry fee……150€

-Transport……...200€

-Accommodation……..…….70€

-Food and beverage……120€

❖ **TOTAL ESTIMATED BUDGET……654.51€**

6.2 Timeframe

Activities	2022																			
	January (in weeks)				February (in weeks)				March (in weeks)				April (in weeks)				May (in weeks)			
	1	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*
Preparing research proposal and gathering authorizations																				
Preparing questionnaire and PowerPoint presentation																				
Meeting with supervisors and nurse staff (informed consent)																				
Initial session																				
Reminder session																				
Data collection sheet completion and gathering																				

Activities	**2022**															
	June (in weeks)				**July (in weeks)**				**August (in weeks)**				**September (in weeks)**			
	1	***2***	***3***	***4***	***1***	***2***	***3***	***4***	***1***	***2***	***3***	***4***	***1***	***2***	***3***	***4***
Data examination and statistical analysis																
Evaluation of results																
Discussion and conclusions																
Reporting session at HUCA																
Publication in online journal																
Participation in a congress																

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8. APPENDICES

Appendix 1. Ethical Committee application form

Oviedo, a 2 de enero de 2022

De: Raquel Rodríguez y Ricardo Baldonedo. Facultad de Medicina y Ciencias de la Salud. Universidad de Oviedo

A: Comité Ético Regional de Investigación.

Asunto: *Proyecto de investigación en Trabajo fin de Máster, Departamento de Medicina, Universidad de Oviedo.*

Adjunto enviamos para su evaluación el proyecto titulado: Nursing care in ventilatorassociated pneumonia and COVID-19: an informative intervention among nurses. Dicho proyecto corresponde a la investigación de un TFM dentro del programa de Master Erasmus Mundus en Enfermería de Urgencias y Cuidados Críticos por la Universidad de Oviedo de la estudiante Raquel Rodríguez Fernández, tutorizada por el Prof. Dr. Ricardo Baldonedo Cernuda. Dada la naturaleza observacional del estudio, no es necesaria una cobertura de seguros adicional a la requerida en la práctica clínica normal. El estudio carece de financiación y de promotor externo a la Universidad de Oviedo.

Se adjunta:

- Memoria del proyecto.

Un saludo.

Fdo. Prof. Dr. Ricardo Baldonedo Cernuda (Tutor)

Contacto: Ricardo Baldonedo: baldonedo@telecable.es Tfno: 686960853

Appendix 2. Informed consent (English version)

INFORMED CONSENT

The study I am willing to participate in, consists of the following:

• The main objective of this study is to determine the impact that an informative intervention among nurses has on different variables related to patients in ICUs number 8 and 9 at HUCA.

• The variables will be collected by the nurses via a data collection sheet supplied by the researcher.

•The study has been approved by the Ethical Committee

• All information collected will be kept anonymous and confidential.

I……. (Name)

□ I have spoken with Raquel Rodríguez (Investigador´s name) and has explained me the whole process.

□ I have received information about the study and have been able to ask questions about it, in such a way that I judge that I have received enough information about it.

□ I agree to participate in the study.

Participant´s Signature	Investigator's signature
----------	----------
Date: / /	Date: / /

Appendix 3. Informed consent (Spanish version)

CONSENTIMIENTO INFORMADO

El estudio en que estoy autorizando a participar consiste en lo siguiente:

• El objetivo principal de este estudio es el de determinar el impacto que tiene una intervención informativa entre el personal de enfermería sobre diferentes variables relacionadas con pacientes ingresados en las UCIs 8 y 9 en el HUCA.

• Las variables serán recogidas por el personal de enfermería a través de una hoja de recogida de datos aportada por la investigadora.

• El estudio ha sido autorizado por el Comité de Ética.

• Toda la información obtenida será confidencial y permanecerá en el anonimato.

Yo……. (Nombre)

 He hablado con Raquel Rodríguez (Nombre de la investigadora) y me ha explicado todo el proceso.

 He recibido información sobre el estudio y he sido capaz de realizar preguntas sobre el mismo de manera que entiendo que he recibido suficiente información sobre el asunto.

 Acepto participar en este estudio.

Firma del participante	Firma del investigador/a
---	---
Fecha: / /	Fecha: / /

Appendix 4. Data collection sheet (English version)

Date: …/…./…….

About nurses:

Signed informed consent: Yes ☐ No ☐

Gender: Male ☐ Female ☐

Age (years): ……..

Academic training: 3 years ☐ 4 years ☐

Job experience in nursing (years): ……

Academic training in critical care: Profile ☐ Master ☐ Other ☐

Job experience in critical care (years): ……

Current position: Permanent ☐ Temporary ☐

About patients:

Gender: Male ☐ Female ☐

Age (years): ……..

Toxic habits: Smoking ☐ Alcohol ☐ Other drugs ☐

Chronic diseases: Diabetes ☐ HTA ☐ Heart disease ☐
COPD/Asthma ☐ Cancer ☐ CKD ☐ Others…….

Initial diagnosis:…… Days since admission:……..

ICU stay (days):……. Ventilator days:……..

Nutrition: Enteral feed ☐ Parenteral feed ☐ Both ☐

Complications: Septic shock ☐ ARDS ☐ Atelectasis ☐

MDR colonization ☐ Pulmonary abscess ☐ Renal insufficiency ☐

Others:……..

Mortality during ICU stay: Yes ☐ No ☐

If so: -Number of days in ICU until death:……...

-Cause of death:……

Appendix 5. Data collection sheet (Spanish version)

Fecha: …/…./…….

Sobre personal de enfermería:

Consentimiento informado firmado: ☐Yes ☐ No

Género: Masculino ☐ Femenino ☐

Edad (años): ……..

Formación académica: 3 años (Diplomatura) ☐ 4 años (Grado) ☐

Experienci laboral como enfermero/a (años) ……

Formación académica en cuidados críticos: Profile ☐ Master ☐ Other ☐

Experiencia laboral en cuidados críticos (años): ……

Posición actual: Fijo/a ☐ Eventual ☐

Sobre los pacientes:

Género: Masculino ☐ Femenino ☐

Edad (años): ……..

Hábitos tóxicos: Tabaco ☐ Alcohol ☐ Otras drogas ☐

Enfermedades crónicas: Diabetes ☐ HTA ☐ Cardiopatía ☐
EPOC/Asma ☐ Cáncer ☐ ERC ☐ Otras…….

Diagnóstico inicial:…… Días desde el ingreso:……..

Tiempo en la UCI (días):……. Días con ventilación mecánica:……..

Nutrición: Enteral ☐ Parenteral ☐ Ambas ☐

Complicaciones: Shock séptico ☐ SDRA ☐ Atelectasia ☐

Colonización por MDR ☐ Abscesos pulmonares ☐ Insuficiencia renal ☐

Otras:……..

Mortalidad durante el ingreso en ICU: Sí☐ No☐

-Si la respuesta es sí: -Número de días hasta fallecimiento:……..

-Causa del fallecimiento:……