PREDICTORS OF OUTCOME OF NON-INVASIVE VENTILATION IN PATIENTS WITH ACUTE HYPOXEMIC RESPIRATORY FAILURE - A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"PREDICTORS OF OUTCOME OF NON-INVASIVE VENTILATION IN PATIENTS WITH ACUTE HYPOXEMIC RESPIRATORY FAILURE – A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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LIST OF ABREVIATIONS

ACPE	-	Acute cardiogenic pulmonary edema
ARDS	-	Acute respiratory distress syndrome
ARF	–	Acute respiratory failure
AHRF	-	Acute hypoxemic respiratory failure
APACHE II	–	Acute physiological and chronic health evaluation
BiPAP	–	Bilevel positive airway pressure
CAP	–	Community acquired pneumonia
COPD	–	Chronic obstructive pulmonary disease
CPAP	–	Continuous positive airway pressure
EPAP	-	Expiratory positive airway pressure
FRC	-	Functional residual capacity
GCS	-	Glassgow coma scale
ICU	-	Intensive care unit
IPAP	-	Inspiratory positive airway pressure
HFNC	–	High flow nasal cannula
LTOT	-	Long term oxygen therapy
NIV	-	Non invasive ventilation
NPPV	-	Noninvasive positive pressure ventilation
OHS	-	Obesity hypoventilation syndrome
PEEP	-	Positive end expiratory pressure
PPV	-	Positive pressure ventilation
qSOFA	-	Quick sequential organ failure assessment
SAPS II	-	Simplified acute physiological score

ABSTRACT:

PREDICTORS OF OUTCOME OF NON-INVASIVE VENTILATION IN PATIENTS WITH ACUTE HYPOXEMIC RESPIRATORY FAILURE - A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY

Background and objective: NIV (Noninvasive Ventilation) is one of the most important modality of ventilation which reduces the need for intubation and complications associated with it. However, NIV can not be used in all patients with acute respiratory failure. Hence there is a need to analyse the incidence of failure of NIV and various factors that predict the success and failure of NIV.

Methods: The patients of acute hypoxemic respiratory failure (AHRF) who received NIV were included in study and various parameters such as PaO2/FiO2 ratio, A-a O2 gradient, APACHE II score, SAPS II score, qSOFA score, CURB 65 score were analysed within first 24 hours of admission.

Results: Among 97 patients 53 had favourable outcome and 44 had unfavourable outcome, the incidence of NIV failure was 45.4%. The baseline mean PaO2/FiO2 ratio and A-a O2 gradient was 158.71 and 298.99 respectively. Among those with favourable outcome the mean values were 193.08 and 196.38 and among those with unfavourable outcome the mean values were 117.32 and 422.59 respectively. This was statistically significant. The various other predictors which were studied were APACHE II, SAPS II, CURB 65 and qSOFA scores whose baseline mean values were 17.29, 39.46, 1.83, 1.46 respectively. Among those with favourable outcome the mean values were lower i.e, 13.30, 32.32, 1.77, 1.17 and among those with unfavourable outcome the mean values were higher i.e, 20.59, 49.14, 2.43, 1.70 respectively and this was statistically significant.

Conclusion: This study concludes that one has to have a high index of suspicion of failure of NIV among patients of acute hypoxemic respiratory failure with low Pao2/Fio2 ratio, high alveolar arterial gradient (A-a O2), high APACHE II, SAPS II, CURB 65 and qSOFA scores, as they determine poor prognosis.

KEY WORDS: NIV, AHRF, ARF, PREDICTORS, APACHE II, SAPS II

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INTRODUCTION

Acute hypoxemic respiratory failure (AHRF) is a clinical condition characterized by severe hypoxemia that is refractory to supplemental oxygen (PaO2 < 60 mmHg, PaO2/FiO2 <300 mmHg). [1]

Acute respiratory failure (ARF) is a life-threatening condition caused by either impaired function of the respiratory muscle pump or lung dysfunction[1]. Respiratory failure is a clinical condition that occurs when the respiratory system fails to perform its primary function of gas exchange, resulting in PaO2 less than 60 mmHg and/or PaCO2 greater than 50 mmHg. **Type 1 respiratory failure** has a PaO2 < 60 mmHg with normal or subnormal PaCO2. **Type 2 respiratory failure** has a PaCO2 > 50 mmHg.[2] The incidence of respiratory failure is approximately 137.1 per 100,000 individuals in the United States and the mortality rate is approximately 29%-42%.

The etiology of respiratory failure can either be due to involvement of nervous system (lack of ventilatory drive or defects in neural transmission or neuromuscular diseases affecting the respiratory muscles) or due to involvement of respiratory system (thoracic cage abnormalities or airway diseases or parenchymal diseases.

Noninvasive ventilation (NIV) provides positive pressure airway support without the use of an endotracheal tube and is used as the first line of treatment for acute hypoxic respiratory failures (AHRF). The benefits of NIV include the elimination of the need for endotracheal intubation (ETI), which reduces the risk of ventilator-associated pneumonia, the duration of stay in the ICUs, and hospitalization costs. Several studies have been published on the use of NIV in AHRF over the last two decades and still there is a debate over whether NIV is appropriate in all forms of AHRF.[3]

Hence NIV cannot be used in all patients with acute respiratory failure. As a result, there is a need to identify the incidence of NIV failure as well as various prognostic indicators determining NIV success or failure.

Noninvasive ventilation (NIV) represents one of the most important advances in the field of pulmonary and critical care medicine of the last 30 years. The efficacy of NIV in appropriately selected patients with acute respiratory failure (ARF) has been widely confirmed by several randomized controlled trials and meta-analyses. Strong evidence supports the application of NIV as a first-line treatment in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and acute cardiogenic pulmonary edema (ACPE). Moreover, NIV has also been proven to be beneficial in patients with respiratory failure following solid organ transplantation and in those who are immunocompromised and to wean chronic obstructive pulmonary disease (COPD) patients from invasive ventilation[2]

The treatment of respiratory failure ranges from nasal prongs, oxygen mask , rebreathing mask , venturi mask, HFNC ,NIV to intubation based on the etiology and severity . Doshi et al[3] published a randomized noninferiority trial of 204 subjects that compared HFNC with NIV and found HFNC to be noninferior for the treatment
of acute respiratory failure.

While NIV also has its own problems such as difficulties in patient ventilator synchrony, mask tolerance, humidification, air leaks, pressure difficulties.

Use of NIV in COPD has become a standard of care setting[4,5]Two recent meta-analyses did not find any strong evidence to support the role of NIV in AHRF and acute lung injury/acute respiratory distress syndrome (ALI/ARDS)[6,7].However, in a few randomized

controlled trials of NIV in AHRF patients of pneumonia in immunocompromised hosts and in patients of AHRF post lung-resection surgery, NIV was found to reduce the need for intubation and even mortality.[8–10] In AHRF due to cardiogenic pulmonary edema, use of NIV has been shown to reduce mortality in meta-analysis. [11]

OBJECTIVES :

1) To find out the incidence of failure of NIV in patients with acute hypoxemic respiratory failure
2) To compare the various factors associated with NIV success and NIV failure

REVIEW OF LITERATURE

Epidemiology of Noninvasive Ventilation

First surveys, conducted in 1998, assessed NIV use and availability in 268 acute care hospitals in the United Kingdom and discovered that, at the time, NIV was only available in half of the hospitals surveyed (particularly in intensive care units (ICUs)) and, when available, were underutilized (used by more than 60 patients per year in only 7% of hospitals).[12,13.]

Though much progress was seen in modifying equipment still use of NIV was not well established till last two decades. A survey in Europe done in 2010 suggested an overall higher utilisation rate of NIV especially among COPD patients and the utilization was more by pulmonologists compared to other physicians (52.9% vs 34.3%).Also in this study it was observed that pulmonologists used more NIV compared to intensivists among all causes of respiratory failure 18.7% vs 7.2% in ACPE , 19.1% vs 6,2% in hypoxemic respiratory failure , 14.4% vs 8.5% when used for weaning [14]

However there was geographical variation in use of NIV in acute respiratory failure which was demonstrated by a study done by Devlin et al in 2007 which suggested that North American clinicians were less likely to utilise NIV compared to European physicians [13]

A study in 2009 among North American respiratory therapists and physicians confirms that factors influencing the use of NIV were barriers in using this technique such as familiarity among physicians, availability of equipment in emergency department, the expenses and the availability of respiratory therapist [15,16]

EVOLUTION OF MECHANICAL VENTILATION

Negative pressure ventilation was the initial mode used for ventilation by using body ventilators such as tanks or cuirasses[17].

Slowly positive pressure ventilators were developed, they only provide volume targeted mode of ventilation.

Later in the 1990s there was evolution into blower driven continuous positive airway pressure (CPAP) devices and Bi level positive pressure (BiPAP) devices.[18] . From then devices have further evolved to have more flexibility in gas delivery and leak compensation abilities and advanced trigger mechanisms.

Negative pressure ventilation:

From 1800 till around 1930 the main device used for ventilation was negative pressure ventilation in form of tanks and cuirasses [19]

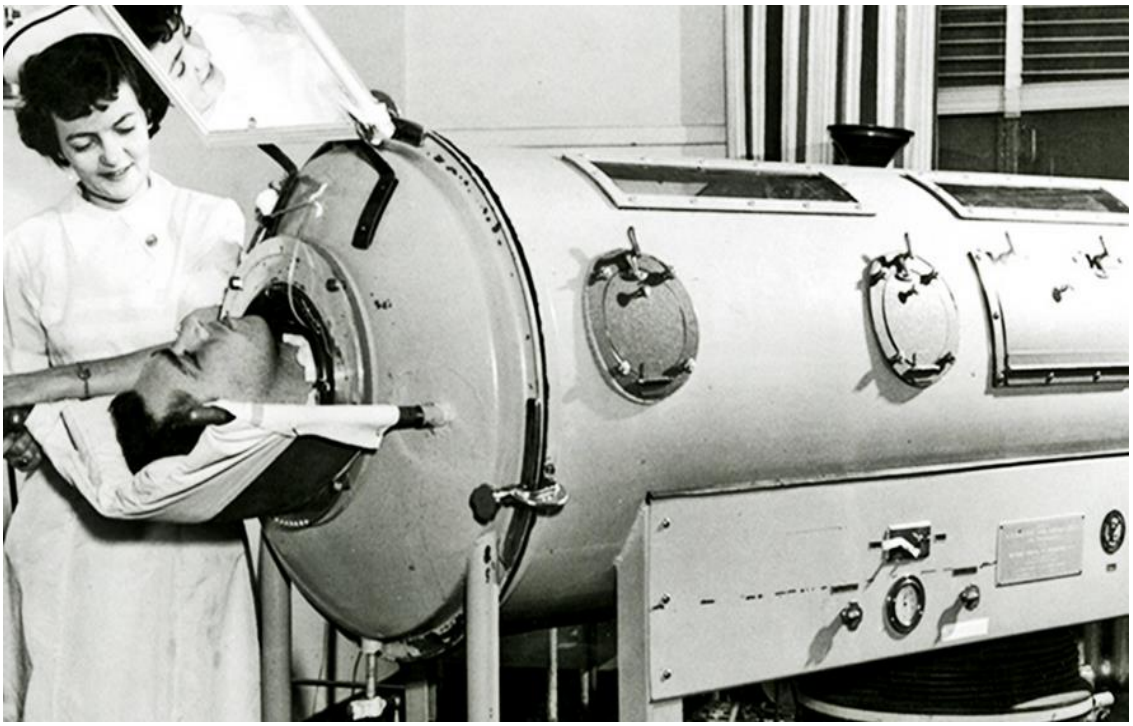


Figure 1: Iron tank device

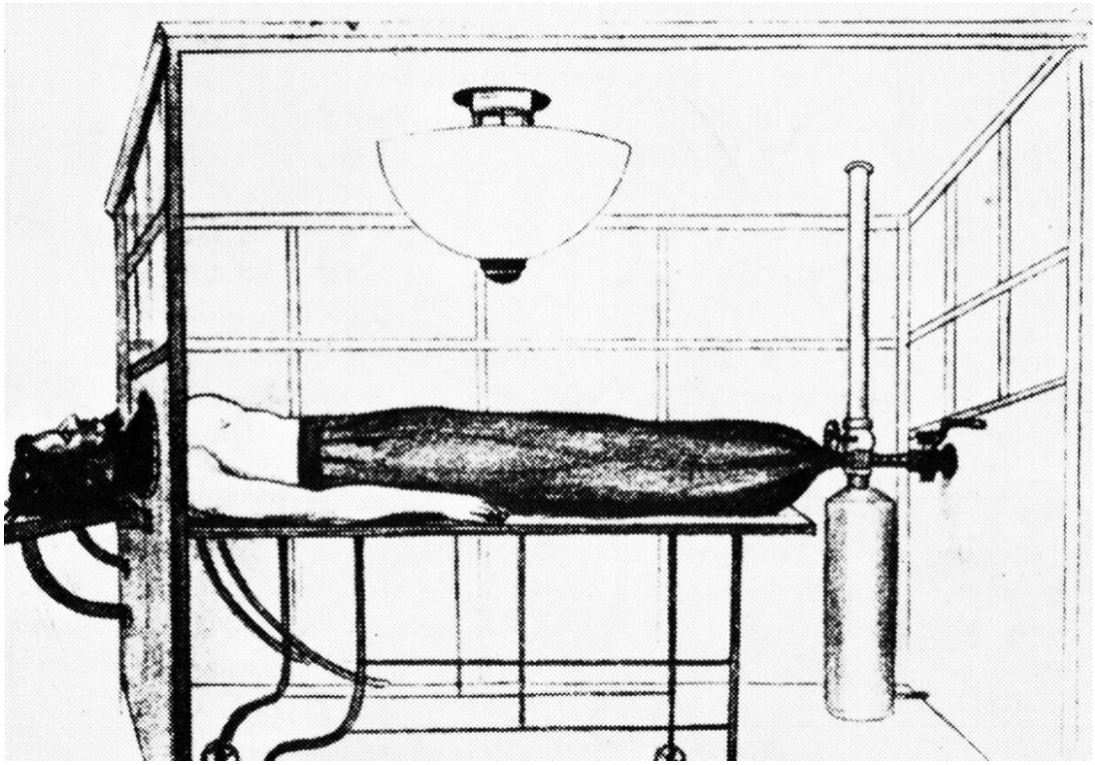


Figure 2 : Negative pressure operating chamber

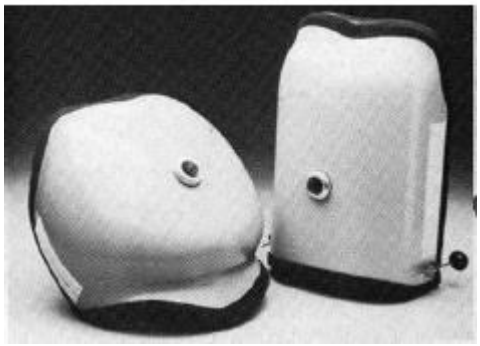


Figure 3: Chest cuirass

Positive pressure ventilation:

First PPV device was as long back as 1780s it was a bag and mask manual ventilator [19]

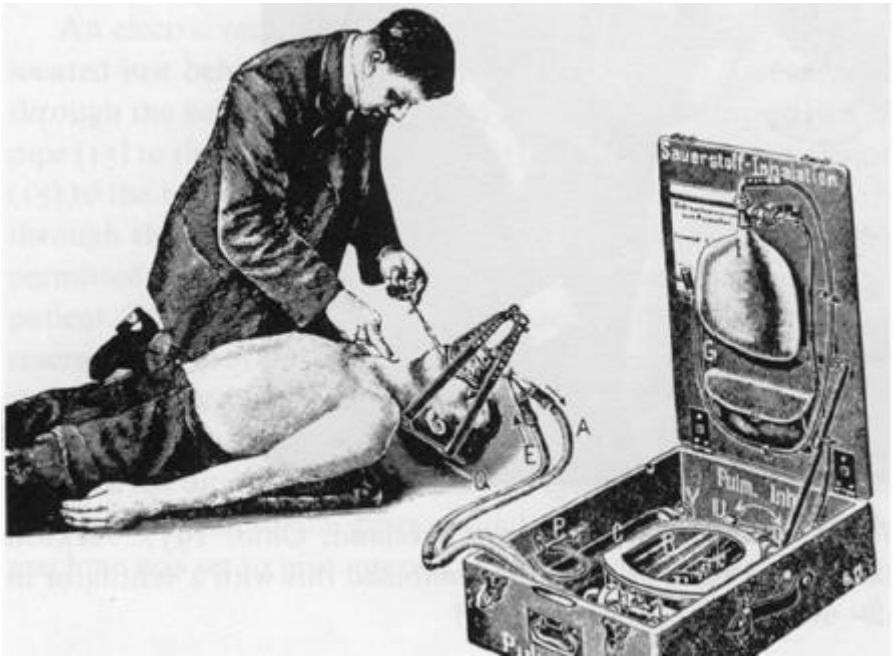


Figure 4: Manual bag and mask ventilator

In 1911 there was development of dragon pulmotor and Green and

Janeway in 1911 developed rhythmic inflation apparatus [19]

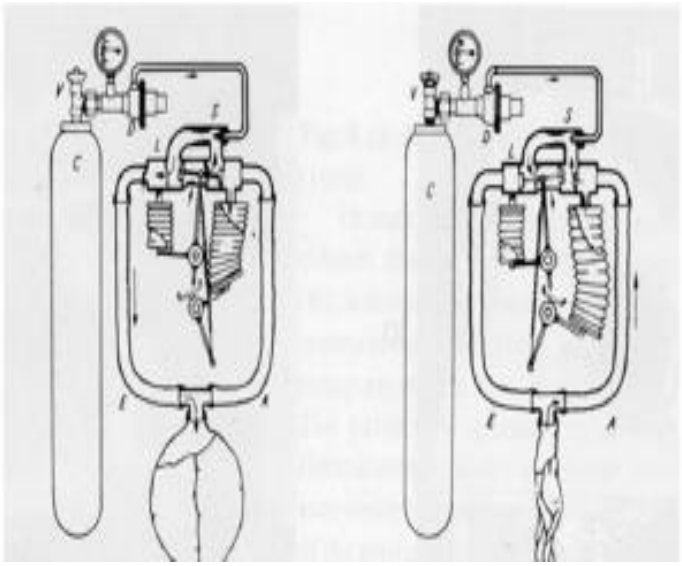


Figure 5: Dragon pulmotor

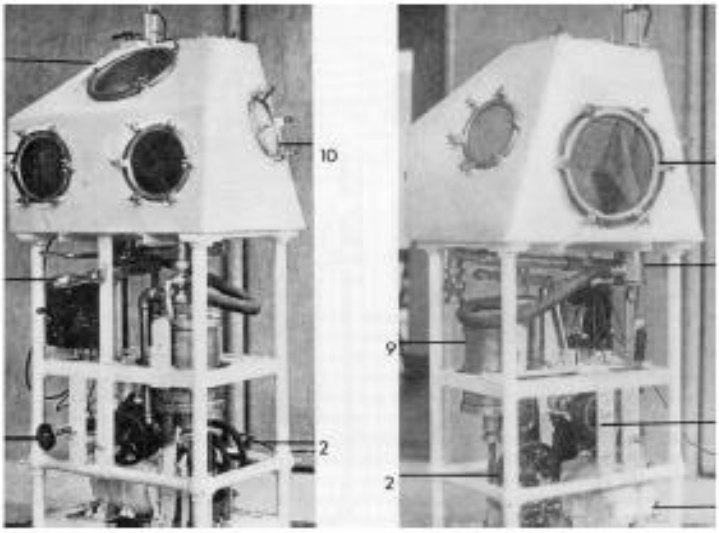


Figure 6: Rhythmic inflation apparatus.

Most popular PPV devices in 1960s and 1970s were Bennett TV and Bird mark ventilators [19]

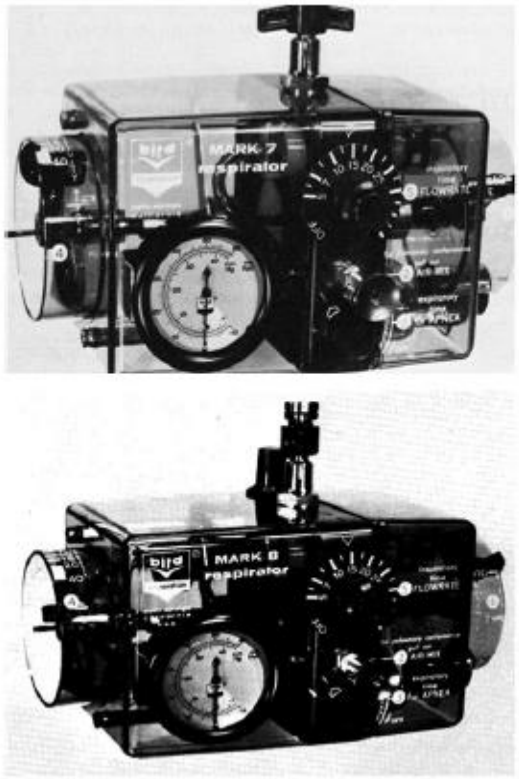


Figure 7: Bird mark ventilator

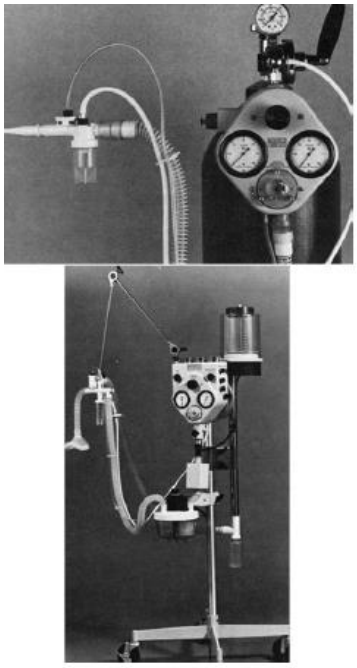


Figure 8: Bennett TV ventilator

But however all these provided only volume controlled ventilation.

From 1990s to present: Devices have further evolved to have more flexibility in gas delivery, leak compensation abilities and have advanced trigger mechanisms.

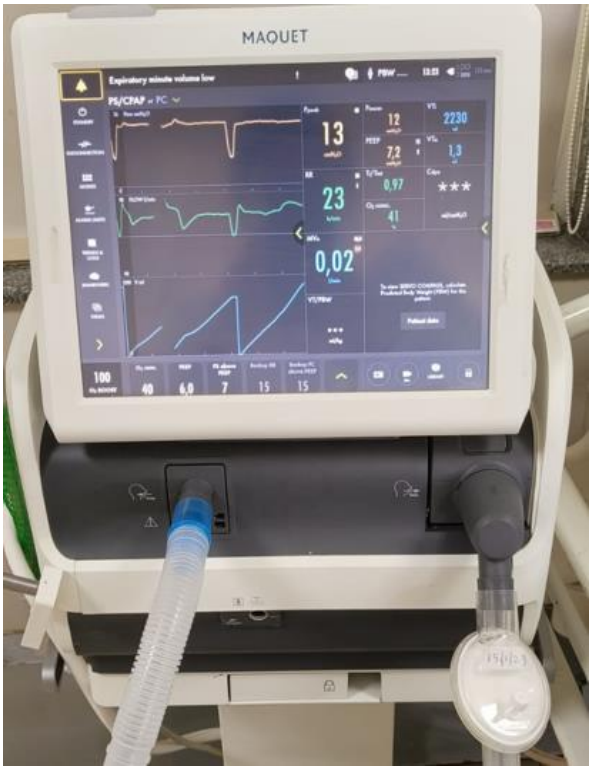


Figure 9: Advanced ICU ventilator

Table 1: Timeline of evolution of ventilators: [19]

Timeline	**Features**
1800 to early 20th century	Negative pressure ventilation
1900s to 1970s (first generation ventilators)	Volume controlled ventilation without patient triggering
1970s to 1980s (second generation ventilators)	Patient triggered ventilation
1980s to 1990s (third generation ventilators)	Development of a microprocessor control
1990s to present (fourth generation ventilators)	Volume targeted modes, pressure targeted modes, hybrid modes , assist and control modes and plethora of new modes

INDICATIONS OF NIV [33]

A) Established efficacy (for most patients, multiple studies)

- Chronic obstructive pulmonary disease (COPD) exacerbations
- Cardiogenic pulmonary edema (CPE)

B) Efficacy in selected patients (effective in subgroups or experience limited)

- Asthma
- Post-extubation; following discontinuation of mechanical ventilation (COPD and hypercapnia)
- Community acquired pneumonia (and COPD)
- Immunocompromised state and infiltrates (known cause of infiltrates)

  Solid organ transplants

  Febrile neutropenic patients
- Postoperative respiratory distress and respiratory failure

  Atelectasis

  Postoperative lung resection

- Rib fractures

Trauma with nonpenetrating chest injury; flail chest

Decompensated obstructive sleep apnea/corpulmonale

C) Efficacy promising or limited (limited reports)

- Acute respiratory distress syndrome (ARDS)
- Do not intubate status
- Cystic fibrosis
- Interstitial lung disease
- Neuromuscular respiratory failure (better in chronic than acute respiratory failure)

Kyphoscoliosis

Muscular dystrophy

- Severe acute respiratory distress syndrome (SARS)
- Mild Pneumocystis jiroveci pneumonia

CONTRAINDICATIONS OF NIV [20]

A) Absolute contraindications

- Coma
- Cardiac arrest
- Respiratory arrest
- Conditions requiring immediate intubation

B) Relative contraindications

- Cardiac instability
- Gastrointestinal bleeding
- Upper airway obstruction
- Decreased sensorium
- Persistent secretions
- Status epilepticus

Cardiopulmonary Function when on NIV

Normally the interstitial and intrapulmonary pressure remain positive during inspiration and returns to normal in expiration however intrapulmonary pressure remains positive even in expiration when PEEP is applied. Hence when positive pressure is applied it leads to changes in the patients physiological effects (as described in table 2) [21,22,.23]

Table 2: Comparing physiological differences during spontaneous breathing vs noninvasive ventilation

Spontaneous breathing	**Noninvasive ventilation**
↓ Intrathoracic pressure	↑↑ Intrathoracic pressure
↓ Blood pressure during inspiration	↓↓ Blood pressure during inspiration
Peripheral vascular resistance (no effect)	↑ Peripheral vascular resistance
↑ Venous return (to right atrium)	↓↓ Venous return (to right atrium)
↑ Right atrium preload	↓ Right atrium preload
↑ Right Ventricle afterload	↑Right ventricle afterload
↑ Right ventricle cardiac output	↓Right ventricle cardiac output
↑ Left ventricle afterload	↓Left ventricle afterload
↓ Left ventricle cardiac output	↑Left ventricle cardiac output

Patients of ACPE benefit from PPV and improve when put on positive pressure ventilation as there is reduction of left ventricle after load hence it significantly improves dyspnoea of patients with left ventricle failure.[24]

Table 3: Effect of NIV on cardiovascular system:

Right heart	**Left heart**
↓Venous return	↓ Left ventricle preload
↓Right atrial preload	↑Raised stroke volume
↑Right ventricle afterload	↓ Oxygen consumption
	↑ Cardiac output
	↓ Left ventricle afterload

[23 24].

Implications of NIV in Pulmonary and Cardiac Diseases:

Pulmonary diseases:

Pulmonary diseases mainly affect the lung elasticity and volume, resistance in the airflow, work of breathing, and right ventricle impedance.[24]

Asthma and COPD:

In patients of asthma and COPD there is raised airway resistance leading to prolonged expiration which opposes deflation of alveoli leading to dynamic hyperinflation and an intrinsic PEEP. This intrinsic PEEP is the minimum pressure the muscles of inspiration have to overcome to start an inspiratory gas flow and hence these patients need higher respiratory effort to maintain alveolar ventilation. Sometimes excessive expiratory effort combined with increased work of breathing can result in respiratory arrest and sudden death.[24] .

Whenever PPV is applied in such patients with severe airflow obstruction there might be further increase in the dynamic hyperinflation and air trapping. Hence the ventilator settings in such patients must be aimed to deliver a low tidal volume with a long expiratory time. The patient has to be put on assisted modes as it reduces the threshold work required for inspiration and hence reduces the inspiratory effort and increases minute volume.[25]

Normally respiration requires only around 1-2% of total oxygen consumption but however the requirement increases to as high as 20% in patients with acute respiratory failure. Such patients benefit from positive pressure mechanical ventilation as it reduces the work of breathing by countering the intrinsic PEEP and decreasing the threshold for inspiration and hence lowering oxygen consumption.

In general work of breathing can be reduced in most patients when a PEEP of 5 cm H2O and inspiratory pressure support of 15 cm H2O is applied as the inspiratory effort comes back to normal.[25]

Pulmonary hypertension:

Pulmonary hypertension is seen in most of the chronic respiratory diseases as they cause significant haemodynamic compromise secondary to persistent hyperinflation. This can further lead to right ventricle ischemia and corpulmonale.

Pulmonary hypertension causes dilatation of the right ventricle and progresses to right ventricle failure, which further decreases pulmonary flow and left ventricle preload finally leading to systemic hypotension [23].

Application of NIV in patients with pulmonary hypertension counteracts the hypoxic pulmonary vasoconstriction and hence decreases the pulmonary vasomotor tone.

ARDS:

ARDS is characterised by increased lung elastance and alveolar collapse, raised metabolic rate, increased work of breathing, excessive airflow limitation and pulmonary hypertension (as the mediators of inflammation cause pulmonary vasoconstriction and systemic hypotension).

In these patients PPV with higher inspiratory pressure is required for alveolar ventilation and parallelly high PEEP levels are used to help in alveolar recruitment by preventing airway collapse.[23]

Cardiac diseases:

In patients of hypovolemia, restrictive cardiomyopathy, tamponade, or valvular stenosis the cardiac output is dependent on venous return and when such patients are on PPV there is further reduction in cardiac output as PPV reduces the venous return

Diseases with reduced ventricular compliance:

But however in cardiac diseases with reduced ventricular compliance such as coronary disease, heart disease with hypertrophy, heart disease with fibrosis there is increase in cardiac output as NIV increases the intrathoracic pressure and reduces the left ventricle afterload. [24]

Acute cardiogenic pulmonary edema:

In patients with left ventricle dysfunction with ACPE application of PEEP increases the cardiac output by reducing left ventricle afterload further in these patients PEEP also helps to maintain lung volume and alveolar patency.[24]

Classification of Ventilators

1. Volume controlled home ventilators: The first devices to deliver PPV were volume-controlled ventilators, which were primarily utilised for domiciliary care. Their ability to apply PPV is largely constrained as they have huge problems with accounting for leaks. As a result, there use is currently limited to home-based patients of neuromuscular diseases, and they are also useful in providing invasive support for tracheostomy patients who are ventilator dependent.[26].

2. Bilevel ventilators: This name "bi-level ventilators" comes from their ability to support spontaneous breathing with two different pressures: an inspiratory positive airway pressure (IPAP) and a expiratory positive airway pressure (EPAP), also known as positive end-expiratory pressure (PEEP). They are the evolution of home-based continuous

positive airway pressure (CPAP) devices. These devices have the ability to account for air leaks.

Addition of "hybrids modes" like volume-assured pressure support ventilation (VAPS), have the ability to deliver various advanced ventilation modalities.[26 27].

3.ICU Ventilators: ICU ventilators were created to provide invasive ventilation through endotracheal or tracheostomy tube. However the conventional ICU ventilators are not able to account for leaks. Hence in order to effectively help acute patients a new generation of ICU ventilators has been created. These ventilators have the ability to counter for leaks, hence they have the ability to correct of air leak-induced patient-ventilator asynchrony.[28]

4.Intermediate Ventilators: These group of ventilators are made by combining the features of bilevel, ICU and volume controlled ventilators (dual-limb circuit, sophisticated alarm and monitoring systems, inner battery, both volume and pressure modes, wide setting of inspiratory and expiratory parameters). The vast majority of more recent intermediate ventilators offer "hybrid modes" of breathing, including VAPS. [26,27].

NIV vs IMV

NIV differs from invasive ventilation in two ways:

1) The system is not airtight, which increases the possibility of unintended leaks; and

2)There is a resistance offered by the upper airways, hence the ventilator and lung cannot be assumed as single compartment

Due to this tidal volume delivered is reduced. Hence when a patient is on NIV increasing the delivered volume need not necessarily increase the effective ventilation of lungs [29]

Patient Ventilator Synchrony

The ventilator and the respiratory muscles of patients are two different ventilatory pumps which work in tandem in delivering mechanical ventilation. These two pumps may complement one other, but they are capable of interacting in a variety of ways, many of which will exacerbate rather than resolve the issues. As a result, during NIV, patient-ventilator asynchrony is extremely common. [30,31]

Asynchronies can happen on two different levels:

1) During inspiratory triggering, when the ventilators triggering and the patients inspiratory effort mismatch (for example, when the patient's inspiratory effort is ineffective or when the ventilator triggers twice or when the patient triggers automatically); or

2) During switch from inspiration to expiration, when the ventilators switch does not coincide with the end of the patient effort (premature or delayed cycling) [31]

TRIGGERING MODES :

Spontaneous Mode

In this mode patient controls the start and stop of inspiration as inspiration starts only when the ventilator is triggered by patients efforts. The patients effort modifies flow in circuit and and subsequently the pressure changes from lower EPAP level to higher IPAP level during inspiration. This pressure of IPAP is maintained as long as there is minimal preset inspiratory flow. When the pressure comes back to EPAP there is switch from inspiration to expiration. The key factors that affect the patients effort of breathing are trigger sensitivity, peak flow, and the degree of ventilatory assistance (IPAP - EPAP). In this mode patient has control over cycle length, depth, and flow profile since each cycle is

stopped by a flow criterion rather than by volume or time. Additionally this mode is known as pressure support ventilation (PSV) [33].

Assist Mode

Here onset of inspiration is controlled by the patient but however the length of inspiration is controlled by operator. A targeted pressure or volume, inspiratory-expiratory (I:E) ratio, inspiratory duration, and inspiratory trigger sensitivity are all selected by the clinician in this mode. [33]

Assist-Control Mode

This is similar to assist mode where the start of inspiration is in patients control and the duration of inspiration is under operators control in addition to that this mode has an added advantage of setting the backup respiratory rate. Hence if the respiratory rate of the patient decreases significantly or when the patient goes into apnoea the device switches to control mode and delivers breaths at a preset backup respiratory rate. [33]

Then, while permitting a backup rate, this mode seeks to provide a minimum minute ventilation while still allowing the patient to activate the ventilator. The clinician must choose an inspiratory trigger sensitivity, backup rate, intended pressure or volume, expiratory pressure, and inspiratory to expiratory (I:E) ratio in this mode.

Control Mode

There is a pre-set automated cycle based on time. In the control mode the ventilator by itself controls the start and stop of inspiration and the respiratory rate. The physician must choose an inspiratory to expiratory ratio, a target volume or pressure, and a fixed respiratory rate in this mode. In this mode, the ventilator is designed to handle entire work of breathing. [33]

MODES OF VENTILATION:

Volume-Targeted Mode

This mode is also known as flow limited mode where a fixed volume is delivered in a predetermined time irrespective of whatever the pressure required to deliver it. Any inspiratory effort will only decrease the airway pressure but will not alter the delivered volumes or flows. The benefit of this mode is the rigorous delivery, of the preset volume when there are no leaks, regardless of patients compliance and resistance. A drawback in this mode is that when there is a leak, it is not compensated as there is no rise in flow rate, and hence the pressure created will remain lower, resulting in delivery of low volumes. [33]

Pressure-Targeted Mode

In this mode the flow is delivered by providing a preset positive pressure for a fixed period of time hence also known as pressure limited mode. When there is a significant difference between the preset target pressure and the circuit target, flow is rapid at the start of inspiration. As the pressure difference gets smaller, the flow slows down until there is no longer any driving flow, at which point the flow stops. Therefore, the volume provided to a patient is not constant and is determined by the combination of the preset pressure, the patients effort during inspiration, the resistance and compliance of the patient, and the inspiratory time. The ability of this mode to account for minor to moderate leakage is a key benefit. In this mode inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) can be adjusted independently to increase alveolar ventilation and maintain patency of upper airway. This mode provides better patient-ventilator synchrony. [33]

Volume Targeting Pressure Mode (HYBRID MODE)

The fact that pressure ventilation cannot ensure a patients tidal volume delivery is one of its limitations. Some bi-level ventilators have a feature called volume targeting that enables to overcome this restriction. This mode has benefits of both pressure and volume modes as it adjusts the pressure support level within the predetermined range to provide a tidal volume as close to the set target[32]

NCPAP INTERFACES: [33]

Oronasal masks:

Advantages:

- Few air leaks
- Provide a stable airway pressure
- Easy to use and cheaper

Disadvantages:

- Lesions over nasal bridge

Full face mask:

Advantages:

- Easy fitting
- Minimal air leak
- Provide a stable airway pressure
- Less noisy

Disadvantages:

- Facial lesions
- Claustrophobia

- Expensive
- Irritation to eyes

Helmet mask:

Advantages:

- Scarce air leaks
- No lesions of skin or nose

Disadvantages:

- Very high flow is needed
- Noisy
- Carbon dioxide rebreathing
- Less stable airway pressure
- Lesions over axilla and neck
- Expensive
- Very high dead space

COMPLICATIONS OF NIV DUE TO NCPAP INTERFACES [33]

- Leaks
- Pressure sores and ulcers
- Discomfort
- Claustrophobia
- Aspiration
- Soft skin tissue damage
- Mucus plugging
- Conjunctivitis

- Keratitis
- Eye irritation
- Oral and nasal dryness
- Nasal congestion
- Vomiting
- Gastric distension
- Aerophagia
- Difficult speaking
- Difficult eating
- Difficult hearing
- Noise
- Aellrgy

NIV in COPD:

Noninvasive ventilation in these group of cases leads to,

1. Reverting hypoventilation

2. Unloading of respiratory muscles

3. Resetting the respiratory center [36]

4. Cardiovascular effects

Correction of Hypoventilation

PPV in pressure support mode can enhance alveolar ventilation in hypercapnic COPD patients by increasing tidal volume and decreasing respiratory rate. [34].

Unloading of respiratory muscles

The intrinsic PEEP of these patients is countered by applying the external positive PEEP and this inspiratory pressure leads to unloading of the respiratory muscles.[35]

Acute COPD Exacerbations

The increase in airway resistance leads to increased work of breathing in cases of acute COPD exacerbations that might end up in acute respiratory failure (ARF).

The respiratory muscles are less effective as a result of lung hyperinflation, and they run the danger of failing and becoming exhausted if the underlying disease does not improve quickly.

PaCO2 rises due to the inability of respiratory muscles to maintain adequate alveolar ventilation. The level of consciousness is typically diminished when PaCO2 is elevated severely and for an extended period of time.

The aim of medical line of treatment when the precipitating cause of acute respiratory failure is reversible is to maximise lung function and reverse the condition, and the the goal of PPV is to buy time for the treatment of the cause and to reduce the effort of breathing and hence to reverse the hypoxemia and acidosis [37]

NIV IN ACPE:

Raised pulmonary capillary pressure and left ventricle filling pressure, and a subsequent overload of fluid in pulmonary interstitial and alveolar spaces are the defining features of acute cardiogenic pulmonary edema. [38]

Hence there is increased airway resistance, decreased lung diffusion capacity, reduced functional residual capacity, and increased intrapulmonary shunt, leading to hypoxia and raised respiratory efforts.

PPV causes decrease in venous return and preload of right ventricle and also reduces the left ventricle afterload which leads to increased myocardial contraction and cardiac output subsequently leading to recruitment of alveoli, improvement in the functional residual capacity, reduced intrapulmonary shunt and work of breathing.[39–41,42].

NIV IN ARDS:[43]

Table 4: Criteria to classify ALI and ARDS[44]

Evaluation of parameter	**ALI**	**ARDS**
Timing	Acute onset	Acute onset
Oxygenation	PaO2/FIO2 <300 mm Hg (irrespective of PEEP level)	PaO2/FIO2 <200 mm Hg (irrespective of PEEP level)
Chest x ray	Bilateral infiltrates	Bilateral infiltrates
Pulmonary capillary wedge pressure	≤18 mmHg when measured or no clinical evidence of left arterial hypertension	≤18 mmHg when measured or no clinical evidence of left arterial hypertension

Lung protection using airway pressure thresholds

High airway pressures during mechanical breathing have been linked to lung damage. One of the major side effects of positive pressure breathing is barotrauma or volutrauma. Due to the low lung compliance in patients with ARDS, significant peak inspiratory pressure is needed. The lung units with normal or high compliance could be harmed by the increase in airway pressures. Additionally, pneumomediastinum, pneumoperitoneum, pneumothorax, tension pneumothorax, and subcutaneous emphysema are also lung

ailments that can result with positive pressure breathing. (Bezzant et al.,[45] 1994; Slutsky, [46]1994).

Lung protection strategy: It is a technique to stop mechanical ventilation from injuring the lungs through pressure or volume. In order to preserve the lungs, it is generally accepted that the lowest pressures or tidal volumes should be used. According to studies, airway pressures should generally be maintained at the following levels: peak inspiratory pressure of 50 cm H2O, plateau pressure of 35 cm H2O, mean airway pressure of 30 cm H2O, and PEEP of 10 cm H2O. (Bezzant et al.,[45] 1994; Slutsky,[46] 1994). (Note: The ARDSNet suggested a plateau pressure of 30 cm H2O in 2000)

Low tidal volume and Permissive Hypercapnia:

Patients who have been on mechanical ventilator for more than 48 hours are at an increased risk for ARDS due to high airway pressure and high tidal volume [47] . Both low tidal volume and permissive hypercapnia can help to some extent to reduce these risk factors hence utilizing these strategies has the main benefit of reducing airway pressures and decreasing the risk of barotrauma. (Feihl et al., [48]1994; Hall et al.,[49] 1987).

Low Tidal Volume

Barotrauma is due to redistribution of mechanical tidal volume to lung units with high compliance. During positive pressure ventilation, the cases of COPD are susceptible to developing overdistention, air trapping, and auto-PEEP hence tidal volume has to be decreased and the peak inspiratory flow should be raised to allow for longer expiratory time for appropriate exhalation in such patients.

Low tidal volume mechanical ventilation enhances dead space ventilation but reduces alveolar ventilation. Disadvantages of low tidal volume approach include acute hypercapnia, respiratory acidosis, increased strain of breathing, dyspnoea, and atelectasis (Kallet et al.,[50]).

Permissive Hypercapnia

When volume-controlled ventilation is used, permissive hypercapnia permits the PaCO2 to climb over the upper-normal limit. The tidal volume employed in permissive hypercapnia ranges from 4 to 7 mL/kg. (Feihl et al.,[48] 1994,Hall, [49]1987; Slutsky,[46] 1994). Permissive hypercapnia can be a secure defence mechanism for ARDS patients lungs since it offers little ventilation with decreased tidal volume and pressure. (Feihl et al., 1994[48]; Hickling et al., [51]1990).

Increased pulmonary vascular resistance, CNS dysfunction, an increase in intracranial pressure, neuromuscular weakness and acidosis are the major disadvantages as a result of raised PaCO2 secondary to permissive hypercapnia. By bringing the pH back into the normal range, either through renal compensation over time or by neutralising the acid with bicarbonate or tromethamine, these problems of permissive hypercapnia may be reduced.

Decremental recruitment maneuver to determine optimal PEEP

ARDS and PEEP

Because various lung units demand diffent pressures, lung damage is a serious risk for ARDS patients. Low compliance lung units need high opening and maintaining pressures. The usual compliant lung units may become overstretched and hurt by these high airway pressures. PEEP is utilised during mechanical breathing to stop the lungs atelectatic region from repeatedly recruiting and derecruiting. PEEP also improves hypoxemia brought on by intrapulmonary shunting, improves alveolar ventilation, and decreases total lung water. PEEP has a number of negative effects when administered to ARDS patients. PEEP's main side effects include pressure- and volume-induced lung injuries because of elevated mean airway pressure (due to overdistension of alveoli).

The increased pulmonary vascular resistance, decreased left ventricular compliance, decreased venous return, decreased cardiac output, and decreased systemic oxygen delivery are all effects of PEEP because it increases the peak inspiratory pressure and transmits the combined pressure to the pleural space. Reduced cardiac output leads to renal insufficiency, decreased urine production, and increased sodium and water retention (Kallet et al., 2007[50]). The choice of an ideal PEEP is essential because of these possible difficulties.

Initial ventilator settings and FIO2 and PEEP combinations for ARDS patients were published by the Acute Respiratory Distress Syndrome Network (ARDSNet) in 2000. In order to get the ideal PEEP based on the patient's needs, consecutive PEEP levels may be titrated after initial setup and stabilisation.

Initial settings of ARDSNET for patients with ARDS [50, 52,53]

1. Volume-controlled mode
2. Assist/Control mode
3. Keep Pplat (peak plateau pressure) <30 mmH2O (reduce Vt as low as 4 ml/kg predicted body weight to reach the target Pplat)
4. Maintain SaO2 or SpO2 88% to 95%
5. Appropriate PEEP as per the FiO2/PEEP combination to be set to obtain O2 saturation > 88%

Table 5: ARDSnet FiO2/PEEP titration

FiO2(%)	30	40	50	60	70	80	90	100
PEEP (cm H2O)	5	5-8	8-10	10	10-14	14	16-18	20-24

Optimal PEEP titration

The techniques for obtaining an ideal PEEP have evolved over time. In earlier techniques, the titration parameters and endpoints were compliance, PaO2, SpO2, lung function, and FRC.

The best PEEP has recently been determined by titrating ventilation homogeneity (total ventilation distribution) using electrical impedance tomography [50,52,53]. A lung recruitment procedure was performed in recent research prior to PEEP titration. The best PEEP for ARDS patients has been identified using both incremental and decremental lung recruitment approaches.

Contraindications of recruitment maneuvers:

According to Meade et al. [54], patients with the severe pulmonary edema and those who are at most risk of passing away from refractory hypoxemia of ALI or ARDS are the ones who benefit from recruitment manoeuvres.

Routine recruitment manoeuvres should not be used in unselected individuals with ALI as only around 10 to 15% of patients with ALI/ARDS die due to refractory hypoxemia as the primary cause of mortality (the majority of deaths are brought on by non pulmonary organ failure). (Stapleton, [55]2008).

Extremely high peak airway pressure, plateau pressure, and PEEP are all results of recruitment techniques. Patients who already have barotraumas, have poor hemodynamic condition, or have blebs or bullae on a chest radiograph should not undergo these techniques. The use of recruiting techniques should be avoided in the presence of elevated intracranial pressure.

Prone positioning

Is carried out by tilting the patient's bed between 15 and 30 degrees in a Trendelenberg position, the bulk of the lower lobes are in a higher position in the prone posture.

This position improves ventilation distribution, lowers the gradient of transpulmonary pressure across the lungs, and lowers the opening pressure of the lower lobes.

Patients with substantial impairments in gas exchange can benefit from this physiological impact. Candidates for prone placement are patients who need a PEEP of >10 cm H2O and a FIO2 of greater than or equal to 60% to maintain supine oxygen saturation of 90%.

NIV in ASTHMA: [33]

- Increases bronchodilation by maintaining airway patency and reducing airway resistance.
- Increases functional residual capacity.
- Reduces work of breathing

NIV IN CAP:

There aren't many randomised controlled trials examining the effectiveness of NIV in treating pneumonia. Most people have taken into account extremely diverse patient populations with a range of ARF causes, including pneumonia to some extent [56] .

Among 105 cases of acute respiratory failure Ferrer et al.[57] found that BiPAP (Bilevel positive airway pressure) reduced the need for intubation and produced a rapid improvement of dyspnoea and oxygenation in patients receiving NIV.

"De novo" group includes patients of pneumonia without a history of cardiac or pulmonary disease. The "Comorbidities" group includes pneumonia cases with associated chronic disorders (such as COPD). "Immunodepressed" group, are the cases of pneumonia with weakened immune systems as a result of hematologic malignancies or being transplant recipients [58,59].

In carefully chosen group of patients with pneumonia, NIV can be administered with caution, this is particularly true for patients of comorbidities group and

immunodepressed group. In patients with severe CAP, predicting the failure of noninvasive ventilation is helpful to lower the risks of delayed intubation.

NIV IN BRONCHIECTASIS

PPV causes alveolar recruitment in bronchiectasis, increasing the total number of functional units and hence expands dependent lung regions where there is very little or no airway opening during inspiration.

By increasing functional residual capacity and residual volume, PPV enhances the respiratory mechanics. [60].

Positive expiratory pressure (PEP) and oscillatory PEP devices (such as flutter device) are just a couple of the positive pressure treatments that are available, and few controlled trials have shown a therapeutic advantage in bronchiectasis.[60],[61] .

NIV IN OHS (Obesity Hypoventilation Syndrome):

The most significant justification for NIV, particularly in individuals who are extremely obese, is hypercapnic respiratory failure. Carillo et al. [62] conducted a study and concluded that NIV was successful in avoiding intubation in patients of decompensated OHS and it also reduced the in hospital mortality in these patients.

NIV IN DISEASES OF CHEST WALL:

Mechanical ventilation has a minimal but consistent therapeutic advantage for patients with chest wall and neuromuscular disease. PPV relieves symptoms of persistent hypoventilation[62]. Lemyze et al. [63], concluded that NIV was superior than LTOT among kyphoscoliosis patients as there was greater reduction in PaCO2 (reduced by 21%) and better one year survival among NIV group compared to LTOT group (100% vs 66%)

NIV IN ATELECTASIS:

The use of CPAP enhances oxygenation and encourages lung recruitment while having no negative hemodynamic effects or pleural leakage. NIMV (Noninvasive mechanical ventilation) reduces the need for tracheal intubation and hospital mortality during cardiac or lung resection surgery [64].

Patients who were prophylactically put on CPAP with pressures of 10 cmH2O for 12–24 hours following thoracoabdominal surgery had considerably higher oxygenation rates, lesser hospital and ICU stay.[65]

NIV IN BLUNT CHEST TRAUMA:

In patients of blunt trauma of the chest the noninvasive ventilation is to be considered only when the patient has no neurological impairment and is haemodynamically stable and when the patient is not in respiratory distress as the advantage of noninvasive ventilation in these patients is seen in early stages before respiratory failure.

Hence there is no benefit of noninvasive ventilation in prevention of intubation in patients with respiratory distress. Early management of pain with appropriate analgesia is important adjunct to the use of noninvasive ventilation in chest trauma. [33]

PREDICTORS OF NIV FAILURE

NIV needs careful monitoring to detect failure at the earliest, different studies have evaluated the predictors of NIV failure which are as follows:[66],[67]

- High severity scores (APACHE II, SAPS II, SOFA scores)
- Older age
- Failure to improve after 1 hour on NIV

• Multiorgan involvement

• Premorbid status

• Mean pH < 7.25, mean PaCO2≥75 mmHg after 2 hours of NIV initiation, in patients with hypercapnic failure.

• Difficult to identify the etiology of acute respiratory failure or when pneumonia / ARDS is the cause.

• PaO2/ FiO2 < 150 mmHg

• Higher Tidal volume generation

Failure of NIV is an important independent risk factor for mortality, hence there has to be a careful selection of patients before initiating non-invasive ventilation.[68]

Table 6: Clinical criteria required before weaning is attempted [69]

	Measure	**Character**
1	Aretrial pH	≥7.35
2	Oxygen saturation	>90%
3	Respiratory rate	<25/min
4	Heart rate	≤120/min
5	Systolic blood pressure	≥90 mmHg
6	Signs of respiratory distress	No agitation, diaphoresis, anxiety

Modes of treatment in respiratory failure:

Oxygen delivery modes:

Low flow:

Nasal prongs

Simple face mask

Partial rebreathing face mask

Non rebreathing mask

High flow:

Venturi mask

High flow nasal cannula

Mechanical ventilation modes:

Noninvasive mechanical ventilation

Invasive mechanical ventilation

High flow nasal cannula:

It is a mode of high flow oxygen delivery which delivers heated (to around 37ºC) and humidified oxygen upto 60L/min

Advantages:

- Comfort and better tolerated
- No claustrophobia

- NIV interface increases the anatomical dead space but HFNC decreases the dead space (washout of the nasopharyngeal dead space) which leads to higher alveolar ventilation, improved carbon dioxide clearance and higher resting oxygen saturation[70]
- Delivers a heated and humidified oxygen
- Provides a flow at higher rate than the normal patients inspiratory flow rate leads to reduced work of breathing [71]
- Minimal skin lesions
- Generation of PEEP as HFNC generates a PEEP of around 5-7cmH2O

Disadvantages:

- Not beneficial in ARDS especially in severe ARDS
- Maintenance of the device

Status of HFNC:

- HFNC is better than conventional oxygen therapy via oxygen mask as it reduces the need for noninvasive ventilation and reduces the rate of intubation compared to conventional oxygen therapy [72,73]
- HFNC has similar efficacy as NIV in reducing the need for intubation and mortality among the patients of acute hypoxemic respiratory failure with PaO2/FiO2<300 mmHg, however the efficacy is not known among moderate to severe ARDS patients when PaO2/FiO2 <200 mmHg.[74–76]
- NIV is the treatment of choice in hypercapnic respiratory failure, HFNC can be used in hypercapnic respiratory failure when NIV is not tolerated
- But however there are no clear guidelines regarding HFNC and hence merits for more studies in this area

SCORES

APACHE II score [77]

Acute physiology and chronic health evaluation (APACHE II) score is one of the most commonly used score in ICU.

Components of scoring:

Age, temperature , pH, heart rate, mean arterial pressure, respiratory rate, electrolyte levels (sodium , potassium), creatinine, acute renal failure, haematocrit, total counts, FiO2, status of intubation and history of severe organ failure (class 4 heart failure, chronic lung disease, cirrhosis, renal disease dependent on dialysis)

Maximum score – 71

Advantages:

- To estimate mortality in ICU
- To determine prognosis
- To compare patients with similar risk characteristics in different ICUs
- Useful for risk stratification of patients

Disadvantages:

- Does not play role in patient management
- Useful only in newly admitted patients to ICU
- Score is applied for generalised ICU patients and hence is less specific for specific subgroup of patients (like hepatic encephalopathy, ARDS etc,)

SAPS II score

Simplified acute physiological score (SAPS II) score is one of the most frequently used score in ICU patients which is comparable to APACHE II score.

Components of scoring:

Age, heart rate, systolic blood pressure, temperature, GCS, PaO2/FiO2 ratio, blood urea nitrogen, urine output, electrolytes (sodium, potassium, bicarbonate), bilirubin , total count, type of admission (medical/surgical) and presence or absence of malignancy and retroviral disease

Maximum score – 163

Advantages:

- It estimates the mortality risk of ICU patients[78,79]
- To assess prognosis
- To compare quality of care in ICU

Disadvantages:

- Cannot predict survival
- Does not play role in patient management
- Presence of chronic organ failure is not taken to consideration in the scoring

qSOFA score [80]

It stands for quick sequential organ failure assessment it includes three components blood pressure, respiratory rate and mental status (GCS). It's a score which helps to identify the infected patients outside ICU who are more likely to be septic.[81–83]

Scoring:

Systolic blood pressure<100mmHG – 1

Respiratory rate- >22 breaths/min – 1

GCS(Glasgow coma score) <15 – 1

Maximum- 3 points

Advantages:

- It's a simple bedside scoring
- Useful to identify high risk patients outside the ICU
- Raises a suspicion of severe infectious process and hence prompts further evaluation
- Used to predict mortality but not to diagnose sepsis

Disadvantages:

- Not useful in ICU patients
- No clinical decision on outcomes can be made based on this score

CURB 65 score [84]

It is a score which was devised for severity scoring among patients with community acquired pneumonia it consists of 5 components which include confusion, blood urea nitrogen , respiratory rate, blood pressure and age

Scoring:

C-Confusion – 1 (if present)

U- Uremia (blood urea nitrogen >19 mg/dl or >7 mmol/L) – 1

R-Respiratory rate (≥ 30breaths/min)- 1

B-Blood pressure (systolic blood pressure<90mmHg) -1

65 -Age (≥65)- 1

Maximum score - 5

Advantages:

- Estimate mortality in pneumonia[85]
- Decide if inpatient treatment is necessary or if it can be treated as outpatient basis
- To stratify the pneumonia patients on basis of risk

Disadvantages:

- The score doesn't take in account the comorbid conditions
- Inability to decide if the patient requires treatment in intensive care unit

RESPIRATORY FAILURE

A condition known as respiratory failure occurs when the respiratory system is unable to perform one or both of its gas-exchanging tasks, namely oxygenating mixed venous (pulmonary arterial) blood and removing carbon dioxide from it. Hence respiratory failure is a phenomenon as opposed to a disease. [86]

Insufficiency in breathing can be sudden or gradual. Patients with acute and chronic respiratory failure typically show in very diverse ways clinically. The signs of chronic respiratory failure might not be evident clinically, in contrast to acute respiratory failure, which is defined by life-threatening abnormalities in arterial blood gases and acid-base balance.[86]

Respiratory failure may be classified as: [86]

Hypercapnic respiratory failure:

When arterial PCO2 (PaCO2) greater than 45 mm Hg.

Hypoxemic respiratory failure:

When arterial PO2 (PaO2) less than 55 mm Hg when the fraction of oxygen in inspired air (FiO2) is 0.60 or greater.

Both these forms of respiratory failure exist together in most cases as diseases affecting the respiratory pump (like COPD) might develop hypoxemia too as a result of complications involving the lung parenchyma (like pneumonia) or vascular complications (like pulmonary embolism) and conversely the diseases that initially cause hypoxemia might also develop respiratory pump failure as a complication.

Table 7: Distinctions Between Acute and Chronic Respiratory Failure[87]

Category	**Characteristic**
Hypercapnic respiratory failure	PaCO2 >45 mmHg
Acute	Develops in minutes to hours
Chronic	Develops in several days to longer
Hypoxemic respiratory failure	Pao2 <55 mm Hg when FiO2 ≥0.60
Acute	Develops in minutes to hours
Chronic	Develops in several days to longer

PATHOPHYSIOLOGY

Respiratory failure results due to defect in any of the effector components of respiration which include:

- Central nervous system
- Peripheral nervous system
- Chest wall including the respiratory muscles
- Airways
- Alveoli

The initial four components together are known as respiratory pump and abnormality in these four components results in development of both hypercapnia and hypoxemia and when the fifth component (alveoli) is affected there is hypoxemia alone.[87,88]

Causes of Respiratory Failure:

I)Defects in ventilatory drive (Drug induced, cerebrovascular accident, OHS)

II)Defects in neural transmission

Spinal cord (trauma, tumors, gullian barre syndrome)

Peripheral nerves (Phrenic nerve injury post surgery, trauma, idiopathic)

Diseases affecting neuromuscular junction:[88–90](Myasthenia gravis, botulism)

III)Defect in ventilatory muscles (muscular dystrophy, poliomyositis, dermatomyositis)

IV)Defects with thoracic cage (kyphoscoliosis, effusion, flail chest)[91]

V)Defect in airways: [91](COPD, asthma)

VI)Defects in lung parenchyma: [92] (Pneumonia, ARDS)

VII)Defects in pulmonary circulation: (Pulmonary embolism, venous air embolism)

HYPOXEMIC RESPIRATORY FAILURE

Four pathophysiological mechanisms account for the hypoxemia which include;

- Alveolar hypoventilation
- Mismatch of ventilation and perfusion
- Shunting
- Factors limiting diffusion.[87]

Alveolar hypoventilation is seen in neuromuscular disorders affecting the respiratory system. The hypoxemia in such diseases have a normal alveolar-arterial gradient in the absence of underlying pulmonary

disease. In contradiction, there is widening of the alveolar-arterial gradient in the disorders affecting any of the other three

mechanisms.

Whenever there is a ventilation-perfusion mismatch there is development of hypoxemia as certain areas have low ventilation relative to perfusion.

Whenever there is a shunt, either intracardiac or intrapulmonary, there is development of venous admixture as the deoxygenated venous blood bypasses the ventilated alveoli leading to hypoxemia.

Finally, diseases that increase the diffusion pathway for oxygen from the alveolar space to pulmonary capillary results in hypoxemia as they impair oxygen transport across the alveolarcapillary membrane. [87]

METHODOLOGY

MATERIALS AND METHODS:

Source of data

Patients admitted at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.

Method of collection of data

STUDY DESIGN: AN OBSERVATIONAL STUDY

STUDY PERIOD: JANUARY 2021 TO DECEMBER 2021.

SAMPLE SIZE: Sample size was estimated by using the incidence of NIV failure in acute respiratory failure patients at 30.6% from the study by Thiago Domingos Corrêa et al. using the formula

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

p = Expected proportion in population based on previous studies or pilot studies.

d = Absolute error or precision – Has to be decided by researcher.

P = 30.6

q = 69.4

d = 10%

Using the above values at a 95% Confidence level a sample size of 82 subjects with acute respiratory failure and critically ill will be included in the study.

Considering 10% Nonresponse a sample size of 82 + 8.2 ≈ 90 subjects will be included in the study.

SAMPLE METHOD: In an observational study, the acute hypoxemic respiratory failure patients who fulfill the inclusion criteria will be included in the study. Data will be entered into a Microsoft excel datasheet and will be analysed using SPSS 22 version software. Categorical data will be represented in the form of Frequencies and proportions. Chi-square will be used as a test of significance. Continuous data will be represented as mean and standard deviation. An Independent t-test will be used as a test of significance to identify the mean difference. Pearson's Correlation will be used to correlate between two quantitative variables. P-value <0.05 will be considered statistically significant.

INCLUSION CRITERIA

All patients with acute hypoxemic respiratory failure with:

- The partial pressure of oxygen (PaO2) in the arterial blood < 60mmHG
- PaO2/FiO2<300 mmHg
- RR >24cpm
- Age >18 years

EXCLUSION CRITERIA

- Need for emergency intubation
- Recent esophageal, facial, or cranial trauma or surgery
- Severely decreased consciousness (Glasgow Coma Score of 11 or less)

- Tracheotomy or other upper airway disorders
- Cardiac/respiratory arrest
- Active upper GI bleeding
- Haemoptysis
- Inability to clear respiratory secretions
- Use of NIV for palliative care
- Usage of NIV for weaning purposes
- Severe hemodynamic instability
- Unstable cardiac arrhythmias

DATA COLLECTION

Patients were subjected to a thorough history and clinical examination and various parameters were analysed which included PaO2/FiO2 ratio, A-a O2 gradient, blood gas analysis, APACHE 2 score, SAPS 2 score, qSOFA score, CURB 65 score within first 24 hours of admission. All the patients were on maquet servo ICU ventilator with oronasal CPAP mask.

OUTCOME VARIABLES:

Primary Outcome variables:

PaO2/FiO2

APACHE II

SAPS II

qSOFA

Secondary outcome variables:

Length of stay in ICU

Length of stay on NIV

RESULTS

Table 8: Baseline demographic characteristics of the patients:

Parameter	Mean	SD	Median	Minimum	Maximum	Range
Age (years)	58.13	17.83	62	18	90	73
HR	104.62	22.09	106	60	210	150
RR	32.31	4.23	32	18	44	26
SBP	123.70	29.71	120	50	210	160
DBP	77.63	22.72	80	0	120	120
SPO2	90.87	7.77	90	50	99	49
PaO2/FiO2	158.71	59.39	165	59	358	299
GCS	14.86	0.41	15	13	15	2
CURB 65	2.07	1.06	2	0	5	5
qSOFA	1.41	0.67	1	0	3	3
A-a O2(mmHg)	298.99	153.34	270	19	578	559
pH	7.29	0.12	7.30	6.90	7.50	0.60
PO2	78.82	29.96	75	30	230	200
HCO3	23.25	10.79	21	7	98	91
SO2	88.95	9.73	92	52	100	48
APACHE II	16.61	6.92	17	06	34	28
SAPS II	39.90	14.69	38	18	98	80
LOS(Total) in days	12.11	9.24	9	1	42	41
LOS(NIV) in days	5.14	5.53	3	1	37	36
LOS(ICU) in days	7.09	6.70	5	1	42	41

A total of 97 patients were included in the study. There were 62 male patients and 35 female patients and the mean age was 58.13±17.83 years.

PaO2/FiO2 – Ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen

GCS- Glassgow coma scale

APACHE II – Acute physiological and chronic health evaluation score

SAPS II – Simplified acute physiological score

qSOFA- quick sequential organ failure assessment score

LOS(total)-total length of stay in hospital

LOS(ICU)- Length of stay in ICU

LOS(NIV)-Length of NIV usage

A-a – Alveolar arterial oxygen gradient

OUTCOME

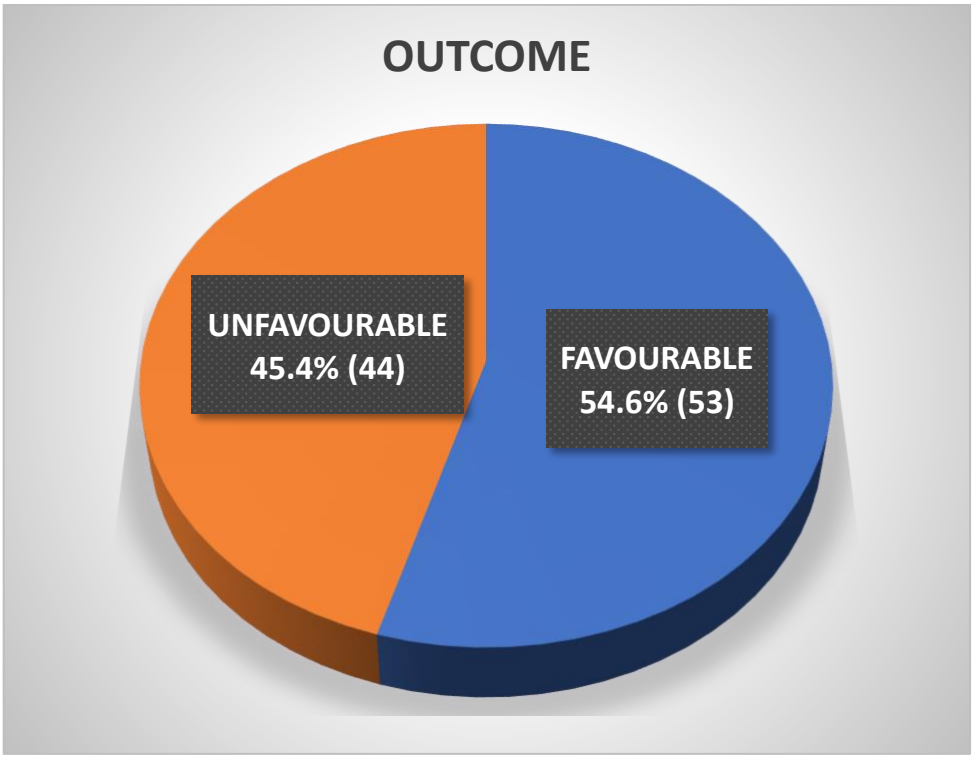
1)Favourable outcome (Success) –

- Discharged from the hospital

2)Unfavourable outcome (Failure)-

- Intubated
- AMA
- Death

Graph 1: A pie diagram showing outcome among patients with acute hypoxemic respiratory failure on NIV



Among 97 patients of acute hypoxemic respiratory failure who were put on NIV, 53 had a favourable outcome and 44 had an unfavourable outcome.

Table 9: Showing outcome among patients with acute hypoxemic respiratory failure on NIV

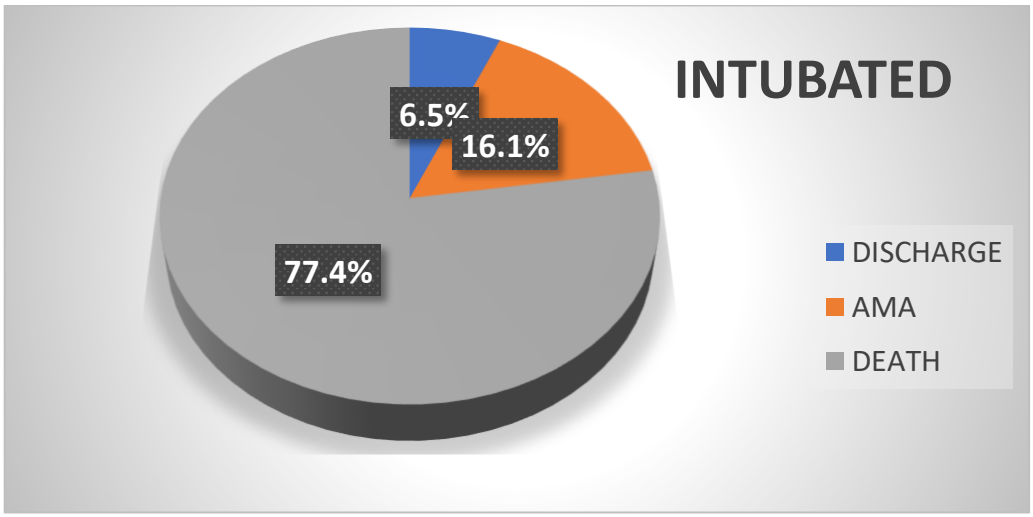
Outcome	N (N%)
Favourable	53 (54.6)
Unfavourable	44 (45.4)
Total	97 (100)

Table 10: Showing the various causes for unfavourable outcome:

Unfavourable outcome	N (N%)
Discharged(but were intubated)	2 (4.5)
AMA(Against medical advice)	9 (20.5)
Death	33 (75)

Among 44 patients with unfavourable outcome 2 patients were discharged (considered unfavourable since they were intubated and recovered and intubation was considered as unfavourable outcome in the study) and 9 patients went against medical advice (AMA) and 33 patients expired.

Graph 2: A pie diagram showing the outcome of intubated patients



A total of 31 patients were intubated of which only 2 (6.5%) patients were discharged, 5(16.1%) went against medical advice and 24 (77.4%) patients expired.

Table 11: Comparison of parameters with respect to outcome

	Outcome						P value
	Favourable			Unfavourable			
	Mean	SD	Median	Mean	SD	Median	
HR	99.66	18.81	102.00	110.59	24.40	110.00	0.014*
RR	30.64	3.35	32.00	34.09	4.44	34.00	<0.001*
SBP	129.60	28.12	130.00	116.59	30.32	115.00	0.031*
DBP	82.26	14.09	80.00	72.05	29.22	80.00	0.027*
SPO2	93.23	3.89	93.00	88.02	10.07	90.00	0.001*
PAO2/FI02	193.08	47.02	190.00	117.32	44.62	97.00	<0.001*
GCS	14.92	0.33	15.00	14.77	0.48	15.00	0.071
CURB65	1.77	0.97	2.00	2.43	1.07	3.00	0.002*
Q-sofa	1.17	0.51	1.00	1.70	0.73	2.00	<0.001*
PH	7.31	0.07	7.30	7.26	0.16	7.25	0.062
PO2	87.19	32.67	83.00	68.75	22.86	65.00	0.002*
PCO2	46.36	18.25	44.00	39.11	19.78	34.00	0.064
HCO3	26.15	12.42	24.00	19.75	7.10	19.50	0.003*
SO2	92.58	5.58	94.00	84.57	11.74	87.50	<0.001*
APACHEII	13.30	5.64	11.00	20.59	6.24	20.50	<0.001*
SAPS II	32.23	10.11	30.00	49.14	14.09	48.00	<0.001*
LOS(Total)	12.81	8.85	9.00	11.27	9.72	9.00	0.417
LOS (NIV)	4.13	3.04	3	6.36	7.36	4	0.047*
LOS (intubated)	0.00	0.00	0	3.93	4.11	3	<0.001*
Time to NIV	1.00	0.00	1.00	0.98	0.15	1.00	0.275
A-a	196.38	89.79	210.00	422.59	118.89	435.00	<0.001*
LOS(ICU)	4.43	3.00	3.00	10.30	8.37	9.00	<0.001*

PaO2/FiO2 – Ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen

GCS- Glassgow coma scale

APACHE II – Acute physiological and chronic health evaluation score

SAPS II – Simplified acute physiological score

qSOFA- quick sequential organ failure assessment score

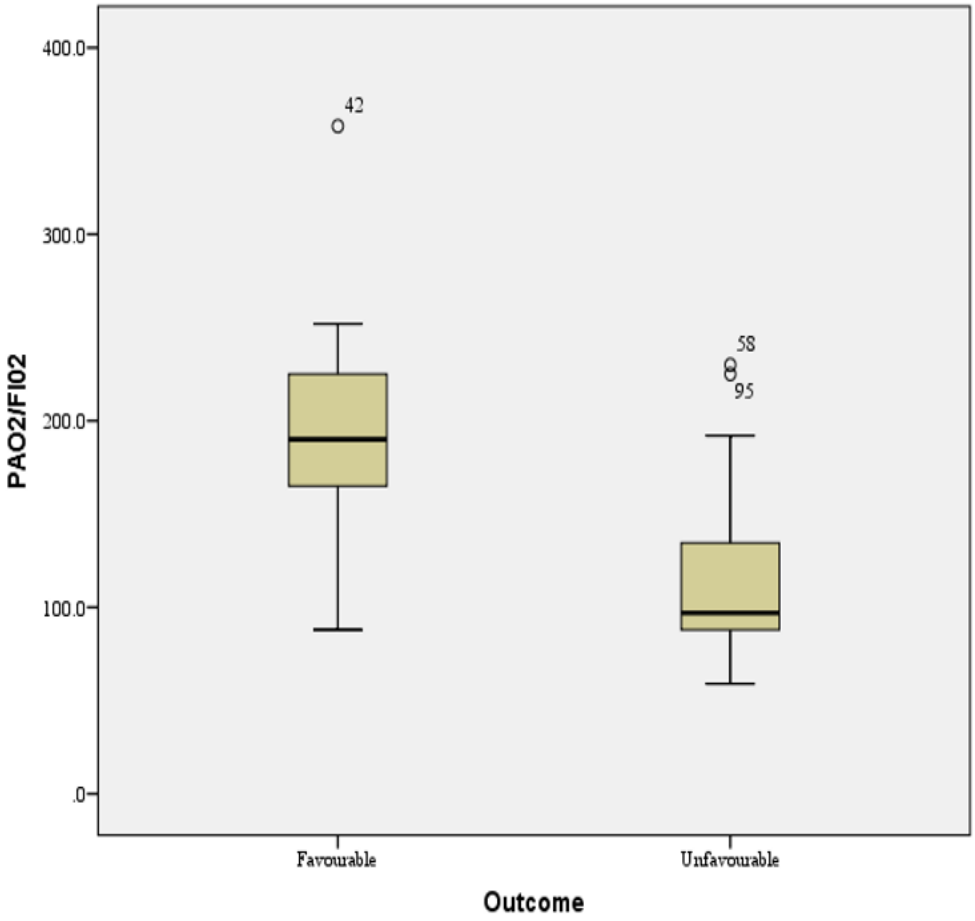
LOS(total)-total length of stay in hospital

LOS(ICU)- Length of stay in ICU

LOS(NIV)-Length of NIV usage

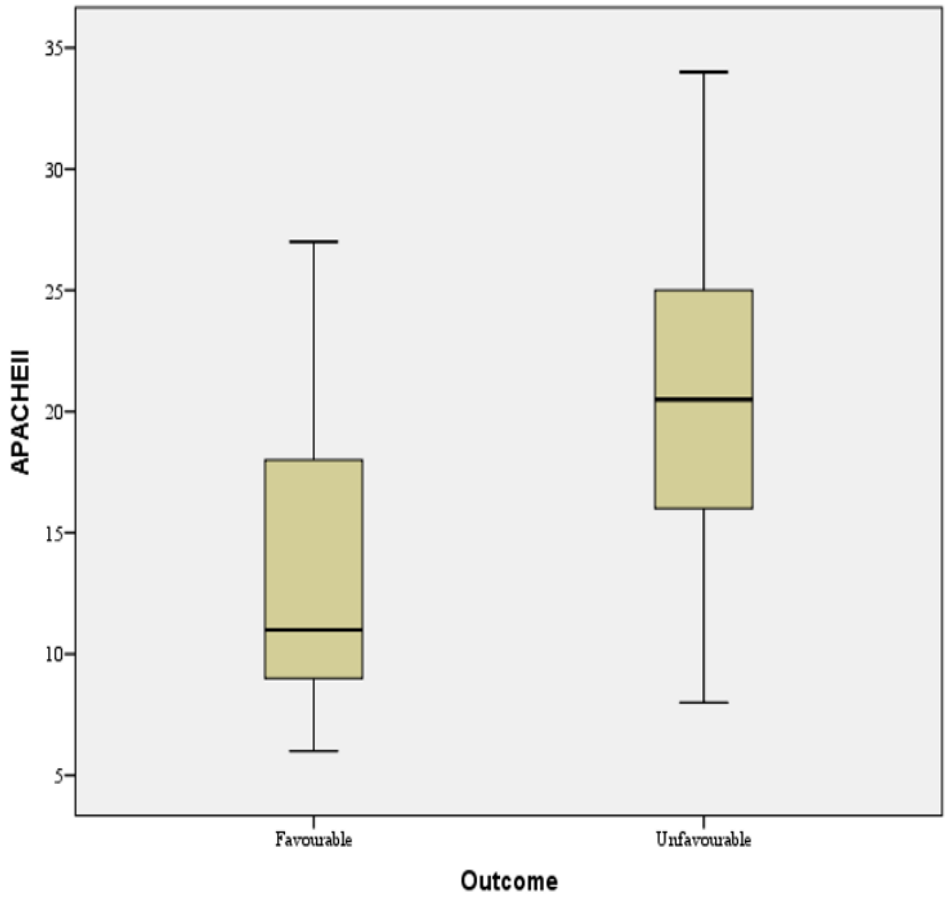
A-a – Alveolar arterial oxygen gradient

Graph 3: A simple bar diagram showing Pao2/FiO2 with respect to outcome



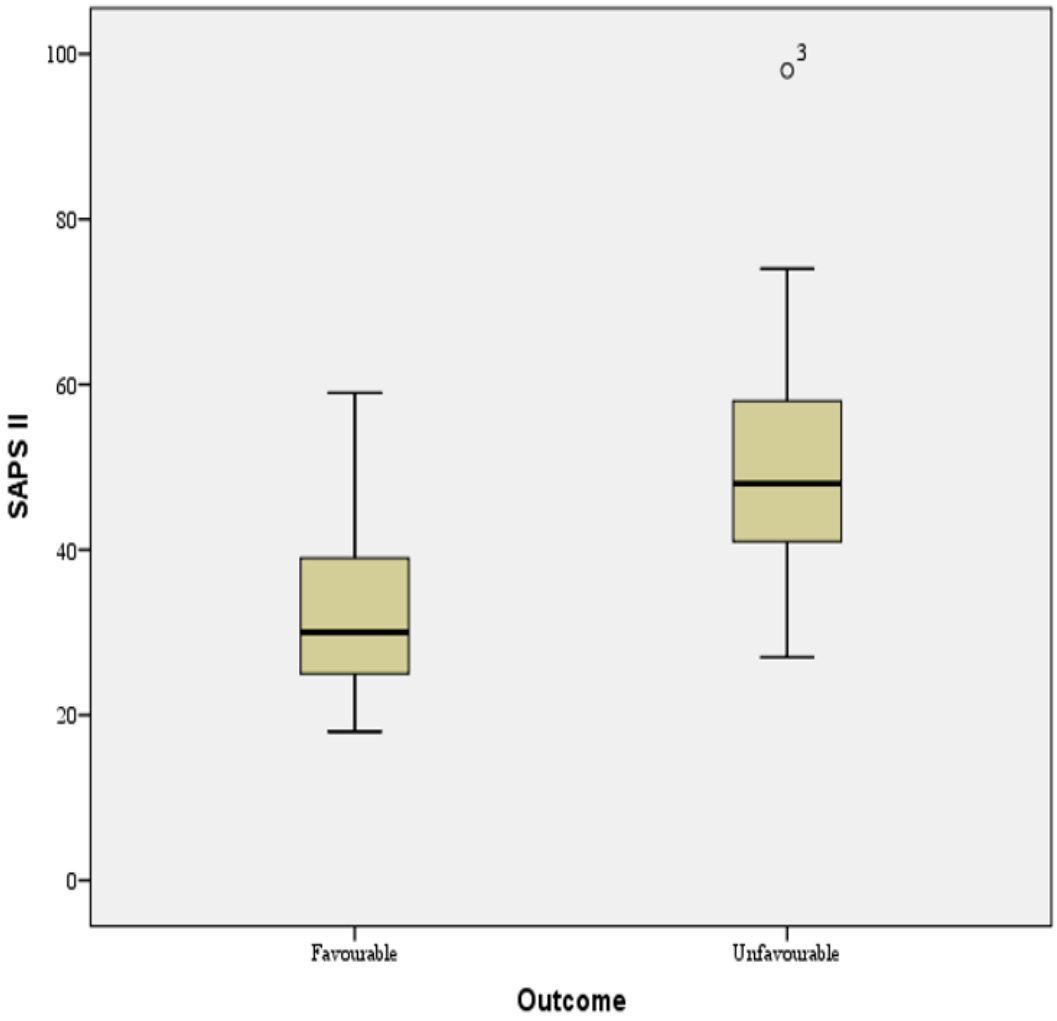
Among the patients with favourable outcome the mean PaO2/FiO2 was 193.08 and the mean PaO2/FiO2 among unfavourable outcome was 117.32 and this was statistically significant with p value <0.001.

Graph 4: A Simple bar diagram showing APACHE II score with respect to outcome



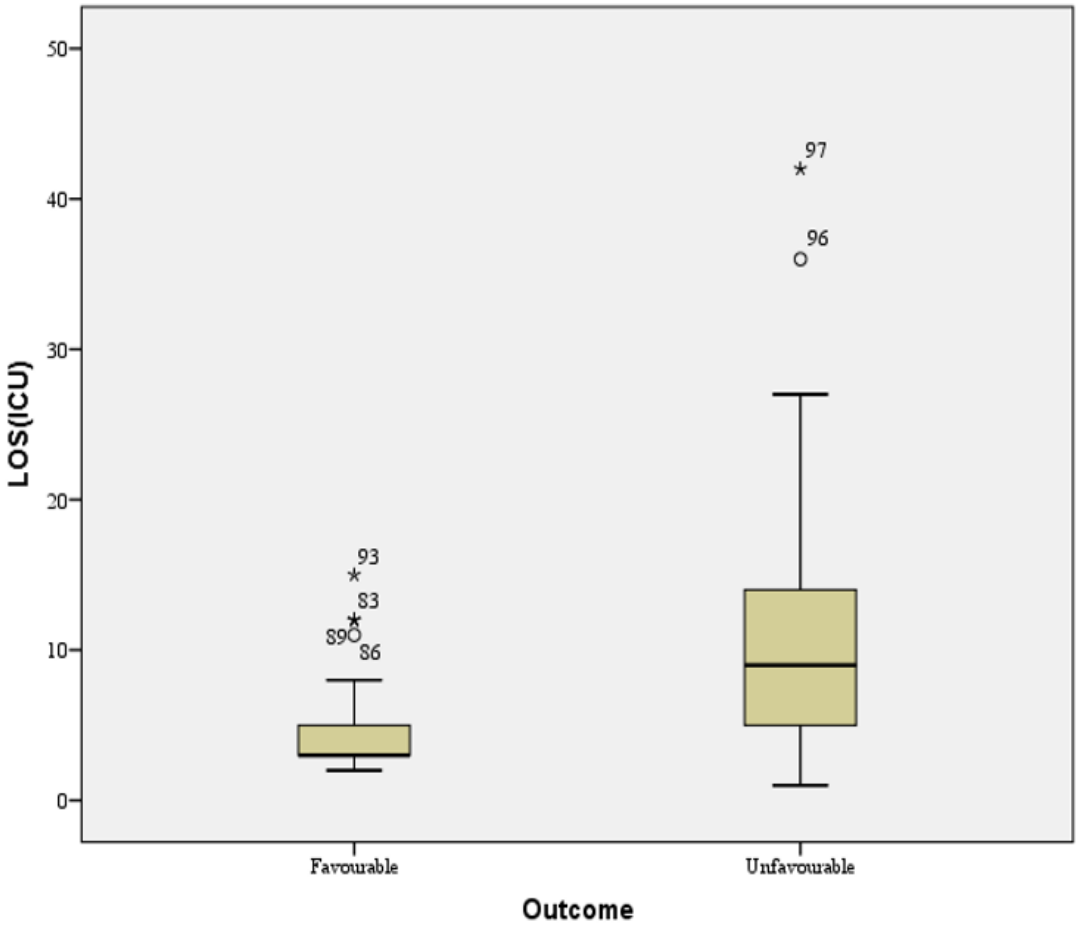
Among the patients with favourable outcome the mean APACHE II score was 13.30 and the mean APACHE II score among unfavourable outcome was 20.59 and this was statistically significant with p value <0.001

Graph 5: A simple bar diagram showing SAPS II score with respect to outcome



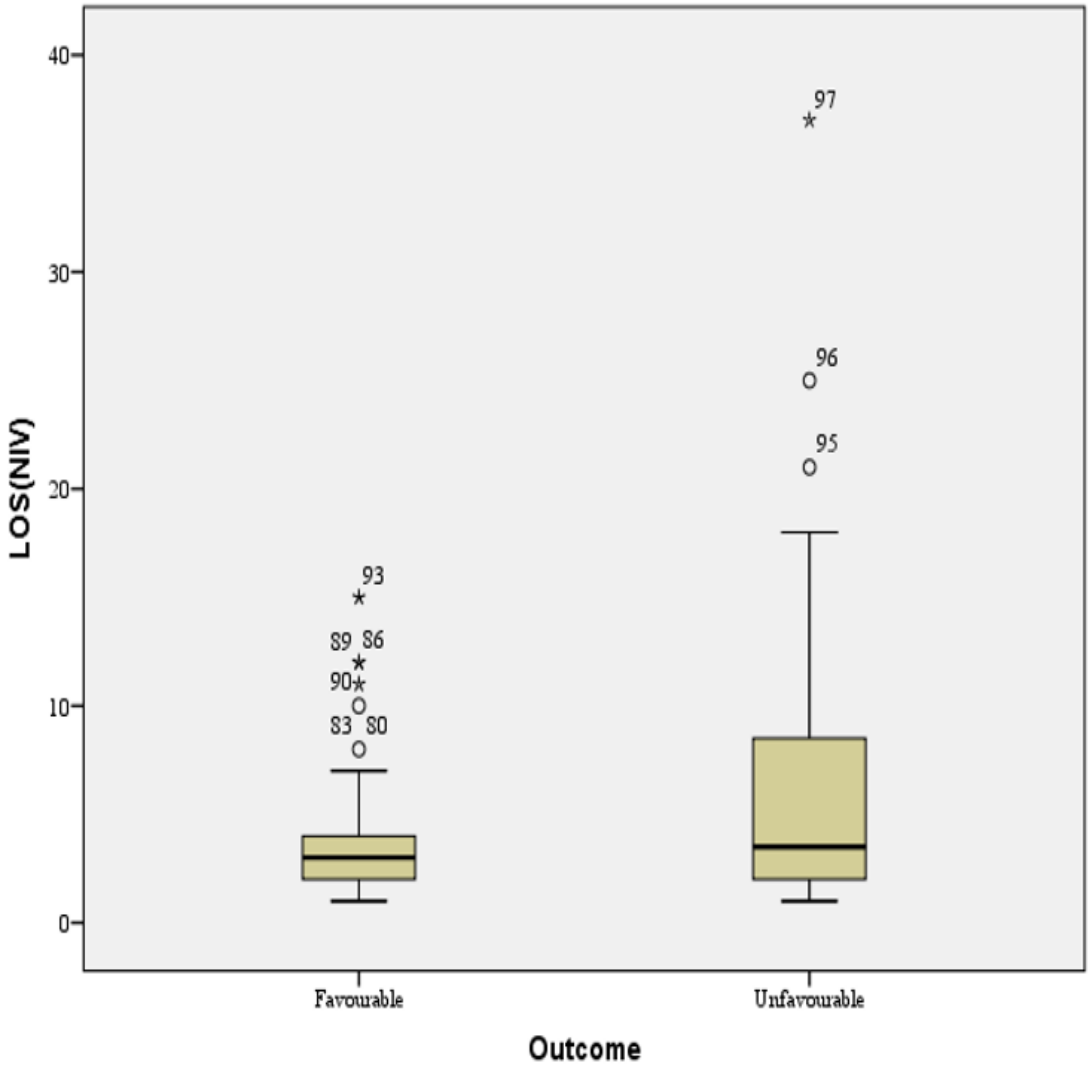
Among the patients with favourable outcome the mean SAPS II score was 32.23 and the mean SAPS II score among unfavourable outcome was 49.14 and this was statistically significant with p value <0.001

Graph 6: A simple bar diagram showing length of stay(LOS) in ICU with respect to outcome



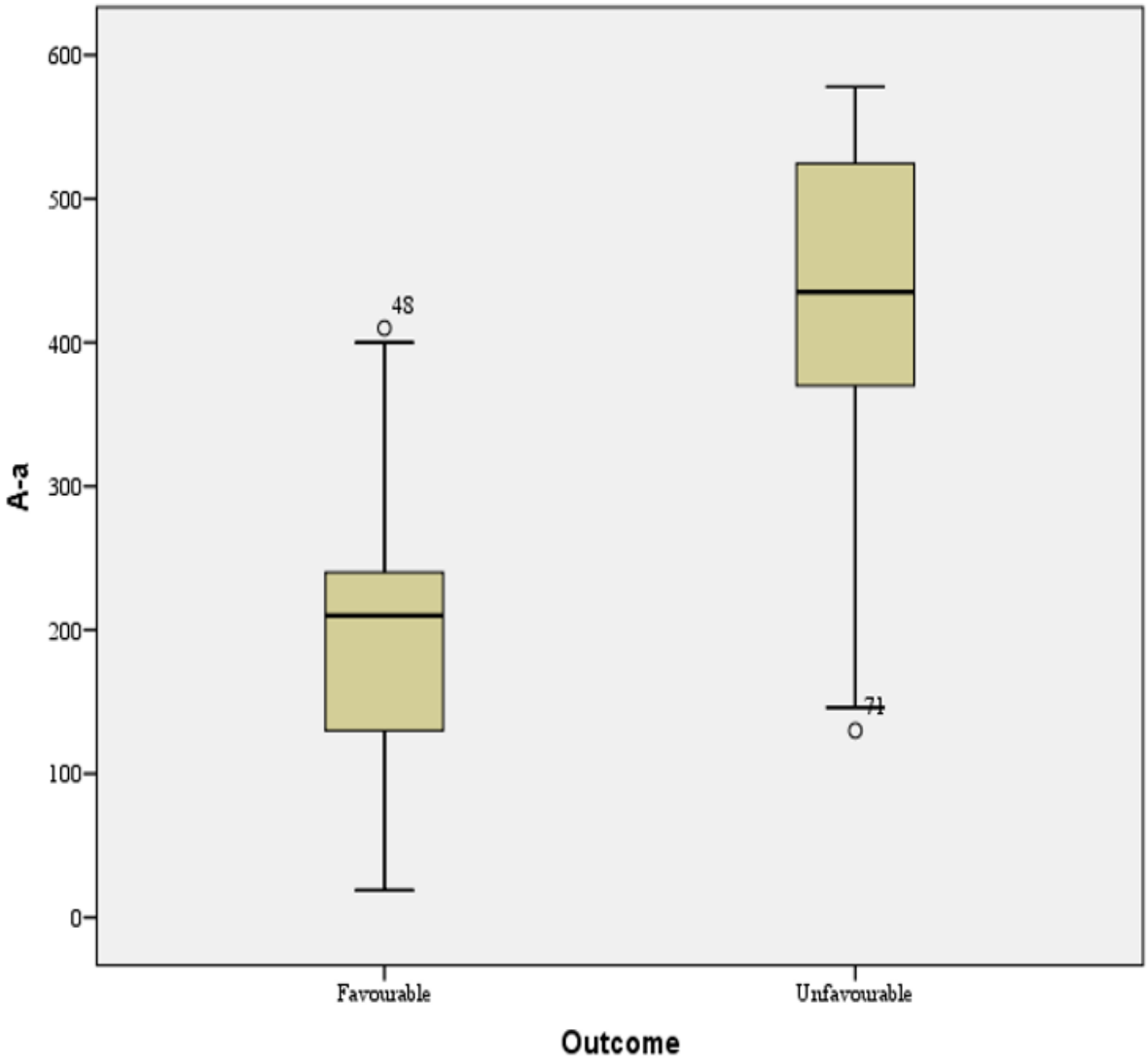
Among the patients with favourable outcome the mean length of stay in ICU was 4.43 days and the mean length of stay in ICU among unfavourable outcome was 10.30 days and this was statistically significant with p value <0.001

Graph 7: A simple bar diagram showing length of stay on NIV with respect to outcome



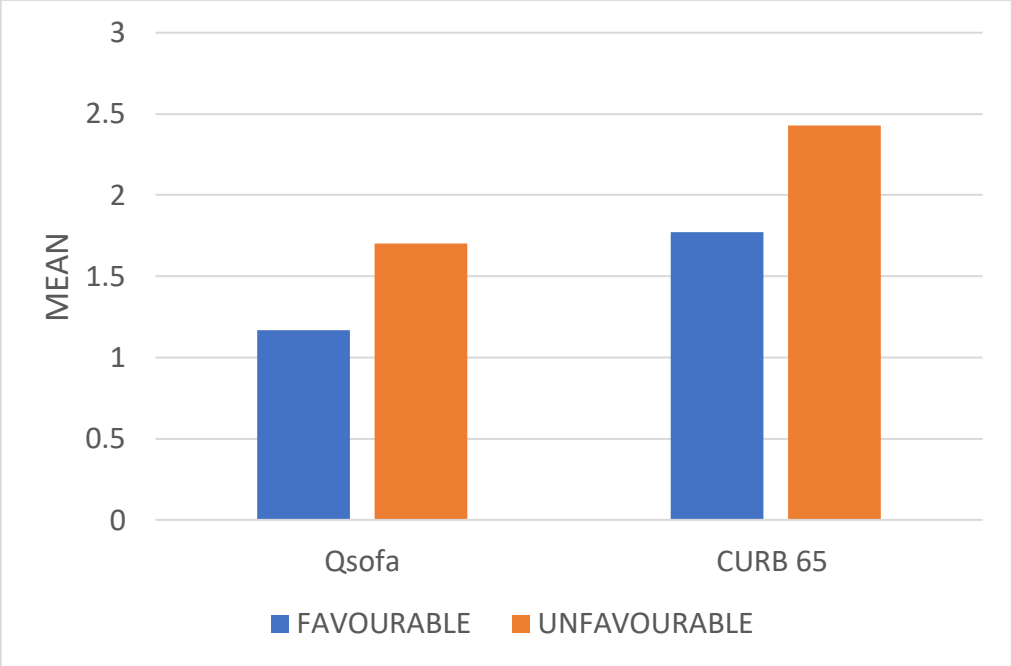
Among the patients with favourable outcome the mean length of stay on NIV was 4.13 days and the mean length of stay on NIV among unfavourable outcome was 6.36 days and this was statistically significant with p value <0.05

Graph 8 : A simple bar diagram showing A-a O2 gradient with respect to outcome



Among the patients with favourable outcome the alveolar arterial oxygen gradient was 196.38 mmHg and the mean alveolar arterial oxygen gradient among unfavourable outcome was 422.59mmHg and this was statistically significant with p value <0.001

Graph 9: A Bar diagram showing qSOFA and CURB65 score with respect to outcome



Among the patients with favourable outcome the mean qSOFA and CURB 65 score was 1.17 and 1.77 and among the patients with unfavourable outcome the mean qSOFA and CURB 65 score was 1.70 and 2.43 this was statistically significant with p value of <0.005

Table 12: Showing distribution of cases in this study

Diagnosis	**N (N%)**
Pulmonary edema	18(18.6)
SARS COV 2 pneumonia	17(17.5)
Other pneumonia	15(15.5)
COPD	13(13.4)
Asthma	6(6.2)
Post TB COAD	4(4.1)
Interstitial lung disease (ILD)	5(5.2)
Pleural effusion	5(5.2)
Haemopneumothorax	4(4.1)
Pneumothorax	2(2.1)
Carcinoma lung	3(3.1)
Silicotuberculosis	1(1)
Miliary tuberculosis	1(1)
Pulmonary tuberculosis	1(1)
Destroyed lung	1(1)
Kyphoscoliosis	1(1)

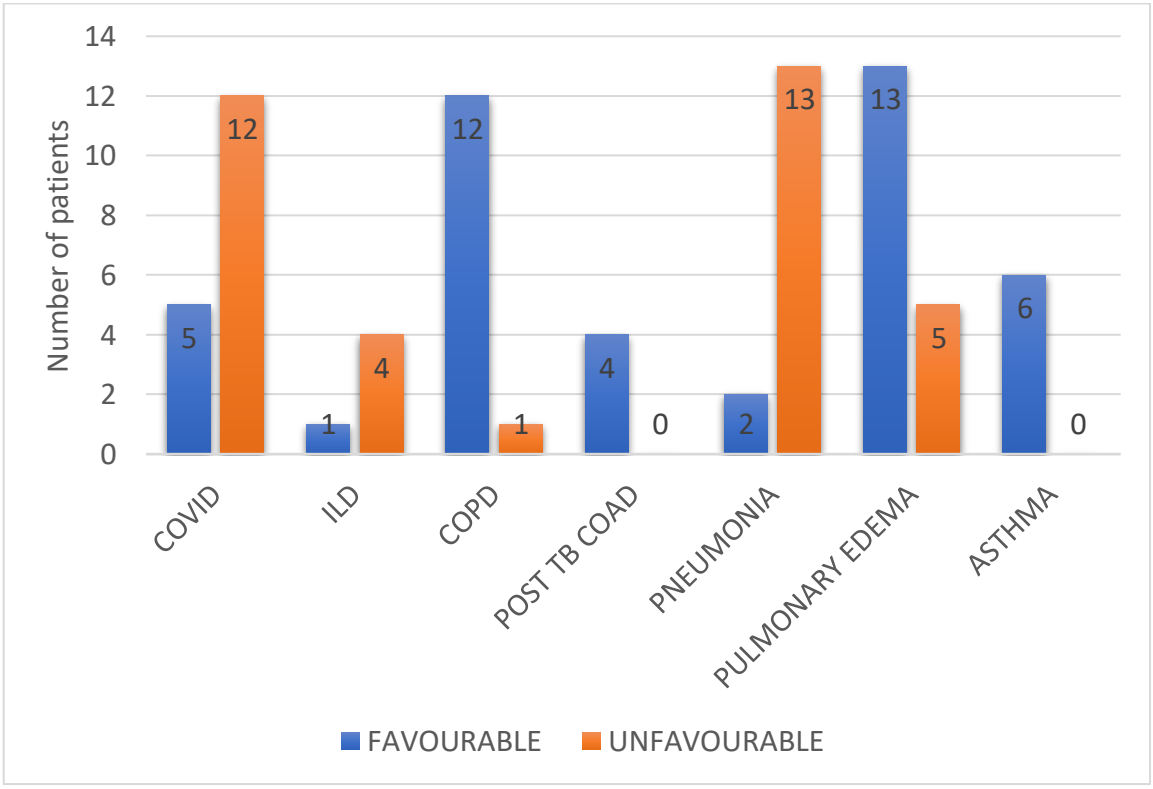
Among 97 patients of acute hypoxemic respiratory failure, majority of patients were cases of pulmonary edema 18 (18.6%), pneumonia 15

(15.5%), SARS COV 2 17 (17.5%) and COPD 13 (13.4%).

Table 13: Showing outcome with respect to different cases

Diagnosis	Favourable N(N%)	Unfavourable N(N%)	P value
Pulmonary edema	13(72.2)	5(27.8)	0.097
SARS COV2 pneumonia	5(29.4)	12(70.6)	0.021
Other pneumonia	2(13.3)	13(86.7)	<0.001
COPD	12(92.3)	1(7.7)	0.003
Asthma	6(100)	0	0.021
Post TB COAD	4(100)	0	0.063
ILD	1(20)	4(80)	0.110
Pleural effusion	2(40)	3(60)	0.500
Haemopneumothorax	3(75)	1(25)	0.404
Pneumothorax	2(100)	0	0.193
Carcinoma lung	1(33.3)	2(66.7)	0.451
Silicotuberculosis	1(100)	0	0.360
Kyphoscoliosis	1(100)	0	0.360

Graph 10: A bar diagram showing outcome distribution in different subgroups



Among the various etiologies of acute hypoxemic respiratory failure, the NIV success rate was higher in patients with obstructive airway diseases 96%(and cardiogenic pulmonary edema 72.2% and the success rate in NIV among denovo respiratory failure (SARS COV 2 pneumonia and other pneumonia) was low 22% .

The present study has 23(23.7%) patients of obstructive airway diseases which included COPD (13,13.4%) , asthma(6, 6.2%) , post TB COAD (4,4.1%) of NIV was success among 12 patients of COPD(92%), all 6 patients of Asthma(100%) and in all the 4 patients of post TB COAD (100%) and hence overall NIV success was seen in 22 patients of obstructive airway disease(96%).

In the present study there were a total of 32 patients of de novo respiratory failure 15 patients of bacterial pneumonia and 17 patients of covid pneumonia. NIV success was seen only in 7(22%) patients of de novo respiratory failure and only among 2(13%) patients of bacterial pneumonia and 5(29%) patients of covid pneumonia.

DISCUSSION:

NIV (Noninvasive ventilation) stands for usage of various noninvasive interfaces for administration of positive pressure ventilation (nasal mask , nasal plugs , face mask). Patients with either acute or chronic respiratory failure may benefit from NIV as ventilatory support. In the last two decades, one of the most significant advancements in the field of mechanical ventilation has been the use of NIV.

Incidence of failure of NIV in AHRF:

The present study included total of 97 patients of acute hypoxemic respiratory failure of various causes.

Among 97 patients 53 (54.6%) had a favourable outcome and 44(45.4%) had an unfavourable outcome. Among 44 patients with unfavourable outcome 2 patients recovered ,9 patients went AMA and 33 patients expired. The 2 recovered patients were considered unfavorable as intubation was considered as unfavourable outcome in the study.

In a similar study conducted by Agarwal et al[93] , among 40 patients with AHRF on NIV. NIV success was seen in 52.5% (21) of patients with acute hypoxemic respiratory failure. These results were similar and comparable with present study where NIV success was 54.6%.

In a study done in South Paulo Brazil conducted by Correa et al [94] , total of 85 patients were included in the study and NIV success was seen in 59 (69.4%) and NIV failure in 26 (30.6%) patients. Compared to present study this study had higher success and it was found

that this study had a lower mean APACHEII score and higher PaO2/FiO2 ratio compared to the present study.

In another Indian study conducted by Kshatriya et al [95] 110 patients of acute respiratory failure who received NIV were included. NIV success was seen in 81 (74%) and failure in 29(26%). This study has a higher rate of NIV success compared to the present study and this study differs from the present study in the baseline patient subgroups as this study has higher number of patients with obstructive airway disease 78(70%) compared to the present study.

In a study conducted in Spain by Ferrer et al[96] , among 51 patients of AHRF who were on NIV, NIV success was seen in 38 (74.5%). The success in this study to was relatively higher compared to the present study and it was found that the mean SAPS II score was lower in this study than the present study (34 vs 40)

Table 14: Comparing the incidence of success and failure of NIV in various studies

Study	**Total patients**	**Group of patients**	**Prevalence of success n(N%)**	**Prevalence of failure n(N%)**
Present study	97	Overall COPD ACPE Pneumonia Covid Others	53(55) 12(92) 13(72) 2(13) 5(29) 21(62)	44(45) 1(7.7) 5(28) 13(87) 12(71) 13(38)
Correa et al [94]	85	Overall COPD ACPE Pneumonia ARDS Others	59(69) 7(70) 15(79) 20(67)	26(31) 3(30) 4(21) 10(33)
Kshatriya et al [95]	110	Overall COPD Other	81(74) 58(85) 23(55)	29(26) 10(15) 19(45)
Ferrer et al [96]	51	Overall	38(74.5)	13(25.5)

Demoule et al [95]	249	Overall (included all patients with ARF including COPD, ACPE, Pneumonia)	139(55.8)	109(44.2)
V K Singh et al [97]	50	Overall	37(74)	13(26)
Ahmed Taha et al [98]	6835	Overall	5480(80)	1355(20)
Shaheen M et al [99]	25	Overall(only COPD patients were included)	19(76)	6(24)
Ibrahim et al [100]	52	Overall (COPD, Pneumonia ,ACPE ,Others)	40(77)	12(23)
Bajaj et al [101]	50	Overall (all patients with AHRF except those with PaCO2>45	31(62)	19(38)
Lt Col S P. Rai et al[102]	59	Overall(only COPD patients were included)	52(88)	7(12)
Wei Sun et al [103]	131	Pneumonia	64(49)	67(51)

Predictors of Outcome of NIV:

The present study included a total of 97 patients who were subjected to thorough clinical examination and were assessed for ABG, SAPSII, APACHE II, qSOFA, CURB 65 scores and PaO2/FiO2 ratio and A-a O2 gradient within first 2 hours of admission.

In our study it was observed that among 97 patients NIV success was seen in 53 patients and failure was seen in 44 patients. The NIV failure group had and lower PaO2/FiO2 ratio and higher APACHE II , SAPS II, qSOFA, CURB 65 scores and higher length of ICU stay and higher duration of stay on NIV compared to success group .

<u>PaO2/FiO2 ratio:</u>

The mean PaO2/FiO2 in our study was 158 and it was 193 among success group and 117 in failure group

A study by Agarwal et al [93], among 40 patients of AHRF found that baseline PaO2/FiO2 was 103 in NIV failure group as compared to NIV success group where the ratio was 144. The findings are similar to present study especially among NIV failure group (103 vs 117).

In an European study conducted by Antonelli et al [104], among 147 patients with ARDS it was found that if PaO2/FiO2 continued to be <175 even after one hour of NIV use , then it was an independent predictor for failure of NIV and need for endotracheal intubation . These findings are similar to the present study.

Several other studies among hypoxemic respiratory failure by Demoulle[105] , Bellani [106] and Carillo[107] conclude that a PaO2/FiO2 ratio < 150 at baseline and after 1hour of NIV use predicts NIV failure .However this value was higher in another study by Frat[74] where failure of noninvasive ventilation was likely to occur when PaO2/FiO2 ratio <200.

Table 15: PaO2/FiO2 ratio as a predictor of outcome in success and failure group:

Study	**Success group**	**Failure group**
Present study	193.08	117.32
Bajaj et al [101]	186.77	120.47
Carillo et al[107]	135	116
Agarwal et al [93]	144.2	103.8
Ibrahim et al [100]	235.6	210.5
Bellani et al [106]	171	145
Wei Sun et al [103]	236	194

APACHE II score:

It is one of the most commonly used score in ICU which estimates the ICU mortality, helps in determining prognosis and useful for risk stratification of patients.

In present study the mean APACHE II score in success group was 13.30 and the mean in failure group was 20.59.

In a study by Correa et al [94] among 85 patients it was observed that the failure group (26) had a higher APACHE II score of 16 compared to the success group 13.4. However this was not as significant difference when compared to the present study

Wei Sun et al [103] studied regarding the predictors of outcome of NIV among pneumonia patients and it was found that NIV success group had a APACHE II score of 14 and failure group had a score of 20 and these results are similar to the present study

However in a study by Agarwal et al [93] among 40 patients the APACHE II score was 14.8 in success group and 15 in failure group, showing no major difference among both groups.

Zhu [108]and colleagues studied on patients of pneumonia, and concluded that higher APACHE II score of >20 was found to be an independent risk factor for failure of NIV. This is comparable with the present study.

Table 16: APACHE II score as a predictor of outcome in success and failure group :

Study	**Success group**	**Failure group**
Present study	13.30	20.59
Bajaj et al [101]	11.06	15.57
Ibrahim et al [100]	18.1	16.9
Agarwal et al [93]	14.8	15
Wei Sun et al [103]	14	20
Correa et al [94]	13.4	16

SAPS II score:

It is one of the most commonly used score in ICU comparable to APACHE II score it helps to estimate mortality, predict prognosis and to compare quality of care in ICU

SAPS II score in present study was significantly higher in NIV failure 49.14 compared to 32.23 in success group and overall mean SAPS II score was 39.90.

In a study by Antonelli et al [104] , SAPS II score of >34 was independent risk factor for failure of noninvasive ventilation and this result is similar to the present study.

Demoule[105] and colleagues did a study in France among 248 patients who were on NIV and concluded that the NIV failure group (109 patients) had significantly higher SAPS II 43 compared to the success group (139) where the value was 34 the results are similar to the present study

In a study conducted in Spain by Carillo et al [107] among 102 patients of De novo ARF the success group (55 patients) had a significantly lower SAPS II score of 38 vs 47 among the failure group (47 patients)

Table 17: SAPS II score as a predictor of outcome in success and failure group:

Study	**Success group**	**Failure group**
Present study	32.23	49.14
Demoule et al [105]	34	43
Carillo et al[107]	38	47
Antonelli et al [66]	30	35

Length of stay (LOS):

In the present study the length of stay in ICU was higher among failure group compared to successive group (10.30 days vs 4.30 days) and subsequently length of stay on NIV was also higher among failure group when compared to success group (4.13days vs 6.36 days). Higher length of stay was predictor for failure of noninvasive ventilation.

A study by Antonelli[104] found that similar results were observed where the length of stay was significantly higher in failure group compared to success group (5 days vs 9 days).

In an observational cohort study done by Correa [94] among patients with acute hypoxemic respiratory failure the length of days (ICU) was 2 days in success group and 12 days in failure group and total length of days was also lower in success group compared to failure group (15 days vs 30 days)

Table 18: Length of stay (LOS) as a predictor of outcome in success and failure group:

Study	**Success group**	**Failure group**
Present study	LOS(ICU) – 4.43 LOS(NIV) – 4.13	LOS(ICU)-10.30 LOS(NIV)-6.36
Carillo et al [109]	LOS(ICU)-6	LOS(ICU)-15
Wei Sun et al [103]	LOS- 15	LOS-17
Antonelli et al [66]	LOS-5	LOS-9
Correa et al [94]	LOS -15 LOS(ICU)-2	LOS-30 LOS(ICU)-12

Other factors:

The other factors that were significant in predicting the outcome were CURB 65 score and qSOFA score.

In our study among the patients with favourable outcome the mean qSOFA and CURB 65 score was 1.17 and 1.77 and among the patients with unfavourable outcome the mean qSOFA and CURB 65 score was 1.70 and 2.43 this was statistically significant.

In a study by Carillo et al [107]among 82 patients of respiratory failure with known respiratory or cardiac disease NIV success was seen in 61(74.4) and failure was seen in 21(25.6) and the success group had a lower CURB 65 score 2.5 vs 3.4 in failure group

In the same study CURB65 score was performed for patients with denovo respiratory failure(102 patients) the success group (55 patients) had a lower CURB 65 score 2.3 compared to failure group(47 patients) 2.7 .

Rate of intubation and mortality:

In present study among total of 97 patients of AHRF who were on NIV 31 patients required intubation (31.97%) and 66 (68.04%)patients were on NIV throughout the hospital stay and among patients who were intubated the mortality was 77.41% (24 of 31) and mortality in NIV group was significantly lower 13.63% (9 of 66).

Agarwal et al[7]. done a meta-analysis that evaluated the effectiveness of NPPV in patients with ALI/ARDS. The literature search for this study was restricted to works released between 1995 and 2009. According to research by Agarwal et al[93] , NPPV treatment reduced mortality in ALI/ARDS patients by 65% and averted intubation in 50% of cases. Similarly in present study the mortality was significantly higher in intubation group (77.41%) than in the NIV group (13.63%)

Table 19: Showing rate of intubation and mortality among patients of acute hypoxemic respiratory failure treated with NIV in different studies

Study	**Total patients who received NIV**	**Number of patients Intubated and percentage of intubated**	**Number of Mortality and percentage of mortality**
Present study	97	31(32)	24(77)
Hilbert et al[110]	64	48(75)	44 (92)
Antonelli et al [104](also included ACPE)	147	68(46)	41(60)
Agarwal et al [93]	40	12(30)	7(58)
Rana et al [111]	54	38	26
Confalonieri et al[112]	24	8	6

NIV in Obstructive airway disease:

The present study has 23(23.7%) patients of obstructive airway diseases which included COPD (13,13.4%) , asthma(6, 6.2%) , post TB COAD(4,4.1%) of NIV was success among 12 patients of COPD(92%), all 6 patients of Asthma(100%) and in all the 4 patients of post TB COAD (100%) and hence overall NIV success was seen in 22 patients of obstructive airway disease(96%). But however the study had very few patients of asthma and post TB COAD.

In patients with COPD in type 2 respiratory failure the usage of noninvasive positive pressure ventilation leads to improvement of patients clinical condition, reduced mortality and rate of intubation and hence noninvasive ventilation has become the standard of care in COPD.[113,114]

Table 20: Showing Success and failure of NIV in different studies of COPD patients

Study	**Success**	**Failure**
Present	12(92)	1(8)
Kshatriya et al[95]	58(85)	10(15)
Correa et al [94]	7(70)	3(30)
Lt Col SP. Rai et al[102]	52(88)	7(12)
Shaheen M et al [99]	19(76)	6(24)

NIV in ACPE:

In present study there were a total of 18 patients of ACPE and success was seen in 13 patients (72%) and failure in 5 (28%).

The 5 systematic reviews by Mehta [115], [116,]concluded that noninvasive ventilation leads to reduction in the need for intubation and mortality among patients with ACPE as NIV by

itself reduces the pulmonary edema and both CPAP and BiPAP have similar effects on outcome.

NIV in De novo respiratory failure:

These are the patients of acute hypoxemic respiratory failure with no prior chronic respiratory disease (a non COPD diagnosis) and neither of ACPE and Post operative respiratory distress. [116]

In the present study there were a total of 32 patients of de novo respiratory failure 15 patients of bacterial pneumonia and 17 patients of covid pneumonia. NIV success was seen only in 7(22%) patients of de novo respiratory failure and only among 2(13%) patients of bacterial pneumonia and 5(29%) patients of covid pneumonia. However the baseline APACHE II scores, SAPS II scores among these patients was significantly higher.

According to an observational research by Thille et al[117]., the milder the degree of ARDS, the greater the likelihood that NIV will be successful in preventing ETI and lowering ICU mortality. They suggested that NIV would be worthwhile to try in patients with moderate ARDS if they had a PaO2/FiO2 ratio more than 150 and there is no hemodynamic instability or altered consciousness. The choice of patients is very important.

In a study by Carillo[107] et al among 102 patients of denovo respiratory failure success was seen in 55(54%) patients and failure in 47(46%).

Role of NIV in de novo respiratory failure is controversial and NIV can be used only in early ARDS (PaO2/FiO2 >200) as a measure to reduce the need for intubation according to a study by Zahn [118]et al.

Dysart et al [119]concluded that high flow nasal cannula was beneficial than NIV as it improves patient tolerance and maintains low tidal volume similarly Frat et al[74] also found that high flow nasal cannula to be superior to NIV but however there was no significant difference in the primary endpoint of intubation.

NIV in De novo acute respiratory failure is associated with risk of delaying intubation and ARDS and pneumonia are associated with higher chances of failure of NIV especially when they have higher APACHEII ,SAPS II scores and when there is failure to recover within one hour of treatment with NIV as demonstrated by Brochard et al[120]

Overall in the present study the incidence of failure of NIV was 45.4% and the factors predicting the failure of NIV were higher APACHE II, SAPS II, qSOFA, CURB 65 scores and lower PaO2/FiO2 ratio and it was found that NIV was more successful when used among patients with obstructive airway disease and ACPE and had higher chances of failure when used in patients with de novo respiratory failure (bacterial pneumonia, SARS COV2 pneumonia).These results were consistent with most other studies.

LIMITATIONS:

This is only an observational study

The number of patients were less

There was no assessment of serial blood gas analysis (ABGs)

There was no assessment made with respect to comorbidities

CONCLUSION:

- In the present study among 97 patients 53 had favourable outcome and 44 had unfavourable outcome and NIV failure rate was 45.4%.
- The patients with low Pao2/Fio2 ratio and high APACHE II , SAPS II ,CURB65 and qSOFA scores and high alveolar arterial (A-a O2) gradient had higher incidence of NIV failure and are predictors for unfavourable outcome.
- The patients with increased length of stay in ICU , increased length of usage of NIV are independent predictors for unfavourable outcome.
- Among the various etiologies of acute hypoxemic respiratory failure NIV success was higher in obstructive airway disease and cardiogenic pulmonary edema and the failure was higher in denovo respiratory failure.
- This study concludes that one has to have a high index of suspicion of failure of NIV among patients of acute hypoxemic respiratory failure with low Pao2/Fio2 ratio, high alveolar arterial gradient (A-a O2) , high APACHE II , SAPS II , CURB 65 and qSOFA scores, as they determine poor prognosis.

SUMMARY:

- Our study is a one year hospital based observational study conducted between January 2021 to December 2021
- The patients of acute hypoxemic respiratory failure after fulfilling the inclusion and exclusion criteria were included in the study
- The patients were subjected for thorough history and clinical examination and various parameters which included Pao2/Fio2 ratio, ABG, A-a O2 gradient, APACHE II score , SAPS II score, qSOFA score, CURB 65 score were analyzed within first 24 hours
- A total of 97 patients were included in study of which 62 were male and 35 were female, mean age of male patients was 61.60 and mean age of female patients was 52.
- The causes of acute hypoxemic respiratory failure in our study majorly were pulmonary edema (18) , SARS COV2 pneumonia (17) , other pneumonias (15) , COPD(13), bronchial asthma(6) and ILD (5).
- The overall incidence of **success** of NIV among patients of acute hypoxemic respiratory failure in our study was 54.6% and **failure** was 45.4%.
- Among various parameters and scores observed PaO2/FiO2 ratio was one of the most significant predictor for NIV failure. Any patients whose PaO2/FiO2 ratio <150 mmHg were more likely to have unfavourable outcome with a mean PaO2/FiO2 ratio being 117.32 with SD±44.62. However in patients whose PaO2/FiO2 ratio >150 mmHg were more likely to have favourable outcome with a mean PaO2/FiO2 ratio being 193.08 with SD±47.02. These values were statistically significant with a p value of <0.001

- The various other scores which were studied were APACHE II, SAPS II, CURB 65 and qSOFA whose baseline mean values in favourable outcome group were 13.30, 32.32, 1.77, 1.17 and the mean values in unfavourable outcome were 20.59, 49.14, 2.43, 1.70 and this was statistically significant with a p value of <0.005.
- Another important parameter was A-a O2 gradient which was 196.38 mmHg in success group and was 422.59 in failure group and was statistically significant with p value of <0.001
- The mean length of stay in ICU (irrespective of NIV use) among success group was 4.43 days and it was 10.30 days in failure group. The mean length of NIV usage in ICU among success group was 4.13 days and it was 6.36 days in failure group and these values were statistically significant with p value of <0.05.
- Among the various etiologies of acute hypoxemic respiratory failure,the NIV success rate was higher in patients with obstructive airway diseases 96% and cardiogenic pulmonary edema 72.2% and the use of NIV among denovo respiratory failure group was questionable as the NIV failure rate was higher 78%
- The incidence of NIV failure in the study was 45.4% and the predictors identified for NIV failure were low Pao2/Fio2 ratio, high APACHE II, SAPS II , CURB 65 and qSOFA scores. Also high alveolar arterial (A-a O2) gradient and increased length of stay in ICU and length of NIV usage in ICU were predictors for NIV failure.

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ANNEXURE 1 : PROFORMA

DATA COLLECTION PROFORMA

PATIENT NAME:

AGE:

SEX:

IP/OP NO:

HR:

PR:

BP:

SPO2:

PaO2/FiO2:

GCS SCORE

Best eye response
If local injury, edema, or otherwise unable to be assessed, mark "Not testable (NT)"
Spontaneously (+4)
To verbal command (+3)
To pain (+2)
No eye opening (+1)
Not testable (NT)

Best verbal response
If intubated or otherwise unable to be assessed, mark "Not testable (NT)"
Oriented (+5)
Confused (+4)
Inappropriate words (+3)
Incomprehensible sounds (+2)
No verbal response (+1)
Not testable/intubated (NT)

Best motor response
If on sedation/paralysis or unable to be assessed, mark "Not testable (NT)"
Obeys commands (+6)
Localizes pain (+5)
Withdrawal from pain (+4)
Flexion to pain (+3)
Extension to pain (+2)
No motor response (+1)

Not testable (NT)

GCS SCORE –

CURB 65 SCORE-

CONFUSION (NO-0,YES-1)
BUN>19mg/dl(>7 mmol/L) (NO-0, YES-1)
RR>30 (NO-0, YES-1)
SBP<90mmHG or DBP <60mmHG (NO-0, YES-1)
AGE >65 YRS (NO-0, YES-1)

qSOFA SCORE

GCS< 15 (NO-0, YES-1)
RR>22 (NO-0, YES-1)
SBP<100 (NO-0, YES-1)

ABG

pH
Po2
Pco2
Hco3
So2

APACHE II SCORE

History of severe organ failure or immunocompromise
Heart Failure Class IV, cirrhosis, chronic lung disease, or dialysis-dependent NO- , YES-

Age
YEARS

Temperature
C

Mean arterial pressure
mmHG

pH

Heart rate/pulse
bpm

Respiratory rate
breaths/min

Sodium

mmol/L

Potassium
mmol/L

Creatinine
micromol/L

Acute renal failure
Note: "acute renal failure" was not defined in the original study. Use clinical judgment to determine whether patient has acute kidney injury. NO - , YES-

Hematocrit
%

White blood cell count
x 10^9 cells/L

Glasgow Coma Scale
points

FiO_2
<50% (or non-intubated)
≥50%

PaO2, mmHg
>70
61-70
55-60
<55

A-a gradient

<200
200-349
350-499
>499

SAPS 2 SCORE

Age, years
<40 0
40-59 +7
60-69 +12
70-74 +15
75-79 +16
≥80 +18

Heart rate
If patient had both cardiac arrest (11 points) and extreme tachycardia (7 points), assign 11 points

<40 +11
40-69 +2
70-119 0
120-159 +4
≥160 +7

Systolic BP, mmHg
Worst value in 24 hours

<70 +13
70-99 +5
100-199 0
≥200 +2

Temperature ≥39ºC (102.2ºF)
Highest temperature in 24 hrs

N0- 0 , YES- +3

GCS

Lowest value in 24 hours; if patient is sedated, record estimated GCS before sedation

14-15	**0**
11-13	+5
9-10	+7
6-8	+13
<6	+26

PaO_2/FiO_2, if on mechanical ventilation or CPAP

Use lowest value in 24 hours; if patient was extubated <24 hours ago, use lowest value while on mechanical ventilation

<100 mm Hg/% (13.3 kPa/%)	+11
100-199 mm Hg/% (13.3-26.5 kPa/%)	+9
≥200 mm Hg/% (26.6 kPa/%)	+6
Not on mechanical ventilation or CPAP within the last 24 hours	**0**

BUN, mg/dL or serum urea, mmol/L

BUN <28 or urea <10	**0**
BUN 28-83 or urea 10-29.6	+6
BUN ≥84 or urea ≥30	+10

Urine output, mL/day

If in ICU <24 hours, calculate for 24 hours (e.g. if 1 L in 8 hours, then mark 3 L in 24 hours)

<500	+11
500-999	+4
≥1000	**0**

Sodium, mEq/L or mmol/L

Worst value in 24 hours

<125	+5
125-144	**0**
≥145	+1

Potassium, mEq/L

Worst value in 24 hours

<3.0	+3
3.0-4.9	**0**
≥5.0	+3

Bicarbonate, mEq/L

Lowest value in 24 hours

<15	+6
15-19	+3
≥20	**0**

Bilirubin

Highest value in 24 hours

<4.0 mg/dL (<68.4 µmol/L)	**0**
4.0-5.9 mg/dL (68.4-102.5 µmol/L)	+4
≥6.0 mg/dL (≥102.6 µmol/L)	+9

WBC, x $10^3/mm^3$

Worst value in 24 hours

<1.0	+12
1.0-19.9	**0**

≥20.0	+3
Chronic disease	
None	**0**
Metastatic cancer	+9
Hematologic malignancy	+10
AIDS	+17
Type of admission	
Scheduled surgical = surgery scheduled ≥24 hours prior; medical = no surgery within 1 week of admission; unscheduled surgical = surgery scheduled ≤24 hours prior	
Scheduled surgical	**0**
Medical	+6
Unscheduled surgical	+8

ANNEXURE II: PHOTOGRAPHS

PHOTOGRAPH 1 :MAQUET SERVO ICU VENTILATOR

PHOTOGRAPH 2: ORONASAL NIV MASK

ANNEXURE III : KEY TO MASTER CHART

PaO2/FiO2 – Ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen

GCS- Glassgow coma scale

APACHE II – Acute physiological and chronic health evaluation score

SAPS II – Simplified acute physiological score

qSOFA- quick sequential organ failure assessment score

LOS(total)-total length of stay in hospital

LOS(ICU)- Length of stay in ICU

LOS(NIV)-Length of NIV usage

A-a O2 – Alveolar arterial oxygen gradient

ANNEXURE IV : MASTERCHART