كليـــــــة الطب
والصيدلة - مراكش
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Analysis of sedation related complications in critically ill patients: Risk assessement and prevention strategies

THESIS

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BY

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Born On 16th of February 2000 in Marrakech

TO OBTAIN THE DEGREE OF DOCTOR OF MEDECINE

KEY WORDS

Sedation – Adult ICU – Complications

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{رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ
وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ وَأَصْلِحْ
لِي فِي ذُرِّيَّتِي إِنِّي تُبْتُ إِلَيْكَ
وَإِنِّي مِنَ الْمُسْلِمِينَ}

سورة النمل الآية : 19

بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

قَالُوا۟ سُبْحَٰنَكَ لَا عِلْمَ لَنَآ إِلَّا مَا عَلَّمْتَنَآ ۖ إِنَّكَ أَنتَ ٱلْعَلِيمُ ٱلْحَكِيمُ ﴿٣٢﴾

صَدَقَ ٱللَّهُ ٱلْعَظِيمُ

سورة البقرة ٢:٢٣

Hippocratic Oath

I swear to fulfill, to the best of my ability and judgment, this covenant :
I will respect the hard-won scientific gains of those physicians in whose steps I walk, and gladly share such knowledge as is mine with those who are to follow.
I will apply, for the benefit of the sick, all measures [that] are required, avoiding thosetwin traps of overtreatment and therapeutic nihilism.
I will remember that there is art to medicine as well as science, and that warmth,sympathy, and understanding may outweigh the surgeon's knife or the chemist'sdrug.
I will not be ashamed to say "I know not," nor will I fail to call in my colleagues whenthe skills of another are needed for a patient's recovery.
I will respect the privacy of my patients, for their problems are not disclosed to methat the world may know.
Most especially must I tread with care in matters of life and death.
If it is given me to save a life, all thanks.
But it may also be within my power to take a life ; this awesome responsibility mustbe faced with great humbleness and awareness of my own frailty.
Above all, I must not play at God.
I will remember that I do not treat a fever chart, a cancerous growth, but a sick
human being, whose illness may affect the person's family and economic stability.
My responsibility includes these related problems, if I am to care adequately for thesick.
I will prevent disease whenever I can, for prevention is preferable to cure.
I will remember that I remain a member of society, with special obligations to all myfellow human beings, those sound of mind and body as well as the infirm.

Geneva, 1948

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291	CHATAR Achraf	Pr Ass	Urologie
292	OUMGHAR Nezha	Pr Ass	Biophysique

293	HOUMAID Hanane	Pr Ass	Gynécologie-obstétrique
294	YOUSFI Jaouad	Pr Ass	Gériatrie
295	NACIR Oussama	Pr Ass	Gastro-entérologie
296	BABACHEIKH Safia	Pr Ass	Gynécologie-obstétrique
297	ABDOURAFIQ Hasna	Pr Ass	Anatomie
298	TAMOUR Hicham	Pr Ass	Anatomie
299	IRAQI HOUSSAINI Kawtar	Pr Ass	Gynécologie-obstétrique
300	EL FAHIRI Fatima Zahrae	Pr Ass	Psychiatrie
301	BOUKIND Samira	Pr Ass	Anatomie
302	LOUKHNATI Mehdi	Pr Ass	Hématologie clinique
303	ZAHROU Farid	Pr Ass	Neurochirugie

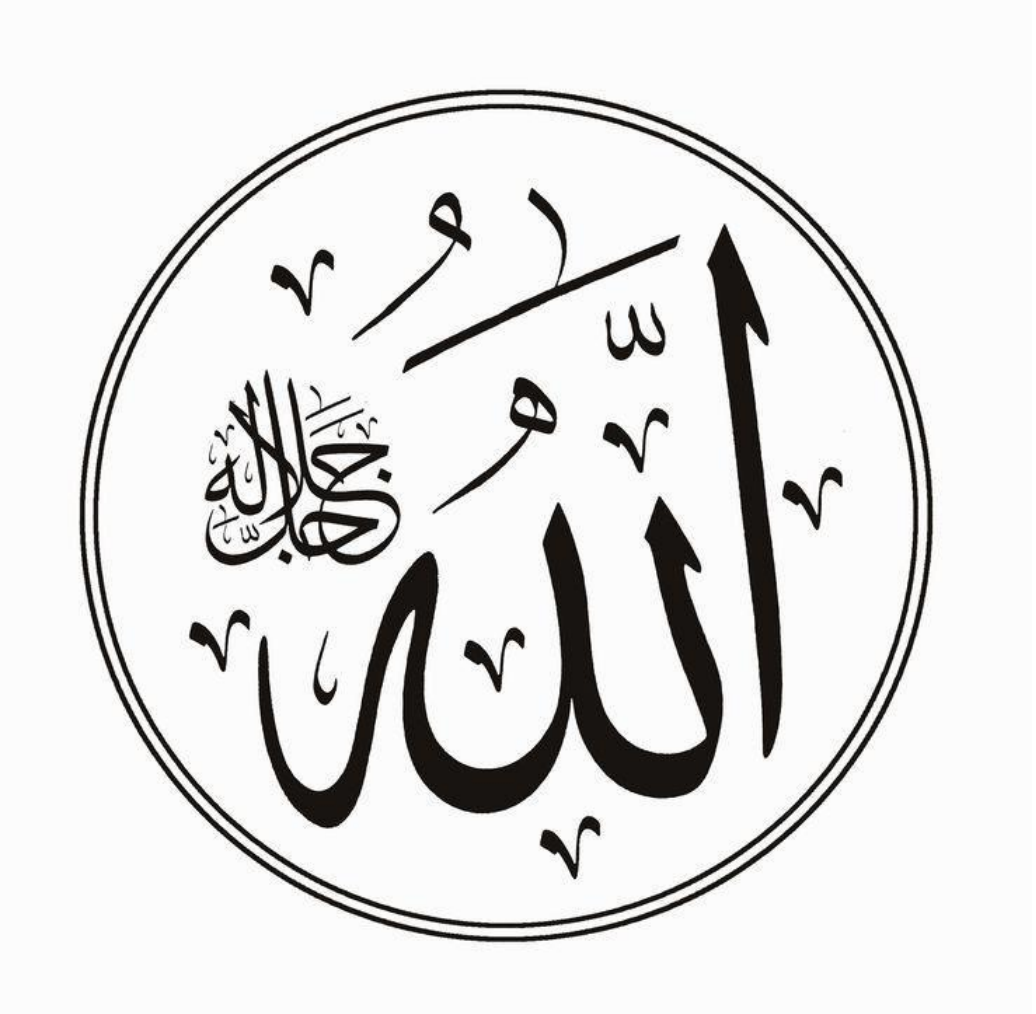
304	MAAROUFI Fathillah Elkarim	Pr Ass	Chirurgie générale
305	EL MOUSSAOUI Soufiane	Pr Ass	Pédiatrie
306	BARKICHE Samir	Pr Ass	Radiothérapie
307	ABI EL AALA Khalid	Pr Ass	Pédiatrie
308	AFANI Leila	Pr Ass	Oncologie médicale
309	EL MOULOUA Ahmed	Pr Ass	Chirurgie pédiatrique
310	LAGRINE Mariam	Pr Ass	Pédiatrie
311	OULGHOUL Omar	Pr Ass	Oto-rhino-laryngologie
312	AMOCH Abdelaziz	Pr Ass	Urologie
313	ZAHLAN Safaa	Pr Ass	Neurologie
314	EL MAHFOUDI Aziz	Pr Ass	Gynécologie-obstétrique
315	CHEHBOUNI Mohamed	Pr Ass	Oto-rhino-laryngologie
316	LAIRANI Fatima ezzahra	Pr Ass	Gastro-entérologie
317	SAADI Khadija	Pr Ass	Pédiatrie
318	DAFIR Kenza	Pr Ass	Génétique
319	CHERKAOUI RHAZOUANI Oussama	Pr Ass	Neurologie
320	ABAINOU Lahoussaine	Pr Ass	Endocrinologie et maladies métaboliques
321	BENCHANNA Rachid	Pr Ass	Pneumo-phtisiologie
322	TITOU Hicham	Pr Ass	Dermatologie
323	EL GHOUL Naoufal	Pr Ass	Traumato-orthopédie

324	BAHI Mohammed	Pr Ass	Anesthésie-réanimation
325	RAITEB Mohammed	Pr Ass	Maladies infectieuses
326	DREF Maria	Pr Ass	Anatomie pathologique
327	ENNACIRI Zainab	Pr Ass	Psychiatrie
328	BOUSSAIDANE Mohammed	Pr Ass	Traumato-orthopédie
329	JENDOUZI Omar	Pr Ass	Urologie

330	MANSOURI Maria	Pr Ass	Génétique
331	ERRIFAIY Hayate	Pr Ass	Anesthésie-réanimation
332	BOUKOUB Naila	Pr Ass	Anesthésie-réanimation
333	OUACHAOU Jamal	Pr Ass	Anesthésie-réanimation
334	EL FARGANI Rania	Pr Ass	Maladies infectieuses
335	IJIM Mohamed	Pr Ass	Pneumo-phtisiologie
336	AKANOUR Adil	Pr Ass	Psychiatrie
337	ELHANAFI Fatima Ezzohra	Pr Ass	Pédiatrie
338	MERBOUH Manal	Pr Ass	Anesthésie-réanimation
339	BOUROUMANE Mohamed Rida	Pr Ass	Anatomie
340	IJDDA Sara	Pr Ass	Endocrinologie et maladies métaboliques
341	GHARBI Khalid	Pr Ass	Gastro-entérologie
342	ATBIB Yassine	Pr Ass	Pharmacie clinique
343	EL GUAZZAR Ahmed (Militaire)	Pr Ass	Chirurgie générale
344	MOURAFIQ Omar	Pr Ass	Traumato-orthopédie
345	HENDY Iliass	Pr Ass	Cardiologie
346	HATTAB Mohamed Salah Koussay	Pr Ass	Stomatologie et chirurgie maxillo faciale

LISTE ARRETEE LE 04/10/2024

DEDICATIONS



First and foremost, I thank Allah Almighty for blessing me with the opportunity to be here today and for granting me the honor of influencing people's lives. I am grateful for His answered prayers and for His mercy throughout this hard and rocky journey.

Alhamdulillah, now and forever.

To my beloved Father Boubker Gallal

Thank you for being my backbone and my unwavering support system.
Becoming a doctor was not only a dream of mine but a choice I made with you in mind, inspired by your strength and dedication.
I know life hasn't always been easy on you, and I'm well aware of the countless sacrifices you've made to give me every opportunity.
I love you more than anything else, and I grew up feeling fearless because I knew I had you to protect me.
I've always been proud of you, and I hope that, through this accomplishment and all that follows, I've made you proud as well.
Every step of this journey has been driven by the example you've set one of resilience, integrity, and compassion.
This dedication is a tribute to your strength and to the love that has made me who I am today.

To my dear Mother : Halima Belhirch

You instilled in me the values that serve as the foundation of this work: the importance of education, the strength that comes from dedication, and the relentless pursuit of excellence.
Your belief in the power of hard work and knowledge has guided me through every challenge and triumph in this journey.
I am endlessly grateful for the wisdom, strength, and passion for learning that you have passed down to me.
This thesis is as much a testament to your influence as it is to my work.

To my brothers Mohamed and Abdolah

You are the joy of our family, and the most beautiful gift from God.
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I hope that through this accomplishment, I can make you as proud as you make me every day. May this work reflect the gratitude I feel for having you in my life and my commitment to making you proud of the person and professional I am becoming.

To my sisters Mohsana and Aya

Growing up together created a bond that I hold dear, and I hope that distance or time never changes that.
We have shared dreams, hopes, and countless memories, and it is my greatest wish that each of our successes be celebrated as a collective achievement.
Your encouragement, love, and laughter have carried me through, and I hope this accomplishment reflects the strength of the bond we share.
Let this be one of the many achievements we can celebrate together, as always.

To my Grandfather Hajj Moukhtar belhirch, may ALLAH bless his soul:

Your absence is an ever-present grief, and the wonderful memories we shared only make it harder to let go.
I wish you were here to witness this milestone and to celebrate this accomplishment with me; I know it was your dream as much as it is mine.
Your prayers and unwavering faith in me have remained with me, guiding me through every step, even beyond your last breath. For that, I can never thank you enough.
Your love and guidance live on in me, and this achievement is as much yours as it is mine.

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You are the sweetness of our family, the warmth that makes your home feel like ours.
Your kindness and love create a place of comfort and refuge, where we can come to ease our minds and hearts.
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You are one of the purest and most genuine souls I have ever encountered.
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To my dear Lamiaa Frej

Thank you for all the beautiful memories we've shared.
Each moment with you has added joy and meaning to my life, and I'm so grateful for every laugh, adventure, and late-night talk we've had together.
Here's to cherishing the memories we've made and to many more to come!"

To all my friends old friends that have blessed me with their support every step of the way
This work is dedicated to you. Thank you for everything
To all my beloved family and friends who have blessed me with their unwavering love and support, To all my professors from university who generously shared their knowledge with us, To all my professors throughout my academic journey, especially those who believed in me, I wouldn't be here without you.
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Thesis Chairman
Head of the Intensive Care Departement – IBN TOFAIL

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MY Mentor and Thesis Supervisor
Head of the Surgical Intensive Care Departement – CHU MED VI

My chief tutor, who welcomed me from the very first day and introduced me to this subject:
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Thank you for your guidance and advice, your unwavering enthusiasm, encouragement, and support whenever needed.
You have made this work less stressful.
Please accept this modest work as a sincere expression of my gratitude and deepest respect.

To Professor H. REBAHI,
Thesis Jury member
Professor of Anesthesia and Intensive Care – CHU MED VI
Thank you for the great honor you bestow upon us by accepting to be part of this esteemed committee. Your willingness to contribute your time, expertise, and valuable insights is truly appreciated.
Please accept my sincerest expression of high esteem, utmost consideration, and deep respect.

Professor M. EL KHAYARI,
Thesis Jury member

Professor of Anesthesia and Intensive Care – CHU MED VI

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Professor M.CHRAA,
Thesis Jury member

Professor of Neurology – CHU MED VI

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I am deeply appreciative of the time and dedication you have given to reviewing my work, as well as the insightful guidance that has enriched this research.

Thank you for your support and for helping me reach this important milestone.

List of tables and figures

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List of Abbreviations

ICU	Intensive care unit
SICU	Surgical intensive care unit
TBK	Tuberculosis
ARDS	Acute Respiratory Distress Syndrome
COPD	Chronic obstructive pulmonary disease
DSI	Daily sedation interruptions
IMV	Invasive mechanical ventilation
VAP	Ventilator-associated pneumonia
VAC	Ventilator-associated conditions
IVAC	Infection-related ventilator-associated complications
PVAP	Possible ventilator-associated pneumonia
HAI	Hospital-associated infection
ETT	Endotracheal tube
HAP	Hospital-acquired pneumonia
UE	Unplanned extubation
AHRF	Acute hypoxemic respiratory failure
CAM-ICU	Confusion Assessment Method for the Intensive Care Unit
ICDSC	Intensive Care Delirium Screening Checklist

VTE	Venous thromboembolism
ICU-AW	ICU acquired weakness
CIP	Critical illness polyneuropathy
CIM	Critical illness myopathy
MOF	Multiple organ failure
LOS	Length of stay
PLOS	Prolonged length of stay
CNS	Central nervous system
SAT	Spontaneous awakening trials
SBT	Spontaneous breathing trials
DSI	Daily Sedative Interruption
NP	Nurse-Protocolize
NIH	National institues of health

OUTLINE

INTRODUCTION

The use of sedative agents in medical practice dates back to the 19th century, when substances such as ether and chloroform were introduced to induce loss of consciousness and insensitivity to pain, allowing surgical procedures to be performed without distress to patients. These early innovations marked the beginning of modern anesthesia and sedation, providing an invaluable tool for the practice of surgery.[1] Over the centuries, significant advances have been made in pharmacology and clinical sedation techniques, progressively refining both the safety and efficacy of sedation protocols.[2]

In recent decades, sedation has evolved from a solely surgical intervention to an essential component of care across various medical fields, particularly in critical care settings. Over the past ten years, the role of sedation in intensive care units (ICUs) has become increasingly well-established as part of routine care. In the ICU, the judicious use of sedative agents is pivotal for ensuring patient comfort, minimizing anxiety, and enabling the successful performance of both diagnostic and therapeutic procedures. For patients requiring prolonged immobility, such as those undergoing mechanical ventilation or invasive procedures, sedation becomes indispensable, contributing to a more manageable and less stressful experience for both patients and healthcare providers.

The therapeutic goals of sedation in the ICU extend beyond mere patient comfort. Proper sedation reduces pain and anxiety, which are known to have deleterious effects on critically ill patients by exacerbating physiological stress responses, potentially leading to adverse outcomes.[3] By mitigating these stressors, sedation can contribute to improved overall outcomes, including faster recovery times, fewer complications, and enhanced patient cooperation dur- ing necessary interventions.

However, despite the clear benefits, the administration of sedation in critical care settings must be approached with caution due to the potential for significant side effects and complications. The pharmacodynamics of sedative agents, particularly in critically ill patients, can be unpredictable, and inappropriate use or dosing can result in adverse outcomes. Common complications related to sedation include respiratory depression, hemodynamic instability, prolonged sedation, delirium, and an increased risk of infections due to immobility and

reduced airway clearance. [4] In addition, patients with pre-existing comorbidities or thosereceiving multiple medications may have an elevated risk of adverse events related to sedation. [5] The challenge for healthcare providers lies in striking a balance between the beneficial effects of sedation and its potential risks. To this end, the development and application ofevidence-based sedation protocols are crucial in optimizing patient care and reducing complications. [2]

The present study aims to address this critical issue by conducting a retrospective analysis of sedation practices in the ICU of University Hospital Center Mohamed VI. By reviewing patient data over a one-year period, we seek to identify and assess the prevalence of sedation-related complications, as well as the factors that may predispose certain patients to these adverse events. In particular, we aim to evaluate the impact of various sedation protocols on patient outcomes, including the duration of sedation, the need for mechanical ventilation, and the occurrence of complications such as respiratory depression, hemodynamic instability, and delirium.

In addition to identifying and assessing complications, this study seeks to provide insights into potential preventive measures. By understanding the patterns and risk factors associated with sedation-related complications, we aim to propose strategies to mitigate these risks and improve patient outcomes. These prevention strategies will be based on the data collected and supported by a review of the existing literature, with the goal of enhancing sedation management protocols in the ICU.

In summary, the objectives of this study are threefold:

1- To analyze data collected from ICU patients to identify specific complications associated with sedation.
2- To assess the prevalence and severity of these complications and identify the risk factors that contributes to their occurrence.
3- To propose evidence-based prevention strategies aimed at minimizing sedation-related complications and improving patient care outcomes in critical care settings.

By addressing these objectives, we aim to contribute to the growing body of knowledge on sedation management in the ICU, ultimately enhancing patient safety and optimizing clinical outcomes.

Patient and Methods

I. Study Design:

This is a retrospective descriptive and analytical study assessing complications due to sedation in surgical intensive care unit of University Hospital Center Mohamed 6.

II. Duration of the study:

The study was conducted over one-year period from june 2022 to june 2023; and Included 104 patients.

III. Inclusion and Exclusion Criteria:

All patients who received sedation in the intensive care unit (ICU) during the specified one-year period.

IV. Exclusion criteria:

- Patients who were not sedated during their admission.
- Patient who were not initialy sedated in surgical intensive care unit.
- Patients with incomplete medical records.

V. Sampling:

All patients who were sedated in the surgical intensive care unit of the Mohamed VI University Hospital in Marrakech and who met the inclusion criteria were included in the study.

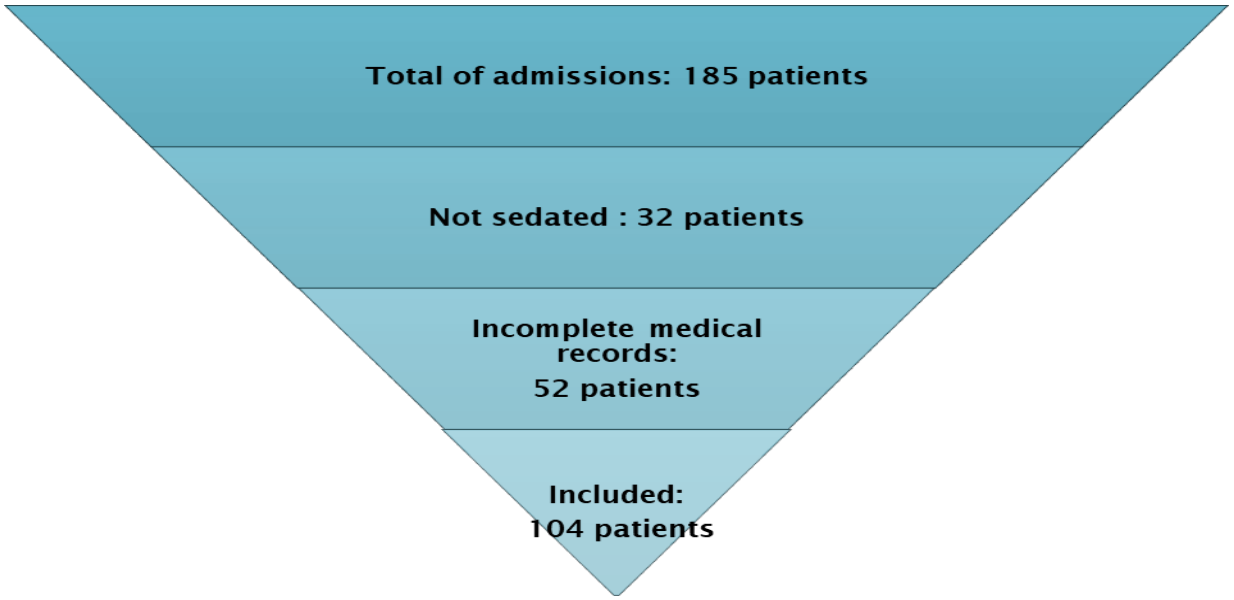


Figure1: Sampling size and characteristics

VI. Measuring methods:

1. Data Collection:

Epidemiological, clinical, paraclinical, and therapeutic data were collected for each patient from medical records and nursing monitoring sheets. These data were gathered using a predefined data collection form. (Annex 1)

Data analysis was conducted using Microsoft Excel, with the Chi-square test applied to determine p-values and evaluate the statistical significance of associations between risk factors and outcomes. This approach facilitated a rigorous examination of the data, enabling the identification of significant relationships and contributing to a comprehensive

2. Variables Studied:

For each record, the studied variables included:

a) Epidemiological Data:

Information collected included the patient's age, sex, and comorbidities.

b) Clinical Data:

A comprehensive clinical examination was conducted on all patients, which included a meticulous assessment of lesions, rigorous monitoring of clinical progression, and close observation of vital signs.

The indications for sedation, the depth and duration of sedation, the co-administration of analgesics, the utilisation of mechanical ventilation, and the administration of concomitant medications were also evaluated.

c) Paraclinical Data:

Biological assessments: conducted based on the patient's condition, progression, and proposed therapies

Radiological assessments: performed as required by the clinical situation.

d) Ethical Aspects:

Data collection was conducted with strict respect for anonymity and confidentiality of patient information.

e) Limitation of the study :

The analysis of the BMI variable was not possible due to the unavailability of the relevant medical records.

During the initial eight-month phase of the study, midazolam was unavailable in the ICU unit. Consequently, propofol was employed as an alternative.

It is common for patients with critical illness to have additional underlying medical conditions. In this case, we could not definitively determine whether the complication was due to sedation or was a manifestation of the patient's pre-existing medical condition.

RESULTS

DESCRIPTIVE RESULTS

I. Demographic results

1. Sex of included patients

A total of 104 patients were included in the study from June 2022 to June 2023. The majority of patients were male (n = 82), representing 80% of the total sample, while only 20% of our study population were female. With a sex ratio of 4/1.

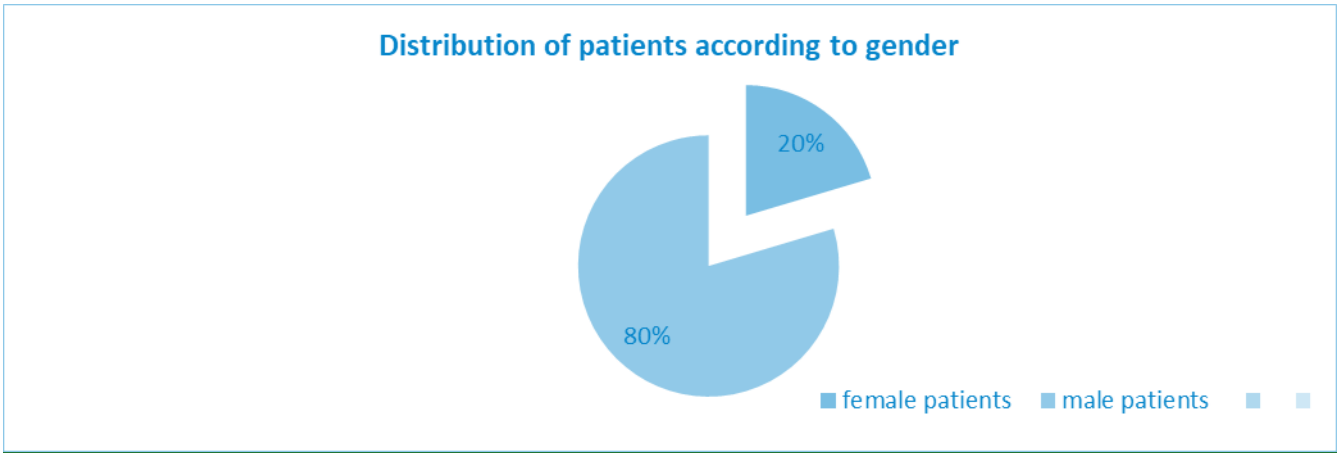


Figure 2: Gender of included patients

2. The age distribution of patients:

The mean age of our study population is 28.84 years, with the majority being under 50 years old. The age range spans from 17 to 84 years.

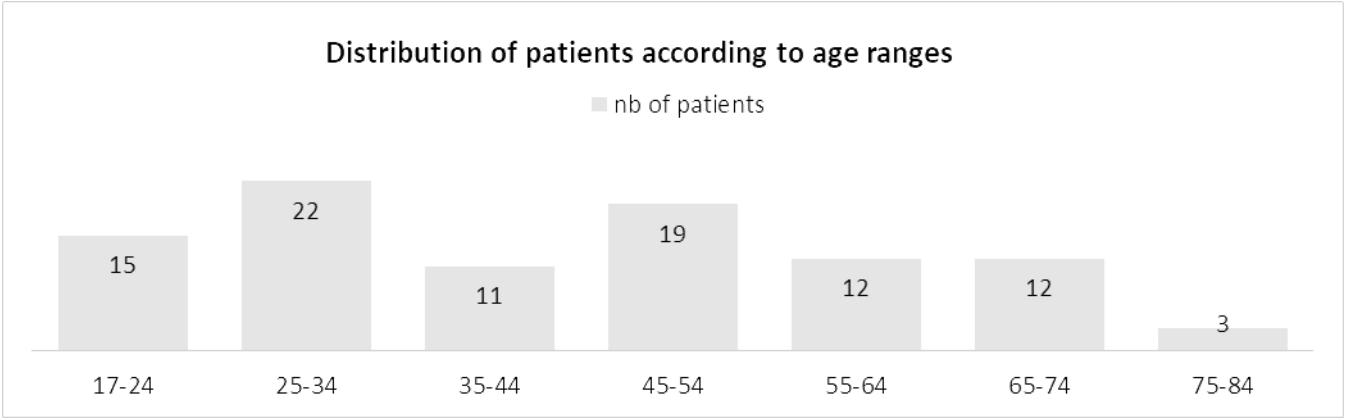


Figure 3: Distribution of patients by age groups

The distribution of patients by age reveals that the study population is predominantly young to middle-aged adults, with the majority of patients in the 25-34 and 45-54 age groups.

The representation of older adults, particularly those aged 75-84 years, is significantly lower.

This distribution suggests a focus on a relatively younger population.

3. Admission diagnostics:

Poly trauma represents the most common diagnosis, affecting 37 patients, approximately 35.9% of the total study population.

Cranial trauma represents the second most common diagnosis, affecting 21 patients (20.4% of the study population).

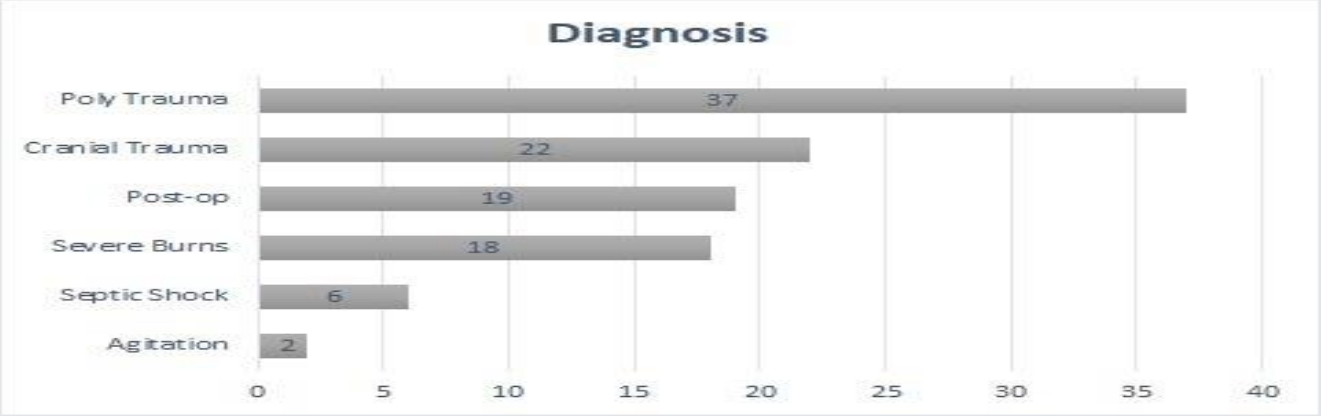


Figure 4: distribution of patients by admission diagnostics

The third most common group of patients is post-operative patients, who account for 19 patients; approximately 18.4% of the overall total.

Severe burns were the cause of admission for 18 patients, representing 17.5% of our total.

Six patients suffered from septic shock, which constituted 5.8% of our total.

Two patients exhibited signs of agitation, representing 1.9% of the study population due to ketoacidosis in one case and intracerebral expansive lesion in the other.

4. Comorbities:

In our series seventy one percent of patients presented with no comorbidities upon admission.

The most prevalent comorbidities were high blood pressure and mellitus diabetes, occurring in 7% of cases each.

Heart diseases in 5% of cases including ischemic and non ischemic cardiopathies.

Thyroid dysfynction, neuropathy such as parkinson desease and epilepsia, COPD and TBK each accounted for 2%.

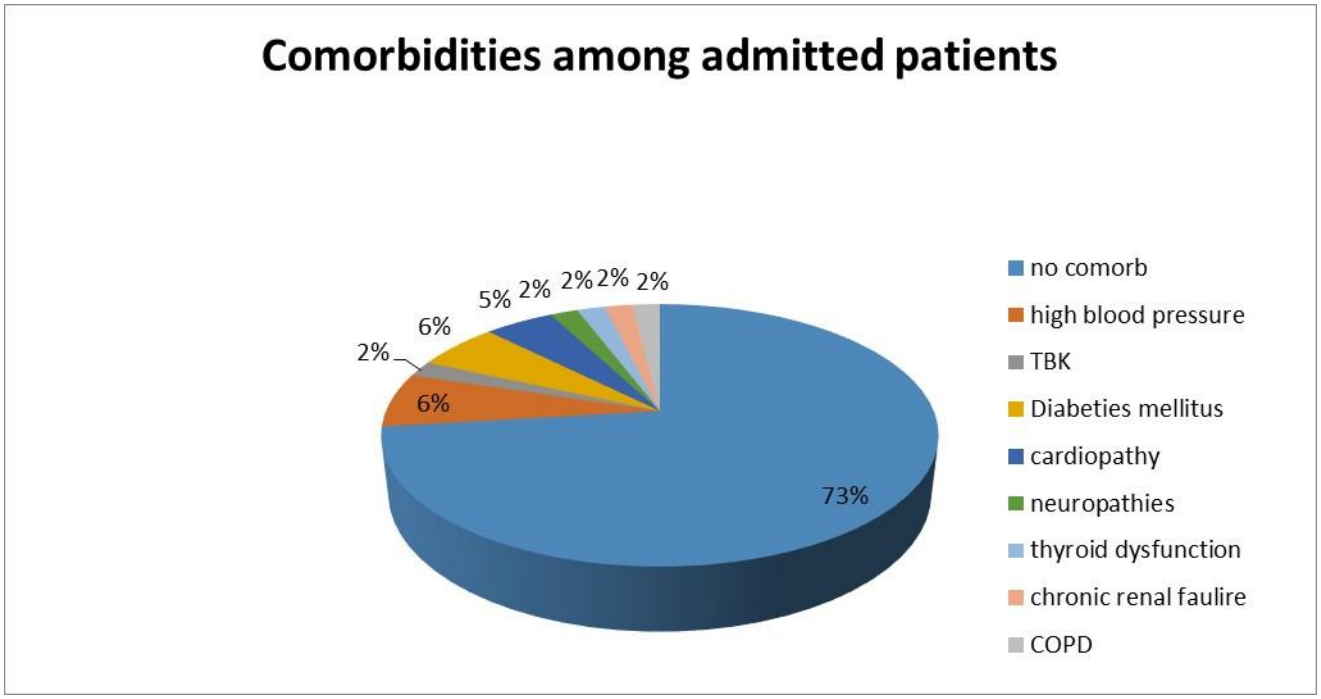


Figure 5: Comorbidities among admitted patients

5. Lenght of stay:

The average length of stay in the ICU is 8.91 days with a minimum of 1 day and a maximum of 53 days.

II. Sedation management

1. Initial sedation indications

HTIC is the most common initial indication for sedation, within 45 patients. This represents 43,27 % of our study population.

HTIC occurs both in severe cranial trauma and in polytrauma with associated severe cranial trauma.

Hemodynamic instability is the second most common reason for sedation with 29 patients; secondary to polytrauma, septic shock and postoperative hypovolaemia.

Mechanical ventilation accounts for 11 patients who have been admitted with acute respiratory distress.

Severely burned patients account for 9 cases where sedation was required for analgesic purposes.

Agitation is the indication for sedation in 5 patients, agitation was secondary to keto acidosis in 2 cases and to refractory epileptic seizure disorder in the 3 remaining.

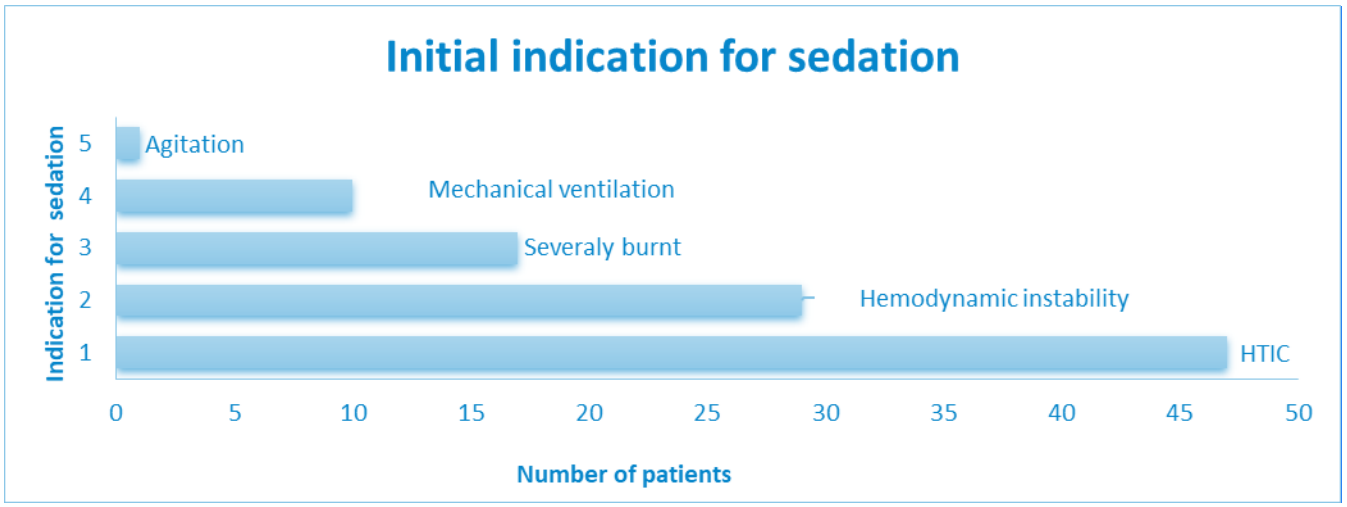


Figure 6: Indications for sedation in intensive care

The predominant reasons for sedation in our population are related to HTIC and hemodynamic instability.

The need for sedation is less common in patients with burns, those on mechanical ventilation or those with agitation.

2. The average duration of sedation

The mean duration of sedation in our series is 5.5 days, with the shortest period being 24 hours and the longest 40 days.

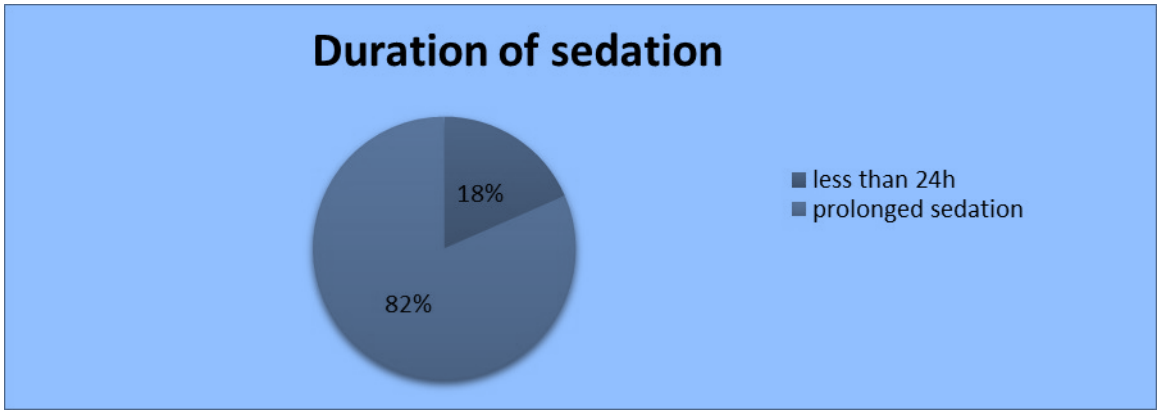


Figure7: Short term vs prolonged sedation

82% of patients underwent prolonged sedation, defined as a period exceeding 24 hours, compared with only 18% who were sedated for a shorter duration.

3. Depth of sedation:

In order to estimate the depth of sedation we used the Ramsay score. [6]

The Ramsay Sedation Scale is a clinical tool used to assess the level of sedation in critically ill patients.

It scores sedation from 1 to 6, with higher numbers indicating deeper levels of sedation.

As following:

1. Patient is anxious and agitated, or restless, or both.
2. Patient is cooperative, oriented, and tranquil.
3. Patient responds to commands only.
4. Brisk response to a light glabellar tap or loud auditory stimulus.
5. Sluggish response to a light glabellar tap or loud auditory stimulus.
6. No response to a light glabellar tap or loud auditory stimulus[6].

A Ramsay score above 4 defines deep sedation.

The majority of our patients were deeply sedated with Ramsay scare not less than 4(92.30%).

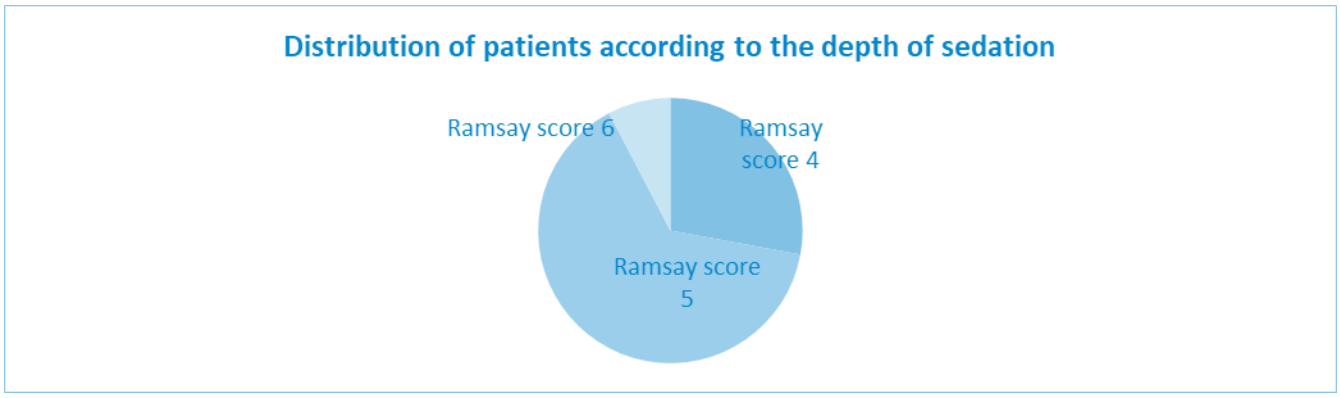


Figure 8: Depth of sedation in our serie of patients

A total of 8 patients (7.69%) were asleep with no response to glabellar tap or loud auditory stimulus corresponding to a Ramsay score of 6.

Sixty seven patients were asleep with slow response to light glabellar tap or loud auditory stim-ulus corresponding to a Ramsay score of 5.

Twenty nine were asleep with rapid response to light glabellar pressure or to a loud auditorystimulus corresponding to a Ramsay score of 5.

4. Distribution of patients according to the protocole used:

A continuous infusion of a sedatives was used in 91.34% of cases (n=95 patients), whereas a bolus administration was used in only 9 patients.

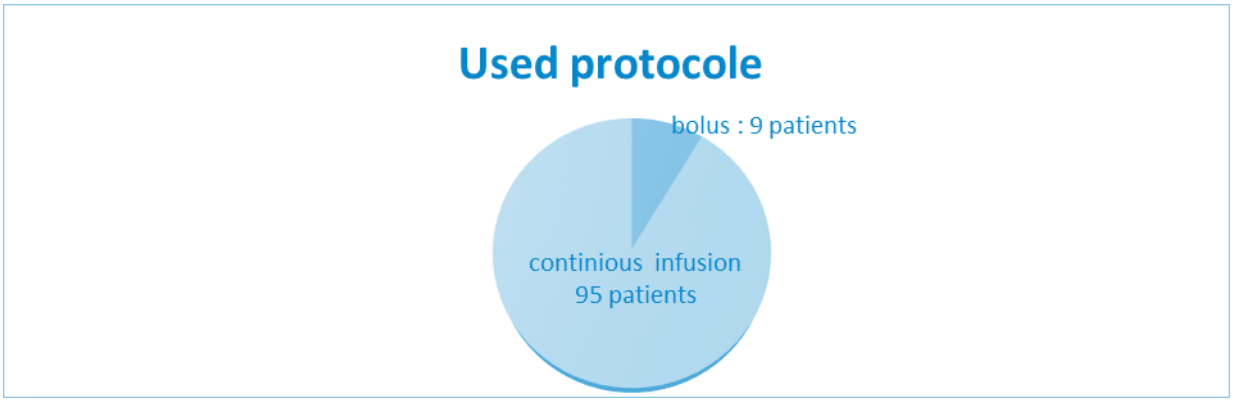


Figure 9: Distribution of patients according to the protocole used.

According to the data cited, the prescription of sedatives is largely dominated by continuous infusion.

5. Distribution of patients according to the sedative medication used

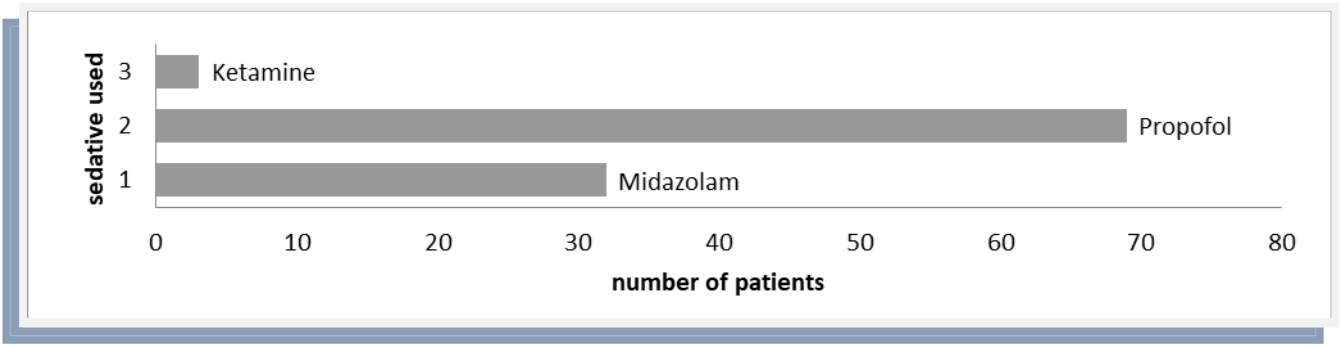


Figure 10: Distribution of patients according to the sedative medication used

Among the patients in our series, 69 were sedated with propofol (66.99 %), 32 with midazolam, and only three with ketamine.

Fentanyl was identified as the analgesic associated with the sedatives among all patients.

6. Use for mechanical ventilation:

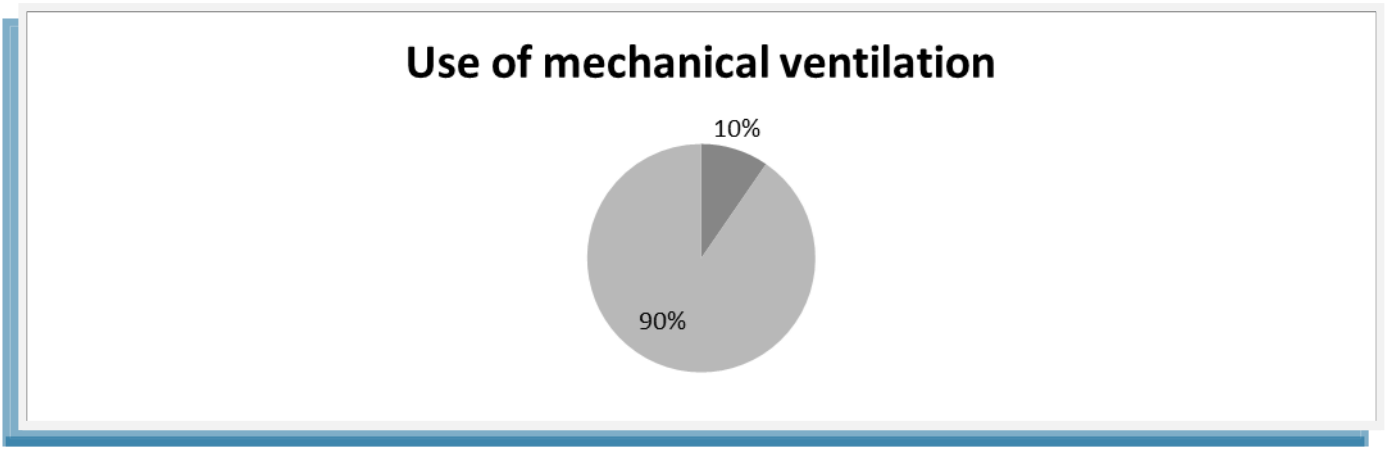


Figure 11: Use of mechanical ventilation

90% of the patients were on mechanical ventilation. While only 10 % received a vigilent sedation.

The mean duration of mechanical ventilation was 5.25 days, with a minimum of 1 day and a maximum of 20 days.

III. Complications assessement

1. Respiratory complications:

A total of 41 patients presented with a respiratory infection, representing 39% of the total number of patients.

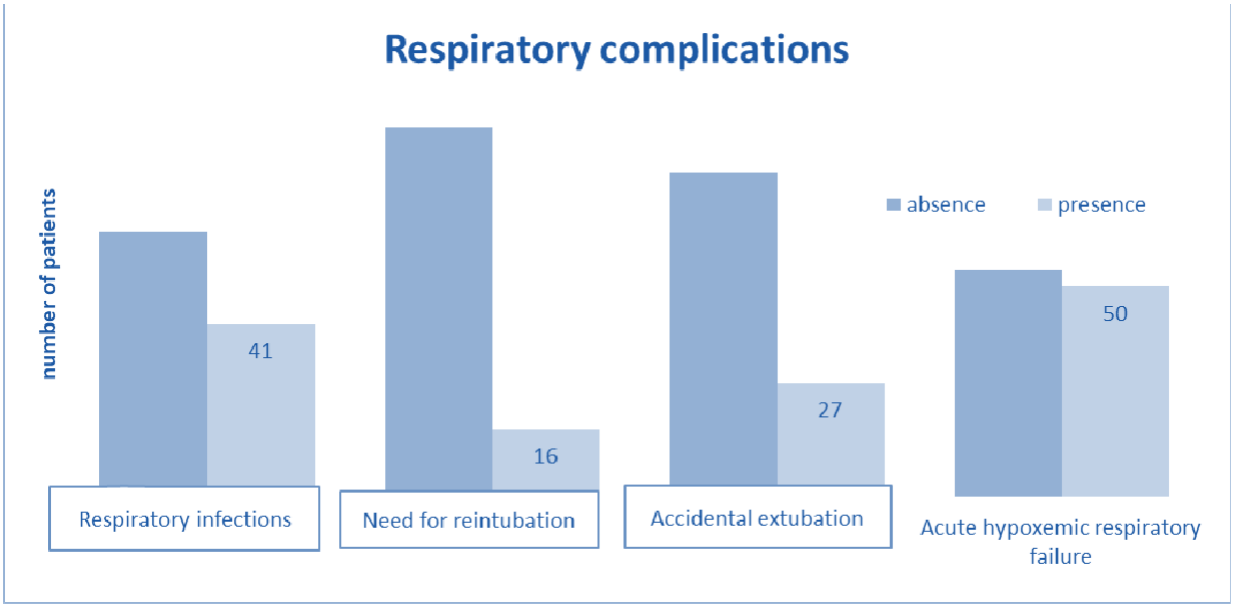


Figure 12: Respiratory complications

Additionally, there were 50 instances of acute hypoxemic respiratory failure during ICU stay counting for 48% among the sedated.

27 patients (25.96%) experienced an accidental extubation, while 16 required reintubation (15.34%).

2. Neurological complications:

a) Delirum assessement

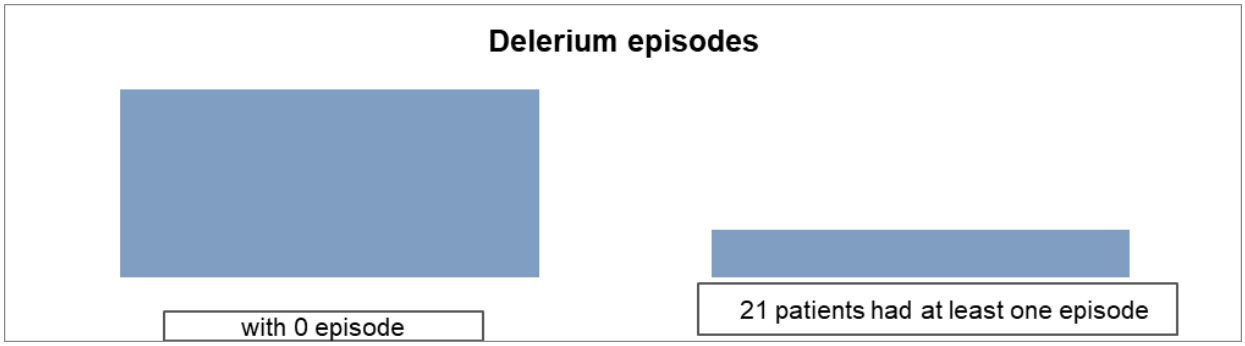


Figure 13: Delirium episodes

A total of 21 patients experienced at least one episode of delirium, representing 20.19% of all admissions.

The mean duration of delirium episodes was 15.85 hours.

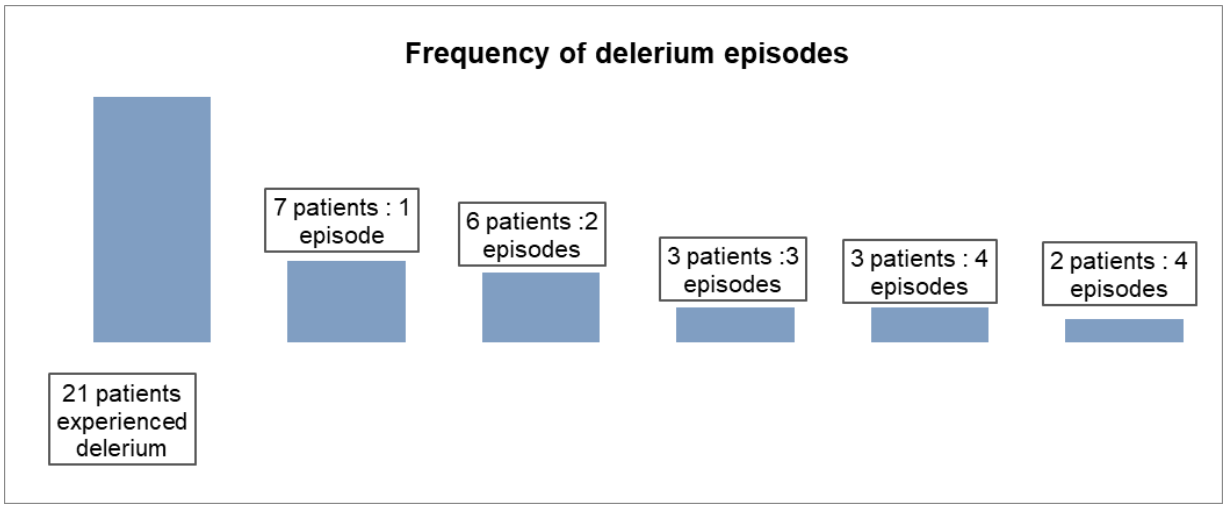


Figure 14: Frequency of delirium episode

Twenty one patients experienced at least one delirium episode.

Recurrent delirium episodes (2 or more) are present in a notable proportion of patients, but fewer patients experience higher numbers of episodes (4 or more).

3. Decubitus complications

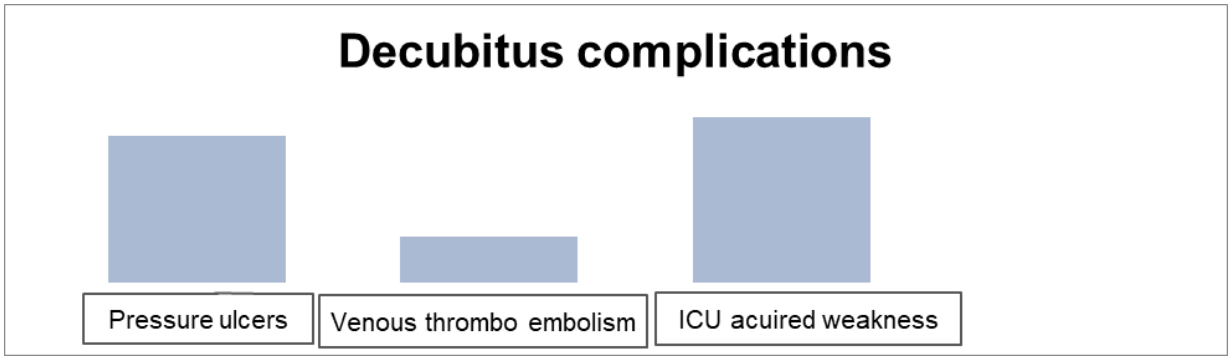


Figure 15: Decubitus complications

The most common complications among patients are ICU-acquired weakness (n=36) and pressure ulcers (n=32); representing respectively 34.62% and 30.76%, possibly related to prolonged bed rest or lack of physiotherapy.

Thromboembolism is less common (n=10), possibly due to prolonged immobilisation or other factors related to the patient's health status.

4. The incidence and prevalence of adverse drug events:

The most common side effects are those related to blood pressure (hy-po/hypertension) and tachycardia.

The occurrence of hyperthermia and delayed awakening may indicate is less common in our study.

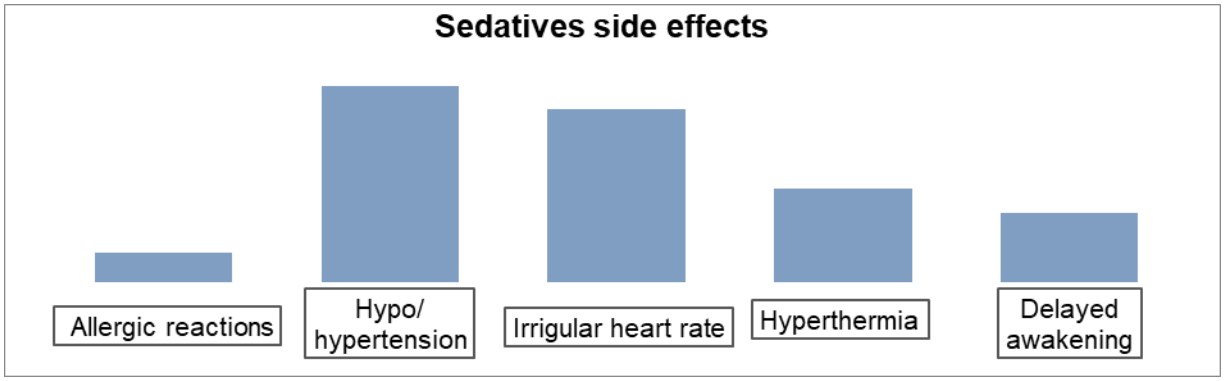


Figure 16: The incidence and prevalence of adverse drug events

Fifty nine patients had experienced at least one side effect, with vascular side effects being the most common (n=59), followed by irrigular hear rate (n=52) ; with tachycardia occuring in38 cases and bradycardia in 14 cases.

Hyperthermia accured within 28 patients; delayed awakening within 21 (20%), while allergic reactions in 9 patients (8.6%).

IV. Outcome measures

1. Cost increase and erros related to sedation:

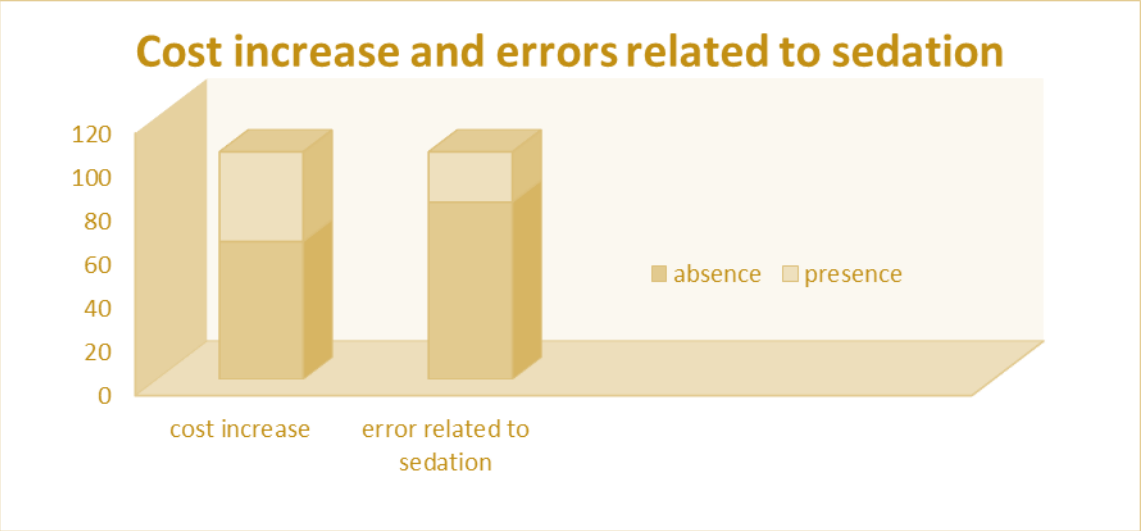


Figure17: Cost increase and errors related to sedation administration

A cost increase was observed in 41 cases, representing 39.42% of patients, cost increased is due to a prolonged length of stay or the occurance of a complication related to sedation.

A total of 23 cases were identified in which errors were made in the administration of sedation.

We counted as errors non-adherence to the indication, prolonged sedation and use of inappropriate medication.

In our series, there were a total of 65 deaths, representing a proportion of 62.5% of our patients.

V. Discharge facilities:

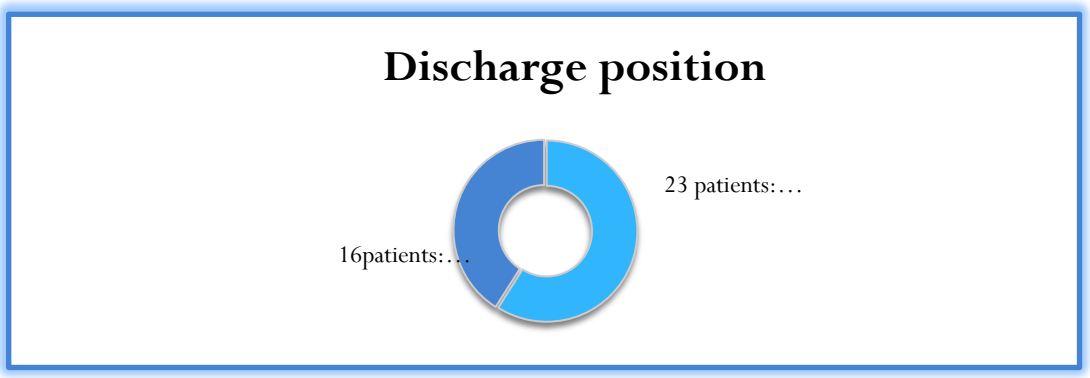


Figure 18: The distribution of patients according to their discharge facilities

Twenty-three patients were discharged to a different hospital facility representing 59%, while 16 were transferred to a rehabilitation facility representing 41%.

Analytical results:

Table 1: Analytical results

	Age <75 years	Age>75 years	p	Comment
	40	1	1.0	Not significant
	No comorbidities	comorbidities		
	28	3	1.0	Not significant
ICU-AP	Vigilent sedation	Ventilated	0.019	Significant
	0	41		
	Short term sedation	Prolonged sedation	0.000034	Highly significant
	2	39		
	Age < 75 years	Age ≥ 75 years	1.0	Not significant
	16	0		
Unplanned Extubation	Midazolam	Propofol	1.0	Not significant
	5	11		
	Short-term sedation	Prolonged sedation	0.0098	Significant
	0	16		
	Age < 75 years	Age ≥ 75 years	0.57	Not significant
	13	3		
	No comorbidities	comorbidities	0.22	Not significant
	10	6		
	Sedation less than 4 days	Sedation over 4 days	0.01	Significant
Need for reintubation	1	15		
	Vigilent sedation	Ventilated	0.001	Highly significant
	0	16		
	Age < 75 years	Age ≥ 75 years	1	Not significant
	42	8		
	No comorbidities	comorbidities		

	34	16	0.368	Not significant
Acute hypoxemic respiratory failure during ICU	Sedation less than 4 days	Sedation over 4 days	0.001	Highly significant
	50	0		
	Vigilent sedation	Ventilated	0.001	Highly significant
	50	0		
Delerium Assessement	Age < 75 years	Age ≥ 75 years	0.269	Not significant
	50	0		
	No comorbidities	Comorbidities	0.277	Not significant
	43	7		
	Propofol	Midazolam	0.884	Not significant
	35	15		
	Other than HTIC	HTIC	0.0199	Significant
	21	29		
	Vigilant sedation	Ventilated	0.0041	Significant
	0	50		
	Short-term sedation	Prolonged sedation	0.00003	Highly significant
	5	45		
Bedsores	Age < 75 years	Age ≥ 75 years	0.591	Not significant
	32	0		
	No comorbidities	Comorbidities	0.536	Not significant
	18	3		
	Vigilant sedation	Ventilated	0.063	Borderline signifi-cant
	0	32		
	Short-term sedation	Prolonged sedation	0.00019	Highly significant
	1	31		
	Length of stay < 4 days	Length of stay ≥ 4 days	0.00015	Highly significant
	0	32		
	Age < 75 years:	Age ≥ 75 years	1.0	Not significant
	10	0		

		No comorbidities	Comorbidities	1.0	Not significant
		7	3		
		Vigilant sedation	Ventilated	0.119	Not significant
	DVT	0	10		
		Short-term sedation	Prolonged sedation	0.029	Significant
		0	10		
		Length of stay < 5 days	Length of stay ≥ 5 days	0.029	Significant
		0	10		
		Age < 75 years	Age ≥ 75 years	0.847	Not significant
		22	0		
		No comorbidities	Comorbidities	0.254	Not significant
	ICU Acquired	13	9		
		Vigilant sedation	Ventilated	0.188	Not significant
	Weakness	0	22		
		Short-term sedation	Prolonged sedation	0.001	Highly significant
		0	22		
		Length of stay < 6 days	Length of stay ≥ 6 days	0.000003	Highly significant
		0	22		
		Propofol	Midazolam		
	Allergic Reaction	6	3	1.0	Not significant
Adverse drug events	Hypo/ Hypertension	Propofol	Midazolam	1.0	Not significant
		40	19		
	Tachycardia	Propofol	Midazolam	0.676	Not significant
		37	15		
	Delayed awake-ning	Propofol	Midazolam	0.512	Not significant
		21	7		
	Length of Stay > 4 days	No sedation-related complication	sedation-related complication	0.000002	Highly significant
Outcome mesures		19	47		
	Mortality	No sedation-related complication	sedation-related complication	0.013	Significant
		24	41		

DISCUSSION

I. Main findings

1. Respiratory complication

A. Hospital-acquired pneumonia:

The National Institutes of Health (NIH) defines nosocomial pneumonia or HAP as pneumonia that occurs 48 hours or more after hospital admission and is not present at the admission time. VAP represents a significant subset of HAP occurring in intensive care units.

Pneumonia was defined-since guidelines of 2005 as the presence of « new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin, which includes the new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation ». [7]

Our data analysis indicates that prolonged sedation (short-term sedation: 2 vs prolonged sedation: 39 / p-value: 0.000034) and mechanical ventilation (vigilant sedation: 0 vs ventilated: 41 / p-value: 0.019) are the primary predisposing risk factors for the development of respiratory infections in our patients.

These two factors significantly compromise the respiratory system, impairing the patients' ability to clear secretions and increasing their susceptibility to infections.

Prolonged sedation is particularly concerning because it leads to reduced patient mobility, suppression of cough reflexes, and weakening of the muscles responsible for respiration.These effects collectively create an environment conducive to infection.

Similarly, mechanical ventilation can bypass the body's natural airway defenses, allowing pathogens to enter the respiratory tract more easily, which further elevates the risk of infection. [8]

Contrary to common assumptions in clinical settings, our study did not find a significant association between advanced age (age $<$ 75 years: 40 vs age $\geq$ 75 years: 1 / p-value: 1.0) or the presence of comorbidities (no comorbidities: 28 vs comorbidities: 3 / p-value: 1.0) and the development of respiratory infections in this cohort.

Although elderly patients and those with multiple health conditions are often considered more vulnerable to complications. [9] Our data suggest that these factors may not independently contribute to infection risk when sedation and mechanical ventilation are already present.

These results underline the critical importance of carefully managing sedation duration and ventilator use to reduce the risk of respiratory infections.

Proactive measures such as optimizing sedation protocols, early weaning from mechanical ventilation, and implementing infection prevention strategies may help mitigate this risk in surgical ICU patients.

B. Unplanned Extubation:

Unplanned extubation is the accidental removal of an endotracheal tube (ETT) or tracheostomy tube that had been placed to provide mechanical ventilation or airway support in a patient. [10]

This can occur either because the patient deliberately removes the tube (self-extubation) or due to accidental displacement by healthcare staff or during patient movement or repositioning.

The data from our study reveal that prolonged sedation is the only significant risk factor associated with accidental extubation in sedated patients.

Patients who were sedated for over 24h exhibited a higher incidence of unplanned extubation, suggesting that the duration of sedation directly impacts the likelihood of this complication (short-term sedation: 0 vs prolonged sedation: 16 / p-value: 0.0098).

Interestingly, our analysis showed that neither advanced age (age $<$ 75 years: 16 vs age $\geq$ 75 years: 0 / p-value: 1.0) nor the specific type of sedative used (midazolam: 5 vs propofol: 11 / p-value: 1) were linked to an increased risk.

C. Need for reintubation:

The data from our study reveal that prolonged sedation (prolonged sedation: 15 vs short term sedation :1 / p-value :0.01) and ventilation for over 5 days(ventilation< 5 days :0 vs ventilation >5 days : 16 / p-value :0.01) are the only significant risk factors associated with reintubation in sedated patients.

Patients who were sedated for over 4 days, and or ventilated over 5 days exhibited a higher incidence of need for reitubation, suggesting that the duration of sedation directly impacts the risk of this complication.

Interestingly, our analysis showed that neither advanced age (age < 75 years: 13 vs age ≥ 75 years: 3 / p-value: 0.57), nor comorbidities (no comorbidities: 10 vs comorbidities: 6 / p-value: 0.22) were linked to an increased risk for this particular complication.

D. Acute hypoxemic respiratory failure:

Similar to reintubation our data reveal that prolonged sedation (especially over 4 days) and ventilation for over 5 days (ventilation< 5 days: 0 vs ventilation >5 days: 50 / p-value: 0.001) are the only significant risk factors associated with AHRF.

Patients who were sedated for over 4 days (prolonged sedation: 50 vs short term sedation: 0 / p-value: 0.001), and or ventilated over 5 days exhibited a higher incidence of this complication, suggesting that the duration of sedation directly impacts its occurance.

Interestingly, our analysis showed that neither advanced age (age < 75 years: 42 vs age ≥ 75 years: 8 / p-value: 1), nor comorbidities (no comorbidities: 34 vs comorbidities: 16 / p-value: 0.37) were linked to an increased risk.

2. Delerium assessement:

ICU delirium is defined as an acute and fluctuating disturbance of consciousness, attention, cognition, and perception that occurs in critically ill patients. It typically develops over a short period (hours to days) and represents an underlying physiological disturbance. [11]

The diagnostic criteria generally include: acute onset and fluctuating course, inattention disorganized thinking and altered level of consciousness. ICU delirium can be classified as hyperactive, hypoactive, or mixed, with the hypoactive form often being underdiagnosed. [12]

Diagnosis is based on clinical assessment, often using validated tools like the Confusion Assessment Method for the ICU (CAM-ICU) or the Intensive Care Delirium Screening Checklist (ICDSC). [13]

Our study highlights that prolonged sedation is the most significant risk factor for the development of delirium in critically ill patients (prolonged sedation : 45 vs short term sedation : 5 / p-value : 0.003).

Additionally, both mechanical ventilation (vigilant sedation: 0 vs ventilated: 50 / p-value: 0.004) and the presence of cranial hypertension (other than HTIC: 21 vs HTIC: 29 / p-value: 0.019) were found to be equally responsible for the occurrence of delirium.

Regarding the type of sedative used, our analysis indicated that there was no excess risk of delirium associated with midazolam or propofol (midazolam: 15 vs propofol: 35 / p-value: 0.88). This suggests that the choice between these two commonly used sedatives may not significantly impact the risk of developing delirium.

Additionaly neither with age (age $<$ 75 years: 50 vs age $\geq$ 75 years: 0 / p-value: 0.26) nor comorbidities (no comorbidities: 43 vs comorbidities: 7 / p-value: 0.27) were linked to an increased risk.

3. Decubitus complications:

A. Bedsores:

Bedsores or pressure ulcers are localized areas of tissue damage that occur due to prolonged pressure on the skin, typically affecting patients who are immobilized. These injuries can develop rapidly in critically ill patients, particularly those with limited mobility and altered consciousness. The combination of pressure, shear forces, and moisture creates an environment conducive to skin breakdown. [14]

In our study, prolonged sedation (prolonged sedation : 31 vs short term sedation : 1 / p-value : 0.0002) ; and extended length of hospital stay (length of stay< 4 days:0 vs length of stay >4 days : 32 / p-value:0.00015) were identified as the two most significant risk factors for the development of pressure ulcers.

The association of mechanical ventilation with pressure ulcer occurrence was determined to be borderline significant (vigilant sedation: 0 vs ventilated: 32 / p-value: 0.063).

Furthermore, neither advanced age (age $<$ 75 years: 32 vs age $\geq$ 75 years: 0 / p-value: 0.59) nor the presence of comorbidities (no comorbidities: 18 vs comorbidities: 3 / p-value: 0.53) were identified as independent risk factors contributing to the development of this complication.

Preventive measures, including regular repositioning, use of specialized mattresses, and diligent skin care, are essential in mitigating the risk of pressure ulcers in this vulnerable population.

Early identification and management of these injuries are crucial to improve patient outcomes and reducing healthcare costs. [15]

B. Venous thrombosis:

Venous thromboses include deep vein throbosis and pulmonary embolism.

Deep vein thrombosis (DVT) refers to the formation of one or more thrombi in one of the body's large veins, most commonly in the lower limbs. [16]

The most serious complication that can arise from DVT is a pulmonary embolism (PE) which occurs in over one-third of DVT patients. [17]

According to our database analysis, prolonged sedation (prolonged sedation: 10 vs short term sedation: 0 / p-value: 0.029) and a hospital stay longer than five days (length of stay< 5 days: 0 vs length of stay >5 days: 10 / p-value: 0.029) have emerged as the only significant independent risk factors for the development of DVT.

These factors likely contribute to a patient's reduced mobility and altered physiological responses, creating conditions favorable for clot formation. [18]

On the other hand, variables such as advanced age (age < 75 years: 10 vs age ≥ 75 years: 0 / p-value: 1.0), the presence of comorbidities (no comorbidities: 7 vs comorbidities: 3 / p-value: 1.0), and the use of mechanical ventilation (vigilant sedation: 0 vs ventilated: 10 / p-value: 0.119), which are often considered potential contributors to DVT, were not found to be statistically significant in our study.

This suggests that while these factors may play a role in overall patient health, they do not independently elevate the risk of DVT in a meaningful way in the population we analyzed.

Our findings emphasize the importance of focusing on patient immobility and extended hospitalization when assessing DVT risk.

C. ICU acquired weakness

Intensive care unit-acquired weakness (ICU-AW), a common neuromuscular complication associated with patients in the ICU, is a type of skeletal muscle dysfunction that commonly occurs following sepsis, mobility restriction, hyperglycemia, and the use of glucocorticoids or neuromuscular blocking agents. [19]

ICU-AW can lead to delayed withdrawal of mechanical ventilation and extended hospitalization. [20]

Our database identifies two key independent risk factors for ICU-AW: prolonged sedation, particularly with increasing duration (prolonged sedation: 22 vs short term sedation: 0 /

P-value: 0.001), and a hospital stay exceeding six days (length of stay< 6 days: 0 vs length of stay >6 days: 22 / p-value: 0.000003).

Prolonged sedation is likely to contribute to muscle atrophy and reduced neuromuscular activity, which in turn increases the vulnerability to weakness.

Similarly, extended hospital stays often reflect more severe or complex illnesses that may require immobilization or extended bed rest, further heightening the risk of ICU-AW. [21]

Conversely, factors such as advanced age (age < 75 years: 22 vs age ≥ 75 years: 0 / p-value: 1.0), existing comorbidities (no comorbidities: 13 vs comorbidities: 9 / p-value: 1.0), and the use of assisted ventilation (vigilant sedation: 0 vs ventilated: 22 / p-value: 0.188) do not appear to independently contribute to the occurrence of ICU-acquired weakness.

While these factors may influence the patient's overall health and recovery, they were not statistically significant in our analysis for this specific complication.

This suggests that interventions to mitigate ICU-AW should prioritize minimizing sedation duration and addressing the challenges associated with prolonged hospital stays, rather than focusing solely on these other variables. [22]

4. Adverse drug events:

Previous study has shown that the use of different analgesic and sedative drugs has a variety of adverse reactions with the most common adverse effects being: allergic reactions, hyperthermia, hypo/hypertension, tachycardia and delayed awakening. [23]

We also assessed the incidence of propofol infusion syndrome, although this is a rare condition due to its severity.

According to our database, the analysis revealed no statistically significant differences in the incidence of key adverse events, including allergic reactions (propofol : vs midazolam : p-value :), hemodynamic events (propofol : 6 vs midazolam : 3 / p-value : 1.0), tachycardia episodes (propofol : 37 vs midazolam : 15 p-value : 0.67), or delayed awakening (propofol : 21 vs midazolam : 7 p-value : 0.51), between patients receiving propofol and those receiving midazolam.

This suggests that both anesthetic agents exhibit a comparable safety profile in these areas.

Furthermore, no instances of propofol infusion syndrome were detected throughout the duration of the study.

5. Outcomes measures:

Sedation-related complications are a significant and independent risk factor for mortality in the intensive care unit (No sedation-related complications: 24 vs sedation-related complications: 41 / p-value: 0.013).

Beyond increasing the risk of death, these complications contribute to prolonged hospital stays (No sedation-related complications: 19 vs sedation-related complications: 47 / p-value: 0.000002), which can lead to further medical complications and delays in recovery.

This extended hospitalization not only affects patient outcomes but also imposes a substantial financial burden on healthcare systems due to increased resource utilization and associated costs.

As a result, minimizing sedation-related risks is critical for improving both patient safety and cost-efficiency in the ICU.

II. Assessement of dermographic characteristics:

1. Age and sex:

Demographic characteristics vary widely between populations; to compare these differences in critically ill patients, we collected the results of previous studies to compare with our findings.

For example, in the multicentre study of Edsberg et al. [24] Involving over 290 000 patients, the population was predominantly older adults, with a mean age of 64.29 years, which is consistent with the studies by Rosa et al. [25] and Gong et al. [26]

In terms of gender, we find an equal distribution between male and female in the USA and Brazil, whereas the ratio M/F is 2/1 in China.

Table 2 : Distribution of age and sex among different ICUs :

First author	Gong et al. (2019) [26]	Rosa et al. (2019) [25]	Edsberg et al (2019) [24]	Our study (2023)
Country	China	Brazil	USA	**Morocco**
Number of patients	749	1685	296,014	**104**
Mean age	62.9	58.5	64.29	**28.84**
Male %	68.4 %	52.8 %	49.4%	**76.9%**
Female%	31.6 %	47.2 %	50%	**23.1%**
M/F ratio	**2/1**	**1**	**1**	**4/1**

The mean age of our 104 patients is approximately 29 years, which is considerably younger than the age distribution observed in other countries.

Our males to females ratio is 4:1. These findings differ from those reported in the literature, which may be attributed to the demographic characteristics of the country.

2. Comorbidities:

It is widely accepted that co-morbidities represent an additional risk factor for the development of complications in intensive care settings. However, the distribution of these comorbidities is highly variable.

To illustrate this, we will examine the study conducted by Ahlstrom et al. [27]
In this study, approximately three-quarters of patients had comorbidities, with heart disease being the most prevalent condition in 30.6% of cases, followed by arterial hyperten- sion and diabetes present in 23.6% and 13.8% of cases, respectively.
while asthma was present in 4.1%. Renal failure and COPD were present in 3.8% of cases each, and organ transplantation was present in 1.2% of patients.

According to our data analysis 71% of our patients presented with no comorbidities.
The most prevalent complications in our serie were high blood pressure and diabetes mellitus, occurring in 7% of cases each.
Heart diseases were present in 5% of cases, including ischaemic and non-ischaemic cardiopathies. Thyroid dysfunction, neuropathy (such as Parkinson's disease and epilepsy), COPD and TBK accounted for 2% each.

Table 3: A comparaison between a swedish study and ours in term of comorbidities

First Author	Ahlström et al. (2024)[27] Sweden	Our series
Number of patient	7382	104
Patients with no co-morbidities	16.2%	71%
Ischemic/ non-ischemic heart disease	30.6%	5%
Hypertension	23.6%	7%
Diabetes mellitus	13.8%	7%
Stroke	2.9%	0%
Chronic renal failure	3.8%	2%
COPD	3.8%	2%
Asthma	4.1%	0%
organ transplant	1.2%	0%

By comparing the data from the two studies we notice a lower prevalence of heart disease and diabetes, these common comorbidities are significantly less prevalent in our study, and the same goes for hypertension and COPD.

Overall, our study population had fewer comorbidities, suggesting a generally healthier baseline than the Swedish cohort study.

This comparison highlights the variability in comorbidity distribution across different populations in intensive care settings.

III. Admission diagnostics:

Admission diagnostics are broadly divided into 3 main categories: medical, post-surgical and traumatic admissions.

Comparing the findings from litterature we notice that most admissions are for medical pathologies, however a dispaty exists between the studies of Nunes et al [28] (82%) and Aragón et al [29] (72.4%) compared to Al-Shareef (43.35%) et al [30] and Hyun et al [31] (48.6%).

The patients admited for traumatic lesions range from 11.6% to 30.5% of the ICU admissions.

The proportion of patients admitted for postoperative care in our study (18.5%) is similar to that reported by Nunes et al. (18%) and Hyun et al. (20.7%), but higher than that observed by Al-Shareef et al. (7.3%) and Aragón et al. (6.9%).

In our series trauma patients represents the most common admission diagnostic, with poly trauma affecting 37 patients (35.9%) and cranial trauma affecting 21 patients (20.4%).

The second most common group is post-operative patients, who account for 19 admissions (18.4%).

Among our patients admitted for medical reasons we find : 18 severely burnt patients (17.5%), 6 cases for acute respiratory distress (5.8%) and 2 patients exhibited signs of agitation due to ketoacidosis in one case and intracerebral expansive lesion in the other one. With a cumulative rate of 25.2% of medical admissions.

Table 4: Distribution of admission diagnostics

First author	Al-Shareef et al [30]	Aragón et al [29]	Hyun et al [31]	Nunes et al [28]	Our study
Number of patients	233	1338	631	152	104
Admission diagnosis	medical 43.35%	medical 72.4%	medical 48.6%	medical 82%	medical 25.2%
	trauma patients 13.3%	trauma 11.6%	trauma 30.5%	post-op and trauma 18%	trauma 56.3%
	post-op 7.3%	post-op 6.9%	post-op 20.7%		post-op 18.5%

Our study reports the highest percentage of trauma patients among all studies, accounting for 56.3% of admissions, compared to 13.3% in Al-Shareef et al. and 11.6% in Aragón et al.

These findings highlight a distinct focus on trauma-related admissions within a younger, predominantly male cohort, with fewer comorbidities.

This demographic profile can be largely explained by the epidemiological context of road traffic accidents, which disproportionately affect younger males.

The high prevalence of trauma admissions in this population is therefore consistent with these risk patterns, making road accidents a leading cause of ICU admissions in younger, otherwise healthier individuals.

IV. Sedation management:

1. Initial indication of sedation:

In the ICU, sedation is used to manage a variety of clinical scenarios. The main indications for sedation in ICU patients include:

- Respiratory indications: sedation is often required to facilitate mechanical ventilation, reduce the discomfort of the endotracheal tube, and improve synchrony with the ventilator. Furthermore; sedation may be used to decrease the patient's oxygen consumption, particularly in conditions like respiratory failure, acute respiratory distress syndrome (ARDS), or shock. [32]
- Hemodynamic stability: sedation may help stabilize patients with cardiovascular instability by reducing the stress response and preventing sympathetic overactivation.[33]
- Anxiety and agitation control: ICU patients can experience anxiety or agitation due to their critical illness, invasive procedures, or the ICU environment itself. Sedation helps maintain calmness and reduces psychological distress.[34]
- Pain Management: sedation is often combined with analgesics to help manage pain, especially in patients undergoing invasive procedures or with traumatic injuries.[34]
- Intracranial Pressure (ICP) Control: in patients with traumatic brain injury, stroke, or other neurological conditions, sedation can help control elevated ICP and prevent secondary brain injury.[35]
- Facilitation of Procedures: sedation is necessary for various diagnostic and therapeutic procedures, such as bronchoscopy, endoscopy, and insertion of central lines.[36]

Each patient’s sedation requirements are individualized based on their condition, clinical goals, and the balance between sedation depth and the need for neurological assessments.

2. Sedative used; protocol and duration:

a. Sedative used

In our study, patients were sedated using either propofol or midazolam, which allowed us to directly compare our results with other studies that employed these two sedatives. The usage patterns of midazolam and propofol for sedation in adult ICUs show considerable variability across different researchs.

The literature review highlights significant variability in sedative use across different studies, underscoring the lack of a universal standard for choosing sedatives in ICU settings.

For example, in a study by Sun et al, 51.9% were sedated with a combination of propofol and fentanyl, while 48.1% received midazolam and fentanyl. [37]

A retrospective analysis from Payen et al reported a similar split, with 51.9% of patients receiving propofol and 48.1% midazolam. [38]

Comparable results were observed in a study conducted by Akhileshwar et al [39] in this case, sedative use was evenly divided, with 50% of patients receiving propofol and the other 50% midazolam.

In contrast, a single-center study from Saudi Arabia [30] marked preference for midazolam over propofol. In this study, 90.99% of patients were sedated with midazolam, while only 9.01% received propofol. This finding stands out as the most divergent from other studies.

These results illustrate the variability in sedative practices across different regions and institutions, suggesting that no single sedative regimen dominates clinical practice globally.

Table 5: Distribution of propofol and midazolam among different studies

First Author	Our serie	Sun et al. [37]	Payen et al. [38]	Akhileshwar et al. [39]	Al-Shareef et al. [30]
Country	Morocco	China	USA	India	Saudi Arabia
Year	2023	2022	2007	2019	2024
Propofol	66,99%	51.9%	51,9%	50%	9,01%
Midazolam	30,76%	48.1%	48,1%	50%	90,99%

In our cohort, 66.99% of patients were sedated with propofol. The high rate of propofol use can be attributed to an 8-month supply disruption that limited the availability of alternative sedatives. This contrasts with data from the USA, India, and China, which indicate a more balanced use of both propofol and midazolam.

Saudi Arabia, however, reports a markedly different trend, with midazolam being the dominant sedative in their ICUs. These findings highlight regional and situational differences in sedative use.

b. Depth of sedation

Sedation assesement scores

The assessment of sedation in clinical settings is crucial for patient safety and effective management. Various sedation scoring systems have been developed, each with unique strengths. The most notable among these are the Richmond Agitation-Sedation Scale (RASS) and the Ramsay Scale, which have shown reliability and validity in different contexts.

The Richmond Agitation-Sedation Scale (RASS) is a tool used to measure the level of agitation and sedation in patients, commonly in critical care settings. It ranges from 0 to -5 (unarousable), with 0 indicating an alert and calm state.

Presented as the following:

Table 6: The Richmond Agitation-sedation score[40]

Score	Clinical manifestation
0	indicating an alert and calm state
-1	Drowsy : Not fully alert, but has sustained (>10 seconds) awakening to voice (eye contact).
-2	Light sedation : Briefly awakens with eye contact to voice (<10 seconds).
-3	Moderate sedation : Movement or eye-opening to voice but no eye contact.
-4	Deep sedation : No response to voice, but movement or eye-opening to physical stimulation.
-5	Unarousable : No response to voice or physical stimulation

Where a score of ≤ -3 indicated deep sedation.

The RASS was first introduced in 2001 has demonstrated excellent interrater reliability (weighted $\kappa = 0.91$) and validity in detecting changes in sedation status over time .It correlates well with the Glasgow Coma Scale and the administered doses of sedatives. [41]

The Ramsay Scale is recommended for clinical use due to its good correlation with objective measures like auditory evoked potentials, showing a coefficient of determination ($r^2 = 0.6$) .It is also noted for its face validity and reliability. [42]

While these scoring systems are widely used, ongoing research is essential to refine and validate new methods for sedation monitoring, particularly objective measures that can complement subjective assessments. [42]

And lastly the PSI (patient state index) score first introduced in 1998, which is the least used scale among ICU professionals.

The PSI provides a real-time numerical value (usually between 0 to 100) based on electroencephalography (EEG) signals. [43]

This score is typically used in conjunction with other clinical parameters to guide anesthetic dosing and ensure patients are neither under- nor over-sedated:

Table 7: Patient index score [43]

PSI score < 60	Deep Sedation
PSI score 61-80	Mild-Moderate Sedation
PSI score > 80	Awake-Alert

Depth of sedation:

In a multicenter study of Hyun et al., 66.2% of patients were deeply sedated, while 33.8% received light sedation. The study also demonstrated that deep sedation was associated with higher mortality rates, with 14.1% mortality in the deeply sedated group compared to 8.4% in the lightly sedated group. [44]

Similar findings were reported in the study by Grap et al., which included 169 patients, with 62% being deeply sedated and 38% receiving light sedation. [45]

A multicenter cohort study reported by Mehta et al. found that early deep sedation occurred in 71% of patients at the first assessment, dropping to 61% at 48 hours post-assessment. [17]

Table 8: The Profil of sedation depth in critically ill Patients

First Author	Hyun et al. [44]	Grap et al. [45]	Metha et al. [17]	Our serie
Country	Korea	USA	Canada	Morocco
YEAR	2023	2012	2012	2023
Included patients	631	169	430	104
Sedation assessement score	RASS	IPS	RASS	RAMSAY
Light sedation	33.8%	38%	29%	7.67%
Deep sedation	66.2%	62%	61%	92.33%

These findings underscore the significant variation in sedation depth between our study and others, with our cohort demonstrating the highest prevalence of deep to very deep sedation.

In particular, the use of deep sedation in our patient population far exceeds what has been reported in other studies.

For instance, this rate is considerably higher than in comparable research, such as the studies by Hyun et al. (66.2% deep sedation) and Grap et al., where 62% of patients were deeply sedated.

The increased use of deep sedation in our cohort could be attributed to several factors, including institutional practices, patient severity, or specific clinical protocols.

Our findings align with concerns raised in the literature about the association between deep sedation and adverse clinical outcomes. Studies, such as those by Mehta et al. and Hyun et al., have reported that deep sedation is linked to higher mortality, longer duration of mechanical ventilation, and increased ICU stay.

The 92.33% prevalence of deep sedation in our cohort raises important questions about sedation practices and the potential risks involved, emphasizing the need to reassess sedation strategies to ensure a balance between patient comfort and safety.

c. Duration of sedation :

There appears to be no significant temporal variation in the duration of sedation when comparing older studies with more recent research.

For instance, earlier studies such as that of Sanchez-Izquierdo-Riera et al. [46] reported an average sedation duration of 6.3 ± 4.0 days in trauma patients receiving either midazolam or propofol. Similarly, Harris et al. [47] demonstrated that propofol sedation was significantly shorter, with a mean duration of 20.2 hours, compared to midazolam, which averaged 84.5 hours.

Buckley et al. also observed that patients sedated with propofol could remain sedated for over 5 days, further supporting the variability in sedation duration depending on the choice of agent. [48]

More recent studies present comparable findings. For example, Jakob et al. reported that midazolam sedation could extend up to 7–12 days, primarily due to drug accu- mulation. [49]

Additionally, a systematic review by Barr et alconfirmed that midazolam seda- tion typically lasted 7–8 days, while propofol, known for its shorter half-life and more rapid onset and offset, averaged 3–5 days of sedation. [50]

Table 9: Mean duration of sedation across diferent studies

Author	Our se- ries	Harris et al.[47]	Sanchez et al.[46]	Buckley et al.[48]	Jakob et al. [49]	Barr et al [50]
Sedation with Midaz olam	5.5 days	3.5 days	6.3 ± 4.0 days	---	7–12 days	7–8 days
Sedation with propofol	5.5 days	20.2 hours	6.3 ± 4.0 days	5 days	---	3–5 days

Our data, reflect a mean sedation duration of 5.5 days with a range of 24 hours to 40 days, aligns with the historical and contemporary findings. This suggests that, despite ad- vancements in sedation protocols and pharmacological agents, the overall duration of seda- tion in ICU settings has remained relatively stable over time.

These findings highlight the need for ongoing assessment of sedation practices, par- ticularly in light of drug pharmacokinetics and patient-specific factors, to optimize sedation strategies and reduce the potential for complications related to prolonged sedation, such as delayed weaning from mechanical ventilation and prolonged ICU stays.

d. Bolus vs continuous infusions :

Several studies, including the seminal work by Schweickert et al. [51], have demon- strated the advantages of protocol-driven sedation strategies in the intensive care unit.

These protocols typically involve the administration of sedation via intermittent boluses as an initial approach, followed by the introduction of continuous infusions if necessary.

This method has been associated with more rapid patient arousal, reduced duration of mechanical ventilation, and shorter ICU stays.

Additionally, these strategies have been shown to minimize the need for further invasive procedures such as tracheostomies.

Alligning with those guidelines the research conducted by Beigmohammadi et al.[52] reported that intermittent bolus dosing was used in approximately 60.87% of patients, while continuous infusion of midazolam was applied in 39.13% of cases.

Table 10: Bolus vs continuous infusion of sedatives

Frist author	Beigmohammadi et al. [52]	Our series
Year	2013	2023
Bolus	60.87%	8.66%
Continuous infusion	39.13%	91.34%

These findings contrasts with ours, in which the majority of patients (91.34%) were sedated via continuous infusions for prolonged periods.

Such practices are well-documented in the literature to contribute to complications, including delayed arousal, extended mechanical ventilation times, and an increased necessity for tracheostomies. The prolonged use of continuous sedative infusions, especially with benzodiazepines like midazolam, is associated with drug accumulation, which can exacerbate these outcomes.

Further supporting this, a 2021 meta-analysis evaluating propofol sedation demonstrated that while continuous infusions provide more consistent levels of sedation, they tend to prolong mechanical ventilation and ICU stays compared to intermittent bolus dosing.[53]

The risk of sedative drug accumulation and related complications, such as prolonged sedation and delayed weaning from mechanical ventilation, is higher with continuous infusion.

Conversely, intermittent bolus dosing, when judiciously administered, has been shown

to result in shorter ICU stays, faster liberation from mechanical ventilation, and a reduced incidence of sedation-related adverse events.

This body of evidence underscores the importance of selecting appropriate sedation strategies, tailored to each patient's needs, to optimize clinical outcomes and minimize the risks associated with prolonged sedative use in critical care settings.

3. Co-administartion of analgesics:

Fentanyl is widely recognized as one of the primary opioids used for analgesia in ICU settings, particularly in patients requiring mechanical ventilation.

Its prevalence in critical care arises from its high potency, rapid onset of action, and relatively short duration, making it an ideal choice for managing acute and procedural pain in critically ill patients.

Additionally, fentanyl is frequently combined with sedative agents to optimize both analgesia and sedation, facilitating ventilator tolerance and patient comfort.

For instance, a large cohort study conducted by Payen et al. reported that 58.5% of ICU patients receiving opioid treatment were administered fentanyl, emphasizing its widespread use in pain management in this setting. [54]

This high percentage reflects clinical preference for fentanyl, particularly due to its ability to provide consistent analgesia with minimal hemodynamic effects, making it suitable for the critically ill.

Further corroborating these findings, a systematic review by Aoki et al. evaluated 534 patients across seven studies, noting that 47% of the patients were treated with fentanyl. [55]

The review underscores fentanyl's continued prominence as one of the most commonly used opioids in critical care settings, especially for mechanically ventilated patients.

Its pharmacological properties, including rapid titration and minimal accumulation in short-term use, render it highly effective in these contexts.

Table 11: Proportion of use of fentanyl as an analgesic

Author	Our series	Payen et al. (2007) [54]	Aoki et al. (2022) [55]
Fentanyl %	100%	58.5%	47%

In our study cohort, 100% of the patients received fentanyl as the primary analgesic, aligning with the broader literature that positions fentanyl as the predominant opioid in ICU settings. This consistency across studies emphasizes the ongoing reliance on fentanyl for managing pain in critically ill patients.

However, it is important to note the concerns associated with the prolonged use of fentanyl in ICUs. As highlighted by Aoki et al., extended administration of fentanyl is associated with longer durations of mechanical ventilation and prolonged ICU stays. [55]

These outcomes are consistent with earlier findings on opioid use in ICUs, where prolonged sedation and opioid administration can contribute to delayed weaning from mechanical ventilation and other complications such as opioid tolerance and withdrawal syndromes.

This highlights the need for cautious, protocolized opioid administration in ICU settings, balancing effective pain management with the risks of prolonged use and associated complications.

V. Use of mechanical ventilation:

1. Prevalence of ventilated patients

Sedation is a standard practice in the ICU to alleviate agitation and pain, particularly among patients who are mechanically ventilated.

In the study by Jakob et al., more than 80% of ICU patients requiring sedation were also on mechanical ventilation. The study emphasized that in critically ill patients, especially those with ARDS or multi-organ failure, deep sedation is often required to optimize ven tilator synchrony and reduce patient discomfort. [49]

This reflects common ICU practices, where deep sedation is frequently used to ensure patient comfort and facilitate effective mechanical ventilation.

However, the study also highlighted the risks associated with prolonged sedation, particularly with drugs like midazolam, which can lead to extended mechanical ventilation durations, prolonged ICU stays, and a more complex recovery process.

Recent studies continue to report a high proportion of mechanically ventilated patients among those receiving sedation.

For example, a comprehensive study in Sub-Saharan Africa found that approximately 97.25% of sedated ICU patients required mechanical ventilation. [56]

Table 12: Place of mechanical ventilation among ICU patients

Author	Jakob et al.[49]	Abate et al.[56]	Our series
Prevalence of ventilated patients	80%	97.25%	90%

Our series is consistent with these findings, with 90% of sedated ICU patients in our cohort being mechanically ventilated, further aligning with recent literature on sedation and ventilation practices in critical care settings.

2. Duration of mechanical ventilation:

The mean duration of mechanical ventilation in sedated ICU patients varies based on several factors, including patient demographics, the severity of illness, and the specific sedation protocols employed.

For instance, the Jakob et al. study demonstrated that patients receiving sedatives such as midazolam often required extended periods of mechanical ventilation, with durations sometimes exceeding 14 days.[57]

In contrast, lighter sedation or protocols promoting early awakening, such as daily sedation interruptions (DSI), have been associated with shorter ventilation durations, typically around 4 to 7 days.

This variability emphasizes the critical role of sedation depth, the type of sedative agents, and the use of structured protocols in minimizing the duration of mechanical ventilation and improving patient outcomes.

In our cohort study, the mean duration of mechanical ventilation was 5.25 days, with a range from 1 to 20 days, aligning with the findings of Jakob et al. Although our results are consistent with those reported more than a decade ago, this raises critical concerns about the stagnation in the evolution of our sedation and ventilation protocols.

The persistence of similar outcomes over such a long period highlights the need for re-evaluating and advancing current clinical practices.

Furthermore, the lack of substantial recent literature addressing this issue suggests that protocol updates may be overdue. Our findings underscore the necessity of revisiting sedation strategies and ventilation management to optimize patient outcomes and reduce complications. It is imperative that we incorporate contemporary evidence and adapt protocols accordingly to ensure that we are delivering the most effective, evidence-based care in the ICU.

Table 13: Impact of DSI in reducing ventilation days

First Author	Our series	Mehta et al.[58]	Jakob et al.[57]
Ventilation days without DSI	5.25 days	9-12 days	14 days
Ventilation days using DSI	---	7 days	4 to 7 days

Further reinforcing these insights, a randomized controlled trial by Mehta et al. explored the impact of daily sedation interruption in mechanically ventilated critically ill patients. [58]

This study found that DSI could reduce ventilation times to an average of 7 days, compared to 9-12 days in patients receiving continuous sedation, highlighting the benefits of lighter sedation strategies in accelerating recovery

Recent literature continues to show significant variability in mechanical ventilation duration, which is largely influenced by sedation practices.

A multicenter study published in The New England Journal of Medicine demonstrated that light sedation, as opposed to deep sedation, may reduce ventilation time and enhance patient outcomes, although differences in outcomes may not always reach statistical significance. This underscores the necessity of individualized sedation management, ensuring that patient comfort is balanced with the goal of reducing mechanical ventilation duration and facilitating faster weaning. [59]

Thus, tailoring sedation strategies to the patient's clinical condition, and utilizing evidence-based protocols, such as daily sedation interruption, plays a crucial role in optimizing recovery and minimizing the complications associated with prolonged ventilation.

VI. Complications assessement

1. Respiratory complications

A. ICU acquired pneumonia

Prevalence of VAP in different countries:

Hospital acquired pneumonia in ICU in other terms ICU acquired pneumonia stands for VAP and NVAP, with VAP by far the most frequant cause of ICU-AP.

VAP is a nosocomial infection that occurs in patients undergoing IMV for more than 48 h and ranks among the most prevalent nosocomial infections in ICU. [60] [61]

Numerous epidemiological studies have demonstrated significant variations in the incidence of VAP across different countries and regions.

For example, Denys et al. conducted a multicenter, prospective study evaluating the incidence of pneumonia in ICUs throughout Western Europe. Their findings revealed that the overall European ICU-acquired pneumonia incidence was 11.8%. Within this study, Belgium reported an ICU-acquired pneumonia rate of 10.2%, while the ICU in Bruges showed a slightly higher rate at 12.8%. [66]

These findings have remained relatively stable over the past two decades, with more recent data, such as that from a Portuguese multicenter study by Mergulhão et al., indicating a cumulative VAP incidence of 9.2%.[63]

In contrast, even lower rates were reported in a Chinese study by He et al., which identified 1882 episodes of VAC with an incidence of 16.7%, 721 episodes of IVAC at 6.4%, and 185 episodes of PVAP at 1.64%. These figures indicate that the burden of VAP in China remains significant but lower compared to European rates. [61]

Meanwhile, a study from Diyarbakır, Turkey, documented 158 episodes of nosocomial infections in 128 of 556 patients over three years, with a total of 9048 ICU hospitalization days. The three-year ICU hospital-associated infection (HAI) rate was calculated to be 29.19%, nearly three times higher than the rates reported in European studies. This highlights the vari-

ability of infection rates in different regions, with Turkey showing considerably higher rates of ICU-acquired infections. [64]

In Egypt, even more alarming figures have been reported. Yacoub et al. [65] studied 356 ICU patients, of whom 133 (37.35%) developed VAP and 76 (21.34%) experienced non-ventilator-associated hospital-acquired pneumonia (HAP), resulting in a total ICU-acquired pneumonia incidence of 58.69%. These rates are substantially higher than those reported in Europe, China, and Turkey, suggesting regional challenges in infection control and ICU practices.

Table 13: Prevalence of VAP in different countries.

First Author	Denys et al.[66]	Mergulhão et al.[63]	He et al.[61]	Yilmaz Aydin et al.[64]	Yacoub et al.[65]	Our series
Country	Belgium	Portugal	China	Turkey	Egypt	Morocco
included patients	----	---	---	556	356	104
Prevalence of VAP	10.2% to 11.8%	9.2%	6.4%	29.19%	37.35%	39%

In our cohort study, we observed that 41 patients developed respiratory infections, representing 39% of the total study population. This alarmingly high rate aligns with the findings of Yacoub et al., further emphasizing the severity of ICU-acquired infections in our setting.

Risk factors associated with ICU-AP :

Not only do VAP rates vary between countries, but the incidence also differs across ICU types. Notably higher VAP rates have been observed in specialized ICUs, particularly in cancer patients (24.5%) and trauma patients (17.8%), as reported by multiple studies. These findings suggest that the prevalence of VAP is heavily influenced by the ICU patient mix, with certain populations being more vulnerable to infections. [67-68]

Despite the fact that more than 56% of our patients were trauma patients; a population already at increased risk for VAP; our infection rates remain significantly higher than those reported in European and Chinese studies.

This stark contrast underscores the urgent need to implement tailored protocols and interventions to address the elevated infection rates in our ICU, particularly given the regional and case-specific variations in VAP incidence.

In terms of risk factors contributing to VAP, a statistically significant association was observed in different cohorts between VAP and the presence of comorbidities such as COPD, diabetes, alcoholism, and obesity. Additionally, the development of multi-organ failure, episodes of respiratory failure during the ICU stay, advanced age, prolonged mechanical ventilation, and an extended ICU length of stay were all identified as significant risk factors. [69-70]

Although demographic characteristics did not have a significant impact on the incidence of VAP in our study such as (age $<$ 75 years: 39.60% vs Age $\geq$ 75 years: 33.33% / P-value: 1.0) and comobidities Comorbidities (no comorbidities: 35.14% vs comorbidities: 42.86% / P-value: 1.0) contrary to the findings of previous research.

Our data analysis indicates that prolonged sedation (Prolonged sedation: 52.11% vs Short-term sedation: 6.45% / P-value: 0.000034) and the use of mechanical ventilation (Vigilant sedation: 0% vs ventilated: 100% / P-value: 0.019) were the primary predisposing factors for the development of respiratory infections in sedated surgical patients.

This finding is consistent with existing literature, which emphasizes the detrimental effect of prolonged mechanical ventilation and sedation on the respiratory system, particularly in vulnerable patient populations.

B. Unplanned extubation (UE):

Prevalence of unplanned extubation

A prospective study conducted on 317 intubated patients in the ICUs of referral hospitals in Addis Ababa, Ethiopia, reported a 19.74% prevalence of unplanned extubation. [71]

The study highlighted risk factors such as male sex, intubation lasting more than 5 days, intubations initially managed by less experienced residents, patient agitation, and the use of physical restraints, all of which significantly contributed to the occurrence of unplanned extubation.

Similarly, a study from the Philippines found an incidence of unplanned extubation of 19%. In that study, competing risk regression analysis identified male sex and advanced age as significant baseline risk factors, with the highest incidence occurring during night shifts. [72]

Table 14: Prevalence of unplanned extubation among different studies

First Author	Minda et al[71]	Uy et al[72]	Our serie
Country	Ethiopia	Philipines	Morocco
Year	2022	2019	2023
Included patients	317	191	104
unplanned extubation	63	36	27
Prevalence	19.74%	19%	25.96%

In contrast, the incidence of unplanned extubation in our cohort was 25.96% (n=27), notably higher than those reported in the aforementioned studies

a. Risk factors :

The literature review revealed that the first and second categories of the Ramsay Sedation Scale (RSS) were associated with a high risk of unplanned extubation (UE). [62]

Additional factors, including male sex, the ICU subunit, length of ICU stay, and the use of midazolam at the time of UE, were also identified as significant risk factors. [71]

Our study findings indicate that prolonged sedation (short-term sedation: 0 vs prolonged sedation: 16 / p-value: 0.0098) is the only statistically significant risk factor associated with accidental extubation in sedated patients.

Especifically, patients who were sedated for more than 24 hours exhibited a higher incidence of unplanned extubation, suggesting that the duration of sedation directly correlates with an increased risk of this complication.

Interestingly, our analysis did not find advanced age (age <75: 18 cases vs. age >75: 9 cases, P-value = 1), comorbidities (no comorbidities: 23 cases vs. comorbidities: 4 cases, P-value = 0.22), or the type of sedative used (protocol: 22 cases vs. midazolam: 5 cases, P-value = 1) to be significant risk factors for unplanned extubation in our population.

Additionally, we were unable to analyze the potential influence of night shifts on UE incidence, as this information was not available in the medical records.

Our study confirms that prolonged sedation and prolonged mechanical ventilation (over 5 days) are the only significant risk factors for accidental extubation in sedated patients.

These findings are consistent with the previous studies, further suggesting that the duration of sedation directly influences the likelihood of unplanned extubation.

C. Need for reintubation:

b. The prevalence of reintubation in different countries

Reported rates of reintubation in the literature range from 10% to greater than 30%.

In a study in Spain including 1152 extubated patients were included in the analysis, 16% required reintubation. [73]

In an other study in Brazil among 169 included patients the incidence of reintubation was 12.4%.[74]

In the USA the need for reintubation reached 39.21% (60/153) [75], however in a more recent study multicenter study including 98,367 ICU patients who received mechanical ventilation 9,907 (10.1%) were reintubated[76] showcasing a significant decease in the prevalence of this complication

Table 15: The prevalence of reintubation in different countries.

Author	Hayashi et al.[74]	Frutos-Vivar et al [73]	Seymour et al [75]	Miltiades et al [76]	Our serie
Country	Brazil	Spain	USA	USA	Morocco
Year	2013	2011	2004	2017	2023
Total of patients	169	1152	153	98367	104
Reintubated patients	20	182	60	9907	16
Prevalence	12.4%	16%	39.21%	10.1%	15.38%

In our study, 16 out of the 104 included patients, representing 15.38%, exhibited this complication. These findings are consistent with prevalence rates reported in Spain.

However, when compared to more recent studies from countries such as Brazil, and the USA, our prevalence rate is significantly higher. This discrepancy highlights the need for heightened awareness and preventative measures to address this particular complication and reduce its occurrence in our patient population. Interstingly, the USA successfully reduced the prevalence of this complication by fourfold over the course of ten years and example to follow.

c. Risk factors :

Common risk factors for reintubation include male sex, age over 65, sepsis, heart disease, cerebral infarction history, as well as mechanical ventilation over 5 days [10] and longer ICU length of stay [76].

The administration of of Midazolam and fentanyl seems to be significant risk factor for reintubation as proven by Halaseh et al. [77]

The data from our study reveal that prolonged sedation (prolonged sedation: 15 vs short term sedation: 1 / p-value: 0.01) and ventilation for over 5 days (ventilation< 5 days:0

vs ventilation >5 days: 16 / p-value:0.01) are the only significant risk factors associated with reintubation in sedated patients.

Interestingly, our analysis showed that neither advanced age (age < 75 years: 13 vs age ≥ 75 years: 3 / p-value: 0.57), nor comorbidities (no comorbidities: 10 vs comorbidities: 6 / p-value: 0.22) were linked to an increased risk for this particular complication.

This may be due to our sampling: It should be noted that over 70% of our sample is made of young adults with no co-morbidities- and the absence of Midazolam use during eight months of the study period, while Fentanyl continued to be used in combination with Propofol.

D. Hypoxemic respiratory failure (AHRF) during ICU

Prevalence of acute hypoxemic respiratory distress (AHRF) in the ICU :

Pham et al. [78] reported that 34.9% of mechanically ventilated patients presented with respiratory failure signs, while Villar et al. [79] found a slightly lower percentage (28.6%) meeting the criteria for acute hypoxemic respiratory failure.

However Azevedo et al. observed a significantly higher prevalence (57%) of respiratory failure among ICU patients. [80]

Table 16: Prevalence of acute hypoxemic respiratory distress in ICU

First author	Azevedo et al.[80]	Villar et al.[79]	Pham et al.[78]	Our series
Country	Brazil	Spain	Canada	Morocco
Year	2013	2022	2021	2023
Included patients	773	4456	12906	104
Episodes of AHRF	440	1271	4504	50
Prevalence	57%	28.6%	34.9%	48%

In our study, we documented 50 episodes of acute hypoxemic respiratory failure (AHRF), representing 48% of the patient cohort.

This prevalence aligns closely with the findings of Azevedo et al.[80], who reported a similarly high rate of acute respiratory failure. However, when compared with the results of Villar et al.[79] and Pham et al.[78], our observed prevalence is notably higher.

The differences in our findings may be attributable to variations in patient characteristics, clinical settings, or diagnostic criteria used to define respiratory failure. Further research is needed to explore these disparities and their potential impact on patient outcomes.

Similar to reintubation our data reveal that prolonged sedation (especialy over 4 days) and ventilation for over 5 days (ventilation< 5 days: 0 vs ventilation >5 days: 50 / p-value: 0.001) are the only significant risk factors associated with AHRF.

Patients who were sedated for over 4 days (prolonged sedation: 50 vs short term sedation: 0 / p-value: 0.001), and or ventilated over 5 days exhibited a higher incidence of this complication, suggesting that the duration of sedation directly impacts the likelihood of its occurance.

This is particularly relevant given the exponential increase in the likelihood of AHRF episodes with both the duration of sedation and the duration of mechanichal ventilation.

Interestingly, our analysis showed that neither advanced age (age < 75 years: 42 vs age ≥ 75 years: 8 / p-value: 1), nor comorbidities (no comorbidities: 34 vs comorbidities: 16 / p-value: 0.37) were linked to an increased risk.

2. Delerium assessement:

A. Prevalence of delerium among ICUs

According to the Diagnostic and statistical manual of mental disorders: DSM-5 delirium is defined as disturbance in attention (top mandatory feature) that develops over a short period of time, is associated with additional disturbances in cognition that are not better explained by another preexisting, established or evolving neurocognitive disorder, and do not occur in the context of a severely reduced level of arousal, and evidence from the history, physical examination or laboratory findings that indicate that the disturbance is a direct physiological consequence of another medical condition, substance intoxication, or withdrawal.[81] Three subtypes have been recognized: hyperactive, hypoactive, and mixed.

The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and the intensive Care Delirium Screening Checklist (ICDSC) are the two most widely used assessment tools for delirium detection in critical care settings worldwide.

The CAM-ICU demonstrates high diagnostic performance with a sensitivity of 100% and 93%, specificity of 98% and 100%, and excellent interrater reliability ($\kappa = 0.96$; 95% CI, 0.92-0.99). [82]

It is both time-efficient, taking under one minute to complete, and can be utilized in non-verbal patients. The CAM-ICU has been adapted for use in pediatric, emergency department, and neurocritical care patients, and translated into more than 30 languages. By comparison, the ICDSC exhibits a sensitivity of 99% and specificity of 64%. [83-84-85-86]

Due to its superior sensitivity and broader validation, the CAM-ICU is the most extensively studied and validated diagnostic tool for delirium in the ICU. However, the accuracy of the CAM-ICU is highly dependent on the proper training of healthcare providers administering the assessment.

Historically, delirium has been reported in 60-80% of mechanically ventilated ICU patients and 20-50% of patients with lower severity of illness. [87-88]

Recent advances, including the increased use of validated diagnostic tools and changes in ICU management aimed at reducing oversedation and immobility, have contributed to a 25% reduction in delirium rates in many ICUs. These changes underscore the importance of diagnostic tools, early mobilization, and both lighter and shorter sedation protocols as key deliriums prevention strategies. [88-89-90]

The variation in delirium incidence seems to depend on whether the study population includes exclusively mechanically ventilated patients. For instance, the prevalence of delirium reached 77% in mechanically ventilated burn patients. [91-92]

Table 17 : Prevalence of delerium among differnt ICUs

First author	Ely et al. [12]	Girard etal. [13] (2008)	Guenther et al. [88] (2010)	Roberts etal. [91] (2005)	Salluh etal. [90] (2015)	Our series (2023)
Country	USA	USA	USA	Australia	USA	Morroco
Enroled patients	275	1658	54	185	16 595	104
Prevalence of delerium	81.7%	71% to 74%	46%	45%	31.8%	20.19%

In contrast to these findings, our study revealed that only 21 patients (20.19% of all admis- sions) experienced at least one episode of delirium, with mean delirium duration of 15.85 hours. This discrepancy may stem from underdiagnosis, as our team primarily recorded hyperactive delirium, while hypoactive and mixed states were not accounted for due to inadequate surveillance.

B. Risk factors:

Several risk factors predispose critically ill adults to delirium, including advanced age, dementia, hypertension, polytrauma, delirium on the previous day, mechanical ventilation, and metabolic acidosis. [11]

Our findings emphasize that prolonged sedation is the most significant risk factor for the development of delirium (short-term sedation: 16.13% vs prolonged sedation: 63.38%; P = 0.00003). Additionally, mechanical ventilation (vigilant sedation: 0.00% vs ventilated: 53.19%; P = 0.004) and the presence of increased intracranial pressure (non-HTIC: 36.84% vs HTIC: 61.70%; P = 0.0199) were found to be significant contributors to delirium development. These results highlight the need for vigilant sedation practices and early detection of delirium in ICU patients to improve outcomes.

3. Decubitus complications

A. Venous Thromboembolism :

Venous thromboembolism (VTE) is a significant complication in critically ill patients, most of whom have compromised cardiac and respiratory function. ICU patients represent a heterogeneous population, inherently at high risk for developing deep vein thrombosis (DVT). Managing this risk presents a dual challenge: on one hand, DVT is associated with an increased risk of bleeding, which complicates the use of anticoagulant prophylaxis; on the other hand, DVT contributes to prolonged hospital stays, extended durations of mechanical ventilation, and an elevated risk of hospital mortality. [93-94-95-96]

- **Prevalence of VTE**

Five studies from various countries have reported the prevalence of venous thromboembolism (VTE) in different patient cohorts.

Al-Dorzi et al. (2022), conducted in Saudi Arabia, included 322 patients and reported the highest VTE prevalence at 26.6%.[97]

In comparison, Gibson et al. (2020) from the USA enrolled 243 patients and found a lower VTE prevalence of 16%.[98]

Another USA-based study by Karcutskie et al. (2017), with a much larger cohort of 1,137 patients, reported an even lower prevalence at 9.1%. [99]

Chu et al. (2021) conducted a study in China with 848 patients and observed a VTE prevalence of 8.13% [100], while the lowest prevalence was reported by Dibiasi et al. (2022) from Australia, where only 1.4% of the 1,352 patients developed VTE. [101]

These differences in VTE prevalence may reflect variations in patient populations, healthcare settings, and VTE prophylaxis practices across countries.

Table 18 : VTE prevalenve in different cohorts :

First author	Al-Dorzi et al.[97]	Gibson et al.[102]	Karcutskie et al.[99]	Chu et al. [100]	Dibiasi et al.[101]	Our series
Country	Saudi Arabia	USA	USA	China	Australia	Morocco
Enrolled patient	322	243	1137	848	1352	104
Prevalence of VTE	26.6%	16%	9.1%	8.13%	1.4%	9.6%

In our cohort study, only 10 venous thromboembolic events were documented, resulting in a reported incidence rate of 9.6%. Consistant with the results of Karcutskie et al. and Chu et al.

However, this low incidence compared to the finding of Al-Dorzi et al. is most likely due to underdiagnosis, making it difficult to ascertain the true incidence of DVT in our study population.

Active screening for DVT using ultrasound has been associated with a reduction in the incidence of proximal DVT and a decreased risk of bleeding, as demonstrated in recent studies. An approch that we rather encourage to adopt in our ICU. [103]

- **Risk factors:**

Recognized risk factors for DVT are tied to the elements of Virchow's triad: stasis, endothelial injury, and hypercoagulability. In ICU patients, stasis plays a predominant role due to immobility resulting from trauma, the use of sedatives, and neuromuscular blockade, all of which significantly reduce venous blood flow velocity in the limbs. Additionally, mechanical ventilation decreases venous return to the heart, further contributing to venous stasis. [18-104].

In our study, prolonged sedation (prolonged sedation : 31 vs short term sedation : 1 / p-value : 0.0002) ; and extended length of hospital stay (length of stay< 4 days:0 vs length of stay >4 days : 32 / p-value:0.00015) were identified as the two most significant risk factors for the development of pressure ulcers.

The association of mechanical ventilation with pressure ulcer occurrence was determined to be borderline significant (vigilant sedation: 0 vs ventilated: 32 / p-value: 0.063).

Furthermore, neither advanced age (age < 75 years: 32 vs age ≥ 75 years: 0 / p-value: 0.59) nor the presence of comorbidities (no comorbidities: 18 vs comorbidities: 3 / p-value: 0.53) were identified as independent risk factors contributing to the development of this complication.

These factors likely exacerbate patient immobility and disrupt normal physiological processes, creating an environment conducive to clot formation, particularly in the absence of effective mechanical prevention strategies.

B. ICU acquired weakness (ICU-AW):

ICU-AW is characterized by symmetrical limb weakness, with more severely affected proximal limb muscles and hips. Moreover, respiratory muscles are often affected, (especially in patients receiving mechanical ventilation) and is associated with difficulty in weaning from the ventilator. [105]

ICU acquired weakness has two electroneuromyographic definitions: critical illness polyneuropathy (CIP) and critical illness myopathy (CIM).

- **Prevalence of ICU-AW:**

Data from medical institutions worldwide show the incidence of ICU-acquired weakness ranging from 25 to 31% [106-107-108-109], however in surgical ICUs, 56-74% of patients show symptoms of ICU-AW [22].

Fan et al. (2014) conducted a study involving 3,095 patients, with ICU-acquired weakness (ICU-AW) diagnosed in 1,019 of them, resulting in a prevalence of 33%. [110]

In contrast, Panahi et al. (2020) enrolled 160 patients in their study, identifying ICU- AW in 72 patients, leading to a higher prevalence of 44.9%. [111] Similarly, Hermans et al. (2014) reported an even greater prevalence of ICU-AW, with 227 out of 415 patients affected, representing 55%. [112]

These variations in prevalence across studies may be influenced by differences in ICU settings, patient populations, and diagnostic criteria. In fact lower rates are reported in medical ICUs compared to surgical ICUs.

Table 19: Prevalence of ICU-AW a litterature review.

First author	Fan et al.[113] (2014)	Panahi et al.[111] (2020)	Hermans et al.[112] (2014)	Our series (2023)
Number of enroled patients	3095	160	415	104
Patients with ICU-AW	1019	72	227	36
Prevalence of ICU-AW	33%	44.9%	55%	34.6%

In our patient cohort, the most frequent complication associated with prolonged immobility was ICU-acquired weakness (n=36), observed in 34.62% of cases. These results are in line with the findings of Fan et al., though their study focused on medical ICU patients. Notably, our prevalence is much lower than the rates reported by Panahi et al. and Hermans et al., both of whom studied surgical ICU populations.

Given that we expected our results to align more closely with findings from other surgical ICUs, this discrepancy highlights that the true prevalence of ICU-acquired weakness is likely underreported, potentially due to underdiagnosis.

- COMMON RISK FACTORS:
- **Multiple organ failure (MOF) :** Multiple organ failure is a clinical syndrome with simultaneous or sequential failure of two or more organs following severe infection, trauma or major surgery. When patients are in the MOF state for a long duration, ICU-AW may occur. [114] .The primary causes of MOF are sepsis and septic shock, and more than 70% of patients with sepsis were reported to develop ICU-AW. [20]
- **Mobility Restriction:** In addition to structural changes, muscle strength also decreases significantly. When a healthy adult is bedridden, the muscle strength is reduced by 1% per day. Long-term muscle inactivity causes changes in mitochondrial function, leading to an increase in reactive oxygen species, inducing muscle atrophy and dysfunction. [115]
- **Hyperglycemia :** Recent studies have shown that hyperglycemia affects the respiratory muscle functions, leading to ICU-acquired respiratory muscle weakness. [116] ICU patients complicated with diabetes or hyperglycemia may develop peripheral neu- ropathies due to metabolic disorders, oxidative stress, neurotrophic factor deficiencies, or vascular injuries. [117]
- **Glucocorticoids (GCs):** GCs have a direct catabolic effect on skeletal muscles, with their long-term use causing amyotrophy and proximal muscle weakness. [118] Keh et al. showed that 34% of patients with sepsis and 45% of non-septic patients de- veloped ICU-AW after GC usage. [119] Other factors increase the incidence of ICU-AW, include long-term mechanical ventila- tion, electrolyte imbalance, aging, parenteral nutrition, inappropriate use of vasoactive drugs. [120]

Our database identifies two key independent risk factors for ICU-AW: prolonged seda- tion, particularly with increasing duration (prolonged sedation: 22 vs short term sedation: 0 / P-value: 0.001), and a hospital stay exceeding six days (length of stay< 6 days:0 vs length of stay >6 days: 22 / p-value:0.000003).

Conversely, factors such as advanced age (age < 75 years: 22 vs age ≥ 75 years: 0 / p-value: 1.0), existing comorbidities (no comorbidities: 13 vs comorbidities: 9 / p-value: 1.0), and the use of assisted ventilation (vigilant sedation: 0 vs ventilated: 22 / p-value: 0.188) do

not appear to independently contribute to the occurrence of ICU-acquired weakness. While these factors may influence a patient's overall health and recovery, they were not statistically significant in our analysis for this specific complication.

These findings are consistent with the results of our literature review. In contrast, age and the presence of comorbidities did not emerge as significant risk factors in our cohort study. However, the effects of glucocorticoid use and the occurrence of multiple organ failure (MOF) were not explored in this study.

C. Pressure ulcers:

A. Prevalence of pressure ulcers:

Pressure ulcers or bedsores are a common complication in critically ill patients, with a prevalence that varies between studies, ranging from 11% to 20% across countries.

For istance in Turkey, Sayan et al. [121] reported the lowest prevalence, 11.43%; followed by Cox et al. [122] in the USA with a pressure ulcer prevalence of 14.3%, similar to Flæten et al. [14] in Norway (15%).

Amini et al. In Iran observed a prevalence of 19.57% among their 440 patients, the highest rate among the studies. [123]

These variations in pressure ulcer prevalence across countries could be attributed to differences in healthcare systems, prevention protocols, and patient demographics.

Table 20: Prevalence of pressure ulcers:

First author	Cox et al.[122] (2022)	Flæten et al.[14] (2024)	Amini et al.[123] (2022)	Sayan et al.[121] (2020)	Our series
Country	USA	Norway	Iran	Turkey	Morocco
total patients	41 866	594	440	1548	104
Pressure ulcers	5995	91	86	177	32
Prevalence	14.3%	15 %	19.57%	11.43%	30.76%

In our study, pressure ulcers were documented among 32 patients, resulting in a prevalence of 30.76%. This rate is notably higher than those reported in the studies mentioned earlier.

The significantly higher prevalence in our study may be attributed to differences in patient care, length of ICU stay, or potentially under-recognized risk factors within our patient population. It may also reflect variability in diagnostic practices or preventive measures, underlining the importance of standardized protocols to reduce the burden of pressure ulcers in critically ill patients.

- **Risk factors:**

Bedsores are caused by prolonged pressure on the skin, particularly over bony areas. Several factors increase the risk of developing these painful sores:

- Immobility: Patients who have limited mobility due to conditions like paralysis, spinal in- juries, or sedative use are at higher risk, as they cannot frequently reposition themselves to relieve pressure on vulnerable areas. [124]
- Incontinence: Excessive moisture from urine or feces irritates and damages the skin, weakening its natural defenses and making it more prone to ulcers. Bacterial contamination from incontinence can also heighten the risk of infection. [125]
- Friction and Shear: Friction, such as from skin rubbing against bed linens, can exacer- bate skin damage, especially when combined with shear forces, which occur when skin moves in one direction and bone in another (like sliding down in a hospital bed). [125]
- Poor Nutrition and Hydration: Malnutrition weakens skin integrity and slows healing. Adequate protein, calories, vitamins, and hydration are essential to maintain skin health and support tissue repair. [124]
- Reduced Sensory Perception: Conditions that reduce the ability to feel pain, such as dia- betes or neuropathies, can prevent a person from noticing and adjusting to pressure, increas-ing the risk of prolonged pressure damage. [15]
- Age: Older adults are more susceptible as skin becomes thinner and more fragile with age, reducing its resilience against pressure and minor injuries. [126]

In our study, prolonged sedation (prolonged sedation: 31 cases vs. short-term sedation: 1 case; $p = 0.0002$) and an extended length of hospital stay (stay < 4 days: 0 cases vs. stay > 4 days: 32 cases; $p = 0.00015$) were identified as the most significant risk factors for devel- oping pressure ulcers. Both factors directly contribute to immobility, reduced sensory percep- tion, and incontinence, all of which increase susceptibility to pressure injuries.

The association between mechanical ventilation and pressure ulcer development showed borderline significance (vigilant sedation: 0 cases vs. ventilated: 32 cases; $p = 0.063$).

Conversely, neither advanced age (age < 75 years: 32 cases vs. age ≥ 75 years: 0 cases; $p = 0.59$) nor the presence of comorbidities (no comorbidities: 18 cases vs. comorbidities: 3 cases; $p = 0.53$) were found to be independent risk factors for pressure ulcer development.

The high prevalence of pressure ulcers underscores areas for improvement, particularly in enhancing mobility support, moisture prevention methods, hydration, and nutritional measures.

4. Adverse drug events:

A. Hypotension:

• Prevalence of Hypotension with Propofol and Midazolam :

Hypotension in ICU patients may arise from their underlying medical conditions or from the well-documented vasodilatory effects of sedatives. This makes it difficult to pinpoint the exact prevalence of this adverse event among critically ill patients. A comprehensive literature review yielded only two relevant studies comparing the incidence of hypotension related to sedative use in this population. The findings from these studies were as follows:

- Hypotension after general anesthesia using either propofol and or midazolam: in the study of Bayable et al. inlucing 311 patients receiving general anesthesia, 28.6% of them experience at least one episode of unintentional hypotension. [127]
- Hypotension with Propofol: In the study of Sneyd et al. (2022), it was found that 36% of procedures involving propofol sedation were associated with episodes of hypotension. [128]
- Hypotension with Midazolam: in the study of Zuin et al. (2017) hypotension occurred in 27.9% of of procedures involving propofol sedation. [129]

In our series hypotension occured in 59 patients sedated patients with a prevalence of 56.7%, in 42 cases with patients sedated with propofol (40%) and 17 cases using midazolam (16.3%).

Table 21 : Prevalence of hypotension due to propofol and midazolam

First author	Sneyd et al. (2022)[128]	Zuin et al. (2017)[129]	Our series
Sedative studied	Propofol	Midazolam	Both
Prevalence of hypotension	36%	27.9%	40%

Comparative Insights:

The meta-analysis of Sneyd et al. included 14 studies comparing propofol with midazolam. The risk ratio for developing hypotension with propofol compared to midazolam was found to be 1.46 (95% confidence interval: 1.18-1.79; P=0.0004). This indicates that hypotension was more likely to occur with propofol than with midazolam. [128]

The prevalence of hypotension in our series is notably higher than reported in the cited studies, likely due to factors beyond sedation alone. Hypotension in our cohort may be influenced by various underlying conditions typical in critically ill patients. However, our findings align with the literature in demonstrating a higher incidence of hypotension with the use of propofol.

The findings suggest that while hypotension is a common occurrence during propofol sedation, the prevalence is lower when using midazolam. This highlights the importance of considering the choice of sedative agent in clinical practice, especially for critically ill patients.

B. Delayed awakening:

Delayed awakening is defined as a persistent disorder of arousal or consciousness 48 to 72 h after sedation interruption in critically ill patients. It's considred a significant issue among ICU sedated patients, especially those on mechanical ventilation. [130]

The prevalence can vary widely depending on the sedative used, the depth of sedation, and patient-specific risk factors such as age, comorbidities, and duration of sedation.

- **Prevalence of delayed awakening:**

Studies report that up to 37% of critically ill patients may experience prolonged recovery from sedation, leading to delayed extubation, increased ICU stays, and complications like delirium.

For instance in the cohort of Paul et al. delayed awakening occurred in 29 % of patients. [130]

While Rey et al.[131] reported a prevalence of 34% among sedated patients. [131]

We observed lower rates of delayed awakening in patients receiving propofol and/or midazolam as sedatives for surgery. This reduced incidence suggests that the prevalence of this complication is proportional to the duration of sedation, as noted by Bayable et al. who reported of a prevalence not over 8.3%.[127]

Table 22: Prevalence of delayed awakening after general anesthesia

First author	Paul et al.[130]	Rey et al.[131]	Bayable et al.[127]	Our series
Enrolled patients	326	402	311	104
Delayed awakening cases	56	137	25	21
Prevalence	29%	34%	8.3%	20%

In our series delayed awakening accured within 21 patients counting for 20% lower than the prevalence reported by et Paul et al. and Rey et al.

In the context of our cohort, where 66.99% of patients were sedated with propofol, the prevalence of delayed awakening is significantly lower than in cohorts using longer-acting sedatives (e.g, midazolam). However, other factors like patient comorbidities or especialy prolonged sedative use still influence the rate.

- Risk factors:

Several risk factors contribute to delayed awakening, including:

- Prolonged sedation duration: Extended use of sedatives like benzodiazepines and opioids is associated with delayed awakening due to their long half-lives and accumulation in the body. Studies have shown that high cumulative doses of these drugs can contribute to slower recovery of consciousness. [132]
- The type of sedative used: Longer-acting sedatives, such as benzodiazepines (e.g., midazolam), are more likely to cause delayed awakening compared to shorter-acting agents like propofol. [133]

- Prolonged duration of sedation: The longer the sedation, the greater the risk of delayed awakening.
- Renal or hepatic dysfunction: These can impair drug metabolism and clearance, pro- longing sedation effects. [134]
- Drug accumulation: Particularly with continuous infusions, lipophilic drugs like pro- pofol or benzodiazepines can accumulate in fat tissue and contribute to longer recovery times. [133]

According to our database, the analysis revealed no statistically significant differences in the incidence of key adverse events, including allergic reactions, hypothermic events, tachy- cardia episodes, or neurological disorders, between patients receiving propofol and those re- ceiving midazolam.

This main difference from the findings of litterature is due to sampling issue, where most patients were sedated with propofol and not equaly distributed into two equal groups one using midazolam and the other using propofol.

C. Irrigular heart rate:

- **Prevalence of irrigular heart rate among sedated patients by propofol or midazolam:**

The prevalence of tachycardia and bradycardia among patients sedated with propofol or midazolam can vary based on the patient population and specific clinical settings, but both sedatives are known to affect heart rate.

- **Bradycardia:**

Propofol is more commonly associated with bradycardia due to its ability to decrease sympathetic nervous system activity and potentially increase the parasympathetic. The re- ported prevalence of bradycardia in patients receiving propofol ranges from 5% to 42%, de- pending on the dose and patient conditions. [135]

Midazolam, being a benzodiazepine, can also cause bradycardia, but it is generally less pronounced compared to propofol. Prevalence of bradycardia with midazolam is typically around 1-10%. [136]

Table 23: Prevalence of bradycardia a comparaison

First author	Duprey et al.[135]	Riker et al.[136]	Our serie
Sedative used	Propofol	Midazolam	Propofol
Prevalence	42%	10%	35%

- **Tachycardia:**

With midazolam tachycardia is more common due to its potential to induce hypotension, leading to compensatory increases in heart rate. The prevalence is cited as up to 25% in critically ill patients. [136]

Tachycardia is less commonly reported with propofol but may occur, particularly if patients experience hypotension due to vasodilation as a compensatory mechanism. The prevalence of tachycardia is usually lower, cited as less than 10%. [137]

Table 24: Prevalence of tachycardia a comparaison:

First author	Duprey et al.135 (2019)	Paramsothy et al.137 (2023)	Our series
Sedative used	Propofol	Midazolam	Midazolam
Prevalence	10%	25%	13%

In our series irregularities in heart rate occured in 52 cases with tachycardia in 14 cases accounting for 13%, bradycardia was more commun repoted in 38 cases with a prevalence of 35%.

The prevalence of bradycardia in our study is significantly higher than reported in the literature, suggesting that its occurrence may not solely be attributed to the sedative used, but likely also to the patients' underlying conditions. In contrast, the observed prevalence of tachycardia aligns closely with previously reported rates in the literature.

D. Allergic reactions:

- **Allergic recations to propofol:**

Propofol is regarded as a remarkably safe drug with a reported incidence of 1 in 60,000 for allergic reactions as reported by Hepner et al. [138]

The main allergens in propofol (Diprivan®) are the active drug itself or the excipients like egg lecithin and soybean oil, used in its formulation.

The overall incidence of anaphylaxis induced by propofol in France is about 1% and 0.65% in the Australia. Another survey estimated that 1.2% of cases of perioperative anaphylactic shocks were attributable to propofol. [139]

- **Allergic recations to midazolam:**

Allergic reactions to midazolam are extremely rare. Reported cases of hypersensitivity are isolated and are estimated to be around 0.01% of cases. Midazolam is mainly associated with localized allergic reactions, such as skin rashes or bronchospasm, but anaphylaxis is very rare. [139]

The data from Hepner and al. review report that allergic reactions to midazolam occured in 0.75% of French patients and no reactions in the Australian patients. [138]

In our series, allergic reactions were reported in 9 patients (8.6%), with no significant difference in prevalence between those sedated with propofol and midazolam. This higher rate, compared to the findings of Hepner et al. and Baldo et al., can be attributed to the overall prevalence of allergic reactions in our patient cohort, rather than being solely related to the sedatives used.

VII. Outcome measures:

1. Hospital stay:

A. Prolonged length of stay (PLOS):

The literature varies in defining the period at which a stay is considered as prolonged. PLOS is defined as LOS ≥ 90th or ≥ 75th percentile or above the median LOS for the entire cohort of population. [140]

The prevalence of PLOS rages from 11.2% to 17.5%, as showed by the series of Aravani et al. (2016), Krell et al. (2014) and Almashrafi et al. (2016). [141-142-143]

Table 25: Prevalence of prolonged ICU length of stay.

First author	Aravani et al. (2016)[141]	Krell et al. (2014)[142]	Almashrafi et al. (2016)[143]	Our series
Country	England	USA	Oman	Morocco
Enrolled patients	240873	2177	600	104
Definition of PLOS	>10 days	>90th percentile	≥5 days	>9 days
Prevalenvce of PLOS in ICU	11.2%	14.5%	17.5%	34.6%

In our study, prolonged length of stay (PLOS) was defined as any ICU stay exceeding the median duration, which we calculated to be 8.91 days. Among our cohort of 104 patients, 36 individuals (34.6%) experienced PLOS, marking the highest rate compared to similar studies from other regions.

This elevated percentage highlights the significant challenges posed by extended hospitalizations, which likely contribute to poorer patient outcomes and increased risk of complications such as infections or bedsores.

Moreover, the extended length of stay places a substantial financial strain on the healthcare system, elevating costs related to staffing, resource use, and bed occupancy.

This observation underscores the critical need for targeted interventions and strategies aimed at reducing PLOS, which could improve both patient recovery and the overall efficiency of healthcare delivery. Enhancing discharge planning, optimizing resource allocation and exploring alternative care pathways could be vital steps in addressing this pressing issue.

B. Errors related to sedation:

Common types of errors include improper dosing, prolonged sedation, use of inappropriate sedatives, and failure to adhere to sedation protocols. These errors can lead to serious complications such as delayed recovery, prolonged mechanical ventilation, increased ICU length of stay, and higher risk of infections or delirium.

In our study, we identified a total of 23 instances where errors occurred in the administration of sedation. These errors were categorized into three main types: non-adherence to the prescribed sedation protocol, the use of inappropriate or non-indicated medications, and the administration of sedation for duration longer than necessary.

Such deviations from standard sedation practices not only increase the risk of adverse events, such as respiratory depression and delayed weaning from mechanical ventilation, but also contribute to prolonged ICU stays and higher healthcare costs.

These findings emphasize the importance of a heightened focus on reducing these errors by implementing standardized sedation protocols, regular staff training, and the use of sedation monitoring tools in order to enhance patient safety and outcomes in critical care settings.

2. Mortality:

Studies on mortality rates in surgical intensive care units (SICUs) across various countries highlight a range of outcomes depending on regional resources and patient demographics.

In Thailand, Apichartvongvanich et al. reported a mortality rate of 23.6% among 276 patients, reflecting outcomes in a middle-income setting with varied patient conditions. [144]

In contrast, a study by Zhang et al. in China observed a higher 28-day mortality rate of 32.6% among 347 surgical ICU patients, suggesting potential differences in patient acuity and healthcare challenges in this setting. [145]

Higher mortality rates are observed in lower-resource regions. For example, Chaker et al. reported a 36% SICU mortality rate among 100 patients in Rabat, Morocco [146], and Shoukat et al. noted an even higher mortality rate of 46.45% among 155 adult patients in the SICU inLahore, Pakistan, potentially reflecting resource constraints and patient severity. [147]

In Brazil, Sousa Neto et al. found a SICU mortality rate of 55.27% in a cohort of 155 patients, underscoring the challenges of managing critically ill surgical patients in resource-limited environments. [148]

These studies illustrate the global variability in SICU mortality rates, which are often influenced by factors such as healthcare infrastructure, access to specialized care, patient severity, and regional practices in critical care.

In our study, there were 65 deaths, accounting for 62.5% of the patient cohort. Among the 39 surviving patients, 23 (59%) were discharged to other hospital facilities, while 16 (41%) were transferred to rehabilitation centers.

Table 26: Prevalence of mortality in different SICUs around the world

First author	Apichartvongvanich et al.144	Zhang et al.145	Sousa Neto et al.148	Shoukat et al147	Chaker et al.146	Our series
Country	Thailand	China	Brazil	Pakistan	Morocco	Morocco
Number of patients	276	347	155	155	100	104
Prevalence of mortality	23.6%	32.6%	55.27%	46.45%	36%	62.5%

In comparison to our study, which showed a notably higher mortality rate, it's important to consider that our sample was exclusively composed of sedated patients, representing a more severe subgroup within the surgical ICU population. This sampling approach likely contributes to the higher mortality observed in our data, as sedation is typically required for patients with complex or critical conditions, which correlates with increased ICU mortality risks.

Thus, the elevated mortality in our study likely reflects the severe baseline condition of the sedated cohort, aligning with evidence that higher acuity levels and sedation-related complications are strong predictors of mortality in ICU settings

Sedation-related complications were found to be a significant and independent risk factor for mortality in the intensive care unit, with mortality rates of 24 among patients without sedation-related complications versus 41 among those with complications ($p = 0.013$).

Review of Literature

I. Definition of sedation:

In critical care, sedation refers to the therapeutic use of medications to reduce patient consciousness and responsiveness, thereby minimizing pain, anxiety, and agitation in a controlled and monitored environment. Sedation is essential for improving patient tolerance to invasive interventions (like mechanical ventilation) and for maintaining stability in patients with severe conditions. [149]

According to the Society of Critical Care Medicine (SCCM), sedation strategies should be individualized, titrated, and regularly assessed to maintain the patient at the minimum sedative level necessary for therapeutic goals. [150]

II. Types and Levels of Sedation in the ICU:

Sedation in ICU patients can be divided into three broad levels, depending on the desired consciousness level:

- Minimal Sedation (Anxiolysis): The patient is calm but responsive to verbal commands. This level is often used to alleviate anxiety without impairing the patient's ability to communicate.
- Moderate Sedation (Conscious Sedation): This level maintains a balance where the patient responds purposefully to verbal commands or light tactile stimulation but has reduced awareness of surroundings.
- Deep Sedation and General Anesthesia: In these states, the patient does not respond to external stimuli, and reflexes may be lost, requiring intensive monitoring to support vital functions and prevent complications like respiratory depression or hemodynamic instability. [151]

In terms of duration, sedation in ICU can be divided to short term and long term sedation:

- Short-Term Sedation (up to 24 hours): This is typically administered during brief ICU stays or short procedures and employs agents with rapid onset and offset like propofol or midazolam, allowing for quick patient arousal post-sedation.
- Long-Term Sedation (more than 24 hours): Often necessary in critically ill patients, this sedation supports prolonged ICU care using agents that have longer half-lives, such as lo- razepam or certain opioids, which are more cost-effective for extended use but may accumu- late in the body over time, necessitating careful dose management and monitoring to avoid adverse effects. [152]

III. Place of sedation in intensive care units:

The ICU environment can appear hostile; the noisy ICU environment, unfamiliar monitoring and support equipment, loss of day and night cycle and painful invasive procedures are associated with a high incidence of psychological problems and sleep deprivation.Sedation and analgesia are important to ensure patient comfort, from both psychological and physical points of view. The stress response can lead to profound changes in endocrine function: hypermetabolism, sodium and water retention, mobilization of substrates from en- ergy stores and increased lipolysis. [153-154-155]

Pain can have many adverse consequences, including sympathetic overactivity with an increase in heart rate and myocardial oxygen consumption, increased respiratory rate and hypoxaemia, altered gastrointestinal motility, impaired urinary tract function, changes in blood viscosity, clotting time and platelet aggregation, diminished immune function and impaired wound healing. [156-157]

The International Association for the Study of Pain defines pain as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. This definition highlights the subjective nature of pain and suggests that it can be present only when reported by the person experiencing it. Most critically ill patients will likely experience pain sometime during their ICU stay and identify it as a great source of stress. [158-159-160]

Many critically ill patients may be unable to self-report pain due to altered consciousness or mechanical ventilation. [161] However, reliably assessing pain is essential for effective treatment. As the International Association for the Study of Pain emphasizes, "the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment". [156]

Thus, clinicians must accurately detect and manage pain in these situations, as pain assessment and management remain top priorities in critically ill adults. Nevertheless, significant pain still occurs in over 50% of medical and surgical ICU patients. [162]

IV. Most commonly used sedatives: pharmacokinetics and protocols:

1. Mecanism of action of midazolam and propofol:

Midazolam and propofol are both commonly used sedative agents in critical care, each with a unique mechanism of action.

A. Midazolam:

Midazolam is a benzodiazepine that works by binding to the gamma-aminobutyric acid type A (GAB*A*-A) receptor. This binding enhances the effect of GABA, the principal inhibitory neurotransmitter in the central nervous system, leading to increased chloride ion influx. This hyperpolarizes the neuron, making it less excitable, which results in sedative, anxiolytic, muscle relaxant, and anticonvulsant effects. [163]

- Binding site: midazolam binds to a specific site on the GABA-A receptor complex, known as the benzodiazepine site. This site is located at the interface of the alpha and gamma subunits of the receptor.
- Action: benzodiazepines like midazolam enhance the frequency of chloride channel opening in response to GABA, which increases chloride ion flow and potentiates GABA's inhibitory effect.

- Selectivity: midazolam has a high affinity for receptors that contain the alpha1, alpha2, alpha3, or alpha5 subunits paired with the gamma subunit, making it more selective for particular GAB*A*-A receptor subtypes. [164]

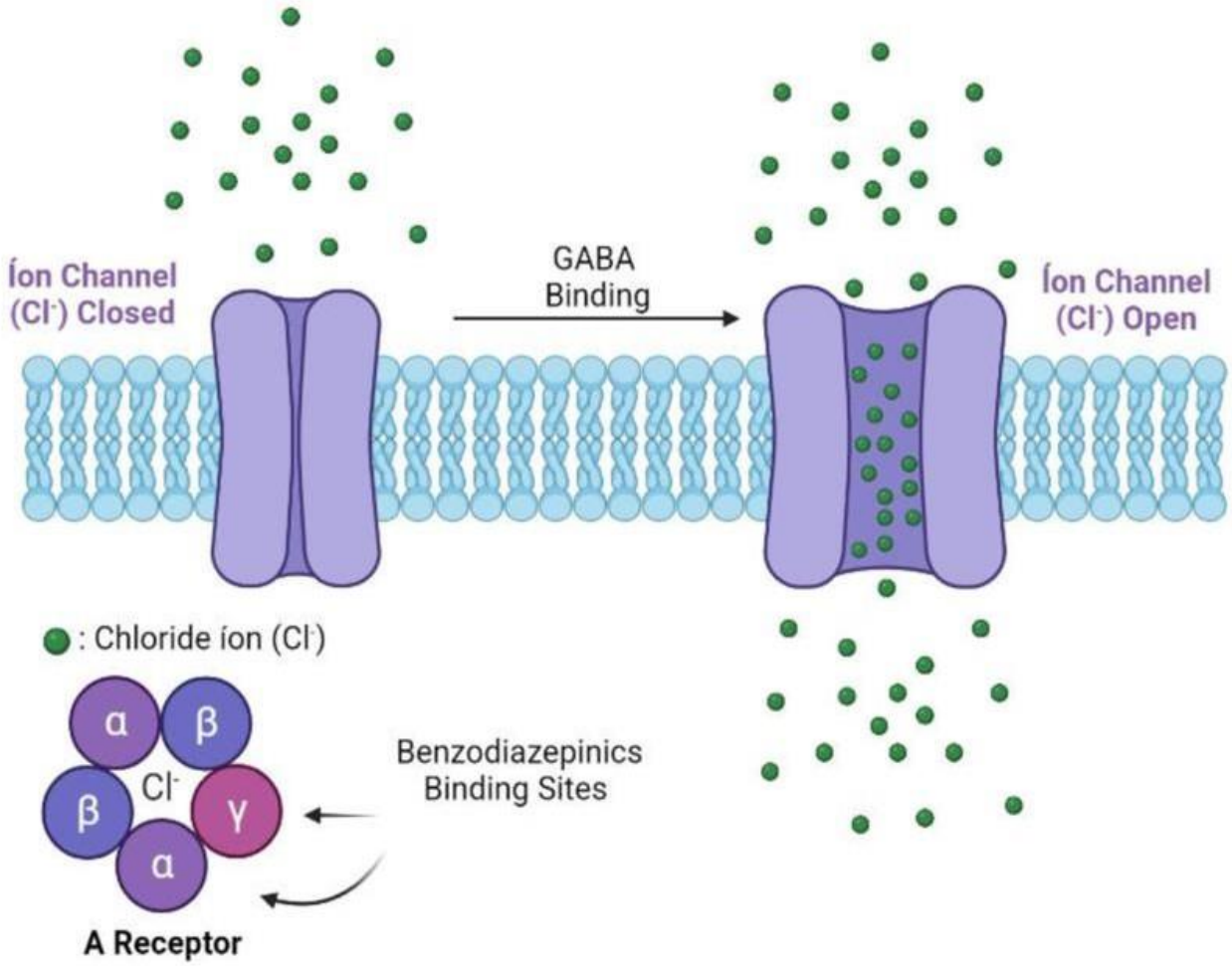


Figure 19: Mecanism of action of midazolam

B. Propofol:

Propofol is a non-benzodiazepine sedative-hypnotic agent, also works through GABA-*A* receptor modulation but at a distinct binding site from benzodiazepines. Propofol enhances GABA-*A* mediated inhibitory effects by increasing the duration of chloride channel opening, leading to neuronal hyperpolarization and sedation. [165-166]

- Binding site: propofol binds to a distinct site on the GABA-A receptor, separate from the benzodiazepine site, which involves the beta subunit interface rather than the alpha-gamma interface.
- Action: propofol enhances GABA's inhibitory effect by increasing the duration of chloride channel opening, leading to sustained chloride influx and a stronger hyperpolarizing effect compared to benzodiazepines.
- Selectivity: propofol interacts more broadly across different GABA-A receptor subtypes, not being as specific as midazolam for particular subunit combinations. [167]

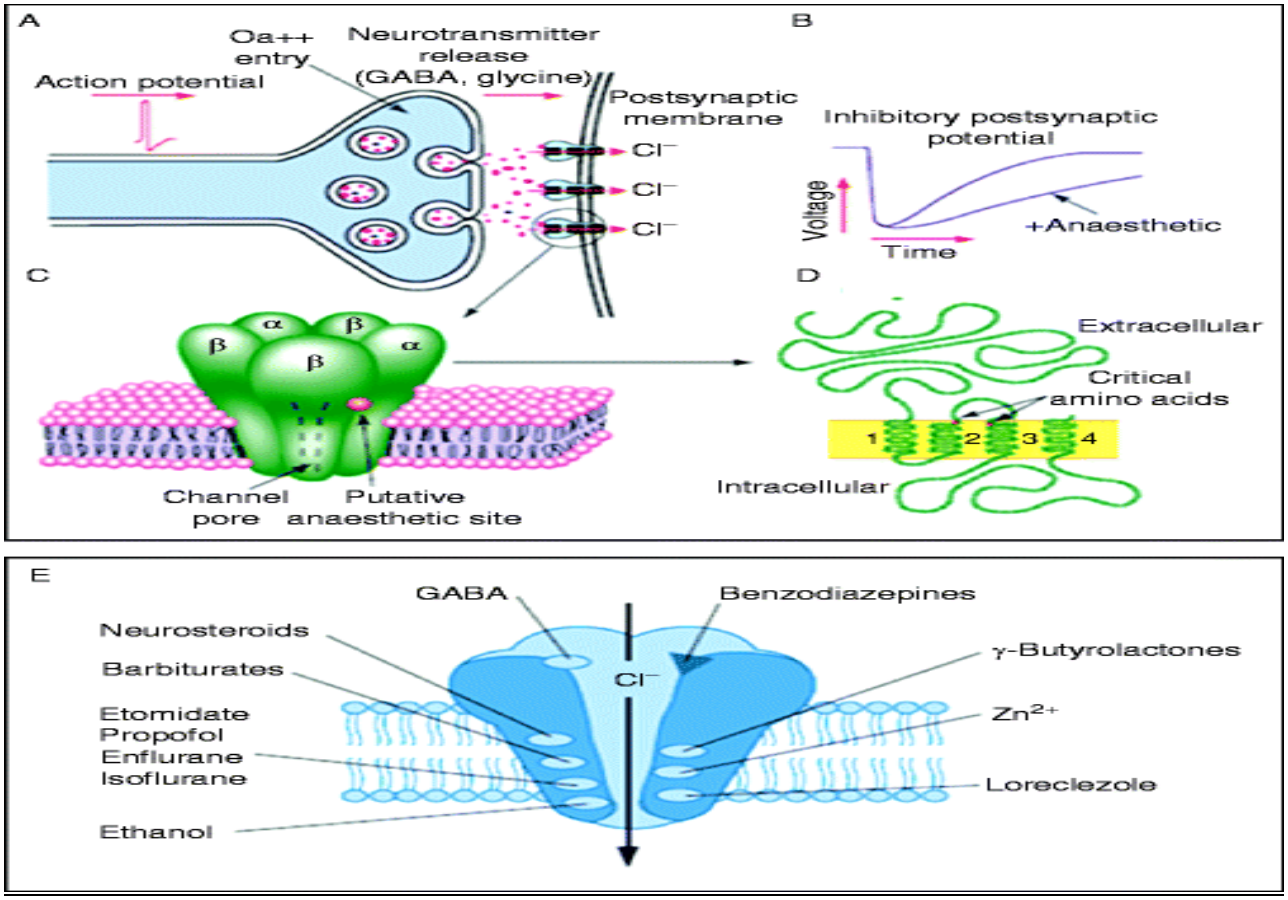


Figure 20: Mecanism of action of propofol (binding sites)

While both drugs potentiate GABA-A receptor-mediated inhibition, midazolam works by increasing the frequency of chloride channel opening via the benzodiazepine binding site (alpha-gamma interface), whereas propofol increases the duration of channel opening through a

distinct site associated with the beta subunit. This difference in binding and modulation leads to variation in the depth, duration, and onset of their sedative effects.

2. Pharmacokinetics:

The pharmacokinetic profiles of midazolam and propofol reveal distinct characteristics that influence their clinical application, particularly in anesthesia.

A. Midazolam:

- Absorption & Distribution: midazolam is rapidly absorbed after intravenous (IV) administration, with peak effects occurring within minutes. It has high lipid solubility, facilitating quick passage through the blood-brain barrier. The drug is widely distributed, with a volume of distribution around 1-3 L/kg, depending on the age and health of the patient. [168]
- Metabolism: midazolam undergoes hepatic metabolism, primarily by the cyto-chrome P450 enzyme CYP3A4, producing an active metabolite, 1-hydroxymidazolam. This metabolite is then further metabolized and excreted renally, thus liver function significantly affects midazolam clearance. [169]
- Elimination: the elimination half-life of midazolam ranges between 1.5-3 hours in adults but can be prolonged in patients with hepatic impairment or in elderly patients. Renal failure impacts the clearance of its metabolite but has minimal effect on midazolam itself. [170]

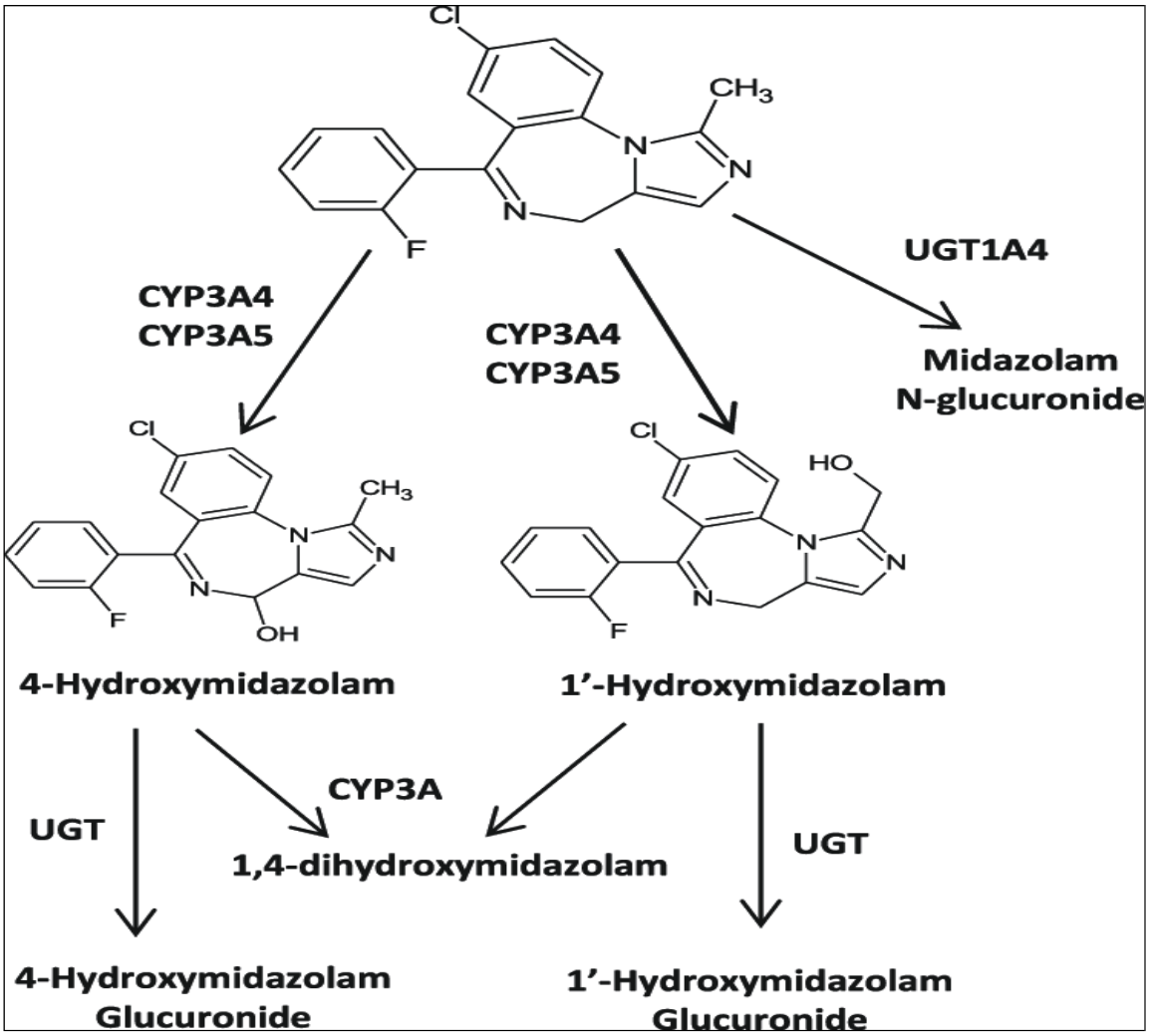


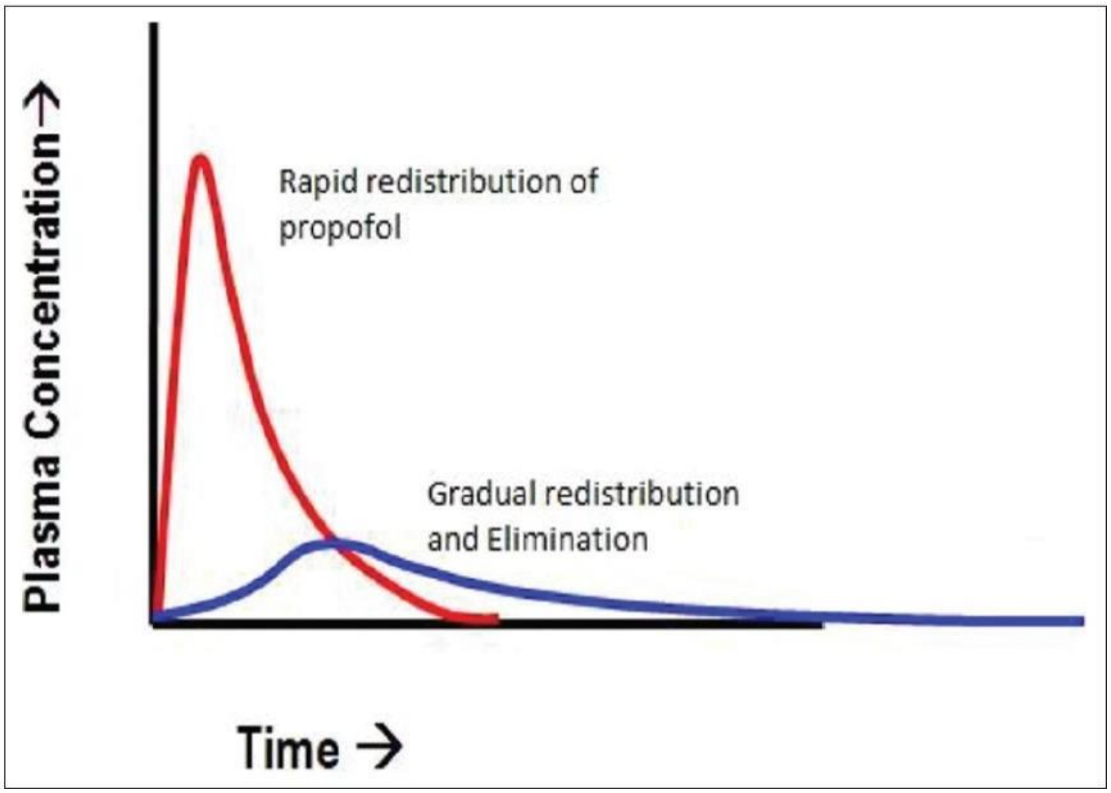
Figure 21: Pharmacokinetics of midazolam

B. Propofol:

- Absorption & Distribution: propofol is administered exclusively by IV due to its lipophilicnature and poor water solubility. It rapidly distributes into highly perfused, reaching peak CNSeffects within 1-2 minutes. Its volume of distribution ranges from 2-10 L/kg, which facilitatesrapid onset and redistribution out of the CNS, resulting in quick recovery after bolus doses. [171]

- Metabolism: propofol undergoes extensive hepatic metabolism primarily via CYP2B6 and CYP2C9, forming inactive metabolites, which are excreted renally. Metabolism also occurs extrahepatically, including in the kidneys and lungs, which allows for rapid clearance despite hepatic impairment. [172]
- Elimination: Propofol has a short half-life of 2-4 minutes for distribution and around 30-60 minutes for the elimination phase. Its clearance rate (around 1.5-2 L/min) exceeds hepatic blood flow, explaining its suitability for continuous infusions. [173]

Figure 22: Pharmacokinetics of propofol



Practice Guidelines

I. Safe practice of sedation:

1. Assess sedation status:

The healthcare provider must determine the specific indication for the use of sedatives. If a sedative is needed, the patient's current sedation status should be assessed and then frequently reassessed using valid and reliable scales. [174-175-176-177]

2. Sedation practice:

A. Target depth of sedation:

The 2013 guidelines suggested targeting light levels of sedation defined as a RASS scale score of greater than or equal to -2 and eye opening of at least 10 minutes. [178-179]

B. Daily sedative interruption / nurse-protocolized sedation:

In critically ill, DSI protocols and NP-targeted sedation can achieve and maintain a light level of sedation.

A DSI or a SAT is defined as a period of time, each day, during which a patient's sedative medication is discontinued and patients can wake up and achieve arousal and/or alertness, defined by objective actions such as opening eyes in response to a voice, following simple commands, and/or having a Sedation-Agitation Scale (SAS) score of 4-7 or a RASS score of -1 to +1.

NP-targeted sedation is defined as an established sedation protocol implemented by nurses at the bedside to determine sedative choices and to titrate these medications to achieve prescription-targeted sedation scores. [180]

C. Choice of sedative:

The 2018 PADIS guidelines recommend using either propofol or dexmedetomidine over benzodiazepines for sedation in critically ill patients. Most studies have administered benzodiazepines as continuous infusions rather than intermittent boluses. In critically ill patients,

clinically significant outcomes were defined for propofol and dexmedetomidine by a time to achieve light sedation within at least 4 hours and a time to extubation within 8–12 hours. [181]

II. Assess, prevent, and manage pain:

Inadequately treated pain can result in delirium as well as several other complications. Pain should be monitored routinely in all adult ICU patients. This can be done by using validated pain scales such as the Behavioral Pain Scale (BPS). [177]

1. Both SAT and SBT:

Spontaneous awakening trials (SATs) are pauses of intravenous narcotics and sedatives. Spontaneous breathing trials (SBTs) are periods of minimal ventilator support.

A randomized controlled trial comparing a daily SAT and SBT protocol with daily SBT plus routine sedation found that patients on the SAT plus SBT protocol spent more days breathing without assistance and less time in the ICU. [182]

2. Choice of Analgesia and Sedation:

Effective management of pain and anxiety is a primary objective in the ICU. There are several validated scales published for assessment of sedation level in the ICU, for example the Richmond Agitation–Sedation Scale (RASS).

The most effective medication and titration protocol for sedation and analgesia is not yet clear, and likely depends on the clinical context and patient characteristics.

III. Assess, Prevent, and Manage delerium:

1. Pharmacological treatment:

In 1978 the use of intravenous haloperidol was reported in a series of 15 delirious patients during recovery from cardiac surgery[183] and this became the mainstay of treatment for delirium in the critically ill. The next several decades saw an increasing reliance on antipsychotic medications for this purpose. In 2002 the SCCM guidelines for use of sedatives and

analgesics in ICU recommended haloperidol as the preferred agent for treatment of delirium. [184]

Based on more recent literature, the current Society of Critical Care Medicine (SCCM) guidelines suggest against routine use of antipsychotics for delirium including haloperidol. Other pharmacologic interventions (e.g., dexmedetomidine, statine and ketamine) are under investigation and their impact is not yet clear. [185]

2. Non Pharmacological treatment :

For decades, nonpharmacologic interventions have been the cornerstone of delirium management and treatment. A key component of delirium management is monitoring for early identification and risk factor modification. The most widely used tool for delirium assessment in the ICU is the Confusion Assessment Method for the ICU (CAM-ICU)[186]. It is important to assess patients regularly to reduce the risk of overlooking hypoactive delirium, and the optimal time for this assessment is during SATs. [187]

Primary delirium prevention principles:

A. Repeated reorientation [181]
B. A sleep promotion [181]
C. Early mobilization: Early mobility consists of a range of activities from passive range of motion to ambulation with assistance. Any member of the care team can perform early mobility; the appropriate level of activity is determined based on the patient's level of sedation. Early mobilization during SATs was associated with improved odds of return to independent functional status by discharge in a series of critically ill adults on mechanical ventilation. [186]
D. Family engagement and empowerment: Empowering family members to be equal participants in patient care can improve ICU team performance and communication, reveal key insights into the patient condition, and keep providers focused on the most salient goals of care for each patient. This intervention may also lead to early

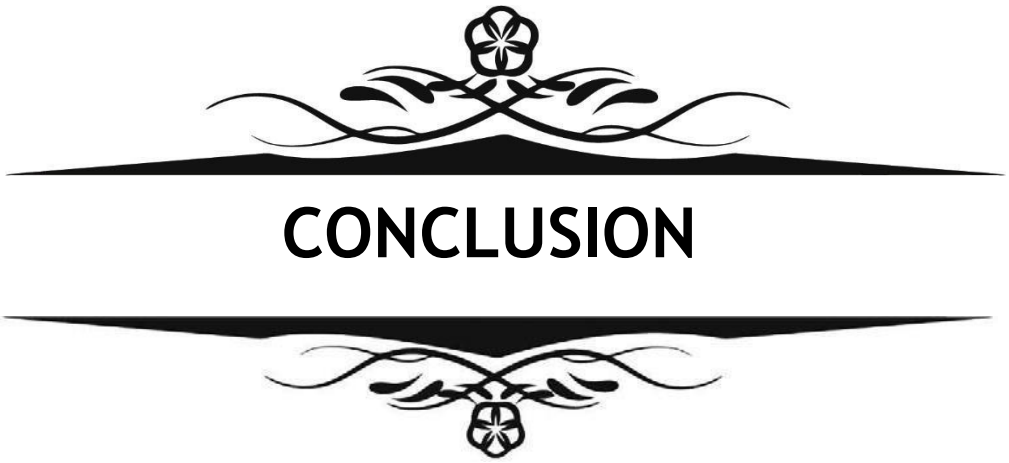
Identification of and reduction in the burden of ICU-related psychological and emotional stress among family members. [188]

E. Timely removal of catheters and physical restraints. [181]

F. Use of eye glasses, magnifying lenses, hearing aids, and earwax disimpaction. [181]

G. Correction of dehydration. [181]

H. Minimization of unnecessary noise and tactile stimuli. [181]



CONCLUSION

Our study highlights key findings regarding sedation practices in an adult surgical ICU, shedding light on important real-world outcomes and implications.

Conducted within a real-world clinical setting and utilizing a precise sampling approach, our research offers a comprehensive analysis of sedation use, specifically emphasizing the increased reliance on propofol during an extended supply disruption.

This detailed evaluation strengthens our understanding of sedation dynamics in surgical ICU environments and presents actionable insights for optimizing care.

Study Strengths:

- **Real-Life Setting:** Conducting the study in a genuine clinical environment enhances the external validity and applicability of our results to everyday ICU practices.
- **Precise Sampling:** Focusing exclusively on adult surgical ICU patients allowed for targeted and relevant analysis, improving the robustness and precision of our conclusions.
- **Adequate Sample Size:** Including 103 patients provided strong statistical power, making our findings reliable and meaningful for similar populations.
- **Access to Own Patient Data:** Leveraging data from our ICU allowed for an in-depth exploration of sedation practices, reflecting the unique characteristics of our healthcare setting.

Study Limitations:

- **Retrospective Design:** The study's retrospective nature limits causal inferences and introduces potential biases inherent to this research approach.
- **Incomplete Medical Records:** Missing data, such as BMI, restricted our ability to analyze certain variables that could influence outcomes.
- **Lack of Long-Term Outcome Analysis:** We did not evaluate long-term complications associated with sedation, limiting the scope of our findings to short-term outcomes.
- **Propofol Supply Disruption:** The unusual period of propofol shortage may have skewed sedation practices, affecting the generalizability of our results.

In summary, while our study provides valuable insights into sedation practices in an adult surgical ICU and highlights the impact of external factors like medication supply disruptions, it also points to areas needing further research.

Future studies should employ prospective designs, consider comprehensive data collection, and explore long-term patient outcomes. Despite its limitations, our research offers critical information for improving sedation strategies in real-world ICU settings.

ABSTRACTS

ABSTRACT:

The judicious use of sedative agents has become essential in modern intensive care units (ICUs), particularly for patients requiring mechanical ventilation. Sedatives are crucial for managing pain, agitation, and physiological stress, facilitating essential procedures and reducing the metabolic demands in critically ill patients.

However, sedation is a double-edged sword: while it provides undeniable clinical benefits, its misuse or prolonged administration can lead to serious complications, influencing patient recovery and increasing healthcare burdens.

This study aims to evaluate sedation practices and related complications in the surgical ICU of University Hospital Center Mohamed VI over a one-year period (June 2022 to June 2023) to better understand their impact on patient outcomes and resources utilization.

We conducted a retrospective, descriptive, and analytical study, analyzing data from 104 patients who met the inclusion criteria. The data collected included epidemiological profiles, clinical and paraclinical parameters, sedation protocols, and incidence of sedation-related complications.

The patient cohort comprised predominantly young adults, with a mean age of 28.84 years, and exhibited a significant gender imbalance, with 79.6% being male.

The demographic characteristics, including a lower prevalence of comorbidities compared to international studies, reflect the epidemiological context of our region, heavily influenced by trauma-related admissions.

Our study revealed that trauma-related conditions, particularly polytrauma (35.9%) and cranial trauma (20.4%), were the most common diagnoses necessitating ICU admission and sedation.

Hemodynamic instability (27.9%) and intracranial hypertension (43.3%) were the leading indications for sedation, highlighting the critical condition of the patient population.

The predominant use of propofol (66.99%) over midazolam (30.76%) was driven by an eight-month supply disruption, affecting protocol consistency.

Sedation depth was assessed using the Ramsay Sedation Scale, and deep sedation (Ramsay score ≥ 4) was reported in 92.3% of cases. This heavy reliance on deep sedation contrasts with international trends emphasizing lighter sedation to minimize complications.

The analysis identified that the mean duration of sedation was 5.5 days, with 90% of patients requiring mechanical ventilation, lasting an average of 5.25 days.

Respiratory complications were the most frequent adverse outcomes, with a 39% incidence of respiratory infections, aligning with studies from regions facing similar infection control challenges.

Additionally, 25.96% of patients experienced unplanned extubation, a significant concern linked to prolonged sedation and mechanical ventilation.

Other notable complications included delirium (20.19%), pressure ulcers (30.76%), ICU-acquired weakness (34.62%), and thromboembolic events (9.6%).

Hemodynamic instability, hyperthermia, and delayed awakening were prevalent adverse drug events.

Analytical results revealed that prolonged sedation was a significant independent risk factor for multiple complications, including respiratory infections (p-value < 0.0001), unplanned extubation (p-value < 0.01), and reintubation (p-value < 0.05).

Mechanical ventilation exceeding five days was strongly associated with adverse outcomes, underscoring the interplay between sedation duration, ventilator dependence, and morbidity.

Conversely, variables such as age and comorbidities, often deemed critical in ICU prognosis, did not independently increase the risk of complications within our cohort, suggesting that the sedation strategy and ventilator management were more influential determinants.

Our study highlights several critical insights into sedation management. The high prevalence of complications associated with deep and prolonged sedation emphasizes the need for refining sedation protocols to balance efficacy and safety.

Recommendations include adopting evidence-based sedation strategies, incorporating daily sedation interruption, and prioritizing lighter sedation where feasible.

Additionally, proactive measures to minimize mechanical ventilation duration and implement infection prevention protocols could significantly reduce respiratory complications and improve patient outcomes.

In conclusion, this comprehensive analysis provides a foundational understanding of sedation practices and their implications in our ICU setting.

By identifying modifiable risk factors and proposing strategic interventions, our research aims to enhance sedation management, improve patient safety, and optimize healthcare resource utilization.

Future research should focus on prospective studies to validate these findings and explore innovative approaches for sedation and ventilator management, ultimately contributing to the global efforts in improving critical care practices.

RESUME:

L'utilisation judicieuse des agents sédatifs est devenue essentielle dans les unités de soins intensifs (USI) modernes, en particulier pour les patients nécessitant une ventilation mécanique. Les sédatifs sont cruciaux pour gérer la douleur, l'agitation et le stress physiologique, facilitant les interventions nécessaires et réduisant les besoins métaboliques chez les patients en état critique.

Cependant, la sédation est une arme à double tranchant : bien qu'elle offre des avantages cliniques indéniables, une administration prolongée ou inappropriée peut entraîner de graves complications, influençant la récupération des patients et augmentant la charge pour les systèmes de santé.

Cette étude vise à évaluer les pratiques de sédation et les complications associées dans l'USI chirurgicale du Centre Hospitalier Universitaire Mohamed VI sur une période d'un an (de juin 2022 à juin 2023), afin de mieux comprendre leur impact sur les résultats des patients et l'utilisation des ressources.

Nous avons mené une étude rétrospective, descriptive et analytique, analysant les données de 104 patients répondant aux critères d'inclusion.

Les données recueillies comprenaient les profils épidémiologiques, les paramètres cliniques et paracliniques, les protocoles de sédation et l'incidence des complications liées à la sédation.

La cohorte étudiée comprenait principalement de jeunes adultes, avec un âge moyen de 28,84 ans, et un déséquilibre marqué entre les sexes, 79,6 % étant des hommes.

Les caractéristiques démographiques, y compris une prévalence plus faible de comorbidités par rapport aux études internationales, reflètent le contexte épidémiologique de notre région, fortement influencé par les admissions liées aux traumatismes.

Notre étude a révélé que les traumatismes, en particulier les polytraumatismes (35,9 %) et les traumatismes crâniens (20,4 %), étaient les diagnostics les plus fréquents nécessitant une admission en USI et une sédation.

L'instabilité hémodynamique (27,9 %) et l'hypertension intracrânienne (43,3 %) étaient les principales indications de sédation, soulignant la gravité de l'état des patients.

L'utilisation prédominante du propofol (66,99 %) par rapport au midazolam (30,76 %) était due à une rupture de stock de huit mois, impactant la cohérence des protocoles.

La profondeur de la sédation a été évaluée à l'aide de l'échelle de Ramsay, et une sédation profonde (score Ramsay $\geq$ 4) a été observée chez 92,3 % des patients. Cette forte dépendance à la sédation profonde contraste avec les tendances internationales qui prônent une sédation plus légère pour minimiser les complications.

L'analyse a révélé que la durée moyenne de la sédation était de 5,5 jours, 90 % des patients nécessitant une ventilation mécanique, d'une durée moyenne de 5,25 jours.

Les complications respiratoires étaient les plus fréquentes, avec une incidence de 39 % d'infections respiratoires, alignée avec les études de régions faisant face à des défis similaires en matière de contrôle des infections.

De plus, 25,96 % des patients ont présenté des extubations accidentelles, une préoccupation importante liée à la sédation et à la ventilation prolongée.

D'autres complications notables comprenaient le delirium (20,19 %), les escarres (30,76 %), la faiblesse acquise en réanimation (34,62 %) et les événements thromboemboliques (9,6 %).

Les événements indésirables hémodynamiques, l'hyperthermie et le réveil retardé étaient également fréquents.

Les résultats analytiques ont révélé que la sédation prolongée était un facteur de risque indépendant significatif pour de multiples complications, y compris les infections respiratoires ($p < 0,0001$), l'extubation accidentelle ($p < 0,01$) et la réintubation ($p < 0,05$).

La ventilation mécanique de plus de cinq jours était fortement associée à des résultats défavorables, soulignant l'interaction entre la durée de la sédation, la dépendance à la ventilation et la morbidité.

En revanche, des variables comme l'âge et les comorbidités, souvent considérées comme critiques dans le pronostic des patients en réanimation, n'ont pas augmenté le risque de complications de manière indépendante dans notre cohorte, suggérant que la stratégie de sédation et la gestion de la ventilation étaient des déterminants plus influents.

Notre étude met en lumière l'importance de revoir les protocoles de sédation pour équilibrer l'efficacité et la sécurité.

Nos recommandations incluent l'adoption de stratégies de sédation basées sur des preuves, la réduction de la durée de la ventilation mécanique, et la mise en œuvre de protocoles de prévention des infections.

En conclusion, cette analyse fournit une compréhension des pratiques de sédation et leurs implications dans notre USI. En identifiant les facteurs de risque modifiables, cette recherche vise à améliorer la sécurité des patients et à optimiser l'utilisation des ressources.

Les recherches futures devraient se concentrer sur des études prospectives pour explorer davantage les stratégies innovantes de gestion de la sédation et de la ventilation en soins intensifs.

ملخص:

أصبح استخدام المهدئات بشكل مدروس ضرورة في وحدات العناية المركزة الحديثة، خاصة لدى المرضى الذين هم بحاجة إلى التنفس الصناعي.

المهدئات لها دور أساسي في إدارة الألم، والقلق، مما يسهل إجراء التدخلات الطبية الأساسية ويقلل الاحتياجات الأيضية للمرضى في حالة حرجة.

رغم منافعها العديدة إلا أن المهدئات تعتبر سيفا ذو حدين إذ أن اعتمادها بشكل غير مدروس ومُطَوَّل قد يؤدي إلى مضاعفات خطيرة تعرقل تعافي المرضى مشكلة بذلك عبئا إضافيا على نظام الرعاية الصحية.

تهدف هذه الدراسة إلى تقييم أنظمة التخدير والمضاعفات المتعلقة بها في وحدة العناية المركزة الجراحية بمستشفى محمد السادس الجامعي خلال فترة عام (يونيو 2022 إلى يونيو 2023) لفهم أفضل لتأثيرها على نتائج المرضى واستعمال الموارد.

أجرينا دراسة استرجاعية وصفية وتحليلية، شملت 104 مريض استوفوا معايير الإدراج. هذا و قد شملت البيانات الملفات الوبائية، المعطيات السريرية والشبه السريرية ، بروتوكولات التخدير المعتمدة و نسبة حدوث المضاعفات المتعلقة بالتخدير.

بمتوسط عمر بلغ 28.84 سنة فإن غالبية المرضى في دراستنا هم شباب مع تفاوت كبير بين نسبتي الجنسين حيث بلغت نسبة الذكور 79.6%.

من جهة أخرى فإن الخصائص الديموغرافية التي تم استبيانها بما فيها نسبة الانتشار الضعيفة للاعتلالات المشتركة لدى المرضى الذين شملتهم دراستنا و هو ما يخالف ما ورد في أغلب الدراسات الدولية ، تعكس السياق الوبائي للمنطقة الذي تغلب عليه حالات الحوادث و الإصابات.

كشفت دراستنا أن الحوادث، لا سيما الإصابات المتعددة (35.9%) وإصابات الرأس (20.4%)، كانت التشخيصات الأكثر شيوعًا التي تتطلب ولوج وحدة العناية المركزة و التخدير.

فيما شكل ارتفاع الضغط داخل الجمجمة (43.3%) و الاضطرابات الهيموديناميةٍ (27.9%) النسبة الاكبر من الحالات التي استوجبت التخدير نظرا لدلالتها على الحالة الحرجة للمرضى .

من جهة أخرى ، فإن استخدام البروبوفول لدى 66.99% من المرضى مقابل استخدام الميدازولام بنسبة أقل تصل إلى 30.76% راجع لانقطاع الامدادات من هذا الأخير لمدة ثمانية أشهر ، مما أثر على اتساق البروتوكولات المعتمدة.

أما فيما يخص تقييم عمق التخدير، فقد اعتمدنا خلال دراستنا مقياس رامساي ، حيث تبَيَّن أن 92.3% من المرضى حصلوا على تخدير عميق (درجة رامساي ≥ 4) . و هو ما يتناقض مع التوجهات الدولية التي تحرص على تخفيف عمق التخدير تفاديا للمضاعفات المصاحبة له.

أما بالنسبة لمدة التخدير فقد أبانت نتائج دراستنا عن متوسط تخدير لمدة 5.5 أيام احتاج خلالها 90% من المرضى للتنفس الصناعي لمدة معدلها 5.25 يوم.

المضاعفات التنفسية كانت الأكثر شيوعا حيث بلغت نسبة حدوث عدوى على مستوى الجهاز التنفسي 39% ، و هي نسبة تتماشى مع نتائج مختلف الدراسات السابقة في مناطق تواجه هي الأخرى صعوبات في مواجهة الالتهابات .

بينما أُدرِج النزع العرضي للتنبيب لدى 25.96% من المرضى مُشكِّلا بذلك شاغِلاً مهما يرتبط أساسًا بالتخدير و التنفس الصناعي المُطوَّل .

كما شملت نتائجنا مضاعفات أخرى كالهذيان (20.19%) ، قرح الضغط (30.76%) ، ضعف العضلات المكتسب في العناية المركزة (34.62%) و الجلطات الدموية (9.6%).

الى جانب ما سبق فإن الاضطرابات الهيموديناميةارتفاع درجة حرارة الجسم و تأخر الاستيقاظ تعتبر هي الأخرى من العوارض المتكرر حدوثها.

من جهتها أوضحت النتائج التحليلية أن التخدير المُطوَّل كان عاملاً مستقلاً لمضاعفات عديدة ، بما في ذلك الالتهابات التنفسية ($p < 0.0001$)، النزع العرضي للتنبيب ($p < 0.01$)، و إعادة التنبيب ($p < 0.05$).

و بهذا فإن ارتباط التهوية الميكانيكية التي تجاوزت خمسة أيام بنتائج سلبية يبرز بشكل كبير العلاقة بين مدة التخدير ، إدارة التهوية الميكانيكية و الاعتلال .

من جهة أخرى فإن العمر و الاعتلالات المشتركة و التي تعتبر عادة من أهم العوامل المؤثرة على تعافي مرضى العناية المركزة ، لم يكن لها دور مباشر في ظهور المضاعفات التي تمت دراستها خلال بحثنا ، و بهذا يكون العامل الأقوى هو استراتيجية التخدير المُتبعة مع حسن تسيير التنفس الصناعي .

تسلط دراستنا الضوء على ضرورية إعادة النظر في البروتوكولات المعتمدة

للتخدير و ذلك للحفاظ على التوازن المطلوب بين فعالية العلاج و سلامة المريض.

تشمل توصياتنا بشكل عام اعتماد استراتيجيات تخدير تستند إلى أدلة ، تقليص مدة التخدير و مدة التنفس الصناعي و تطبيق منهجيات تمكن من الوقاية من التعفنات .

ختاما ، تمكن هذه الدراسة من فهم ممارسات التخدير و مكانتها داخل وحدتنا الصحية . كما تهدف لضمان سلامة المرضى و الحرص على استغلال أفضل للموارد، و ذلك من خلال تحديدها لعوامل الخطر القابلة للتعديل.

لذا وجب التركيز مستقبلا على إجراء دراسات استطلاعية لمواصلة استكشاف و تحليل الاستراتيجيات المبتكرة فيم يخص التخدير و التنفس الصناعي داخل وحدات العناية المركزة .

APPENDIX

1-Patient Identification:

- Patient identifier :
- Full Name:
- Date of admission :
- Date of discharge:
- ICU admission diagnosis:

2-Demographic Information:

- Age:
- Gender:
- O/ R:
- Profession:
- Health care insurance:
- Body mass index (BMI):
- Comorbidities:
  Medical:
  Surgical :
- Medication intake:
- Allergies:
- intoxications:

3-Sedation Management:

- Indication for sedation:
- Sedation protocol used:

Bolus ☐
IV continuous infusion ☐

- Sedative medications administered:

Propofol ☐
Midazolam ☐

- Sedation depth monitoring tools utilized:

Ramsay scale ☐
Richmond Agitation-Sedation Scale ☐
Sedation-Agitation Scale ☐

- Duration of sedation

- Use of mechanical ventilation:
- Duration of mechanical ventilation:
- Co-administration of analgesics:
- Co-administration of other medications:

4.Complications:

a-Respiratory Complications:

- Incidence of ventilator-associated pneumonia:
- Episodes of unplanned extubation:
- Need for reintubation:
- Acute hypoxemic respiratory failure (AHRF):

b-Delirium Assessment:

- Frequency of delirium episodes:
- Duration of delirium episodes:
- Use of non-pharmacological strategies for delirium prevention:

- Early mobilization ☐
- Sleep promotion ☐

c- Decubitus complications:

Bedsores ☐
Venous thromboembolism ☐
ICU acquired weakness ☐
Delayed awakening ☐

d- Cost increase:

e-Adverse Drug Events:

- Specific adverse drug events associated with sedatives:

Allergic reaction ☐
Hypotension / Hypertension ☐
Tachycardia ☐
Delayed awakening ☐

- Medication errors related to sedative administration

f- Prolonged Sedation:

5. Outcome Measures:

- Length of stay in the intensive care unit:
- Mortality rate:

- Discharge disposition:

  Home ☐

  Rehabilitation facility ☐

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أقْسِم بِالله العَظِيم

أن أراقبَ الله في مِهْنَتِي.

وأن أصُونَ حياة الإنسان في كآفّة أطوَارهَا في كل الظروف والأحَوال باذلة وسْعِي في إنقاذها مِن الهَلاك ِوالمرَضِ والألَم والقَلَق.

وأن أحفَظَ لِلنَاسِ كرَامَتهُم، وأسْتر عَوْرَتهُم، وأكتمَ سِرَّهُمْ.

وأن أكونَ عَلى الدوَام من وسائِل رحمة الله، باذلة رعايتي الطبية للقريب والبعيد، للصالح والطالح، والصديق والعدو.

وأن أثابر على طلب العلم، وأسَخِّرَه لِنَفْعِ الإنْسَان لا لأذَاه.

وأن أُوَقّر َمَن عَلَّمَني، وأُعَلّمَ مَن يصغرني، وأكون أختا لِكُلّ زَميلٍ في المِهنَةِ الطِّبِيّة مُتعَاونِينَ عَلى البرّ والتقوى.

وأن تكون حياتي مِصْدَاق إيماني في سِرّي وَعَلانيَتي، نَقِيَّة مِمّا يشينها تجَاهَ الله وَرَسُولِهِ وَالمؤمِنين.

كليـــــــة الـطـب
والصيدلة - مراكش
FACULTÉ DE MÉDECINE
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UNIVERSITÉ CADI AYYAD

سنة 2024 أطروحة رقم : 544

تحليل المضاعفات المتعلقة بالتخدير في المرضى الذين يعانون من حالات حرجة: تقييم المخاطر واستراتيجيات الوقاية

الأطروحة

قدمت ونوقشت علانية يوم 2024/11/

من طرف

السيدة مريم كلال

المزداد في 2000/02/16 بمراكش

لنيل شهادة الدكتوراه في الطب

الكلمات الأساسية:

التخدير-وحدة التخدير و الإنعاش للكبار-المضاعفات

اللجنة

السيد	م. الخلوقي أستاذ في الإنعاش والتخدير	الرئيس
السيد	ي. الزروقي أستاذ في الإنعاش والتخدير	المشرفة
السيد	ح. رباحي أستاذ في الإنعاش والتخدير	الحكام
السيدة	م. الخياري أستاذ في الإنعاش الطبي	
السيد	م. شرع أستاذة في طب الاعصاب	