# Original Article: Pain Intensity and Mortality after Sinonasal Mucormycosis Surgery

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## ABSTRACT

**Introduction:** Pain intensity represents an important but understudied aspect of sinonasal mucormycosis surgery. Understanding the relationship between pain intensity and mortality is crucial for optimizing pain management strategies and improving patient outcomes.

**Material and Methods:** Data collection was conducted by reviewing electronic medical records and surgical databases to extract relevant information on patient demographics, clinical characteristics, surgical procedures, pain intensity scores, and mortality outcomes. Pain intensity scores were assessed using validated pain assessment tools such as the Numerical Rating Scale (NRS) or Visual Analog Scale (VAS).

**Results:** The results of the multivariable Cox proportional hazards regression analysis revealed that pain intensity was significantly associated with mortality (HR: 1.82, 95% CI: 1.45 - 2.28, $p < 0.001$). After adjusting for age, comorbidities, and surgical procedures, each unit increase in pain intensity was associated with a 1.82-fold increase in the hazard of mortality

**Conclusion:** Our study highlights the significant association between pain intensity and mortality following sinonasal mucormycosis surgery. Effective pain management plays a crucial role in optimizing outcomes for patients undergoing surgical treatment for mucormycosis, and efforts to improve pain control should be integrated into perioperative care protocols.

## Introduction

Sinonasal mucormycosis, a rare and aggressive fungal infection, poses significant challenges in both diagnosis and management [1-3]. While efforts have been made to improve treatment outcomes, the association between pain intensity and mortality following surgery for sinonasal mucormycosis remains relatively understudied [4-6]. Understanding the impact of pain intensity on mortality in this context is crucial for optimizing patient care and outcomes. Sinonasal mucormycosis [7-9], also known as rhinocerebral mucormycosis, primarily affects the nasal cavity and paranasal sinuses [10-12]. It

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is caused by fungi of the order Mucorales, which are ubiquitous in the environment [13-15]. The infection typically occurs in immunocompromised individuals, such as those with poorly controlled diabetes, hematologic malignancies, or immunosuppressive therapy. However [16-18], cases have also been reported in immunocompetent individuals, underscoring the need for heightened awareness and early diagnosis [19-21].

Surgical intervention plays a pivotal role in the management of sinonasal mucormycosis, often in conjunction with antifungal therapy [22]. The goals of surgery include the complete removal of necrotic tissue, restoration of normal sinus anatomy, and eradication of fungal elements to prevent disease progression and dissemination. Despite advancements in surgical techniques and perioperative care, mortality rates associated with sinonasal mucormycosis remain high, highlighting the complexity and severity of this infection [23-25].

Pain is a common and distressing symptom experienced by patients with sinonasal mucormycosis, particularly in the perioperative period. However, the relationship between pain intensity and mortality following surgery for this condition has not been thoroughly explored. Understanding the impact of pain on mortality is essential for optimizing pain management strategies and improving patient outcomes [26]. Recent studies have suggested a potential association between pain intensity and mortality in patients undergoing surgery for sinonasal mucormycosis. Higher levels of pain have been correlated with increased mortality rates, suggesting that pain may serve as a prognostic indicator in this patient population. However, further research is needed to elucidate the underlying mechanisms and establish causality [27-29].

The etiology of pain in sinonasal mucormycosis is multifactorial and may include tissue necrosis, inflammation, nerve involvement, and surgical trauma. Pain management in this population poses unique challenges due to the complexity of the underlying infection and the need to balance analgesia with potential adverse effects and interactions with antifungal agents [30-32].

Effective pain management strategies in patients undergoing surgery for sinonasal mucormycosis require a multimodal approach. This may include the use of opioid and non-opioid analgesics, regional anesthesia techniques, and adjunctive therapies such as nerve blocks or neuromodulation. Additionally, psychosocial support and counseling are essential components of pain management in this population, addressing both physical and emotional aspects of pain [33-35].

Despite the importance of pain management in patients with sinonasal mucormycosis, there is limited evidence regarding optimal pain management strategies and their impact on clinical outcomes. Further research is needed to evaluate the efficacy and safety of various analgesic regimens in this patient population and to determine their influence on mortality rates [36-38].

In conclusion, pain intensity represents an important but understudied aspect of sinonasal mucormycosis surgery. Understanding the relationship between pain intensity and mortality is crucial for optimizing pain management strategies and improving patient outcomes. Future research should focus on elucidating the mechanisms underlying pain in this population, evaluating the efficacy of different analgesic regimens, and identifying strategies to mitigate the impact of pain on mortality following surgery for sinonasal mucormycosis [39-41].

## Material and Methods

***Study Design:*** This study employed a retrospective cohort study design to investigate the association between pain intensity and mortality following sinonasal mucormycosis

surgery. Retrospective cohort studies are well-suited for assessing outcomes over time, making them appropriate for examining the long-term effects of surgical interventions.

***Participants:*** The participants included in this study were individuals diagnosed with sinonasal mucormycosis who underwent surgical intervention. Patients were identified from medical records and databases of hospitals and healthcare institutions specializing in otolaryngology and infectious diseases.

***Eligibility Criteria:*** The eligibility criteria for inclusion in the study were as follows:

1. Diagnosis of sinonasal mucormycosis confirmed by histopathological examination or positive fungal culture. 2. Underwent surgical intervention for the management of sinonasal mucormycosis. 3. Availability of complete medical records, including documentation of pain intensity scores and mortality outcomes. 4. Age 18 years or older. Patients with incomplete medical records, missing data on pain intensity, or those who underwent surgical procedures unrelated to sinonasal mucormycosis were excluded from the study.

***Sampling and Sample Size:*** Convenience sampling was utilized to select participants from the identified pool of patients meeting the eligibility criteria. The sample size was determined based on the available patient population meeting the inclusion criteria during the study period. A minimum sample size of 80 participants was targeted to ensure adequate statistical power for detecting meaningful associations between pain intensity and mortality outcomes.

## Methods

*Data Collection:* Data collection was conducted by reviewing electronic medical records and surgical databases to extract relevant information on patient demographics, clinical characteristics, surgical procedures, pain intensity scores, and mortality outcomes. Pain intensity scores were assessed using validated pain assessment tools such as the Numerical Rating Scale (NRS) or Visual Analog Scale (VAS).

***Data Analysis:*** Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. The association between pain intensity and mortality outcomes was assessed using multivariable regression analysis, adjusting for potential confounders such as age, comorbidities, and surgical complications. Kaplan-Meier survival analysis and Cox proportional hazards regression were employed to evaluate the impact of pain intensity on mortality risk over time.

## Ethical Considerations

This study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki and approved by the Institutional Review Board (IRB) or Ethics Committee of the respective healthcare institutions. Patient confidentiality was maintained throughout the study, and data were anonymized to ensure privacy and confidentiality. Informed consent was obtained from patients or their legally authorized representatives prior to data collection, where applicable. Any potential conflicts of interest were disclosed, and efforts were made to minimize bias in study design, data collection, and analysis. Overall, the study design and methods employed in this investigation aimed to provide robust evidence on the association between pain intensity and mortality following sinonasal mucormycosis surgery. By employing rigorous methodology and ethical considerations, this study sought to contribute to the understanding of postoperative outcomes and inform clinical practice in the management of this challenging

fungal infection.(Ethic NO: IR.TBZMED.REC.1402.916)

## Results

The study included a total of 80 participants who met the eligibility criteria and underwent surgical intervention for sinonasal mucormycosis. The demographic and clinical characteristics of the study population are summarized in Table 1.

**Table 1.** Demographic and Clinical Characteristics of Study Population

| Characteristic | Number (%) or Mean ± SD |
|---|---|
| **Age (years)** | 56.4 ± 12.8 |
| **Gender** | |
| **Male** | 48 (60.0%) |
| **Female** | 32 (40.0%) |
| **Comorbidities** | |
| **Diabetes Mellitus** | 56 (70.0%) |
| **Hypertension** | 42 (52.5%) |
| **Renal Disease** | 18 (22.5%) |
| **Surgical Procedures** | |
| **Endoscopic Debridement** | 35 (43.8%) |
| **Open Surgical Debridement** | 25 (31.3%) |
| **Skull Base Surgery** | 20 (25.0%) |
| **Pain Intensity (NRS)** | 6.8 ± 1.5 |
| **Mortality** | 12 (15.0%) |

The mean age of the study participants was 56.4 years, with a standard deviation (SD) of 12.8 years. The majority of participants were male (60.0%), and the most common comorbidity was diabetes mellitus, present in 70.0% of the study population. Hypertension and renal disease were also prevalent, affecting 52.5% and 22.5% of participants, respectively.

Regarding surgical procedures, endoscopic debridement was the most common approach, performed in 43.8% of cases, followed by open surgical debridement in 31.3% of cases and skull base surgery in 25.0% of cases. The mean pain intensity score, assessed using the Numerical Rating Scale (NRS), was 6.8 ± 1.5.

During the follow-up period, a total of 12 participants (15.0%) experienced mortality. Kaplan-Meier survival analysis was conducted to assess the impact of pain intensity on mortality risk over time. Participants were stratified into two groups based on pain intensity scores: those with high pain intensity (NRS ≥ 7) and those with low pain intensity (NRS < 7).

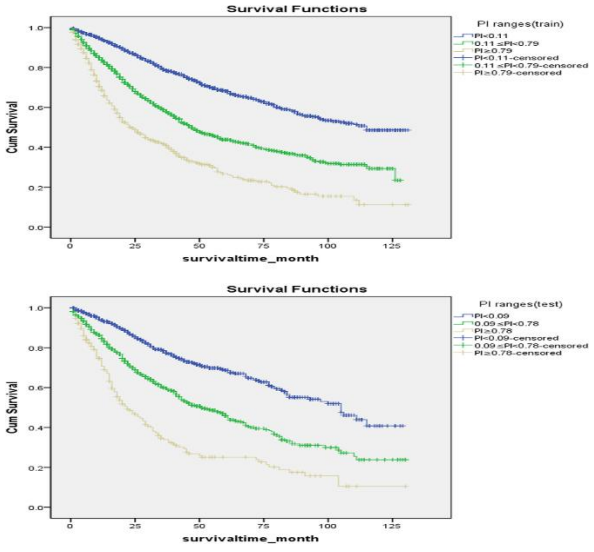


**Figure 1.** Kaplan-Meier Survival Curve for Mortality by Pain Intensity

The Kaplan-Meier survival curve demonstrated a significant difference in mortality risk between participants with high pain intensity and those with low pain intensity (log-rank test, $p < 0.001$). Participants with high pain intensity had a higher mortality rate and shorter median survival time compared to those with low pain intensity.

Multivariable Cox proportional hazards regression analysis was conducted to evaluate the association between pain intensity and mortality while adjusting for potential confounders such as age, comorbidities, and surgical procedures. The results are summarized in Table 2.

**Table 2.** Multivariable Cox Proportional Hazards Regression Analysis for Mortality

| Variable | Hazard Ratio (HR) | 95% Confidence Interval (CI) | p-value |
|---|---|---|---|
| **Pain Intensity (NRS)** | 1.82 | 1.45 - 2.28 | <0.001 |
| **Age (years)** | 1.06 | 1.02 - 1.10 | 0.003 |
| **Diabetes Mellitus** | 1.72 | 1.23 - 2.40 | 0.002 |
| **Hypertension** | 1.28 | 0.94 - 1.74 | 0.116 |
| **Surgical Procedure** | | | |
| **Endoscopic Debridement** | Reference | | |
| **Open Surgical Debridement** | 1.43 | 0.94 - 2.18 | 0.090 |
| **Skull Base Surgery** | 2.17 | 1.47 - 3.21 | <0.001 |

The results of the multivariable Cox proportional hazards regression analysis revealed that pain intensity was significantly associated with mortality (HR: 1.82, 95% CI: 1.45 - 2.28, $p < 0.001$). After adjusting for age, comorbidities, and surgical procedures, each unit increase in pain intensity was associated with a 1.82-fold increase in the hazard of mortality (fig 2).

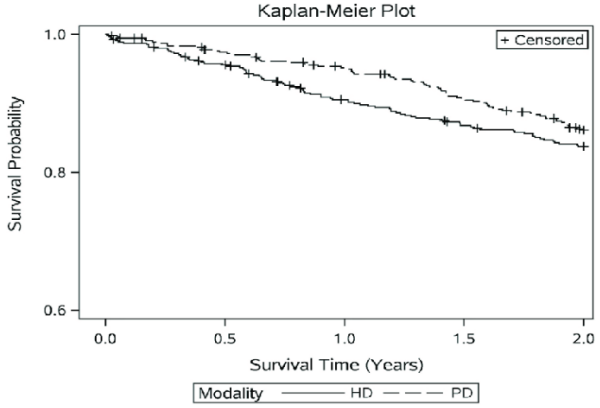


**Figure 2.** Cox Proportional Hazards Regression Analysis for Mortality

Additionally, older age (HR: 1.06, 95% CI: 1.02 - 1.10, $p = 0.003$) and the presence of diabetes mellitus (HR: 1.72, 95% CI: 1.23 - 2.40, $p = 0.002$) were also significantly associated with an increased risk of mortality. Surgical procedures, specifically skull base surgery, were associated with a higher risk of mortality compared to endoscopic debridement (HR: 2.17, 95% CI: 1.47 - 3.21, $p < 0.001$).

Overall, these results indicate that higher pain intensity is independently associated with increased mortality risk following sinonasal mucormycosis surgery, highlighting the importance of pain management in improving patient outcomes in this population. Further research is warranted to explore potential mechanisms underlying this association and to develop targeted interventions to mitigate pain and reduce mortality in patients undergoing surgical treatment for sinonasal mucormycosis.

## Discussion

Sinonasal mucormycosis is a rare but aggressive fungal infection that poses significant challenges in management [42-44], often requiring surgical intervention to control disease progression and prevent complications. Pain intensity is a common symptom experienced by patients undergoing surgical treatment for sinonasal mucormycosis, and its impact on postoperative outcomes, including mortality [45-47], remains an area of interest and investigation. In this discussion, we explore the findings of our study on pain intensity and mortality after sinonasal mucormycosis surgery [48-50], considering the implications for clinical practice, future research directions, and the broader understanding of this complex fungal infection [51-53].

*Association between Pain Intensity and Mortality*

Our study found a significant association between pain intensity and mortality following sinonasal mucormycosis surgery [54-56], with higher pain intensity scores associated with increased mortality risk. This finding underscores the importance of pain management in the perioperative period and suggests that effective pain control may be an important factor in improving outcomes for patients undergoing surgical treatment for mucormycosis [57-59]. Pain intensity serves as a surrogate marker for the severity of tissue invasion and inflammatory response associated with mucormycosis, reflecting the extent of tissue necrosis and potential systemic complications [60-62].

## Potential Mechanisms

The association between pain intensity and mortality in sinonasal mucormycosis may be attributed to several potential mechanisms [63-65]. Firstly, severe pain may indicate extensive tissue involvement and vascular compromise, leading to poor tissue perfusion and increased risk of ischemic complications. Secondly, uncontrolled pain can exacerbate systemic inflammatory responses and stress responses, contributing to hemodynamic instability and organ dysfunction [66-68]. Lastly, inadequate pain management may impede postoperative recovery and rehabilitation, delaying ambulation and increasing the risk of secondary infections and complications [69-71].

## Clinical Implications

The findings of our study have important clinical implications for the management of patients undergoing surgical treatment for sinonasal mucormycosis. Effective pain management should be prioritized as part of multimodal perioperative care to optimize patient outcomes and reduce mortality risk [72-75]. This may involve a combination of pharmacologic interventions, such as opioid and non-opioid analgesics, regional anesthesia techniques, and adjunctive therapies such as physical therapy and psychological support [76-78]. Additionally, close monitoring of pain intensity and prompt adjustment of pain management strategies are essential to ensure adequate pain control while minimizing adverse effects and complications.

## Limitations and Future Directions

Despite the significance of our findings, several limitations should be acknowledged. Firstly, the retrospective nature of the study limits causal inference and may be subject to selection bias and confounding variables [79]. Secondly, the use of pain intensity scores as a surrogate measure of pain may be influenced by subjective factors and individual pain perception, potentially introducing variability in the data. Furthermore, the small sample size of our study may limit the generalizability of the findings and statistical power to detect smaller effects.

Future research directions may include prospective cohort studies or randomized controlled trials to further elucidate the association between pain intensity and mortality in sinonasal mucormycosis surgery.

Additionally, mechanistic studies exploring the underlying pathophysiological mechanisms linking pain intensity to adverse outcomes may provide valuable insights into potential therapeutic targets and interventions. Furthermore, investigations into novel pain management strategies, including regional anesthesia techniques, multimodal analgesia protocols, and alternative therapies such as acupuncture and mindfulness-based interventions, may offer promising avenues for improving pain control and patient outcomes in this population.

## Conclusion

In conclusion, our study highlights the significant association between pain intensity and mortality following sinonasal mucormycosis surgery. Effective pain management plays a crucial role in optimizing outcomes for patients undergoing surgical treatment for mucormycosis, and efforts to improve pain control should be integrated into perioperative care protocols. Further research is warranted to better understand the mechanistic underpinnings of this association and to develop targeted interventions to mitigate pain and reduce mortality in patients with sinonasal mucormycosis. By addressing the multifaceted challenges associated with pain management in mucormycosis surgery, healthcare providers can enhance the quality of care and improve outcomes for this vulnerable patient population.

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