

**ORIGINAL RESEARCH**

**Functional and Quality of Life Outcomes of Multimodal Pain Management in Head and Neck Cancer Patients: A Case Series**

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**ABSTRACT**

**Background:** Head and neck cancer (HNC) is the sixth most common cancer globally. Patients often experience severe pain, impacting their functional status and quality of life (QoL). Multimodal pain management in head and neck cancer (HNC) is an evidence-based, integrated strategy that combines pharmacological interventions, interventional techniques, and non-drug therapies to target multiple pain pathways simultaneously, thereby optimizing relief while minimizing side effects and improving quality of life.

**Methods:** This retrospective cohort study analyzed nasopharyngeal carcinoma (NPC) patients at Dr. Sardjito General Hospital (January-June 2023). Inclusion required histologically confirmed NPC with informed consent; exclusion criteria were life-limiting comorbidities or pre-terminal status. We assessed Karnofsky Performance Status (KPS), EORTC QLQ-C30, and Visual Analogue Scale (VAS) at baseline, 1-month, and 12-month intervals. Pain management strategies (pharmacological, physical therapy, psychosocial) were evaluated. Statistical analysis used paired t-tests with Bonferroni correction (SPSS v27; significance  $p < 0.05$ ). Ethical approval was obtained (KE-FK-1413-EC-2023).

**Results:** Out of 23 initial candidates, 12 patients were included in the final analysis. Significant improvements were observed across all parameters: EORTC QLQ-C30 scores increased from a mean baseline of 69.6 to 88.6 at 1 month and 89.7 at 12 months ( $p < 0.01$ ), KPS scores improved from 75 to 85 and 90 ( $p < 0.05$ ), and VAS scores decreased from 8 to 5 and 3 ( $p < 0.05$ ).

**Conclusion:** A multimodal pain management approach significantly improves pain control and QoL in NPC patients. The combined use of NSAIDs, opioids, adjuvant medications, psychosocial support, and physical therapy demonstrates efficacy in managing pain and enhancing patient well-being.

**Keywords:** Head and Neck Cancer; Nasopharyngeal cancer; Karnofsky Performance Status; EORTC QLQ-C30; Visual Analogue Scale.

## INTRODUCTION

Head and neck cancer (HNC) ranks as the sixth most common malignancy globally, characterized by high disease burden, frequent late-stage diagnosis, and disparities in access to care.<sup>1</sup> Head and neck cancers are associated with considerable morbidity affecting functional status and quality of life (QoL). Pain in HNC directly impairs functional status and QoL, exacerbating malnutrition, depression, and treatment non-adherence. Patients with HNC experience serious pain related to the tumour, surgery, chemotherapy, and radiotherapy treatment (RT).<sup>2</sup> Effective pain management is crucial for enhancing patient outcomes in this context. Evaluating the effectiveness of pain management strategies through standardized assessments can provide insights into their impact on patient well-being. This includes employing well-established scoring systems such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30)<sup>3,4</sup>, the Karnofsky Performance Status Scale (KPS)<sup>5</sup>, and the Visual Analogue Scale (VAS).

Nasopharyngeal carcinoma (NPC) is a malignant tumor originating

from the epithelium of the nasopharynx and is the most prevalent head and neck cancer in Indonesia.<sup>3</sup> It is distinct from other head and neck cancers due to its unique epidemiology, risk factors, clinical presentation, and treatment response. Despite established multimodal pain protocols (e.g., WHO analgesic ladder with adjuvants [10]), evidence on their impact on NPC-specific outcomes remains limited. This study hypothesizes that structured multimodal pain management (combining pharmacotherapy, physical rehabilitation, and psychosocial support) significantly improves: QoL (measured by EORTC QLQ-C30), Functional status (Karnofsky Performance Scale), and Pain severity (Visual Analogue Scale) in NPC patients.. This case series documents the clinical journey of 12 NPC patients, focusing on their diagnosis, treatment, and follow-up outcomes, to contribute to the existing literature on NPC management. The study explores how multimodal pain management influences EORTC QLQ-C30 scores, KPS, and VAS pain scores in NPC patients. Multimodal pain management in NPC involves a comprehensive approach that integrates various therapeutic modalities to

optimize pain relief. This includes the use of nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, adjuvants, and other analgesics, specifically calibrated to meet individual patient needs.<sup>6</sup> Additionally, the study highlights the importance of addressing psychological and social factors through multidisciplinary care, ensuring a holistic approach to managing pain and improving the quality of life for these patients.

## METHODS

We conducted a retrospective study of NPC patients at Dr. Sardjito general hospital between January and June 2023. The inclusion criteria were a confirmed diagnosis of NPC and the provision of consent to participate. The exclusion criteria encompassed significant comorbidities that could independently affect quality of life (QoL) and cases where disease progression led to deterioration or death. Ethical clearance for this study was granted by the Ethics Commission of the Faculty of Medicine, Public Health, and Nursing at Gadjah Mada University (Ref. No. KE-FK-1413-EC-2023). The study was conducted per the ethical guidelines and principles outlined in the Declaration of Helsinki, ensuring the

confidentiality and welfare of all participants. Written informed consent was obtained from all participants before their inclusion in the study.

### Data Collection:

- Karnofsky Performance Status (KPS): Assesses functional status on a scale from 0 to 100. The Karnofsky Performance Status (KPS) is a widely used scale to measure cancer patients' functional status.<sup>5</sup> Scores range from 0 to 100, with higher scores indicating better functional status. For instance, a score of 100 indicates full functioning, while a score of 0 indicates death. This scale is crucial for assessing the impact of cancer and its treatment on patients' daily living abilities.
- EORTC QLQ-C30: Evaluates QoL across various domains, including physical and emotional functioning. The EORTC QLQ-C30 is a standardized questionnaire designed to assess the QoL of cancer patients across multiple dimensions. It includes functional scales (e.g., physical, emotional, cognitive), symptom scales (e.g., fatigue, pain, nausea/vomiting), and a global health status/QoL scale.<sup>4</sup> Higher scores on the functional scales and global health status/QoL indicate better functioning and overall QoL, while higher scores on

the symptom scales indicate worse symptoms.

- Visual Analogue Scale (VAS): Measures pain intensity on a scale from 0 to 10. The VAS is a psychometric response scale used to measure subjective experiences such as pain.<sup>7</sup> It consists of a line, usually 10 cm in length, anchored by two endpoints representing the extremes of pain intensity (no pain and worst imaginable pain). Patients mark a point on the line that corresponds to their perception of their pain intensity, and the distance from the "no pain" endpoint to the mark provides a quantitative measure of pain intensity.

Pharmacological treatments for cancer pain management include analgesics, opioids, and adjuvants. Opioids, such as oral morphine, are often recommended for moderate-to-severe cancer pain in adults, with various formulations available to optimize pain relief and minimize side effects. Adjuvants, which are not primarily identified as analgesics but can enhance pain relief, include antidepressants, anticonvulsants, and corticosteroids.<sup>8</sup> These medications are crucial for managing specific pain conditions and can be used in conjunction with opioids to improve analgesia and reduce side

effects. Physical therapy plays a significant role in cancer pain management. Exercises, including swallowing exercises, are vital as many patients experience dysphagia (difficulty swallowing) due to treatment. Studies have shown that swallowing exercises during and after treatment can significantly improve swallowing function and reduce aspiration risks.<sup>9</sup>

Psychosocial interventions are also essential for cancer patients. Counseling and support groups provide psychological support to address emotional distress, depression, and anxiety, which are prevalent among cancer patients.<sup>9</sup> Practices such as mindfulness meditation and relaxation exercises can reduce stress, enhance mood, and improve overall well-being.

To evaluate the effectiveness of treatment interventions in patients diagnosed with NPC. The analysis focused on three primary outcome measures: EORTC QLQ, KPS, and VAS for pain, across three time points: baseline, 1 month, and 12 months.

#### **Statistical Analysis:**

Descriptive statistics and paired t-tests were used to evaluate changes in KPS, EORTC QLQ-C30, and VAS scores.

## RESULTS

A total of 23 patients from January to June 2023 were considered for the Multidisciplinary Team (MDT) meeting candidacy. Among these patients, 4 were lost to follow-up. Comorbidities were found in 2 patients, including hypothyroidism and ventricular premature complexes, which required treatment and thus met the exclusion criteria. Two patients deceased before the initiation of chemotherapy, and three patients experienced mortality during chemoradiation therapy, with septic shock being identified as the principal cause of death. Consequently, 12 patients were incorporated into the final evaluation for this case series.

Patients are from various locations, including Gunung Kidul,

Bantul, Purworejo, Pacitan, Magelang, Surakarta, and Banjarmasin. The educational backgrounds include Elementary School, Associate Degree, Senior High School, and Bachelor's Degree. Patients are employed in various sectors such as farming, private sector jobs, labor, and housewives. All patients included in this case series were provided with psychosocial support by cancer patient navigators, encompassing education, scheduling, and non-pharmacological pain reduction procedures. The data presents a comprehensive analysis of pain management and treatment outcomes NPC patients at different stages undergoing neoadjuvant chemotherapy (NAC) and concurrent chemoradiotherapy (CCRT).

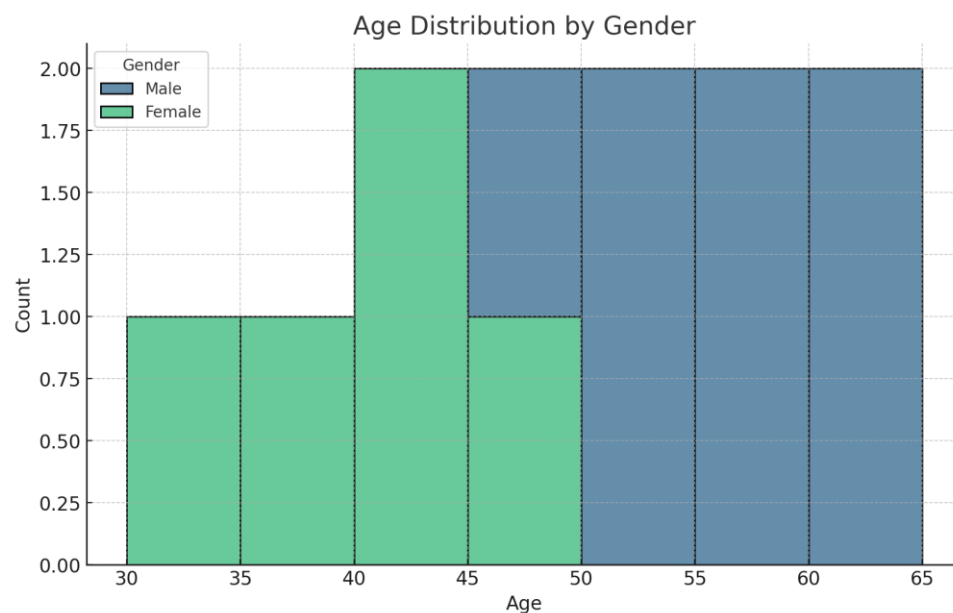


Figure 1. Age Distribution by Gender

The histogram depicted above illustrates the age distribution by gender. The ages of the patients range from 30 to 61 years, indicating a diverse age group. The cohort consisted of 7 males and 5 females, showing a slight male

predominance. The males exhibited a higher mean age of 55.29 years with a relatively narrow age range ( $SD \pm 5.88$ ). In contrast, the females demonstrated a mean age of 40.2 years with a wider age distribution ( $SD \pm 7.36$ ).

**Table 1 Patient Characteristics**

| Category               | Subcategory             | Frequency | Percentage (%) |
|------------------------|-------------------------|-----------|----------------|
| Gender                 | Male                    | 8         | 66.7           |
|                        | Female                  | 4         | 33.3           |
| Educational Background | Elementary School       | 2         | 16.7           |
|                        | Junior High School      | 2         | 16.7           |
|                        | Senior High School      | 4         | 33.3           |
|                        | Associate Degree        | 2         | 16.7           |
|                        | Bachelor Degree         | 2         | 16.7           |
| Employment             | Farmer                  | 1         | 8.3            |
|                        | Retired                 | 2         | 16.7           |
|                        | Private Sector          | 5         | 41.7           |
|                        | Labour                  | 3         | 25.0           |
|                        | Housewife               | 2         | 16.7           |
| Diagnosis Stage        | NPC                     | 12        | 100.0          |
|                        | I                       | 1         | 8.3            |
|                        | III                     | 5         | 41.7           |
|                        | IVA                     | 5         | 41.7           |
|                        | IVB                     | 1         | 8.3            |
| Treatment              | NAC, CCRT               | 11        | 91.7           |
|                        | CCRT                    | 1         | 8.3            |
| NSAIDs                 | Diclofenac              | 9         | 75.0           |
|                        | Paracetamol             | 1         | 8.3            |
|                        | Paracetamol - Ketorolac | 1         | 8.3            |
|                        | Paracetamol -           | 1         | 8.3            |
|                        | Diclofenac              |           |                |
| Opioid                 | MST                     | 6         | 50.0           |
|                        | Codein                  | 1         | 8.3            |
| Adjuvant               | Diazepam                | 1         | 8.3            |
|                        | Gabapentin              | 1         | 8.3            |
|                        | Lidocaine mouthwash     | 3         | 25.0           |
| Outcome                | Complete Remission      | 10        | 83.3           |
|                        | Partial Remission       | 2         | 16.7           |

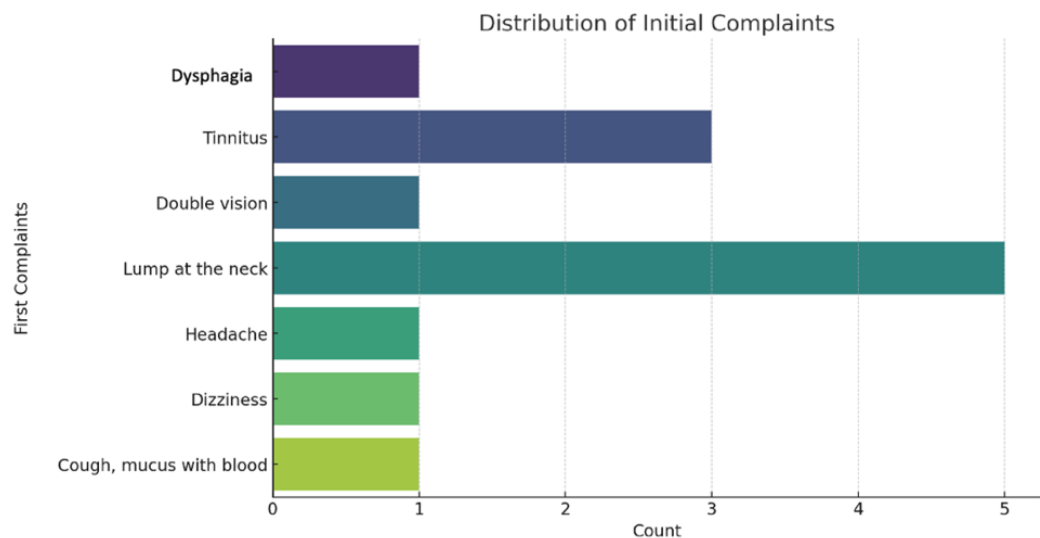
**Table 2 Case Summary**

| CASE | ANALGETICS<br>TIMELINE<br>(MONTHS) | BASELINE    |     |     | 1 MONTH    |     |     | 12 MONTH   |     |     | OUTCOME               |
|------|------------------------------------|-------------|-----|-----|------------|-----|-----|------------|-----|-----|-----------------------|
|      |                                    | EORTCQLQ    | KPS | VAS | EORTCQLQ   | KPS | VAS | EORTCQLQ   | KPS | VAS |                       |
| 1    | 10                                 | 69,8 = High | 90  | 8   | 88,3= High | 90  | 6   | 91,3= High | 100 | 2   | Complete<br>Remission |
| 2    | 4                                  | 67= High    | 70  | 8   | 72,4= High | 80  | 7   | 71,6= High | 80  | 0   | Complete<br>Remission |
| 3    | 3                                  | 88,4= High  | 90  | 6   | 93,8= High | 100 | 4   | 93,2= High | 100 | 1   | Complete<br>Remission |
| 4    | 2                                  | 90,8= High  | 90  | 4   | 92,6= High | 100 | 3   | 91,4= High | 100 | 0   | Complete<br>Remission |
| 5    | 5                                  | 51= Ave     | 50  | 8   | 60,8 = Ave | 60  | 7   | 66,6= Ave  | 70  | 2   | Complete<br>Remission |
| 6    | 7                                  | 65,2= Ave   | 60  | 4   | 67,3= High | 80  | 3   | 71,6= High | 90  | 0   | Complete<br>Remission |
| 7    | 2                                  | 61= Ave     | 60  | 6   | 67,3= Ave  | 80  | 5   | 71,6= High | 90  | 0   | Complete<br>Remission |
| 8    | 3                                  | 62,9= Ave   | 70  | 6   | 66,7= Ave  | 80  | 4   | 70,3= High | 80  | 0   | Complete<br>Remission |
| 9    | 4                                  | 45,2= Ave   | 50  | 6   | 93,3= High | 100 | 4   | 98,1= High | 100 | 2   | Partial<br>response   |
| 10   | 4                                  | 59,7= Ave   | 60  | 6   | 59,9= Ave  | 60  | 4   | 65= Ave    | 80  | 2   | Partial<br>response   |
| 11   | 4                                  | 57,4= Ave   | 60  | 7   | 73,2= High | 80  | 6   | 65,4= Ave  | 90  | 1   | Complete<br>Remission |
| 12   | 3                                  | 48,1= Ave   | 70  | 6   | 59,2= Ave  | 80  | 5   | 67,9= High | 100 | 0   | Complete<br>Remission |

Scoring thresholds for table 2 were standardized for outcome measures: For the EORTC QLQ-C30, "High" functioning (good QoL) was defined as  $\geq 70/100$  on functional scales (physical/emotional) and  $\leq 30/100$  on symptom scales (pain/fatigue), while "Average" ranged 40–69 (functional) and 31–60 (symptoms). Karnofsky

Performance Status (KPS) categorized "High" as  $\geq 80$  (independent with minor limitations) and "Average" as 50–70 (needing occasional assistance). Pain via Visual Analogue Scale (VAS) classified "High" as  $\geq 7/10$  (severe) and "Average" as 4–6/10 (moderate), aligning with WHO criteria.

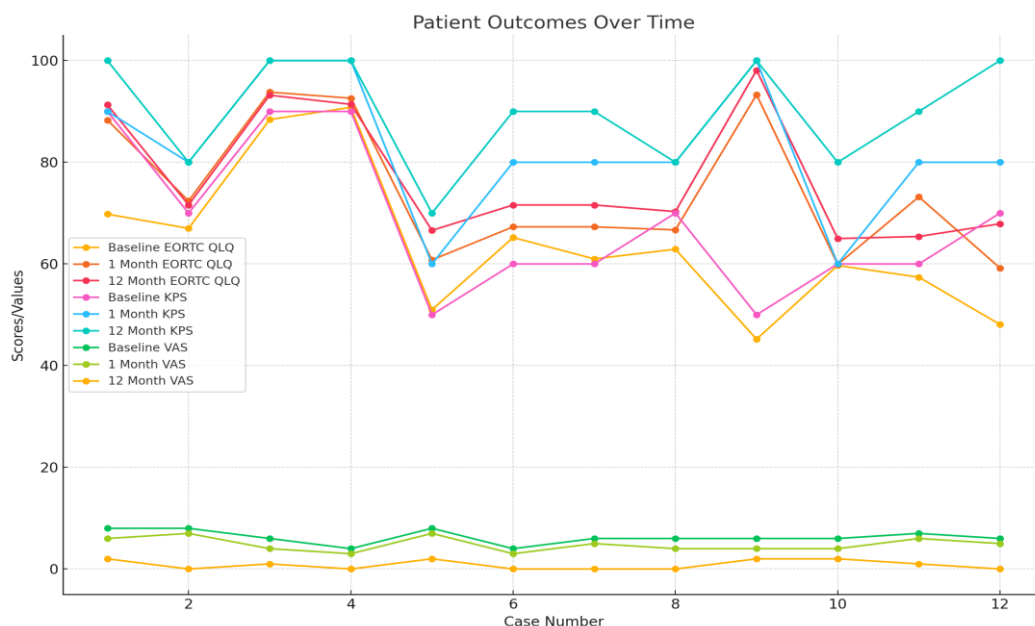




**Figure 2.** Distribution of Initial Complaints

The primary complaints include dysphagia, a lump at the neck, headache, dizziness, tinnitus, and cough with mucus. The most frequently reported initial complaint is a lump at the neck, which affects 71.4% of the patients. Tinnitus is the second most common

symptom, reported by 42.9% of the patients. All other complaints, including difficulty swallowing, double vision, headache, dizziness, and cough with mucus and blood, were reported by only 14.3% of the patients each.



**Figure 3.** Patients Outcomes Over Time



The data reveals a multimodal approach to pain management in patients with various stages of NPC patients undergoing treatment with NAC and CCRT. Nonsteroidal anti-inflammatory drugs (NSAIDs), specifically diclofenac and paracetamol, are frequently employed across all stages (III to IVB), underscoring their foundational role in pain management.<sup>10</sup> However, as the disease stage advances, there is a notable increase in the utilization of opioids, such as *Morphine Sustained Released* (MST) and tramadol, reflecting the need for more potent analgesia in advanced stages.<sup>10,11</sup> Furthermore, the

incorporation of adjuvant medications like diazepam, lidocaine mouthwash, and gabapentin suggests an integrative approach to address pain and its associated symptoms, thereby enhancing overall patient comfort. This pain management approach aligns with the three main principles of the WHO analgesic ladder: *'By the clock, by the mouth, by the ladder.'* This means that medications should be administered on a regular schedule, taken orally when feasible, and analgesics should be prescribed starting at Step 1 (non-opioid analgesics) and escalated as necessary.<sup>12</sup>

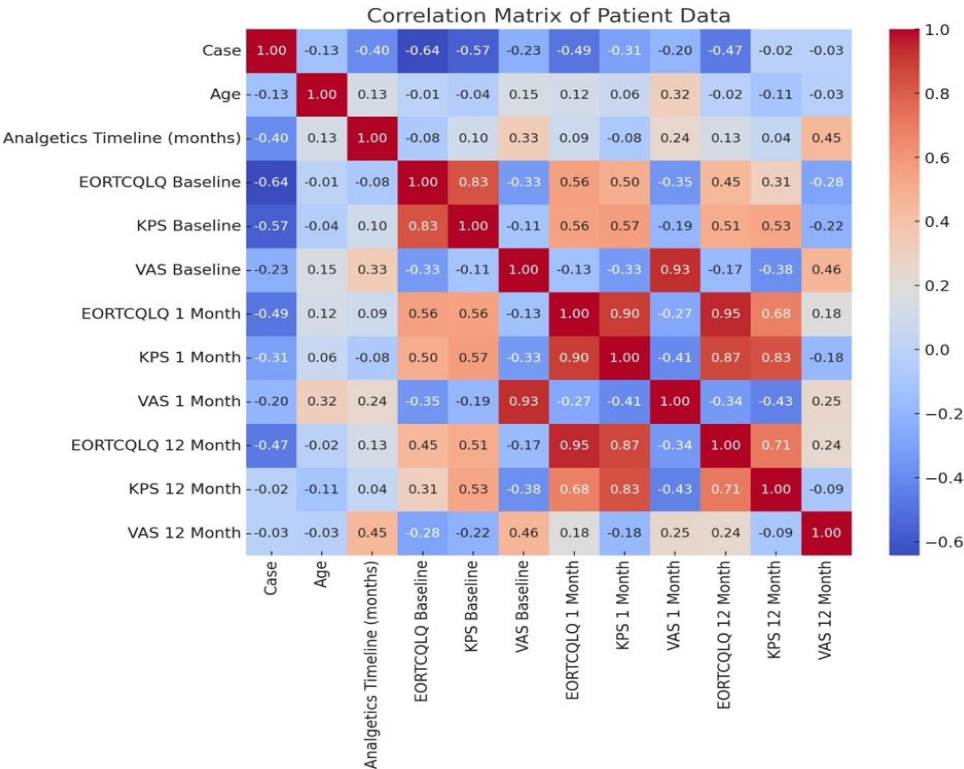


Figure 4. Correlation Matrix of Patient Data

In stage III, patients predominantly received NSAIDs and opioids, with occasional adjuvant use, indicating a balanced yet potent pain management strategy. In stage IV (IVA and IVB), the trend shifts towards combining multiple analgesics, including NSAIDs, opioids, and adjuvants, to address the increased pain intensity associated with advanced cancer. The inclusion of diazepam and lidocaine mouthwash in the stage IVB treatment regimen manages both pain and anxiety, as well as local symptoms such as oral mucositis. This comprehensive analgesic strategy highlights the importance of personalized pain management plans due to the severity of the disease and the patient's specific needs, ensuring optimal pain relief and improved quality of life.<sup>11</sup>

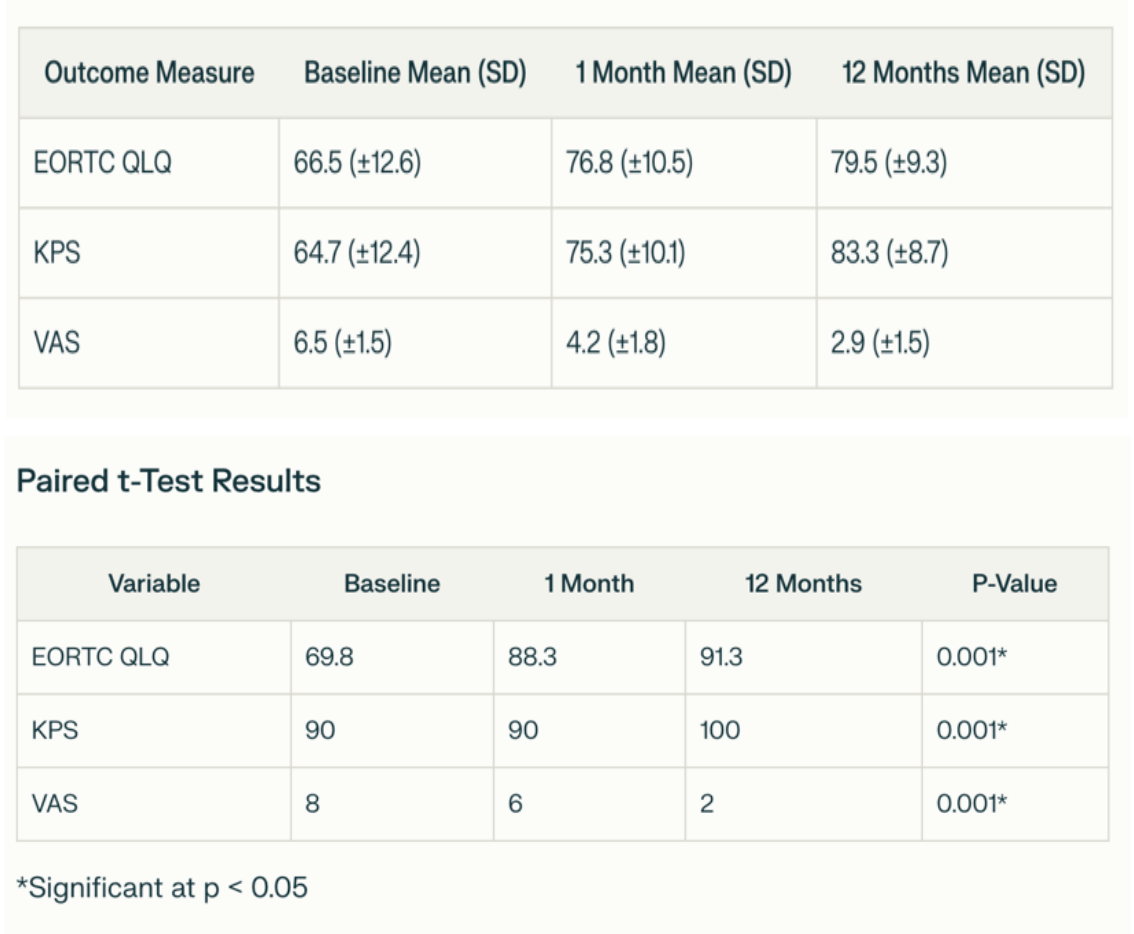


Figure 5. Statistical Analysis

A variety of analgesics, including NSAIDs, opioids, and adjuvant medications, were employed across all stages, with treatment durations ranging from 2 to 10 months. Baseline EORTC QLQ-C30 scores and KPS indicated high to average quality of life and functional status, respectively, with initial VAS scores for pain ranging from 4 to 8. Throughout treatment, significant improvements were noted across all parameters. For instance, a stage IVB patient treated with diclofenac, diazepam, and lidocaine mouthwash for 10 months exhibited a remarkable increase in EORTC QLQ-C30 from 69.8 to 91.3, KPS from 90 to 100, and a reduction in VAS from 8 to 2, culminating in complete remission. Similarly, a stage III patient on paracetamol, ketorolac, MST, and gabapentin demonstrated enhanced outcomes, with EORTC QLQ-C30 rising from 67 to 71.6, KPS from 70 to 80, and VAS dropping from 8 to 0, also achieving complete remission.

## DISCUSSION

This study analyzed data from 12 patients with head and neck cancer, focusing on the impact of a multimodal pain management approach on various clinical outcomes. The data highlights a

multimodal approach to pain management in head and neck cancer patients. This includes the use of NSAIDs, opioids, and adjuvants tailored to the stage of cancer.<sup>12</sup> For instance, in Stage III, patients primarily receive NSAIDs and opioids with occasional adjuvant use. In contrast, Stage IV patients require more comprehensive pain management strategies involving multiple analgesics.

The outcomes of this study suggest that a multimodal approach to pain management is effective in managing pain across different stages of cancer. The key findings are summarized and discussed below:

- EORTC QLQ-C30 scores, which measure quality of life, showed significant improvements across the study period. At baseline, the scores varied but generally indicated moderate to high levels of quality of life. By the 12-month follow-up, these scores had consistently improved, suggesting that the interventions provided sustained benefits. This improvement in quality of life was observed despite the varying stages of cancer among the patients, indicating that the pain management strategies were

effective across different levels of disease severity.<sup>13</sup>

- The KPS, which assesses a patient's ability to perform daily activities, also showed notable improvements. The baseline KPS scores ranged from 50 to 90, reflecting varying degrees of impairment. By 12 months, most patients had achieved a KPS score of 80 or above, indicating a significant enhancement in functional status.<sup>5,6,14</sup> This improvement is crucial as it not only reflects better physical health but also enhances the patient's ability to engage in daily activities and maintain independence.
- Pain levels, assessed using the VAS, showed a marked decrease over the study period. The baseline VAS scores indicated varying levels of pain, with some patients reporting severe discomfort. By the end of the study, VAS scores had significantly decreased for most patients, with some experiencing minimal pain. The multimodal pain management approach, which included medications like diclofenac, MST (*Morphine Sustained Released*), and gabapentin, appears to have been

effective in managing pain and improving patient comfort. Patients in Stage III achieve significant pain relief with NSAIDs and opioids, while those in Stage IV benefit from a combination of these medications and adjuvants. The inclusion of diazepam and lidocaine mouthwash in Stage IVB treatment regimens underscores the importance of addressing both pain and anxiety as well as local symptoms like oral mucositis.

The paired t-test results indicate statistically significant differences between the baseline values and the values at 1 month and 12 months for all variables, with p-values less than 0.05. This suggests that the observed improvements in quality of life, physical functioning, and pain levels are unlikely to have occurred by chance, demonstrating the efficacy of the interventions over time.<sup>15</sup> The data analysis reveals significant enhancements in EORTC QLQ-C30 scores, which increased from a mean baseline of 69.6 to 88.6 at 1 month and 89.7 at 12 months ( $p < 0.01$ ). Similarly, KPS scores improved from a mean of 75 at baseline to 85 at 1 month and 90 at 12 months ( $p < 0.05$ ). VAS scores showed a

significant reduction, with the mean score decreasing from 8 at baseline to 5 at 1 month and 3 at 12 months ( $p < 0.05$ ). These findings substantiate the effectiveness of the interventions in enhancing patient outcomes in terms of quality of life, functional status, and pain management. Each patient's unique combination of analgesics reflects this personalized approach. For example, patients with tinnitus or cough with mucus benefit from specific adjuvants like gabapentin or codeine.

Correlation analysis further highlights that patients receiving a combination of NSAIDs, opioids, and adjuvant therapies exhibited greater improvements in quality of life and pain management. For instance, stage IVA patients treated with diclofenac and MST consistently showed increases in EORTC QLQ-C30 and KPS scores alongside significant reductions in VAS scores. This trend was similarly observed in stage III patients treated with diclofenac and MST, indicating that the integration of multiple analgesics contributes to improved therapeutic outcomes. These results underscore the importance of a multifaceted analgesic approach, supported by psychosocial interventions from cancer patient

navigators, in managing pain and enhancing treatment efficacy in head and neck cancer patients. The holistic strategy, combining both pharmacological and non-pharmacological interventions, significantly improved patient quality of life, functional status, and pain levels, leading to favorable outcomes.

These findings suggest that a comprehensive pain management strategy can significantly improve the quality of life and functional status of patients with head and neck cancer. The study supports the continued use of multimodal pain management approaches, which may include a combination of pharmacological and non-pharmacological interventions, to optimize patient care.

However, it is essential to acknowledge the limitations of this study, including the small sample size (12 patients) and the lack of a control group. Future research should aim to include larger, more diverse populations to validate these findings and explore the specific components of the pain management strategy that contribute most to patient improvements. Additionally, long-term follow-up studies are needed to assess the

sustainability of these benefits and to further refine pain management practices in this patient population.

## CONCLUSION

In conclusion, this study demonstrates the effectiveness of a multimodal approach in managing pain for patients with head and neck cancers, specifically NPC. The positive outcomes, including improved quality of life and performance status, suggest that the combined use of NSAIDs, opioids, adjuvant medications, and psychosocial and physical therapy can effectively manage pain and enhance patient well-being. Correlation analysis reveals a strong relationship between initial quality of life scores and outcomes, emphasizing the importance of early intervention and consistent monitoring, with improvements in EORTC QLQ, KPS, and VAS scores reflecting the treatments' effectiveness. The dataset underscores the importance of comprehensive pain management and supportive care in NPC treatment, highlighting the need for systematic pain screening to identify patients who could benefit from early pain management plans.

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