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Optimal timing of postoperative radiotherapy initiation in maxillary sinus cancer patients

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ABSTRACT

Introduction: Maxillary sinus cancer is a relatively rare head and neck malignancy. Despite advances in treatment, it remains a therapeutic challenge. This study aimed to evaluate treatment outcomes in maxillary sinus cancer patients depending on the timing of radiotherapy initiation after surgery.

Material and methods: A retrospective analysis of 91 patients treated for maxillary sinus cancer was performed. Depending on the treatment modality, patients were divided into 3 groups: I — surgery + adjuvant radiotherapy (n = 77), II — palliative radiotherapy (n = 10), and III — radical radiotherapy only (n = 4). Overall survival (OS) was assessed.

Results: The longest median OS (30.6 months) was observed in group I. It was demonstrated that the timing of radiotherapy initiation after surgery is crucial — with 3–4 weeks interval OS was 75 and 60.4 months, respectively. Patients with treatment failure in the form of distant metastases had shorter median OS (4.4 months) compared to those with local recurrence (10.9 months).

Conclusions: Combined treatment with surgery + adjuvant radiotherapy provides the best results. Postoperative radiotherapy should be initiated no later than 4 weeks after surgery, which significantly prolongs median overall survival. Commencing radiotherapy within 3–4 weeks after surgery markedly improves the prognosis. Patients who developed local recurrence have better prognosis compared to those with distant metastases.

Keywords: Maxillary sinus cancer, radiotherapy, combined modality treatment, treatment timing, time factors

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Introduction

Maxillary sinus cancer is a relatively rare head and neck malignancy, accounting for approximately 0.5–1% of all cancers [1]. Despite advances in diagnosis and treatment, it remains a therapeutic challenge with poor prognosis, especially in advanced stages [2]. The standard management includes radical surgery, followed by adjuvant radiotherapy [3]. However, there are still controversies regarding the optimal timing between surgery and radiotherapy.

Previous studies have not demonstrated the significance of the interval from surgical resection to adjuvant radiotherapy [4–6].

However, ensuring timely delivery of adjuvant treatment can be challenging due to waiting times for radiotherapy planning and scheduling [7–9]. Moreover, some patients may require a prolonged recovery period after extensive surgery. On the other hand, initiating irradiation too early poses a risk of impaired wound healing and other postoperative complications. Therefore, the optimal timing of adjuvant radiotherapy after surgery remains to be established.

This retrospective study aimed to evaluate the impact of the interval from surgery to adjuvant radiotherapy on outcomes in maxillary sinus cancer patients treated with a combined modality approach. The results may help optimize postoperative management and radiotherapy planning to improve the prognosis of this rare malignancy.

Material and methods

The study group consisted of 91 patients treated between April 2009 and November 2015 at the Oncology Centre, diagnosed with maxillary sinus cancer. A retrospective analysis of the clinical and pathological data of all patients was performed. Information about the patients was obtained from the extensive medical database of the Oncology Centre.

The stage of maxillary sinus cancer and final diagnosis were determined based on histopathological examination of surgical specimens and additional tests such as computed tomography and magnetic resonance imaging.

The clinical staging of maxillary sinus cancer was based on the TNM classification for maxillary sinus tumours from the 7th edition of the AJCC (American Joint Committee on Cancer).

Patients were divided into three groups depending on the treatment modality:

Group I — 77 patients who underwent radical macroscopic surgical resection of the tumour with modified neck dissection for clinically stage III cancer.

Group II — 10 patients who underwent palliative radiotherapy with a total dose of 20 Gy in 5 fractions per week due to significant advancement of the neoplastic process.

Group III — 4 patients who could not undergo surgery due to medical contraindications. They received radical radiotherapy with a total dose of 68–70 Gy in 34–35 fractions given 5 times a week.

The data was statistically analysed using STATISTICA v.13.0. T-student and Mann-Whitney U tests were used for comparisons. Survival was assessed by the Kaplan-Meier method and compared using the log-rank test. The significance level was set at $p < 0.05$.

Results

In the study group, 51% were women and 49% were men. The mean age at diagnosis was 66 years for women and 61 years for men. The most common symptoms were pain (76%), nasal bleeding (65%), and nasal obstruction (51%).

Cervical lymph node involvement was found in 48.9% of patients. Histological examination showed squamous cell carcinoma in all patients.

Treatment results

Group I included 77 stage III patients treated with surgery (maxillectomy with modified neck dissection)

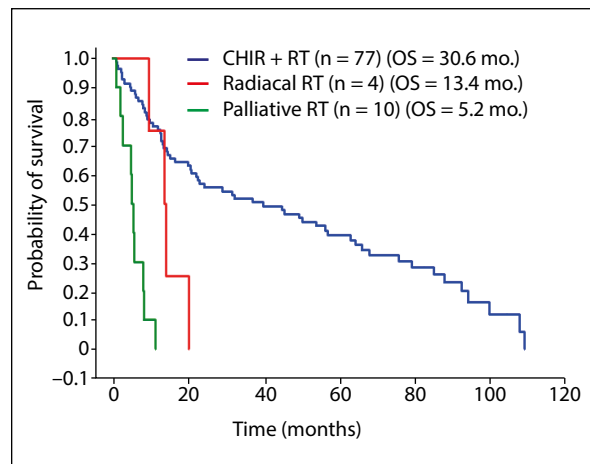


Figure 1. Probability of overall survival in patients treated with combined surgery and adjuvant radical radiotherapy (CHIR + RT) (group I), patients treated with palliative radiotherapy only (group II), and patients treated with radical radiotherapy only (group III)

followed by radiotherapy. Adjuvant radical radiotherapy was initiated at various times after surgery, from 2 to over 12 weeks.

The median overall survival for group I was 30.6 months. In this group, local recurrence occurred in 32% of patients and distant metastases in 27%.

Group II included 10 patients who underwent palliative radiotherapy only due to advanced cancer with distant metastases at diagnosis. The median overall survival was 5.2 months.

In group III, consisting of 4 patients treated with radical radiotherapy alone, the median overall survival was 13.4 months.

The probability of overall survival according to treatment modality is shown in Figure 1. Comparison between groups demonstrated significantly longer survival in patients treated with combined surgery and radiotherapy. The 5-year overall survival was 22% and 3-year survival was 31%. Nine patients received re-irradiation due to local recurrence without distant metastases. The overall survival in this group ranged from 12 to 19 months.

In group III patients who underwent radical radiotherapy alone due to medical contraindications for surgery under general anaesthesia, overall survival ranged from 9.2 to 19.2 months. All patients died. The median OS was 13.4 months (Fig. 2).

Local recurrence occurred in 32% of patients and distant metastases in 27%. Local recurrence was observed in 26 patients (10 women, 16 men) within 2–104.5 months from diagnosis. It was most frequently seen in patients with T4 disease (84.6%), less commonly in T3 (3.8%) and T2 (11.6%). The median overall survival (OS)

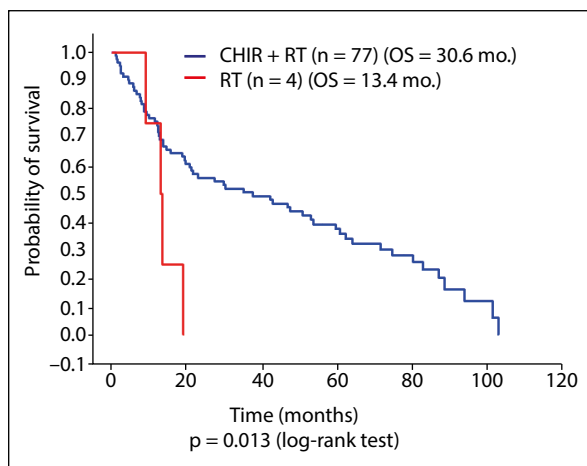


Figure 2. Comparison of patient prognosis between patients treated with combined modality surgery + radical radiotherapy (CHIR+RT) and patients treated with radical radiotherapy (RT) alone. Overall survival clearly differed between the combined modality group and the combined modality group. The median survival in this cohort was 30.6 months, while in patients treated with radiotherapy alone, it was more than twice as short at 13.4 months. These results confirm the advantage of combined treatment over radiotherapy alone for maxillary sinus cancer treatment. These findings indicate that, in most patients, surgical removal of the primary tumor along with neck dissection followed by adjuvant radiotherapy provides better local control and prolongs survival compared to irradiation alone

in this group was 10.9 months. Distant metastases developed in 22 patients (7 women, 15 men) and were associated with a median survival of 4.4 months. Figure 3 illustrates the worse prognosis in the case of distant metastases compared to local recurrence. The results confirm that progression to disseminated disease significantly impairs prognosis and shortens the OS of maxillary sinus cancer patients.

Patients with disease progression received palliative radiotherapy. In 9 patients, radical re-irradiation was used due to local recurrence without distant metastases. The OS in this small group ranged from 12 to 19 months.

A detailed analysis of group I patients treated with combined surgery and adjuvant radical radiotherapy was performed. The aim was to assess the impact of the timing of radiotherapy initiation after surgery on median OS. Weekly intervals from surgery to the start of irradiation were analysed. Significant differences in median overall survival were found depending on when radiotherapy was administered (Fig. 4). The most favourable results were achieved in patients starting irradiation at 3–4 weeks after surgery.

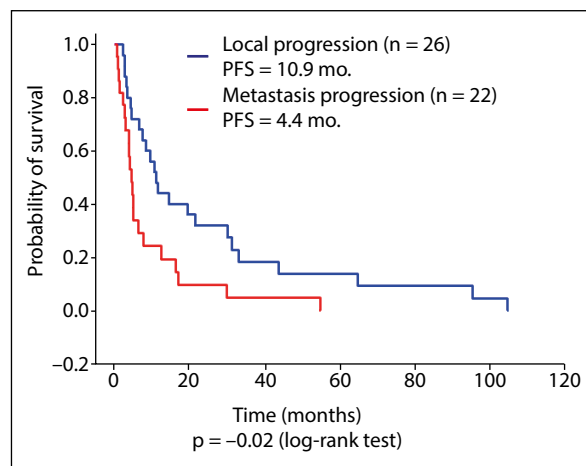


Figure 3. Time to disease progression (local progression vs distant metastases). The probability of local recurrence or distant metastasis in patients previously treated with surgery or radical radiotherapy. Patients who developed local recurrence had a slightly better prognosis (PFS = 10.9 months) than did those with distant metastases (PFS = 4.4 months) after treatment

Discussion

Maxillary sinus cancer is a relatively rare malignancy, accounting for approximately 0.5–1% of all cancers [10]. Due to non-specific symptoms, it is often detected at an advanced stage, which negatively affects the prognosis [10]. Despite progress in diagnosis and treatment, it remains a therapeutic challenge [11].

In the present study, similarly to other reports [12, 13], the peak incidence was in the 6th decade of life, with a slight predominance of women [12].

In this study, at diagnosis, the tumour stage in most patients corresponded to T3 (68%) and T4 (28%) according to the TNM classification. This indicates that despite diagnostic advancements, maxillary sinus cancer remains challenging regarding early detection. The obtained data is consistent with other studies [14, 15], which also observed a high percentage of patients with locally advanced primary tumours at diagnosis. This may indicate the need to increase awareness of maxillary sinus cancer symptoms among primary care physicians and implement early detection programs in high-risk groups.

Current standards for maxillary sinus cancer management recommend combined treatment with radical surgical resection and adjuvant radiotherapy [16, 17]. In this study, the longest median OS (30.6 months) was observed in the group of patients undergoing such combined treatment. However, this median was slightly

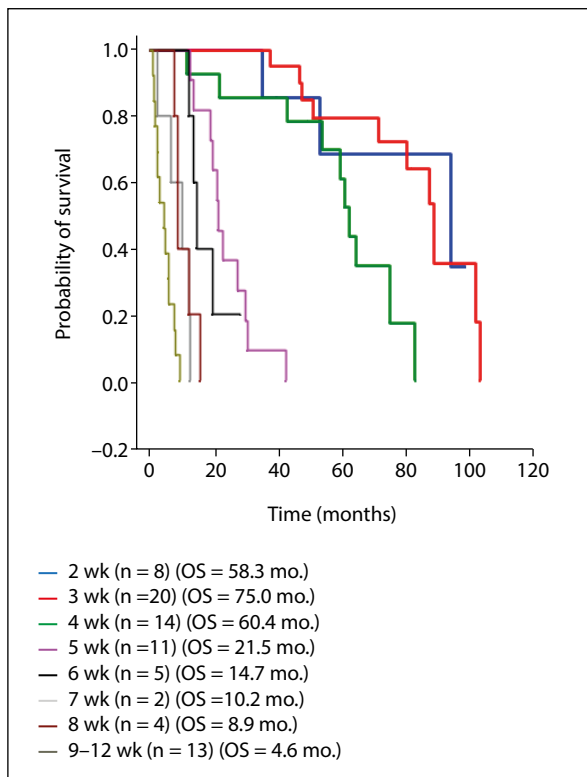


Figure 4. Effect of time from surgery to start of radiotherapy on median overall survival in group I patients. The survival curves markedly differ depending on the interval between surgery and radiotherapy. The longest medians of overall survival, 75 and 60.4 months, were observed when irradiation was initiated at 3 and 4 weeks after surgery, respectively. The later the start of radiotherapy, the worse the prognosis. The median decreased to 21.5 months at 5 weeks, 14.7 months at 6 weeks, and did not exceed 10 months at 7 weeks or later. The results unequivocally indicate that early initiation of radiotherapy within 3–4 weeks after surgery significantly improves prognosis in maxillary sinus cancer patients

lower than that reported by other authors, Kreppel et al. (57.8 months) [18].

It should be emphasized that despite the same clinical tumour stage, substantial variability in OS was found in this group depending on the timing of radiotherapy initiation after surgery (Fig. 4). It was demonstrated that starting irradiation at 3–4 weeks after surgery had a key impact on prognosis (OS medians 75 and 60.4 months, respectively). Only 42% of patients received radiotherapy at this optimal time.

This indicates a clear need for better coordination between surgical and radiotherapy centres [19]. The solution may be establishing comprehensive cancer centres enabling integrated, coordinated treatment.

Moreover, this study showed that in patients with distant metastases, the median OS was 4.4 months, while in those with local recurrence, it was over twice as long at 10.9 months. The results are consistent with other reports [20, 21] and confirm that the presence of distant metastases is associated with a worse prognosis in maxillary sinus cancer. This may indicate the need for early detection of N0 disease and optimization of adjuvant systemic treatment regimens to minimize the risk of distant spread. Further research should focus on identifying prognostic factors related to metastatic progression risk and developing effective methods for early micrometastasis detection.

Conclusions

It was demonstrated that the timing of radiotherapy initiation after surgery is crucial for prognosis in maxillary sinus cancer patients. The longest OS was observed in patients who started radiotherapy at 3–4 weeks post-operatively (OS medians of 75 and 60.4 months, respectively). Only 42% of patients received radiotherapy at this optimal time, indicating the need for better synchronization of surgical treatment and radiotherapy. The solution may be establishing comprehensive cancer centres enabling integrated, coordinated care. The results are pivotal for treatment optimization and improving outcomes in maxillary sinus cancer patients.

Article information

Data availability statement: *The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.*

Ethics statement: *All research involving patients described in this work was accepted by the Bioethics Committee at Nicolaus Copernicus University in Toruń (opinion no. KB/825/2018 of 18.12.2018). The research was conducted by the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine of 1997, and based on Art. 29 of the Act of 5 December 1996 on the Medical Profession (Journal of Laws 1997 No. 28 item 152 with later amendments), and the ordinance of the Minister of Health and Social Welfare of 11 May 1999 on the detailed principles of appointing and financing and the mode of operation of bioethics committees (Journal of Laws No. 47 item 480).*

Author contributions: *conceptualization — KBM, KR. methodology — KBM, KR, ZD. software PE, ZD; collection data — KBM, KR, ZD, PE. Visualization KBM, KR, ZD, PE; Validation KR, Formal analysis: KBM, KR; writing original draft preparation — KBM, KR; writing review and editing — KBM, KR; verification — KR; supervision — KR. All authors have read and agreed to the published version of the manuscript.*

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