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Management of Nasal Complications after Irradiation of Head and Neck Cancers - A Literature Review

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Abstract: ***Nasopharyngeal carcinoma (NPC) constitutes a mere 0.7% of all reported cancers globally. Neoplasms affecting the nasal and paranasal sinus regions are infrequent and represent a small fraction of head and neck cancers. While radiation therapy is pivotal in treating head and neck cancers, it can induce mucosal damage, resulting in severe complications during and after treatment, including common side effects like rhinosinusitis and alterations in smell. Advancements in radiotherapy techniques, transitioning from 3D - conformal planning to intensity - modulated radiation therapy (IMRT), signify notable progress. This review zeroes in on nasal complications arising from radiotherapy in head and neck cancer patients, encompassing sinonasal mucosal disorders, olfactory disturbances, choanal atresia, and synechia. A thorough literature review, incorporating databases like PubMed, Embase, Cochrane, and Scopus, identified 5736 papers, with 46 meeting eligibility criteria. After a meticulous full - text assessment, 30 articles were included in qualitative synthesis, while 16 were excluded for various reasons. The review underscores that the incidence and severity of olfactory dysfunction and chronic rhinosinusitis peak at the conclusion of radiotherapy and three months post - treatment, gradually diminishing over time. Procedures like Functional Endoscopic Sinus Surgery (FESS) and interventions involving fluticasone propionate aqueous nasal spray coupled with irrigation have demonstrated efficacy in mitigating symptoms and improving the quality of life for nasopharyngeal carcinoma patients grappling with post - irradiation rhinosinusitis. Additionally, endoscopic surgeries have reported favorable outcomes in addressing sinonasal complications, including chronic sinusitis and choanal stenosis. For nasopharyngeal stenosis (NPS) ensuing from radiation treatment, endoscopic excision and carbon dioxide laser excision with balloon dilation have displayed success rates of 80 - 100% and 40 - 60%, respectively. In conclusion, the management of nasal complications post - irradiation necessitates early identification and treatment through surgical and endoscopic approaches.***

Keywords: nasal complications, review, irradiation, Nasopharyngeal carcinoma, rhinosinusitis, synechia, head and neck cancer

1. Introduction

Neoplasms affecting the nose and paranasal sinuses are exceedingly rare, constituting a mere 0.2–0.8% of all tumors and comprising less than 3% of total head and neck cancers. These conditions, often presenting symptoms akin to common disorders like chronic rhinosinusitis, frequently experience delays in diagnosis. Predominantly occurring in the fifth and sixth decades of life, these tumors exhibit a male predilection with a male - to - female ratio of 2: 1. Among the sinuses, the maxillary sinus is the most involved (70%), followed by the ethmoid sinus (20%), and less frequently, the frontal and sphenoid sinuses. Squamous Cell Carcinoma (SCC) emerges as the most prevalent malignant tumor within this category. [1]

Nasopharyngeal carcinoma (NPC) boasts distinctive epidemiology, pathogenesis, and evolving treatment modalities that have undergone significant shifts over the past three decades. Globally, NPC is a rarity, contributing to 0.7% of all reported cancer cases with approximately 130, 000 new cases annually. [2] Notably, NPC exhibits a unique geographical distribution pattern, with low incidence rates in non - endemic regions like North America and Europe (less than 1 case per 100, 000 population), contrasting sharply with high - risk areas such as Hong Kong and Southern China where the annual incidence rates among males can reach 20–30 cases per 100, 000 population. The most common sites affected by NPC are the fossa of Rosenmüller and the superior posterior wall of the nasopharynx. [3, 4]

Treatment approaches for Head and Neck Cancer (HNC) encompass surgery, radiotherapy (RT), and chemotherapy (CT), with the chosen modality dependent on tumor stage and primary site involvement. Early - stage cancers are typically managed with a single modality, either surgery or radiotherapy. Conversely, locally advanced tumors necessitate multimodal treatments, such as surgery followed by adjuvant radiotherapy or chemo - radiotherapy (CT - RT), or definitive CT - RT. For recurrent and metastatic diseases unsuitable for surgical intervention, chemotherapy or immunotherapy is recommended. In recent years, electrochemotherapy (ECT) has emerged as a curative or palliative option for select cases of recurrent oral and oropharyngeal cancer. [5, 6, 7]

Radiation therapy plays a pivotal role in HNC treatment but can induce mucosal damage, leading to severe complications during and post - RT. Additionally, concomitant chemotherapy may exacerbate toxicity due to its cytotoxic effects on rapidly growing non - cancer cells, particularly mucosal cells. In the sinonasal region, CT - RT can impair mucociliary clearance by causing destruction of mucosal cilia in epithelial cells, elevating the risk of chronic rhinosinusitis. Nasal cytology may reveal an inflammatory infiltrate as well. [8, 9, 10]

This literature review aims to comprehensively summarize and analyze the current understanding of complications associated with radiation therapy for Head and Neck Cancers and its management.

2. Materials and Methods

A comprehensive review of the English - language literature was conducted utilizing prominent databases, including PubMed, Embase, and Scopus, with the last access date being December 11, 2023. The objective was to identify articles published prior to this date. The primary search strategy involved the use of specific terms: " (head and neck cancer) AND (radiotherapy OR radiation therapy) AND (nasal OR sinus OR rhinitis OR rhinosinusitis OR smell OR olfactory) AND (Management OR Treatment)."

Individualized search strategies were tailored for each database. Inclusion criteria encompassed clinical trials, cohort studies, case - control studies, and case series or reports pertaining to olfactory dysfunction, chronic rhinosinusitis, and other nasal complications resulting from Radiotherapy in Head and Neck Cancer (HNC) patients. Non - human studies, literature not in English, and olfactory disorders unrelated to Radiotherapy for HNC were among the exclusion criteria. Abstracts of potentially relevant articles were scrutinized against the inclusion criteria for relevance.

3. Results of the Literature Review

A total of 5736 published papers published between 1975 and 2021 were identified using database searches. After abstract screening for eligibility, 71 articles were considered eligible. Among these, we included 46 articles in qualitative synthesis after a full-text assessment. The other 16 papers were excluded because they were systematic reviews (6), they were not in English (6), they did not include HNC patients (4). Table 1 highlights the main results concerning the nasal complications and its management post - radiotherapy of the included studies in the literature review.

Author, Year, Country	Study Design	Characteristics of the study participants	Tumor (Site andStage)	Treatments	Outcome Measurement	Time of Assessment	Results
Ophir et al., 1988, Israel [11]	Prospective	n = 12 M: 9 (75%), F: 3 (25%) Age - 54.8 (38–76)	Nasopharynx (n = 9), pituitary gland (n = 7) (stage NR)	2D - RT (66 Gy) No CT Dose to olfactory area: 25–28 Gy (Nasopharyngeal carcinoma)	ODT (amyl acetate and eugenol)	Before RT, within a week after RT end, 1, 3 and 6 months later	1. The Olfactory Detection Threshold (ODT) exhibited a notable increase for both compounds as the treatment concluded. 2. The nadir of olfactory acuity was observed during the initial week and persisted up to one month post the completion of Radiotherapy (RT). **3.** Even at the six - month mark post Radiotherapy (RT) cessation, the baseline levels of Olfactory Detection Threshold (ODT) had not fully rebounded, indicating a prolonged impact on olfactory function.
Sagar et al., 1991, UK [12]	Retrospective	**Study group:** n = 25 NR **Control group:** n = 40 NR	Nasopharynx, pituitary fossa, maxillary sinus (n = 25) (stage NR)	2D - RT (doses NR) No CT Dose to olfactory area: 50–75 Gy (study group)	Self - reported smell (ad hoc questionnaire)	During RT	1. A majority of the cohort, specifically 15 patients (60%), experienced a modulation in their sense of smell commencing with the initial treatment fraction. This alteration gradually waned as Radiotherapy (RT) progressed and ultimately ceased post RT completion. The characterized odor was unanimously described as disagreeable, aligning consistently with the qualities associated with ozone.
Stringer et al., 1995, USA [13]	Cross - sectional	**Study group:** n = 9 **Control group:** n = 9 **Study group:** M: 6 (77%) F: 3 (33%) **Control group:** NR **Study group:** Age – 80	Nasal vestibule or ala (n = 7), nasal cavity (n = 2), nasopharynx (n = 1) (stage NR)	RT (63.8–74.8 Gy) Dose to nasal cavities: NR	- MCC (saccharine test) - Subjective nasal symptoms	Before RT (Subjective symptoms) and 20–117 months after RT (Saccharine test and subjective symptoms)	1. Post Radiotherapy (RT), there was a discernible decrease in mucociliary clearance, indicating an impact on the efficient clearing mechanism of the respiratory tract. 2. Following Radiotherapy (RT), there was an elevated incidence of nasal congestion, drainage, and facial pain, suggesting an association between the treatment and an increased prevalence of

		(36–81) **Control group:** NR					these symptoms.
Lou et al., 1999, Taiwan [14]	Cross - sectional	**Study group:** n = 10 (all with sinusitis) **Control group:** n = 6 (3 patients with sinusitis and 3 without) **Study group** M: 7 (70%) F: 3 (30%) **Control group:** NR **Study group:** Age - 45 (28–70) **Control group:** NR	Nasopharynx (stage NR)	RT (70–80 Gy) Dose to nasal cavities: Mean dose to infundibulum 21 Gy (17.5–25 Gy)	Biopsy of infundibulum mucosa (light and electron microscope views)	5.9 (0.8–23) years after RT	1. Following Radiotherapy (RT), there was a notable escalation in the accumulation of dense collagenous fibers within the lamina propria, indicating a structural change in the tissue composition. 2. Post Radiotherapy (RT), a transformation in the arrangement of epithelial cells was observed, transitioning into a stratified configuration, accompanied by a progressive reduction in cytoplasmic volume. 3. Subsequent to Radiotherapy (RT), distinctive pathological changes were identified, including areas exhibiting ciliary loss, intercellular and intracellular vacuolation, and ciliary dysmorphism, signifying a complex spectrum of cellular alterations.
Hua et al., 1999, China [15]	Prospective	**Study group (n = 49):** - group 1 (awaiting RT): n = 24 - group 2 (after RT): n = 25 **Control group:** n = 36 **Group 1:** M: 16 (67%) F: 8 (33%) **Group 2:** M: 23 (92%) F: 2 (8%) **Control group:** M: 26 (72%) F: 10 (28%) **Group 1:** Age - 40.9 (27–59) **Group 2:** Age - 45.2 (28–60) **Control group:** Age - 43.6 (28–67)	Nasopharynx (T1 - T3)	2D - RT (68–72 Gy) Dose to olfactory area: NR	ODT (N - butyl alcohol), Odour Quality Discrimination test (5 odorants), Odour Recognition Memory Test, Odour - Visual Matching test, Odour - Tactile Matching test, OI (10 odorants), Odour Function test (edibility, function and identity)	Before RT (n = 24 NPC, group 1), after RT (n = 25 NPC, group 2)	Patients with Nasopharyngeal Carcinoma (NPC) undergoing Radiotherapy (RT) exhibited a spectrum of olfactory impairments, encompassing Olfactory Detection Threshold (ODT), cross - modal matching of odors with tactile sensations, verbal identification of odors, as well as challenges in the recall and recognition of the identity of odors. This comprehensive array of affected olfactory functions highlights the multifaceted impact of RT on the olfactory capabilities of individuals with NPC.
Kamel et al., 2004, Egypt [16]	Retrospective	n = 32 M: 19 (59%) F: 13 (39%) Age - 36 (7–65)	Nasopharynx (stage NR)	RT (doses NR) Dose to nasal cavities: NR	- MCC (saccharine test) - Nasal endoscopy - Computed Tomography scan (Lund - Mackay score)	**Group I (n = 23):** Saccharine test and nasal endoscopy before RT and at 2–6 weeks, 3 and 6 months, 1 and 2 years after RT; Computed Tomography scan 6–12 months after RT	1. The saccharine delay time exhibited a notable increase, persisting up to 6 months post Radiotherapy (RT), after which it stabilized. 2. A correlation was observed between the mucociliary clearance (MCC) delay times before and after RT, indicating a continuity in the impact of treatment on this physiological process. 3. Manifestations of early edema and discharge were evident within the 2–6 weeks post RT, followed by delayed occurrences of crusting and adhesions emerging at the 6 - month mark after RT. 4. The most affected regions, post

						Group II (n = 9): 4–12 years after RT	RT, included the maxillary sinus, anterior ethmoid sinus, and ostiomeatal complex. 5. No discernible correlation was found between the Radiotherapy (RT) dose and both the mucociliary clearance (MCC) delay time and the endoscopic findings, as well as the Lund - McKay score, suggesting a nuanced relationship between the treatment dosage and these specific outcomes.
Hu et al., 2008, Taiwan [17]	Prospective	**Study group:** n = 21 **Control group:** n = 10 Study group M: 13 (62%) F: 8 (28%) **Control group:** NR **Study group:** Age - 49.5 (43–58) **Control group:** NR	Nasopharynx (stage NR)	RT (70–80 Gy) Dose to nasal cavities: NR	- MCC (saccharine test) - Mucosal specimens during FESS (electron microscope views)	Before and 1 year after FESS 2.1 (1.2–4.0) years between RT and FESS	1. Following Radiotherapy (RT), choanal stenosis manifested in 5 patients, and nasal synechiae were observed in 6 cases, indicating structural alterations in the nasal passages. 2. Post RT, there was a reduction in the number of submucosal gland openings and the ciliary area, suggesting morphological changes in the nasal mucosa. 3. Cilia regeneration was noted 1 year after Functional Endoscopic Sinus Surgery (FESS), indicating a restorative process in the ciliary structure. 4. The number of goblet cells remained unchanged after the intervention, suggesting a relative stability in this particular cellular component. 5. Saccharin transit time experienced a decrease after Radiotherapy (RT), implying an alteration in the rate of mucociliary clearance post - treatment.
Xiang et al., 2013, China [18]	Retrospective	n = 40 M: 22 (55%) F: 18 (45%) Age - 46 (23–65)	Nasopharynx (stage NR)	RT (68–72 Gy) Dose to nasal cavities: NR	- Nasal endoscopy - Computed Tomography/ MRI scan - Subjective nasal symptoms (VAS)	3.4 (0–9) months after RT	1. Post Radiotherapy (RT), the occurrence of nasal synechiae was widespread, observed between the inferior turbinate and septum in all cases (100%), between the middle turbinate and septum in 70% of cases, between the inferior turbinate and nasal floor in 50% of cases, and between the middle turbinate and inferior turbinate in 42.5% of cases. This highlights the diverse locations of adhesions in the nasal passages post - RT. 2. Following surgery, nasal cavities were patent in an overwhelming majority, with 95% of patients experiencing unobstructed nasal passages. 3. A noticeable decrease in the Visual Analog Scale (VAS) scores for nasal symptoms was observed post - operatively, indicating an improvement in subjective perceptions of nasal well - being after the surgical intervention.
Riva et al., 2015, Italy [19]	Cross - sectional	**Study group:** n = 30 **Control group:** n = 30 **Study group:** M: 24 (80%) F: 6 (20%)	Nasopharynx (stage I–IV)	CT - RT (cisplatin - based regimens): - 2D - RT/3D - CRT (n = 10): 70.2 Gy - IMRT (n = 20):	- ODT, OI, OD (Sniffin'sticks) - Subjective reduced or altered	59 (24–124) months after RT	1. The study group exhibited a higher percentage of reduced smell, although not significantly altered, compared to the control group, indicating a nuanced impact on olfactory function within this cohort.

		Control group: M: 20 (67%) F: 10 (33%) **Study group:** Age - 53.5 (37–75) **Control group:** 52.3 (42–76)		69–70 Gy Dose to olfactory area: NR	smell		2. There were no discernible differences in subjective hyposmia among different radiation techniques, suggesting a comparable impact on the self - reported reduction in smell across these modalities. 3. In contrast, the control group demonstrated higher Olfactory Detection Threshold (ODT) and Total Discrimination Index (TDI) scores, while no significant differences were observed in Odor Identification (OI) and Odor Discrimination (OD) between the control and study groups. Additionally, there were no variations in ODT, OI, and OD among different radiation techniques, highlighting a distinct pattern in olfactory performance between the groups.
Feng et al., 2016, China [20]	Prospective	**Intranasal steroid group** (fluticasone propionate): n = 32 **Nasal irrigation group:** n = 31 **Intranasal steroid group** M: 13 (41%) F: 19 (59%) **Nasal irrigation group** M: 14 (45%) F: 17 (55%) **Intranasal steroid group:** Age - 38.86 ± 9.26 **Nasal irrigation group:** Age - 39.36 ± 7.28	Nasopharynx (stage I–IV)	RT: - Intranasal steroid group: 67.57 ± 2.94 Gy - Nasal irrigation group: 66.28 ± 3.91 Gy Dose to nasal cavities: NR	- Subjective nasal symptoms (VAS) - Nasal endoscopy (Lund endoscopic staging system) - Computed Tomography scan (Lund - Mackay score) - SNOT - 20	Before, and 3 and 6 months after RT	1. The group receiving steroids exhibited fewer nasal complaints, including overall symptoms, blocked nose, and headache, coupled with an improved quality of life and less severe endoscopic findings at both the 3 and 6 - month marks post Radiotherapy (RT), indicating a positive impact of steroid treatment on these outcomes. 2. There were no discernible differences in the Lund - Mackay score between pre - and post - RT evaluations in both the steroid and non - steroid groups, suggesting that this particular scoring system did not capture significant changes in sinonasal pathology over the course of treatment in either group.
Kuharet al., 2017, USA [21]	Retrospective	Total = 114 **CRSr:** n = 15; M: 6 (41%), F: 9 (59%) Age - 58.1 (range NR) **CRSsNP:** n = 43; M: 21 (49%), F: 22 (51%); Age - 50.3 (range NR) **CRSwNP:** n = 56; M: 25 (45%), F: 31 (55%) Age - 50.9 (range NR)	Nasal cavity and paranasal sinuses (n = 12), nasopharynx (n = 1) (stage I–IV)	RT (30.75–129 Gy) Dose to nasal cavities: NR	- Computed Tomography scan (Lund - Mackay score) - Biopsy of sinonasal mucosa during FESS (light microscope views) - SNOT - 22	5.73 ± 7.2 years after RT	1. Comparative analysis revealed heightened occurrences of squamous metaplasia and subepithelial edema in Chronic Rhinosinusitis with Recurrent Exacerbations (CRSr) when juxtaposed with Chronic Rhinosinusitis without Polyps (CRSsNP), suggesting distinct histopathological variations between these subtypes. 2. Chronic Rhinosinusitis with Recurrent Exacerbations (CRSr) demonstrated fewer eosinophils per high - power field, reduced basement membrane thickening, and a lower prevalence of eosinophil aggregates compared to Chronic Rhinosinusitis with Nasal Polyps (CRSwNP), indicating differential inflammatory patterns and tissue changes. 3. Chronic Rhinosinusitis with Recurrent Exacerbations (CRSr)

							exhibited a higher Lund - Mackay score in contrast to Chronic Rhinosinusitis without Polyps (CRSsNP), implying a more extensive involvement of sinuses in the recurrent exacerbation subtype. 4. Prior to Functional Endoscopic Sinus Surgery (FESS), no significant differences were observed in the SinonasalOutcome Test - 22 (SNOT - 22) scores between Chronic Rhinosinusitis with Recurrent Exacerbations (CRSr) and the other groups, suggesting comparable subjective symptomatology among these subtypes before surgical intervention.
Shemesh et al., 2018, Israel [22]	Prospective	n = 9 M: 5 (55%) F: 4 (45%) 44.2 (15–74)	Nasopharynx	RT (66–70 Gy): - 2D - RT (n = 4) - IMRT (n = 5) Dose to nasal cavities: NR	- Computed Tomography scan (Lund - Mackay score) - SNOT - 16	Before and 6 months after surgery	1. Among the cohort of 93 patients who underwent Radiotherapy (RT), 9 individuals necessitated surgery for sinonasalcomplications, encompassing 6 cases of Chronic Rhinosinusitis (CRS), 4 instances of choanal stenosis, and 2 occurrences of skull base osteoradionecrosis, underscoring the diverse nature of complications arising post - RT. 2. Subsequent to surgery, there was an observable reduction in the Lund - Mackay score, indicative of improved sinonasalradiological findings. Additionally, a concurrent enhancement in the quality of life, as measured by the Sinonasal Outcome Test - 16 (SNOT - 16), was noted, reflecting the positive impact of the surgical intervention on patient well - being.
Lakhdar et al., 2019 [23]	Case report	54 years old man	undifferentiated carcinoma of the nasopharynx (T1)	Radiotherapy – 65Gy	Computed Tomography (CT)		The computed tomography (CT) scan of the nose and paranasal sinuses revealed stenosis in both choanae, indicating a narrowing or constriction in these nasal passages.
Nassif et al., 2023 [24]	Literature review	N = 59 patients M: 24 (48%) F: 25 (52%) Mean age - 48years	Nasopharyngeal carcinoma (Stage 1 to 4)	IMRT - 60–70Gy	-	-	The most prevalent symptoms associated with the diagnosis of Nasal Polyposis Syndrome (NPS) included nasal obstruction, reported by 100% of cases, chronic sinusitis in 23% of cases, hyponasal speech in 8% of cases, and anosmia in 8% of cases.

Abbreviations: 2D - RT, Two - dimensional Radiotherapy; 3D - CRT, Three - Dimensional Conformal Radiotherapy; CRS, Chronic Rhinosinusitis; CRSr, radiation - induced Chronic Rhinosinusitis; CRSsNP, Chronic Rhinosinusitis without Nasal Polyps, CRSwNP, Chronic Rhinosinusitis with Nasal Polyps; F, Female; FESS, Functional Endoscopic Sinus Surgery; Gy, Gray; IMRT, Intensity Modulated Radiation Therapy; M, Male; MCC, Mucociliary Clearance; MRI, Magnetic Resonance Imaging; NPC, Nasopharyngeal carcinoma; NR, Not reported; RT, Radiotherapy; OI, Odor identification; OD, Odor discrimination; ODT, Odor detection threshold; RT, Radiotherapy; SNOT, Sino - Nasal Outcome Test; SNOT, Sino - Nasal Outcome Test; VAS, Visual Analog Scale

Out of the 14 publications addressing nasal complications following Radiotherapy in Head and Neck cancer patients, five studies were conducted prospectively [11, 15, 17, 20, 22], three were cross - sectional studies [13, 14, 19], and four were retrospective studies [12, 16, 18, 21]. Additionally, there was one case report (23) and one literature review (24) (refer to Table 1). The sample sizes across these studies varied, ranging from 1 to 114 patients. Predominantly, men were the focal gender in most publications, with three exceptions found in papers [20, 21, 24]. The age of participants spanned from 7 to 81 years. Notably, five studies included a control group [11, 15, 17, 20, 22].

The predominant cancer sites were the nasopharynx, nasal cavity, and paranasal sinuses, with additional occurrences in the oropharynx, oral cavity, larynx, hypopharynx, skull base, and parotid gland. Nasopharynx was the primary focus in most articles, with one article concentrating on both nasopharynx and nasal cavity [13], and another on nasal cavity and paranasal sinuses [21]. Tumor stages, as reported by six articles, varied from I to IV based on TNM classification [15, 19, 20, 21, 23, 24].

Treatment modalities encompassed two - dimensional radiation therapy (2D - RT) in five studies [11, 12, 15, 19, 22], three - dimensional conformal radiation therapy (3D - CRT) in one paper [19], and intensity - modulated radiation therapy (IMRT) in three studies [19, 22, 24]. Radiation therapy doses specifically to nasal cavities were detailed in only five studies, ranging from 30.75 to 129 Gy.

Radiological assessments were conducted using computed tomography in six articles [16, 18, 20 - 23], MRI in one article [18], and both computed tomography and MRI in one paper [18]. The Lund - Mackay staging system, evaluating opacification of each sinus, was employed to assign scores between 0 and 2 (0, no abnormality; 1, partial opacification; 2, total opacification), resulting in a total score range of 0 to 24. Computed tomography was generally the preferred method for rhinosinusitis staging.

Olfactory function assessments utilized psychological tests, self - report instruments, or a combination of both. Psychological tests measured the main olfactory abilities—odor detection threshold (ODT), odor discrimination (OD), and odor identification (OI). ODT was evaluated using amyl acetate and eugenol, n - butyl alcohol, or n - butanol. Studies employing Sniffin' sticks for olfactory assessment calculated a total score (TDI—Threshold Discrimination Identification). Other objective measurements included olfactory event - related potential testing and olfactory bulb volume in MRI [11, 12, 15, 19]. One study reported no differences in ODT, OI, and OD among radiation techniques [19], while two papers focusing on nasopharyngeal carcinoma (NPC) patients with radiotherapy noted olfactory impairments [11, 15].

In their study titled "Effect of endoscopic sinus surgery on irradiation-induced rhinosinusitis in patients with nasopharyngeal carcinoma, " Ko - Hsin Hu and colleagues (2008) investigated the impact of functional endoscopic sinus surgery (FESS) on nasopharyngeal carcinoma (NPC) patients with postirradiation rhinosinusitis. They found that FESS led to a reduction in the number of submucosal gland openings in the antral mucosa, although the count remained higher than in the control group. The surgery was effective in improving ventilation and drainage of the paranasal sinuses, addressing symptoms of chronic sinusitis unresponsive to antibiotics. The study included 21 NPC patients with previous radiotherapy and chronic rhinosinusitis. FESS was shown to enhance the regeneration of the sinus mucosa in patients with irradiation - induced rhinosinusitis [17].

In a study by Shaoyan Feng and colleagues (2016), fluticasone propionate aqueous nasal spray combined with irrigation was found effective in alleviating symptoms and enhancing the quality of life in nasopharyngeal carcinoma patients experiencing post - irradiation rhinosinusitis. The group receiving the nasal spray exhibited lower endoscopic and visual analogue scale scores, along with improved Sino - Nasal Outcome Test - 20 scores. Although computed tomography scores did not significantly differ between the groups, the treatment proved beneficial in managing the common side effects of radiotherapy, ultimately impacting patients' well - being [20].

The study "Endoscopic Surgery for Delayed Sinonasal Complications of Radiation Therapy for Nasopharyngeal Carcinoma" conducted by Rachel Shemesh and her team (2018) explored the efficacy of endoscopic surgery in addressing delayed sinonasal complications, such as chronic sinusitis, choanal stenosis, and osteoradionecrosis, in NPC patients unresponsive to medical treatment. The results highlighted favorable subjective outcomes with surgical intervention, emphasizing the importance of recognizing symptoms and promptly referring patients for evaluation and treatment [22].

Samih Nassif and colleagues from Tufts University (2023) reported on the occurrence of nasopharyngeal stenosis (NPS) after radiation treatment for nasopharyngeal carcinoma. They found that primary excision of scarring was the most effective management method for NPS, demonstrating a lower rate of revision surgery compared to balloon dilation. The study identified common symptoms of NPS, including nasal obstruction, chronic sinusitis, hyponasal speech, and anosmia. Endoscopic excision showed a success rate of 80 - 100%, while carbon dioxide laser excision with balloon dilation had a success rate of 40 - 60%. The etiology of NPS remains unclear and may be associated with an epithelial inflammatory reaction from radiation therapy along the nasopharynx and choana [24].

4. Discussion

The management of head and neck cancer poses considerable challenges, typically requiring multimodal approaches, such as radiation therapy and chemotherapy [5]. Advances in radiotherapy techniques, evolving from 3D - conformal planning to intensity - modulated radiation therapy (IMRT), have significantly reduced complications related to organs at risk (OARs) [25].

In a meta - analysis comprising 8 studies involving 3, 570 patients with nasopharyngeal tumors, Zhang et al demonstrated superior 5 - year overall survival and local control in individuals treated with IMRT compared to those receiving 2D or 3D conformal RT [26]. These findings were corroborated by a recent meta - analysis, albeit with limitations of a small sample size and low statistical power. Notably, nasopharyngeal tumors exhibited a more favorable response in overall survival and locoregional control with IMRT [27].

A study led by Youssef Lakhdar (2019) addressed the occurrence of choanal stenosis following radiotherapy for nasopharyngeal carcinoma. While acquired choanal stenosis is rare, this study found a 15% incidence post - radiation

treatment for nasopharyngeal cancer. Diagnosis involves endoscopy and CT scans, with treatment requiring video - assisted endonasal surgery for nasal cavity calibration. Endoscopic surveillance is crucial for early detection of this rare complication [23]. In a 2014 study exploring various late nasal - sinus complications post - radiation, choanal stenosis was reported in 15% of patients.

A retrospective analysis of postirradiated nasopharyngeal carcinoma (NPC) patients employed endoscopic surgery for those with rhinosinusitis unresponsive to conservative medical treatment. Similar positive outcomes were reported in another retrospective study by Gray et al, demonstrating significant postoperative improvement in Lund - Mackay scores and the absence of recurrent mucocele collection in patients treated for sinonasal malignancy [28]. Kamel et al supported these findings, revealing a decline in mucociliary clearance in all NPC patients undergoing irradiation, with continued deterioration over time independent of radiation dose [16].

Su et al conducted endoscopic surgery for post - radiation chronic rhinosinusitis, observing partial symptom relief in 7 out of 9 patients and improved computed tomography scores in 12 of 14 evaluated operative sides [29]. Postirradiated NPC patients with chronic rhinosinusitis typically receive antibiotics and nasal douching, with aggressive medical treatment leading to improvement in most cases.

The nasal mucociliary clearance (NMCC) of the nasal cavity and paranasal sinuses relies on proper mucosal cilia functioning, mucus properties, and their interactions. Various factors, including infection, dry air, and irradiation, can impair NMCC. Irradiation - induced ciliary dysmorphism may compromise NMCC and lead to sinusitis, while chronic sinusitis may induce dysmorphic cilia formation, creating a reciprocal and exacerbating cycle in irradiation - induced sinusitis pathogenesis.

5. Conclusion

This review identifies sinonasal mucosal disorders, olfactory disturbances, choanal atresia, and synechia as nasal complications arising from the irradiation of head and neck cancers. The incidence and severity of olfactory dysfunction and chronic rhinosinusitis were most pronounced at the conclusion of radiotherapy (RT) and three months post - treatment, gradually diminishing over time. The decline in smell acuity and the occurrence of chronic rhinosinusitis post - RT appeared to be correlated with radiation dosage on the olfactory area and nasal cavities, albeit with varying degrees of recovery. Consequently, it is crucial to ascertain the severity of chronic rhinosinusitis and olfactory dysfunction to formulate strategies that provide support to patients and enhance their quality of life. Further investigations are imperative to better evaluate the efficacy of medical, surgical, and endoscopic management approaches for nasal complications following radiotherapy.

Declaration of conflicting interests

The author declare that there is no conflict of interest

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