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The Epidemiological and Therapeutic Profile of Oropharyngeal Cancers: Experience of the Onco-Radiotherapy Department of the Mohamed VI University Hospital, Marrakech: A Report on 46 Cases

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Abstract **Original Research Article**

Oropharyngeal squamous cell carcinoma (OPSCC), commonly known as throat cancer or tonsil cancer, is a type of head and neck cancer that refers to the cancer of the base and posterior one-third of the tongue, the tonsils, soft palate, and posterior and lateral pharyngeal walls. The incidence of OPSCC is increasing in both old and young populations at an alarming level. Radiotherapy is the traditional treatment for oropharyngeal cancer because of its ability to preserve anatomic form and function compared with other conventional curative options. The patterns of presentation, stage distributions, tumor bulk, biology and tolerance to intensive radical treatment may differ in developing countries and different ethnic populations.This activity aim to illustrate the evaluation and management of oropharyngeal squamous cell carcinoma in our context and highlights the role of conventional radical radiotherapy in the treatment.

Keywords: Squamous cell carcinoma, Oropharyngeal cancer, HPV, radiotherapy.

INTRODUCTION

OPSCC is a common malignancy of the head and neck. Worldwide age-adjusted incidence rates for men and women are 1.8 and 0.4 per 100 000 populations respectively, with a substantial variation in different regions and countries. In the Northern Africa, the age-adjusted incidence rates for men and women are 0.31 and 0.16 per 100 000 populations respectively (Sung, H *et al*., 2021). Although the strongest etiological association of this cancer is with the abuse of tobacco and alcohol, there is now an established association with human papilloma virus (HPV) infection as well (Gillison, M. L. *et al*., 2000) (Pintos, J. *et al*., 2008). All over the world, most cases of this cancer present in locoregionally advanced disease. This is especially true for developing countries (Agarwal, J. P. *et al*., 2009).

Oropharyngeal cancers comprise a substantial proportion of head and neck malignancies at our institute, and we decided to retrospectively analyze outcomes in the patient population receiving radical radiation to identify its epidemiological and clinical characteristics in our context, as well as to generate our treatment outcomes with conventional radiotherapy techniques.

MATERIAL AND METHODS

Patients

The medical records of a single radiotherapy unit in the institute between 2018 and 2022 were reviewed retrospectively. The records of 46 consecutive patients with oropharyngeal carcinoma treated with radical radiotherapy were isolated for analysis. The decision of treatment with radical RT in each case was based on a multidisciplinary joint clinic assessment. Prior to treatment all the patients had detailed evaluation that included a) complete history; b) documentation of risk factors especially tobacco or alcohol abuse (tobacco abuse was defined as a chronic abuse of one or more forms of smoked or smokeless tobacco); c) comprehensive clinical examination including a flexible endoscopy; d) histological diagnosis; e) staging workup including blood chemistry, CT TAP and appropriate imaging of the face and neck. Patients were staged according to the prevalent American Joint Committee for Cancer (AJCC)/International Union Against Cancer (UICC) staging system. For the purpose of this analysis

they were reclassified according to the current AJCC 8th edition.

Radiotherapy treatment

All the patients were irradiated with megavoltage beams (6 MV photons) with 2 parallel opposed lateral fields and 1 anterior vertical for the irradiation of lower cervical lymph nodes. Spinal cord was shielded at 46 Gy. Appropriate immobilization was used during the treatment. They were treated with conventional daily fractionation of 2 Gy, 5 fractions per week, to a dose of 70 Gy to the gross primary and nodal disease as well as adjacent nodal regions at high risk of microscopic metastasis. The remaining electively treated neck received between 54 Gy at 1.8 Gy daily fractions. A posterior neck electron portal with appropriate energies was added after spinal shielding when indicated on the basis of pretreatment nodal extent.

Chemotherapy

Chemotherapy was administered with radiation in a proportion of patients either in neoadjuvant or concomitant setting. The practice of chemotherapy varied with the time period, and was individualized according to the age, performance status and stage of the disease. The most commonly used regimen consisted of concurrent cisplatinum, at a dose of 100 mg/m^2/21days.

Follow-up

During treatment, all patients were reviewed weekly or more frequently depending on the need and evaluated for tolerance and compliance to treatment, weight loss, performance status, skin and mucosal reactions, blood counts and need for symptomatic treatment. The patients were followed-up at 6 to 8 weeks from completion of therapy to assess response and persistent toxicity. Acute toxicity was reported utilizing the Radiation Therapy Oncology Group (RTOG)/ European Organization for Research and Treatment of Cancer (EORTC) toxicity criteria [14]. Response was documented by the WHO response grading. Subsequent follow-up visits were scheduled at 3 monthly intervals for the first 2 years, then every 6 months till the 5th year and annually thereafter. All efforts were made to update the disease status of patients by the medical records department through telephonic contact. Patients not responding to above measure were considered lost to follow-up and censored for statistical analysis.

RESULTS

Details of 47 patients with oropharyngeal cancer receiving radical radiotherapy as the primary treatment were analyzed. The median age was 64.5 years (range 37-92 years) and the sex ratio was 1.5:1 in favor of males. History of tobacco abuse was present in 62.5% of the patients, whereas 20.8% of the patients had a history of alcohol consumption. 2% presented with syphilis. Only 20% had a KPS of 80 or more. The majority (75%) had T3 or T4 tumors. Node-positive disease was seen in 58.3% of the patients. Overall nearly 62.5% had stage III and 8.3% had stage IV disease. Tonsillar carcinoma (63,5%) outnumbered the base of tongue and vallecular primaries (30,5%). Whereas soft palate carcinoma and posterior pharyngeal wall counted for 3% each. All tumors were squamous cell carcinoma on histopathological examination of biopsy specimens including 81,8% of conventional non-keratinizing subtype.

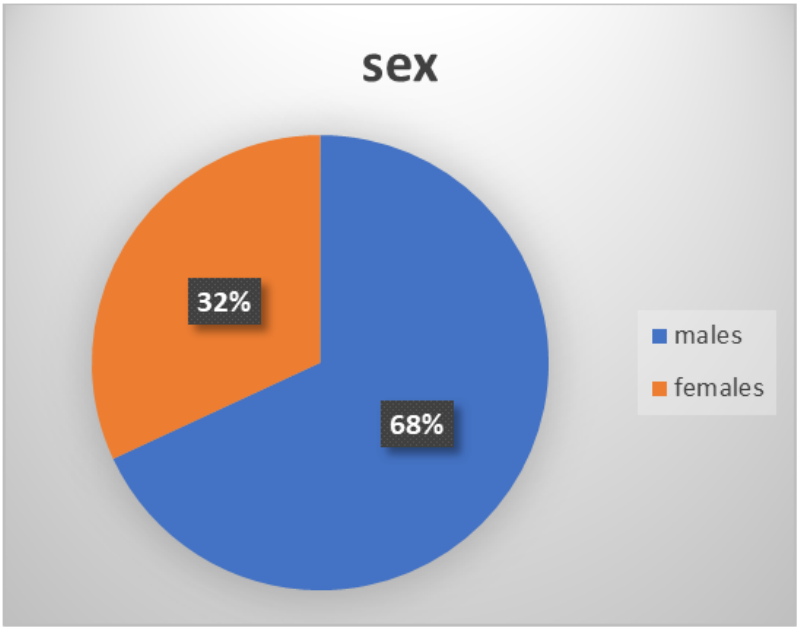

Figure 1: Distribution of OPSCC by gender

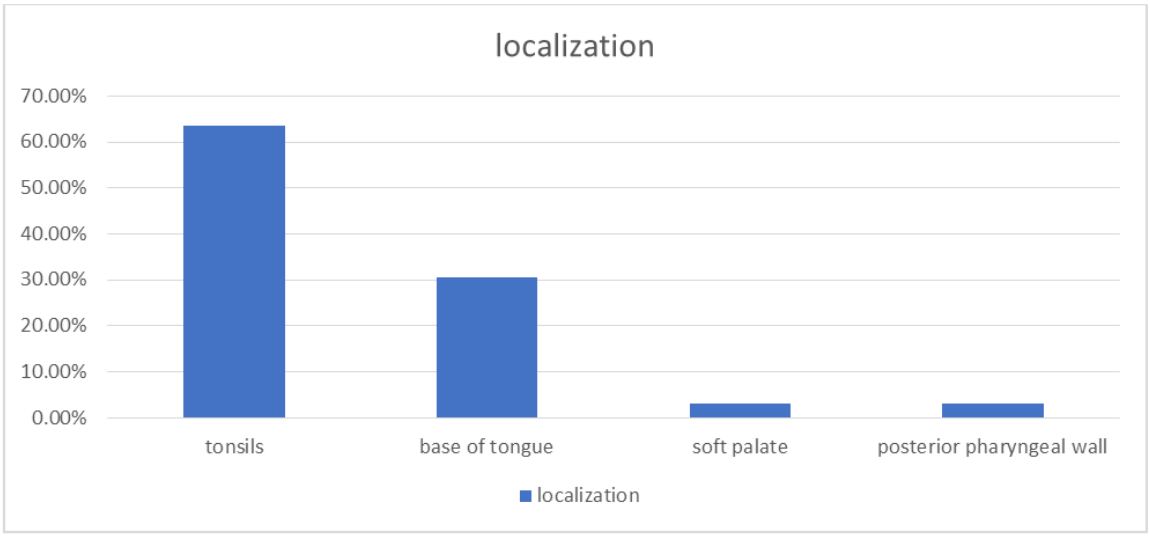

Figure 2: Distribution of OPSCC by location

Treatment Characteristics

All patients were planned for radical radiotherapy with or without chemotherapy. Radical RT alone was the treatment modality for 8.3% of the patients as a postoperative therapy. The remaining received either concomitant (31,3%) or neoadjuvant (60.4%) chemotherapy. The total dose of radiation delivered was 70 Gy. The overall treatment time ranged from 35-102 days (median 68.5 days). In the group receiving concomitant chemotherapy, the median number of chemotherapy cycles was 2 (range 1 to 4).

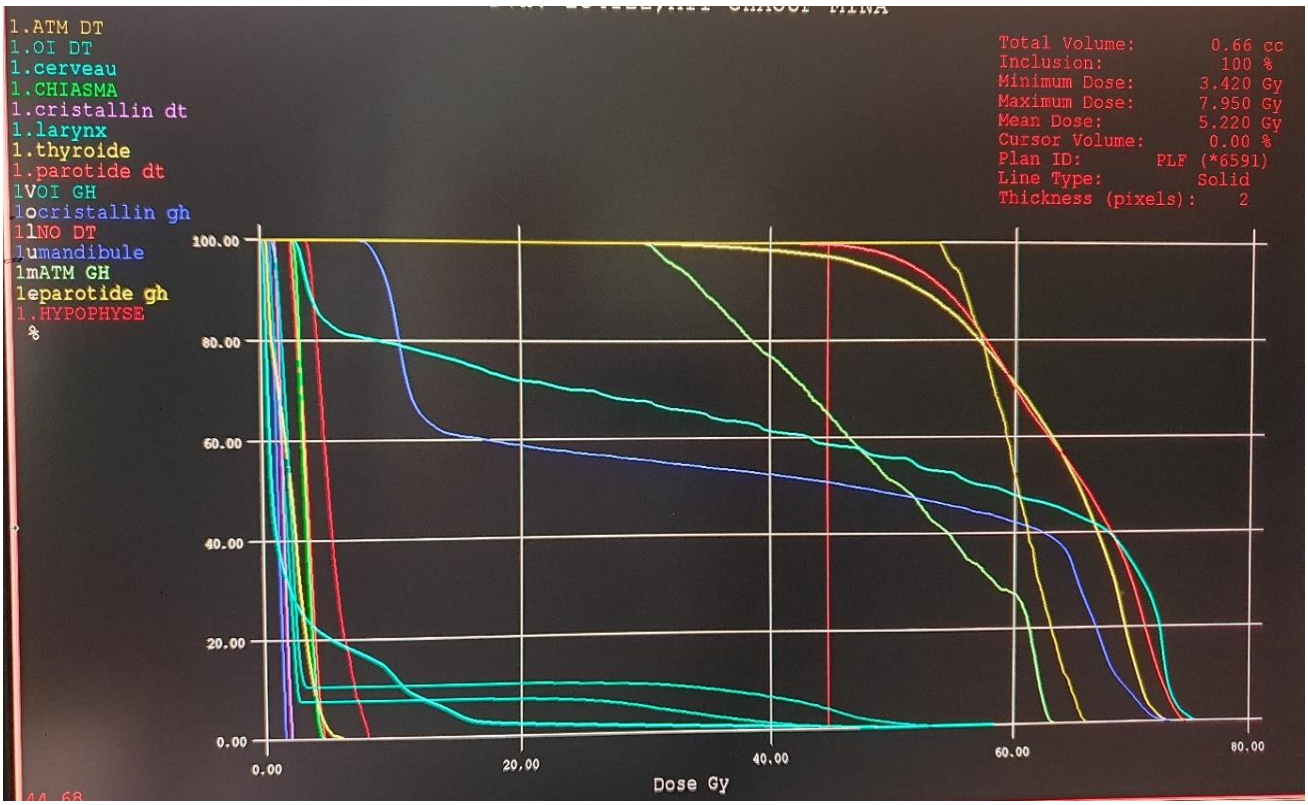

Figure 3: The dose received by the organs at risk of a 37-years-old patiente with a squamous cell carcinoma of the right tonsil

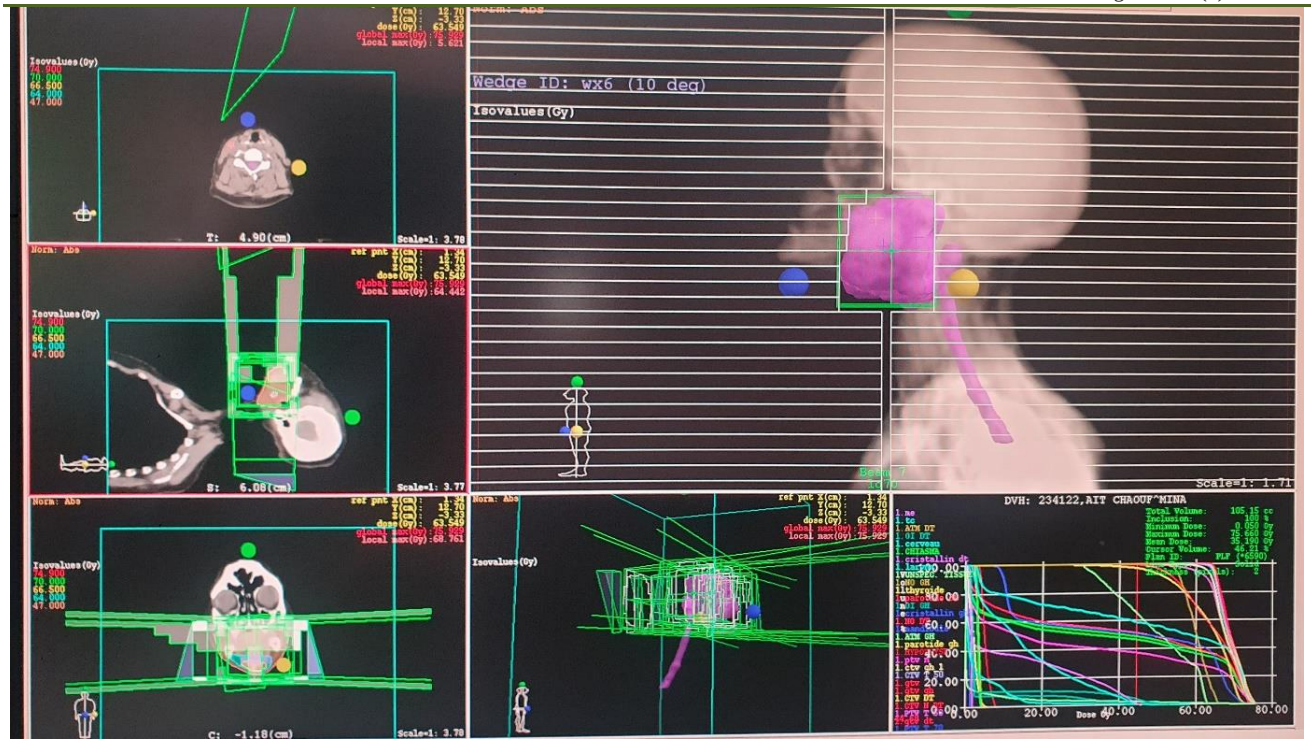

Figure 4: Dosimetry of a squamous cell carcinoma of the right tonsil in a 37-years-old patiente

Acute toxicity

The overall incidence of RTOG grade I-II skin and mucosal reactions were 90.5% and 87,9% respectively. The incidence of grade III acute skin toxicity was 9.5% and grade III mucositis was seen among 12.1% of patients. Patients who had grade III mucosal toxicity with impaired nutritional intake were admitted for nutritional support.

Response and Survival

Complete response was seen in 46% of patients. Locoregional residual disease was seen in 32.9% of patients, a progressive disease was seen among 9.1% of patients, whereas 12% died.

DISCUSSION

OPSCC represents more than 90% of oropharyngeal cancers (Shibahara T. *et al*., 2017). It develops in the posterior third of the tongue, tonsils, soft palate, and posterior pharyngeal wall (Amin, M. B. *et al*., 2017). Within these subsites of the oropharynx, the tonsil and tongue base are the most common sites to be affected by carcinoma (Stevens, T. M *et al*., 2017). Oropharyngeal cancer is the sixth most common cancer worldwide and the prevalence is higher in males than females (Chimenos-Küstner, E *et al*, 2019) (Yete, S *et al*., 2018). The etiology of oropharyngeal carcinoma is broadly categorized into two categories, HPV associated and non-HPV associated carcinomas. HPV associated OPSCC occurs in patients who have been infected with the human papillomavirus. Among the many types of human papillomavirus, HPV16 is the most common type found in oropharyngeal cancers (Isayeva, T *et al*., 2012). HPV-associated OPSCC tends to occur in a younger population that smoke and drink less; a higher percentage of them are males and report more oral sex partners (Taberna, M *et al*., 2017).

On the other hand, smoking tobacco and alcohol consumption have been widely identified as the major risk factors for non-HPV-associated oropharyngeal carcinomas (Barón, A. E *et al*., 1993). Other less common risk factors include a diet low in vegetables and fruits, betel quid chewing, poor nutrition, marijuana smoking, asbestos exposure, certain genetic mutations such as P53 mutation, and CDKN2A (p16) mutations (Mizukawa, N *et al*., 2017) (Helgadottir, H *et al*.., 2014) (Marks, M. A *et al*., 2014).

The recent edition of the American Joint Committee on Cancer (AJCC) staging system defined HPV-positive (HPV+) and HPV-negative (HPV–) OPSCCs as separate entities, with distinct molecular profiles, tumour characteristics and outcomes. Importantly, the HPV+ former is associated with a more favourable prognosis (Fenton, T. R *et al*., 2022).

Patients with oropharyngeal cancer can present with a variety of symptoms depending on the location of the tumor. The most common presentation include persistent sore throat, dysphagia, odynophagia, dysarthria, presence of a lump in the neck, and otalgia. In addition, the patients may also complain of voice changes (hoarseness), unexplained weight loss, and hematemesis

Diagnosis is made on the basis of biopsy results of the affected tissue. The American Society of Clinical

Oncology recommends that HPV testing should be done on all the newly diagnosed oropharyngeal cancers. This is done by polymerase chain reaction, which detects the HPV DNA (Jamal, Z *et al*., 2023).

Treatment involves surgery, radiotherapy, chemotherapy, or a combination of these therapies. Treatment was typically with surgery, as most tumors were locally advanced at presentation. Radiotherapy was used post-operatively to optimize loco-regional control. With developments in the delivery of radiation and the recognition that primary non-surgical management was feasible, a move away from traditional open resection was seen. Two multi-center randomized controlled trials in 2004 also showed a survival advantage with the addition of postoperative chemoradiotherapy in high-risk patients (Bernier, J *et al*., 2004) (Cooper, J. S *et al*., 2004).

Radiation based approaches were adopted more commonly with surgery reserved for salvage. A report of the outcomes and complications comparing surgical and radiotherapy-based approaches in 2002 showed that while both approaches had similar survival and local control rates, surgery was associated with an increased rate of complications (Parsons, J. T *et al*., 2002).

Further interest in radiation treatments for OPSCC was stimulated by advancing technologies in the delivery of radiotherapy. Intensity-modulated radiotherapy treatment (IMRT) was introduced in the early 2000s. Specific potential advantages of this targeted method of delivering radiation include avoidance of high-dose exposure to the parotid glands to minimize xerostomia and to the pharyngeal constrictors in an attempt to minimize swallowing dysfunction (Nutting, C. M *et al*., 2011) (Petkar, I *et al*., 2016).

The overall five-year survival rate in oropharyngeal carcinoma is around 60%. However, the prognosis varies depending on the etiology. In comparison to HPV negative OPSCC, HPV-positive oropharyngeal carcinoma shows a better prognosis and increased response to the treatment. The higher survival with HPV-associated cancer is because of favorable tumor biology and a healthier and younger patient population (Jamal, Z *et al*., 2023).

CONCLUSION

OPSCC is an increasing health problem in the developing and developed world. In recent years, there have been major changes in the treatment paradigms for OPSCC, especially as our understanding of HPV-related tumors has improved. Conventional radiotherapy is a key therapeutic modality used in the treatment. Although it is a proven, effective treatment of cancer control, it can result in significant acute and late toxicities.

REFERENCES

- Shibahara, T. (2017). Oral cancer-diagnosis and therapy-. *Clinical calcium*, *27*(10), 1427-1433.
- Amin, M. B., Greene, F. L., Edge, S. B., Compton, C. C., Gershenwald, J. E., Brookland, R. K., Meyer, L., Gress, D. M., Byrd, D. R., & Winchester, D. P. (2017). The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA: a cancer journal for clinicians*, *67*(2), 93–99.
- Stevens, T. M., & Bishop, J. A. (2017). HPV-related carcinomas of the head and neck: morphologic features, variants, and practical considerations for the surgical pathologist. *Virchows Archiv: an international journal of pathology*, *471*(2), 295–307.
- Chimenos-Küstner, E., Marques-Soares, M. S., & Schemel-Suárez, M. (2019). Consideraciones sobre etiopatogenia y prevención del cáncer orofaríngeo [Aetiopathology and prevention of oropharyngeal cancer]. *Semergen*, *45*(7), 497–503.
- 5- Yete, S., D'Souza, W., & Saranath, D. (2018). High-Risk Human Papillomavirus in Oral Cancer: Clinical Implications. *Oncology*, *94*(3), 133–141.
- Isayeva, T., Li, Y., Maswahu, D., & Brandwein-Gensler, M. (2012). Human papillomavirus in non-oropharyngeal head and neck cancers: a systematic literature review. *Head and neck pathology*, *6 Suppl 1*(Suppl 1), S104–S120.
- Taberna, M., Mena, M., Pavón, M. A., Alemany, L., Gillison, M. L., & Mesía, R. (2017). Human papillomavirus-related oropharyngeal cancer. *Annals of oncology : official journal of the European Society for Medical Oncology*, *28*(10), 2386–2398.
- Baron, A. E., Franceschi, S., Barra, S., Talamini, R., & La Vecchia, C. (1993). A comparison of the joint effects of alcohol and smoking on the risk of cancer across sites in the upper aerodigestive tract. *Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*, *2*(6), 519-523.
- Mizukawa, N., Swe Swe Win, Zaw Moe Thein, Moe Thida Htwe, Yoshioka, Y., Kimata, Y., Iida, S., Myo Khin, Okada, S., & Than Sein (2017). The Incidence of Oral and Oropharyngeal Cancers in Betel Quid-Chewing Populations in South Myanmar Rural Areas. *Acta medica Okayama*, *71*(6), 519–524.
- Helgadottir, H., Höiom, V., Jönsson, G., Tuominen, R., Ingvar, C., Borg, A., Olsson, H., & Hansson, J. (2014). High risk of tobacco-related cancers in CDKN2A mutation-positive melanoma families. *Journal of medical genetics*, *51*(8), 545–552.
- Marks, M. A., Chaturvedi, A. K., Kelsey, K., Straif, K., Berthiller, J., Schwartz, S. M., Smith, E., Wyss, A., Brennan, P., Olshan, A. F., Wei, Q., Sturgis, E. M., Zhang, Z. F., Morgenstern, H., Muscat, J., Lazarus, P., McClean, M., Chen, C., Vaughan, T. L., Wunsch-Filho, V., … D'Souza, G. (2014). Association of marijuana smoking with oropharyngeal and oral tongue cancers: pooled

analysis from the INHANCE consortium. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*, *23*(1), 160–171.

- Fenton, T. R., Liu, J., Masterson, L., & Fenton, T. R. (2022). HPV-associated oropharyngeal cancer: epidemiology, molecular biology and clinical management. Nature Reviews Clinical Oncology, *19*(5), 306–327.
- Jamal, Z., & Anjum, F. (2023). Oropharyngeal Squamous Cell Carcinoma. In *StatPearls*. StatPearls Publishing.
- Hay, A., & Nixon, I. J. (2018). Recent advances in the understanding and management of oropharyngeal cancer. *F1000Research*, *7*, F1000 Faculty Rev-1362.
- Bernier, J., Domenge, C., Ozsahin, M., Matuszewska, K., Lefèbvre, J. L., Greiner, R. H., Giralt, J., Maingon, P., Rolland, F., Bolla, M., Cognetti, F., Bourhis, J., Kirkpatrick, A., van Glabbeke, M., & European Organization for Research and Treatment of Cancer Trial 22931 (2004). Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *The New England journal of medicine*, *350*(19), 1945–1952.
- Cooper, J. S., Pajak, T. F., Forastiere, A. A., Jacobs, J., Campbell, B. H., Saxman, S. B., Kish, J. A., Kim, H. E., Cmelak, A. J., Rotman, M., Machtay, M., Ensley, J. F., Chao, K. S., Schultz, C. J., Lee, N., Fu, K. K., & Radiation Therapy Oncology Group 9501/Intergroup (2004). Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *The New England journal of medicine*, *350*(19), 1937–1944.
- Parsons, J. T., Mendenhall, W. M., Stringer, S. P., Amdur, R. J., Hinerman, R. W., Villaret, D. B., Moore-Higgs, G. J., Greene, B. D., Speer, T. W., Cassisi, N. J., & Million, R. R. (2002). Squamous cell carcinoma of the oropharynx: surgery, radiation therapy, or both. *Cancer*, *94*(11), 2967–2980.
- Nutting, C. M., Morden, J. P., Harrington, K. J., Urbano, T. G., Bhide, S. A., Clark, C., Miles, E. A., Miah, A. B., Newbold, K., Tanay, M., Adab, F., Jefferies, S. J., Scrase, C., Yap, B. K., A'Hern, R. P., Sydenham, M. A., Emson, M., Hall, E., & PARSPORT trial management group (2011). Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. *The Lancet. Oncology*, *12*(2), 127–136.
- Petkar, I., Rooney, K., Roe, J. W., Patterson, J. M., Bernstein, D., Tyler, J. M., Emson, M. A., Morden, J. P., Mertens, K., Miles, E., Beasley, M., Roques, T., Bhide, S. A., Newbold, K. L., Harrington, K. J., Hall, E., & Nutting, C. M. (2016). DARS: a phase III randomised multicentre study of dysphagia-optimised intensity- modulated radiotherapy (Do-IMRT) versus standard intensity- modulated radiotherapy (S-IMRT) in head and neck cancer. *BMC cancer*, *16*(1), 770.