Upper aerodigestive tract bleeding in head and neck – a tertiary Center Reality

Original Article

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Abstract

Objective: To characterize hospital admissions due to tumoral hemorrhage from head and neck squamous cell carcinoma (SCC) in a tertiary center.
Study design: Retrospective.
Material and Methods: Review of clinical files with a diagnosis of oral cavity hemorrhage (ICD 10 R04.1) associated with head and neck SCC, from 2018 to 2023.
Results: 36 admissions were analyzed. The most frequent tumor location was the oropharynx (61%). Most of the tumors were stage IV (89%). 50% of patients had undergone CRT. With regard to hemostasis treatment, 17% received local measures; 14% also required systemic antifibrinolytic therapy; in 36% tamponade was performed. Surgical hemostasis was required in 17% of episodes and 11% underwent hemostatic radiotherapy. 25% needed emergent tracheostomy.
Conclusions: Factors such as oropharyngeal tumor location, stage IV and previous CRT were prevalent in patients requiring hospitalization for tumor hemorrhage.

Keywords: tumor hemorrhage; squamous cell carcinoma; head and neck cancer

Introduction

Head and neck cancer is the seventh most common cancer worldwide.[1] Portugal has an incidence of over 10 cases per 100,000 population, while the global incidence is over 20 cases per 100,000 population.[2] Squamous cell carcinomas represent >90% of head and neck tumors.[3]

Tumor-related bleeding has an overall incidence of 6%-14%.[4] In head and neck tumors, it is considered one of the main complications, particularly after tumor-directed therapy, with an incidence ranging from 0.5% to 10%.[3,5] This is a potentially fatal event and may present as either low-volume bleeding or catastrophic hemorrhage. [3,6,7] It occurs most frequently in primary tumors of the oral cavity and in advanced-stage neoplasms, and it is a

common reason for emergency department visits, with a significant risk of recurrence and mortality. [4,6,7,8,9] Treatment for these patients varies and is often multimodal. Following local treatment and supportive therapy, radiological intervention (angioembolization), surgery, or hemostatic radiotherapy may be considered.[6,10]

Material and Methods

In this retrospective observational study, we reviewed the electronic health records of patients hospitalized for oral cavity hemorrhage (ICD-10 R04.1) associated with head and neck cancer over a 6-year period (2018–2023). Hospitalizations with incomplete data or histological diagnoses other than squamous cell carcinoma (SCC) were excluded. Subsequently, a statistical analysis was performed using Microsoft Excel®.

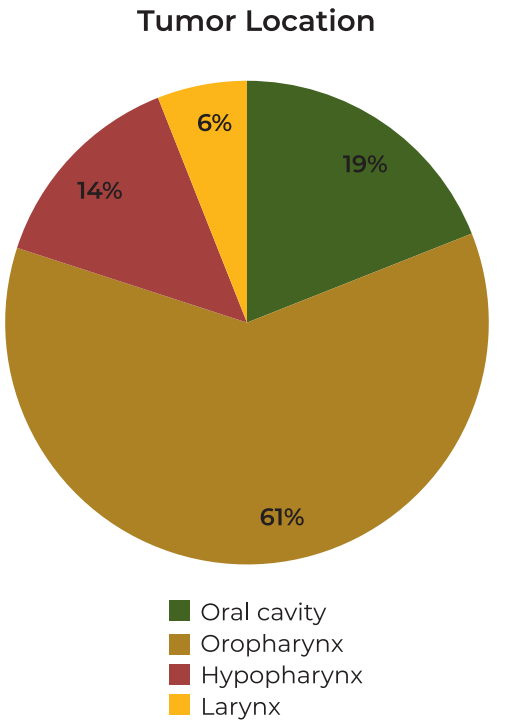
Results

A total of 36 patient admissions were analyzed; 83% of the patients (N=30) were male, and 17% (N=6) were female. The sample had a mean age of 60 years, with a range of 37 to 87 years.

In 83% (N=30) of these admissions, the patients had a diagnosis of head and neck SCC prior to admission. In the remaining 17% (N=6), hemorrhage was the presenting sign of cancer. In 11% (N=4) of these admissions, radiation-induced ulcers were present, without active neoplastic disease.

As shown in Figure 1, the most frequent tumor location was the oropharynx (N=22, 61%), followed by the oral cavity (N=7, 19%), hypopharynx (N=5, 14%), and larynx (N=2, 6%) (Figure 1). Most tumors were T4 (N=27, 75%) or were at stage IV (N=32, 89%). Overall, 17% (N=6) had bleeding risk factors related to hematologic disease or concomitant antiplatelet or anticoagulant therapy. Current smokers accounted for 47% (N=17), while 31% (N=11) were former smokers. As shown in Table 1, 78% (N=28) of the 36 hospitalized patients with carcinomas had received prior oncological treatment. The average length of stay was 15 days, with 47% (N=17) of the sample staying

Figure 1
Tumor Location



for less than 8 days (Table 2). Patients with oropharyngeal SCC hemorrhages required longer average hospital stays (20 days) than those with hemorrhages originating in other anatomical areas, specifically the oral cavity (8 days), hypopharynx (7 days), and larynx (5 days).

Hemorrhage was resolved using a sequential approach: first, local measures, specifically cryotherapy; second, systemic antifibrinolytic therapy (tranexamic acid or aminocaproic

Table 1
Prior treatment

Treatment	N (%)
Untreated	8 (22%)
ChT	3 (8%)
RT	3 (8%)
CRT	18 (50%)
IT	1 (3%)
CRT + IT	3 (8%)

Legend: ChT: chemotherapy, RT: radiotherapy, CRT: chemoradiotherapy, IT: immunotherapy

Table 2
Length of stay

Location	≤ 7 days	8-28 days	>28 days
Total	17 (47%)	15 (42%)	3 (11%)
Oral cavity	4 (57%)	3 (43%)	
Oropharynx	8 (36%)	10 (46%)	4 (18%)
Hypopharynx	3 (60%)	2 (40%)	
Larynx	2 (100%)		

acid); third, packing (with gauze pads or petrolatum gauze); fourth, hemostasis in the operating room and/or angioembolization and/or hemostatic radiotherapy (RT).

As described in Figure 2, 31% (N=11) of the events were managed with only local measures (N=6, 17%) (cryotherapy) or systemic antifibrinolytic therapy (aminocaproic acid or tranexamic acid) (N=5, 14%). However, in 53% of cases, more invasive local measures were required, such as packing with gauze soaked in aminocaproic acid (N=13, 36%) or surgical hemostasis (N=6, 17%) conducted via bipolar cauterization (N=4), internal jugular vein ligation (N=1), or thyrolinguofacial trunk ligation (N=1). Hemostatic radiotherapy was also performed in 11% of the sample (N=4). Angiography was performed in 11% (N=4) of cases, revealing a lingual artery aneurysm and an external carotid artery pseudoaneurysm. Subsequently, angioembolization successfully controlled the hemorrhage in 50% (N=2) of these patients. Local measures alone were effective for 43% (N=3) of oral cavity tumors. In contrast, oropharyngeal SCC required packing in 32% (N=7) and surgical exploration in 27% (N=6) of cases. Similarly, packing was the most common treatment for hypopharyngeal tumor hemorrhages (N=4, 80%).

Half of the patients (50%, N=18) had a history of tracheostomy, and 25% (N=9) underwent emergency tracheostomy. Consequently, 8 (22%) of the 36 patients did not undergo a tracheostomy.

Figure 2
Therapeutic approach

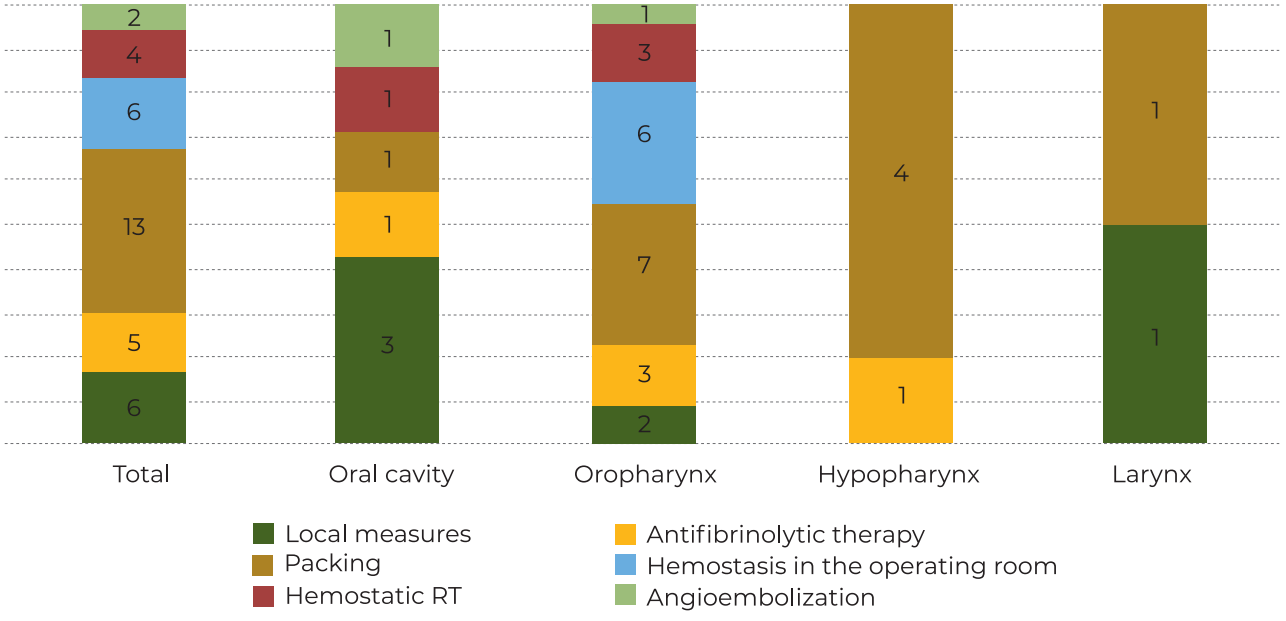


Table 3
Hemorrhagic Recurrence

Recurrent hemorrhage	Oral cavity	Oropharynx	Hypopharynx	Larynx
Yes	**3 (43%)**	**11 (50%)**	**4 (80%)**	
No	4 (57%)	11 (50%)	1 (20%)	2 (100%)

During hospitalization, 50% of patients experienced rebleeding (Table 3). The mortality rate due to tumor hemorrhage was 33% (N=12).

Discussion

Among the 36 hospitalized patients, most patients were men with a mean age of 60 years, which is consistent with populations reported in the literature.[6,8]

SCC diagnosis was known prior to admission in 83% of the sample. A high number of patients (78%) had undergone previous tumor-directed therapy, including chemotherapy, radiotherapy, and immunotherapy, with four patients presenting with radiation-induced ulcers. These results can be explained by the well-known adverse effects of these treatments.[5,6,7,9] Vascular sequelae—specifically premature atherosclerosis, arterial wall weakening due to adventitial fibrosis, elastic filament fragmentation, and destruction of the *vasa vasorum*—along with mucosal erosion and ulceration exposing susceptible vessels to injury, can result in up to a 7.6-fold increased risk of hemorrhage.[5,6,9] Additionally, chemotherapy-induced thrombocytopenia contributes to these hemorrhagic episodes.[9]

In contrast to the findings of Wang *et al.*, oropharyngeal tumors were more common (61%) than those of the oral cavity (19%).[6] Unlike oropharyngeal hemorrhages, particularly those in the base of the tongue, hemorrhages originating in the oral cavity are generally located in areas accessible via direct visualization, which often allows for effective source control without the need for hospitalization. Since the sample in this study excludes outpatients, the frequency of oral cavity tumors may be lower than would be expected in a broader population.

Hemorrhages are frequently reported in tumors with a T3 or T4 TNM classification or advanced stages, as reflected in the study results.[4,6,7,9] During tumor growth, progressive infiltration and invasion of the surrounding tissues occur concurrently; crossing certain anatomical barriers can cause the nearby vessels to ulcerate.[9] This destruction can, by itself, lead to potentially catastrophic hemorrhages of large-caliber vessels.[9] Additionally, more aggressive and larger neoplasms may require higher doses of radiotherapy, posing an increased risk of hemorrhage.[9]

In such events, particularly in high-volume hemorrhages, the airway may be compromised due to the aspiration of blood. Therefore, in accordance with critical care protocols, the airway must always be secured early on.[11] In non-tracheostomized patients, large volumes of clots can obscure the larynx, precluding orotracheal intubation.[11] In these situations, cricothyroidotomy or surgical tracheostomy should be considered.[11] In the present study, most patients were already tracheostomized, allowing for airway control by inflating the tracheostomy tube cuff. However, a quarter of the patients required an emergency tracheostomy, which demonstrates the importance of considering this procedure when managing these types of patients.

Regarding hemostasis, if general supportive measures (anti-fibrinolytics) and less invasive local techniques (cryotherapy, Surgicel®, packing) fail, other options should be considered, such as ligation/cauterization in the operating room, hemostatic radiotherapy, or angioembolization.[10] Our findings on the treatments used for patients in our sample corroborate the relevance of considering all therapeutic options, as all are frequently used as well as the importance of a multidisciplinary

approach. In collaboration with the radiology team, four patients underwent angiography; however, only 50% had findings amenable to treatment by angioembolization. *Cannavale et al.*, in agreement with other authors, reported a small number of candidates for angioembolization, with 87.5% and 33% of the candidates showing no active bleeding on CT angiography and angiography, respectively.[6,12] Following discussion with radiation oncology, four patients underwent hemostatic radiotherapy. The efficacy of this treatment is proven in several studies, particularly in patients receiving palliative care. [3,13,14] The low rate of patients undergoing surgery is also demonstrated by *Wang et al.*, with over 82.7% of cases resolved with supportive treatmen.[6]

The oropharynx and hypopharynx are difficult to access in an awake patient, making bleeding points in these regions difficult to access and control under these same conditions. Consequently, while oral cavity SCCs are primarily managed with local measures, oropharyngeal and hypopharyngeal tumors usually require more invasive local treatments, such as packing or surgical intervention. Likely due to the greater complexity of treating tumors in these anatomical areas, hemorrhages from oropharyngeal SCCs resulted in longer hospital stays (average of 20 days) than oral cavity hemorrhages (average of 8 days).

The present study demonstrated higher rates of hemorrhage recurrence (50%) and mortality rate (33%) than those reported by *Yen et al.* (recurrence 21.2%, mortality 16%).[4] The discrepancy in the mortality rate may be explained by differences in the study populations. Our sample, which was limited to inpatients, likely represents more severe cases, whereas *Yen et al.* included only emergency department patients, some of whom may have been considered fit for discharge and therefore did not require inpatient monitoring.

Conclusion

Tumor hemorrhage was a significant cause of mortality in the sample studied. Oropharyngeal tumor location, stage IV disease, and previous chemoradiotherapy were frequent factors among patients requiring hospitalization for tumor hemorrhage. Compared with oral cavity hemorrhages, oropharyngeal hemorrhages more often required more complex or invasive management approaches. Tracheostomy ensured airway protection in 75% of patients and was performed as an emergency in 25% of cases. The high rate of hemorrhage recurrence during hospitalization highlights the challenges associated with managing these episodes.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

Privacy policy, informed consent and Ethics Committee Authorization

The authors declare that they have written consent for the use of photographs of patients in this article.

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Statement on the Use of Generative AI and AI-Assisted Technologies in the Writing Process

No generative AI or AI-assisted technologies were used at any stage of the project.

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