Internal or common carotid artery encasement (CAE) is observed in almost 2-7% of head and neck cancers (HNC) and designates the tumor with the T4b category. This clinical scenario is associated with a dismal prognosis, owing to the risk for thrombosis and bleeding that usually characterizes such an advanced cancer. Standardized radiological criteria to infer invasion of the carotid artery are lacking. Complete surgical resection in the context of a multimodality treatment is supposed to offer the greatest chances of cure. Surgery can either be carotid-sparing or include carotidectomy. Data on probability of cerebrovascular and non-cerebrovascular complications, risk of carotid blowout, poor oncologic outcomes, and less-than-certain efficacy of diagnostic and interventional preventive procedures against cerebral infarction make it difficult to define surgery as the recommended option among other therapeutic strategies. Non-surgical therapies based on radiation therapy possibly combined with chemotherapy are more frequently employed in HNC with CAE. In this context, carotid blowout is the most feared complication, and its probability increases with tumor stage and cumulative radiation dose received by the vessel. The use of highly conformal radiotherapies such as intensity-modulated particle therapy might substantially improve the manageability of HNC with CAE by possibly reducing the risk of late sequelae. Despite evidence is frail, it appears
observed in 71% of patients (6). In 2010, Pons et al. reported focusing on cases with >270° encasement, CA invasion was between 180° and reported that when tumor surrounded the CA for <180° or these aspects based on the most relevant current evidence.

INTRODUCTION

Internal or common carotid artery encasement (CAE) by head and neck cancers (HNCs), including salivary gland and sinonasal cancers, designates the tumor with the T4b category (1). Carotid artery (CA) can be encircled, and its walls potentially invaded by the primary tumor and/or nodal metastases with extranodal extension. CAE has a low but non-negligible incidence, accounting for approximately 2–7% of advanced HNCs (2), more often in patients affected by recurrent or persistent disease. In all cases, a comprehensive, multidisciplinary plan is necessary to pursue the optimal patient-centered approach (3). This clinical scenario is generally associated with a very poor prognosis, which is determined by both the risk for fatal exsanguination when cancer erodes CA walls and the abrupt tumor progression which usually characterizes such an advanced neoplastic stage (4, 5). Moreover, CAE is usually not specified as an inclusion or stratifying criteria in trials assessing the role of non-surgical therapies.

Criteria to define CAE at imaging, mastering various therapeutic approaches for locally advanced disease with CAE, management options to prevent CA blowout (CB), as well as knowledge of potential cerebrovascular risks related to permanent CA occlusion are all contemporary aspects that should raise the interest of different physicians who deal with advanced HNCs. The present perspective will emphasize on these aspects based on the most relevant current evidence.

CAE DEFINITION CRITERIA

So far, there are no standardized radiological criteria to distinguish simple CAE from frank vessel involvement. Preoperative magnetic resonance imaging (MRI) has been demonstrated capable in predicting involvement of the CA in cases with near-circumferential encasement (6). In contrast, despite computed tomography (CT) is more commonly used to stage HNCs, its utility in predicting CA invasion has been questioned (7). In 1995, Yousem et al. analyzed 49 MRI (53 CAs) and reported that when tumor surrounded the CA for <180° or between 180–270°, no CA invasion was found at surgery. When focusing on cases with >270° encasement, CA invasion was observed in 71% of patients (6). In 2010, Pons et al. reported on 22 patients preoperatively staged through both CT and MRI. They found that combination of CA deformation, >180° encasement, and segmental obliteration of the fat separating the vessel from the adenopathy or primary tumor was highly predictive of invasion of the CA wall. On the other hand, the isolated finding of >180° encasement or fat obliteration could not reliably indicate an invasion of the CA (8). Other studies reported similar results (2, 9, 10). However, standardized and validated radiological criteria to infer CA invasion are lacking. Thus, radiological definition of CAE is challenging and not founded upon sound data. Therefore, beside counting on a head and neck imaging-trained radiologist, the multidisciplinary team should also include vascular surgeons and interventional radiologists and be equipped with the necessary resources to assess on a case-by-case basis the resectability and curability of a CA-encasing tumor.

THERAPEUTIC OPTIONS FOR PATIENTS WITH CA-ABUTTING CANCERS AND THEIR COMPLICATIONS

The therapy reported to offer the greatest chances of cure in patients with resectable HNC with CAE is surgery aimed to obtain a complete tumor resection, which can be achieved through sub-adventitial dissection or CA resection when the tumor only abuts or frankly invade/encase the vessel, respectively (Figure 1). The most relevant, life-threatening complication of CA-sparing surgery is CB, which has an average incidence of 3-4.5% (0-2.4% in naïve patients, 4.5-21.1% in previously irradiated patients) and mean lethality rate as high as 50% (11). In an animal study published in the 1970s, sub-adventitial dissection to peel the tumor off CA combined with infection of the surgical site have been hypothesized as being the main determinants of postoperative CB (12). Thus, one could hypothesize abutted CA to be resected irrespective of its genuine invasion by cancer, with the twofold advantage of preventing CB and providing a wider margin of resection. However, resecting the CA does not compensate the advanced stage and biological aggressiveness of HNC determining CAE. In fact, several series of HNCs, mostly represented by squamous cell carcinoma (SCC), treated through CA resection-including surgery reported a 2-year overall survival rate as low as 11.1-50.0% (13–16). On the other hand, perioperative mortality (10-25%) (17–19) and risk for cerebrovascular (12.5-33%) (13–16) and non-cerebrovascular complications (25-60%) (13, 14, 16, 20) are non-negligible in patients receiving CA resection-including surgery. Despite cerebral revascularization is supposed to reduce the incidence of cerebrovascular events (19, 21), the comparative study by Aslan et al. was unable to demonstrate a significant difference (17). Cerebral revascularization can be achieved through either CA reconstruction, which is
technically feasible when common CA and/or extracranial (i.e., parapharyngeal) internal CA are resected, or bypass surgery, which consists of creating a communication between a donor arterial system, such as the external carotid one, and the cerebral vascularization (e.g., to the middle cerebral artery) via an interpositional vascular graft. Moreover, prior to indicate CA resection without cerebral revascularization in a patient tolerating a temporary balloon occlusion test, one should consider that the rate of delayed cerebrovascular events in patients with negative occlusion test accounts for 15-22% (22–24). Of note, more than one study demonstrated that morbidity and mortality in patients receiving CA resection-including surgery had a decreasing trend after the 1990s (18, 19). These data taken altogether suggest that only meticulous selection of patients and minimization of surgical morbidity, which cannot prescind from involvement of a neurologist and neurosurgeon in the multidisciplinary team, could lead CA resection-including surgery to be a valuable therapeutic option for some patients with CAE-determining HNC. As an example of the need to accurately select patients, Yokoyama et al. reported a series of 10 patients receiving CA resection and reconstruction through a superficial femoral vein graft: the 5-year overall survival rates of patients affected by SCC and non-SCC cancers were <20% versus 100%, respectively (25). These data witness that histology represents one of the factors to consider when CA resection-including surgery is proposed.

Nonsurgical modalities, mainly represented by photon-based radiotherapy (RT), delivered either alone or in combination with chemotherapy (CRT), are aimed at avoiding complications of CA resection. An HNC may be labelled as “unresectable” either because genuinely unsuitable for a wide-margin resection (i.e., invasion of the skull base, nasopharynx, prevertebral space or cervical spine, fixation of nodes, massive bilateral nodal involvement) or due to the estimated unfavorable balance between risks of surgery and its potential benefits from an oncologic standpoint. Over one-third of these patients are
usually treated by neoadjuvant chemotherapy followed by CRT (26–29).
However, there are few data regarding the outcome of nonsurgical treatments in patients affected by HNC with CAE. Roh et al. reported a cohort of patients with CA-invading HNC: the median survival was 16.5 months in patients treated with surgery (n=11) with or without reconstruction or ligation of the CA, possibly combined with (neo)adjuvant (C)RT, 11.5 months for patients receiving definitive (C)RT (n=6), and 3 months for those treated palliatively (n=6) (p<0.05). CA was not occluded in patients receiving RT, some of them undergoing a temporary balloon occlusion test prior to treatment (5). In addition, no separate outcome analysis was performed for naïve and recurrent patients. Manzoor et al. also reviewed the outcomes of 44 consecutive de novo and recurrent HNC patients with CA involvement. Survival outcome was not significantly different between patients treated with definitive CRT and surgery with or without postoperative RT (p=0.47), although a trend was found in favor of CRT, possibly because of the treatment-naïve nature of these patients. Of note, imaging was assessed in 7/8 patients treated with radical CRT, and all had near-total circumferential CAE (30).

No data on CB events were reported in non-surgically treated patients in these two latter series (5, 30). However, CRT can determine the obliteration of the carotid vasa vasorum, leading to fibrosis of the adventitia and subsequent weakening of the arterial wall (31). Indeed, in a study on 1072 patients receiving CRT with conventional fractionation for HNC, the cumulative incidence of CB increased stepwise from 1.4% to 6.1% considering T1 to T4 cancers, suggesting that locally advanced tumors are associated with a higher risk of CB (32). The overall incidence of CB further increases in patients undergoing re-irradiation for HNC (11, 33), with CAs receiving a cumulative dose of 120 Gy or higher blowing out in 25% of cases within 1 year (34). Of note, the highest CB rates published were in patients affected by recurrent nasopharyngeal cancer re-irradiated through hypofractionated stereotactic RT. These data pose a considerable dilemma to the radiation oncologist, who is forced to either delivering a suboptimal dose or putting the patient at risk of CB, particularly in the re-irradiation setting. This concern could be tempered when delivering high precision RT, like protons and carbon ions. High-linear energy transfer carbon ions RT (CIRT) has recently entered the clinical practice. It enables dose escalation due to specific ions physical properties (allowing highly conformal dose distributions) and offers superior relative biological effectiveness by at least a 2-3-fold factor in comparison to conventional RT (35). There is some evidence that radioresistant HNCs and skull base tumors, such as adenoid cystic carcinoma, may benefit from CIRT, usually using hypofractionated regimen, in terms of outcome and safety. This is particularly true in inoperable/unresectable tumors, macroscopic residues, and recurrences (36–38). So far, there are scant data on the occurrence of vascular complications after CIRT. Jensen et al. reported a CB incidence of 3.8% in 52 patients receiving CIRT-based re-irradiation for recurrent adenoid cystic carcinoma. One-year local control and overall survival were 70.3% (2-year estimate: 47.4%) and 81.8% (2-year estimate: 63.3%), respectively, which is higher compared to conventional RT (39). In another paper, only 1/229 patients re-treated with CIRT had a CB. This was a patient with a recurrent adenoid cystic carcinoma of the right base of the skull already treated with 2 courses of RT. The patient recovered quickly from a post-interventional stroke and survived for 9 months after CB. Median local progression-free survival after CIRT was 24.2 months and the median overall survival 26.1 months (40).

Neither of these two studies analyzed the radiological relationship between CA and the tumor, nor was the possibility to stent or occlude CA before starting re-treatment discussed. The latter strategy should be considered in view of the potential benefits in terms of local control and survival in certain histologies candidates to CIRT (Figure 2).

**CONCLUSIONS**

Patients with naïve or recurrent advanced HNC with CAE may still have a chance to be cured if treated with modern surgical and RT techniques. In particular, this should be taken into account in young patients with a relatively indolent disease, who may potentially have a relatively long life expectancy. In this clinical scenario, a careful evaluation of the available management strategies to secure CA should be put in place to achieve the best oncological results while minimizing the risk of

**FIGURE 2** | Locally recurrent nasopharyngeal squamous cell carcinoma diagnosed 5 years after the initial diagnosis (cT3N1). (A) Axial T1-weighted, fat-saturated, contrast-enhanced image shows the recurrence (red line) extending through the left foramen rotundum and vidian canal and involving the foramen ovale and cavernous sinus. Left cavernous internal carotid artery (ICA) is encased by the tumor. (B) Axial CT simulation image showing the tumor (red line) and the left ICA occluded with endovascular coils following a well-tolerated temporary balloon occlusion test. (C, D) CT axial and coronal images showing the tumor and the cumulative dose distribution according to the primary photon RT plan and the definitive re-irradiation through intensity-modulated proton therapy (54 GyE). Isodose levels are represented by different colors.
cerebrovascular and non-cerebrovascular sequelae. Precise analysis of tumor extension, adequate treatment planning, and proper counseling should save patients an ineffective invasive treatment, such as an unintentional R2 surgery, and the risk of dangerous and potentially life-threatening complications, such as CB. These prerequisites are best fulfilled in tertiary referral centers, where the multidisciplinary team can handle very advanced cancers with CAE by exploiting the available strategies and customizing treatment based on special characteristics of the single case. It is authors’ opinion that prospective studies are needed to objectively assess the risk-benefit ratio of CA securing strategies (e.g., stenting or occlusion) that are adopted to deliver the locoregional treatment of HNC with CAE.

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DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

Authors contributed as follows: conception (EO, MF, EL, LP, MBe, BV, MBo, VR, AS, LL, and PN). Perspective design (EO and MF). Paper draft (EO and MF). Draft correction (EL, LP, MBe, BV, VR, and AS). Supervision (LL and PN). All authors contributed to the article and approved the submitted version.
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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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