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RESEARCH ARTICLE

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# Salvage neck dissection for isolated neck recurrences in head and neck tumors: Intra and postoperative complications

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## Abstract

**Background and Objectives:** The current evidence regarding complications after salvage neck dissection (ND) for isolated regional recurrences (IRRs) in head and neck cancers is poor. The aim of this study is to evaluate the incidence and differences in complication rates of salvage ND after primary surgery, radiotherapy, chemoradiotherapy, or combined treatments.

**Methods:** This was a multicentric retrospective study on 64 patients who underwent salvage ND for IRR in three Italian institutes between 2008 and May 2020.

**Results:** Complications were detected in 7 of the 34 patients (20.8%) and surgeons described difficult dissection in 20 patients (58.82%). Accidental vascular ligations or nervous injury during surgery were never detected. None of the variables analyzed were statistically significant in predicting the risk of complications, disease-free survival, or overall survival.

**Conclusions:** IRR represents a rare entity among total relapses. The incidence of complications after salvage ND for IRR is higher than after primary surgery but at an acceptable rate in experienced hands. However, an adequate balance between functional and oncological outcomes is mandatory.

KEYWORDS

head and neck tumors, isolated neck recurrence, salvage neck dissection, salvage surgery, surgical complications

## 1 | INTRODUCTION

Neck dissection (ND) represents a potentially life-threatening procedure in head and neck surgery; however, careful and thorough anatomic knowledge, as well as surgical experience and expertise, ensure that complication rates remain reasonably low.[1–5]

In recent years, radiotherapy (RT), whether or not associated with chemotherapy (CHT), is increasingly being used as the primary treatment for head and neck tumors, guaranteeing survival rates comparable to surgery alone and related to a better functional outcome in selected tumors.[6–11] On the other hand, in the case of regional or locoregional recurrence, previous RT/CHT treatments might increase salvage treatment-related complications.[12–14] In fact, previous studies[15–17] have largely demonstrated that radiotherapy and chemotherapy induce tissue reworking and increase local fibrosis which could make surgery

  

particularly complex by affecting the vascularization and healing capacity of the tissues.

Although complications brought about by salvage surgery after primary conservative laryngeal and pharyngeal cancer treatment have been studied in the literature,[18–20] evidence regarding the adverse events of salvage ND alone is currently poor. In our opinion, including patients with both regional and locoregional recurrence could lead to an overestimation of the complication rate for ND after RT/CHT since any adverse events are more attributable to surgery on the tumor site, rather than on cervical node recurrence.

In this setting, we have undertaken a multicentric retrospective study to analyze the complication rates after salvage ND for isolated regional recurrences (IRRs) in head and neck cancer patients. Our primary aim was to assess the differences, if any, between the incidence of complications after a salvage neck procedure following primary surgery with or without adjuvant treatment versus primary single modality RT or concurrent RT-CHT. Our secondary end point was to identify any factors affecting recurrence and survival.

## 2 | MATERIALS AND METHODS

We retrospectively analyzed all of the patients who underwent salvage ND for isolated neck recurrences in three different second-level Italian institutes (University Hospital in Verona, Careggi University Hospital in Florence, and University Hospital in Modena) between 2008 and May 2020.

This study was conducted in accordance with the current revision of the Declaration of Helsinki and with approval from the local Ethics Committee (registration number: 17798_oss).

The indications for salvage ND included the presence of IRR at preoperative evaluation without any other concomitant site of relapse, regardless of primary treatment performed (surgery and/or RT/CHT). Patients had been informed of the risks, alternatives, and goals of treatment, and they had provided informed consent before initiation of treatment.

Preoperative management included magnetic resonance imaging and/or computed tomography (CT), followed by positron-emission tomography (PET) and/or fine-needle aspiration. The decision regarding the best suitable therapy was made by the multidisciplinary tumor board of each institute.

Treatable patients received salvage ND (with or without postoperative re-irradiation) with curative intent for isolated neck recurrence of head and neck squamous cell carcinoma (HNSCC). All primary tumor subsites of HNSCC were included. Neck recurrences were confirmed at the final histological report. Exclusion from this study encompassed the following criteria: any concomitant locoregional or isolated local or distant recurrences; histology other than squamous cell carcinoma; patients who received extra-boost salvage RT; cervical recurrence of primary tumors other than head and neck; incomplete reports on recurrence stage and surgical salvage strategy such as onset time and type of postoperative complication; absence of histologically confirmed relapse; absence of consent to join the study.

Specific tumor and treatment characteristics were recorded, including: (1) patient preoperative assessment; (2) type and stage of primary and recurrent tumors; (3) surgical data (type of treatment, type of neck dissection performed, surgical time, and intraoperative details such as involvement of other structures, need for free flap reconstruction, presence of difficult dissection, accidental vascular or nervous injury); (4) length of hospital stay and postoperative complications (surgical and systemic complications, need for revision surgery, drainage tube volume and removal, nasogastric tube and tracheal cannula removal, hospital stay); (5) adjuvant postoperative treatments. In particular, comorbidity was recorded and classified according to the Charlson Comorbidity Index version validated for head and neck.[21]

### 2.1 | Statistical analysis

The following end points were considered: complication rate after salvage ND, including both surgical and systemic complications; post-recurrence overall survival (OS), defined as the time between the date of salvage surgery and the date of death/last visit; post-recurrence disease-free survival (DFS), defined as the time between the date of salvage surgery and the date of any recurrence/last visit.

The lymph node ratio (LNR) was calculated as the ratio of positive lymph nodes out of the total number of lymph nodes removed. Based on the median LNR value of 10.3, a LNR cut-off value of 10% was selected to stratify patients into roughly equal-sized groups.[22]

The influence of type of primary and recurrence treatment was estimated through the computation of OS and DFS curves using the Kaplan–Meier method and comparisons using the $\chi^2$ test. Univariate analysis regarding the most clinically relevant factors for re-recurrence and risk of death or development of complications was performed using the regression Probit test with 95% confidence intervals (CIs).

All of the tests were two-tailed, and $p$ values <.05 were considered to be statistically significant. Data were analyzed using Stata 14.0 software.

## 3 | RESULTS

### 3.1 | Study population

In total, 64 patients underwent salvage ND for suspected isolated neck recurrence of head and neck tumor at our institutes during the study period. Of these, 34 met our inclusion criteria, while the remaining cases were excluded because they had no histologically proven disease in the final histological report (9 cases) or presented histology other than squamous cell carcinoma (30 cases).

Our study population included 29 male and 5 female patients (M:F = 5.8:1) and the mean age at the diagnosis of single neck recurrent disease was 65.35 years (SD 9.001 ± 1.54; range 46–83 years); most patients reported current or previous smoking habits

**TABLE 1** Demographic, clinical, and treatment characteristics of primary tumor

| | No. of patients | % |
|---|---|---|
| Epidemiology and risk factor | | |
| Gender | | |
| M | 29 | 70.59 |
| F | 5 | 14.71 |
| Age | 68.0 (median); 65.35 (mean) (*SD* 9.00 ± 1.54) | |
| Charlson comorbidity index | | |
| 0 | 0 | 0.00 |
| 1–2 | 8 | 23.52 |
| 3–4 | 13 | 38.24 |
| ≥5 | 13 | 38.24 |
| Smoke | | |
| No smoker | 4 | 11.76 |
| Ex smoker | 20 | 58.82 |
| Current smoker | 6 | 17.64 |
| Not available | 4 | 11.76 |
| Primary tumor | | |
| Location | | |
| Oral cavity | 10 | 29.41 |
| Pharynx p16- | 11 | 32.35 |
| Pharynx p16+ | 5 | 14.71 |
| Larynx | 7 | 20.59 |
| Cervical esophagus | 1 | 2.94 |
| cT (27 patients) | | |
| cT1 | 4 | 14.81 |
| cT2 | 12 | 44.44 |
| cT3 | 4 | 14.81 |
| cT4 | 7 | 25.93 |
| cN (27 patients) | | |
| cN0 | 11 | 40.74 |
| cN1 | 5 | 18.52 |
| cN2 | 8 | 29.63 |
| cN3 | 3 | 11.11 |
| Primary treatment | | |
| Surgery | 6 | 17.65 |
| RT or RT/CHT | 16 | 47.06 |
| Surgery + adj RT/CHT | 12 | 35.29 |
| Type of neck dissection | | |
| No neck dissection | 19 | 55.88 |
| Ipsilateral ND | 7 | 20.59 |
| Bilateral ND | 8 | 23.53 |
| pN (15 patients) | | |
| pN0 | 6 | 40.00 |
| pN+ | 7 | 46.67 |
| Not available | 2 | 13.33 |
| ENE | | |
| ENE− | 15 | 100.00 |
| ENE+ | 0 | 0.00 |

Abbreviations: ENE, extranodal extension; ND, neck dissection.

(almost 76% of the total number of cases). Table 1 summarizes their demographic, clinical and treatment characteristics.

Regarding the primary tumor, the pharynx was the most frequently affected site (47.06%), followed by oral cavity (29.41%). There was a slightly higher percentage of T1 and T2 stages (14.81% and 44.44%, respectively), whereas advanced stages were less frequent (T3 and T4 in 14.81% and 25.93% of cases, respectively). In 40.74% of the cases, there was no evidence of lymph node metastasis at primary diagnosis.

Primary treatment included (1) surgery, (2) single modality RT or concurrent RT/CHT, or (3) surgery followed by adjuvant treatment in 17.65%, 47.06%, and 35.29% of cases, respectively. Primary neck dissection was performed in 44.12% of cases; all patients underwent selective neck dissection (either ipsilateral or bilateral). Both postoperative RT and single modality RT treatments included prophylactic neck irradiation.

## 3.2 | Salvage neck dissection

Ipsilateral regional recurrence was detected in 85.29% of cases whereas contralateral or bilateral relapse affected 14.71%. Preoperative staging detected single (58.82%) and multiple (38.25%) suspected cervical nodes. Even though 21 of 34 patients had only one metastatic lymphadenopathy (rcN1), 5 of them (23.8%) were classified clinically as extranodal extension (ENE) positive (rcN3), showing an advanced nodal stage despite single cervical recurrence. Overall, clinical staging of recurrent disease was recorded as follows: rcN1 (32.35%), rcN2 (41.18%), and rcN3 (17.65%).

A mean posttreatment interval of 17.82 ± 15.29 months (mean ± *SD*; range 2–60 months, median 13 months) for onset of IRRs was observed in our study population; 44.12% of the cases

experienced IRR within the first 2 years of follow-up. In particular, the mean time to relapse for rcN1, rcN2, and rcN3 stages was 15.90 months (*SD* 12.87 ± 4.07), 19.86 months (14.52 ± 3.88), and 11.83 months (*SD* 14.29 ± 5.83), respectively. As shown in Figure 1, 66.66% of rcN3 recurrences were observed within 6 months, compared to 16.66 at both 6–24 and >24 months; there were no rcN3 recurrences after 2 years. Figure 2 reports time distribution of recurrences based on pathological stage. The rpN3 stage was recorded in 8 of 13 early recurrences (72.72%) with a decreasing frequency over time; as opposite, rpN1/2 stages resulted more frequent at 24 months.

Table 2 summarizes the characteristics of the documented IRRs and the therapeutic procedures performed.

A total of 40 neck dissections were performed in the 34 patients, and among them, selective neck dissection was the most frequent procedure carried out (27 of 40, 67.5% of cases). Total parotidectomy with facial nerve preservation was associated with the main procedure in 2 patients (5.88%); 3 of 34 patients (8.82%) required free flap reconstruction due to skin cancer infiltration.

The histological reports confirmed rpN1, rpN2/2a, rpN2b, rpN2c, and rpN3/N3b in 26.47%, 17.65%, 0%, 8.82%, and 47.06% of cases, respectively. ENE was detected in 23 of 34 patients (67.65%). Four of 11 patients (36.36%) presenting preoperative rcN1 disease were up-staged at the final histological report because they presented microscopic ENE (2 rpN2a and 2 rpN3b) in the specimens. Moreover, 11 of 22 patients (47.83%) with a single suspected lymph node at preoperative imaging, were rpN3b at final histology. A lymph node ratio >10% was observed in 44.12% of cases: these patients often presented a single lymphadenopathy (80%) frequently associated with ENE (73.3%) or advanced rpN stage (33.33%); no evidence of difference in time to relapse was observed. Positive margins (R1) were detected in 4 of 34 patients, 3 of them in patients with a lymph node ratio >10%. According to histological findings, previous treatment, and patient's comorbidity, adjuvant therapy (RT ± CHT) was administered after salvage ND in 11.76% of cases.

### 3.3 | Surgical details and complications

Mean surgical time was 207.97 min (*SD* ±117.39, range 70–520 min). Details regarding the need to sacrifice vascular, neural, or muscular structures are presented in Table 3. In total, 18 of 34 patients (52.9%) underwent extensive dissections, based on preoperative tumor staging and intraoperative assessment of neighboring soft or vascular tissue infiltration. Among these patients, 72.2% were rpN3b (rpN2a, rpN2b/c and rpN1 in 11.1%, 5.5% and 11.1%, respectively) and 50% (9 of 18) presented a lymph node ratio >10%. Surgeons described difficult dissection in 20 of 34 patients (58.82%). Accidental damage to vascular structures or nerves during surgery was never detected. Excluding one patient with prolonged hospitalization (over two months) due to pharyngo-cutaneous fistula, mean length of hospital stay was 8.6 days (*SD* 10.40 ± 1.81; range 2–54 days). Two patients (5.88%) needed prolonged use (15.5 days, *SD* 2.12 ± 1.50) of the naso-gastric feeding tube and one patient (2.94%) underwent permanent gastrostomy for incoercible dysphagia; 8 patients (23.53%) required temporary tracheostomy: mean time to tracheal

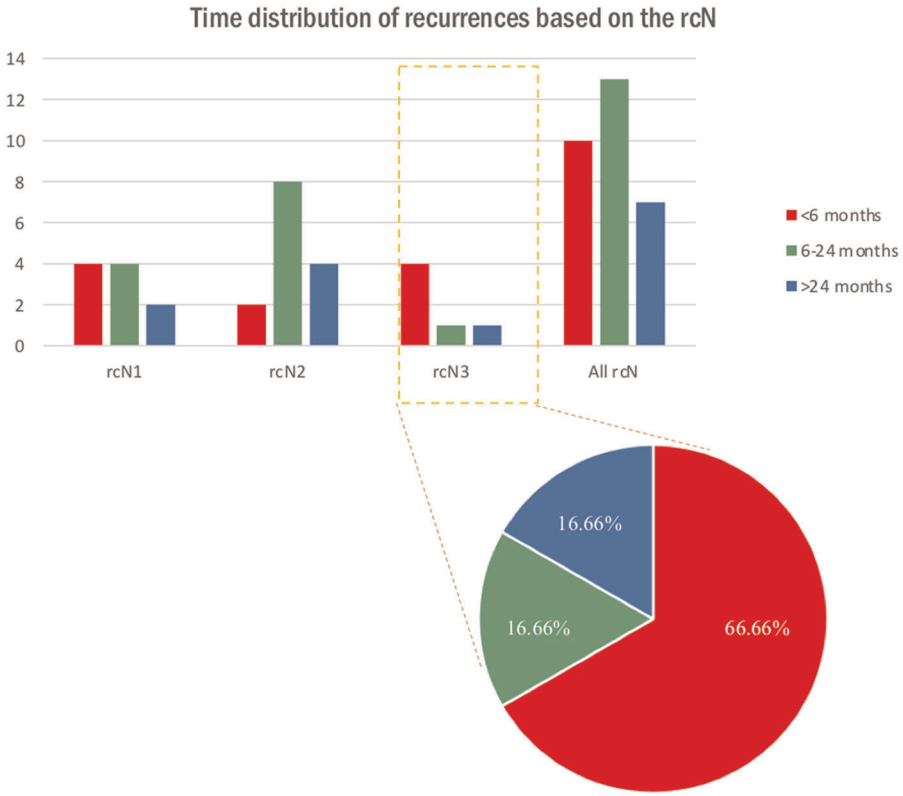


**FIGURE 1** Time distribution of IRR. Colored lines distinguish clinical stage of neck recurrence and pie-chart highlights the distribution of recurrences in the first 6 months [Color figure can be viewed at wileyonlinelibrary.com]

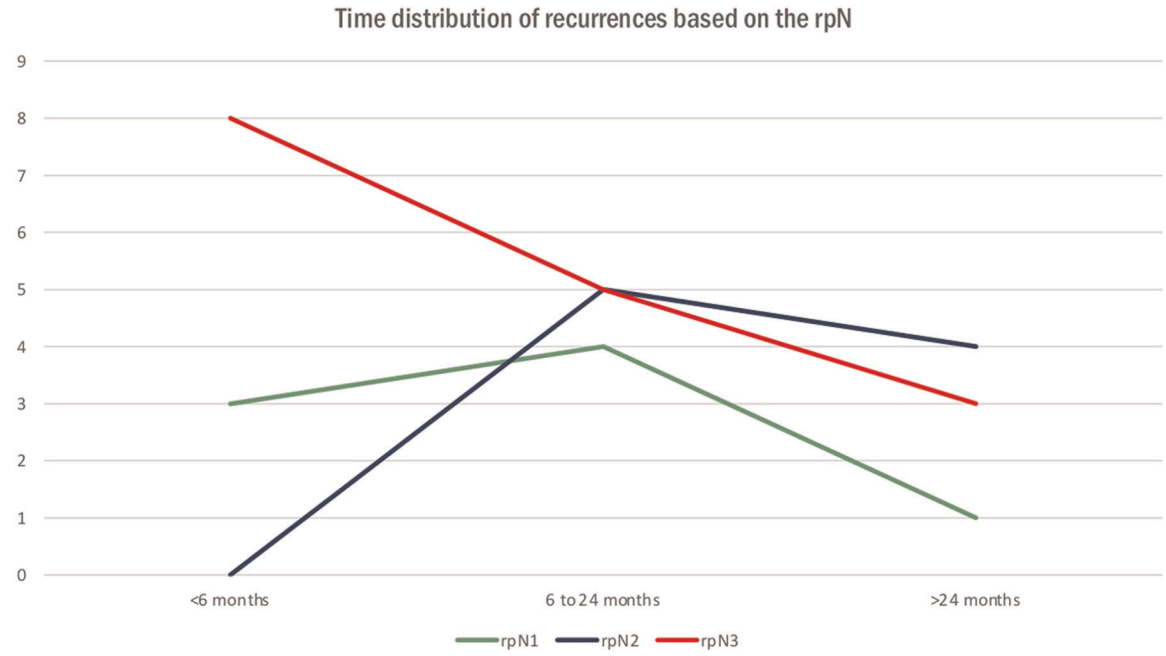


**FIGURE 2** Time distribution of IRR based on clinical stage at diagnosis of neck recurrence. Colored lines distinguish time to relapse [Color figure can be viewed at wileyonlinelibrary.com]

cannula removal was 16.43 days (*SD* 18.82 ± 7.1; range 5–54 days), while one patient had a permanent tracheostomy.

Perioperative complications were detected in 7 of 34 patients (20.58%). Table 4 summarizes the surgical and general complications observed. The most common postoperative complication was wound dehiscence (3 of 34 patients, 8.82%), followed by bleeding (2 of 34 patients, 5.88%). Only 1 of 34 patients (2.94%) required surgical revision: this patient experienced free flap necrosis and underwent regional flap (PMF) reconstruction. Systemic complications were observed in only one patient.

Univariate analysis was performed to determine whether there was a possible relationship between the most relevant preoperative clinical and surgical factors and the occurrence of adverse events, but none of the variables analyzed statistically significantly predicted the risk of perioperative complications. In particular, primary treatment did not affect the complication rate, and previous radiotherapy or chemotherapy, both as curative or adjuvant treatment, was not related to a higher risk of adverse events ($p = .150$ in the case of RT or RT/CHT and $p = .232$ in the case of surgery + RT/CHT).

### 3.4 | Oncological outcomes

Mean follow-up time after salvage treatment was 21 months (*SD* 22.46 ± 2.54; range 1–88 months; median 13 months). In total, 21 of 34 patients (61.76%) were alive and free from disease at the end of follow-up; 16 patients experienced locoregional or distant re-recurrences after salvage treatment (47.06%), local and distant re-recurrence being the most frequently observed. The distribution of relapses is shown in Figure 3.

Thirteen (38.24%) died, 10 of them from tumor-related events and 3 from other causes. Regarding survival, 1-year DFS and OS were 71.22% and 83.07%, respectively, and 2-year DFS and OS were 45.22% and 54.07%, respectively. Salvage treatment did not seem to have an impact on DFS (Figure 4), and primary type of treatment did not appear to significantly affect OS (Figure 5).

Nevertheless, it is important to note that all of the patients who underwent salvage surgery plus adjuvant treatment were alive at the end of follow-up.

Finally, we performed univariate analysis to detect possible factors related to re-recurrence and survival. None of the variables were statistically significantly related to survival; in particular, side of recurrence, type of salvage treatment, presence of rENE, number of pathological nodes, lymph node ratio, and rpN stage were not related to DFS. Similarly, none of the factors significantly affected OS.

## 4 | DISCUSSION

IRRs of head and neck malignancies are quite unusual, representing only 5.2% of all relapses; nevertheless, IRRs are associated with better survival compared to single local, or concomitant locoregional recurrences, as well as the onset of distant metastases.[23]

Predictive factors for IRRs are actually unknown. Our aim was first to highlight their characteristics of presentation in our multicentric study population; second, to outline their treatment and oncologic outcomes, with the final purpose to lay the foundation for definition of their onset and predictive factors.

**TABLE 2** Clinical and histological characteristics of IRRs and their treatment

| | No. of patients | % |
|---|---|---|
| Recurrent tumor | | |
| Time to relapse | | |
| <6 months | 10 | 29.41 |
| 6–24 months | 15 | 44.12 |
| >24 months | 8 | 23.53 |
| Not available | 1 | 2.94 |
| Side | | |
| Ipsilateral nodes | 29 | 85.29 |
| Contralateral/bilateral nodes | 5 | 14.71 |
| rcN | | |
| rcN1 | 11 | 32.35 |
| rcN2 | 14 | 41.18 |
| rcN3 | 6 | 17.65 |
| Not available | 3 | 8.82 |
| Salvage treatment | | |
| Type of salvage therapy | | |
| Surgery alone | 30 | 88.24 |
| Surgery + adj RT/CHT | 4 | 11.76 |
| Ipsilateral ND | | |
| No ND | 3 | 8.82 |
| SND | 20 | 58.82 |
| mRND | 4 | 11.76 |
| RND | 7 | 20.59 |
| Contralateral ND | | |
| No ND | 25 | 73.53 |
| SND | 7 | 20.59 |
| mRND | 1 | 2.94 |
| RND | 1 | 2.94 |
| Histological characteristics | | |
| No. pN+ | | |
| 1 node | 22 | 64.71 |
| 2–5 nodes | 9 | 26.47 |
| >5 nodes | 3 | 8.82 |
| Lymph node ratio | | |
| <10% | 17 | 50.00 |
| >10% | 16 | 47.06 |
| Not available | 1 | 2.94 |
| rENE | | |
| ENE− | 11 | 32.35 |
| ENE+ | 23 | 67.65 |
| N + level | | |
| I–III | 23 | 67.65 |
| IV–V | 11 | 32.35 |
| rpN | | |
| rpN1 | 9 | 26.47 |
| rpN2a/2 | 6 | 17.65 |
| rpN2b | 0 | 0.00 |
| rpN2c | 3 | 8.82 |
| rpN3/3b | 16 | 47.06 |
| Surgical margins | | |
| R0 | 30 | 88.24 |
| R+ | 4 | 11.76 |

*Note:* R0, resection margin free to disease; R+, positive resection margin (both macro or microscopical tumor residue detect at resection margin).

We recorded a prevalence of advanced pathological recurrent nodal stages (47.06% of rpN3, followed by 26.47% of rpN1), despite the reasonably high percentage of primary early stages at both T (cT1/T2 stage in 59.25%, comprehensively) and N (40.74% of cN0) status. Moreover, even though a single suspected lymph node was detected at the preoperative evaluation in 20 of 34 patients (58.82%), 16 of them presented extranodal extension at the final histology, with a global under-staging bias of 80%. Furthermore, the time distribution of relapses showed that recurrences were more frequent within the first 2 years of clinical follow-up after the primary treatment and they showed an unequal distribution of their nodal stage: in the first 6 months, advanced nodal disease was more common with a prevalence of rpN3 stage (8 of 11 early recurrences, 72.72%) while lower stages were rarely observed (rcN1/2 accounted for 27.27% of early relapses). The rate of rpN3 decreased over time; on the other hand, the early nodal stage was rare in the first 6 months and more frequently observed thereafter.

Our results are in accordance with the recent literature.[24–26] Giger et al.[25] reported advanced rcN stage in up to 60% of isolated neck recurrences, despite there being 56.6% of cN0 detection at the primary tumor diagnosis; a mean interval of 18.1 months was observed between initial tumor treatment and histological/cytological diagnosis of the IRR. Similarly, Léon et al.[24] previously recorded rcN2/3 in 97 of 123 IRRs (78.86%) with 66.7% of ENE+, even though no regional involvement of primary tumor was detected in 60.98% of cases; moreover, those authors did not find any relationship between the presence of nodes with extracapsular spread and the local or regional extension of the primary tumor, the initial therapy, or time to regional recurrence on multivariate analysis.

**TABLE 3** Intraoperative details regarding vascular, nerve and soft-tissue sacrifice

| Vascular ligation | | Nerve resection | | Muscolar resection | |
|---|---|---|---|---|---|
| **Total patients** | **15/34 (44.12%)** | **Total patients** | **8/34 patients (23.53%)** | **Total patients** | **12/34 (35.94%)** |
| Multiple vascular ligation | 2/15 (13.33%) | Multiple nerve resections | 5/8 (62.50%) | Multiple muscular resection | 0 (0%) |
| IJV | 14 | VII n.c | 0 | SCM muscle | 9 |
| ECA | 3 | X n.c. | 3 | Other | 3 |
| ICA | 0 | XI n.c. | 7 | | |
| | | XII n.c. | 2 | | |
| | | Frenic nerve | 1 | | |

Abbreviations: ECA, external carotid artery; ICA, internal carotid artery; IGV, internal jugular vein; SCM muscle, sternocleidomastoid muscle.

**TABLE 4** Postoperative complication in salvage neck dissection for IRR

| | No. of patients |
|---|---|
| Surgical complications | |
| Total surgical complications | 7/34 (20.59%) |
| Bleeding | 2 |
| Dehiscence | 3 |
| Vocal cord palsy | 1 |
| Flap necrosis | 1 |
| General complications | |
| Total general complications | 1/34 (pneumonia) |
| Surgical revision | |
| No | 6/7 (85.71%) |
| Yes | 1/7 (14.29%) |

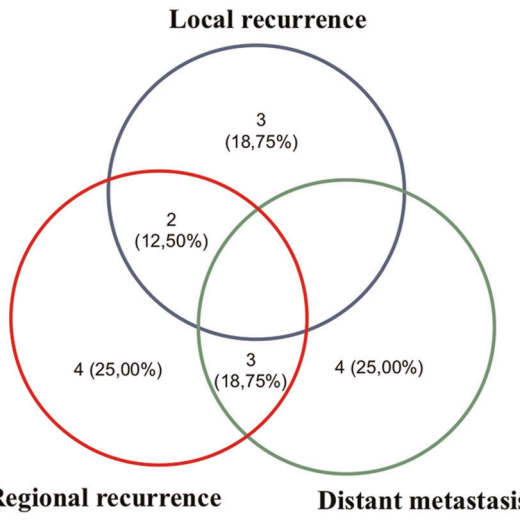


**FIGURE 3** Distribution of site to re-relapse after salvage surgery for isolated regional recurrence (IRR) [Color figure can be viewed at wileyonlinelibrary.com]

Although primary stage has not been investigated in the literature as a predictive factor for timing of onset of isolated neck recurrences, based on our experience, we would like to recommend careful follow-up during the first 6 months after primary treatment to promptly recognize advanced recurrences. Moreover, it would be of the utmost importance to identify predictive factors for advanced recurrences of primary tumors to effectively contain relapses, largely represented by the rN3 stages, in the first 6 months. Furthermore, diagnosis of early recurrent disease could also represent an undoubted advantage in the treatment and outcome of limited relapses.

Despite the advanced nodal stage at presentation, surgery represents the gold standard for treatment in these patients, eventually followed by adjuvant therapy.[6,23,25,27–32] However, salvage ND could be challenging and potentially dangerous in pretreated neck because of the structural changes in tissues undergoing radio(chemo) therapy and/or surgery.

In particular, dose-dependent soft-tissue hypoxia and impaired leucocyte migration in previously irradiated patients seem to play an important role in delayed wound healing and, consequently, in the development of deep infection and prolonged hospitalization.[3,15] Furthermore, several conditions related to previous surgery or RT including local pain, dysgeusia, xerostomia, dysphagia, inappetence, as well as alcohol consumption, may lead to malnutrition, which is an additional independent risk factor for wound healing and related complications.[16] Moreover, RT-induced fibrosis was recently observed in 58% of patients at 1-year follow-up together with a linearly increasing development of this disorder up to 8 years afterward.[17] Radiation-related or postsurgical fibrosis may potentially lead to nervous injury or dysfunction through unintended lesions from difficult anatomic localization or devascularization during neck dissection.[4]

In our study, complications after salvage ND for IRRs were observed in 23.52% of patients, 87.5% of them (20.59% of all cases) were local and only 1 of 34 patients (2.94%) experienced systemic complications. The most frequent postoperative complication was wound dehiscence (42.86%), followed by postsurgical bleeding (28.57%), while other events were rarely encountered; most were managed conservatively. In 52.9% of patients, a planned resection of nerves and/or vessels and/or muscles was performed; up to 70% of

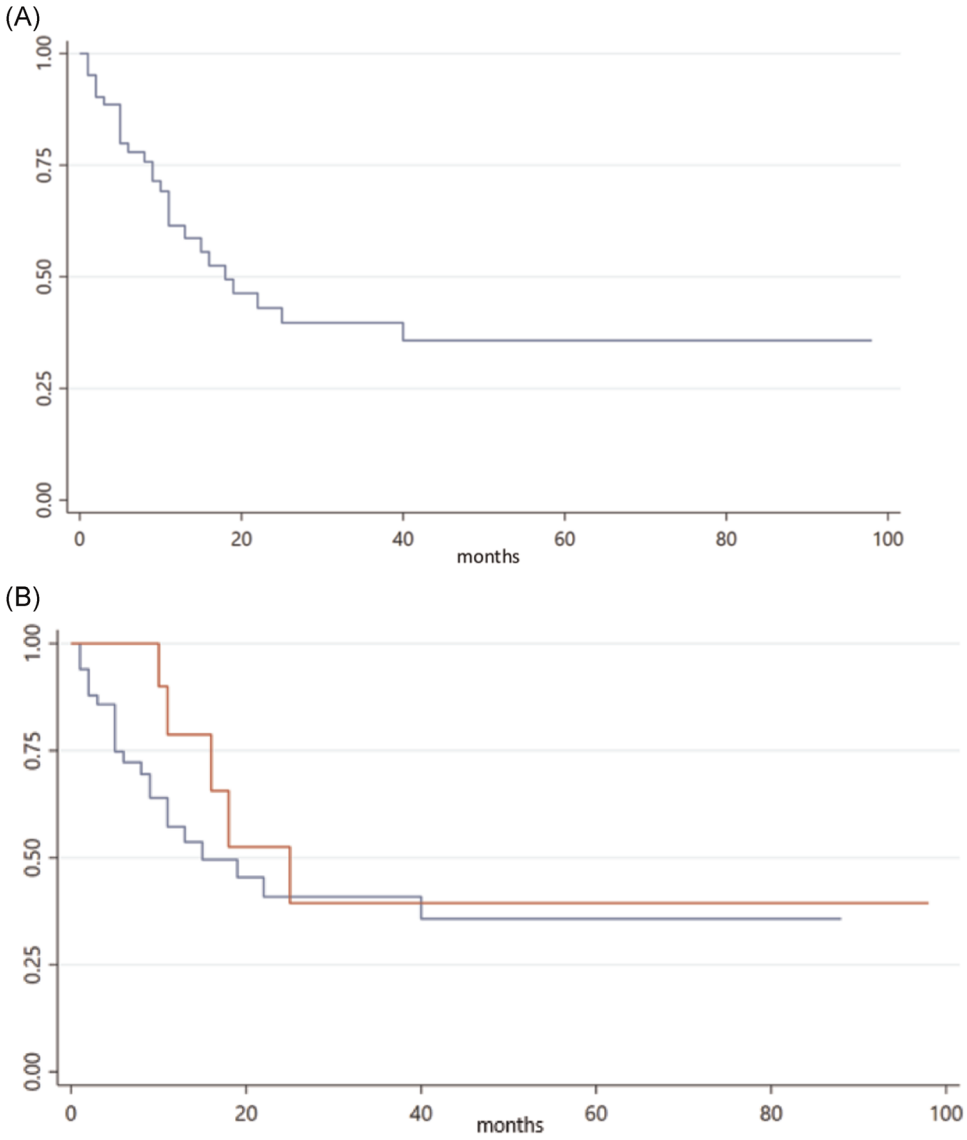


**FIGURE 4** (A) Disease-free survival in all patients. (B) Disease-free survival in salvage neck dissection alone (blue) and surgery + adjuvant RT/CHT (red) [Color figure can be viewed at wileyonlinelibrary.com]

them were rpN3b, and 50% presented a lymph node ratio >10%. In addition, in our series, rN3 stage did not show a statistically significant association with an increased risk of postoperative complications or a poorer oncological outcome.

Although, to the best of our knowledge, only a few studies have reported complications in salvage ND for IRRs, our results were in line with those of previous authors.[26,33,34] Chung et al.[26] detected an overall postoperative complication rate of 20%, where wound infection was the most frequently occurring event; moreover, perioperative mortality occurred in 2 of 55 patients (3.6%) due to sepsis. According to our results, a high rate of extensive dissections was observed, leading to nerve resection and vascular sacrifice in 23.53% and 44.12% of patients, respectively. Moreover, considering the involvement of neighboring structures, the frequency of dissection of glandular structures in our series resulted comparable to previous studies (5.88% vs. 3.64%, according to Chung et al.). These results confirmed the need for adequate preoperative counseling to properly inform patients about possible postsurgical functional impairments; nevertheless, experienced and skilled surgeons with a high-volume workload have to be preferred in salvage surgery for IRRs due to the frequent involvement of vascular and nervous structures by advanced-stage cervical disease.

According to the previous literature, our analysis did not show a statistically significant difference in complication rate between patients who had primary RT/CT ± surgery compared to surgery alone. On the other hand, van den Bovenkamp et al.[34] recognized the extent of neck dissection as an independent predictor of surgical complications in salvage surgery for IRRs ($p = .010$), even though, in our opinion, their results need to be confirmed by further studies including multicentric investigations.

None of the previous reports studying salvage surgical treatment for isolated neck recurrences reported the incidence of

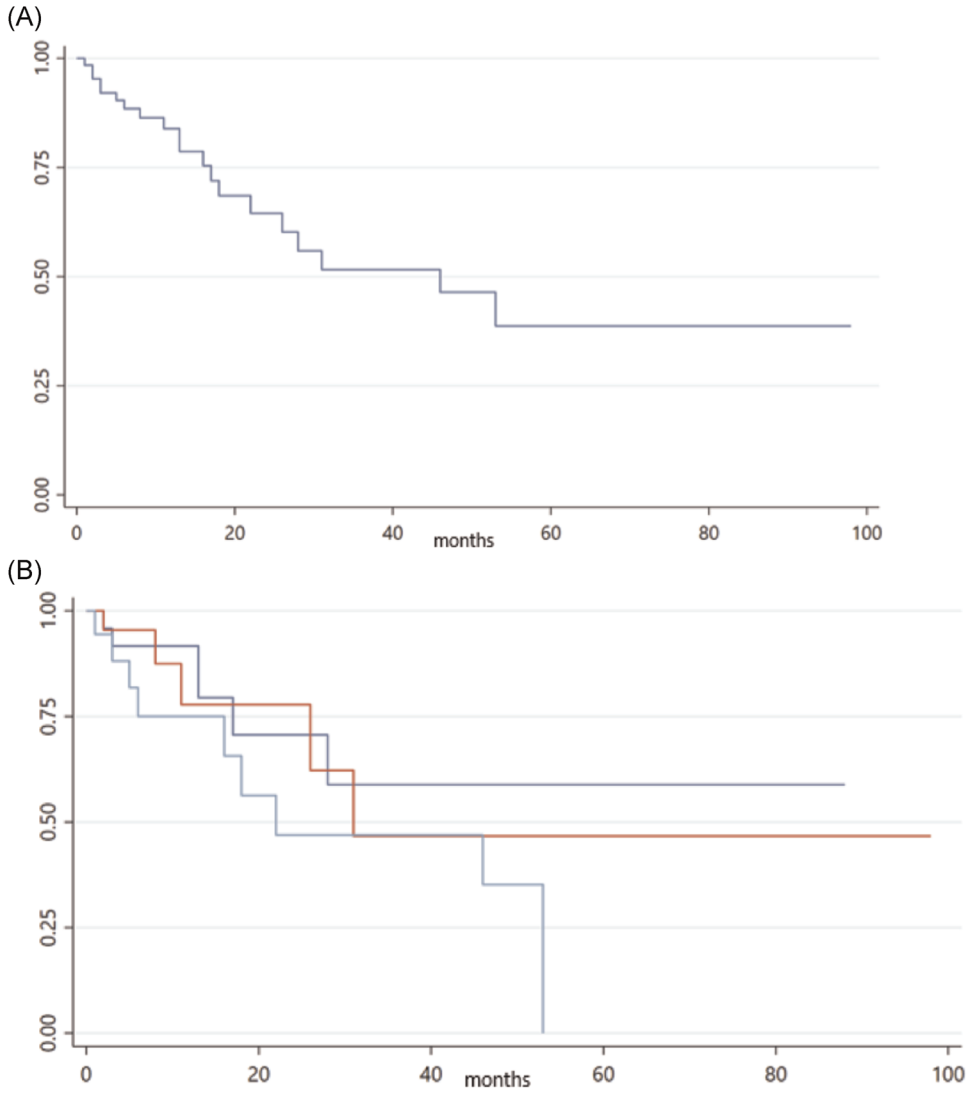


**FIGURE 5** (A) Overall survival in all patients. (B) Overall survival depending on primary treatment [Color figure can be viewed at wileyonlinelibrary.com]

accidental nerve or vascular injuries. Despite the high rate of planned nerve resection for malignant infiltration (23.53% of cases), accidental damage to vascular structures or nerves during surgery was never detected. This result should be analyzed with caution, given the small sample size; however, in agreement with our experience, Prim et al. reported 1.68% of intraoperative spinal accessory nerve lesion in a court of 442 patients underwent neck dissection for laryngeal/hypopharyngeal tumor. Nevertheless, we strongly recommended a careful dissection because of the difficult location and isolation of vascular and nervous structures within fibrotic tissue, confirmed by the fact that difficult resection was frequently reported by surgeons (58.82%).

Comparing the onset of complications after salvage ND in the case of regional recurrence to salvage surgery performed for local or locoregional relapses, we easily observed an increased risk in the latter in agreement with the literature.[19,20] Salvage surgery after both primary surgery plus adjuvant treatment, and radiotherapy plus bioradiotherapy showed comparable evidence to salvage surgery after primary RT ± CHT.[35,36]

Finally, in comparison to previous studies on survival in salvage ND in HNSCC patients, our study showed a slightly poorer outcome with a lower OS and DFS (3-year and 5-year OS and DFS of 47.31%, 27.04% and 45.22%, 38.76%, respectively).[23–26,32,37,38] This difference might be due to the high rate of LNR > 10% (47.06%) recorded in our series; this agrees with Ding et al.[22] who indicated that the LNR was the most important prognostic factor for OS and DFS in salvage treatment HNSCC patients, having a significant relationship with advanced stage of recurrent disease.

The pitfalls of our study mainly include its retrospective nature and the limited number of patients enrolled, in addition to the involvement of three institutes. This might be explained by the relativity low incidence of IRR even in high-volume oncologic centers. Other potential biases are represented by the short follow-up period (21 months; *SD* 22.46 ± 2.54), low rate of primary neck dissections in

the surgical group, and incomplete data regarding type and dose of radiotherapy and chemotherapy when performed.

On the other hand, the major strengths of our study are the extensive and accurate description of surgical details, complications, and hospital stay records. Moreover, according to recent evidence, we only included neck recurrences staged by PET–CT and confirmed by histopathological report, whereas previous studies included rcN0 patients and suspect relapses investigated only by chest X-ray and CT.

## 5 | CONCLUSIONS

To the best of our knowledge, this is the first study that reports a complete analysis of surgical complications in IRR management, these complications representing a rare entity among total relapses. We believe that an adequate consideration of the balance between functional costs and oncological outcomes is mandatory in these patients. The incidence of complications after salvage ND for IRR is higher than for primary surgery but at an acceptable rate in experienced hands.

Nevertheless, our experience provides only preliminary results and further studies, based on larger databases with longer follow-up, are needed to confirm our findings.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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