CHAPTER 8

Paratracheal lymph node dissection during laryngectomy after previous (chemo)radiotherapy: a retrospective analysis of complications and histopathological results

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ABSTRACT

Objectives: To evaluate complications and histopathological results of paratracheal lymph node dissection (PTLND) at laryngectomy after (chemo)radiotherapy.

Design, setting and participants: In a retrospective analysis, complications and histopathological results of paratracheal lymph node dissections were analysed in 191 patients with a recurrent or second primary laryngeal or hypopharyngeal carcinoma following radiotherapy with or without chemotherapy.

Main outcome measures: The percentage of complications in patients with bilateral, unilateral or without PTLND.

Results: Forty-seven patients underwent laryngectomy with bilateral paratracheal lymph node dissection, 52 with unilateral and 92 without paratracheal lymph node dissection. Although the difference in total complications was not significant, significantly more fistulae developed in patients with bilateral paratracheal lymph node dissection (40% versus 22%; P = 0.016). In multivariate analysis, this difference maintained significant (P = 0.038). Pathological examination of the lymph node dissection specimen showed tumour in 3 of the 96 ipsilateral dissections (3%) and in 1 of the 50 contralateral dissections (2%). This suggests that if unilateral instead of a bilateral paratracheal lymph node dissection had been performed, 17% less fistulae would have occurred in this group of patients, while paratracheal lymph node (PTLN) metastases would have been missed in one patient. Three of four patients with paratracheal lymph node metastases had glottic carcinoma, all with subglottic extension.

Conclusion: Because of the low incidence of lymph node metastases and the increased risk of fistulae, there is a need for a strict selection of patients who need a bilateral paratracheal lymph node dissection at laryngectomy after previous (chemo)radiotherapy.
INTRODUCTION

The reported incidence of paratracheal lymph node (PTLN) metastases in (mainly previously untreated) patients with total laryngectomy ranges from 9% to 20% (1-5). The indications for and extent of paratracheal lymph node dissections (PTLND) are not well defined and mainly depend on the surgeon’s preference. Previous studies identified the presence of PTLN metastases as a significant prognostic factor for worse survival (1,6,7). Plaat et al. (2) found that PTLN metastases with extranodal spread was associated with poorer overall survival. Paratracheal lymph node dissection was shown to significantly adversely affect disease-free survival as an independent factor (8). Also, metastatic disease involving the PTLN has been seen in recurrent disease, particularly peristomal recurrence (9,10), suggesting the likely prognostic significance of positive paratracheal metastatic spread (5). Because the role of PTLND is not clear, the risks associated with this procedure should also be considered. To our knowledge, the relation between laryngectomy with PTLND and complications has not been evaluated before. It is known that salvage laryngectomy, compared to laryngectomy in previously untreated patients, carries a high risk of postoperative (local) complications (11,12).

The goal of this study was to retrospectively evaluate the incidence of complications in a group of patients with laryngectomy after previous (chemo)radiotherapy with no, unilateral or bilateral PTLND.
Chapter 8

PATIENTS AND METHODS

From November 1990 to June 2007, 191 patients underwent laryngectomy after previous (chemo) radiotherapy for a laryngeal or hypopharyngeal carcinoma at the VU University Medical Center in Amsterdam. Forty-seven patients underwent laryngectomy with bilateral PTLND, 52 patients with unilateral PTLND and 92 patients without PTLND (Fig. 1).

Laryngectomy was performed for residual disease (≤3 months after radiotherapy) in 15 patients, recurrent disease (>3 months after radiotherapy) in 143 patients and primary tumour in 33 patients. The median detection time from the last radiation was 9.6 months (range 1.1–347.9 months). Patients were followed for recurrent disease after laryngectomy for a median of 29 months (range 0.5–177.7 months).

![Flow diagram of patients and paratracheal lymph node dissections (PTLND).](image)

Table 1 gives the details of patient, tumour and previous treatment characteristics. Serious medical comorbidity (ASA > 2) was present in 37% of the patients. The majority reported use of alcohol and tobacco at the time of laryngectomy. For staging the pre-treatment, TNM classification was used. Overall, 74% of patients were irradiated for T1 or T2 tumours; 14% of patients had a clinically positive neck (cN+). While the vast majority of patients with laryngeal carcinoma had early-stage disease, patients with hypopharyngeal cancer were staged T3–T4 in 54% and N+ in 46%.
Twenty-one patients underwent accelerated radiotherapy, and one underwent hyperfractionated radiotherapy. The median dose of definitive radiotherapy was 68 Gy, ranging from 51 to 74.4 Gy. Most patients were irradiated with a daily fraction dose of 2 Gy (range 1.8–4 Gy). Table 2 gives details of the surgery performed during salvage laryngectomy. Most patients underwent total laryngectomy (82%) with partial pharyngectomy (93%) and hemithyroidectomy (67%), in 18% of the patients combined with flap reconstruction.

If a PTLND was performed, this involved dissection of the lymph nodes between the trachea and the carotid artery from the cricoid to thoracic inlet. Landmarks of the distal margins along the paratracheal gutter were the superior mediastinum as far inferiorly as possible, through the cervical approach. The surgical rationale for performing this procedure was based on the personal preference and judgement of the head and neck surgeon, because guidelines for PTLND were not available during the study period.

Complications were retrospectively assessed and categorised. All complications in the operation area were defined as local complications: with and without re-intervention. Local complications were subdivided into pharyngocutaneous fistulae, haemorrhage, wound dehiscence (without infection or fistula) and wound infection (without fistula).

**Statistics**

Statistical difference between two independent groups was calculated by the chi-square test. The trend test was used where appropriate. Variables put in univariate analyses are listed in Table 3. Variables excluded from multivariate analyses were not significant in univariate analyses. To investigate confounding, multivariate analyses were conducted. For this, logistic regression was used in two steps: in the first step, only the variable of interest was entered in the model. In a second step, a potentially confounding variable was added to the model. Subsequently, the relative change in the coefficient of the variable of interest was assessed. An increase or decrease of 10% was used to determine confounding. Variables put in multivariate analyses are listed in Table 5. Statistical analyses were carried out using spss 15.0 (Statistical Package for the Social Sciences; IBM, Somers, NY, USA).
Table 1. Patient, tumour and previous tumour stage and treatment characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients (n = 191) (%)</th>
<th>No PTLND (n = 92) (%)</th>
<th>Unilateral PTLND (n = 52) (%)</th>
<th>Bilateral PTLND (n = 47) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>167 (87)</td>
<td>84 (91)</td>
<td>43 (83)</td>
<td>40 (85)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (13)</td>
<td>8 (9)</td>
<td>9 (17)</td>
<td>7 (15)</td>
</tr>
<tr>
<td>Smoking (at the time of laryngectomy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>125 (65)</td>
<td>60 (65)</td>
<td>35 (67)</td>
<td>30 (64)</td>
</tr>
<tr>
<td>Yes</td>
<td>66 (35)</td>
<td>32 (35)</td>
<td>17 (33)</td>
<td>17 (36)</td>
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<td>Alcohol (at the time of laryngectomy)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>61 (32)</td>
<td>25 (27)</td>
<td>22 (42)</td>
<td>14 (32)</td>
</tr>
<tr>
<td>Yes</td>
<td>130 (68)</td>
<td>67 (73)</td>
<td>30 (58)</td>
<td>33 (68)</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>121 (63)</td>
<td>58 (63)</td>
<td>34 (65)</td>
<td>29 (62)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>70 (37)</td>
<td>34 (37)</td>
<td>18 (35)</td>
<td>18 (38)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>13 (7)</td>
<td>3 (3)</td>
<td>5 (10)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Supraglottic</td>
<td>51 (26)</td>
<td>25 (27)</td>
<td>16 (31)</td>
<td>10 (21)</td>
</tr>
<tr>
<td>Glottic</td>
<td>126 (66)</td>
<td>64 (70)</td>
<td>31 (59)</td>
<td>31 (66)</td>
</tr>
<tr>
<td>Subglottic</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
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<tr>
<td>Initial T-stage (at the time of radiotherapy)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>62 (33)</td>
<td>40 (43)</td>
<td>13 (25)</td>
<td>9 (19)</td>
</tr>
<tr>
<td>T2</td>
<td>78 (41)</td>
<td>34 (37)</td>
<td>23 (44)</td>
<td>21 (45)</td>
</tr>
<tr>
<td>T3</td>
<td>31 (16)</td>
<td>12 (13)</td>
<td>12 (23)</td>
<td>7 (15)</td>
</tr>
<tr>
<td>T4</td>
<td>20 (11)</td>
<td>6 (7)</td>
<td>4 (8)</td>
<td>10 (21)</td>
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<tr>
<td>Initial N-stage (at the time of radiotherapy)</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>N0</td>
<td>165 (86)</td>
<td>81 (88)</td>
<td>48 (92)</td>
<td>36 (77)</td>
</tr>
<tr>
<td>N1</td>
<td>17 (9)</td>
<td>5 (6)</td>
<td>3 (6)</td>
<td>9 (19)</td>
</tr>
<tr>
<td>N2a</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>N2b</td>
<td>3 (2)</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>N2c</td>
<td>5 (3)</td>
<td>4 (4)</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>N3</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Prior treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Radiotherapy</td>
<td>182 (95)</td>
<td>88 (96)</td>
<td>52 (100)</td>
<td>42 (89)</td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>9 (5)</td>
<td>4 (4)</td>
<td>0 (0)</td>
<td>5 (11)</td>
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Table 2. Details of surgical procedure during salvage laryngectomy

<table>
<thead>
<tr>
<th>Feature</th>
<th>All patients (n = 191) (%)</th>
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<tr>
<td>Laryngectomy</td>
<td></td>
</tr>
<tr>
<td>Partial laryngectomy</td>
<td>35 (18)</td>
</tr>
<tr>
<td>Total laryngectomy</td>
<td>156 (82)</td>
</tr>
<tr>
<td>Pharyngectomy</td>
<td></td>
</tr>
<tr>
<td>Partial pharyngectomy</td>
<td>177 (93)</td>
</tr>
<tr>
<td>Total pharyngectomy</td>
<td>14 (7)</td>
</tr>
<tr>
<td>Thyroidectomy</td>
<td></td>
</tr>
<tr>
<td>No thyroidectomy</td>
<td>46 (24)</td>
</tr>
<tr>
<td>Partial thyroidectomy</td>
<td>127 (67)</td>
</tr>
<tr>
<td>Total thyroidectomy</td>
<td>18 (9)</td>
</tr>
<tr>
<td>Neck dissection</td>
<td></td>
</tr>
<tr>
<td>No neck dissection</td>
<td>92 (48)</td>
</tr>
<tr>
<td>Unilateral neck dissection</td>
<td>53 (28)</td>
</tr>
<tr>
<td>Bilateral neck dissection</td>
<td>46 (24)</td>
</tr>
<tr>
<td>Flap reconstruction</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>156 (82)</td>
</tr>
<tr>
<td>Yes</td>
<td>35 (18)</td>
</tr>
</tbody>
</table>

RESULTS

One hundred and eleven patients (58%) developed 137 complications after laryngectomy. Local complications were pharyngocutaneous fistulae (n = 51; 27%), haemorrhage (n = 11; 6%), wound dehiscence (n = 9; 5%) and wound infection (n = 5; 3%).

Univariate analyses (Table 3) showed significantly more local complications in case of women, smoking, no alcohol, primary tumour on other location than glottis, advanced T-stage, N+ neck, high radiotherapy total and fraction dose, total laryngectomy and pharyngectomy and bilateral lymph node dissection. More pharyngocutaneous fistulas were seen in case of smoking, primary tumour on other location than glottis, N+ neck, high radiotherapy total and fraction dose, and bilateral lymph node dissection. There were more wound infections in patients with the age below the median 63 years. Univariate analyses showed more haemorrhage in women, advanced T-stage, chemoradiotherapy and bilateral lymph node dissection. Univariate analyses showed no significant difference in complications between patients with radiotherapy and patients with chemoradiotherapy.

The occurrence of overall complications was not significantly different in the groups of patients with unilateral or bilateral PTLND and the group of patients without PTLND (Table 4). A significant difference in local complications was found between the three subgroups (P = 0.05), mainly caused
Table 3. Univariate analyses of complications after laryngectomy. Variables in the box with significant P-values are the factors with more complications

<table>
<thead>
<tr>
<th>Variable</th>
<th>Local complications (P-value)</th>
<th>Pharyngocutaneous fistulae (P-value)</th>
<th>Wound dehiscence (P-value)</th>
<th>Wound infection (P-value)</th>
<th>Haemorrhage (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.02 (female)</td>
<td>0.20</td>
<td>0.89</td>
<td>0.61</td>
<td>0.01 (female)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.02 (smoking)</td>
<td>0.01 (smoking)</td>
<td>0.94</td>
<td>0.23</td>
<td>0.43</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.04 (no alcohol)</td>
<td>0.10</td>
<td>0.41</td>
<td>0.56</td>
<td>0.31</td>
</tr>
<tr>
<td>Glottic</td>
<td>0.03 (other location)</td>
<td>0.01 (other location)</td>
<td>0.44</td>
<td>0.50</td>
<td>0.87</td>
</tr>
<tr>
<td>T-stage</td>
<td>0.03 (advanced)</td>
<td>0.19</td>
<td>0.88</td>
<td>0.56</td>
<td>0.02 (advanced)</td>
</tr>
<tr>
<td>N-stage</td>
<td>0.02 (N+)</td>
<td>0.04 (N+)</td>
<td>0.22</td>
<td>0.37</td>
<td>0.65</td>
</tr>
<tr>
<td>RT total dose</td>
<td>0.01 (high)</td>
<td>0.003 (high)</td>
<td>0.62</td>
<td>0.79</td>
<td>0.36</td>
</tr>
<tr>
<td>RT fraction dose</td>
<td>0.02 (high)</td>
<td>0.01 (high)</td>
<td>0.39</td>
<td>0.92</td>
<td>0.10</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0.64</td>
<td>0.28</td>
<td>0.49</td>
<td>0.61</td>
<td>0.03 (chemotherapy)</td>
</tr>
<tr>
<td>ASA</td>
<td>0.36</td>
<td>0.92</td>
<td>0.23</td>
<td>0.43</td>
<td>0.20</td>
</tr>
<tr>
<td>Laryngectomy</td>
<td>0.01 (total)</td>
<td>0.70</td>
<td>0.53</td>
<td>0.96</td>
<td>0.44</td>
</tr>
<tr>
<td>Pharyngectomy</td>
<td>0.002 (total)</td>
<td>0.31</td>
<td>0.34</td>
<td>0.82</td>
<td>0.13</td>
</tr>
<tr>
<td>Flap reconstruction</td>
<td>0.12</td>
<td>0.89</td>
<td>0.76</td>
<td>0.20</td>
<td>0.43</td>
</tr>
<tr>
<td>Age</td>
<td>0.17</td>
<td>0.70</td>
<td>0.67</td>
<td>0.03 (age &lt; 63 yr)</td>
<td>0.31</td>
</tr>
<tr>
<td>PTLND</td>
<td>0.05 (bilateral)</td>
<td>0.03 (bilateral)</td>
<td>0.82</td>
<td>0.81</td>
<td>0.05 (bilateral)</td>
</tr>
</tbody>
</table>

PTLND, paratracheal lymph node dissection; Glottic, initial tumour glottic versus other locations; N-stage, N+ versus N0, RT, radiotherapy; ASA, ASA > 2 versus ASA 1–2; PTLND, No or unilateral versus bilateral PTLND. Bold values are considered statistically significant (P < 0.05).
by high percentage of complications in the group with bilateral dissection. The same increase was found in univariate analyses of the relation between the three subgroups and haemorrhage (P = 0.05) and fistulae (P = 0.03).

As in all previous analyses, post hoc significance was only found between the group with bilateral PTLND and the other two groups (no and unilateral PTLND), the last two groups were combined in one group to evaluate the specific effect of a bilateral PTLND (Table 4).

For local complications the T-status, N-status, total and fraction dose of radiotherapy were identified as confounding factors in multivariate analysis. The relation between bilateral PTLND and local complications lost its significance after correction for these confounders (Table 4).

**Table 4.** Univariate and multivariate analyses of complications after laryngectomy (overall, local and specific) in patients with no, unilateral and bilateral paratracheal lymph node dissection (PTLND)

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>All patients (%)</th>
<th>No PTLND (%)</th>
<th>Unilateral PTLND (%)</th>
<th>Bilateral PTLND (%)</th>
<th>Univariate analysis (P-value)</th>
<th>Multivariate analysis (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>80 (42)</td>
<td>43 (47)</td>
<td>20 (38)</td>
<td>17 (36)</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>111 (58)</td>
<td>49 (53)</td>
<td>32 (62)</td>
<td>30 (64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>120 (63)</td>
<td>62 (67)</td>
<td>35 (67)</td>
<td>23 (49)</td>
<td>0.05</td>
<td>0.74</td>
</tr>
<tr>
<td>Yes</td>
<td>71 (37)</td>
<td>30 (33)</td>
<td>17 (33)</td>
<td>24 (51)</td>
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<tr>
<td>Pharyngocutaneous fistulae</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>140 (73)</td>
<td>72 (78)</td>
<td>40 (77)</td>
<td>28 (60)</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Yes</td>
<td>51 (27)</td>
<td>20 (22)</td>
<td>12 (23)</td>
<td>19 (40)</td>
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<tr>
<td>Wound dehiscence</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>182 (95)</td>
<td>88 (96)</td>
<td>50 (96)</td>
<td>44 (94)</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 (5)</td>
<td>4 (4)</td>
<td>2 (4)</td>
<td>3 (6)</td>
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<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>186 (97)</td>
<td>90 (98)</td>
<td>50 (96)</td>
<td>46 (98)</td>
<td>0.92</td>
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<td>2 (2)</td>
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<td>1 (2)</td>
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</tr>
<tr>
<td>Haemorrhage</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>180 (94)</td>
<td>88 (96)</td>
<td>51 (98)</td>
<td>41 (88)</td>
<td>0.05</td>
<td>0.19</td>
</tr>
<tr>
<td>Yes</td>
<td>11 (6)</td>
<td>4 (4)</td>
<td>1 (2)</td>
<td>6 (13)</td>
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<td></td>
</tr>
</tbody>
</table>

Bold values are considered statistically significant (P < 0.05).

Pharyngocutaneous fistulae, which was the most frequent complication, occurred significantly more frequently in patients with a bilateral PTLND (40%), compared to patients with no or unilateral PTLND (22%) (P = 0.016). In multivariate analysis, N-status before previous (chemo)radiotherapy...
(N0 versus N+) and total and fraction dose of radiotherapy appeared to be confounding factors (Table 5). Although confounding was present, the difference between bilateral and no or unilateral PTLND maintained its significance (P = 0.038, Table 3). For haemorrhage, where T-status and radiotherapy fraction dose were identified as confounding factors, correction for confounding factors resulted in a loss of significance of the relation between bilateral PTLND and postoperative haemorrhage (Table 4).

Table 5. Confounding analyses for the relation between fistulae and bilateral paratracheal lymph node dissection (PTLND). N-status (N0 versus N+ before radiotherapy), radiotherapy total dose and radiotherapy daily fraction dose were identified as confounding factors.

<table>
<thead>
<tr>
<th>Confounder</th>
<th>(P)</th>
<th>B-solo</th>
<th>B-conf</th>
<th>RelDiff</th>
<th>P-s</th>
<th>P-c</th>
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<td>Smoking</td>
<td>+</td>
<td>0.865</td>
<td>0.879</td>
<td>+</td>
<td>+</td>
<td></td>
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<tr>
<td>Alcohol</td>
<td></td>
<td>0.865</td>
<td>0.898</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td>0.865</td>
<td>0.865</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Glottic</td>
<td>+</td>
<td>0.865</td>
<td>0.902</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>0.865</td>
<td>0.803</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>+</td>
<td>0.865</td>
<td>0.761</td>
<td>+</td>
<td>+</td>
<td></td>
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<tr>
<td>RT total dose</td>
<td>+</td>
<td>0.915</td>
<td>0.771</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>RT fraction dose</td>
<td>+</td>
<td>0.956</td>
<td>0.817</td>
<td>+</td>
<td>*</td>
<td>+</td>
</tr>
</tbody>
</table>

ASA, ASA > 2 versus ASA1–2; Glottic, initial tumour glottic versus other locations; N-stage, N+ versus N0, RT, radiotherapy.  
(P), significance of relation between the potential confounder and the outcome; B-solo, coefficient of variable of interest without the confounder in the model; B-conf, coefficient of variable of interest with the confounder in the model; RelDiff, magnitude of relative change of B-raw into B-confounded as indication for confounding; P-s, significance of B-raw; P-c, significance of B-confounded.  
P: +<0.05, *<0.01.  
RelDiff: +>10%, *>50%.

The locations of the 51 pharyngocutaneous fistulae were retrospectively determined. Fistulae mainly developed above the stoma (55%); 37% were located in the margins of the stoma and 8% under the stoma. No statistical correlation was found between the location of the fistulae and the type of PTLND (no, uni- or bilateral).

Paratracheal lymph node metastases were found in 4 of the 146 PTLND specimens. Three patients had ipsilateral metastases, while 93 other ipsilateral paratracheal dissections were free of tumour. Of the 50 contralateral paratracheal dissections, one patient had a contralateral metastasis. In two patients, the PTLN metastasis was the only regional localisation of tumour. The primary tumours of the patients with PTLN metastases were located in the glottic area in three patients, all with subglottic extension, and hypopharynx in one patient. The initial T- and N-stage of these tumours were T1 (n = 1), T2 (n = 1) and T3 (n = 1) with N0 (n = 2) and N1 (n = 1) for the ipsilateral positive patients, and T1N0 for the contralateral positive patient.

Retrospectively, performing a unilateral instead of a bilateral PTLND would seem to increase the risk of missing contralateral paratracheal metastases with 4% (95% confidence interval: 1–15%).
DISCUSSION

Laryngectomy is often combined with neck dissection (especially in advanced stage disease), but the paratracheal nodal group is not routinely included in the dissection. The rate and extensiveness of PTLND mostly depend on the personal preference of the surgeon (13). If high-risk factors are present, the surgeon will probably be more reluctant to perform PTLND. In patients with subglottic extension, the risk of PTLN metastases is 27% (13). For laryngeal tumours, the ‘at-risk’ nodal groups include the paratracheal area (4,14), and the presence of PTLN metastases, especially with extra nodal spread (2), is associated with stoma recurrence (4,6,9,10,15–17) and poor survival (5,7,8).

Synopsis of new findings

While the above-mentioned arguments plead for a routine PTLND, we found significantly more postoperative fistulae after laryngectomy with bilateral PTLND. Forty percent of the patients with bilateral PTLND developed a fistulae, compared to 22% with no or unilateral PTLND. Despite confounding factors, bilateral PTLND appeared to be an independent risk factor for the development of fistulae in multivariate analyses. Local complications and postoperative haemorrhage lost significance in multivariate analyses but might be associated with bilateral PTLND when evaluated in a larger patient group. All patients with proven PTLN metastases and glottic carcinoma had subglottic extension.

Comparisons with other studies

To our knowledge, the present study is the first to analyse the relationship between PTLND and postoperative complications in patients who underwent laryngectomy after previous (chemo)radiotherapy. Biermann et al. (18) described the complications of thyroidectomy with PTLND. All reported complications, e.g. permanent pareses of the recurrent nerve, permanent hypocalcaemias and short-term tracheotomy, seemed to be related to the thyroidectomy and not specifically to the PTLND.

Based on our findings of a markedly increased rate of fistulae in patients with bilateral PTLND, we would not recommend performing contralateral PTLND. In our study, only 1 of the 50 contralateral PTLND contained metastases. However, Plaat et al. (2) found contralateral PTLN metastases in 21% of the PTLND. It is difficult to weight reduction in the risk of fistulae with increase in the risk of peristomal recurrence when PTLN metastases are not surgically removed after failed radiotherapy.

An argument in favour of routinely performing contralateral PTLND is the limited accuracy of preoperative diagnostics to identify PTLN metastases. Timon et al. (4) found positive paratracheal nodes with diameters varying from 0.3 to 3 cm, the majority measuring <1 cm and appearing negative preoperatively. Other authors also reported the difficult and limited estimation of PTLN status with preoperative palpation, ultrasonography, CT and MRI (19), owing to the limitations in the assessment of small lymph nodes (16). Okada et al. (20) compared PET/CT with contrast-enhanced CT for lymph node metastases (including PTLNs) in patients with oesophageal cancer. Sensitivity and specificity were 60% and 100% for PET/CT and 56% and 97% for contrast enhanced CT. The smallest lymph node metastasis detectable by PET/CT was 6 mm. In previously irradiated patients, it might be even more difficult to assess the lymph node status preoperatively.
The presence of PTLN metastases does not seem to be related to the presence of cervical lymph nodes in other levels. Our study had a relatively low rate of PTLN metastases (4/146), but despite this, in two patients this was the only localisation of lymph node metastases. This was supported by previous studies, in which 16% to 38% of the patients with PTLN metastases had no other lymph node metastases (2,4).

We included only patients with laryngectomy after previous (chemo)radiotherapy. Most studies reported on PTLND in patients without previous therapy, or in a combined patients group with and without previous therapy. Salvage laryngectomy is accompanied by an increased rate of complications, compared to laryngectomy in untreated patients (11). The increased rate of fistulae after bilateral PTLND in our study might not be present in previously untreated patients with laryngectomy. Also, the rate of PTLN metastases was less than that described in other studies, which might be related to a different lymph node drainage structure in previously irradiated patients (21). Also, lymph node metastases might have been eradicated as a result of previous (chemo)radiotherapy, while there was residual tumour on the primary site. Radiotherapy combined with chemotherapy might result in an additional risk of complications. However, the present study did not support this hypothesis. It must be borne in mind, however, that the small number of chemotherapy patients (n = 9) might have biased these data. Another difference compared to the previously untreated patients is the increased risk of complications after radiotherapy in a previously irradiated area. To prevent stoma recurrence in case of PTLN metastases, postoperative radiotherapy is suggested (4,5,9,15,16). However, re-irradiation is known to result in increased rate of complications (22).

**Drawbacks of the study**

The main drawback of this study is the retrospective analyses. The present study is the first to explore the relationship between PTLND after (chemo)radiotherapy and complications, but further research is necessary to draw further conclusions. Also, to be able to evaluate a large group of patients, a wide time window was used in which a variety of surgeons have been performing the operations with small modifications of techniques over the years. Moreover, because the borders of level VI are not clearly defined, the extent of a PTLND may vary somewhat (23). A more homogeneous group would have been preferable. In this study, all patients with salvage laryngectomy were included. Inclusion of patients with hypopharyngeal carcinoma as primary tumour site might be argued because these tumours have a different lymphatic drainage and because this concerned a small number of patients (7%) with potential bias. However, in univariate analyses, no significant difference was found for different primary tumour sites. And also in multivariate analyses, no significant difference was found between glottic tumour and other sites showed no significance. The results should also be interpreted with caution for hypopharyngeal carcinoma because this study included largely early-stage disease (T1–2: 74%, N0: 86%), while the included hypopharyngeal carcinomas concerned more advanced-stage tumours (T1–2: 46%, N0: 54%). In general, it should be kept in mind that this study concerned mainly early-stage initial disease.
Clinical applicability of the study

The results of this study emphasise the need to make a well-considered decision to perform PTLND. Survival rates are important for patients undergoing extensive surgery as (salvage) laryngectomy, but complication rates should also be kept in mind.

CONCLUSIONS

Bilateral PTLND in patients undergoing laryngectomy after previous (chemo)radiotherapy is shown to significantly adversely affect the risk of postoperative pharyngocutaneous fistulae. As the incidence of contralateral PTLN metastases was low, a strict selection of patients undergoing contralateral PTLND is warranted. If subglottic extension is diagnosed, patients should certainly undergo PTLND, because all patients with glottic carcinoma and PTLN metastases had subglottic extension.
REFERENCES


