Morbidity and mortality of cervical lymphadenectomy. Analysis of 311 cases

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Abstract

Objective: To determine the morbidity and mortality and the risk factors associated with cervical lymphadenectomy.
Method: Cross-sectional study; patients undergoing cervical lymphadenectomy were included in any of its variants, secondary to the recurrence of some neoplastic entity; from January 2011 to November 2016. Results: 311 patients were included of which 65.3% were women and 49 ± 17.2 years old. The most frequent diagnoses were thyroid cancer 194 (62.4%) and recurrent laryngeal cancer 22 (7.1%). Asymptomatic patients had 53.4% of the patients and 119 (38.3%) presented masses or nodules in the neck, with level III being the most affected with 276 (88.7%) patients. Overall morbidity was 17% and mortality was 5.8%. The factors related to mortality were: present symptomatology (p = 0.006), involvement of level I (p = 0.005), extensive lymph node dissection (p = 0.01), and vascular complications (p = 0.0001) and the wound (p = 0.01).

Conclusions: Due to the lymphatic dissemination pattern of head and neck tumors, selective lymphadenectomy plays a crucial role in the treatment of these neoplasms. We have opted to perform more conservative surgeries, as long as the main oncological objectives are preserved.

Key words: Cervical lymphadenectomy. Ganglion levels. Morbidity. Mortality.

Resumen

Objetivo: Determinar la morbimortalidad y los factores de riesgo asociados a la linfadenectomía cervical. Métodos: Estudio transversal analítico en el que se incluyeron pacientes sometidos a linfadenectomía cervical en cualquiera de sus variantes, secundarios a la recurrencia de alguna enfermedad neoplásica, desde enero de 2011 hasta noviembre de 2016. Resultados: Se incluyeron 311 pacientes, de los cuales 203 (65.3%) eran mujeres, con una edad de 49 ± 17.2 años. Los diagnósticos más frecuentes fueron cáncer de tiroides, en 194 (62.4%) casos, y cáncer de laringe recurrente, en 22 (7.1%). Cursaron asintomáticos 166 (53.4%) pacientes, y 119 (38.3%) presentaron masas o nódulos en el cuello, siendo el nivel III el más afectado, con 276 (88.7%) pacientes. La morbilidad general fue del 17% y la mortalidad fue del 5.8%. Los factores relacionados con la mortalidad fueron la sintomatología presente (p = 0.006), la afectación del nivel I (p = 0.005), la disección ganglionar.
Introduction

The presence of lymph node metastases has been estimated to indicate a 50% decrease in overall survival in patients with any nosological entity, and contralateral lymph node involvement indicates another 50% decrease. Therefore, it is important to perform cervical lymph node dissection, which contributes to the staging of certain tumors and is considered a prognostic factor. Dissection of the neck in its various forms is the standard procedure for surgical treatment of cervical lymph node metastases, since it allows extensive clearance of all lymph nodes with macroscopic growth and offers accurate histological information about the nodes at risk of developing micrometastases in a clinically negative neck, and whose purpose is local control of the disease. Opinions vary with regard to indications for neck dissection and the type of dissection for different situations.

Currently, cervical lymphadenectomy is classified in four categories: radical neck dissection, modified radical neck dissection, selective neck dissection and extended neck dissection. The transition from radical to selective neck dissection has resulted in a fewer number of complications and less morbidity, while surgical efficacy and compliance with oncological principles are preserved.

Operative complications, such as vessel or nerve injury, are a cause of higher morbidity, coupled with medical complications unrelated with the procedure that may occur after cervical lymphadenectomy. Although infrequent, death can occur as a consequence of severe morbidity.

The purpose of this study was to assess the complications and mortality associated with the cervical lymphadenectomy procedure, since in our institution it constitutes one of the main reasons for consultation, as well as for surgical procedures, and it is therefore necessary to detect the various risk factors associated with morbidity and mortality with the purpose to implement improvements that decrease their frequency.

Method

An analytical cross-sectional study was carried out. The surgical oncology department database was reviewed and all patients who had undergone cervical lymphadenectomy in any of its variants as a surgical procedure, due to lymph node recurrence of any neoplasm during the period from January 1, 2011 to November 30, 2016 were included. Patients who had unresectability criteria, such as spine or spinal cord compromise, and those with serious comorbidity preventing said procedure were excluded.

Variables such as age, gender, presentation symptoms, primary neoplasm and type of performed surgery (radical, modified, selective, supraomohyoiod, lateral, posterolateral, central and posterior dissection) were collected and compared with the histopathology result, postoperative complications associated with procedure (of the wound itself, vascular, nervous and chylous fistula) and postsurgical mortality.

Statistical analysis

The variables were captured on an electronic database and were subjected to statistical analysis using the SPSS program (version 21.0; IBM Corp., Armonk, NY, USA). Raw numbers and percentages were obtained for qualitative variables, and means with their standard deviation for quantitative variables. The inferential phase was carried out through a univariate analysis with the chi-square test or Fisher’s exact test for qualitative variables and odds ratios (OR) and 95% confidence intervals (CI) calculation. Any p-value < 0.05 was considered statistically significant.

Ethical considerations

Ethical aspects in this study are based on the Regulations of the General Statute Law in Matters of Health Research and on the Declaration of Helsinki and its
amendments, as well as on national and international codes in force for good research practice. The study was approved by the Local Research and Ethics in Health Research Committee with registration number R-2016-1301-117. The study was carried out with the institution’s own resources, and thus it is declared that there is no conflict of interest.

Results

Three-hundred and eleven patients were included, 108 (34.7%) of the male gender and 203 (65.3%) of the female gender. Age was 49 ± 17.2 years. The most common diagnosis was thyroid cancer in 194 patients (62.4%), followed by recurrent laryngeal cancer in 22 patients (7.1%), and cervical metastases of unknown primary in 16 patients (5.1%). With regard to symptoms, 166 patients (53.4%) were asymptomatic and 119 (38.3%) referred the presence of masses or nodules in the neck; out of them, 26 (8.4%) had symptoms such as dysphagia or dysphonia.

As for surgical dissection, 108 (34.7%) underwent lateral lymph node dissection, 78 (25%), type 3 modified radical dissection and 48 (15.4%).

| Variable                        | n (%) |
|---------------------------------|-------|
| Gender                          |       |
| Males                           | 108 (34.7) |
| Females                         | 203 (65.3) |
| Age (years)                     | 49 ± 17.2 |
| Hospital stay (days)            | 4.2 ± 4  |
| Diagnosis                       |       |
| Thyroid cancer                  | 194 (62.4) |
| Larynx cancer                   | 22 (7.1)  |
| Cervical metastasis of unknown primary tumor | 16 (5.1) |
| Parotid cancer                  | 11 (3.5)  |
| Melanoma                        | 11 (3.5)  |
| Tongue cancer                   | 9 (2.9)   |
| Others                          | 48 (15.6) |
| Clinical presentation           |       |
| Asymptomatic                    | 166 (53.4) |
| Masses or nodules               | 119 (38.3) |
| Others                          | 26 (8.4)  |
| Morbidity                       |       |
| Vascular complications          | 23 (7.4)  |
| Nerve complications             | 11 (3.5)  |
| Wound complications             | 19 (6.1)  |
| Mortality                       | 18 (5.8)  |
| Comorbidity                     |       |
| Diabetes mellitus (DM)          | 21 (6.8)  |
| High blood pressure (HBP)       | 37 (11.9) |
| DM and HBP                      | 36 (11.6) |
| Other                           | 12 (3.8)  |
| Type of surgery                 |       |
| Type I radical dissection       | 3 (1)   |
| Type III modified radical dissecion | 78 (25) |
| Supraomohyoid dissection        | 48 (15.4) |
| Lateral dissection              | 108 (34.7) |
| Posterolateral dissection       | 29 (9.3)  |
| Anterior dissection             | 25 (8)   |
| Lateral and anterior dissection | 19 (6.1)  |
| Posterior dissection            | 1 (0.3)  |
| Histopathological result        |       |
| Positive                        | 264 (84.9) |
| Negative                        | 47 (15.1) |

Vascular complications

Risk factors associated with vascular complications were analyzed, out of which high blood pressure (OR: 2.7; 95% CI: 1.1-6.5; p = 0.02), clinical symptoms (OR: 2.8; 95% CI: 1.1-7.1; p = 0.01), type III radical dissection (OR: 3; 95% CI: 1.2-7.1; p = 0.01) and supraomohyoid dissection (OR: 0.9; 95% CI 0.8-0.9; p = 0.01) were found to be, as seen in table 2.

Nerve complications

Major hypoglossal nerve lesions were found in 9 patients (2.8%) and recurrent laryngeal nerve lesion was found in 1 (0.3%), which were associated with level I (OR: 19.1; 95% CI: 4.0-91.2; p = 0.00) and level II resection (OR: 1; 95% CI: 1.0-1.1; p = 0.002).

Wound complications

Surgical wound complications were infection in 3 patients (0.9%), surgical wound dehiscence in 8 (2.5%) and seroma in 2 (0.6%). A higher risk was observed in male patients (OR: 0.2; 95% CI: 0.1-0.7; p = 0.009), with diabetes mellitus (OR: 2.8; 95% CI: 1.0-7.5; p = 0.04) and with lateral dissection (OR: 0.3; 95% CI 0.09-1.1; p = 0.05).
Chylous fistula

In the 12 (3.85%) patients who developed chylous fistula, male gender (OR: 0.2; 95% CI: 0.7-0.8; p = 0.02) and type III radical dissection (OR: 3.1; 95% CI: 0.9-10; p = 0.05) were found to be risk factors.

Mortality

Eighteen patients died (death rate of 5.8%), out of which eight died due to severe postoperative hemorrhage, five due to sepsis, two due to complications associated with a chylous fistula and the rest due to complications unrelated to the procedure. The factors that were associated with mortality were presence of clinical symptoms (OR: 4.32; 95% CI: 1.3-13.4; p = 0.02), level I metastases (OR: 4.41; 95% CI: 1.5-10.9; p = 0.005), type 3 modified radical dissection (OR: 3.2; IC 95%: 1.2-8.5; p = 0.01) and vascular (OR: 11; 95% CI: 3.7-32.2; p = 0.0001) and wound complications (OR: 5.29; 95% CI: 1.5-18.0; p = 0.01), as observed in table 3.

Discussion

Cervical lymphadenectomy in patients with head and neck tumors continues to be considered the first line of treatment for lymph node metastases of tumors of this region, as well as one of the main tools for staging, which is considered the most important prognosis factor of aerodigestive tract neoplasms malignancy1,2.

As it could be observed in our study, there is a large number of tumors that cause metastases in cervical lymph nodes, among which the vast majority are found
to correspond to thyroid-origin tumors, which account for 62% in our population, while in world literature percentages of up to 72% can be found, which are associated with low lethality but high incidence6. If we consider aerodigestive tract tumors in general, we find an incidence of cervical metastases of around 16%, which is higher when compared to the literature, which reports 12%; however, in contrast with the results obtained in studies carried out in other countries, we observe that larynx neoplasms in our study rank second6,10,11.

According to the classification proposed since 1987 by the American Head and Neck Society (AHNS) and the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), it could be appreciated that the most affected levels are II, III and IV, which, if the lymphatic drainage of each tumor is analyzed, corresponds to the natural evolution of its dissemination7,12,13, since they have a predictable and sequential pattern, as observed in thyroid, tongue, gum, larynx and parotid tumors, which have drainage towards these levels and therefore there is correlation with the resected lymph node levels, with a lower proportion of levels V, VI and VII. When analyzing asymptomatic patients in comparison with those who have cervical nodules or masses, we see that these are a recurrence prognostic parameter, since all those who have symptoms are positive for malignancy in the histopathological examination, with this difference being statistically significant, which is consistent with Sugitani et al. findings13, who found that 20.6% of patients with palpable lymph nodes developed nodal recurrence, this way considering those presenting with lymph nodes of 3 cm or more as high-risk patients.

According to lymphadenectomies surgical evolution, conservative management is increasingly being preferred, since previous studies have shown that the resection of lymph node-unrelated structures, such as the spinal nerve, muscles or blood vessels, offers no advantage in terms of overall survival or disease-free period14-16. We agree with the world literature by performing more conservative surgeries, with resection of lymph node levels by groups depending on the affected levels and the possibility of metastasis contiguous, and this is why levels II, III and IV lateral dissection continues to be the most performed surgery, followed by type 3 modified radical dissection, which includes lymph node levels I to V, preserving lymph node-unrelated structures, or supraomohyoid dissection for higher levels. The extent of lymphadenectomy directly influences morbidity, mainly with vascular conditions, when performing extensive dissections such as modified radical dissection.

The presence of nodules at jugular levels and their resection significantly affect the increase of hematomas and incidental perforations in the jugular vein, which in correlation with the extent of lymphadenectomy in a radical dissection can occur in up to 4% according to the literature6,11 (5% in our study).

The incidence of surgical complications is variable, dependent on each surgeon and each hospital, in addition to being correlated with tumor histological type. In our study, we found a complication rate of 17%, which include nerve and vascular complications and those inherent to the wound, in contrast with observations reported by Dedivitis et al.18, who found a frequency of up to 28%. The most common complications in our population were vascular, unlike the previously mentioned study18, where nerve complications

### Table 3. Univariate analysis of factors associated with mortality in the study population

| Variable                                      | n   | p* | OR (95% CI) |
|-----------------------------------------------|-----|----|-------------|
| Gender                                        |     |    |             |
| Males                                         | 9/108 | 0.12 | 0.5 (0.1-1.3) |
| Females                                       | 9/203 |    |             |
| Diagnosis                                     |     |    |             |
| Thyroid cancer                                | 9/194 | 0.19 | 0.58 (0.2-1.5) |
| Melanoma                                      | 2/11 | 0.12 | 3.94 (0.7-19.7) |
| Laryngeal cancer                              | 2/22 | 0.36 | 1.7 (0.3-7.9) |
| Squamous cell cancer                          | 1/5 | 0.25 | 4.2 (0.4-40.1) |
| Type of surgery                               |     |    |             |
| Type III radical dissection                    | 9/78 | 0.01 | 3.24 (1.2-8.5) |
| Supraomohyoid dissection                      | 3/48 | 0.54 | 1.10 (0.3-3.9) |
| Lateral dissection                            | 4/108 | 0.18 | 0.51 (0.16-1.6) |
| Anterior dissection                           | 1/25 | 0.56 | 0.65 (0.08-5.1) |
| Posterolateral dissection                     | 0/29 | 0.16 | 0.93 (0.9-0.9) |
| Lateral and anterior dissection               | 1/19 | 0.69 | 0.89 (0.1-7.1) |
| Complications                                 |     |    |             |
| Vascular                                      | 7/23 | 0.0001 | 11 (3.7-32.2) |
| Nerve                                         | 1/11 | 0.48 | 1.66 (0.2-13.7) |
| Wound                                         | 4/19 | 0.01 | 5.29 (1.5-18.0) |
| Chylous fistula                               | 2/12 | 0.14 | 3.53 (0.7-17.5) |
| Pathology result                              | 17   | 0.21 | 3.16 (0.4-24.3) |
| Symptoms present                              | 14   | 0.006 | 4.32 (1.3-13.4) |
| Lymph node level                              |     |    |             |
| I                                             | 9    | 0.005 | 4.41 (1.5-10.9) |
| II                                            | 12   | 0.27 | 1.52 (0.5-4.2) |
| III                                           | 14   | 0.81 | 2.94 (0.8-7.7) |
| IV                                            | 6    | 0.54 | 1.05 (0.3-2.9) |
| V                                             | 3    | 0.21 | 2.14 (0.5-7.9) |
| VI                                            | 2    | 0.50 | 0.72 (0.1-3.2) |
| VII                                           | 0    | 0.61 | 0.94 (0.9-0.9) |

*By chi-square test or Fisher’s exact test.
CI: confidence interval; OR: odds ratio.
Cervical lymphadenectomy is the ideal treatment for regional control in patients with lymph node metastases, avoiding unnecessary resection of non-lymphatic structures. An overall morbidity of 17% was observed, which is similar to that recorded in other specialized centers. Performing more conservative surgeries has been chosen, as long as regional control of disease is achieved, given the direct relationship between lymph node metastases and the increase in both neoplastic persistence and recurrence. Since cervical lymphadenectomy is an element to stage neoplasms originating in the head and neck, and in those that are metastasis of distant neoplasms, the importance of its performance stands out, since the benefit of lymph node resection outweighs the low rate of complications expected from said surgery.

Conclusions

Cervical lymphadenectomy is the ideal treatment for regional control in patients with lymph node metastases, avoiding unnecessary resection of non-lymphatic structures. An overall morbidity of 17% was observed, which is similar to that recorded in other specialized centers. Performing more conservative surgeries has been chosen, as long as regional control of disease is achieved, given the direct relationship between lymph node metastases and the increase in both neoplastic persistence and recurrence. Since cervical lymphadenectomy is an element to stage neoplasms originating in the head and neck, and in those that are metastasis of distant neoplasms, the importance of its performance stands out, since the benefit of lymph node resection outweighs the low rate of complications expected from said surgery.

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