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Complications following lymphadenectomy: a prospective study in canine patients.

Complicanze delle linfoadenectomie: studio prospettico nel cane.

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Sommario

Abstract

Lymphadenectomy is an essential procedure to assess the lymph nodes (LNs) status in many clinical situations, as staging of neoplasia.

The aim of this prospective study was to describe the complications associated with lymphadenectomy of peripheral lymph centers, evaluating their occurrence, duration, and treatment.

The study includes patients undergoing lymphadenectomy between April 2021 and August 2022 at the Veterinary Teaching Hospital of Parma.
Postoperative complications were evaluated in the immediate postoperative period and during the month after surgery.
A total of 64 lymphadenectomies performed in 50 dogs could be considered for the statistical analysis. The complication rate was 69% (44/64 cases), and the total number of complications was 44. Complications were oedema (89%), lameness (7%), dehiscence (2%) and seroma (2%).
Only 1 of 64 lymphadenectomies had a severe complication caused by a dehiscence that required a revision surgery, while 2 of 64 had a moderate complication that required medical treatment with corticosteroids.
The median time to onset of the complications was 1 day (range 1-7), and the median duration of the complications was 4.5 days (range 1-35).

Even if any of the variables evaluated were statistically significant, the risk of oedema seemed to be increased in case of *en bloc* excision of mandibular and retropharyngeal LNs, the use of methylene blue dye and the mandibular lymphadenectomy alone. Lymphadenectomy of the popliteal LN appeared to be the safest surgery. The lameness was correlated with axillary lymph node dissection, and this could be explained with the anatomical site of LN close to nerves and vasculature.

Time of lymphadenectomy (LT) seemed to play an important role in the occurrence of complications, although not statistical significance was found.

The results of the present study show that lymphadenectomy of superficial LNs is a safe procedure, despite the high rate of minor complications. All these complications seem to be self-limiting and resolve completely during the month of follow-up.

Introduction

Lymph nodes (LN) are the draining site for all inflammatory and neoplastic diseases of the organism. Knowing their physiological state is important to define the extent of a disease and to plan the appropriate therapy. In oncology, knowing the LN status is becoming more and more important, therefore, lymphadenectomy has become a very common practice, both in human and veterinary medicine. This step plays a pivotal role in the staging of cancers and is crucial in establishing a correct treatment plan for oncologic patients. [1,2]

The lymphatic vessels comprise a one-way transport system for fluid and proteins by collecting them from the interstitial space and returning to the blood circulation. If the lymphatic is blocked or dysfunctional, interstitial proteins accumulate, leading to continual increase of osmotic pressure, and fluid accumulation (oedema) ensues.

The smallest lymphatic vessels are still much larger than blood capillaries and flow velocities are orders of magnitude slower. Lymph fluid is nearly identical to interstitial fluid and promotes cell viability. [3–5]

Tumor cell dissemination is mediated by several mechanisms, including local tissue invasion, lymphatic spread, hematogenous spread, or direct seeding into body cavities or surfaces. [6]

The lymphatic system serves as the primary route for the metastasis of most cancers, and the spread of tumor cells via lymphatics to the regional LNs is one of the most important indicators of tumor aggressiveness for the majority of human malignancies,[7] and it represents one of the most important prognostic indicators of survival and risk of recurrence. [3–5].

While the majority of sarcomas disseminate by vascular invasion, carcinomas and round cell tumors primarily spread through the lymphatic system and initially metastasize to the regional LNs. [8,9]

In the pre-sentinel node era, it was assumed that cancer would spread from the primary site to the regional LNs (RLN) first, then to the distant sites.[10]

In the 19th century Virchow was the first to describe the role of LNs in filtering lymph and serving as a major barrier for cancer cells, assuming that the RLNs were the first site to be affected by metastases [11,12].

The sentinel LN (SLN) is defined as the first LN within the lymphatic basin that drains the primary tumor, therefore, its evaluation is indicated to early and more precisely detect the presence of

loco-regional metastasis. Thus, accurate methods for detecting the SLNs may provide crucial information on tumor prognosis and may guide the clinician on treatment selection. For these reasons SLN mapping has successfully been established in human oncology, becoming an integral part of treatment decision-making and prognosis of certain malignancies.

In human medicine, LNs dissection represents a debated topic, in particular for the treatment plan of breast cancer in women, and for this reason, it is widely studied.[9, 13]

Axillary LN dissection (ALND) is an effective method of maintaining regional control in this disease, but it is associated with a significant risk of complications such as infection, lymphedema, numbness, axillary seroma, axillary paresthesia, axillary web syndrome, brachial plexus nerve injuries (BPI) and decreased upper-extremity range of motion. This fact has a strong impact on the patient's quality of life, and symptoms magnitude is proportional to the extent of the dissection. [14-18] Thus, over the last 30 years, a gradual de-escalation in axillary LN surgery has been proposed, that lead to the replacement of the ALND with the sentinel lymph-node biopsy (SLNB), which is the current best practice standard of care for women with early-stage breast cancer associated with modern chemotherapy and radiotherapy.[13]

Although SLN mapping has reduced complications, they may still develop during and after lymphadenectomies, depending on the extent of the approach and the location of the LNs. [14,15,18] For instance, inguinal and ilio-inguinal lymphadenectomy is associated with a high complication rate, which potentially include seroma, lymphocele, lymphocyst, lymphorrea, lymphatic fistula, hematoma, hemorrhage, infection, cellulitis, wound dehiscence, wound breakdown, skin edge necrosis and, in the most severe cases, venous thromboembolism. [19,20] The removal of LNs within body cavities, such as tracheobronchial or iliac and sacral LNs, is considered a more complex procedure, with greater morbidity and increased surgical time. [1]

In veterinary medicine, there is a lack of standardization in LNs assessment, and both cytology and histopathology are validated techniques to detect nodal metastases.[21]

Despite this, LN dissection combined with mapping techniques to identify SLNs is becoming the gold standard technique for the diagnosis of LN metastasis also in veterinary medicine, even in the absence of clinical suspicion of metastasis, especially for some malignancies with high metastatic potential, such as mast cells tumors.[2,8,21-25]

The excision of metastatic LN may, therefore, have a therapeutic role, as it translates into a lower risk of distant spread, may result in better regional tumor control, thus increased survival time. [1,21,26,27]

Lymphadenectomy following SLN mapping has become part of the diagnostic and therapeutic protocol for the treatment of many malignant neoplasms, mainly of epithelial and round cell origin. The lymphadenectomy of peripheral LNs is considered a safe procedure with a low incidence of complications, although there are not many detailed published studies.

The same trend in complication development found in human medicine, would, therefore, be expected in veterinary patients, although there are not many published studies yet. [1,22–24,26]

The aim of this study was to describe the complications associated with lymphadenectomy of peripheral lymph centers in veterinary patients undergone lymphadenectomy for any reasons, and to report their incidence in relation to anatomic location, number and size of LNs removed.

Methods and Materials

Data collection

This prospective study was conducted from April 2021 to August 2022 at the Veterinary Teaching Hospital of the University of Parma. All owners signed a written informed consent, agreeing to submit their dogs to the procedures described and for their data to be used for scientific purposes.

Dogs undergoing lymphadenectomy of a superficial lymph center for diagnostic or therapeutic purposes, such as staging a solid neoplasms or lymphoma, were enrolled.

Lymphadenectomies were performed by one Professor of Small Animal Surgery, one ECVS resident and one PhD student.

Data collected on all patients included: breed, sex, neutered status, age, body weight, body condition score (BCS, range 1–9), histotype and anatomic localization of the primary tumor, anatomic location and laterality of LN and if they were palpable/no-palpable during physical examination, type of pre-operative diagnostic imaging (ultrasound, peritumoral injection of aqueous contrast and indirect computed tomography lymphangiography), number of identified LN with imaging techniques, peritumoral injection of methylene blue dye (MBD) to identify the LN, time of lymphadenectomy (LT), number of excised LNs and their maximum diameter (measured *ex vivo* with a caliper after surgical resection), histopathologic status of dissected LNs in case of neoplastic disease, perioperative treatment.

Time of lymphadenectomy (LT) was recorded for each removed lymph center. LT was recorded from the start of research to the definitive excision of LN(s), if only one incision was performed to remove both the tumor and the lymph center. If the lymph center was located in a different anatomic area from the primary tumor, LT was recorded from the skin incision over the LN to the end of skin suture. If several LNs had to be removed from different sites, LT was recorded for each site and each LN was considered as a different enrolled case.

Unless needed for other reasons, antibiotics were used only at induction of anesthesia (cephazolin e.v., 20 mg/kg), while NSAIDS were administered for 2-7 days after surgery, depending on the concurrent surgery performed. In these cases, NSAIDS administration has not

been considered as a treatment for the complication. Only in case of lymphoma, corticosteroids were administered instead of NSAIDS.

Each lymph center was considered as a single case, if lymphadenectomy required different skin incisions on the same dog. Different lymph centers accessed from the same skin incision were considered as a unique case (i.e., mandibular and medial retropharyngeal lymph centers).

Evaluation of complications

The type of complications considered were infection, dehiscence, oedema, seroma formation, hematoma, lymphedema, lameness, and hemorrhage, and for each complication, the onset from the day of surgery, duration (days), and treatments performed were recorded.

Patients were followed for 30 days post-surgery and visited by one of the team surgeons at 24 hours, 3, 7 dys, 15 and 30 days.

Post-operative complications were graded into three levels of severity: mild (Grade 1), moderate (Grade 2) and severe (Grade 3), in accordance with the Veterinary Cooperative Oncology Group—Common Terminology Criteria for Adverse Events (VCOG-CTCAE v2) guidelines. [28]

Lameness was scored into 4 levels (0, no detectable lameness; 1, mild weightbearing lameness; 2, moderate weightbearing lameness; 3, marked weightbearing lameness; and 4, no weightbearing lameness). [29]

Only in case of ALND, due to the possible BPI, thoracic limb reflexes were evaluated before and after surgery (Withdrawal reflex, Biceps tendon reflex, Triceps tendon reflex, Extensor carpi radialis response), and any alterations recorded. Dogs already presenting with preoperative lameness were recorded and re-evaluated after surgery.

The database was completed on 8th august 2022.

Statistical Analyses

All the analyses reported below were performed in Python exploiting the statsmodel package for the statistical analysis and especially for the logistic regression.

Initially, a correlation analysis between all the continuous variables to quantify the association was performed. Then, the most correlated variables were selected, in order to be removed from

the list of predictors in the subsequent logistic regression model to avoid multi-collinearity issues. This was additionally detected using the Variance Inflation Factor (VIF) technique.

The statistical relationship of signalment, surgical time, localization and number of LN removed with the presence of surgical complications was evaluated with a set of logistic multivariate regressions.

Variables with a P-value smaller than 10% in the univariate analysis were included in a multivariate logistic regression model to assess their statistical relation with presence/absence or wound-related complications. Logistic regression results are reported specifying the odds ratios and the associated P-values. Odds ratios (OR) are used to compare the relative odds of the occurrence of the outcome of interest (i.e., complications), given the exposure to the variable of interest.

In conclusion, specific multivariate logistic regressions focused on LT and oedema were performed, in order to understand the surgical time threshold more influential on the onset of complications and if specific factors specifically influenced the presence of oedema, being the complication observed in the vast majority of sample cases.

Results

Description of the population

A total of 50 dogs on which 64 lymphadenectomies were performed were included in this study. Median age of enrolled dogs was 9.5 years (range 1-17 years), and median body weight was 30 Kg (range 4.5-70 Kg). Twenty-nine (58%) dogs were females, 16 of which spayed, and 21 (42%) dogs were males, 5 of which castrated. The median body condition score was 4 (range 3-7).
The most represented breeds were crossbreed (13), followed by Labrador retriever (7), Jack Russell terrier (5), golden retriever (3), Corso (3), boxer (2), Bernese mountain dog (2), German shepherd (2), Rottweiler (1), dachshund (1), Belgian shepherd dog (1), Dobermann (1), Airedale terrier (1), Bracco Italiano (1), Samoyed (1), Lagotto Romagnolo (1), Lhasa Apso (1), Segugio (1), Siberian Husky (1), Welsh Corgi(1) and York Shire terrier (1).

LN Localization and Evaluation

The 64 lymphadenectomies included the access to 19 Inguinal lymph centers (30%), 16 axillary lymph centers (25%), 8 superficial cervical LN (13%), 7 *en bloc* mandibular and retropharyngeal lymph centres (11%), 7 popliteal LN (11%), 4 mandibular LN (6%), 3 retropharyngeal LN (5%).
Localization was left sided in 29 cases (45%), right sided in 25 (39%) and bilateral in 10 cases (16%),
At the physical examination, 34 lymph centers were considered palpable (53%) and 30 no-palpable (47%).

The median of number of LNs excised was 1 (range 1-11); in 54 cases (84%) less than 4 LNs from a single lymph center were extirpated, and in 10 cases (16%) 4 or more LNs were removed.

Preoperative diagnostic imaging included ultrasound in 1 case and peritumoral injection of aqueous contrast and indirect computed tomography lymphangiography in 32 cases, of which 27 were identify as SLNs and 5 were not detected as SLNs.

In 38 cases blue dye was used to identify the lymph centrum intraoperatively, in particular, 16 in case of the axillary lymph center, 14 for inguinal lymph center, 5 for superficial cervical lymph center, 2 for popliteal lymph center, 1 for mandibular lymph center.

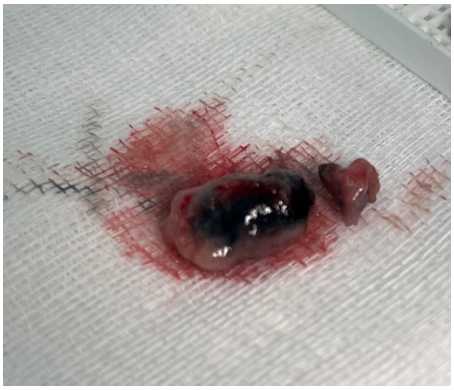

Figure 1: example of LN extirpated after peritumoral injection of MBD.

Table 1: Signalment, Maximum Diameter of LNs, Localization of LNs, Number of LNs removed and LT of the 64 cases included in this study related to complications.

Group Class	Number of Complication	Number Of Cases	% complicanze
Age <8	15	23	34,1
Age 8-10	16	20	36,4
Age 10-17	13	21	29,5
Maximum diameter <15	15	22	34,1
Maximum diameter 15-29 mm	13	21	29,5
Maximum diameter >29 mm	16	21	36,4
Localization -Bilateral	8	10	18,2
Localization- DX	14	25	31,8
Localization- SX	22	29	50,0
Axillary LN	14	16	31,8
Inguinal LN	12	19	27,3
Mandibular LN	3	4	6,8
Mandibular+ retropharyngeal LNS	6	7	13,6
Popliteal LN	1	7	2,3
Retropharyngeal LN	3	3	6,8
Superficial cervical LN	5	8	11,4
Number removed- 1	27	39	61,4
Number removed- 2	5	12	11,4
Number removed- 3	4	3	9,1
Number removed- 4	2	3	4,5
Number removed- 5	1	1	2,3
Number removed- 6	1	1	2,3
Number removed -7	2	2	4,5
Number removed- 8	1	1	2,3
Number removed- 9	0	1	0,0
Number removed - 11	1	1	2,3
SEX - F	12	16	27,3
SEX - FS	14	20	31,8
SEX- M	15	22	34,1
SEX - MC	3	6	6,8
Weight class <13,6 kg	14	22	31,8
Weight class 13,6-35 kg	21	28	47,7
Weight class 35-70 kg	9	14	20,5
Palpable NO	27	37	61,4
Palpable YES	17	27	38,6
LT class < 10	10	23	22,7
LT class 10-25	19	21	43,2
LT class > 25	15	20	34,1

Lymphadenectomy time and Histopathology

The median lymphadenectomy time (LT) was 19 minutes (range 1.5-61).

At histopathology, tumor types included: 27 mast cell tumors (MCT) (25 cutaneus, 1 subcutaneus, 1 oral), 6 malignant oral melanomas (OMM), 5 mammary benign tumors, 4 lymphomas, 3 soft tissue sarcomas, 2 Canine Apocrine Gland Anal Sac Adenocarcinomas (AGASACA), 2 squamocellular carcinomas (SCC), 2 mammary carcinomas, 2 thyroid gland carcinomas, 2 adenomas of the hepatoid cells, 1 mammary myoepithelioma, 1 oral osteosarcoma (OSA), 1 acanthomatous ameloblastoma, 1 lymphangiosarcoma, 1 plasmacytoma. Four lymphadenectomies were performed in non-oncologic patients.

The median maximum diameter measured *ex vivo* with a caliper after surgical resection was 14 mm (range 1-55 mm).

Complications rate

There were 40 out of 64 (63%) surgical procedures that showed at least one adverse event, while the total number of complications was 44.

Oedema was the most frequent complication, observed in 39/44 cases (89%), followed by lameness in 3 cases (7%), 1 seroma (2%) and 1 dehiscence (2%).

No neurological complications were observed in any patients, nor infections, hematoma, lymphedema, hemorrhage, or intraoperative death.

Complications were recorded in lymphadenectomies of the Inguinal lymph center in 12/19 cases, axillary lymph center in 8/16 cases, *en bloc* mandibular and retropharyngeal in 6/7 cases, mandibular lymph centers in 3/4 cases, superficial cervical lymph centers in 5/8 cases, retropharyngeal in 2/3 cases and popliteal in 1/7 cases.

Of the lymphadenectomies that had complications, 20 were left sided (n=20/29), 12 right sided (12/25) and 8 bilateral (n=8/10).

Lymphadenectomies associated with complications occurred in 32/54 cases (59%) when less than 4 LNs were removed, and in 8/10 cases (80%) when 4 or more LNs were removed.

Three dogs with BCS=3, twenty with BCS=4, fifteen with BCS=5 and two with BCS=6 developed complications. The BCS score was not statistically correlated to the occurrence of complications.

The median time to onset of complications was 1 day (range 1-5), and the median duration was 4.5 days (range 1-30).

Complications occurred in 25/38 cases (66%) in which MBD was used; of these, 11/16 were axillary, 10/14 inguinal, 3/5 superficial cervical, and 1/1 mandibular. In lymphadenectomies in which MBD was not used, complications occurred in 15/26 cases (58%); of these, 6/7 were *en bloc* mandibular and retropharyngeal, 2/5 inguinal, 2/3 mandibular, 2/3 retropharyngeal, 2/3 superficial cervical, and 1/5 popliteal.

Twenty three of the 32 surgeries with LT >20 minutes (72%) developed complications, compared with 17/32 (53%) of those with LT < 20 minutes.

LNs localization	**Number of cases**	**%**	**Complicated cases**	**% Complication**
Retropharyngeal	3	5%	2	67%
Mandibular	4	6%	3	75%
en bloc Mandibular+ retropharyngeal	7	11%	6	86%
Popliteal	7	11%	1	14%
Superficial cervical	8	13%	5	63%
Axillary lymph centre	16	25%	8	50%
Inguinal lymph centre	19	30%	12	63%

Table 1: LNs localization and complication rate.

Of the 64 lymphadenectomies, 37 (58%) had mild complications, including oedema and lameness, which were self-limiting and did not require medical treatment. All mild complications resolved in a median time of 5.5 days.

Two lymphadenectomies (3%) developed moderate complications; oedema in one case, both oedema and seroma in the other; all were treated by corticosteroid therapy and resolved in of 21 days.

Figura 2: Moderate seroma in patient after retropharyngeal lymphadenectomy.

Only one lymphadenectomy (2%) had a severe complication caused by wound dehiscence that required surgical revision.

Statistical Results

In the set of univariate analysis, only *en bloc* extirpation of mandibular and retropharyngeal LNs, BCS, the use of MBD, age, popliteal lymphadenectomy, maximum diameter, LT, bilateral, left sided lymphadenectomy have a P-value <0.10, and a restricted model only including these variables was then used (Table 2).

Logistic Regression	**P value**	**OR confidence interval at 95%**	**OR**
LT	0.44	0.97 - 1.06	1.01
MBD	0.85	0.32 - 3.93	1.12
Number removed	0.53	0.32 - 3.93	0.83
en bloc Mandibular and Retropahringeal	0.54	0.06 - 200	3.49
BCS	0.82	0.56 - 1.56	0.94
median maximum diameter	0.61	0.97- 1.03	1.00
Age	0.88	0.84 - 1.21	1.01
Popliteal	0.06	0.008-1-16	0.10
SX	0.14	0.72 - 8.72	2.51
Bilateral	0.74	0.10 - 21.9	1.55

Table 2: Logistic regression of the selected variables with p-value ≤ 0.10 in the univariate statistical analysis.

In the multivariate logistic regression, no variables had a statistically significant P-value (<0.05). Looking at the latter regression results, popliteal lymphadenectomy had an OR of 0.1, which indicates that this variable decreases the probability of complication. On the contrary, the *en bloc* excision of mandibular and retropharyngeal LNS and left sided lymphadenectomy, with an OR of 3.49 and 2.6, respectively, were more likely to develop complications.

In order to address the specific question regarding the effect of the surgical time on the occurrence of complications each data points were classified in 3 equal-sized buckets, based on sample quantiles; the first collects data with surgical time less than 10 mins, the second one more than 10 and less than 25 mins and the last one more than 25 mins. (Table 3).

The LT in the class of 10-25 minutes had statistically significant a P-value (0.02), with an OR of 3.2, while in class of LT < 10 minutes the P-value was not statistically significant.
Therefore, as LT increases, the rate of complications increases. In the class above 25 minutes the P-value was slightly higher and the OR was over 1 but lower the previous class. This should be only a spurious data caused by a limited number of cases.

Logistic Regression	P value	OR confidence interval at 95%	OR
LT < 10 minutes	0.53	0.337 – 1.754	0.76
LT between 10 -25 minutes	0.02	1.172 – 8.734	3.20
LT > 25 minutes	0.08	0.896 – 6.071	2.33

Table 3: Logistic regression focused on LT.

In conclusion, given the vast majority of the cases that developed oedema as the only complication, a logistic regression focused only on the presence of oedema was performed. (Table 4).

Logistic Regression	P value	OR confidence interval at 95%	OR
Mandibular	0.74	0.074 – 37.105	1.66
Popliteal	0.15	0.002 – 2.493	0.08
en bloc Mandibular and Retropahringeal	0.62	0.048 – 157.48	2.7
Superifical cervical	0.75	0.045 - 9.516	0.66
Axillary	0.79	0.037 – 7.714	0.67
Inguinal	0.65	0.037 – 7.714	0.54
LT	0.46	0.969 – 1.070	1.01
MDB	0.43	0.388 – 9.135	1.88
median maximum diameter	0.62	0.975 – 1.042	1.0
BCS	0.82	0.617- 1.830	1.06
Palpable	0.87	0.258 – 3.149	0.9
Number removed	0.67	0.472 – 1.622	0.87

Table 4: Logistic Regression focused on Oedema.

When all the predictive variables were included, none of them appeared to be statistically significant. Anyway, the *en bloc* excision of mandibular and retropharyngeal LN with an OR 2.7, MBD with an OR 1.88, and mandibular lymphadenectomy with an OR 1.6 were associated with an increased risk of oedema complications after surgery.

Discussion

Lymphadenectomy is increasingly used in veterinary medicine for any case where histopathologic LN evaluation is needed.

Despite this, there are few studies on postoperative complications secondary to lymphadenectomies in veterinary medicine. Quite the opposite, these complications are well described in human literature and a more conservative approach, compared to complete regional lymphadenectomy, is now being attempted to improve patient's quality of life.

In this study, the authors reported an overall complication rate of 69%, with 36 surgeries out of 64 (56%) that showed at least one complication. These results are similar to those found in the human literature.[26]

Oedema was the most frequent complication and developed in 39 cases (89%) followed by lameness in 3 cases (7%), 1 seroma (2%) and 1 dehiscence (2%); most of these events were self-limiting and resolved in few days.

In this study, 37 surgeries experienced mild complications, two moderate (grade2), that needed oral corticosteroid therapy, and only one case developed severe (grade 3) complication that required a revision surgery.

Oedema occurred on average 1 day after surgery (min: 1, max: 7 days) and it resolved in a mean of 7 days (min:1, max: 21 days; median 5,5).

The *en bloc* excision of mandibular and retropharyngeal LNs (OR= 2.7) and of the mandibular alone (OR =1.66) seemed to increase the risk of oedema, even if these variables were not found to be significative (P value >0.05) in both multivariate and univariate logistic regression. This is probably due to the anatomy of the neck area, which requires a wider surgical exposure and tissue manipulation to reach all LNs. Indeed, the retropharyngeal LNs are located deep in the neck, covered by muscles and in close relation with mandibular salivary gland, hypoglossal nerve and carotid sheath.[30]

The same goes for the use of MBD (OR =1.88). A possible explanation is that the intraoperative use of MBD requires a wider surgical exposure to detect the afferent lymphatic vessel and because authors used the blue dye to detect the LNs considered more difficult to find, as axillary or inguinal.

Lameness had a 7% complication rate. All cases occurred in 3/16 during ALND. Of these, 2/3 were non-palpable LNs, with a maximum diameter less than 18 mm. Lameness occurred on average the day after surgery and it resolved in a median of 2 days (min:1, max: 5).
The relation between ALND and lameness could be explained by the anatomical location of the ALN, being deep in the axilla, at the intersection of *pectoralis profundus* and *latissimus dorsi* muscle and surrounded by muscle as pectoralis, caudal to the brachial vein and in proximity to lateral thoracic nerve, thoracodorsal nerve and intercostobrachial nerve.[25] The lateral thoracic nerve is probably the nerve most at risk during ALND in dogs and its resection would compromise the effective innervation of the deep pectoral and cutaneous truncus muscles, but the deep pectoral is also innervated by the caudal pectoral nerves, which probably preserves its function.

LT was one of the most important variables affecting the occurrence of complications. Above 10 minutes the probability of developing complication increased by 3 times (OR = 3.2).
These results are probably related to the fact that surgical time may increase in difficult cases where identification of the lymph node is not easy, such as if the LN location was deeper or if there were multiple LNs to be removed, or of very small in size, resulting in a more extensive and challenging excision and more manipulation of the surrounding tissues.

Nerve injuries were never reported in this study in case of axillary surgeries, although axillary paresthesia is a very common complication in human patients. [14,15]
The intercostobrachial nerve supplies the skin overlying the long head of the triceps brachii muscle; damage to this nerve would result in loss of sensitivity of the cutaneous area overlying the long head of the triceps brachii muscle[25]. In human medicine there are several studies reporting that the preservation of the interbrachial nerve reduces the incidence of postoperative paresthesia[14]. Beyond the anatomy of ALND, the assessment of neuropathic pain in people relies heavily on self-report, which our veterinary patients are unable to do, so these conditions remain an underestimated morbidity in veterinary patients.[31]
The rare nature of this major nerve damage and the difficulty in the diagnosis of axillary paresthesia in the dog is probably the reason why neurologic dysfunctions were never reported in the case of axillary lymphadenectomy in the study population.

No lymphedema cases were reported in this study, as opposed to what is reported in human patients. [32,33] However, it seems clear that there are differences in the anatomy of the lymphatic system as well as in the anatomic structures associated with the immunity between human and dogs.[34] In fact, one study shows that following a lymphadenectomy, the lymphatic vessels of the obstructed territory drained by the LNS removed, will connect to LNs in adjacent territories and create a spontaneous lymphatic-venous shunt. These collateral vessels are believed to act as bypass to prevent the manifestation of lymphedema. The rerouted vessels are reminiscent of the process of vascular remodeling in flap surgeries, in which choke vessels are dilated and then linked to adjacent territories to compensate for the lost vascular supply in the source territory.[34]

Limitations of this study include the small number of cases enrolled, while the unique aspects included the standardized inclusion criteria and the uniform surgical technique and judgement of the severity of the same complication.

Conclusion

In conclusion, lymphadenectomy of the superficial LNs is associated with a high rate (58%) of self-limiting mild complications, that usually resolve in few days without treatment, and a low rate of moderate (3%) and severe (1.5%) ones.
A prolonged surgical time may affect the complication rate, but the increase of the use of more sophisticated techniques of LN detection may reduce it in a near future. The *en bloc* excision of mandibular and retropharyngeal LNs, mandibular alone LNs and the use of MBD seems to be associated with a higher rate of complications.

Therefore, given the limited number of predictive factors identified in this study, other possible risk factors should be explored in future studies with larger numbers of cases to identify whether there is a statistically significant correlation between complications and some variables. Further prospective studies are needed to validate the results before attempts can be made to develop a clinical prediction rule.

Overall, lymphadenectomy can be considered a safe and easy procedure for qualified surgeons, worth being performed for diagnostic purposes, although a standardized approach to lymphadenectomy of different sites would be needed.

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