Original Article

Mediastinal lymph node distribution, size and number: definitions based on an anatomical study*

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Abstract

Objective: To create a reference map of mediastinal lymph nodes through the analysis of their size, number and distribution in various lymph node stations. **Method:** A total of 50 cadavers, 38 males and 12 females, were studied. Of those 50, 39 were Caucasian. The mean age was 59.9 ± 14.1 years, the mean height was 173.1 ± 7.6 cm, and the mean weight was 71.0 ± 12.0 kg. A bilateral mediastinal dissection was performed in order to resect and isolate all lymph nodes. The area, as well as the major and minor transverse diameters, of each lymph node was determined by radiographic imaging analysis. **Results:** In a sample of 485 stations, 1742 lymph nodes were dissected (2.58 ± 1.89 lymph nodes/station), revealing a mean number of 21.2 ± 8.5 lymph nodes on the right and 13.6 ± 6.3 on the left. The lymph node stations 1, 2R, 4R, 5, and 7 were present in more than 90% of the sample. Only the 4R and 7 lymph node stations were always present. The lymph node stations 2L, 3p, and 8 were present in 32, 36, and 54% of the sample, respectively. Mediastinal lymph nodes were present in greater numbers in the 2R, 4R and 7 lymph node stations. In addition, these stations presented the largest mediastinal lymph nodes. **Conclusion:** Composing a reference map for lymph node sizes was feasible. No alterations were observed in the distribution, number, or size of lymph nodes in the age brackets studied, regardless of gender, race, weight, or height.

Keywords: Lymph nodes; Mediastinum; Cadaver; Anatomy.

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Introduction

The importance of a study of the mediastinal lymph node groups derives from their active involvement in various neoplastic and infectious processes. Mediastinal lymph node enlargement is a well known characteristic of such situations.

However, the distribution, size, and number of the mediastinal lymph nodes have yet to be clearly defined. This results from the great variability in the distribution of lymph nodes in certain mediastinal regions. In addition, there is no systematization in the dissection of lymph nodes, previous studies having used different designations for each region. This, together with the fact that different techniques, such as autopsy, thoracic surgery, and chest X-ray, have been employed to study the lymph node stations, has made it difficult to draw comparisons among the results.

In addition, the concept of lymph node enlargement is fundamental to the understanding of several diseases. Although there is controversy regarding the definition of an ideal value, various authors have adopted a maximum of 1 cm on the short axis to define normal lymph node size.[1-6] However, the patient samples evaluated in Brazilian studies of diseases with mediastinal lymph node involvement are not comparable in size to those evaluated in American, English, and Japanese studies.

One single anatomical study to determine the size and number of mediastinal lymph nodes, conducted in Japan, involved 40 cadavers.[7] The authors observed that the larger lymph nodes were located in the subcarinal station (station 7), followed by the tracheobronchial station (station 10R), equivalent to station 4R on the map created by the American Thoracic Society. The mediastinal lymph nodes were larger in the inhabitants of the urban zone than in those of the rural zone, suggesting that local factors can alter these characteristics.[7]

There seems to be some factor that interferes in the size of the lymph nodes of Brazilians. A study carried out with the aim of comparing the role of computed tomography and mediastinoscopy in the mediastinal lymph node staging in lung cancer showed that only 23% of the lymph nodes larger than 20 mm in diameter presented neoplasia, compared with over 80% for lymph nodes of the same size in the Japanese, American and European populations. This could be attributed to the fact that, due to the high incidence of inflammatory diseases in Brazil, mediastinal lymph node enlargement is common in this population.[8,9]

The definition of the size and number of mediastinal lymph nodes found after anatomical dissection has not been established. Studies on lymph node drainage still need to define the number of lymph nodes, which would serve as a reference to characterize the radicality of the resection.

Based on the localization of each lymph node in the anatomical examination of the mediastinum, it is possible to define their distribution, size, and number in the various mediastinal stations. In the present study, we will attempt to determine whether any of the data collected correlate with age, gender, weight, height, race, or cause of death. It will soon be possible to establish a reference map to be used as a standard of normality for the population studied.

Methods

A total of 50 adult cadavers, in which death was not the direct result of diseases with mediastinal lymph node involvement, were dissected during the period from March of 2001 to June of 2003. Of those 50 cadavers, 38 (76%) were males. The age ranged from 36 to 90 years (mean, 59.9 ± 14.1 years; median, 60 years). Thirty-nine were White, seven were Black, and four were of mixed ethnicity. Heights ranged from 150 cm to 185 cm (mean, 173.1 ± 7.6 cm). Weights ranged from 31 to 114 kg (mean, 71 ± 12 kg). In 50% of the cases, the ultimate cause of death, determined in the autopsy, was pulmonary edema.

This study was conducted according to the guidelines for research involving human beings (health research) established in Brazilian National Health Council Resolution nº 196/96,[10] as well as in Law 8501 (11/30/92), which addresses the use of cadavers. The Ethics Committee for the Analysis of Research Projects of the Clinical Board of the University of São Paulo School of Medicine *Hospital das Clínicas* approved the present study.

Consecutive posterior lateral thoracotomies were performed, and the right mediastinum was initially dissected in the craniocaudal direction. The lymph node dissection was based on the definitions of anatomical repair suggested by the map adopted by the American Joint Committee on Cancer and

the *Union Internationale Contre le Cancer*.[11] The topography of the various mediastinal lymph node stations was preserved by the in situ dissection of the mediastinal structures, according to the modifications of dissection techniques already described.[12] The lymph node dissection and resection was radical, that is, all the lymph nodes were removed, together with the circumjacent mediastinal fat, within the defined anatomical limits. The visceral block of the mediastinum was not removed. This made it possible to maintain the syntropy of the lymph node stations, and their limits, with the anatomical structures and divisions of the mediastinum.

The lymph nodes were fixed in an aqueous solution of formalin and separated from the mediastinal fat tissue by a thorough dissection on a plank, after which they were digitally photographed. The lymph nodes were counted on a per-station basis. The possibility of lymph node shrinkage, as a result of the fixation, was studied in 84 lymph nodes, prior to and after seven days of immersion in 10% buffered formalin solution. Sizes were compared using a nonparametric test. There were no significant differences between the two time points in terms of the dimensions of the lymph nodes.

All of the lymph nodes were embedded in paraffin and identified according to their station. The paraffin blocks containing the lymph nodes identified in each mediastinal station were stained with hematoxylin and eosin for histological study. The observation of the slides under a magnifying loupe allowed the lymph node counts after fixation, in order to determine the presence or absence of lymph node coalescence.

Histological analysis under optical microscopy was performed by an independent pathologist who was blinded as to the cause of death. Lymphatic tissue without active pathological process was identified. In addition, the analysis allowed the separation of nonlymphatic tissues that had been inadvertently included in the dissection. The nonlymphatic tissues were photographed and their images were demarcated. They were then excluded from the measurements.

The images were processed using the Image Toll program for Windows, version 3.0, developed by the Health Science Center of the University of Texas at San Antonio. The measurements were calibrated against a line drawn over a known distance (10 mm) on a millimeter ruler on each image. The perimeter of each lymph node was demarcated, the area was calculated, and the minimum/maximum diameters were measured by the computer.

Regarding the descriptive analysis, the minimum and maximum values were observed, and the calculation of means and standard deviation was used for quantitative variables. The coefficient of variation (standard deviation*100/mean) was calculated in order to determine the parameter that presented the smallest differences among values of comparable dimensions. For the qualitative variables, relative and absolute frequencies were calculated. Regarding the statistical analysis, the homogeneity of the groups in relation to the proportions was tested by using the chi-square test or Fisher's exact test. This was indicated for the comparison of the proportions when the response fields presented expected frequencies <5.

All of the tests were performed at a significance level of 5%.[13]

Results

A total of 485 stations were dissected. The mean presence of the various stations upon mediastinal dissection was 74.6%. Stations 2R, 4R and 7 were the most frequently found upon dissection, being resected in 98 and 100% of the cases. Stations 2L, 3p, and 8, in turn, were found only in 32, 36 and 54% of the cases, respectively.

A total of 1742 lymph nodes were found (mean, 2.58 ± 1.89 lymph nodes per station; mean, 34.8 ± 12.2 lymph nodes per case). The mean number of lymph nodes found in the right mediastinum was 21.2 ± 8.5, compared with 13.6 ± 6.3 in the left mediastinum. The station containing the most lymph nodes was station 2R, accounting for 15.6% of the lymph nodes dissected (Table 1). Over 158 lymph nodes were added to the number of lymph nodes, when recounted on the slide, totaling 1900 lymph nodes. Consequently, 8.3% coalescent lymph nodes were found.

A total of 73.2% of the lymph nodes were oval- or kidney-shaped. Approximately 9.7% presented an irregular or mixed shape. The lymph nodes were rectangular or triangular in 11% of the cases, and elongated or figure-eight shaped in 6.1%.

For the definition of a reference value on the size of the mediastinal lymph nodes per stations, lymph node sizes were determined for the maximum

Table 1 - Number of lymph nodes, including means, standard deviations, and percentages of the total, by station.

Station	Lymph nodes	Mean	SD	%
1	116	2.58	1.89	6.66
2R	276	5.52	4.48	15.84
2L	55	3.24	1.95	3.16
3a	87	2.29	1.56	4.99
3p	36	1.89	1.33	2.07
4R	229	4.58	3.02	13.15
4L	150	3.49	2.93	8.61
5	188	4.09	2.06	10.79
6	210	5.00	3.37	12.06
7	205	4.10	2.68	11.77
8	57	2.04	1.45	3.27
9R	61	2.03	1.71	3.50
9L	72	2.12	1.74	4.13
Total	1742	2.58	1.89	100.00

Table 2 - Maximum standard size per area (long axis and short axis).

Region	Area (mm^2)	Axis (mm)	
		Long	Short
1	117.73	16.23	10.66[a]
2L	80.17	13.53[a]	8.71
2R	149.17	17.79	10.78[a]
3a	188.51	23.42	11.42[a]
3p	112.99	15.35[a]	10.59
4L	124.29	17.74	10.31[a]
4R	268.76[a]	29.54	15.87
5	165.13	19.75	11.68[a]
6	116.77	17.20	9.56[a]
7	348.56[a]	33.30	19.02
8	164.04	23.63	10.67[a]
9L	145.77	18.76	10.53[a]
9R	106.55	17.31	9.19[a]

[a]Values with lower coefficients of variation.

pattern at a 95% confidence interval (mean + 2*SD). We found values for the short axis of over 10 mm in most of the stations, except for stations 2L and 9R. Coefficients of variation per area, short axis, and long axis, were determined in order to choose the type of measurement that presented the least variability. The coefficient of variation expresses the variation percentage for each type of measurement. The measurements of the short axis presented fewer variations in most lymph node stations (Table 2).

We attempted to determine whether the number of lymph nodes correlated with the variables age, weight, and height. We found no significant correlation with any of these factors. Nor was the presence or absence of stations found to correlate with any of these demographic variables.

We also attempted to determine whether gender, race, and congestion were associated with the number of lymph nodes per station. There were no differences between genders or among races regarding the number of lymph nodes. The cadavers were divided into two groups by cause of death (congestive and noncongestive diseases). No difference was found between these two groups in terms of the number of lymph nodes.

The size of the lymph nodes was analyzed by gender, race, and cause of death. These were not associated with the variations in the lymph node sizes. Lymph node size was not found to be correlated with age, height, weight, or coalescence.

The analysis of variance revealed significant difference in the size of the lymph nodes ($p < 0.001$). In a multiple-comparison test, a significant difference was found between station 7 and the remaining stations ($p < 0.05$). Station 4R differed significantly from almost of the other stations ($p < 0.05$), the exceptions being stations 3a, 3p, and 5. The remaining stations did not differ among themselves.

Discussion

This is the first anatomical study conducted in Brazil with the aim of determining the distribution, number, and size of lymph nodes. Although a wider number of studies use tomography, which is a noninvasive procedure with a wide number of patients available, we opted to carry out a dissection study. Since it is a more complicated process, with few cadavers available for study, anatomical studies are fewer in number. Nevertheless, such studies allow the anatomical location to be more clearly defined, and the results are more precise in relation to the definition of size and number. Such studies also allow the histopathological confirmation of lymph node tissue free of active pathological processes.

Most authors who have conducted anatomical studies of mediastinal lymph nodes in Brazil had the objective of elucidating aspects of the treatment and prognosis of the bronchogenic carcinoma.

The number of lymph nodes unilaterally resected during surgical procedures in the treatment of lung neoplasms is smaller when compared to that of specific studies on lymph node dissection. In this study, an average of 21.2 lymph nodes in the right mediastinum, and 13.6 in the left mediastinum, were dissected via thoracotomy. These findings are similar to those of other authors who studied mediastinal lymph nodes (Table 3). Authors who analyzed patients with lung neoplasms found lower numbers of lymph nodes.[7,14,15] This suggests that the mediastinal lymph node drainage is not radical, that a dissection conducted in a cadaver is an easier approach to the mediastinum, or that the histological analysis did not consider coalescence in the lymph node counts.

The lymph node count was affected by fusion or coalescence; therefore, different numbers were found in the count and recount of dissected lymph nodes on the slides. Lymph node fusions were found frequently (in 32.2% of the stations dissected in the present study).

There were no differences in the number of lymph nodes in relation to age or gender, as was suggested in one study.[2] The sample presented a higher mean age. In addition, there were fewer women. This might have resulted in the selection of a population in which the variation in the number of lymph nodes was not significant.

The measurements of the long axis were significantly higher when granulomatous scar tissue was observed in the lymph nodes. The incidence of granulomatous diseases can affect the reference value adopted for the size of the lymph node.

The lymph node sizes were greater than those found by other authors. Figure 1 shows the comparison of the mean sizes of the lymph node short axes observed in the present study and reported by other authors, considering the modifications of the descriptors on the maps of the lymph node stations.

The size of the lymph nodes was not uniform among the stations. Therefore, the short axis means for station 7 were significantly higher than the others. Station 4R presented the second greatest mean, which coincides with the observation made by other authors, who reported a significant difference in the dimension of the lymph nodes located in the upper mediastinum when compared to that of the nodes adjacent to the carina.[20]

Although it was expected that the values obtained for the area would more accurately represent the lymph node size,[2] the measurements presented higher coefficients of variation for most stations. Only the lymph nodes of stations 4R and 7 presented lower variation. Therefore, they represented a safer parameter for the evaluation of the size alterations in large lymph nodes, which were generally irregular. In most mediastinal stations, the short axis is the value with greater reliability. The data we gathered made it possible to define a reference

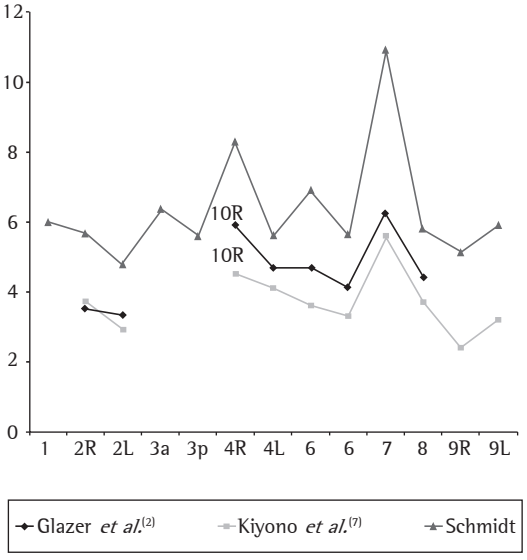

Figure 1 - Mean sizes of the short axis of the mediastinal lymph nodes, by author.

Table 3 - Mean number of mediastinal lymph nodes resected, by author.

Author	Numbers of lymph nodes		Approach
Kiyono *et al.*[7]	30.1 (bilateral)		Thoracotomy
Hoksch *et al.*[16]	31 (bilateral)		Video-assisted thoracoscopy
Namori *et al.*[17]	20 ± 8 (r)[a]	15 ± 3 (l)[a]	Video-assisted thoracoscopy
Sgawa *et al.*[18]	40.3 (r)[a]	37.1 (l)[a]	Video-assisted thoracoscopy
Schmidt[19]	21.2 ± 8.5 (r)	13.6 ± 6.3 (l)	Thoracotomy

[a]Hilar lymph nodes included.

value for the size of the mediastinal lymph nodes by station. For each station, the lymph nodes sizes were determined as the maximum standard value at a 95% confidence interval (mean + 2*SD). The maximum reference values found for the short axis were greater than 10 mm in most stations, except for stations 2L and 9R (Figure 2).

The population studied, comprising Brazilian adults, presented 21.2 ± 8.5 mediastinal lymph nodes on the right and 13.6 ± 6.3 on the left. Stations 1, 2R, 4R, 5, and 7 were present in more than 90% of the cases. Only stations 4R and 7 were always present. Stations 2L, 3p, and 8 were present in 32, 36, and 54% of the cases, respectively. The mediastinal lymph nodes were present in higher numbers in stations 2R, 4R, and 7. These same stations also aggregate the larger mediastinal lymph nodes. The fact that 8.3% of the lymph nodes were coalescent must be considered in the analysis of chest imaging tests and pathological findings.

We were successful in composing a reference map for mediastinal lymph node sizes. No significant alterations were observed in the distribution, number, or size of lymph nodes among any of the age brackets studied, regardless of gender, race, weight, height, or cause of death.

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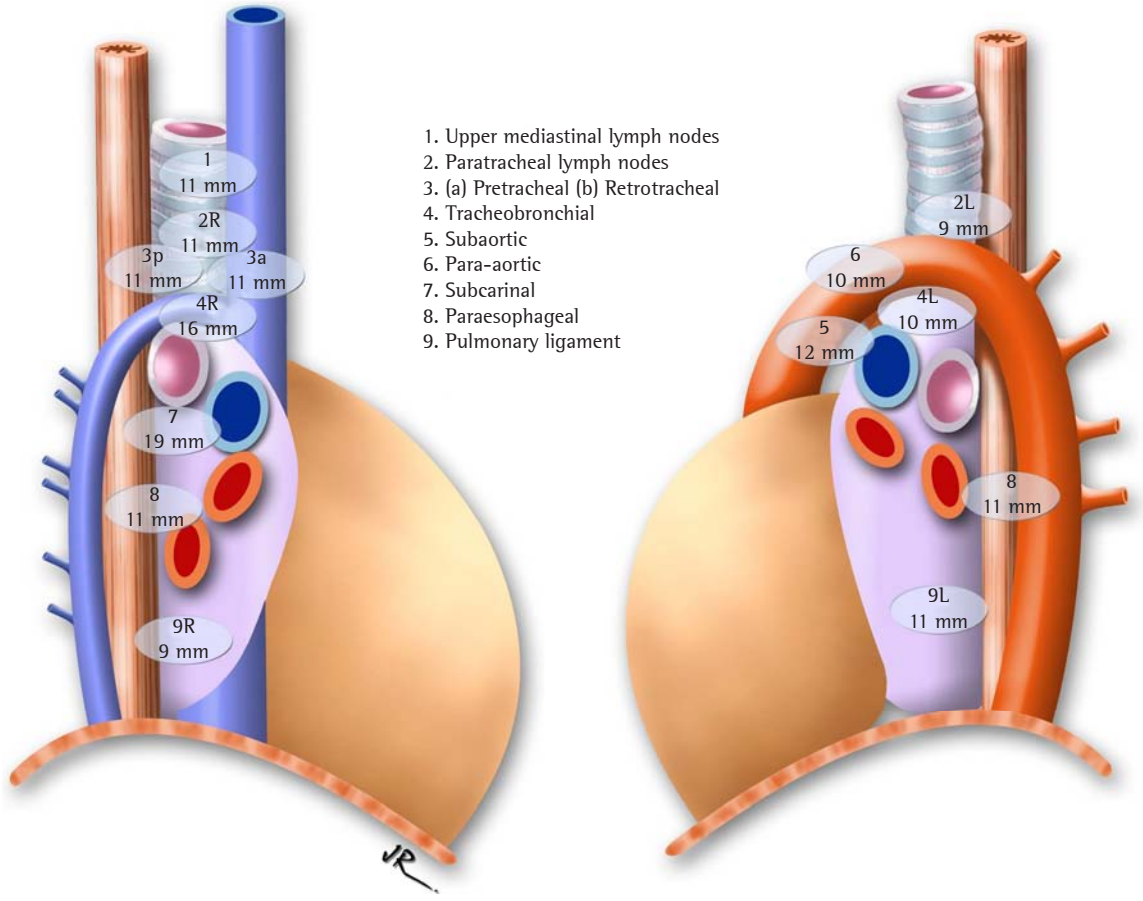

Figure 2 - Map of the mediastinal lymph node stations with the maximum size of the short axis.

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