An Analysis of Lymphographic Signs for Differentiating Cancerous, Lymphomatous, and Normal Lymph Nodes

立崎，英夫；中島，禎一；奧村，敏之；秋貞，雅祥

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Osaka University
An Analysis of Lymphographic Signs for Differentiating Cancerous, Lymphomatous, and Normal Lymph Nodes

Hiče Tatsuzaki, Teiichi Nakajima, Toshiyuki Okumura and Masayoshi Akisada
Department of Radiology, Institute of Clinical Medicine, University of Tsukuba

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Key Words: lymphography, Multivariate analysis, Heshi's quantification scaling

Introduction

Currently, computed tomography (CT) is commonly used for the detection of lymph node metastases or involvements. However, the resolution of CT image is limited, thus CT is not adequate for revealing fine structure. On the contrary, lymphograms give us a direct image, thus enabling us to obtain more precise information about internal structure.

In order to determine what the important factors are and to make differential diagnosis more systematically, we studied lymphographic signs. Two hundred and four lymph node images were chosen from among...
lymphograms of cancerous, malignant lymphomatous or normal patients. Each lymph node was studied with respect to 24 factors, i.e. items. In order to differentiate among cancerous, malignant lymphomatous, and normal lymph nodes, the data were analyzed through univariate analysis using correlation coefficient and Hayashi's quantification scaling type 2 multivariate analysis. We derived discriminant functions from the results.

Materials and Methods

Two hundred and four evaluable lymph nodes were chosen for analysis from the lymphograms. Based on pathological or follow-up examinations, 51 of them were diagnosed ultimately as cancerous, 59 as malignant lymphomatous, and 94 as normal. Lymph nodes of reactive benign changes were excluded from this study.

Examinations

By means of Kinmonth's method, a 15mm skin incision was made on both pedals, and the lymph vessels were prepared for infusion. After puncturing the lymph vessels gently with a small needle, an oily contrast medium was infused directly into the lymph vessels. Five ml of Lipiodol Ultrafluid® was administered via an infusion pump in a period of 50 minutes. Radiograms were then taken, at two different phases. One was a lymph-vascular phase lymphogram, which primarily revealed the lymph vessels, and the other was a lymph nodal phase lymphogram. Four directional views were taken below the diaphragm level and two views were taken above the diaphragm.

Regions of interest were analyzed by macroradiography. Macroradiography was conducted with a Toshiba Macro-Stereography Unit DRX-431HD. The conditions were as follows: Focus=50 micrometer,
Table 2  Categories

Item 1, Clinical diagnosis
Category  1. Bladder cancer
          2. Prostate cancer
          3. Cervical cancer
          4. Endometrial cancer
          5. Ovarian cancer
          6. Testicular tumor
          7. Malignant melanoma
          8. Paget's disease of pubis
          9. Squamous cell cancer of skin
         10. Cancer other than above
         11. Hodgkin's disease
         12. Non-Hodgkin's disease
         13. Suspected malignant lymphoma
         14. Benign disease other than above

Item 2, Region
Category  1. Lumbar paraaortic lymph node
          2. Common iliac lymph node
          3. External iliac lymph node
          4. Internal iliac lymph node
          5. Rosenmüller's lymph node
          6. Deep inguinal lymph node
          7. Superficial inguinal lymph node
          8. Axillary lymph node
          9. Others

Item 3, Nodal size*
Category  1. Enlargement
          2. Minimal enlargement
          3. Normal
          4. Small
**5. Indeterminable
   * in comparison with the normal range
   ** for example, a lymph node in which
   the defect is too large to determine the
   size.

Item 4, Nodal shape
Category  1. Circular shape from both frontal and
          lateral (oblique) views ** (spheroid type)
          2. Circular shape from frontal view, flat
             shape from lateral (oblique) view **
             (saucer type);
          3. Elliptic shape from both frontal and
             lateral views
          4. Elliptic shape from frontal view, flat
             shape from lateral (oblique) view
          5. Others
             * Category 2 includes lymph nodes that
             are round from the frontal view and
             flat from the lateral view.

Item 5, Deformity
Category  1. Deformity is detected
          2. Deformity is not detected
          *3. Equivocal
**4. Indeterminable
   * Category 3 includes lymph nodes for
   which it is not possible to determine
   whether the deformity is in the lymph
   node itself or is a marginal defect.
** Category 4 includes lymph nodes that
   are too small to discriminate.

Item 6, Conglomeration
Category  1. Detected
          2. Uncertain
          3. Equivocal
          4. Indeterminable

Item 7, Granularity
Category  1. Fine granular
          2. Coarse granular
          *3. Others
             * Category 3 includes lymph nodes which
             have defects large enough to make its
             inner structure unrecognizable.

Item 8, Deficiencies in capsules
Category  1. Irregularities or deficiencies in cap-
           sules or marginal sinuses are detected.
          2. Uncertain
          3. Equivocal
          4. Indeterminable

Item 9, Size of defect
Category  1. Minimal
          2. Half of the node
          3. Most part of the node
          4. Almost all of the node

Item 10, Character of defect
Category  1. Predominantly marginal
          2. Predominantly central
          3. Both marginal and central
          4. Complete defect

Item 11, Special pattern
Category  1. Single central defect
          2. Microlacunary pattern
          3. Coarse granular pattern
          4. Lacy pattern
          5. Foamy pattern
          6. Category 4 mixed with 5
          7. Crescent type or rim sign
          8. Complete defect
          9. Hal sign
          10. Necrosis droplets
          11. Microlacunary defect
          12. Greasy pattern
          13. No such pattern
          14. Indeterminable

Item 12, Sharpness of defect
Category  *1. Sharp margin
          2. Invasive margin
          3. Indeterminable
             * including microlacunary pattern

Item 13, Nodal contrast(compared with the other
         lymph node in same region)
Category  1. Thick
          2. Normal
          3. Thin

Item 14, Ectopic lymph node
Category  1. Detected
2. Undetected

Item 15. Early visualization of the lymph node
Category 1. Early visualization
2. Normal
3. Late visualization
4. Equivocal
5. Indeterminable

Item 16. Block of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 17. Stasis or preservation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 18. Encasement of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 19. Capillary nets of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 20. Extravasation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 21. Number of lymph vessels
Category 1. Increase
2. Normal
3. Decrease
4. Indeterminable

Item 22. Dislocation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 23. Collateral lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 24. Defect in lymph vascular and nodal phase
Category 1. Combination
2. Isolation
3. Equivocal
4. Indeterminable

Item 25. Soft tissue shadow
Category 1. The defect is visualized as a positive soft tissue shadow and there are lymph vessels around the node.
2. The defect is visualized as a positive soft tissue shadow and there are no lymph vessels around the node.
3. The defect is visualized as a positive soft tissue shadow but lymph vessels are indeterminable.
4. A soft tissue shadow is not detected.
5. Indeterminable, due to bone shadow or smallness of lymph nodes.

Item 26. Final diagnosis
Category 1. Metastasis of cancer
2. Involvement of malignant lymphoma
3. Normal or benign change

Magnifying power = 2.5, FFD = 105 cm, voltage = 90 kVp (routinely), current = 10mA, exposure time = 1.6 second. Three directional views were taken for each lesion.

Analysis

Each lymph node was examined by two radiologists (T.N. and M.A.) with respect to 24 items listed in Table 1 (Item 3—26). Each item has categories as shown in Table 2 and one category was chosen for each lymph node. Some of the signs in Table 2 are shown in the figures. 'Item 4. Nodal shape'—'Category 1. Circular shape from two projections' and 'Category 3. Elliptic shape from two projections' are shown on Fig. 3. 'Item 8. Deficiencies in capsules'—'Category 1. Irregularities or deficiencies in capsules or marginal sinuses' are shown on Fig. 3. 'Item 11. Special pattern'—''Category 4 and 5. Lacy pattern and foamy pattern' are shown in Fig. 1. 'Item 11. Special pattern'—'Category 10. Necrosis dropless' means a round deposit of contrast material in defect. Item 13. Nodal contrast' is shown in Fig. 4. 'Item 15. Early visualization of the lymph node' is shown in Fig. 1. 'Item 17. Stasis or preservation of lymph vessels' is shown in Fig. 2b. 'Item 24. Defect in lymph vascular and nodal phase'—'Category 1. Combination' is shown in Fig. 2. 'Item 25. Soft tissue shadow' is shown in Figs. 1 and 5.

The data were analyzed by univariate analysis and multivariate analysis. A four-fold point correlation coefficient between each category and 'Final diagnosis' was calculated in order to reveal typical signs for diagnosis. (See Appendix)

For deriving discriminant functions, Hayashi's quantification scaling (type 2) multivariate analysis was used. An SPSS (Statistical Package for the Social Sciences) program was employed for the analysis on...
Fig. 1 Lymph node involved with malignant lymphoma. a: lymph-vascular phase, b: Nodal phase. Enlarged nodal size, lacy and foamy pattern, early visualization of the lymph node. Dislocation of lymph vessels (arrow), soft tissue shadow (arrowhead) are observed.

Fig. 2 Lymph node metastasis from ureteral cancer. a: lymph-vascular phase, b: Nodal phase. Stasis or preservation of lymph vessels (arrow) and combination defects (arrowheads) are observed.
Fig. 3 Lymph node metastasis from malignant melanoma. a: RAO, b: LAC. Irregularities or deficiencies in capsules or margins, sinuses (arrow), elliptic shape from two projections (arrow), circular shape from two projections (arrowhead) are observed. Contrast material after hysteroscopy remained in the pelvic space.

Fig. 4 Lymph node involved with malignant lymphoma: Nodal phase. Thick contrasted lymph nodes are observed (arrow).
main frame computer Fujitsu M-380 at University of Tsukuba. The 'Final diagnosis' was established as an outside criterion, and analysis was made between two groups at a time: Cancer-normal, malignant lymphoma-normal, cancer-malignant lymphoma. Variables were selected from the 23 items in a stepwise fashion. The item making the greatest contribution to the separation of the groups was chosen to be the first variable. After it was entered into the discriminant function, the variable with the next largest correlation ratio was selected, and so on, until 5 variables were ranked according to their relative discriminatory importance. Based on the 5 variables, we derived the optimal discriminant function.

Results

Univariate analysis

With regard to the discrimination between cancerous and normal lymph nodes, categories with a four-fold point correlation coefficient greater than 0.6 are showed in Table 3a. As for the discrimination between malignant lymphomatous and normal ones, such categories are showed in Table 3b. As for the discrimination between cancerous and malignant lymphomatous ones, the category which has a correlation coefficient of over 0.4, is only 'marginal defect'. The correlation coefficient of this category is ±0.54 and the category is typical for cancer.

Multivariate analysis

The five most important discriminant items were found to be as follows (in order of discriminatory importance). For the differentiation between cancerous and normal lymph nodes, 'Defect in lymph-vascular and nodal phase', 'Special pattern', 'Granularity' 'Nodal shape', and 'Stasis or preservation of lymph vessels' were found to be important. For distinguishing between malignant lymphomatous and normal lymph nodes,
Table 3a. Factor with four-fold point correlation coefficient greater than 0.6 at discrimination between cancer and normal

<table>
<thead>
<tr>
<th>Factor</th>
<th>Corr. coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enlarged nodal size</td>
<td>+0.60</td>
</tr>
<tr>
<td>Irregularities or deficiencies in capsules or marginal sinuses</td>
<td>+0.68</td>
</tr>
<tr>
<td>Block of lymph vessels</td>
<td>+0.62</td>
</tr>
<tr>
<td>Extravasation</td>
<td>+0.72</td>
</tr>
<tr>
<td>Combination defect in both phase</td>
<td>+0.77</td>
</tr>
</tbody>
</table>

Table 3b. Factor with four-fold point correlation coefficient greater than 0.6 at discrimination between malignant lymphoma and normal

<table>
<thead>
<tr>
<th>Factor</th>
<th>Corr. coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enlarged nodal size</td>
<td>+0.71</td>
</tr>
<tr>
<td>Elliptic shape from 2 projections</td>
<td>+0.76</td>
</tr>
<tr>
<td>Irregularities or deficiencies in capsules or marginal sinuses</td>
<td>+0.79</td>
</tr>
<tr>
<td>Extravasation</td>
<td>+0.71</td>
</tr>
</tbody>
</table>

'Deficiencies of capsules', 'Nodal shape', 'Special pattern', 'Dislocation of lymph vessels', and 'Nodal contrast' were found to be valuable. In differentiating between cancerous and malignant lymphomatous lymph nodes, 'Character of defect', 'Special pattern', 'Deforrricity', 'Soft tissue shadow', and 'Nodal shape' were important.

The discriminant functions are expressed by the following formula:

\[ Y = X1 + X2 + X3 + X4 + X5 \] (Positive Y indicates the former diagnosis)

The numeric values of each X are presented in Table 4a, Table 4b, and Table 4c.

Discussion

Lymphography provides more information concerning lymph nodes than CT. This information deals mainly with internal structure of lymph nodes or lymph vessels, and is useful for determining whether a lymph node is cancerous, malignant lymphomatous or normal. Furthermore, we can use this information for the detection of minimal nodal involvement with malignant lymphoma. Therefore, analyses of lymphographic findings and the derivation of a discriminant function were thought to be useful for making more accurate diagnosis possible.

Four-fold point correlation coefficient has almost the same meaning as Pearson's correlation coefficient. Thus, the factors chosen by univariate analysis indicate the typical character of lymph nodes afflicted by each disease. The categories chosen for discrimination between cancerous and malignant lymphomatous lymph nodes are in accordance with results of previous studies. In these factors, 'extravasation' and 'combination defect' have very high correlation coefficients. These two factors are highly specific for cancer. In the discrimination between malignant lymphomatous and normal, 'elliptic shape from two projections' showed a high correlation coefficient with lymphoma, in contrast to cancer. This reveals that lymph nodes of malignant lymphoma tend to become spherical. Wiljasalo has reported that cancerous lymph nodes tend to become spherical. In the results of this study, the correlation coefficient between cancer and 'elliptic shape from two projections' was slightly high, +0.48. But this sign was more closely related to malignant lymphoma (correlation coefficient = +0.76) in the discrimination between cancerous and malignant lymphomatous lymph nodes, there was no category which showed a strong correlation. It follows that lymph nodes of these two diseases have similar character.

The multivariate analysis identified the items with the greatest value for discrimination. They were...
<table>
<thead>
<tr>
<th>Table 4a Numeric values for differentiation of cancer from normal</th>
<th>numeric value</th>
</tr>
</thead>
<tbody>
<tr>
<td>X1: Item 24, Defect in lymph-vascular and nodal phase</td>
<td>Category 1: 0.586</td>
</tr>
<tr>
<td></td>
<td>Category 2: -0.307</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.370</td>
</tr>
<tr>
<td></td>
<td>Category 4: -0.208</td>
</tr>
<tr>
<td>X2: Item 11, Special pattern</td>
<td>Category 1: -0.355</td>
</tr>
<tr>
<td></td>
<td>Category 2: 0.201</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.300</td>
</tr>
<tr>
<td></td>
<td>Category 4: -0.283</td>
</tr>
<tr>
<td></td>
<td>Category 5: 0.300</td>
</tr>
<tr>
<td></td>
<td>Category 6: 0.377</td>
</tr>
<tr>
<td></td>
<td>Category 7: -0.302</td>
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<td></td>
<td>Category 8: 0.367</td>
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<td></td>
<td>Category 9: 0.485</td>
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<tr>
<td></td>
<td>Category 10: -0.263</td>
</tr>
<tr>
<td></td>
<td>Category 11: -0.256</td>
</tr>
<tr>
<td></td>
<td>Category 12: -0.285</td>
</tr>
<tr>
<td></td>
<td>Category 13: 0.000</td>
</tr>
<tr>
<td></td>
<td>Category 14: 0.000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4c Numeric values for differentiation of cancer from malignant lymphoma</th>
<th>numeric value</th>
</tr>
</thead>
<tbody>
<tr>
<td>X4: Item 22, Dislocation of lymph vessels</td>
<td>Category 1: 0.357</td>
</tr>
<tr>
<td></td>
<td>Category 2: -0.144</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.257</td>
</tr>
<tr>
<td></td>
<td>Category 4: 0.229</td>
</tr>
<tr>
<td>X5: Item 13, Nodal contrast</td>
<td>Category 1: 0.152</td>
</tr>
<tr>
<td></td>
<td>Category 2: -0.197</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.175</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4b Numeric values for differentiation of malignant lymphoma from normal</th>
<th>numeric value</th>
</tr>
</thead>
<tbody>
<tr>
<td>X3: Item 7, Granularity</td>
<td>Category 1: -0.198</td>
</tr>
<tr>
<td></td>
<td>Category 2: 0.452</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.385</td>
</tr>
<tr>
<td>X4: Item 4, Nodal shape</td>
<td>Category 1: 0.375</td>
</tr>
<tr>
<td></td>
<td>Category 2: -0.311</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.344</td>
</tr>
<tr>
<td></td>
<td>Category 4: -0.284</td>
</tr>
<tr>
<td></td>
<td>Category 5: -0.159</td>
</tr>
<tr>
<td>X5: Item 17, Steal or preservation of lymph vessels</td>
<td>Category 1: 0.154</td>
</tr>
<tr>
<td></td>
<td>Category 2: -0.145</td>
</tr>
<tr>
<td></td>
<td>Category 3: 0.354</td>
</tr>
<tr>
<td></td>
<td>Category 4: 0.309</td>
</tr>
</tbody>
</table>

| X1: Item 10, Character of defect                                              | Category 1: 0.228 |
|                                                               | Category 2: -0.311 |
|                                                               | Category 3: 0.255 |
|                                                               | Category 4: 2.252 |

| X2: Item 11, Special pattern                                                 | Category 1: 0.060 |
|                                                               | Category 2: -0.555 |
|                                                               | Category 3: 0.060 |
|                                                               | Category 4: -0.317 |
|                                                               | Category 5: -0.714 |
|                                                               | Category 6: -0.453 |
|                                                               | Category 7: 0.099 |
|                                                               | Category 8: 1.663 |
|                                                               | Category 9: -0.600 |
|                                                               | Category 10: 0.878 |
|                                                               | Category 11: -0.071 |
|                                                               | Category 12: -1.568 |
|                                                               | Category 13: 0.748 |
|                                                               | Category 14: -1.232 |

| X3: Item 5, Defibrininity                                                    | Category 1: -1.233 |
|                                                               | Category 2: -1.099 |
|                                                               | Category 3: -1.188 |
|                                                               | Category 4: 2.748 |

| X4: Item 25, Soft tissue shadow                                              | Category 1: 3.585 |
|                                                               | Category 2: -0.090 |
|                                                               | Category 3: -3.883 |
|                                                               | Category 4: 3.368 |
|                                                               | Category 5: -3.393 |

| X5: Item 4, Nodal shape                                                     | Category 1: 0.621 |
|                                                               | Category 2: 0.600 |
|                                                               | Category 3: 0.047 |
|                                                               | Category 4: -0.234 |
|                                                               | Category 5: -0.435 |
Defect in lymph-vascular and nodal phase for cancer-normal differentiation, deficiencies in capsules for lympho-lemnormal differentiation, and 'character of defect' for cancer-lymphoma differentiation. These factors have been said to be important. 'Deficiencies in capsules' is implicated in destruction of internal structure. Therefore, it is important to make a minute examination of the lymph node. The items chosen are different from that of the univariate analysis. The reason is that intercorrelations between categories influenced the results of multivariate analysis. Therefore, unnoticed items such as 'nodal contrast' were involved in the discriminant functions. However, these factors give the most effective discriminant functions. By these functions, our examined lymph nodes were diagnosed with an accuracy of 98.6%, 98.7%, and 91.8% for cancer-normal, lymphoma-normal, and cancer-lymphoma differentiation, respectively. The efficacy of these functions should be confirmed further with other data not included in this study.

Appendix

The four-fold point correlation coefficient (r) was calculated with the below formula as showed in Table 5.

\[
r = \frac{f_{11} \cdot f_{22} - f_{12} \cdot f_{12}}{\sqrt{n_1 \cdot n_2 \cdot n_3 \cdot n_4}}
\]

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5 Example of point correlation coefficient

References