

Lymphographic-Histologic Correlation in Patients with Hodgkin's Disease and Non-Hodgkin's Lymphoma Undergoing Staging Laparotomy

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Summary

This report briefly describes the results of an on-going prospective study of the accuracy of lymphography in unselected, previously untreated patients with Hodgkin's disease and non-Hodgkin's lymphoma. Careful lymphographic-histologic correlation of material obtained at staging laparotomy revealed a diagnostic accuracy of greater than 90%. Almost all errors occurred as false-positive diagnoses.

Since 1968, patients with previously untreated, biopsy proven Hodgkin's disease have been admitted to a treatment protocol in which lymphography followed by staging laparotomy is part of the pre-treatment staging (4). More recently, beginning July 1971, patients with previously untreated, biopsy proven non-Hodgkin's lymphoma have entered a treatment protocol which also employs lymphography followed by staging laparotomy (5). An essential feature of these protocols is that the patients are consecutive and not selected in any manner. Bipedal lymphography is performed in all patients, unless medically contraindicated. At times, patients in these protocols will not undergo laparotomy if there is documented stage IV disease; or, if the patients are considered too ill for such a procedure.

At the time of laparotomy, an attempt was made to biopsy those lymph nodes which were of most concern on the lymphogram; as well as any lymph node which appeared suspicious to the surgeon during exploration. Metallic clips were placed at the various biopsy sites so that post-operative abdominal roentgenograms clearly defined which lymph nodes had been surgically removed. Thus, an accurate and detailed radiologic-histologic correlation could be made.

Beginning January 1970, a prospective study was undertaken to determine lymphographic accuracy in Hodgkin's disease; and, beginning July 1971, a similar study was initiated in the non-Hodgkin's disease; and, beginning July 1971, a similar study was initiated in the non-Hodgkin's lymphomas. Both groups consist of patients with biopsy proven and previously untreated disease. Also, these patients represent a consecutive, non-selected population studied in a prospective fashion.

The lymphograms were interpreted and placed into one of three diagnostic categories: (1) normal; (2) abnormal due to non-specific changes, such as various types of reactive hyperplasia, fibrosis, fatty infiltration, etc. ("benign change"); and (3) abnormal due to tumor. No "equivocal" diagnostic category was utilized.

Lymphograms in Hodgkin's Disease (Table 1)

From January 1970 through December 1972, 176 unselected patients with previously untreated Hodgkin's disease were admitted to this study. In 16 patients, no opacified lymph nodes were removed, most often because a staging laparotomy was not performed or the laparotomy was performed prior to the lymphogram. In 11 patients the lymph nodes of radiographic concern were not excised, and therefore no lymphographic-histologic correlation could be made. Therefore, 149 patients remained for analysis.

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Table 1. Lymphographic-histologic correlation in 176 consecutive patients with Hodgkin's Disease

Exclusions - No opacified nodes excised 16
 - Inappropriate nodes removed 11
 27

		Lymphographic Diagnosis		
		Normal	Benign Δ	Tumor
Histology	(Jan. 1970 - Dec. 1972)			
	Normal (89)	87	0	2
	Benign changes (21)	0	11	10
	Tumor (39)	0	0	39
Total (149)		87	11	51

↓	↓
98	51
(0 false neg)	(12 false pos)
100%	76%
(92%) Overall accuracy	

Of 87 lymphograms interpreted as being normal, there was histologic confirmation in all. Likewise, in 11 studies interpreted as representing "benign changes", non-specific reactive changes were histologically confirmed in all instances. Therefore, of 98 lymphograms interpreted as not representing tumor, there was histological confirmation in all (100% accuracy), with no false-negative studies.

However, of 51 lymphograms interpreted as representing tumor, there was histologic confirmation in only 39 (76% accuracy), with twelve false-positive studies. In 10 cases the excised lymph nodes demonstrated non-specific histologic reactive alterations. The lymph nodes from the remaining two patients whose lymphograms were considered representative of tumor were, in fact, unremarkable histologically.

The overall lymphographic accuracy, therefore, in this group of 149 patients was 92%. All errors occurred as false-positive studies.

Lymphography in Non-Hodgkin's Lymphoma (Table 2)

From July 1971 through September 1972, 92 unselected, previously untreated patients with non-Hodgkin's lymphoma were entered into this study. In 23 patients, no opacified lymph nodes were excised, the vast majority being in patients with pre-existing documented stage IV disease. In six patients, the lymph nodes of radiographic concern were not removed at the time of surgery. Therefore, a lymphographic-histologic correlation could not be performed in these 29 patients, leaving 63 patients in whom this analysis could be carried out.

Of 30 lymphograms interpreted as being normal, there was histologic confirmation in 29. The one false-negative study represented a case in which there was microscopic involvement of several para-aortic lymph nodes, where the tumor did not alter the macroscopic

Table 2. Lymphographic-histologic correlation in 92 consecutive patients with non-Hodgkin's lymphoma

Exclusions	- No opacified nodes excised	23
	- Inappropriate nodes removed	<u>6</u>
		29

		Lymphographic Diagnosis		
		Normal	Benign Δ	Tumor
Histology	Normal (29)	29	0	0
	Benign changes (6)	0	2	4
	Tumor (28)	1	0	27
	Total (63)	30	2	31

↓
↓
32
31
(1 false neg)
(4 false pos)
97%
87%
(92%
)
(overall accuracy)

appearance of the node. In two patients, the lymphographic diagnosis of "benign change" was histologically confirmed. Therefore, of 32 lymphograms interpreted as not representing tumor, there was one false-negative study (97% accuracy).

Of 31 lymphograms interpreted as representing tumor, there was histologic confirmation in 27 (87% accuracy). The four false-positive studies were all associated with lymph nodes which demonstrated pronounced nonspecific reactive changes histologically.

Therefore, the overall accuracy in non-Hodgkin's lymphoma was 92%, with most errors occurring as false-positive studies.

Discussion

The role of lymphography in Hodgkin's disease and non-Hodgkin's lymphoma has been reassessed with the advent of the staging laparotomy (1). We disagree with the argument that [1] the lymphogram is unnecessary since surgical biopsies will be undertaken in any case and [2] the lymphogram is too inaccurate to provide meaningful information. Regarding the former statement, not only does the lymphogram serve as guide to surgical sampling and in radiotherapy treatment field planning; but, in the post-treatment follow-up period, changes in residually opacified retroperitoneal lymph nodes play an irreplaceable role in the diagnosis of relapse. Indeed, 15% of our patients with Hodgkin's disease who suffered relapse had their initial relapse detected only by radiographic changes in their opacified retroperitoneal lymph nodes (2).

The importance of the lymphogram to guide surgical sampling cannot be overemphasized, since involvement is commonly focal and not readily detected by surgical palpation.

Also, the limitations of surgery are such that even with the lymphogram as intraoperative guidance, the appropriate lymph nodes are not biopsied in a substantial number of instances. In this study, there were 17 cases in which the excised lymph nodes were not those of concern on the lymphogram. These 17 patients, representing 7% of those undergoing laparotomy, were excluded from the analysis concerning accuracy. In these patients, those specific lymph nodes which were removed appeared normal lymphographically; and were histologically unremarkable in each case.

Regarding the second statement, our experience with consecutive, unselected, previously untreated patients with Hodgkin's disease and non-Hodgkin's lymphoma indicates a greater than 90% overall lymphographic accuracy. Of interest is that most errors occurred in the false-positive category. The reasons for a less favorable accuracy rate noted in other studies with laparotomy correlation might be attributed to one or more of the following: [1] the lack of routine utilization of lymphography in the initial evaluation of every patient; [2] the inclusion of previously treated patients in the study group; [3] the performance of laparotomy in selected cases, the basis for selection at times being difficult or bizarre appearing lymphograms; [4] the lack of detailed correlation with a postoperative abdominal radiograph to determine whether or not the lymph nodes of radiographic concern were in fact biopsied; [5] substantial time lapses between performance of the lymphograms and the laparotomy; and [6] the labeling of a lymphogram interpreted as normal as being a "false-negative" when the para-aortic lymph nodes are histologically normal, but tumor is found in lymph node groups not opacified by lymphography, such as those in the splenic hilus, mesentery, and porta hepatis.

Table III. Lymphographic accuracy in Hodgkin's Disease and non-Hodgkin's lymphoma

	True Negative	True Positive	Benign Change/ False Positive
Hodgkin's Disease	98/98 (100%)	39/51 (76%)	10/12 (85%)
non-Hodgkin's lymphoma	31/32 (97%)	27/31 (87%)	4/4 (100%)
	129/130 (99%)	66/82 (80%)	14/16 (88%)
	195/212 (92%)		

Conclusion

To summarize our experience (Table 3), lymphographic accuracy in unselected, previously untreated patients with Hodgkin's disease and non-Hodgkin's lymphoma had a greater than 90% overall accuracy. Those studies interpreted as demonstrating no evidence of tumor had a virtual 100% accuracy rate. Virtually all errors occurred as false-positive interpretations. It is of interest that in the majority (88%) of the biopsied lymph nodes which were incorrectly interpreted as containing lymphoma on the lymphogram, pronounced "reactive" changes were seen histologically. The causes for these false-positive studies are being investigated, with the hope that they will become suitable for analysis and lymphographic recognition so as to further increase lymphographic accuracy in Hodgkin's disease and the malignant lymphomas (3).

References

- 1 *Castellino, R.A., and N. Blank*: Roentgenologic aspects of Hodgkin's Disease I: Current role of lymphangiography. International Symposium on Hodgkin's Disease. National Cancer Institute Monographs No. 36 (in press)
- 2 *Castellino, R.A., N. Blank, J.R. Cassady and H.S. Kaplan*: Roentgenologic aspects of Hodgkin's Disease II. Role of routine radiographs in detecting initial relapse. *Cancer* 31 (1973) 316-323
- 3 *Castellino, R.A., M. Billingham and R.F. Dorfman*: Benign reactive lymph nodes as a cause of (most) false positive lymphograms in Hodgkin's Disease and malignant lymphoma. (Submitted for publication.)
- 4 *Glatstein, E., H.W. Trueblood, L.P. Enright, S.A. Rosenberg and H.S. Kaplan*: Surgical staging of abdominal involvement in unselected patients with Hodgkin's Disease. *Radiology* 97 (1970) 425-432
- 5 *Goffinet, D.R., R.A. Castellino, H. Kim, R.F. Dorfman, Z. Fuks, S.A. Rosenberg, T. Nelsen, and H.S. Kaplan*: Staging laparotomies in unselected previously untreated patients with non-Hodgkin's lymphomas. *Cancer* (in press)

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Lymphographic Demonstration of the Inferior Epigastric Lymphatics: A Case Report

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Summary

The inferior epigastric lymph nodes and vessels were demonstrated by foot lymphography in a patient without obstruction of the main iliac lymph flow. Histologic examination of the ipsilateral iliac lymph nodes showed normal findings. In patients scheduled for lymphadenectomy with control films taken during the operation, the inferior epigastric nodes may, unless recognized preoperatively, be mistaken for internal iliac nodes, with the result that the surgeon searches in vain for non-existent pelvic lymph nodes.

Exact knowledge of the normal anatomy and variations of the lymphatic system is a prerequisite when lymphography is used as an aid for surgeons during lymph node dissection, e.g. in radical operations for carcinoma of the uterine cervix.

The main peripheral lymphatic trunks lie along the branches of the arterial tree and in the pelvis the lymph nodes are named after the adjacent arteries.

The external iliac artery has two branches: the deep circumflex iliac artery and the inferior epigastric artery. The deep circumflex iliac artery originates behind the inguinal ligament and runs laterally and backwards along the iliac crest, anastomosing peripherally