

## The Role of Lymphography in "Apparently Localized" Prostatic Carcinoma

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### Summary

The preliminary results of an ongoing protocol which is attempting to determine the incidence of lymph node metastases in unselected patients with previously untreated, "apparently localized" carcinoma of the prostate are briefly presented. All patients have disease confined to the prostate gland or periprostatic bed, without evidence of metastasis by standard clinical, laboratory, and radiographic (excluding lymphography) tests. Following lymphography, a "staging laparotomy" is performed which permits histologic documentation of lymph node metastasis and provides data for the evaluation of lymphographic accuracy.

Experimental and clinical studies in prostate cancer have shown the lymphatic system to be an important route for dissemination in this disease (1, 4). However, the ability to identify lymph node metastases in these patients remain a perplexing diagnostic problem of major therapeutic importance. This communication presents our experience with lymphography in predicting lymph node metastases in patients with apparently localized prostate cancer who have undergone exploratory laparotomy and lymph node biopsy.

### "Feasibility" Study (Table 1)

We began by *retrospectively* reviewing all patients with prostatic carcinoma who had undergone lymphography prior to January 1972. (2) Of 94 such patients, 18 previously untreated patients with apparently localized disease underwent staging laparotomy with lymph node biopsy within several weeks of the lymphogram. The preoperative assessment included history and physical examinations, routine laboratory tests, chest radiographs, axial skeletal radiographs, and in some patients percutaneous bone marrow biopsy. Based on these examinations, no patient had evidence of distant metastasis. As determined by digital examination, nine patients had disease limited to the prostate gland and nine had extracapsular extension to the immediate periprostatic bed.

At laparotomy, lymph nodes were biopsied which were abnormal on the lymphogram as well as those suspicious during exploration to the surgeon. In addition, random sampling of other lymph node groups was performed. The positions of the excised lymph nodes were marked with metallic clips, thus permitting accurate radiologic-histologic correlation.

The lymphographic interpretations were placed into one of three diagnostic categories: (1) normal; (2) non-neoplastic abnormality, such as fatty infiltration or inflammatory change ("benign change"); and (3) metastatic tumor. No "equivocal" diagnostic category was utilized.

When evaluating the ability of the lymphogram to distinguish between those lymph nodes which contain metastasis from those which do not, the diagnostic categories of "normal" and "benign change" can be collectively considered as *negative lymphograms*; and the diagnostic category of "tumor" would be the *positive lymphogram*. Of the nine negative lymphograms, there was histologic confirmation in eight (89% accuracy). In the one false-negative study, one of the excised

Supported by Grant No. CA-05338 of the National Cancer Institute, National Institute of Health

\*Presented at the 4th Congress of the International Society of Lymphology, Tucson, Arizona, March 1973

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Table 1 Lymphographic-histologic correlation in 18 *selected* patients with "apparently localized" prostatic cancer evaluated *retrospectively*. There were 4 patients with DLP (disease limited to the prostate) and 5 with ECE (extracapsular extension) who had histologically proven lymph node metastasis. Overall lymphographic accuracy was 89%.

Lymphogram Diagnosis			
HISTOLOGY	NORMAL	BENIGN Δ	TUMOR
NORMAL (6)	5	0	1
BENIGN Δ	0	3	0
TUMOR (9)	1	0	8
<b>TOTAL (18)</b>	<b>6</b>	<b>3</b>	<b>9</b>

	ILIAC	PARA - ORTIC
= 9	DLP <sup>4/9</sup> - 4	3
	ECE <sup>5/9</sup> - 5	4
	9	7

↓	↓
9	9
(1 FALSE NEG)	(1 FALSE POS)
89%	89%

lymph nodes demonstrated a microscopic focus of metastasis. Of the nine positive lymphograms, there was histologic confirmation in eight (89% accuracy) with one false-positive study. Therefore, overall lymphographic accuracy was 89%.

Of the nine patients with lymph node metastasis, four had disease limited to the prostate and five had extracapsular extension as determined by digital examination of the prostate gland. All nine patients had iliac lymph node metastasis. In addition, seven of these patients had cephalad extension with histologically confirmed metastasis to the para-aortic lymph node groups. There was no instance of para-aortic lymph node metastasis without iliac lymph node involvement.

Table 2 Lymphographic-histologic correlation in 16 *consecutive* patients with "apparently localized" prostate cancer studied *prospectively*. There were 3 patients with DLP (disease limited to the prostate) and 2 with ECE (extracapsular extension) who had histologically proven lymph node metastasis. Overall lymphographic accuracy was 75%.

Lymphogram Diagnosis			
HISTOLOGY	NORMAL	BENIGN Δ	TUMOR
NORMAL (9)	9	0	0
BENIGN Δ (2)	0	1	1
TUMOR (5)	3	0	2
<b>TOTAL (16)</b>	<b>12</b>	<b>1</b>	<b>3</b>

	ILIAC	PARA - ORTIC
= 5	DLP <sup>3/11</sup> - 3	2
	ECE <sup>2/5</sup> - 2	0
	5	2

↓	↓
13	3
(3 FALSE NEG)	(1 FALSE POS)
77%	66%
( 75% )	
( OVERALL ACCURACY )	

*"Protocol" Study (Table 2)*

Based upon these encouraging results of the lymphographic accuracy in these selected patients, as well as the surprisingly high incidence of lymph node metastasis in patients with supposedly localized disease, a prospective evaluation of lymphography was undertaken as part of a new treatment protocol which is attempting to evaluate the efficacy of radiotherapy in controlling prostatic cancer. Eighteen unselected, previously untreated patients have been *prospectively* studied in this protocol. Of these, 16 had successful bilateral lymphograms followed by staging laparotomy. The preoperative clinical staging, excluding the lymphogram results, of these 16 patients was 11 with disease limited to the prostate and five with extracapsular extension.

There were 13 patients with *negative lymphograms*, of which 10 were histologically confirmed (77% accuracy). Of the three false-negative studies, in two the lymph node metastases were microscopic foci of tumor limited to the subcapsular marginal sinus, without macroscopic distortion of the lymph node. There were three *positive lymphograms*, with histologic confirmation in two. The false-positive lymphogram demonstrated bulky para-aortic lymph nodes which contained multiple filling defects. At laparotomy, the surgeon noted enlarged, matted adenopathy. Histologic examination failed to demonstrate metastatic tumor but, instead, revealed extensive sinus hyperplasia and fibrosis of the excised lymph nodes. Overall lymphographic accuracy, therefore, in this prospectively studied group of unselected patients was 75%.

Of the five patients with lymph node metastasis, three had disease limited to the prostate and two had extracapsular extension. The iliac lymph nodes were involved in all five instances, with extension to the para-aortic lymph node groups in two patients.

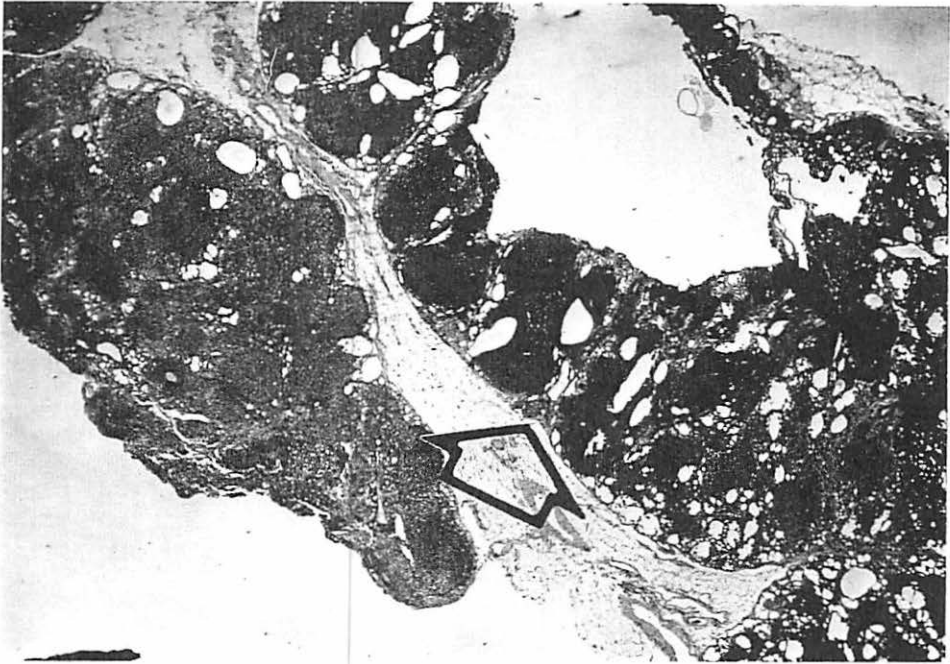
*Discussion*

The incidence of lymph node metastasis in both groups of patients with clinically localized prostate cancer ranged from 31-50%. Of those patients with lymph node metastasis, from 40-78% had involvement of the para-aortic, as well as pelvic, lymph nodes. No skip lesions, that is, para-aortic lymph node metastasis without pelvic lymph node metastasis, were noted. The overall lymphographic accuracy ranged from 75-89%.

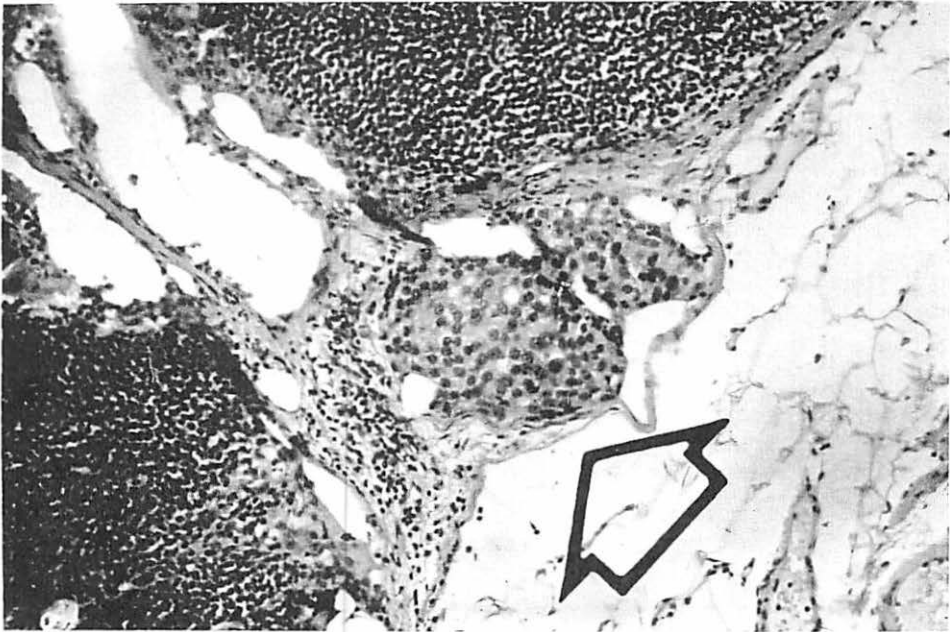
The disparity between the results of the "feasibility" and "protocol" study is probably due to the manner in which these groups were evaluated. The first was a retrospective study evaluating selected patients, whereas the second was a prospective study involving a group of consecutive, unselected patients. Therefore, one might expect that the results from the "protocol" group would more closely approximate the realities of the every day clinical situation. Even so, lymph node metastases were histologically documented in 1/3 of these patients, and the lymphogram demonstrated an overall 75% accuracy. It must be re-emphasized that these patients, by all other parameters, were considered to have localized prostatic carcinoma without lymph node metastasis.

Most false-negative lymphograms were caused by microscopic metastasis to the subcapsular marginal sinus (Fig. 1). Such metastatic lesions do not sufficiently alter the internal architectural structure of the lymph node to permit radiographic identification, and will continue to be a source of false-negative studies with current techniques. The common appearance of irregular-appearing pelvic lymph nodes in lymphograms performed on older patients does not facilitate the lymphographic interpretation.

Since the number of patients in the prospective "protocol" study is small, the results of this analysis are as yet only suggestive. More definitive information regarding the incidence of lymph node metastasis in patients with apparently localized prostate cancer, and the accuracy of lymphography in this setting, depends upon the study of larger groups of unselected, previously untreated patients. Such a prospective clinical study is being continued at the Stanford Medical Center.



a



b

Fig. 1 (a) Low power photomicrograph of excised iliac lymph nodes shows effects of prior lymphogram without any gross alterations in architecture. The lymphogram was interpreted as normal.

(b) High power photomicrograph shows one focus of metastatic prostatic carcinoma (arrows) in the subcapsular marginal sinus. Note lack of distortion of adjacent lymphatic follicles and sinuses.

### References

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Lymphology 8 (1975) 20-23  
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## Lymphocele: A Significant Complication Following Renal Transplantation

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### Summary

Six pelvic lymphoceles occurred in a series of 88 renal transplants. All of the patients had ipsilateral leg edema and one-half had a urinary tract infection and/or pain. Displacement of the urinary bladder away from the kidney with or without some degree of ureteral obstruction was diagnostic. External or internal drainage resulted in relief of the symptoms.

As early as 1958, lymphoceles were reported as an annoying and sometimes fatal complication following pelvic lymphadenectomy (1-4). Since the advent of renal allotransplantation, and the implantation of the kidney in the retroperitoneal pelvis, lymphoceles have reappeared in the literature (5-10). These loculations of lymph may produce symptoms from their increasing mass in the narrow confines of the pelvis.

In this report of six patients with lymphoceles, one patient lost his renal transplant and another eventually died from a pulmonary embolus. Both of these complications probably resulted from retroperitoneal pelvic lymphoceles.

### Patient Population

The records of 70 patients, 46 males and 24 females, having a total of 88 renal transplants, were reviewed. The six male patients with lymphoceles represented 8.6% of the transplant population and 6.8% of the total number of transplants performed.

In all patients the donor kidney was placed in a retroperitoneal location in the pelvis as described by *Hume* (6). The pelvic lymphatic chains along the external iliac vessels were ligated. In two patients, the lymphocele occurred on the left side following a second transplant. The tissue typing match ranged from A to D.