Role of Lymphography in Carcinoma of the Prostate

R. M. PAXTON, GRANT WILLIAMS, J. S. MACDONALD

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Summary

The results of bilateral pedal lymphography in 83 patients with adenocarcinoma of the prostate gland are presented. The patients were divided into two groups: 45 new cases and 38 late or old cases presenting several years after the onset of the disease. Altogether 25 of the new patients and 29 of the late patients had lymphographic evidence of lymph node metastases. The lymphogram results in relation to local tumour size, histological grade, the presence of skeletal metastases, and acid phosphatase levels are discussed. Of the new patients with T1 and T2 tumours—that is, those still localized within the prostatic capsule—41% had positive lymphograms. The inaccuracy of acid phosphatase estimations in detecting early extraprostatic spread is shown and compared with the greater accuracy of lymphography. Lymphography should be used as an initial investigation in all cases where aggressive therapy is being considered, and the importance of regular follow-up radiographs is emphasized.

Introduction

Adenocarcinoma of the prostate gland spreads directly through the capsule to involve adjacent structures, by the vertebral venous plexus—giving rise to distant metastases—and by lymphatic drainage to the internal iliac lymph nodes on each side of the pelvis and then to the common iliac and paraaortic groups. Lymphatic spread of carcinoma of the prostate has received scant attention in the British literature. Our series shows that there is a high incidence of lymphatic spread even in early cases.

Now that localized radiotherapy to the prostate is an accepted form of definitive treatment (Bloom and Hendry, 1973; Ray *et al.*, 1973) and chemotherapy with methotrexate is being used in the later stages of the disease at the Royal Marsden Hospital an accurate pretreatment description of the regional lymph nodes and beyond seems desirable. Nodes shown to be involved by tumour deposits should be included in any therapy plan or a different mode of treatment may have to be considered in the light of lymphographic evidence of tumour spread. Similarly, if radical prostatectomy is contemplated in early cases pre-operative demonstration of lymph node involvement may alter treatment plans.

Though lymphography opacifies only the external iliac, common iliac, and paraaortic groups and not the regional nodes our figures show that there is a sufficiently high incidence of involvement of the opacified nodes to warrant routine pre-treatment lymphography in any case where aggressive therapy is considered.

When lymphograms are performed with an oily fluid containing iodine (iodized oil fluid injection) the lymph nodes retain

the contrast medium in diagnostic amounts for about a year. Thus, plain radiographs of the abdomen and pelvis afford a simple means of assessing the effects of treatment in those patients with involved nodes. In addition, initially normal lymphograms when followed-up regularly by repeat radiographs may reveal new and clinically unsuspected lymphatic metastases.

The technique and complications have been previously described by Macdonald (1973). Patients with carcinoma of the prostate are often elderly, but in only a few cases were we unable to perform the investigation because of concurrent cardio-respiratory illness. The technique is repeatable and "refill" lymphograms are not technically difficult. No significant complications were encountered in the series though complications do occur and sensible precautions must be taken (Fischer, 1969; Macdonald, 1974).

Patients and Methods

Bilateral pedal lymphography was performed in 83 patients with histologically proved adenocarcinoma of the prostate seen at the Royal Marsden Hospital since 1968.

Previous reports on the results of lymphography have not separated new cases from those with longstanding, advanced disease and we felt that this distinction was important if a true perspective of lymphatic involvement was to be achieved. Forty-five of our patients were new cases—that is, referred immediately after histological evidence of the disease had been found for the first time or presenting directly to the hospital with no previous evidence of disease. They had received no treatment except a biopsy, transurethral resection, or open prostatectomy (five cases). The remaining 38 patients were classified as late or "old" cases, having been referred for radiotherapy or chemotherapy because of failure of hormonal treatment.

The case records and radiographs of these patients were reviewed by two of us (R.P. and G.W.). Tumour staging, histological confirmation and grade, and acid phosphatase estimations at the time of lymphography were recorded. The lymphograms were reviewed to detect the presence of tumour deposits in the opacified lymph nodes and follow-up films were reviewed to assess progress. Skeletal surveys and bone and liver scans were also reviewed for possible metastases.

The classification of carcinoma of the prostate has been the subject of much debate. The U.I.C.C. classification, which incorporates the T.N.M. system, received final approval in May 1974, and was used in this series. The clinical classification of the primary tumour is as follows: T, primary tumour; TX, incidental finding of carcinoma in an operative specimen with no preoperative evidence or suspicion of carcinoma; T0, metastatic disease with no evidence of primary disease; T1, solitary nodule with smooth surface occupying less than one lobe and surrounded by compressible tissue; T2, tumour with smooth surface confined to the prostate and occupying one lobe or more; T3, tumour extending beyond the prostate with or without involvement of the seminal vesicles or the bladder; T4, tumour fixed to the pelvic wall or involving adjoining organs. The histopathological grades are: GX, no information available; G0, ungradeable; G1 low grade; G2, medium grade; G3, high grade.

Histological confirmation of metastatic involvement of lymph nodes was obtainable in only six of the new cases and 10 of the late cases. In experienced hands, however, with meticulous

Department of Radiodiagnosis, Royal Marsden Hospital and Institute of Cancer Research, Fulham Road, London

R. M. PAXTON, M.B., F.F.R., Senior Registrar in Radiodiagnosis
J. S. MACDONALD, M.B., F.F.R., Consultant Radiologist

Department of Surgery, Royal Marsden Hospital and Institute of Cancer Research, Fulham Road, London

GRANT WILLIAMS, M.S., F.R.C.S., Consultant Urologist

technique and the evaluation of the nodes on follow-up films lymphography is a very accurate investigation. The persistence of the contrast medium in the nodes allows their behaviour as well as their initial appearance to be assessed and involvement by a deposit should only be diagnosed if the suspicious area not only looks like tumour but behaves like tumour.

Results

Not unexpectedly there was a higher overall incidence of lymphatic involvement in the late cases, 76.3%, than in the new cases, 55.6% (tables I and II). New cases with T1 and T2 tumours—that is, those still localized within the capsule—had an overall 41% (7/17) incidence of lymph node metastases shown by lymphography. This coincides with the experience of Castellino (1974) who in a prospective study still to be published quotes a 35-40% incidence of histologically documented lymph node metastases, often to the paraaortic glands, in patients with disease clinically, biochemically, and radiologically confined to the prostate—that is, T1 and T2.

TABLE I—Extent of Local Tumour and Lymphogram Results in New Cases

Local Tumour Grade	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
TX	5	0	5 (100)
T1	4	1 (25)	3 (75)
T2	13	6 (46.2)	7 (53.8)
T3	10	6 (60)	4 (40)
T4	13	12 (92.3)	1 (7.7)
Total	45	25 (55.6)	20 (44.4)

TABLE II—Extent of Local Tumour and Lymphogram Results in Late Cases

Local Tumour Grade	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
T2	2	2 (100)	0
T3	13	9 (69.2)	4 (30.8)
T4	23	18 (78.3)	5 (21.7)
Total	38	29 (76.3)	9 (23.7)

Altogether 60% (6/10) of new T3 tumours and 92.3% (12/13) of new T4 tumours showed lymphatic deposits. Involvement of paraaortic nodes as well as pelvic nodes in 15.4% of T2 tumours and 61.5% of T4 tumours in new cases should be noted (tables III and IV). There did not seem to be any firm correlation between the degree of malignancy of the primary tumour and the incidence of lymphatic metastases (table V).

The incidence of lymphatic metastases compared with the incidence of skeletal metastases as shown by skeletal surveys and radioisotope bone scans is shown in tables VI and VII. Altogether 46.9% of new cases and 64.3% of late cases without bony metastases had lymphographic evidence of lymph node deposits. Of those new cases with bony deposits 76.9% had involved nodes at lymphography.

Grossman *et al.* (1974) showed that serum acid phosphatase

TABLE III—Distribution of Involved Nodes in New Cases

Local Tumour Grade	No. of Patients	No. (%) with Pelvic Nodes Involved	No. (%) with Paraortic and Pelvic Nodes Involved	No. (%) Negative on Lymphography
TX	5	0	0	5 (100)
T1	4	1 (25)	0	3 (75)
T2	13	4 (30.8)	2 (15.4)	7 (53.8)
T3	10	5 (50)	1 (10)	4 (40)
T4	13	4 (30.8)	8 (61.5)	1 (7.7)
Total	45	14 (31.2)	11 (24.4)	20 (44.4)

TABLE IV—Distribution of Involved Nodes in Late Cases

Local Tumour Grade	No. of Patients	No. (%) with Pelvic Nodes Involved	No. (%) with Paraortic and Pelvic Nodes Involved	No. (%) Negative on Lymphography
T2	2	2 (100)	0	0
T3	13	5 (38.4)	4 (30.8)	4 (30.8)
T4	23	14 (60.9)	4 (17.4)	5 (21.7)
Total	38	21 (55.3)	8 (21.1)	9 (23.6)

TABLE VI—Bone Metastases* and Lymphogram Results in New Cases

	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
Bone metastases present	13	10 (76.9)	3 (23.1)
Bone metastases absent	32	15 (46.9)	17 (53.1)

*As measured by skeletal survey and radioisotope bone scan.

TABLE VII—Bone Metastases* and Lymphogram Results in Late Cases

	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
Bone metastases present	24	17 (70.8)	7 (29.2)
Bone metastases absent	14	9 (64.3)	5 (35.7)

*As measured by skeletal survey and radioisotope bone scan.

levels were not as accurate an indicator of the early spread of the disease as lymphography and we confirmed this (tables VIII and IX). Of new cases with normal acid phosphatase levels at the time of lymphography 48.3% had lymph node deposits whereas 81.8% of new cases with raised acid phosphatase levels had positive lymphograms.

Two patients with advanced disease and liver metastases had positive lymphograms, but out of two patients with histologically proved involved cervical lymph nodes only one had lymphographic evidence of involved abdominal nodes. One patient with lung and bone metastases had a normal lymphogram which was confirmed at necropsy.

Six new cases (13.3%) with initially normal lymphograms subsequently developed lymph node deposits visible on follow-up radiographs, but there was no clinical evidence of lymphatic spread. Five of them developed pelvic lymph node deposits and the remaining patient developed a deposit in an opacified left supraclavicular node visible on a chest x-ray picture. The

TABLE V—Pathological Tumour Grading and Lymphogram Result in All Cases. Results are Numbers of Patients

Local Tumour Grade	No. of Patients	G1		G2		G3		GX	
		Lymphogram Negative	Lymphogram Positive	Lymphogram Negative	Lymphogram Positive	Lymphogram Negative	Lymphogram Positive	Lymphogram Negative	Lymphogram Positive
TX	5	1		2		2			
T1	4			2		1			
T2	15	5	2	2	5		1		
T3	23	4	4	4	9		2		
T4	36		8	4	17	2	1		4
Total	83	10	14	14	32	5	4		4

TABLE VIII—*Acid Phosphatase Estimation at Time of Lymphogram in 40 New Cases*

	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
Raised acid phosphatase	11	9 (81.8)	2 (18.2)
Normal acid phosphatase	29	14 (48.3)	15 (51.7)

TABLE IX—*Acid Phosphatase Estimation at Time of Lymphogram in 29 Late Cases*

	No. of Patients	No. (%) Positive on Lymphography	No. (%) Negative on Lymphography
Raised acid phosphatase	18	16 (88.9)	2 (11.1)
Normal acid phosphatase	11	9 (81.8)	2 (18.2)

deposits appeared between six and 15 months after the lymphograms. (These cases are not included in the tables as having positive results.)

Discussion

In 1959 Flocks *et al.* demonstrated the spread of prostatic cancer by the lymphatic system and later that year Whitmore and MacKenzie (1959) confirmed this finding. Arduino and Glucksman (1962) reported lymph node involvement in 32% (14/44) of patients with disease clinically within the prostatic capsule who had undergone pelvic lymphadenectomy. Only two of these cases had deposits limited to the internal iliac group. Grossman *et al.* (1974) published the results of bilateral pedal lymphography in 58 patients with prostatic cancer and showed an 81% incidence of lymphatic involvement. McCullough *et al.* (1974) in a surgical series of 61 patients had histological proof of lymph node involvement in 61%; stage B had a 25% incidence, stage C 51%, and stage D 82%. Castellino *et al.* (1973) published a smaller series of 18 patients with cancer confined to the prostatic bed. All patients had lymphograms and then underwent staging laparotomy; nine patients had histological proof of lymph node metastases, and in eight of these cases the preoperative lymphograms showed involved lymph nodes. The remaining case had one opacified node involved by a microscopic deposit which would not have been demonstrable by lymphography.

In our series of 45 new cases 55.6% had lymphographic evidence of lymph node metastases. A higher figure of 76.3% was seen in the late cases. This gives an overall incidence of 65% (54/83), which is lower than that given by Grossman *et al.* (1974) but is comparable to that of McCullough *et al.* (1974). Involvement of the paraaortic lymph nodes in 15% of T2 tumours seemed to be important information in the management of these patients, as was the 41% incidence of lymph node deposits in new T1 and T2 tumours.

Whitmore and MacKenzie (1959) showed that patients with normal serum acid phosphatase levels may have extraprostatic spread of cancer. McCullough *et al.* (1974) described 56 patients with normal serum acid phosphatase levels of whom 59% (33/56) had histological proof of lymph node deposits. We have shown that 46.9% of new cases without skeletal metastases and

48.3% of new cases with normal serum acid phosphatase levels at the time of the lymphogram have lymphographic evidence of lymph node spread. Higher incidences were seen in the late cases and many of these patients were thought clinically, radiologically, and biochemically to have disease limited to the local tumour site.

Criticism may be levelled at these results because of the lack of histological proof of the lymphatic metastases shown by the lymphogram. This information is, however, impossible to obtain unless a staging laparotomy is performed with radiographic control (Castellino *et al.* 1973), and in addition patients dying from advanced prostatic cancer do not in this country often come to necropsy. We feel that with regular follow-up radiographs, however, the difference between nodes affected by metastasis, reactive hyperplasia, infection, and fatty replacement soon becomes apparent. The importance of follow-up films cannot be overemphasized if a time-consuming technique is not to lose half its value. Six of our new cases (13.3%) developed radiographically demonstrable lymphatic metastases between six and 15 months after the lymphogram without clinical or biochemical evidence of tumour spread.

Conclusions

If any radical treatment is proposed for carcinoma of the prostate it would seem desirable that a lymphogram should be performed as part of the initial series of investigations since if lymphatic involvement is shown treatment may have to be modified. Irradiation of the pelvis and prostate gland may well fail if paraaortic metastases (24.4% of our new cases) are present and, similarly, radical prostatectomy is inadvisable without a negative lymphogram having been first obtained. In addition, the results of radiotherapy and chemotherapy in those patients with involved nodes may be simply followed up by repeat radiographs and treatment modified as necessary.

Lymphography also gives the clinician an added dimension in investigating early cases. Slightly less than 50% of new patients with normal acid phosphatase levels and no evidence of skeletal metastases have been shown to have lymphographic evidence of lymph node deposits. Lymphography seems to give an earlier and more accurate indication of extraprostatic spread than measurement of the acid phosphatase level.

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