

Staging Laparotomy in Hodgkin's Disease

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Staging laparotomy was performed at the University of Virginia Medical Center on 111 patients with Hodgkin's disease. The operation included multiple liver and lymph node biopsies and, excepting three patients, splenectomy. The histopathology was reviewed and the 111 patients were classified as follows: nodular sclerosis, 74; mixed cellularity, 28; lymphocyte predominance, 7; and undetermined, 2. There were no deaths. Wound, pulmonary or urinary tract complications occurred in 11 patients. One case of postoperative thrombophlebitis occurred and in another case small bowel obstruction developed, and resolved without reoperation. The pathologic stage (PS) following laparotomy was unchanged from the clinical stage (CS) in 64%, reduced in 20%, and advanced in 16%. The therapy, however, was altered in 38% of the patients. Lymphangiography in 103 patients was interpreted as showing lymph node involvement in 38, equivocal involvement in 11, and no involvement in 54. Among the 92 examinations reported as either positive or negative, 77% were confirmed histopathologically, 21% were falsely positive, and 2% were falsely negative. The spleen was positive for Hodgkin's disease in 39% of cases, and in these patients with positive spleens there was no reason to suspect intra-abdominal involvement preoperatively in 21%.

TRADITIONALLY, THE FUNCTION OF THE SURGEON in Hodgkin's disease has been to obtain tissue for pathologic examination, or, rarely, to resect localized disease.

The observations of an interdisciplinary group at the Stanford University Medical Center^{2,4} begun in the 1960's have now expanded the surgical role to include assessment of the presence or absence of the process within the abdominal cavity and, if present, its extent.

In 1969, stimulated by the work in progress at Stanford and other institutions, laparotomy was introduced as a part of the Hodgkin's disease staging protocol at the University of Virginia Medical Center.

Patients and Methods

Clinical Staging

Clinical staging (CS)³ in patients with histopathologically documented Hodgkin's disease included a his-

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tory with special attention to fever, night sweats and weight loss; physical examination with special attention to all peripheral lymph node chains, liver, spleen, and bony tenderness; chest roentgenograms and whole lung tomography if mediastinal and/or hilar adenopathy was present; complete blood counts with differential and platelet count; erythrocyte sedimentation rate; liver function tests: PPD skin testing with anergy determination if indicated; bilateral lower extremity lymphangiography; and bone marrow biopsy. Optional studies included radioisotopic scans and in cases where liver involvement was suspected, liver biopsy either percutaneous or under direct vision at laparoscopy. On the basis of these studies each patient was given a clinical stage.

Pathological Staging (PS)³

A staging laparotomy was next recommended on all patients except for those in whom stage IV disease was established or apparent, or in whom a major diagnostic operation was considered ill-advised because of the patient's general health status. Based on these laparotomy findings each patient is given a final pathological stage.

Operative Technique

The operative incision varied with the preference of the surgeon. A left paramedian rectus muscle retracting incision was used in 62% of the patients, and in one instance was combined with a lateral transverse extension. The midline approach was employed in 36%; in the remaining two patients a left subcostal incision was used.

Initially a complete intra-abdominal exploration was carried out. Open wedge biopsies were taken from the anterior edge of the right and left lobes of the liver and deeply from the liver substance using a

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TABLE 1. *Clinical Stage Compared with Pathological Stage*

Clinical stage	Pathological Stage									
	IA	IB	IIA	IIB	IIIA	IIIB	IVB	IIA _E	IIIB _E	
IA	13				6					19
IB		2					2			4
IIA			18		4					22
IIB				8		1	1			10
IIIA	4		9		14					27
IIIB				1			7	2		10
IVB		1				4	6			11
IIA _E								2		2
IIIB _E									1	1
IIIA _E			1					1		2
	17	3	28	9	24	14	9	3	1	108*

* Three other patients are not included in this table. Two were in complete clinical remission at the time of laparotomy. In one, disease was found in the spleen; in the other, no disease was found. The third patient although in clinical remission at the time of laparotomy, had a positive lymphangiogram (CS IIA) but no disease was found at laparotomy.

biopsy needle. Additionally, any focal involvement or suspicious area was biopsied.

Access to the paraaortic area was gained by dividing the ligament of Treitz, retracting the retroperitoneal duodenum cephalad and incising the posterior peritoneum along the left side of the aorta to the level of the bifurcation. This permitted visualization of nodes along the left side of the aorta and on the right between the aorta and vena cava, and provided access to the iliac nodes. Grossly abnormal paraaortic or iliac lymph nodes were readily identified and were excised either singly or in groups of nodes. When grossly abnormal nodes were obtained further search for nodes was abandoned. If no enlarged nodes were apparent the preoperative lymphangiogram was an invaluable guide to node sampling. Lymph nodes that were positive or equivocal on lymphangiogram were excised. Metallic clips were used to obtain hemostasis and to serve as radiopaque markers. Intraoperative x-rays were obtained to identify the site of the excised node and to ascertain whether or not the desired node had been obtained, but the search was not concluded until the abnormal-appearing lymph node had been removed. If there were no questionable nodes, either on inspection or on preoperative lymphangiogram, several single nodes or a short chain of nodes lying along the left side of the aorta were excised. Other sampling was directed at nodes in the region of the celiac axis, the porta hepatis, the mesentery, near the tail of the pancreas, and in the splenic hilum; nodes in the latter region frequently accompanied splenectomy.

Splenectomy was accomplished after dividing the short gastric vessels, the splenocolic ligament and the posterior peritoneal attachments of the spleen. The

splenic artery and vein were divided and ligated individually. For purposes of subsequent radiographic identification, several metallic clips were placed on the splenic pedicle. The splenic bed was not drained routinely. Bone marrow biopsy was performed as a part of the preoperative clinical staging but in a few instances when preoperative specimens were not entirely satisfactory an open biopsy from the ilium was performed.

Transposition of the ovaries was not a part of the initial staging protocol but in more recent staging operations it was offered to women of reproductive age and younger. The appendix was removed in 71 patients. Other incidental procedures, when indicated, were carried out; these included tubal ligation in five; cholecystectomy in two; renal cystectomy in two; umbilical hernioplasty in one; excision of liver hemangioma in one, and uterine dilatation and curettage in one.

Closure of the abdominal incision also varied with the preference of the surgeon but in all instances interrupted nonabsorbable suture material was used for the principal fascial layers. Systemic prophylactic antibiotics were administered to 13 patients but the remaining ones received none.

Results

During the period from April 1969 through June 1977, 111 patients with histopathologically verified Hodgkin's disease had a staging laparotomy performed at the University of Virginia Hospital. Ages ranged from five to 72 years; 60 were males and 51 were females; 105 were white and six were black.

Histopathological Subclassification

The original microscopic slides and/or additional sections from the paraffin blocks were available for review in all 111 cases. The slides were reviewed separately and independently by two of us (WLM and TWT), without knowledge of the original histopathological subclassification. Lesions were classified according to the criteria of Lukes⁷ and the Rye Conference⁶ on Hodgkin's disease as follows: nodular sclerosis (NS), 74; mixed cellularity (MC), 28; lymphocyte predominance (LP), 7; lymphocyte depletion (LD), none; undetermined, 2.

The Effect of Laparotomy on Staging

Table 1 compares the clinical stage determined by the preoperative clinical staging evaluation with the final pathological stage determined by laparotomy.

The information in this table is summarized in Figure 1. The clinical stage was unchanged in 71 patients (63.9%), reduced in 22 (19.8%), and advanced in 18 (16.2%).

Complications

There were no deaths. However, early or late post-operative complications did occur in 13 patients as follows: superficial wound infection in four patients, superficial wound infection and urinary tract infection in one, superficial wound infection and pneumonia in one, deep wound infection in one, pneumonia in three, atelectasis and pleural effusion in one, thrombophlebitis in one, and partial small bowel obstruction (at four and six months following operation) in one patient.

The deep wound infection occurred in an obese male with a thick abdominal panniculus in whom lateral transverse extension of the left paramedian incision was necessary to obtain adequate exposure. On the seventh day following operation purulent material was evacuated from the deep fascia; culture yielded *Bacteroides fragilis* in large numbers. An incidental appendectomy had been performed during the staging laparotomy. Immediate recovery occurred without other untoward events and the patient tolerated a full course of radiation therapy. An incisional hernia developed later.* Complications in all other patients including the one patient with thrombophlebitis and the one with small bowel obstruction resolved without residual stigmata.

Lymphangiography

Bipedal lower extremity lymphangiography was performed in 103 patients. These studies were interpreted as positive in 38 patients, equivocal in 11, and negative in 54. Among the 92 examinations reported unequivocally as positive or negative, 77.1% were confirmed histopathologically, while 20.6% were falsely positive and 2.1% falsely negative.

Splenic Involvement

Splenectomy was performed in 108 patients, and was positive for Hodgkin's disease in 42 (38.8%). Of the three patients who did not have splenectomy, two had gross involvement of the liver at laparotomy and one had a negative exploration with a small grossly normal spleen.

The weights of the positive spleens are compared with the negative ones in Figure 2. It is of interest to note that there is considerable variability in the size

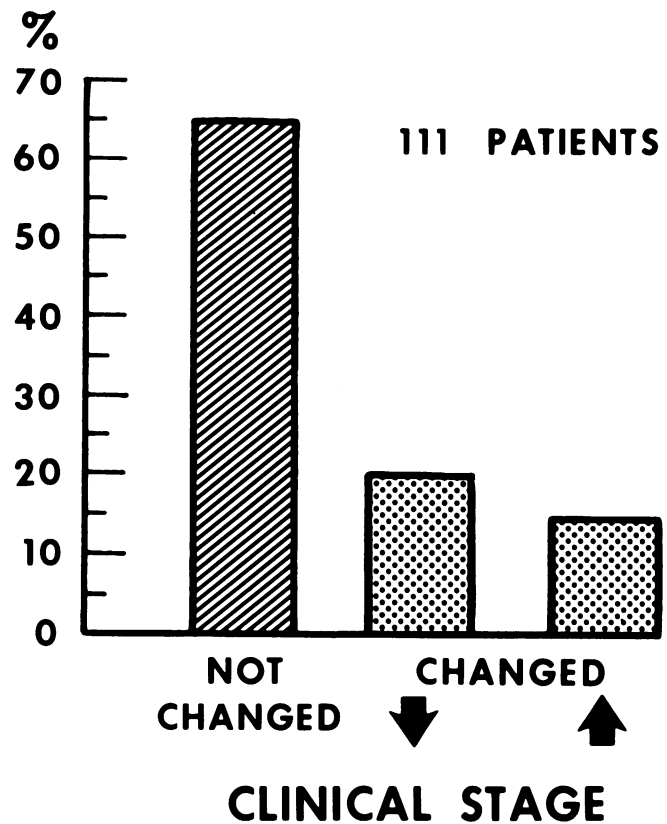


FIG. 1. Comparison of the clinical stage, determined by preoperative evaluation, with the pathological stage, determined by laparotomy.

of the uninvolved spleens and that many small spleens were positive for Hodgkin's disease.

Splenic palpability on physical examination depends not only on the size of this organ but also on the habitus of the patient and the skill of the examiner. Preoperatively the spleen could be felt in 18 patients; in eight of these the spleen was histopathologically positive for Hodgkin's disease and in ten negative. Of the 90 patients with nonpalpable spleens, 34 were histopathologically positive and 56 were negative. Thus, the physical examination is not a reliable indicator of splenic involvement with Hodgkin's disease.

Radioisotopic scanning of the spleen was done preoperatively in only 12 patients, too few in number to draw conclusions. Four tests were positive and confirmed histopathologically, four were negative and confirmed, and four were falsely negative. There were no falsely positive scans.

The spleen was positive in nine patients in whom there had been no reason to suspect intra-abdominal pathology on the basis of preoperative evaluation. In each of these patients the spleen was not palpable (one also had a negative splenic scan), the liver was

* Since presentation of this paper the hernia has been successfully repaired.

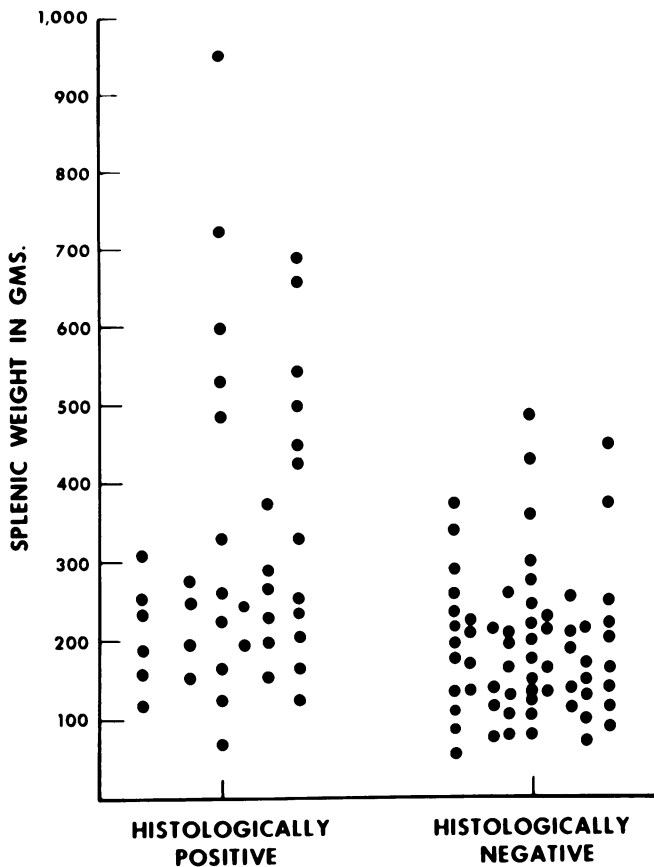


FIG. 2. The weights in grams of 41 spleens histologically positive for Hodgkin's disease compared with the weights of 65 histologically negative spleens.

not enlarged, liver function tests were normal, and the lymphangiogram was negative.

Discussion

In this series of 111 patients with Hodgkin's disease, staging laparotomy resulted in a change of stage in 36%. This figure is in essential agreement with that reported from other institutions.^{4,9} The immediate clinical utility of this information is limited unless it is related to treatment. In other words, did laparotomy alter therapy and to what extent?

Retrospectively, the treatment plan that would have been used if a staging laparotomy had not been performed was compared with the treatment actually administered. In 69 of 111 patients there was no change but in the remaining 42 patients therapy was altered. Planned radiation therapy was decreased in 17 patients, increased in nine, changed to chemotherapy in six, and combined with chemotherapy in seven. In three patients planned chemotherapy was changed to radiation therapy.

These data offer convincing testimony that staging

laparotomy does alter therapeutic strategy. However, potential mortality and morbidity from laparotomy must not be minimized. Although there were no deaths in the University of Virginia series, complications occurred in 12% of the patients. Kawarada et al.⁵ collecting data from 719 patients who had staging laparotomy for Hodgkin's disease found that there were seven deaths (0.9%) and 73 complications (10.1%). Using questionnaires, Rosenstock et al.⁸ surveyed members of the Section of Surgery of the American Academy of Pediatrics with reference to complications associated with staging laparotomy in children with Hodgkin's disease. In 347 procedures there were no operative deaths while 7.5% of the patients had complications. The largest experience from a single institution is from Stanford. In this series of 400 patients, Cannon and Nelsen² report no deaths; one per cent required reoperations for complications, 3.7% had major complications, and 14% minor complications.

The use of total nodal plus splenic irradiation would eliminate the need for staging laparotomy, but at the risk of overtreatment of those in whom no disease was found below the diaphragm, and inadequate treatment of those in whom stage IV disease or mesenteric node involvement was confirmed at laparotomy. Moreover, the adverse effects of radiation therapy and chemotherapy which include the risk of second malignancy, particularly acute leukemia, are not to be minimized.¹

Conclusions

The value of exploratory laparotomy combined with liver and lymph node biopsies and splenectomy in obtaining information leading to a precise therapeutic strategy in Hodgkin's disease needs to be balanced against the potential mortality and morbidity of this operation. In the setting of currently available diagnostic and therapeutic options, a staging laparotomy will continue to be recommended for all patients with Hodgkin's disease excepting those in whom Stage IV disease is established or apparent or in whom a major diagnostic operation is considered ill-advised because of medical and other reasons.

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DISCUSSION

DR. RICHARD G. MARTIN (Houston, Texas): We at the Anderson Hospital have been very active in staging patients with Hodgkin's disease, and our findings are very similar to those that have just been presented.

Of course, the main question that has not been answered is: Does staging increase life expectancy in these cases? And I don't believe we will have that answer for some time as yet. But, certainly, we do think that staging is very important.

We do not routinely stage all of ours; only those adults with negative lymphangiograms and clinical Stage I, II, and III [sic] in children over six years of age. And as has been pointed out, I feel that the surgeon has a great responsibility in choosing which patients are to be staged and which are not. And every patient sent to us must be examined to be sure that he is physically capable of undergoing such a procedure, because, as you have seen, it is not an innocuous procedure, and it is an elective surgical procedure.

Any patient that has mediastinal involvement must carefully be evaluated for adequate respiratory function and, if necessary, this area should be treated before performing a staging laparotomy.

We feel that staging laparotomy is very important, even though we do not know the answer as to life expectancy, because if you treat the abdomen with x-ray therapy, we want to make sure that there is a reason for it. And as many know, I am certainly one who does not like to see x-ray therapy given to the abdomen unless it's necessary.

One brief word may be mentioned in comparing staging of Hodgkin's disease with non-Hodgkin's lymphoma. The non-Hodgkin's lymphoma patient is usually much sicker, and the complication rate is a lot higher. However, here again it is important, because often the mesenteric nodes are positive in the non-Hodgkin's, compared to the Hodgkin's, and these do not show up on lymphangiogram.

DR. ARTHUR J. DONOVAN (Mobile, Alabama): I would like to discuss one facet of intraoperative management of the patient who has a positive lymphangiogram. In the past, at the post-celiotomy conference for decision as to therapy, I have been embarrassed to be shown on the abdominal films the same opacified lymph nodes that were supposed to have been removed, based on the positive lymphangiogram. These nodes had not been removed during the operation. The radiotherapist then adopted the position that Stage 3 disease must be assumed and the patient be treated with total nodal radiation.

Several years ago, I adopted a policy that a scout film of the abdomen be obtained before closing the abdomen. On three occasions I have found that the specific lymph nodes that I was supposed to remove were still within the abdominal cavity. In two of these instances, the lymph nodes were posterior to the right renal vein; in one of these cases the lymph nodes were positive.

I would recommend this procedure and ask the group from Charlottesville if, when there is positive lymphangiogram, they obtain an abdominal scout film on the operating table and prior to the closing of the abdominal wall. To reiterate, the purpose is to assure that the suspicious lymph nodes have been removed.

DR. J. ALEX HALLER, JR. (Baltimore, Maryland): I would like to ask Dr. Sandusky if he would comment on his feeling about the splenectomy involved in the staging laparotomy for patients with Hodgkin's disease.

He and his associates over the years have helped us a great deal in understanding the problem of postsplenectomy infections, and one of the major complications in children and young adults with Hodgkin's disease who have had splenectomy has been the problem of overwhelming sepsis following splenectomy.

I would like to ask him how he feels currently about *excluding* splenectomy. I know he commented upon the difficulty in deciding by inspection which spleens were involved with Hodgkin's. Would he consider doing hemisplenectomies, or partial splenectomies? What is his current feeling about the necessity for removing the spleen in patients with Hodgkin's disease?

DR. J. SHELTON HORSLEY, III (Closing discussion): I would certainly agree with what Dr. Martin said, that we would like to avoid irradiation of the lymph nodes in the abdomen if at all possible. I think it's tremendously important that the surgeon, the medical oncologist, hematologist, and radiation therapist talk to one another. It's of primary importance, particularly in this disease. This should be a multidisciplinary approach. The surgeon is really a technician in Hodgkin's Disease. This is a diagnostic procedure. We should not be doing staging laparotomies unless our results will affect the ultimate treatment of the patient.

Dr. Donovan, bless your heart! This is one point that we wished to stress. You must take an intraoperative x-ray of the patient before you close the abdomen, if you are going to get the suspicious nodes seen on the preoperative lymphangiogram.

Dr. Tegtmeyer, who does the lymphangiograms at the University of Virginia, and did the vast majority of these, was one of us. He's a surgeon who, as he said, "saw the light and went into radiology." It's a real pleasure to work with him because he gives you a definitive diagnosis. We review these films preoperatively with him. If he outlines a suspicious node, at the time of surgery we remove this node, mark the area with metallic clips, get a radiograph, and if that node is still there, we pursue it until it's removed, and again confirmed by an intraoperative x-ray.

Dr. Haller's question is a very pertinent one. We have had very little experience with staging Hodgkin's disease in children. The few that we have done have been otherwise quite healthy. We have removed the spleens and placed them on long-term prophylactic antibiotics.

In the adults, we have had no patients in whom we could attribute any significant or serious infection to splenectomy. As Dr. Sandusky has shown on one of his slides, we were unable to correlate size with involvement of the spleen. We feel, therefore, that we must do a splenectomy and give the entire spleen to the pathologist for definitive histologic study.

I would like to emphasize again that this is a diagnostic test. As other diagnostic tests become more accurate, we will do fewer staging laparotomies in Hodgkin's disease. I refer particularly to bone marrow biopsies, lymphangiography and laparoscopy with direct needle biopsies of the liver.