Comparison of Laparoscopic and Open Staging in Hodgkin Disease

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Background: Staging laparotomy provides useful information for management of Hodgkin disease but has fallen into disfavor because procedure-related morbidity exceeds that of new chemotherapeutic regimens.

Objective: To determine the feasibility, effectiveness, and safety of laparoscopic staging for Hodgkin disease compared with those of open staging.

Patients: Fifty-five patients with Hodgkin disease of cell types including nodular sclerosis in 43 (78%), mixed cellularity in 9 (16%), and lymphocyte predominance in 3 (5%).

Study Design: Concurrent evaluation of laparoscopic staging (n=15) and retrospective review of open staging (n=40).

Interventions: Laparoscopic and open techniques of surgical staging for Hodgkin disease, including splenectomy, liver biopsies, and lymph node sampling.

Main Outcome Measures: Operative time, duration of postoperative ileus and of postoperative hospitalization, morbidity, number of lymph nodes retrieved, alteration in pathologic stage, recurrence, and survival.

Results: For laparoscopic staging vs open staging groups, mean operative time was 202 vs 144 minutes (P=.001); mean postoperative ileus was 1.9 vs 3.2 days (P<.001); mean postoperative hospitalization was 4.4 vs 6.7 days (P<.001); complications occurred in 3 patients (20%) vs 11 patients (28%) (P=.57); and mean number of lymph nodes retrieved was 8.5 vs 4.6 (P=.05). In the laparoscopic staging group, 2 cases (13%) were upstaged and 2 cases (13%) were downstaged. In the open staging group, 6 cases (15%) were upstaged and 3 cases (7.5%) were downstaged. Follow-up data were available for all patients in the laparoscopic staging group, at a mean of 23.5 months postoperatively. All were alive, none had recurrent disease below the diaphragm, and 2 (13%) had residual mediastinal disease. Follow-up data were available for 31 patients (78%) in the open staging group at a mean of 52.5 months postoperatively. All were alive, 27 (87%) were disease free, 3 (10%) had had relapses above the diaphragm, and 1 (3%) had residual mediastinal disease.

Conclusions: Compared with open staging, laparoscopic staging of Hodgkin disease is oncologically equivalent and functionally superior. These data should encourage reappraisal of the role of operative staging in the management of Hodgkin disease.

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PATIENTS AND METHODS

We reviewed records of patients who underwent staging laparotomy for HD at Cedars-Sinai Medical Center, Los Angeles, Calif, and at the University of Udine, Udine, Italy, between December 5, 1991, and December 20, 1996. Laparoscopic staging (LS) procedures were performed by a single surgical team in each institution, whereas open staging (OS) procedures were performed by a single team at Udine and by several teams at Cedars-Sinai. Cases were unselected and consecutive. All cases referred after 1992 were staged laparoscopically at Cedars-Sinai and after 1994 at Udine. Preoperative tumor characteristics included sites of initial appearance of the HD, histological type, and clinical stage. Laparotomies were classified as primary or restaging; the latter were performed after patients had received chemotherapy and radiotherapy for massive mediastinal involvement at the time of initial examination. Operative data included number and location of lymph nodes removed, liver biopsy, splenic weight, and duration of the procedure. Postoperative data included duration of ileus, defined as the period before resumption of oral intake; duration of postoperative hospitalization; and major complications, defined as a complication requiring intervention or delaying discharge. Pathologic data included lymph node retrieval and an analysis of the number of patients in whom the pathological stage was different from the clinical stage. All patients had their disease staged clinically and pathologically according to the Ann Arbor classification. Statistical analysis was performed with the unpaired, 2-tailed Student t test, the Fisher test, and/or the χ² test.

LAPAROSCOPIC STAGING

Of 15 procedures begun laparoscopically, 2 (13%) were converted to open operations because of bleeding from the splenic vein. These occurred early in our experience. Subsequently, only 1 patient experienced bleeding during splenic hilar dissection, and this was controlled laparoscopically. The mean blood loss during the LS operations was 220 mL (range, 0-800 mL). The mean operative time was 202 minutes, including the 2 converted cases.

All of the patients began a clear liquid diet between postoperative days 1 and 3 (mean, 1.9 days after surgery). The patients were discharged from the hospital between 1 and 7 days after operation (mean, 4.4 days), including the 2 patients who required conversion for bleeding. Complications in 3 patients included bleeding in 2 and a left lower-lobe pneumonia treated with antibiotics in 1. No patients required reoperation for intra-abdominal bleeding, and none received transfusions.

During the laparoscopic staging, biopsies were performed on a mean of 8.5 abdominal lymph nodes. In 1 case (6.5%), an accessory spleen was found in the lesser sac and was removed by laparoscopy. All specimens were sent for pathologic examination; 2 patients (13%), both female, had their disease upstaged on the basis of laparoscopic findings. One had involvement of spleen and hilar nodes, and the other had infiltration of the spleen and celiac and porta hepatitis lymph nodes. Two patients (13%), 1 male and 1 female, had their disease downstaged after laparoscopy, because of the absence of any lymph node involvement, despite a preoperative computed tomographic scan that was interpreted as showing involved periaortic nodes.

The mean follow-up time was 23.5 months (range, 5-63 months). Eleven patients (85%) had no recurrence, whereas 2 (15%) had residual mediastinal disease and were undergoing radiotherapy for the primary disease. No patients had recurrence of HD below the diaphragm.
OPEN STAGING

Average operative time was 144 minutes (range, 80–240 minutes). There were no intraoperative complications, and 4.6 lymph nodes per patient were retrieved. Postoperative complications occurred in 11 patients (28%) and included left pleural effusion in 7 patients and left lower-lobe atelectasis, left iliac abscess, left subphrenic abscess, and elevation of amylase level in 1 patient each. Reoperation was required in 2 patients (5%) to drain the abscesses. Liquid diets were begun between 2 and 4 days (mean, 3.2 days) postoperatively, and patients were discharged between 4 and 13 days (mean, 6.7 days) postoperatively.

Six patients (15%), 3 male and 3 female, had their disease upstaged and 3 (7.5%), 2 female and 1 male, had it downstaged. Upstaging findings included involvement of spleen and nodes in 3 patients, spleen only in 2, and porta hepatitis nodes only in 1. Follow-up data were available for 31 patients (78%) in the OS group at a mean of 52.5 months postoperatively (range, 28–95 months). All were alive; 27 (87%) were disease free, 3 (10%) had had relapses above the diaphragm, and 1 (3%) had residual mediastinal disease.

COMPARISON OF TECHNIQUES

Laparoscopic operations were significantly longer (Table 3). Patients in the LS group had earlier resumption of liquid diet, shorter hospitalization, and fewer complications. Lymph node yield was also significantly greater.

RESTAGING

Eighteen of the 54 patients in the series underwent operative restaging after therapy (4 by LS and 14 by OS). When patients who underwent restaging by LS and OS were compared, there were no significant differences in splenic weight, operative duration, ileus, hospitalization, complications, node retrieval, upstaging, or downstaging. One patient in each group had their disease upstaged; one patient in the LS group and 3 in the OS group had their disease downstaged. There was 1 complication in the LS group (bleeding requiring conversion) and 4 complications in the OS group (pleural effusions in 3 and iliac abscess in 1).

**COMMENT**

In 1969, Glatstein et al11 reported the value of liver biopsies, lymph node biopsies, and splenectomy in the staging of HD. However, in recent years, a complex debate has arisen about the need for surgical staging. With improved noninvasive radiologic diagnosis, infrequency of disease sites below the diaphragm,9,10 substantial morbidity of staging laparotomy, and effective salvage chemotherapy producing survival equivalent to that with initial chemotherapy, surgical staging for HD is less often used. This strategy accepts the morbidity of salvage chemotherapy and ignores the observation that the stage of HD will be changed by laparotomy in 30% of patients.2

A review of staging laparotomy by Multani and Grossbard12 showed a mortality of 0.3% to 1%, major morbidity of 3% to 18%, and minor morbidity of 6% to 19%. Morbidity-related delays of subsequent treatment occurred in 5% to 10% of patients. Jockovich et al12 reported surgical complications in 26% of 133 consecutive patients, including atelectasis in 13%, small-bowel obstruction in 10% (requiring reoperation in 7%), subphrenic abscesses in 2%, and wound dehiscence in 1%.

Several studies have evaluated treatments based on clinical or pathological staging. In the H-6 European Organization for Research and Treatment of Cancer trial,13 patients with clinical stages I and II HD were random-
ized to undergo laparotomy or clinical staging. Patients in the laparotomy group had significantly longer disease-free intervals, although there was no statistical difference in survival. Murrell et al\(^2\) also showed that relapse-free survival was longer after pathological staging.

Two studies demonstrated the importance of staging in the treatment of HD and the superiorit of radiation alone as primary therapy for appropriate patients. A National Cancer Institute\(^3\) study, in which 136 patients with pathological staging I or II disease were randomly assigned to receive 6-course chemotherapy or radiation alone, showed that acute toxic reactions were significantly greater in the chemotherapy arm. Betti et al\(^4\) compared extended field radiation with 6 cycles of mechlorethamine, vincristine, procarbazine, and prednisone in 89 patients with pathological stage IA or IIA disease. No significant difference in relapse-free survival was shown, but overall survival was improved significantly with radiation alone.

In contrast to reports\(^5,6\) suggesting that there is no difference in survival after salvage chemotherapy, Valgussa et al\(^7\) showed a 15.5% cumulative actuarial incidence of secondary leukemia in patients treated with primary radiotherapy who later received salvage chemotherapy. Additionally, most large series\(^8,9\) show long-term salvage rates of less than 70% in relapses after radiation. These studies show that primary chemotherapy in patients with stage III disease is less morbid than salvage chemotherapy after radiation. The morbidity of radiation therapy and the increased morbidity of salvage are avoided in patients with accurate pathological staging.

Another advantage of surgical staging\(^10,11,12\) is that the splenectomy allows delivery of a smaller radiation dose to the abdomen, decreasing injury to the left kidney and lung in those patients who still require subdiaphragmatic radiotherapy after laparotomy for staging. Cho et al\(^13\) reported that portal radiation size was greater for patients who underwent clinical staging than for patients treated after staging laparotomy.

The present series reports on 15 consecutive patients who underwent laparoscopic staging for HD and compares them with 40 patients who received open staging. The laparoscopic procedures included our learning curve, with 2 (13%) converted cases. Stage was changed in a similar number of patients in each group at a rate that was consistent with reported data.\(^15,16\) The significantly increased lymph node retrieval with laparoscopy demonstrates that the commitment of the surgeon to sample nodes is more important than the operative route. The absence of any disease recurrence below the diaphragm in the laparoscopic group suggests high accuracy in detecting pathologic abdominal lymph nodes and supports its oncologic equivalence to open staging. The postoperative morbidity was lower after laparoscopy than after open surgery, although this difference did not reach statistical significance. Moreover, the type and severity of the morbidity events were different: wound dehiscence and intra-abdominal abscesses were not seen after LS.

These data show that laparoscopic staging for HD is feasible, effective, and safe. Cosmesis was improved, and hospitalization was shortened. Confirmation of these results by larger trials should stimulate a reconsideration of the role of pathological staging for HD.

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### REFERENCES


Mark M. Connolly, MD, Chicago, Ill: Dr Carroll and his colleagues are to be congratulated for investing the time and effort to revisit the value of pathological staging in Hodgkin disease from a new approach, that is, to employ a minimally invasive technique to reduce procedure-related morbidity while maintaining oncologic validity of the results. Laparoscopic staging of Hodgkin disease is a logical next step after the growth of experience and good outcomes of laparoscopic splenectomy and node dissections for other indications. Although this initial experience is small with relatively short mean follow-up, their objective of demonstrating oncologic equivalence to the open procedure in detecting pathological lymph nodes and retrieving intact spleen appears to be valid.

Reduction in postoperative ileus and length of stay were clearly an improvement. The longer operative time should also decrease with experience. Although infrequently performed at many centers, pathological staging through laparotomy is the gold standard, but its cost was no longer felt to justify its use. The presence or absence of a set of adverse prognostic factors is now commonly being used to determine treatment. Staging laparotomy remains the most precise way to determine the presence and extent of abdominal involvement, allowing the therapy to be tailored to the extent of the disease. Twenty to thirty percent of early clinical stage IA and IIA patients will have occult abdominal disease not detected by modern imaging techniques. Downstaging is also significant. Although select subgroups with low risk for occult abdominal disease have been identified that do not require pathological staging, 75% to 80% of all early clinical stage I and II patients remain at substantial 24% to 36% risk for splenic or lymph node involvement. Of the 20 randomized trials of radiation therapy vs combination chemotherapy and radiation therapy, none has demonstrated an overall survival difference. The treatment and subsequent survival of patients with early-stage Hodgkin disease has been so successful that the current direction of studies is to reduce long-term adverse effects of treatment, such as leukemias. Aggressive staging minimizes the treatment needed. Radiation therapy alone with smaller fields has many long-term advantages. It would be too risky without surgical staging for most patients. The arguments against routine staging laparotomy should be considerably diminished with the laparoscopic approach.

Would staging laparoscopy be more appropriately limited to specific centers, since adequate training, patient selection, and appropriate credentialing are important issues to maintain oncologic validity and minimize complications? What do you feel is the future role of pathological staging? In which patients will the outcome influence treatment? Are you developing a protocol for selecting patients? And, finally, how were you able to persuade the medical oncologists to participate in this trial? What is needed to persuade others to reconsider this procedure?

Raymond J. Jochl, MD, Chicago: Do you use the harmonic scalpel in mobilizing the spleen and taking down the short gastric vessels? Your operative time was: what is the skin-to-skin time, or was it in-the-room to out-of-the-room time? Do you use nasogastric tubes postoperatively? In this trial? What is needed to persuade others to reconsider this procedure?

James E. Goodnight, Jr, MD, PhD, Sacramento, Calif: To pick up on a question Dr Connolly asked, if your staging laparotomy is negative, will the radiation oncologist limit the radiation fields? In other words, will they do less than total nodal therapy if it is negative? Secondly, since one of the major beneficial impacts that would come from the laparoscopic procedure would be removal of the spleen, should you in fact consider doing that only, removing the spleen and foregoing the node biopsies?

Theodore X. O’Connell, MD, Los Angeles, Calif: Although this paper looks like it is comparing open staging to laparoscopic staging, it suffers from the same problem as other studies that are not nonrandomized prospective studies in that there are other variants that are introduced into the process. In many ways you are comparing apples and oranges. One of the biggest variations that you have here is that the majority of the open procedures were performed in Italy, and they may have a different approach to staging, different complication rates, etc, compared to what is done at Cedars. Also, some surgeons at Cedars may be doing open staging, while a different group may be doing laparoscopic staging. This variation in surgeons may...
have an impact on morbidity and also may have an impact on number of nodes retrieved. The number of nodes retrieved is up to the surgeon; one can retrieve 50 if he wants to, or 3 if he wants to. So it is completely up to the surgeon and not whether one is doing it open or laparoscopically.

Second is the time to feeding. Were the same criteria used to determine when to feed in both groups? I think if you are using a protocol situation where you feed everybody on the second day in the laparoscopic group, you can achieve that. If you are waiting for bowel sounds, etc, in the open group, it may take longer. But if you use the same protocol in both groups to start feeding, many times you can feed at the same time.

The third point is the time to leave the hospital. Again, this may be a variation between Italy and the United States. They may not be under the same utilization management procedures that we are to get the patients out early. Is there a real variation between Italian and American health care guidelines rather than a difference in procedure? Also, many of the laparoscopic procedures may have been done later in the time period, when utilization management was even more concerned about getting patients out of the hospital. These variations may have more impact on the differences in results than open vs laparoscopic.

James R. DeBord, MD, Peoria, III: What, if any, is the role of positron emission tomographic scanning in staging lymphoma patients?

Armando E. Giuliano, MD, Santa Monica, Calif: The reason we are not doing staging laparotomy is that it rarely affects the way medical oncologists manage the disease. How often did the authors’ staging affect treatment?

Did they look at the patients in whom staging was altered and see whether it altered therapy?

Dr Phillips: I would like to start first with Dr Connolly’s questions and comment on his specific questions: should laparoscopic staging be performed at specific centers and have specific credentialing? What is the future role of laparoscopic staging? How do we persuade oncologists to reassess the role of staging? Unless we pick a few centers to do a good randomized prospective study, we will not win the support of the oncology community. So, yes, we should have specific centers that are trained, that can do the operations safely, mutually credentialed, and develop the proper protocol that is accepted by surgeons, radiotherapists, and oncologists.

Dr Joehl, regarding technique, we do use the harmonic scalpel in lymph node dissection. I find that it is an excellent instrument to use in the retroperitoneum around some major vessels. We tend not to use the harmonic scalpel for the splenectomy only because we prefer the endovascular cutters with formed staples. Once you have the cutter open, it is very inexpensive to use additional cartridges rather than open the harmonic scalpel. It is very cost-effective to use the harmonic scalpel and not the endovascular cutter, or use the endocutter and not the harmonic scalpel. We are trying to use just the endovascular cutter because we feel a little bit more secure using it on the splenic vein, and we are trying to get away from using the harmonic scalpel to cut costs. But the harmonic scalpel is an excellent technology, and we certainly use it for the short gastric vessels in antireflux surgery. In an obese patient, it facilitates lymph node sampling.

Regarding the operative time, this was a skin-to-skin operative time, not the time into the OR and out of the OR.

Regarding nasogastric tubes, no, we did not use nasogastric tubes, but they were used selectively in Italy in the open cases.

Dr Goodnight asked if negative staging did change the radiation field, and we can conclusively say “yes,” they did get smaller portals and radiation doses. Regarding the question, I think, of the decade, should we just do splenectomy as staging in all of our Hodgkin patients? Our results are similar to other published studies. All but 1 of our patients was positive in the spleen. There was 1 patient who was positive in the periaortic nodes who was not positive in the spleen. We have to include splenectomy alone as an arm in the prospective randomized trial of laparoscopic staging vs clinical staging.

Dr O’Connell, yes, there is naturally a variation between the United States and Italy. We do need a randomized, prospective trial, but there was amazing congruity in Udine University, where the surgeons are excellently trained. They attempted to discharge their patients in a timely manner, as is evidenced by their postsurgical stay of 6.7 days, which was the same length of stay as in the few patients we did open. So, though there was no specific protocol to feeding or discharge, there were similarities. In the laparoscopic group, we did wait for passage of flatus to start oral alimentation so that there would be some sort of general comparison.

To answer Dr DeBord regarding the role of positron emission tomographic scanning, we unfortunately do not have experience in that, but we suspect that it would be positive in lymphoma, but I’m not sure of the size of lesion needed to be imaged.

Dr Giuliano, yes, the treatment was changed in approximately 28% of patients in our study, both upstage and downstage changes in the therapy from radiation alone when they were scheduled for chemotherapy, or for chemotherapy when they were scheduled for radiation.


Surgical Anatomy

Peripheral nerves receive their vascular supply from a succession of anastomosing nutrient vessels (arteriae nervorum) derived from the nearest arteries which are seldom more than one-fourth to one-half inch away. On reaching a nerve, the artery usually divides into ascending and descending branches, which by anastomosing with longitudinal chains near the surface of the nerve and between the nerve bundles, form a series of arterial ladders. The veins (venae nervorum) have an intraneural pattern similar to that of the arteries.