# Postoperative Respiratory Complications in Patients with Hodgkin's Disease: Relationship to the Size of the Mediastinal Tumor\*

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Abstract—Postoperative respiratory complications were investigated in patients with Hodgkin's disease, stages I-III, presenting with a mediastinal mass. By measuring the ratio between the widest diameter of the mediastinal mass and the width of the thorax at T5-6 (mediastinal thoracic ratio, MTR) in a PA chest X-ray, patients were divided into three groups: I: MTR < 0.35 (41 patients); II: MTR 0.35-0.49 (33 patients); and III: MTR > 0.50 (23 patients). Five patients of group II and eight of group III received preoperative radiation therapy (RT) to the mediastinum due to severe clinical or radiological findings associated with the mediastinal mass. No patient of group I received preoperative RT. Without preoperative RT, group III had a significantly higher incidence of respiratory complications (7/15) compared to groups I (7/41) and II (2/28). Respiratory complications were not significantly different after preoperative RT in group III (1/8) compared to that observed in groups I plus II without preoperative RT (9/69).

### INTRODUCTION

EXPLORATORY laparotomy with splenectomy was introduced in the staging of Hodgkin's disease mainly to limit the extent of radiation therapy [1, 2]. Patients with laparotomy, stages I and II-A, are treated with regional radiation therapy (mantle, extended mantle), whereas patients with more advanced disease are treated with chemotherapy or combinations of chemotherapy and radiotherapy. Staging laparotomy in experienced hands has been reported to have a low morbidity and mortality. Overall, the reported incidence of morbidity ranges from 2 to 27% and the reported mortality is 0.6% [3-9]. In large studies, 52-68% of patients with early stage Hodgkin's disease present with mediastinal involvement [10-13]. Patients with massive

mediastinal tumors are reported to have a significantly higher morbidity and potential mortality following general anesthesia [6, 7]. For this reason, preoperative radiation therapy to the mediastinum has been given to symptomatic patients with large mediastinal masses before staging laparotomy (either complete course or the first part of a split course).

The purpose of this report was to study the relationship existing between postoperative respiratory complications and the size of the mediastinal mass in a large series of patients with Hodgkin's disease undergoing surgical procedures under general anesthesia.

# **MATERIALS AND METHODS**

Of 583 patients with a diagnosis of Hodgkin's diseases (all stages) evaluated at Roswell Park Memorial Institute, Buffalo, NY between April 1970 and June 1981, 103 patients with clinical stages I-III presenting radiologic evidence of a mediastinal mass underwent staging laparotomy at this institution. Six patients had incomplete follow-up or the chest X-rays were not available for review. The remaining 97 patients were

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retrospectively analyzed and are the basis of this report.

These patients ranged in age from 9 to 62 yr (median 23 yr). Fifty were males and 47 were females. Staging was conducted according to the recommendations of the Ann Arbor Conference [14].

Patients' data were evaluated for mediastinal mass size, symptoms, and radiologic abnormalities thought to be associated with the mediastinal mass, and for postoperative respiratory complications that were demonstrated clinically and radiographically.

To have an objective measure of the size of the mediastinal tumor, the mediastinal thoracic (MT) radio was obtained by measuring the widest transverse diameter of the mediastinal mass divided by the thoracic width at the level of T5-6 in a PA chest X-ray [11]. MT ratios ranged from 0.19 to 0.86 (median 0.37). Patients were grouped according to the MT ratio as follows: group I, small mediastinal mass, those with an MT ratio of <0.35 (41 patients); group II, large mediastinal mass, MT ratio of 0.35-0.49 (33 patients); and group III, massive mediastinal mass, those with an MT ratio >0.50 (23 patients).

Fifty-seven (59%) of the 97 patients had one or more symptoms and/or radiologic abnormalities on the chest X-ray associated with the mediastinal mass. Table 1 shows incidence of symptoms and radiologic findings in the three groups. As expected, patients in group III were the most symptomatic and had more radiologic abnormalities. The most frequent manifestations observed were cough, tracheal deviation and dyspnea. Symptoms or radiologic abnormalities such as stridor, dyspnea, superior vena cava syndrome, large pericardial or pleural effusions and tracheal deviation were severe enough to

warrant a full course of preoperative radiation (3600 rads) to the mediastinum in 13 patients; five of these 13 were in group II, eight in group III. None of the patients in group I received preoperative radiation therapy.

Respiratory complications were defined as those occurring within 10 days following surgery which required additional medical treatment such as reintubation, bronchoscopy or antibiotics and which were directly responsible for a longer hospital stay in these patients.

Statistical comparisons among the different groups were established with the Fisher exact probability test [15].

#### **RESULTS**

There was no operative mortality. Seventeen of the 97 patients (18%) developed postoperative respiratory complications. Table 2 shows the incidence of respiratory complications according to the size of the mediastinal mass and according to whether or not preoperative radiotherapy was given. None of the 41 patients of group I had received preoperative radiation therapy. Seven of these (17%) developed respiratory complications postoperatively: pneumonia (three patients, one with pleural effusion) and atelectasis (four patients, one with pleural effusion). Two of the 28 patients (7%) of group II who did not receive preoperative radiotherapy developed respiratory complications (pleural effusion and atelectasis respectively), while none of the five patients who received preoperative radiotherapy developed postoperative respiratory complications. In group III 7/15 patients (47%) who did not receive preoperative radiotherapy developed respiratory complications: acute life-threatening airway obstruction after extubation was observed in two patients, both requiring reintubation and assisted

Table 1. Clinical and radiologic manifestations according to MT ratio in 97 patients with Hodgkin's disease (%)

	Group I MT < 0.35 MT	Group II 0.35-0.49	Group III $MT > 0.50$	Total
Patients:	41	33	23	97
Clinical manifestations				
Cough	7 (17%)	14 (42%)	12 (52%)	33 (34%)
Dyspnea	1 (2%)	6 (18%)	6 (26%)	13 (13%)
Dysphagia	4 (10%)	0	3 (13%)	7 (7%)
SVC syndrome	0	1 (3%)	1 (4%)	2 (2%)
Stridor	0	1 (3%)	1 (4%)	2 (2%)
Vocal cord paralysis	0	0	1 (4%)	1 (1%)
Radiologic manifestations				
Tracheal deviation	3 (7%)	5 (15%)	8 (35%)	16 (16%)
Pleural effusion	0	2 (6%)	5 (22%)	7 (7%)
Tracheobronchial narrowing	0	2 (6%)	2 (9%)	6 (6%)
Atelectasis	l (2%)	2 (6%)	3 (13%)	6 (6%)
Pericardial effusion	0	1 (3%)	1 (4%)	2 (2%)

	Group I	Group II	Group III	Total
No preop. RT Preop. RT	7/41 (17%)	2/28 (7%) 0/5 (0%)	7/15 (47%) 1/8 (12%)	16/84 (19%) 1/3 (7%)
Total	7/41 (17%)	2/23 (6%)	8/23 (35%)	17/97 (18%)

Table 2. No. of patients presenting severe respiratory complications/total No. of patients (%)

ventilatory support. One was extubated successfully only after treatment with combination chemotherapy was started. Other complications were pneumonia in two patients, one of these with empyema, the other with effusion, atelectasis with large pleural effusion in two patients, and large pleural effusion alone in one patient. In contrast, only one of the eight patients (13%) who had received preoperative radiotherapy had respiratory complication (pneumonia).

The incidence of respiratory complications among the patients who did not receive preoperative RT to the mediastinum was significantly higher in group II (7/15) than in group I (7/41, P = 0.036) or group II (2/28, P = 0.005). The incidence of severe respiratory complications which occurred after preoperative radiation therapy was similar in group II (1/8) to that observed in group II (0/5, N.S.). Patients of groups I plus II who did not receive preoperative radiation therapy had a similar incidence of postoperative respiratory complications to that observed in patients in group III who were given preoperative radiation therapy.

## **DISCUSSION**

Acute life-threatening airway obstruction from general anesthesia by endotracheal intubation was reported in as high as 33% among patients with MT ratios exceeding 0.45 [6]. In group III (MT ratio >0.50) the incidence of this acute lifethreatening complication was much lower than that reported by Piro et al. [6]. Two of 15 patients (13%) whose MT ratios exceeded 0.50 (MT ratio of 0.56 and 0.67) and who did not receive preoperative radiation therapy required reintubation and assisted ventilatory support. The MT ratios were measured with different techniques in our study and in the above-mentioned study; however, patients of our group III had MT ratios somewhat larger than those with an MT >0.45 in Piro's study. No acute life-threatening episodes were observed after preoperative radiation in patients presenting with an MT ratio larger than 0.50, or with smaller mediastinal masses, but with severe symptoms or radiologic abnormalities. We found, however, a significantly higher incidence (5/15, 33%) of other postoperative respiratory complications among those patients with an MT ratio of ≥0.50 who were not considered to have severe symptoms or radiography changes requiring preoperative radiation therapy. These complications produced longer hospitalization, delay in treatment, possible tumor progression and potential mortaltiy.

Other postoperative surgical complications (wound dehiscence, ventral hernia, small bowel obstruction requiring surgery, upper gastro-intestinal bleeding, ileus, phlebitis, etc.) were not related to the size of the mediastinal mass and were equally distributed among the three groups: six in group I (14%), four in group II (12%) and three in group III (13%). These latter postsurgical complications are no different from other reported series which include all patients with Hodgkin's disease undergoing staging laparotomy with splenectomy [3–5, 8, 9]. The higher level of respiratory complications reported here is the result of the selection of patients for this study.

Preoperative radiation therapy to the mediastinum decreased substantially the incidence of respiratory complications in patients presenting with massive mediastinal masses (see Table 2). However, the long-term follow-up of patients with Hodgkin's disease presenting with MT ratios over 0.30 shows a relapse rate of 50-70% when the treatment given was radiation therapy alone [10-13, 16]. In contrast, in the same group of patients, programs of combined modality treatment have shown a significantly longer duration of remission [10, 16] and longer survival [16]. In addition, patients with large mediastinal masses require wide and large radiation ports, which encompass a large volume of lung and heart. The incidence of radiation pneumonitis, pericarditis and myocardial damage is higher in this group of patients than observed in patients with smaller or no mediastinal mass [11, 16, 17]. Indeed, four of the 13 patients (31%) of groups II and III who had received preoperative radiation therapy developed severe radiation pneumonitis. The use of a split course of radiation therapy may decrease somewhat the incidence of these toxicities [18]. On the other hand, Carmel and Kaplan [19] have demonstrated that the in-field relapse increases significantly when the radiation treatment to the mantle area is interrupted as compared to when it is delivered on time. For the above-mentioned reasons, the use of combined modality treatment is now recommended in the therapy of patients with large mediastinal masses [12, 16]. Closed staging with lymphangiogram, tomodensitometry studies, bone marrow biopsy and radionucleide scintigrams should provide sufficient

diagnostic accuracy in these patients identifying abdominal involvement. The finding of pathologic involvement with Hodgkin's disease in the lymph nodes of the abdomen or in the spleen of these patients will not modify the therapeutic approach, thus staging laparotomy is unnecessary.

#### REFERENCES

- 1. Glatstein E, Guerney JM, Rosenberg SA, Kaplan HS. The value of laparotomy and splenectomy in the staging of Hodgkin's disease. *Cancer* 1969, **24**, 709-718.
- Desser RK, Golomb HM, Ultmann JE et al. Prognostic classification of Hodgkin's disease in pathologic stage III based on anatomoc considerations. Blood 1979, 49, 883-893.
- 3. Green DM, Ghoorah J, Douglas HO et al. Staging laporotomy with splenectomy in children and adolescents with Hodgkin's disease. Cancer Treat Rev 1983, 10, 23-38.
- 4. Martin JK Jr, Clark SC, Beart RW Jr, ReMine WH, White WL, Ilstrup DM. Staging laparotomy in Hodgkin's disease. *Arch Surg* 1982, 117, 586-591.
- 5. Nelson RW, Townsend CM Jr, Eakin DL, Costanzi JJ. Is staging laparotomy for Hodgkin's disease still justified? Am J Surg 1982, 143, 288-292.
- 6. Piro AJ, Weiss DR, Hellman S. Mediastinal Hodgkin's disease: a possible danger for intubation anesthesia. *Int J Radiat Oncol Biol Phys* 1976, 1, 415.
- 7. Bittar D. Case history number 84: respiratory obstruction associated with induction of general anesthesia in a patient with mediastinal Hodgkin's disease. *Anesth Analg (Cleve)* 1975, 54, 399-403.
- 8. Slavin R, Nelsen TS. Complications from staging laparotomy for Hodgkin's disease. *Natl Cancer Inst Monogr* 1973, **36**, 457-459.
- 9. Urlaub BJ, Mack E. Evaluation and complications of 107 staging laparotomies for Hodgkin's disease. *Ann Surg* 1979, 190, 45-47.
- 10. Hoppe RT, Coleman CN, Cox RS, Rosenberg SA, Kaplan HS. The management of stage I-II Hodgkin's disease with irradiation alone or combined modality therapy: the Stanford experience. *Blood* 1982, **59**, 455-465.
- 11. Lee CKK, Bloomfield CD, Goldman AI, Levitt SH. Prognostic significance mediastinal involvement in Hodgkin's disease treated with curative radiotherapy. *Cancer* 1980, 46, 2403-2409.
- 12. Mauch P, Goodman R, Hellman S. The significance of mediastinal involvement in early stage Hodgkin's disease. *Cancer* 1978, 42, 1039-1045.
- North LB, Fuller LM, Hagemeister FB, Rodgers RW, Butler JJ, Shullenberger CC. Importance of initial mediastinal adenopathy in Hodgkin's disease. AJR 1982, 138, 229-235.
- 14. Carbone PO, Kaplan HS, Mushoff K, Smither DW, Tubiana M. Report of the committee on Hodgkin's disease staging classification. *Cancer Res* 1971, 31, 1860-1861.
- 15. Taub TW. Computation of two-tailed Fisher test. J Qual Technol 1979, 11, 44-47.
- Gomez GA, Panahon AM, Stutzman L et al. Large mediastinal mass in Hodgkin's disease results of 2 treatment modalities. Am J Clin Oncol 1984, 7, 65-73.
- Gomez GA, Park JJ, Panahon AM et al. Heart size and function after radiation therapy to the mediastinum in patients with Hodgkin's disease. Cancer Treat Rep 1983, 67, 1099-1103.
- 18. Johnson R, Ruhl U, Johnson SK, Glover M. Split course radiotherapy in Hodgkin's disease. *Cancer* 1976, 37, 1713-1717.
- 19. Carmel RJ, Kaplan HS. Mantle irradiation in Hodgkin's disease. An analysis of technique, tumor eradication and complications. *Cancer* 1976, 37, 2813-2825.