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Staging laparotomy for Hodgkin's disease in adults: One center experience

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The results of 124 staging laparotomies (SL) for Hodgkin's disease (HD) in adults, 95 with supradiaphragmatic clinical state (CS) I-II, and 29 with CS III, performed at the Institute of Oncology in Ljubljana in the years 1974–1989 are presented in a retrospective analysis. After SL, clinical stage was changed in 36 % of all cases, with 34 % of CS I-II cases upstaged and 45 % of CS III cases downstaged. 88 % (28/32) of CS I-II patients with positive SL had upper abdominal involvement (pathological stage – PS III_1) most frequently in the spleen, 84 % (27/32); in 31 % (10/32) the spleen was the only localization of HD. Only 5 % of the patients had early, while 5 % had late complications after SL; there were no procedure-related deaths.

Key words: Hodgkin's diseases; staging laparotomy

Introduction

The extent of Hodgkin's disease (HD) at the time of diagnosis is one of the most important data needed to determine therapy Staging laparotomy (SL) is the most accurate method for diagnosis of HD in the subdiaphragmatic sites. The first experiences with SL were published by the Stanford University in 1969.[1] Since then SL has become accepted in many centers. Considering great differences in the experience and competence of therapeutic teams in different centers as well as in the quality of investigations and the accuracy of SL, the evaluation of our own results seems to be all the more important.

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The purpose of this study was to review the results of SL in our center, and to compare them with those obtained by other authors, in order to establish the degree of realiability of this method in our hands.

Patients and methods

From January 1974 to December 1989, 421 formerly untreated adult patients with HD were treated at the Institute of Oncology in Ljubljana. Their age ranged between 15 – 83 yrs (mean 40 yrs). The diagnosis was histologically[2] confirmed in all except 17 patients. SL has been performed since 1974 in patients with clinical stage (CS) I-II above the diaphragm, and in those suspected of having HD under the dia-

phragm (suspected CS III), whereas SL was never indicated in clear CS III and CS IV. SL was performed in a third, 31% (130/421) of all patients with CS I-IV; 43% (95/219) of these were with CS I-II above the diaphragm, and only 20% (29/144) with CS III (Table 1). For various reasons SL was performed in less than a half of patients with early stages, the selection of candidates for SL was not randomised. Six of 130 patients with CS I-II under the diaphragm had only diagnostic laparotomy performed, and were excluded from the study. Thus, our retrospective study was carried out in 124 patients with CS I-III (95 with supradiaphragmatic CS I-II, and 29 with suspected CS III) who underwent SL. Their age ranged from 15–63 (mean 32.4) years.

Preoperative evaluation comprised a complete history, physical examination, routine laboratory tests, chest X-ray, bone marrow biopsy, and in the majority of patients also pedal lymphography (99/124), Ga-scintiscan of the whole body (103/124), and in last years also CT and/or US of the abdomen.

Stage was determined according to Ann Arbor criteria.[3] For the needs of this study, five supradiaphragmatic lymph node regions were defined as follows: 1. left neck and/or supraclavicular: 2. right neck and/or supraclavicular; 3. left axillary and/or subclavicular; 4. right axillary and/or subclavicular; 5. mediastinal and/or hilar nodes on the right/left or bilaterally.

Laparotomy consisted of wedge and needle biopsy of both liver lobes, splenectomy, biopsy of multiple lymph nodes (celiac, portal, splenic, paraaortic, mesenteric and iliac), biopsy of all lymph nodes that appeared to be involved with disease or the involvement was suspected on lymphangiogram and appendectomy. Metallic clips were placed at biopsy sites. An oophoropexy was performed in premenopausal women. Pneumococcal vaccine has been administrated preoperatively to patients since 1984.

Results

After laparotomy 34% (32/95) of patients with supradiaphragmatic CS I-II were upstaged (Table 2) while 45% (13/29) of patients with CS III were downstaged (Table 3).

Table 4 shows the distribution of HD by subdiaphragmatic site. The distribution by the frequency of subdiaphragmatic lymph node involvement is presented in Table 5, while the number and sites of biopsies are shown in Table 6.

Early complications were noted in 5% (7/130) and late in 5% (6/130) of patients; there were no SL-related deaths (Table 7). Three of 291 non–splenectomized patients had acute myeloblastic leukemia, and one of 130 splenectomized patients had refractory anemia with myeloblastostis; all four patients received chemotherapy according to MOPP schedule, and radiotherapy.

Because of laparotomy, the beginning of treatment had to be postponed for more than 3 weeks on average (Table 8).

Discussion

The reassessment of stage after SL may alter the treatment, which remains the major argument in favor of SL.

According to the data from literature, 25–35% of patients with supradiaphragmatic CS I-II are found to have HD under the diaphragm.[4-10] These findings are consistent with our results (34%) (Table 2). However, when comparing our findings by stage (CS I 44%, CS II 27%) with data from literature (CS I 17–32%, CS II 27–30%)[6,7,11] a high rate of positive SL in our patients with CS I is clearly evident. Perhaps the reason for this is a diffe-

Table 1. Hodgkin's disease: Number of staging laparotomies by clinical stage (Ljubljana, Sovenija 1974–1989).

Clinical Stage	Lapartomy	Non--laparotomy	Total
I-II supradiaphragmatic	95	124	219
subdiaphragmatic	6	16	22
III	29	115	144
IV	0	36	36
Total	130 (31%)	291 (69%)	421

Table 2. Hodgkin's disease with clinical stage I-II: Results of laparotomy.

CS	No. of pts.	Unchanged stage PS I	Unchanged stage PS II	Upstaging PS III	Upstaging PS IV	Upstaging %
I	36	20	0	15	1	44
II	59	0	43	16	0	27
Total	95	20	43	31	1	34

CS = clinical stage, PS = pathological stage

Table 3. Hodgkin's disease with clinical stage III: Results of laparotomy.

CS	No. of pts.	Unchanged stage PS II	Upstaging PS IV	Downstaging PS I	Downstaging PS II	Downstaging %
III	29	12	4	5	8	45

CS = clinical stage, PS = pathological stage

Table 4. Hodgkin's disease with clinical stage I-III (n = 124): Sites of subdiaphragmatic disease after laparotomy.

Site	CS I 16 + SL/36 SL No.	CS II 16 + SL/59 SL No.	CS I-II 32 + SL/95 SL No.	CS III 16 + SL/29 SL No.
Spleen alone	6	4	10	0
Spleen + lgl III_1	9	6	15	7
Spleen + lgl III_2	0	0	0	1
Spleen + lgl III_{1+2}	1	1	2	5
Lgl alone III_1	0	3	3	0
Lgl alone III_2	0	1	1	1
Lgl alone III_{1+2}	0	0	0	1
PS III_1	15	13	28	6
PS III_2	1	2	3	6
PS IV	1	0	1	4

CS = clinical stage, SL = staging laparotomy, PS = patological stage, lgl = lymph nodes

Table 5. Hodgkin's disease with clinical stage I-III (n = 124): Subdiaphragmatic lymph node sites after laparotomy.

Site	CS I 16 + SL/36 SL No.	CS II 16 + SL/59 SL No.	CS I-II 32 + SL/95 SL No.	CS III 16 + SL/29/ SL No.
III_1:				
celiac	6	9	15	7
splenic hilus	3	4	7	10
liver hilus	1	0	1	2
III_2:				
paraaortal	1	1	2	7
mesenteric	0	0	0	0
iliac R	0	0	0	2
iliac L	0	0	0	1

CS = clinical stage, R = right, L = left

Table 6. Hodgkin's disease with clinical stage I-III (n = 124): Number and sites of biopsies, and rate of histologically positive biopsies on laparotomy.

Site of biopsy	Rate of histologically positive biopsies	
	No.	%
Liver	4/124	3
Spleen	40/124	32
Bone-marrow	1/124	0.8
Lymph nodes:		
periportal	3/11	27
spleenic hilus	17/49	35
celiac	22/64	34
paraaortal	10/94	11
iliac right	2/41	5
iliac left	2/38	5
mesenteric	0/75	0

Table 7. Hodgkin's disease with clinical stage I-III (n = 130): Laparotomy related complications.

Complications		No.	%
Early (5%):	bleeding from a. lienalis (surg)	1	0.8
	bronchopneumonia	3	2.3
	dehiscence	2	1.5
	severe wound infection	1	0.8
Late (5%):	ileus	3	2.3
	requiring surgery	2	
	herniation in the surgical scar	3	2.3
	sepsis	–	–
Death (0%)		–	–

Table 8. Hodgkin's disease with clinical stage I-II:Time from diagnosis to the beginning of therapy – laparotomized vs. non-laparotomized patients.

Laparotomy	No. of pts	Range days	$\bar{x}$ days	Chi^2	df	p
Yes	95	22–334	66.8			
				3.75	1	0.0002
No	124	23–243	43.3			

rent definition for the number of involved regions. For instance, we defined the localizations in the mediastinum and/or right and/or left hilus as one site, while other authors may have defined them differently.

In our patitents with advanced disease, the stage after Sl was found to have decreased in 45% (Table 3) while other authors[5,6,11] report decrease in only 11–27% of patients. A high percent of downstaging in our patients probably indicates a high false positive rate of diagnostic procedures under the diaphragm.

In approximately one third of patients with supradiaphragmatic CS I-II, i.e. in 28% (27/95) of our cases (Table 4) and 26%–30% of those reported by other authors,[6,11] HD in the spleen is confirmed by SL. This fact actually proves how difficult it is to prove the presence of splenic involvement by menas of clinical examinations. In patients with CS I-II and positive SL, the spleen was affected most frequently; in our series this was the case in 84% (27/32) (Table 4), while in other reports the rate ranges between 85–100% of patients.[4,6,10,12] The spleen was found to be the only subdiaphragmatic HD site in 31% (10/32) of our patients and in 20–50% of those reported by others.[10–12] According to our data, which are consistent with other reports,[11] all patients with HD in the liver also had splenic involvement. In CS I-II, HD was most frequently localized in the upper abdomen (pathological stage – PS III_1) 88% (28/32) in our series (Table 4) vs. 75–86% in other reports),[6,11] and rarely also in the lower abdomen (PS III_2) 9% (3/32) in our series vs. 8.5–18% in other reports)[6,11] while the extranodal involvement (PS IV) was rare 3% (1/32) in our series vs. 5.3–6.5% in others).[6,11] In our patients (Table 5) as well as in those reported by other authors,[5,11,13] lymph nodes of the splenic hilus and celiac lymph nodes among those of the upper abdomen (PS III_1), and the paraaortal among the lower abdominal lymph nodes (PS III_2), were affected most frequently. According to Smithers, HD, which is initially situated supradiaphragmatically, spread hematogenously under the diaphragm, first into the spleen, thereafter lymphogenously (or hematogenously) into the lymph nodes of the splenic hilus and further into other lymph nodes (but not vice versa) as well as into extranodal organs (liver, bone-marrow).[4] This theory is supported by the following facts: 1. in 25–35% of patients with CS I-II the disease is situated under the diaphragm, 2. the spleen is the most frequent and often the only site of involvement, 3. upper abdominal lymph nodes are most frequently affected together with the

spleen and rarely alone, 4. liver involvement always goes hand in hand with splenic involvement, and 5. the spleen is supplied only by efferent lymphatics.

The quality of SL can be evaluted by the assessment of its technical performance, and in patients with PS I-II treated by mantel field irradiation (MFI) also by the number of subdiphragmatic recurrences outside the radiotherapy field.

The basic criteria for quality SL were fulfilled. All the patients underwent splenectomy, biopsy of both liver lobes, biopsy of the bone marrow and biopsy of all suspicious lymph nodes, while biopsy of all lymph nodes was not done (Table 6). Premenopusal women had "oophoropexy". In ours as well as in other centers[11, 14] biopsy was most frequently performed in the following lymph nodes: those of the splenic hilus, celiac, paraaortal and mesenterial.

However, it would be unrealistic to base our assessment of the quality of SL solely on the number of subdiaphragmatic recurrences, taking into account that 2/3 of laparotomized patients were treated with subtotal nodal irradiation (STNI), for which it is difficult to find a reason. In those patients the radiation field included upper abdominal lymph nodes, which are most frequently affected in CS I-II.

Our data for the occurence of early and late SL-related complications (Table 7) are comparable to those reported by other centers.[5, 6, 10, 13] None of our patients had sepsis, though some authors[5, 10, 13, 15–17] associate splenectomy with an increased risk of sepsis (0.1–10%), while others[18] failed to prove any difference in the frequency of infection between splenectomized and non-splenectomized patients. SL is associated with 0–3% mortality[5, 10, 13, 19–22] although no procedure-related deaths have been registered by the majority of centers in the last decade, probably due to advanced SL technique, better pre- and postoperative care, as well as due to a more appropriate selection of SL candidates.[5, 10] None of our patients have died.

Some authors[23, 24] report an increased incidence of acute myeloblastic leukemia in splenectomized patients receiving MOPP chemotherapy, however, no such association has been confirmed by our results.

The onset of primary (initial) treatment was postponed for almost a month due to SL (Table 8); this data is consistent with other reports.[25]

Conclusion:

There are great differences between individual centers with respect to ghe quality of diagnostic workup, accuracy of SL performance, and the experience and competence of therapeutic team. Nevertheless, the fact that our results are comparable with those obtained elsewhere confirms our competence to perform SL safely. Despite new diagnostic procedures, SL remains the most accurate albeit aggressive diagnostic method for the verification of subdiaphragmatic spread of HD. However, the opinions about when and whether this method is still indicated at all are controversial.

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