Incidence of Disease Outside Modified Retroperitoneal Lymph Node Dissection Templates in Clinical Stage I or IIA Nonseminomatous Germ Cell Testicular Cancer

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Purpose: We evaluated the incidence, sites and histology of disease outside 5 modified retroperitoneal lymph node dissection templates for patients with low stage nonseminomatous germ cell tumors of the testis.

Materials and Methods: Our cohort consisted of 500 consecutive patients with clinical stage I to IIA nonseminomatous germ cell tumors who underwent primary retroperitoneal lymph node dissection from 1989 to 2004. We analyzed 191 patients with pathological stage II disease and defined the incidence of disease outside 5 modified retroperitoneal lymph node dissection templates, 3 described for open surgery (Testicular Tumor Study Group, Indiana University and Memorial Sloan-Kettering Cancer Center) and 2 for laparoscopic surgery (University of Innsbruck and The Johns Hopkins University).

Results: Of 191 patients with pathological stage II disease, 111 (58%) had clinical stage I disease and 80 (42%) had clinical stage IIA disease. Depending on the template applied, extra-template disease ranged from 3% to 23% of all patients and was 1% to 11% of patients with pN1 disease. Regardless of template, histological distribution of extra-template disease was not significantly different from in-template disease with approximately 90% viable germ cell tumor, 10% teratoma only and 20% with any teratoma. For right side templates inclusion of para-aortic, preaortic and right common iliac regions decreased the incidence of extra-template disease to 2%. For left side templates inclusion of interaortocaval, precaval, paracaval and left common iliac regions decreased the incidence of extra-template disease to 3%.

Conclusions: A significant number of men with clinical stage I to IIA nonseminomatous germ cell tumors and retroperitoneal metastases have disease present outside the limits of modified templates, including 20% to 30% with chemoresistant teratomatous elements. The data suggest that more extensive nerve sparing templates optimize oncological efficacy and ejaculation preservation, and minimize overall treatment morbidity.

Key Words: neoplasms, germ cell and embryonal; lymph node excision; testicular neoplasms; laparoscopy

Cure rates for men presenting with clinical stage I or IIA NSGCT of the testis approach 100%. The retroperitoneum is the initial, and often only, site of metastases in up to 90% of patients, therefore a properly performed retroperitoneal lymph node dissection has a diagnostic and therapeutic role. Conversely, an uncontrolled retroperitoneum can result in the need for reoperation,[1] late relapse[2] and the bulky retroperitoneal disease present in approximately 80% of patients dying of GCT.[3]

Historically bilateral infrahilar RPLND templates were associated with significant ejaculatory morbidity due to interruption of the sympathetic trunks, hypogastric plexus and/or postganglionic efferent nerves. To reduce rates of retrograde ejaculation, numerous side specific modified templates have been proposed,[4–7] variably limiting contralateral dissection, particularly below the inferior mesenteric artery. Many of these templates were based on nodal anatomical mapping studies.[8–10]

More recently, prospective nerve sparing RPLND techniques have been described and result in near uniform preservation of antegrade ejaculation.[11] We analyzed anatomical nodal mapping data to evaluate the incidence, sites and histology of disease found outside 5 modified RPLND templates.

METHODS

Following institutional review board approval, we reviewed our institutional prospective RPLND database and identified 500 patients with CS I or IIA NSGCT undergoing primary RPLND at Memorial Sloan-Kettering Cancer Center between 1989 and 2004. RPLND was performed with therapeutic intent and usually all nodal regions in a full infrahilar bilateral template except the contralateral common iliac nodes were resected. Nodal packets were resected from prespecified anatomical regions (see figure), individually labeled and submitted separately for pathological evaluation.

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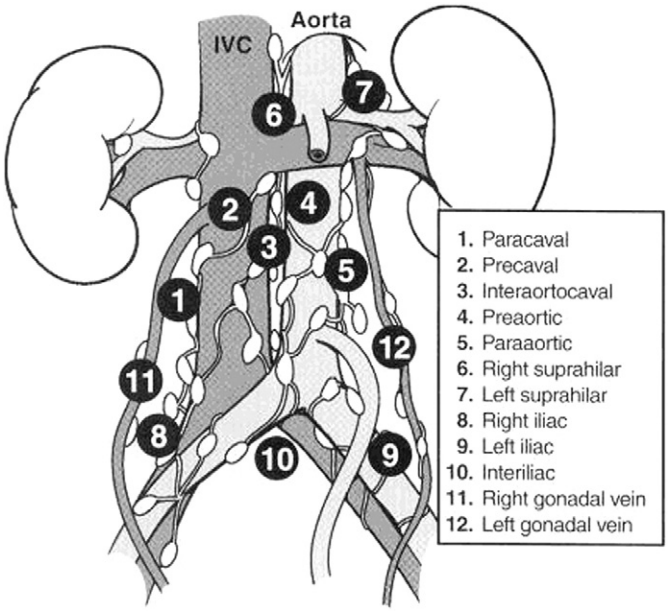

Anatomical regions of the retroperitoneum. Reprinted with permission.[19]

Median followup was 54 months (IQR 25 to 99) after RPLND.

Clinical stage and pathological stage were assigned according to the 2002 American Joint Committee on Cancer classification. CS I was defined as retroperitoneal lymph nodes less than 1 cm on cross-sectional imaging and CS IIA was defined as single or multiple retroperitoneal nodes 1 to 2 cm in diameter. PS was defined as pN1 (5 or fewer positive nodes, all less than 2 cm in diameter), pN2 (positive lymph nodes 2 to 5 cm diameter or more than 5 positive nodes all less than 5 cm, or extranodal tumor extension) and pN3 (positive lymph node more than 5 cm diameter). At present patients with pN1 disease generally undergo observation unless there are concerns regarding compliance with the followup regimen. A few compliant patients with pN1 disease receive adjuvant chemotherapy particularly if there are concerns regarding their ability to tolerate full induction chemotherapy in the event of relapse. Patients with pN2/3 disease almost invariably receive adjuvant chemotherapy.

We analyzed the anatomical distribution of disease in our cohort (see figure) and applied these findings to 5 modified templates to determine the incidence of disease outside of each template (see Appendix). The 3 open templates studied are those described by the Testicular Tumor Study Group (Weissbach et al),[8] Indiana University (Donohue et al)[4] and Memorial Sloan-Kettering (Sheinfeld et al),[12] and for laparoscopic RPLND those described by University of Innsbruck (Janetschek et al)[5] and The Johns Hopkins University (Nelson et al).[6] Disease outside the template was defined as a nodal region with viable GCT or teratoma not included in the template, or extra-template retroperitoneal disease recurrence without in-template recurrence.

RESULTS

Characteristics at Orchiectomy

Mean age (SD) at orchiectomy was 30.3 (8.8) years. The primary tumor was left side in 270 (54%) and right side in 230 (46%) patients (table 1). CS was I in 364 (73%) patients and IIA in 136 (27%). In the orchiectomy specimen 255 (51%) had teratoma, 228 (46%) yolk sac, 190 (38%) seminoma, 421 (84%) any embryonal carcinoma, 73 (15%) pure embryonal carcinoma, 31 (6%) choriocarcinoma and 305 (61%) lymphovascular invasion.

Characteristics of Patients With PS II Disease at RPLND

Of the 500 patients undergoing a primary RPLND, 191 (38%) had PS II, of which 107 (56%) received cisplatin based adjuvant chemotherapy (table 1). Nodal histology was only viable GCT in 148 (77%) patients, viable GCT and teratoma in 26 (14%), and only teratoma in 17 (9%). Teratomatous elements were present in 43 (23%) patients. Pathological stage following RPLND was pN1 in 91 (47%), pN2 in 97 (51%) and pN3 in 3 (2%).

Among the 364 patients with CS I, 111 (31%) had PS II (58 with pN1 and 53 with pN2) and of the 136 patients with CS II, 80 (59%) had PS II (33 with pN1, 44 with pN2 and 3 with pN3). For the 88 patients with right side primary tumors and PS II disease, 37 (42%) had pN1, 50 (57%) pN2 and 1 (1%) pN3, and for the 103 patients with left side primary tumors and PS II disease, 54 (52%) had pN1, 47 (46%) pN2 and 2 (2%) pN3. Before 1998, 20 (4%) patients with elevated serum tumor markers (9 α-fetoprotein, 3 β-human chorionic gonadotropin, 8 both) underwent RPLND, CS I in 7 patients and IIA in 13. Pathological stage was pN0 in 4 (20%), pN1 in 3 (15%) and pN2/3 in 13 (65%).

Extra-Template Disease

In PS II cases disease was found outside the TTSG template in 43 (23%), Indiana in 21 (11%), MSKCC in 6 (3%), Innsbruck in 43 (23%) and JHU in 37 (19%) (table 2). Depending on the template applied, extra-template disease for CS I cases (364) was 1% to 5% and for CS IIA (136) 3% to 18%. Extra-template disease for pN1 cases (91) ranged from 1% to

TABLE 1. *Clinicopathological characteristics at orchiectomy and RPLND*

	No. Pts (%)	
	All RPLND	PS II RPLND
Primary testis tumor side:		
Rt	230 (46)	88 (46)
Lt	270 (54)	103 (54)
Clinical stage:		
I	364 (73)	111 (58)
IIA	136 (27)	80 (42)
Orchiectomy histology:		
Teratoma	255 (51)	74 (39)
Yolk sac	228 (46)	65 (34)
Seminoma	190 (38)	64 (34)
Any embryonal Ca	421 (84)	47 (25)
Pure embryonal Ca	73 (15)	169 (88)
Choriocarcinoma	31 (6)	15 (8)
Lymphovascular invasion	305 (61)	130 (68)
Increased serum tumor markers at RPLND	20 (4)	16 (8)
Pathological stage:	Not applicable	
pN1		91 (47)
pN2/3		100 (53)
RPLND pathology:	Not applicable	
Viable germ cell tumor		174 (91)
Teratoma only		17 (9)
Any teratoma		43 (23)
Adjuvant postop chemotherapy	Not applicable	107 (56)

TABLE 2. *Metastatic sites outside of side specific RPLND templates*

	No. Pts Open (%)			No. Pts Laparoscopic (%)	
	TTSG	Indiana	MSKCC	Innsbruck	JHU
Extra-template disease all pts	43 (23)	21 (11)	6 (3)	43 (23)	37 (19)
Orchiectomy side:					
Rt (88)	17 (19)	17 (19)	2 (2)	17 (19)	25 (28)
Lt (103)	26 (25)	4 (4)	4 (4)	26 (25)	12 (12)
Clinical stage:					
I (364)	19 (5)	10 (3)	2 (1)	19 (5)	19 (5)
IIA (136)	24 (18)	11 (8)	4 (3)	24 (18)	18 (13)
Pathological stage:					
pN1 (91)	10 (11)	2 (2)	1 (1)	10 (11)	9 (10)
pN2/3 (100)	33 (33)	19 (19)	5 (5)	33 (33)	28 (28)
Rt template extra-template disease:	17 (19)	17 (19)	2 (2)	17 (19)	25 (28)
Preaortic	Included in template	Included in template	Included in template	Included in template	17 (68)
Para-aortic	17 (100)	17 (100)	Included in template	17 (100)	17 (68)
Rt iliac	Included in template	Included in template	Included in template	Included in template	5 (20)
Lt iliac	2 (11)	2 (11)	2 (50)	2 (11)	2 (8)
Lt template extra-template disease:	26 (25)	4 (4)	4 (4)	26 (25)	12 (12)
Interaortocaval	23 (88)	Included in template	Included in template	23 (88)	Included in template
Lt iliac	10 (38)	Included in template	Included in template	10 (38)	10 (83)
Precaval	5 (19)	Included in template	Included in template	5 (19)	5 (42)
Rt iliac	3 (12)	3 (75)	3 (75)	3 (12)	3 (25)
Paracaval	2 (8)	2 (50)	2 (50)	2 (8)	2 (17)

11% and for pN2/3 was 5% to 33%. Extra-template disease for patients with increased serum tumor markers at RPLND ranged from 0% to 31%.

Right side templates: Of the 88 patients with a right side testis tumor and PS II disease, retroperitoneal disease was found outside the TTSG template in 17 (19%) men, Indiana in 17 (19%), MSKCC in 2 (2%), Innsbruck in 17 (19%) and JHU in 25 (28%). Among the 17 patients with extra-template disease using the TTSG, Indiana or Innsbruck templates, 17 (100%) had disease in the para-aortic nodes and 2 (11%) had additional disease in the left common iliac nodes. For the 25 patients with extra-template disease using the JHU template, disease was present in the preaortic nodes in 17 (68%) men, para-aortic in 17 (68%), right common iliac in 5 (20%) and left common iliac in 2 (8%). If the preaortic, para-aortic and right common iliac regions were included in right side templates, the incidence of extra-template disease for patients with PS II disease would decrease to 2%.

Left side templates: Of the 103 patients with a left side testis tumor and PS II disease, retroperitoneal disease was found outside the TTSG template in 26 (25%) men, Indiana in 4 (4%), MSKCC in 4 (4%), Innsbruck in 26 (25%) and JHU in 12 (12%). For the 26 patients with extra-template disease using the TTSG or Innsbruck templates, disease was present in the interaortocaval nodes in 23 (88%) men, left common iliac in 10 (38%), precaval in 5 (19%), right common iliac in 3 (12%) and paracaval in 2 (8%). For the 4 patients with extra-template disease using Indiana and MSKCC templates, disease was present in the right common iliac nodes in 3 (75%) and paracaval in 2 (50%). For the 12 patients with extra-template disease using the JHU template, disease was present in the left common iliac nodes in 10 (83%), precaval in 5 (42%), right common iliac in 3 (25%) and paracaval in 2 (17%). If the interaortocaval, precaval, paracaval and left common iliac regions were included in left side templates, the incidence of extra-template disease for patients with PS II disease would decrease to 3%.

In-Template and Extra-Template Disease

Extra-template disease without evidence of in-template disease was present for the TTSG template in 5 (3%) men, Indiana and MSKCC in 0 (0%), Innsbruck in 5 (3%) and JHU in 6 (3%), most commonly as preaortic, para-aortic or ipsilateral iliac disease for right side templates, and as interaortocaval or precaval disease for left side templates (table 3). The histological distribution of extra-template disease was nearly identical to in-template disease. Depending on the template applied, the extra-template disease contained viable GCT in 80% to 92%, teratoma only in 8% to 20% and any teratoma in 18% to 29% (table 4).

DISCUSSION

For patients with CS I to IIA NSGCT, meticulous RPLND provides critical staging information and therapeutic benefit. A thorough RPLND alone without adjuvant chemotherapy results in an approximately 90% cure rate for patients with low volume retroperitoneal disease and virtually eliminates the retroperitoneum as a site of disease relapse.[13] More recently, by selecting only patients whose serum tumor markers have normalized before RPLND and with CS IIA or less, the proportion of pN1 disease in patients with PS II disease has increased from 40% to 65%.

Historically bilateral RPLND led to normal postoperative ejaculatory function in only 10% of patients.[14] Based on

TABLE 3. *Extra-template without intra-template disease*

	No. (%)		
	Lt	Rt	Total
TTSG	5 (5)	0 (0)	5 (3)
Indiana	0 (0)	0 (0)	0 (0)
MSKCC	0 (0)	0 (0)	0 (0)
Innsbruck	5 (5)	0 (0)	5 (3)
JHU	1 (1)	5 (6)	6 (3)

TABLE 4. *Site-specific histology based on template type and in-template versus extra-template disease, JHU*

	No. (%)			
	Germ Cell Tumor	Teratoma Only	Any Teratoma	p Value
TTSG:				
In-template (186)	171 (92)	15 (8)	42 (23)	0.9
Extra-template (38)	35 (92)	3 (8)	7 (18)	
Indiana:				
In-template (191)	174 (91)	17 (9)	43 (23)	0.5
Extra-template (17)	14 (82)	3 (18)	5 (29)	
MSKCC:				
In-template (191)	174 (91)	17 (9)	43 (23)	0.7
Extra-template (5)	4 (80)	1 (20)	1 (20)	
Innsbruck:				
In-template (185)	170 (92)	15 (8)	41 (22)	0.8
Extra-template (33)	29 (88)	4 (12)	7 (21)	
JHU:				
In-template (186)	171 (92)	15 (8)	42 (23)	0.9
Extra-template (37)	34 (92)	3 (8)	7 (18)	

Five patients did not have site specific histology available. Patients with in-template disease and total patients may not be equal due to patients with extra-template and no in-template disease.

anatomical mapping studies of retroperitoneal metastases by Ray,[10] Donohue[9] and Weissbach[8] et al a number of modified RPLND templates were described,[4–7] intended to maximize rates of antegrade ejaculation by limiting dissection in areas considered at reduced risk for metastatic disease.

These mapping studies have significant limitations that may not have been fully appreciated. The mapping studies lack adequate postoperative followup, therefore the rate of extra-template retroperitoneal recurrence is unknown.[8–10] Without clinical followup sample error by surgeon and/or pathologist cannot be assessed. Studies by Ray[10] and Donohue[9] et al did not report any clinical followup while Weissbach et al reported a relatively short median followup of 22 months for patients with PS I disease.[8] In addition, it is not possible to accurately assess additional potential sites of metastatic disease in patients who received postoperative chemotherapy. All patients with PS IIB disease in the study by Weissbach et al received either 2 or 4 cycles of PVB (cisplatinum, vinblastine, bleomycin) in a randomized adjuvant chemotherapy study.[15] Finally, since the report by Weissbach et al was a multicenter study of 50 surgeons from 46 participating centers, significant surgical variability may have confounded their findings.

Several investigators have used modified templates based on mapping studies but their findings are similarly limited by the frequent use of adjuvant chemotherapy. Combining the Innsbruck[16] and Johns Hopkins[6] studies, 36 of 38 (95%) patients with PS II disease received postoperative adjuvant chemotherapy, making it impossible to accurately assess additional potential sites of metastatic disease or elucidate the true therapeutic impact of RPLND. Furthermore, by unnecessarily leaving unresected retroperitoneal disease, the full therapeutic potential of RPLND is not realized. In the Johns Hopkins study patients underwent abbreviated dissection when positive lymph nodes were found on frozen section[6] and the Innsbruck group considered RPLND a diagnostic measure only.[16]

Incomplete resection of retroperitoneal disease has multiple implications. It is an independent predictor of disease relapse.[17] The potential consequences of unresected viable GCT include reoperation and systemic cisplatin based chemotherapy. Patients requiring reoperative RPLND have decreased survival rates,[1] and those requiring chemotherapy are at increased risk for peripheral sensory neuropathy, Raynaud's phenomenon, ototoxicity, cardiovascular disease and development of a secondary solid tumor or leukemia.[18] Lastly, the potential risks of unresected teratoma, present in approximately 30% of patients with PS II disease, include late relapse, reoperation and risk of malignant transformation of teratoma, all associated with decreased survival rates.[1,2] Therefore, the importance of RPLND with resection of all disease cannot be overstated and should never be compromised to preserve antegrade ejaculation.

With prospective nerve sparing techniques resulting in antegrade ejaculation for approximately 95% of all patients,[11] the need for reduced templates to maximize ejaculatory function is debatable. Nerve sparing techniques combined with more extensive templates of nodal resection result in maximum benefit from the dual standpoints of cancer control and ejaculatory function while potentially minimizing the need for adjuvant chemotherapy. These subsequent oncological and ejaculatory outcomes are more appealing compared to the potential for suboptimal cancer control with modified templates.

To achieve complete eradication of retroperitoneal disease, our findings support inclusion of the preaortic, paraaortic and right common iliac regions in right side templates and, similarly, the interaortocaval, precaval, paracaval and left common iliac in left side templates. By doing so, the incidence of extra-template disease decreases to 2% for right side templates and 3% for left side templates. Accompanied by nerve sparing techniques, the full therapeutic potential of RPLND can be realized while reducing the risk of compromising ejaculatory function. In the presence of positive or suspicious nodes, the senior author (JS) performs a bilateral nerve sparing RPLND. If frozen sections are negative in the setting of a right side template, only the contralateral iliac nodes are omitted. For left side templates paracaval and right common iliac nodes are resected since a nerve sparing technique requires a split and roll of the inferior vena cava.

Based on anatomically specific nodal data, the data show that a substantial proportion of men with CS I to IIA NSGCT undergoing primary RPLND have extra-template disease if modified templates are applied. The incidence of disease outside 3 modified open templates ranged from 3% to 23% and for 2 modified laparoscopic templates was 19% to 23%. Disease outside of modified templates occurs even in patients presumably at low risk, in up to 5% of patients with CS I and up to 11% of those with pathological stage N1 disease. Additionally, extra-template disease can be present without evidence of in-template disease in up to 3% of patients.

Extension of surgery beyond the described limits of the 5 templates may be variably influenced by intraoperative findings, predisposition to adjuvant chemotherapy in pN1 disease, individual surgeon practice and other variables that are difficult to quantify at the respective institutions. Our data demonstrate the potential for residual unresected retroperitoneal metastases with strict adherence to 5 published modified templates. The most prudent oncological approach with pathological stage II NSGCT is bilateral infrahilar RPLND.

Our estimates of disease outside the modified templates represent the lowest possible incidence and could potentially be higher since not every patient in our study underwent full bilateral RPLND template that included the contralateral

common iliac regions. More than half of the patients with retroperitoneal disease received adjuvant chemotherapy, and with intermediate-term followup (median 54 months) some patients may yet experience an extra-template late relapse.

Furthermore, nerve sparing techniques require an initial split over the inferior vena cava to prospectively identify, dissect and preserve the postganglionic sympathetic fibers, right sympathetic chain and hypogastric plexus. The anterior split over the aorta necessarily follows and may also have led to an underestimation of extra-template disease in right side primary templates since the right half of the preaortic package is rolled into the interaortocaval package.

CONCLUSIONS

Thus, to achieve maximum oncological benefit from primary RPLND, less restrictive templates appear to be a more prudent approach. Based on the data we continue to advocate infrahilar nerve sparing RPLND for patients with clinical stage IB or IIA NSGCT and surveillance or RPLND for compliant patients with clinical stage IA NSGCT. The results of our study suggest that for patients with clinical stage I or IIA NSGCT of the testis, reducing the RPLND template increases the risk of residual retroperitoneal disease while infrahilar nerve sparing templates appropriately maximize cancer control. Restrictive templates may result in unresected disease, an increased overall treatment burden and morbidity, residual chemoresistant teratoma, and potentially compromised survival.

APPENDIX 1

Open and Laparoscopic RPLND Templates

	Institution	Reference	Abbreviation
Open	Testicular Tumor Study Group	8	TTSG
	Indiana University	4	Indiana
	Memorial Sloan-Kettering Cancer Center	12	MSKCC
Laparoscopic	University of Innsbruck	5	Innsbruck
	The Johns Hopkins University	6	JHU

APPENDIX 2

Description of Templates

	Open			Laparoscopic	
	TTSG	Indiana	MSKCC	Innsbruck	JHU
Right side					
precaval	✓	✓	✓	✓	✓
paracaval	✓	✓	✓	✓	✓
interaortocaval	✓	✓	✓	✓	✓
preaortic	✓	✓	✓	✓	
para-aortic			✓		
ipsilateral iliac	✓	✓	✓	✓	
contralateral iliac					
right hilar					
gonadal vein	✓	✓	✓	✓	✓
Left side					
precaval		✓	✓		
paracaval					
interaortocaval		✓	✓		✓
preaortic	✓	✓	✓	✓	✓
para-aortic	✓	✓	✓	✓	✓
ipsilateral iliac		✓	✓		
contralateral iliac					
left hilar					
gonadal vein	✓	✓	✓	✓	✓

Check mark denotes inclusion in template.

Abbreviations and Acronyms

CS	=	clinical stage
GCT	=	germ cell tumor
JHU	=	The Johns Hopkins University
MSKCC	=	Memorial Sloan-Kettering Cancer Center
NSGCT	=	nonseminomatous germ cell tumors
PS	=	pathological stage
RPLND	=	retroperitoneal lymph node dissection
TTSG	=	Testicular Tumor Study Group

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EDITORIAL COMMENT

This excellent article raises several issues about the proper treatment for clinical stage I NSGCT. One issue is whether retroperitoneal lymphadenectomy should be done at all in the compliant patient. Indeed many excellent urology groups now advocate surveillance for low risk clinical stage I NSGCT and surveillance or 2 courses of chemotherapy for the high risk case (eg with greater than 50% embryonal cancer and/or vascular invasion) presumably because the survival with this approach is said to be basically the same as algorithms involving primary RPLND, and the morbidity from the extra chemotherapy that could be given by these newer approaches (eg neuropathy, infertility, auditory or cardiovascular problems, secondary malignancy) seem to be acceptable in reports involving short and intermediate length followup.

I do not agree and I think neither does the MSKCC group. Until the long-term followup is truly known, especially in the patient who might be genetically susceptible to cancer or cardiovascular, auditory or neuropathic conditions, chemotherapy should be avoided when possible. Our calculations suggest that primary RPLND avoids chemotherapy about 25% of the time compared to surveillance, and about 75% of the time compared to 2 courses of chemotherapy. For low risk NSGCT, RPLND avoids chemotherapy in about 5% to 15% compared to surveillance.[1,2] While these estimates may vary depending on the initial numbers used for calculation, there is no doubt that initial RPLND can avoid chemotherapy in substantial numbers of men. Thus, unless the long-term effects of chemotherapy are better known and of little consequence, I believe RPLND is the preferred initial treatment for most high risk disease and an acceptable alternative even for low risk disease.

This brings us to the primary issue of this report, namely if primary RPLND is performed, how should it be done. This MSKCC group contends that the templates for surgery should be a thorough modified bilateral RPLND initially, which must then be converted to a complete bilateral procedure if positive nodes are found. In this conclusion I think the authors imply that a movement toward embracing laparoscopic RPLND should be discouraged. This group carefully mapped out the distribution of lymph nodes found in 500 consecutive men who underwent the MSKCC relatively extensive open RPLND. They also tabulated the location of those rare cases of short-term retroperitoneal lymph node recurrence and categorized those events as lymph nodes missed in their series. The frequency of lymph nodes they calculated would have been missed had the patients been operated on with the reported templates of 4 other groups (2 who do open RPLNDs and 2 who pioneered the laparoscopic RPLND approach) rather than the more extensive templates of the MSKCC group were 23% in the TTSG group (open), 11% in the Indiana group (open), 23% in the Innsbruck group (laparoscopic) and 19% in the Hopkins group (laparoscopic). The authors contend that these data advocate for a more thorough RPLND template than practiced by these other groups and especially by the laparoscopic groups.

I take issue with their conclusions for a variety of reasons. We have performed more than 50 laparoscopic RPLNDs and the dissection within the templates is just as good as the open approach and nerve preservation within these templates is doable.[1] In addition, ipsilateral common iliac dissections are now performed by laparoscopic groups. Whatever the initial modified templates, if positive nodes are found at surgery, then complete bilateral RPLND at least to the inferior mesenteric artery should be done in most cases. For the laparoscopic approach this may require repositioning the patient. Finally, the major template areas of disagreement for the initial modified RPLND are the para-aortic area for right side tumors, and the precaval and paracaval areas for left side tumors. While these areas may be hard to reach laparoscopically and, thus, sometimes not done, the real question is how frequently these areas are the sole site of lymph node metastasis. I believe this situation is rare (in fact in this article it seems to be less than 5%). Thus, I believe that the laparoscopic RPLND in experienced hands is a legitimate alternative to open RPLND provided that those groups leading this effort continue to reassure us of that conclusion by reporting their results regarding complications, cancer control and the percentage of patients getting chemotherapy.[3]

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REPLY BY AUTHORS

In testing the lower bounds of therapeutic efficacy[1] and by conducting randomized trials, medical oncologists have successfully developed less toxic but equally effective chemotherapy regimens for testicular cancer. Unfortunately, serial and often arbitrary modifications of retroperitoneal surgical templates and techniques have been largely based on mapping studies rather than controlled trials assessing clinical outcomes (references 6 and 8 in article).[2,3] Emerging data on late relapse[4,5] and reoperative retroperitoneal surgery (reference 1 in article) highlight the limitations and dangers of this suboptimal approach. The most common site for late relapse is the retroperitoneum,[4–6] up to a quarter of retroperitoneal recurrences are in areas outside a modified tem-

plate (reference 1 in article) and the liberal application of effective cisplatin based therapy will not reliably avert these often catastrophic events (reference 1 in article).[4,5]

In 1984 Lange et al described one of the first modified ipsilateral surgical templates that minimized contralateral dissection with the aim of reducing the incidence of ejaculatory dysfunction.[7] Specifically, these templates avoided surgery in areas with less than 10% prevalence of NSGCT containing nodes according to the mapping study by Donohue et al (reference 9 in article). Given the obscure followup data and frequent use of postoperative chemotherapy, it is now clear that mapping studies underestimate the extent of retroperitoneal disease. Therefore, the prevalence of NSGCT in areas deliberately avoided in the report by Lange et al probably exceeded 10%. Of note, most subsequent templates described are even more restrictive (reference 6 in article).[3] Furthermore, the assumption that chemotherapy will provide long-term cure in patients with residual postoperative disease is not supported by the data, since approximately 20% to 30% of NSGCT containing nodes harbor chemorefractory teratomatous elements.[8,9]

Our study demonstrates that the distribution of teratoma within and outside modified templates is not different. Despite benign histological appearance, teratoma can grow and invade local structures. It is always aneuploid,[10] has a highly variable proliferative index as measured by Ki67 expression[11] and malignant transformation cannot be predicted.[12] Therefore, teratoma cannot be known *a priori* to be clinically benign.[9] In many unfortunate cases late relapse and/or reoperative retroperitoneal surgery has provided the ultimate testimony to the strategy of reduced templates (reference 1 in article).[4,5]

Lange correctly points to the growing and compelling body of evidence regarding the significant long-term toxicity of chemotherapy. Although he argues (and we agree) against its use as monotherapy for CS I NSGCT and states that "chemotherapy should be avoided when possible," he appears to disregard the same toxicity when condoning its liberal use after RPLND, particularly in the setting of the reduced surgical templates routinely used for laparoscopic RPLND. A properly performed RPLND without adjuvant chemotherapy is curative in almost 90% of patients with low volume (pN1) disease and approximately 50% of patients with high volume (pN2-3) disease (reference 13 in article).[13] Furthermore, recent data show an improved ability to detect occult systemic disease by staging CT chest scans and excluding patients with persistently elevated markers from RPLND (reference 13 in article). This approach has resulted in an overall systemic relapse rate of less than 5% after primary RPLND and a 10% relapse rate in patients with pN1 disease without adjuvant chemotherapy. Therefore, adjuvant chemotherapy and its associated morbidity are reserved for patients with high volume retroperitoneal disease or selected patients with pN1 disease (anticipated noncompliance or other special circumstances).

Lange discusses nerve sparing laparoscopic RPLND as "doable." The critical issue is not what is doable, but what is actually done and reported. A review of the literature on laparoscopic RPLND reveals a consistent and troubling lack of therapeutic intent and highlights the over use of and over reliance on chemotherapy to compensate for restricted dissections. Less than 2% of reported laparoscopic RPLND cases have involved bilateral dissections despite almost 25% having positive nodes and, therefore, at risk for multifocality and contralateral disease (reference 6 in article).[14,15] Overall nearly 99% of patients with positive nodes received adjunctive chemotherapy regardless of retroperitoneal disease volume.

Retroperitoneal surgery must always be performed with therapeutic intent. Recent studies demonstrate that the potential consequences of unresected retroperitoneal disease are late relapse, reoperation and avoidable loss of life. The data suggest that restricted templates unnecessarily increase the incidence of unresected retroperitoneal disease, increase the demands for subsequent chemotherapy and potentially compromise long-term cure.

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