available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Opinion – EAU Guidelines' View

Role of Retroperitoneal Lymph Node Dissection in Clinical Stage IIA/B Seminoma: Recommendations from the European Association of Urology Guidelines Panel on Testicular Cancer

Axel Heidenreich [a,*], *Anna Patrikidou* [b,c], *Torgrim Tandstad* [d]

[a] *Department of Urology, Uro-Oncology, Robot-assisted and Specialized Urologic Surgery, University Hospital Cologne, Cologne, Germany;* [b] *Genitourinary Oncology Team, Department of Cancer Medicine, Gustave Roussy, Villejuif, France;* [c] *Department of Early Drug Development, Gustave Roussy, Villejuif, France;* [d] *Medical Oncology Department, St. Olav's Hospital, Trondheim, Norway*

1. Background

Chemotherapy with three cycles of platinum, etoposide, and bleomycin (PEB) or four cycles of platinum and etoposide is the standard treatment option for clinical stage IIA/B seminoma, with relapse rates of 0–8% in clinical stage IIA and 8–14% in clinical stage IIB [1]. Historical use of radiation therapy with doses of 30 Gy for clinical stage IIA and 36 Gy for clinical stage IIB has resulted in relapse rates of 9–24% [1]. Despite low relapse rates and high cure rates, both treatment options are associated with a risk of long-term toxicities such as secondary malignancies and cardiovascular disease [2].

In an attempt to de-escalate the treatment burden while maintaining oncological efficacy, the potential role of primary retroperitoneal lymph node dissection (RPLND) has been explored in four prospective and two retrospective clinical studies involving a total of 296 patients [3–8]. The majority of patients underwent RPLND for marker-negative seminoma of clinical stage IIA or small-volume clinical stage IIB, and only 34/296 (11.5%) received adjuvant chemotherapy, which consisted of one cycle of PEB in the majority of cases. The surgical approach was open transperitoneal or extraperitoneal laparotomy for 238 patients (80%), and robot-assisted surgery for 58 patients (20%). Median follow-up among all the studies was 33 mo, with a range of 23–58 mo for the prospective studies, and 18–22 mo for the retrospective studies.

The frequency of all surgery-related Clavien-Dindo complications of grade $\geq$3a was low in all studies (ranging from 5% to 12%), with antegrade ejaculation preservation in 90–97% of cases. More than 90% of complications were related to prolonged lymphorrhea or lymphocele.

Between 84% and 98% of patients harbored lymph node micrometastases in the resected specimens; interestingly, up to 5% of patients had nonseminomatous histology in their resected specimens. With regard to oncological outcomes, 48 patients (16%) experienced relapse; >90% of the recurrences developed within the first 2 yr of follow-up. Analysis of preoperative clinical, serological, and pathohistological characteristics did not identify any marker predictive for relapse. All of the patients were rescued by salvage chemotherapy. Only ten patients (3.4%) had in-field relapses, which underlines the generally high surgical quality for procedures performed by experienced surgeons at high-volume testicular cancer centers. The majority of relapses were lymphonodular and developed retroperitoneally outside the field of resection; the minority developed as systemic metastases. Relapse rates were 0–7.5% and 14–30% for patients undergoing surgery with and without adjuvant chemotherapy, respectively (Table 1).

2. Critical issues for primary nerve-sparing RPLND

RPLND in early metastatic seminoma represents an oncologically effective treatment if performed at high-volume centers by surgeons experienced in testicular

* Corresponding author. Department of Urology, Uro-Oncology, Robot-assisted and Specialized Urologic Surgery, University Hospital Cologne, Kerpener Strasse 62, 50937 Cologne, Germany.
E-mail address: axel.heidenreich@uk-koeln.de (A. Heidenreich).

https://doi.org/10.1016/j.eururo.2025.08.013

Table 1 Summary of prospective and retrospective studies investigating primary nerve-sparing retroperitoneal lymph node dissection in clinical stage IIA/B seminomas

Study and design	*N*	Dissection templates	Histology (%)	aCTx, *n* (%)	mFU, mo (IQR)	Relapses, *n* (%)	CDC ≥3a,[a] *n* (%)	AGE (%)
COTRIMS [5] Prospective	34	Unilateral	pN0: 8.9 pN+: 91.2	0	43.2 (12–81)	4 (11.8)	4 (12)	91
PRIMETEST [4] Prospective	33	Unilateral	pN0: 9 pN+: 91	0	58 (all >36 mo)	10 (30)	3 (9)	94
SEMS [3] Prospective	55	36 unilateral 19 bilateral	pN0: 16 pN+: 84	0	33 (12–61.6)	12 (21.8)	4 (7)	94
SWENOTECA [8] Prospective	62	60 unilateral 2 bilateral	pN0: 1.6 pN+: 98.4	18 (29)	23 (16–30)	6/44 (13.6) 0/18 (0)[b]	3 (4.8)	No data
Indiana [6] Retrospective	67	36 unilateral 31 bilateral	pN0: 1.5 pN+: 98.5	0	22 (12.3–36.1)	11 (16.9)	3 (4.5)	97
MSKCC [7] Retrospective	45	bilateral	pN0: 4.4 pN+: 95.4	16 (35)	18.5 (12–42)	4/29 (13.8) 1/16 (7.5)[b]	5 (11)	No data
Overall	296	199 unilateral 97 bilateral	pN0: 6.9 pN+: 93.1	34 (11)		36 (13.7) 1 (2.9)[b]	22 (7.4)	94

aCTx = adjuvant chemotherapy; AGE = antegrade ejaculation; CDC = Clavien-Dindo complications by grade; IQR = interquartile range; mFU = median follow-up; PS = prospective study; RS = retrospective study.
[a] Clavien-Dindo ≥ 3a, [1]prospective, [2]retrospective.
[b] Patients who received aCTx.

cancer surgery. Therefore, primary nerve-sparing RPLND (nsRPLND) needs to be concentrated in tertiary referral centers, as recommended in the European Association of Urology (EAU) guidelines [1]. The EAU guidelines panel is currently evaluating primary RPLND as a treatment option in early-stage metastatic seminoma, and the next update will probably include this as a treatment option.

Besides surgical experience, patient selection is another key factor for high oncological efficacy in patients with pN1 disease and for avoidance of unnecessary surgery for pN0 cases. According to published studies, more than 90% of patients had small-volume disease (≤3 cm) and negative tumor markers. In addition, among patients with relapse after initial clinical stage I, only 5% had received adjuvant carboplatin, with the remainder followed on surveillance. These characteristics should be considered when counseling patients regarding primary nsRPLND. To avoid unnecessary surgery for pN0 disease, patients with small clinical stage IIA masses should undergo guideline-recommended repeat imaging studies 6–8 wk apart [1]. Active treatment is definitively indicated for progressing masses, and this strategy should be discussed on an individual basis for persisting masses. Furthermore, measurement of serum concentrations of the biomarker miR371 might be helpful in identifying individuals who harbor metastases despite small lymph nodes [9]. Preoperative positron emission tomography/-computed tomography is also being prospectively evaluated in this setting and may provide additional information on patient selection.

The relapse rate of 12–30% is another issue that needs to be thoroughly discussed with patients. The relapse rate can be improved by performing an anatomically adequate nsRPLND that respects the lymphatic landing zones of a right-sided or left-sided primary tumor. The Indiana group recently redefined the anatomical templates via a mapping study of the nodal distribution in 65 patients with seminoma who underwent RPLND [10]. The authors identified lymph node metastases outside the typical templates in up to 20% of cases. Para-aortic metastases for a right-sided primary tumor, interaortocaval metastases for a left-sided primary tumor, and pelvic metastases for both represented the most common "unusual" locations. Interestingly, this nodal distribution correlated with the anatomical location of nodal relapses in other trials. The optimal templates for right-sided and left-sided primary tumors are summarized in Table 2. More extensive dissection is not needed.

Finally, the indication for adjuvant chemotherapy needs to be better defined, which is an issue that can only be clarified in a prospective randomized trial. The two groups that offered adjuvant chemotherapy in up to 30% of patients used the presence of extranodal extension or pathological stage IIB as criteria. Relapse rates were fundamentally lower with one cycle of adjuvant chemotherapy in comparison to surgery alone (Table 1). However, until validated criteria have been developed, the correct indication for adjuvant chemotherapy remains unclear.

3. Conclusions

In summary, nsRPLND for marker-negative clinical stage IIA/B seminoma is associated with a low rate of treatment-associated morbidity and a chemotherapy-free survival rate of 80–85% if performed in expert hands. Both the American Urological Association and National Comprehensive Cancer Network guidelines include primary nsRPLND in their evidence-based recommendations for

Table 2 Lymph node dissection templates for right-sided and left-sided marker-negative clinical stage IIA/B seminomas

Right-sided primary tumor	Left-sided primary tumor
Paracaval	Para-aortic
Interaortocaval	Preaortic with IMA as distal boundary
Para-aortic	Interaortocaval
Common and external iliac artery	Gonadal vessels
Gonadal vessels	Lateral to the left ureter
Lateral to the right ureter	

IMA = inferior mesenteric artery.

the management of low-volume clinical stage IIA/B seminomas [11,12]. The EAU guidelines panel is currently evaluating primary RPLND as a treatment option in early-stage metastatic seminoma and will probably include this as an option in the next update. Primary RPLND can significantly reduce the treatment burden: only 24% of patients receive adjuvant or salvage chemotherapy. Of the 36 relapses that occurred following RPLND alone (Table 1), 50% could have been avoided by extending the dissection fields, so the need for chemotherapy could be reduced to approximately 15% of clinical stage IIA/B seminomas. In the future, we still have to define risk factors associated with relapse to identify patients who might be better served by upfront chemotherapy.

Conflicts of interest: The authors have nothing to disclose.

Funding/Support and role of the sponsor: This work was supported by the European Association of Urology. The sponsor played a role in collection and management of the data, and approval of the manuscript.

References

[1] Patrikidou A, Cazzaniga W, Berney D, et al. European Association of Urology guidelines on testicular cancer: 2023 update. Eur Urol 2023;84:289–301.
[2] Hellesnes R, Myklebust TÅ, Fosså SD, et al. Testicular cancer in the cisplatin era: causes of death and mortality rates in a population-based cohort. J Clin Oncol 2021;39:3561–73.
[3] Daneshmand S, Cary C, Masterson T, et al. Surgery in early metastatic seminoma: a phase II trial of retroperitoneal lymph node dissection for testicular seminoma with limited retroperitoneal lymphadenopathy. J Clin Oncol 2023;41:3009–18.
[4] Hiester A, Che Y, Lusch A, et al. Phase 2 Single-arm trial of primary retroperitoneal lymph node dissection in patients with seminomatous testicular germ cell tumors with clinical stage IIA/B (PRIMETEST). Eur Urol 2023;84:25–31.
[5] Heidenreich A, Paffenholz P, Hartmann F, Seelemeyer F, Pfister D. Retroperitoneal lymph node dissection in clinical stage IIA/B metastatic seminoma. Results of the Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma (COTRIMS). Eur Urol Oncol 2024;7:122–7.
[6] Tachibana I, Alabd A, Tong Y, et al. Primary retroperitoneal lymph node dissection for stage II seminoma: is surgery the new path forward? J Clin Oncol 2023;41:3930–8.
[7] Matulewicz RS, Benfante N, Funt SA, et al. Primary retroperitoneal lymph node dissection for seminoma metastatic to the retroperitoneum. J Urol 2024;211:80–9.
[8] Thor A, Negaard HFS, Grenabo Bergdahl A, et al. Primary retroperitoneal lymph node dissection as treatment for low-volume metastatic seminoma in a population-based cohort: the Swedish Norwegian Testicular Cancer Group experience. Eur Urol Open Sci 2024;65:13–9.
[9] Seelemeyer F, Pfister D, Pappesch R, Merkelbach-Bruse S, Paffenholz P, Heidenreich A. Evaluation of a miRNA-371a-3p assay for predicting final histopathology in patients undergoing primary nerve-sparing retroperitoneal lymphadenectomy for stage IIA/B seminoma or nonseminoma. Eur Urol Oncol 2024;7:319–22.
[10] Zeng J, McFadden J, Thakker P, Tachibana I, Masterson TA, Cary C. Retroperitoneal nodal distribution for metastatic seminoma: is modified template appropriate? A retrospective study. J Urol 2025;213:753–65.
[11] Stephenson A, Eggener SE, Bass EB, et al. Diagnosis and treatment of early stage testicular cancer: AUA guideline. J Urol 2019;202:272–81.
[12] Gilligan T, Lin DW, Adra N, et al. NCCN guidelines insights: testicular cancer, version 2.2025. J Natl Compr Cancer Netw 2025;23:e250018.