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ORIGINAL ARTICLE

Post-chemotherapy retroperitoneal lymph node dissection in the management of metastatic testis cancer: the 16-year experience in an Irish setting

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Abstract
Introduction Post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND) is an important tool in the management of advanced germ cell testis cancer, particularly non-seminoma.
Aim We present the 16-year experience with PC-RPLND in a single Irish tertiary referral centre, and compare our results to the major speciality centres worldwide.
Methodology All 78 patients undergoing PC-RPLND for the treatment of metastatic testis cancer between January 1996 and December 2011 were included. Medical records were reviewed and up to date follow-up obtained from primary referral centres, patient's GPs and individual patient interview.
Results The mean age at diagnosis was 28.5 ± 7 years. Initial pathology included non-seminoma 62.8 %, seminoma 6.4 % and combined 19.2 %. All patients underwent pre-operative chemotherapy. The resection template utilised was bilateral infra-hilar in 29.5 %, unilateral infra-hilar in 46.2 % and supra-hilar in 20.5 %. Complete abdominal remission was achieved in all but one patient. Additional procedures were required in 38.5 % of patients ($n = 30$). Clavien Dindo grade three or four complications were seen in 8.9 %, including five patients who required early reoperation. Histology of RPLND specimen showed mature teratoma (41 %) and active cancer (11.5 %). Follow-up data were available for 66 patients (85 %). Median follow-up was 101 (11–207) months. Nine patients relapsed with median time to relapse 15 (8–60) months. Overall 5-year survival rate was 95.2 % (four deaths).
Conclusion In this relatively small series due to small population and low disease incidence, we have shown acceptable peri-operative course, morbidity and oncological outcomes with PC-RPLND compared to major international centres.

Keywords Urology · Oncology · Retroperitoneal lymph node dissection · Testicular cancer · Nonseminomatous germ cell tumour · Teratoma · Seminoma

Introduction

Historic papers confirm the lethal potential of metastatic testis cancer. There were improvements in prognosis in Ireland in the mid 80s with the introduction of chemotherapy and surgery but survival rates did not match the favourable prognosis now reported with modern staged multidisciplinary management. Considering the young population affected and the high potential for cure, there should be clear guidelines relating to management of metastatic testis cancer not least when considering the associated morbidity with oncological and surgical intervention. The role of post-chemotherapy RPLND in the management of metastatic testis cancer has become clearly defined in recent decades. The bulk of data on the topic comes from large series from major international specialist centres.

Testis cancer metastases follow a predictable path to the retroperitoneal lymph nodes [1]. The primary treatment for non-seminoma clinical Stage 1 and low volume retroperitoneal nodal disease remains controversial. The choice of active surveillance, primary chemotherapy or primary RPLND (laparoscopic or open) varies between countries

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and is influenced by tradition and available expertise and resources [2]. For sizeable or advanced metastatic disease (>Stage T2b) there is consensus that in seminoma, non-seminoma and combined tumours, initial treatment should involve platinum based chemotherapy [3]. While primary chemotherapy can achieve complete remission in low volume metastatic disease, partial remission is more common for more sizeable lesions. Optimal management of residual retroperitoneal mass lesions after primary chemotherapy in non-seminoma involves retroperitoneal lymph node dissection at appropriate interval. Such surgery involves complete extirpation of residual masses and the appropriate nodal drainage field. The rationale of post-chemotherapy RPLND is to achieve histopathological diagnosis of residual masses. The presence of active tumour, residual teratoma, or fibrosis/necrosis is of prognostic value. The early histopathological identification of residual cancer allows prompt intervention with salvage chemotherapy. Retroperitoneal lymph node dissection, by achieving complete remission, is therapeutic when pathology confirms teratoma. Such tumour is chemo-resistant but has potential to enlarge ("growing teratoma") and present later as germ cell cancer [4]. Post chemotherapy RPLND also facilitates follow-up, in that relapse should not occur within the resection field. Any subsequent potential relapse in the thorax or pelvis is easier to detect with CT scanning than the retroperitoneum.

In America the majority of RPLND surgeries are performed by a small number of surgeons [5]. In the UK 18 centres have been identified to perform this complex surgery including one in Belfast [6]. Less well described is the role for this operation in Ireland, a country with a small population, and combined with the low incidence of testis cancer (7.3 per 100,000; 176 cases per year) [7], a small number of patients requiring RPLND.

In this study, we describe the experience of a single Irish centre with the performance of post-chemotherapy RPLND in the management of metastatic testis cancer. We aim to characterise the patient cohort with advanced testis cancer and their characteristics of disease in terms of histological subtypes, staging, sites of spread and response to chemotherapy.

Initial data from Ireland were reported by Casey et al. [8]. This follow-up study has increased duration of follow-up and narrowed inclusion criteria to obtain a more homogeneous patient cohort, by including only patients undergoing post-chemotherapy surgery.

Methodology

Data in this retrospective series were prospectively collected including follow-up data in line with the STROBE guideline for observational studies [9].

Table 1 The royal marsden staging system for testis cancer

Stage	Description
I	Tumour confined to testis
II	Abdominal nodal metastases
a	<2 cm
b	2–5 cm
c	>5 cm
III	Supra-diaphragmatic nodal metastases
IV	Extra-lymphatic metastases

All patients undergoing RPLND for metastatic testis cancer of all histological sub-types between January 1996 and December 2011 in a single centre by a single surgeon were included. All patients must have undergone neo-adjuvant primary chemotherapy prior to RPLND. Data were collected by review of medical records, clinical correspondence, operative records, radiology and histology reports. Follow-up data were accrued from the initial referring oncology service. Where unavailable, the patient's primary care practitioner was contacted. Finally, when required, individual patients were contacted personally. Follow-up data were available on 85 % ($n = 66$) of patients.

Staging was by the Royal Marsden staging system [10] with stage migration defined as change of pre-chemotherapy stage by at least one sub-classification following completion of chemotherapy (Table 1). Complications were defined as early (less than 30 days) and late (more than 30 days), with severity classified by the Clavien Dindo Classification of morbidities [11]. Recurrence of disease was defined as confirmed evidence of new metastases at a time remote from RPLND. Finally, sub-group analyses were performed to identify differences in outcomes relating to disease stage and template of resection.

Data were coded to ensure confidentiality. Statistical analysis was performed using Stata 12 Statistical Package (StatCorp, Texas, version 12.0). Mean comparison was performed using *T* test for parametric variables. Categorical variable comparison was performed using Chi Squared testing. All *P* values were reported as two tailed. Survival analysis was performed using Kaplan–Meier survival functions and expressed as 1-, 5- and 10-year survival rates. Data were then censored for recurrence, allowing calculation of time to recurrence and disease free survival. A hospital ethics approval was granted for this study.

Results

Seventy-eight patients were identified for inclusion. Mean age was 28.5 ± 7.5 years at time of diagnosis. Initial presenting complaints included testis mass (74.3 %), testis

pain (38.4 %) and back pain (10.2 %). Less common presentations included neck or supra-clavicular mass, weight loss and haematuria.

Radical orchiectomy was performed as primary diagnostic and therapeutic management in 89.7 % of patients ($n = 70$). 12 alternative pathological diagnostic procedures other than orchiectomy included supra-clavicular or cervical lymph node biopsy, retroperitoneal mass biopsy and testis biopsy. In 10.3 % ($n = 8$) of cases orchiectomy was delayed until the time of post-chemotherapy RPLND. A single patient underwent bilateral orchiectomy for bilateral synchronous tumour. The pathology of primary tumour demonstrated non-seminomatous germ cell (NSGCT) (62.8 %, $n = 49$), seminoma (6.4 %, $n = 5$) and combined tumour (19.2 %, $n = 15$).

The remainder includes nine patients with presumed burned out primary testis tumour because histology demonstrated undifferentiated tissue, fibrotic tissue or calcification.

Disease stage at presentation by Royal Marsden staging system was Stage 1 (16.67 %, $n = 13$), Stage 2a (1.28 %, $n = 1$), Stage 2b (20.52 %, $n = 16$), Stage 2c (21.79 %, $n = 17$), Stage 3 (14.10 %, $n = 11$) and Stage 4 (25.64 %, $n = 20$). All 13 patients with Stage 1 disease at presentation progressed while on surveillance. Most common sites of extraretroperitoneal lymph node metastases included supra-clavicular or cervical ($n = 8$) and mediastinal ($n = 3$). Sites of visceral metastases included lungs ($n = 16$), liver ($n = 3$), brain ($n = 1$) and spine ($n = 1$). Primary chemotherapy in 53 patients (68 %) involved standard four cycle drug regime with Bleomycin, Epirubicin and Cisplatin (BEP). Twelve patients (15.4 %) were given Epirubicin and Cisplatin alone to prevent Bleomycin toxicity. Another 11.5 % of patients ($n = 9$) were unable to complete full course of BEP, with Bleomycin omitted during latter cycles. The remaining four patients (5.1 %) received alternative individualised chemotherapy regimes.

Following completion of chemotherapy, partial remission was achieved in 29.5 % of cases ($n = 23$), with stable disease in 55.1 % ($n = 43$) and disease progression in 15.4 % ($n = 12$). Clinical re-staging post-chemotherapy revealed Stage 1 (0 %), Stage 2a (23.1 %, $n = 18$), Stage 2b (30.77 %, $n = 24$), Stage 2c (16.67 %, $n = 13$), Stage 3 (7.69 %, $n = 6$) and Stage 4 (21.79 %, $n = 17$).

All patients underwent RPLND via an anterior transabdominal approach. The extent of resection template was dependent on the pattern of metastatic spread delineated on imaging, and gross appearance at exploration. The boundaries of resection followed those templates described by Donohue et al. [12].

Intra-operative complications ($n = 4$) included ureteric injury ($n = 2$) and significant bleeding ($n = 2$).

No peri-operative deaths occurred. Re-operation was required in five patients, three for early haemorrhage within 6 h, one for wound dehiscence at 1 week and one patient who required fasciotomy under local anaesthetic for lower limb compartment syndrome at 1 day post-op.

Twenty-three patients (29.5 %) underwent bilateral infra-hilar nodal template resection, 36 cases (46.2 %) underwent modified unilateral resection. Additional supra-hilar dissection was performed in 16 patients (20.5 %), while the template also included pelvic dissection in 3 patients (3.8 %). Disease volume and location mandated 34 further procedures be performed in 30 patients including; nephrectomy ($n = 16$), ureteric repair ($n = 3$), nephroureterectomy, aortic replacement, caval resection, ureterolysis, Boari flap reconstruction and lower lung lobectomy ($n = 1$ each). Another eight patients underwent orchiectomy at time of post-chemotherapy RPLND having had initial pathological diagnosis by other means. Complete surgical abdominal remission was achieved in all but one case in whom the extent of local invasion precluded a complete resection. In this case of seminoma the procedure was abandoned and the patient referred for further oncological measures. This patient is excluded from relapse calculations.

Median hospital stay was 10.5 days (range 5–50 days). Four patients had prolonged admission of 50, 47, 34 and 27 days. There were no peri-operative deaths. Early post-operative complications were observed in 29.5 % cases ($n = 23$). Using the Clavien Dindo classification of complication severity [11] these included grade 1 10.3 %, $n = 8$, grade 2 10.3 %, $n = 8$, grade 3a 1.3 %, $n = 1$, grade 3b 5.1 %, $n = 4$, grade 4 2.5 %, $n = 2$ and grade 5 0 %. Three patients underwent early abdominal re-exploration within 24 h for suspected haemorrhage. One case required control of a lumbar artery and another control of a mesenteric vein. The third case did not have haemorrhage confirmed. One patient developed partial wound dehiscence, requiring repair. One patient developed lower limb compartment syndrome requiring fasciotomy. This patient had undergone iliac artery resection because of densely adherent tumour necessitating an aorto-iliac graft during RPLND. One patient with chylous ascites and pleural effusions required prolonged ventilation for 10 days, a chest drain (removed early) and peritoneal drain (removed after 12 weeks) [13]. Minor complications included atelectasis, respiratory tract infection, minor wound infection and prolonged ileus.

Other early complications included DVT ($n = 3$), transient lower limb oedema ($n = 3$), transient lower limb paresthesia ($n = 2$) and pulmonary embolism ($n = 1$).

Owing to peripheral follow-up of the majority of patients, the incidences of late complications may not be

comprehensive. One patient with recurrent adhesional bowel obstruction required five subsequent laparotomies elsewhere. Three patients were reported to develop small bowel obstruction elsewhere which settled with conservative measures. One patient underwent repair of a small incisional hernia elsewhere. One patient describes ongoing chronic back pain.

Histopathological analysis of RPLND specimens revealed; fibrosis/necrosis ($n = 37$, 47.4 %), mature teratoma ($n = 32$, 41.1 %) and active cancer ($n = 9$, 11.5 %).

Thirteen patients with Stage 1 disease at initial presentation progressed to metastatic disease while on surveillance. They are assumed to have harboured occult micrometastatic disease at the time of orchiectomy. In this subgroup, testis histology was NSGCT in 11 (84.6 %) and mixed in 2 (15.4 %). RPLND showed fibrosis in 5 (38.4 %), mature teratoma in 6 (46.2 %) and active disease in 2 (15.4 %). One patient had progression during primary chemotherapy, one patient had stable disease while all others had a partial response.

Follow-up data were available on 66 patients (85 %). Median duration was 100 months (range 11–207 months).

Disease relapse following RPLND was observed in nine patients (13.6 %). Testis histology was NSGCT in 6 (66.6 %), Seminoma in 2 (22.2 %) and burnt out primary in 1 (11.1 %). Disease stage following primary chemotherapy was Stage 2b $n = 2$ (22.2 %), Stage 2c $n = 2$ (22.2 %), Stage 3 $n = 2$ (22.2 %) and Stage 4 $n = 3$ (33.3 %). RPLND histology showed fibrosis in 4 (44.4 %), teratoma in 2 (22.2 %) and active disease in 3 (33.3 %). Median time to relapse was 15 months (range 8–60 months) (Fig. 1). Sites of relapse included retroperitoneal (outside field of resection) $n = 2$, supra-diaphragmatic nodal $n = 1$, pulmonary $n = 2$, disseminated $n = 1$, combined pulmonary/retrocrural $n = 1$, and combined pulmonary/supra-diaphragmatic nodal relapse $n = 1$ and tumour marker elevation alone $n = 1$. Median disease free survival was 95 months (range 8–204 months).

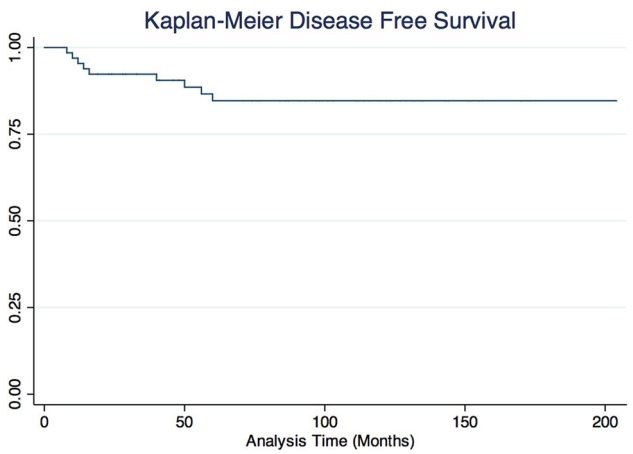

Fig. 1 Kaplan–Meier for disease free survival

Four patients died with median time to death 30 months (11–96 months) post-surgery.

Case 1 who died was aged 50 and had extended bilateral RPLND for non-seminoma clinical Stage 2a disease post-chemotherapy. Complete abdominal surgical remission was achieved but pathology confirmed active germ cell cancer. The patient did not tolerate salvage chemotherapy and died at 11 months due to advancing Stage 4 supra-diaphragmatic and visceral disease.

Case 2 mortality was aged 34 and underwent a partial resection/biopsy of bulky residual seminoma (Stage 2b) post primary chemotherapy. Pathology confirmed active seminoma. This patient died at 36 months despite salvage chemotherapy for advancing widespread disease.

Case 3 mortality was aged 48 and underwent extensive bilateral RPLND for clinical Stage 2c NSGCT post primary chemotherapy. Pathology confirmed active cancer. The patient received salvage chemotherapy but dose modified due to toxicity. He subsequently died at 96 months due to disseminated disease.

Fourth mortality case, age 23, underwent extensive bilateral RPLND for non-seminoma Stage 4 disease including bilateral supra-hilar thoracoabdominal dissection. Pathology confirmed teratoma without active germ cell tumour but the patient died at 24 months despite salvage chemotherapy when he developed advancing lung metastases.

Time specific Kaplan–Meier survival rates (including only patients with follow-up data at that time) were; 98.5 % at 1 year ($n = 65$), 95.2 % at 5 years ($n = 49$) and 92.6 % at 10 years ($n = 25$). The Kaplan–Meier Curve with 95 % confidence interval for the entire cohort demonstrates a plateau at 100 months with no delayed mortalities after 96 months post-operative (Fig. 2). Stratification of survival based on disease stage revealed for Stage 2 disease survival was 98 % at 1 year, 95.4 % at 5 years and 91.2 % at 10 years. For Stage 3 disease, survival was 100 %. For Stage 4 disease, survival was 100 % at 1 year, 91.6 % at 5 years and 91.6 % at 10 years. These variations do not reach statistical significance. There were also no statistically significant associations between complication rates ($P = 0.43$) or rate of disease relapse ($P = 0.89$) and resection template.

Discussion

The Irish National Cancer Registry indicate an incidence of testicular cancer in Ireland of 7.3 cases per 100,000 per year (176 new cases per year) and a lifetime risk of <0.1 %

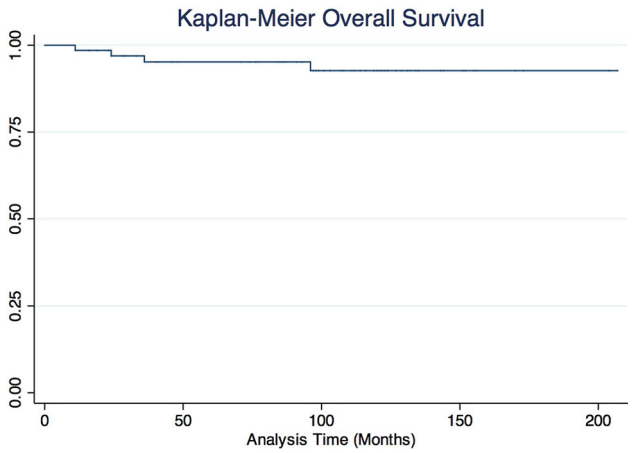

Fig. 2 Kaplan–Meier for overall survival

for all [7]. It constitutes 0.5 % of registered malignancies per year and less than 2 % of male cancers [14]. As expected, most patients were aged 20–39 years at diagnosis [15, 16]. This disease prevalence data therefore yields a small total number of patients who require RPLND post-chemotherapy. The bulk of patients who never require RPLND include those with Stage 1 NSGC testis cancer, those cases of seminoma (with few exceptions) and those who achieve complete remission after primary chemotherapy for metastatic NSGC testis cancer.

Our series confirms the complexity of RPLND in the post-chemotherapy setting when extensive desmoplastic reaction and tumour itself cause significant distortion of tissue planes. Residual nodal masses post-chemotherapy may invade local structures including ureter, aorta, and vena cava. Thus, a complex dissection may be required, involving additional procedures including nephrectomy, aortic replacement, caval resection or ureteric repair. Djaladat et al. in the University of Southern California demonstrate that 30 % of patients require adjuvant procedures at the time of post-chemotherapy RPLND [17]. In that series 15 % of adjuvant procedures were vascular such as aortic or caval resection/replacement while nephrectomy comprised 14 %. Our overall rate of additional procedures at RPLND (28 %) is in line with this series, although we report a higher rate of concomitant nephrectomy (20 versus 14 %) but lower incidence of vascular procedures (2.6 versus 15 %).

Despite the extensive nature of RPLND surgery, mortality remains low. Five major studies report peri-operative mortality rate less than 1 % [18]. The relative young age and lack of co-morbidities of patients are relevant. There were no peri-operative mortalities in the 16 years of this study, although we acknowledge our cohort is relatively small. Our early complication rate of 29.5 % appears high but when Clavien Dindo grade 1 and 2 minor complications are excluded, the rate drops to 8.9 %, which is lower than reported by Baniel et al. in their large post-chemotherapy cohort [19]. They described a higher complication rate with post-chemotherapy RPLND (18 %) than with primary RPLND (8 %), reflecting the complexity of surgery in the post-chemotherapy setting.

The incidence of viable malignant tissue, teratoma and fibrosis/necrosis reported by histopathology following RPLND is similar in our series to the ranges reported by Winter et al. [20]. Most recent studies have shown the percentage of patients with residual malignant disease decreasing to between 2 and 15 %. Approximately 35–60 % have residual mature teratoma and 35–50 % have fibrotic tissue alone. This beneficial trend in recent decades is largely due to improvements in chemotherapy regimes and their delivery. Thus, 51.2 % of patients in our series (with residual germ cell tumour or teratoma in resected specimens) achieved complete abdominal remission by surgery and as such derived a therapeutic benefit. In the absence of a reliable non-invasive procedure to ascertain the nature of residual masses after chemotherapy, RPLND remains the diagnostic method of choice. Algorithms for predicting residual malignant disease in post-chemotherapy masses using statistical models with combinations of variables report variable success [21–24]. The 75–83 % accuracy achieved in some models still renders false negative rates too high to safely avoid RPLND in this setting. Our relapse rate after RPLND surgery is comparable to that of Flechon et al. [25] at 18.5 % with median follow-up 6.1 months (range 1.3–39 months) post PC-RPLND. Regarding sites of relapse post RPLND, three patients did suffer relapse within the abdomen but these were outside the resection template. Another five of nine patients who relapsed developed disease in the supra-diaphragmatic region. There was no documented isolated pelvic recurrence in this series.

Our overall survival (92.6 % at median 100 months) compares with that in Flechon's report (87 %, median follow-up 77 months and range 1.3–187 months) [25]. Similarly the 95 % 5-year survival rate in our series is reassuring because overall 5-year survival for all patients with testis cancer is reported at 97 % at 5 years [26]. Considering the relative advanced stage of disease of our patient cohort, these results are encouraging.

Our study suggests a higher survival for Stage 4 disease than less advanced disease at RPLND. This apparent contradiction did not reach statistical significance and could be due to selection bias where a proportion of Stage 4 patients continue with salvage chemotherapy without having RPLND. Also, risk factor analyses in metastatic testis cancer highlight the importance of disease bulk and elevated tumour marker status [27]. Prognosis is not governed by the presence of distal metastases alone.

Rates of testis cancer in the UK closely mirror those in Ireland (7.1 versus 7.3 per 100,000) [28]. Given the low

number of patients in Ireland who will require this surgery, as well as its complexity and high rates of secondary procedures required, we advocate this procedure only be performed in one or two supra-regional centres in Ireland, an approach that has been the standard in the UK since 2002 [6].

Conclusion

We present the experience of a single Irish hospital in performing post-chemotherapy retro-peritoneal lymph node dissection for the management of testicular cancer over a 16-year period.

In terms of both peri-operative management and overall prognosis, the results of our series can stand alongside those from the major international urological centres.

Compliance with ethical standards

Conflict of interest Shane Considine declares that he has no conflict of interest. Roisin Heaney declares that she has no conflict of interest. Ronan Conroy declares that he has no conflict of interest. John Thornhill declares that he has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Donohue JP, Zachary JM, Maynard BR (1982) Distribution of nodal metastases in nonseminomatous testis cancer. J Urol 128(2):315–320
2. Stephenson AJ, Bosl GJ, Motzer RJ, Kattan MW, Stasi J, Bajorin DF, Sheinfeld J (2005) Retroperitoneal lymph node dissection for nonseminomatous germ cell testicular cancer: impact of patient selection factors on outcome. J Clin Oncol 23(12):2781–2788. doi:10.1200/jco.2005.07.132
3. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Fizazi K, Horwich A, Laguna MP, Nicolai N, Oldenburg J (2015) Guidelines on testicular cancer: 2015 update. Eur Urol 68(6):1054–1068. doi:10.1016/j.eururo.2015.07.044
4. Motzer RJ, Amsterdam A, Prieto V, Sheinfeld J, Murty VV, Mazumdar M, Bosl GJ, Chaganti RS, Reuter VE (1998) Teratoma with malignant transformation: diverse malignant histologies arising in men with germ cell tumors. J Urol 159(1):133–138
5. Flum AS, Bachrach L, Jovanovic BD, Helenowski IB, Flury SC, Meeks JJ (2014) Patterns of performance of retroperitoneal lymph node dissections by American urologists: most retroperitoneal lymph node dissections in the US are performed by low-volume surgeons. Urology 84(6):1325–1328. doi:10.1016/j.urology.2014.07.054
6. Hayes M, O'Brien T, Fowler S (2014) Contemporary retroperitoneal lymph node dissection (RPLND) for testis cancer in the UK—a national study. J Urol 191(4):e89–e90. doi:10.1016/j.juro.2014.02.404
7. The National Cancer Registry Ireland (2015) Testis cancer fact-sheet. http://www.ncri.ie/sites/ncri/files/factsheets/FACTSHEET_testis_1.pdf.2015
8. Casey RG, Aktar M, Hegarty P, Butler M, Thornhill JA (2008) A prospective 10 year audit of a single Irish centre's experience of retroperitoneal lymph node dissection for metastatic testis cancer. Surgeon 6(5):294–296
9. Vandenbroucke JP, von Elm E, Altman DG, Gotzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M (2007) Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. Ann Intern Med 147(8):W163–W194
10. Horwich A (1995) Testicular cancer. Oncology—a multidisciplinary textbook. Chapman and Hall, London, pp 485–498
11. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibanes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M (2009) The Clavien-Dindo classification of surgical complications: 5-year experience. Ann Surg 250(2):187–196. doi:10.1097/SLA.0b013e3181b13ca2
12. Donohue JP (1993) Nerve-sparing retroperitoneal lymphadenectomy for testis cancer. Evolution of surgical templates for low-stage disease. Eur Urol 23(Suppl 2):44–46
13. Browne KM, Casey RG, Thornhill JA (2009) Prolonged lymphatic leak after retroperitoneal lymph node dissection: a case report. J Med Case Rep 3:8704. doi:10.4076/1752-1947-3-8704
14. The National Cancer Registry Ireland (2013) Age standardised incidence rates: testis cancer. http://www.ncri.ie/data.cgi/client/generate_stats.php. Accessed 20 May 2013
15. The National Cancer Registry Ireland (2013) Age specific incidence rates: testis cancer. http://www.ncri.ie/data.cgi/client/generate_stats.php. Accessed 20 May 2013
16. La Vecchia C, Bosetti C, Lucchini F, Bertuccio P, Negri E, Boyle P, Levi F (2010) Cancer mortality in Europe, 2000–2004, and an overview of trends since 1975. Ann Oncol 21(6):1323–1360. doi:10.1093/annonc/mdp530
17. Djaladat H, Nichols C, Daneshmand S (2012) Adjuvant surgery in testicular cancer patients undergoing postchemotherapy retroperitoneal lymph node dissection. Ann Surg Oncol 19(7):2388–2393. doi:10.1245/s10434-012-2284-8
18. Gels ME, Nijboer AP, Hoekstra HJ, Sleijfer DT, Molenaar WM, Plukker JT, Droste JH, Schraffordt Koops H (1997) Complications of the post-chemotherapy resection of retroperitoneal residual tumour mass in patients with non-seminomatous testicular germ cell tumours. Br J Urol 79(2):263–268
19. Baniel J, Sella A (1999) Complications of retroperitoneal lymph node dissection in testicular cancer: primary and post-chemotherapy. Semin Surg Oncol 17(4):263–267
20. Winter C, Raman JD, Sheinfeld J, Albers P (2009) Retroperitoneal lymph node dissection after chemotherapy. BJU Int 104(9 Pt B):1404–1412. doi:10.1111/j.1464-410X.2009.08867.x
21. Toner GC, Panicek DM, Heelan RT, Geller NL, Lin SY, Bajorin D, Motzer RJ, Scher HI, Herr HW, Morse MJ et al (1990) Adjunctive surgery after chemotherapy for nonseminomatous germ cell tumors: recommendations for patient selection. J Clin Oncol 8(10):1683–1694
22. Fossa SD, Aass N, Ous S, Hoie J, Stenwig AE, Lien HH, Paus E, Kaalhus O (1989) Histology of tumor residuals following chemotherapy in patients with advanced non-seminomatous testicular cancer. J Urol 142(5):1239–1242
23. Steyerberg EW, Gerl A, Fossa SD, Sleijfer DT, de Wit R, Kirkels WJ, Schmeller N, Clemm C, Habbema JD, Keizer HJ (1998) Validity of predictions of residual retroperitoneal mass histology in non-seminomatous testicular cancer. J Clin Oncol 16(1):269–274

24. Albers P, Weissbach L, Krege S, Kliesch S, Hartmann M, Heidenreich A, Walz P, Kuczyk M, Fimmers R (2004) Prediction of necrosis after chemotherapy of advanced germ cell tumors: results of a prospective multicenter trial of the German Testicular Cancer Study Group. J Urol 171(5):1835–1838. doi:10.1097/01.ju.0000119121.36427.09
25. Flechon A, Tavernier E, Boyle H, Meeus P, Rivoire M, Droz JP (2010) Long-term oncological outcome after post-chemotherapy retroperitoneal lymph node dissection in men with metastatic non-seminomatous germ cell tumour. BJU Int 106(6):779–785. doi:10.1111/j.1464-410X.2009.09175.x
26. The National Cancer Registry Ireland (2011) Testicular cancer, malignant (ICD10 C62): 5-year relative survival by diagnosis year and age at diagnosis. http://www.ncri.ie/survival/Relsurvival_testis_19942007.htm. Accessed 20 May 2013
27. Spiess PE, Brown GA, Liu P, Tannir NM, Tu SM, Evans JG, Czerniak B, Kamat AM, Pisters LL (2006) Predictors of outcome in patients undergoing postchemotherapy retroperitoneal lymph node dissection for testicular cancer. Cancer 107(7):1483–1490. doi:10.1002/cncr.22182
28. Znaor A, Lortet-Tieulent J, Jemal A, Bray F (2014) International variations and trends in testicular cancer incidence and mortality. Eur Urol 65(6):1095–1106. doi:10.1016/j.eururo.2013.11.004