Pergamon

European Journal of Cancer Vol. 31A, No. 10, pp. 1599–1604, 1995
Elsevier Science Ltd
Printed in Great Britain.

0959-8049(95)00330-4

# Original Paper

# Clinical Stage B Non-seminomatous Germ Cell Testis Cancer: The Indiana University Experience (1965–1989) Using Routine Primary Retroperitoneal Lymph Node Dissection

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**Between 1965 and 1989, 1180 patients at Indiana University, U.S.A., underwent retroperitoneal lymph node dissection (RPLND) for non-seminomatous germ cell (NSGC) testis cancer of whom 638 cases had primary RPLND. A subset of 174 cases were considered clinical stage B (or II) before surgery (retroperitoneal nodal metastases by clinical staging). Surgery revealed that 23% ($n$ = 41) had pathological stage A disease (no cancerous nodes). This error rate in clinical staging has decreased somewhat with improved techniques, but remains approximately 20% over the last decade. The relapse rate in pathological stage A ($n$ = 41) was 5% ($n$ = 2), both of whom were cured by chemotherapy. The relapse rate in pathological stage B without postoperative adjuvant treatment ($n$ = 54) was 35% ($n$ = 19); 2 patients died. This indicates that 65% of pathological stage B cases were cured by RPLND alone. From 1979 to 1989, the 140 pathological stage B cases participated in a randomised prospective trial of post-RPLND adjuvant chemotherapy versus no postoperative treatment. Forty two per cent ($n$ = 59) received postoperative platinum-based therapy (two cycles), and there has been no relapse after RPLND for stage B disease. While advances in chemotherapy for NSGC testis cancer have led to its application by several study groups to clinical stage B (or II) testis cancer (with surgery reserved only for those in partial remission), the equivalent cure rate with RPLND surgery with chemotherapy rescue reserved for those who relapse appears to have both cost and risk–benefit advantages.**

**Key words: clinical stage B testis cancer, retroperitoneal lymph node dissection, comparison to primary chemotherapy**

*Eur J Cancer*, Vol. 31A, No. 10, pp. 1599–1604, 1995

## INTRODUCTION

CLINICAL STAGE B non-seminomatous germ cell (NSGC) testis cancer is defined as metastatic disease limited to the retroperitoneal lymph nodes at clinical staging by computed tomography (CT) scanning. Most series also include patients without radiological evidence of chest metastases, but who have persistently elevated serum tumour markers after orchiectomy, indicating the possible presence of occult retroperitoneal micrometastases. Community-based reports indicate that clinical stage B cases comprise 25–40% of all patients presenting with NSGC testis cancer [1].

The optimal choice of management for clinical stage B NSGC disease is not universally agreed. Primary chemotherapy with a platinum combination is standard treatment in the U.K. and follows a historical tradition there of initial non-operative management for testis cancer. Formerly, such cases received irradiation before cisplatinum chemotherapy was introduced in the late 1970s [2]. Surgery is restricted to cases with a partial response to chemotherapy (approximately one-third) who then undergo resection of residual masses to achieve complete remission [3, 4]. In contrast, elsewhere, and particularly in the U.S.A. where primary retroperitoneal lymph node dissection (RPLND) was popularised in the 1920s [5], primary surgery remains the most common initial treatment of choice for clinical stage B disease [1]. The exceptions to this surgical approach are cases with bulky disease who then receive primary chemotherapy. In practice, resectable clinical stage B patients are combined with clinical stage A cases as "low stage" clinical groups and are managed with primary RPLND. The rationale of primary RPLND in clinical stage B disease is 4-fold. There is greater precision in

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Revised 7 Feb. 1995; accepted 9 Jun. 1995.

retroperitoneal disease staging (our experience indicates one-fifth of these are false positive and, in fact, pathological stage A); hence, subsequent treatment requirements are more clearly and promptly defined. There is therapeutic benefit when resected nodes are positive (two-thirds being cured with RPLND alone). Follow-up is easier for the patient and clinician because regular re-assessment of the retroperitoneum by CAT scan is unnecessary following surgery. Lastly, the disease model is altered in the event of relapse. Very rarely does relapse occur in the retroperitoneum (0–2%). Instead, it occurs in the lungs, which is easily detected early and virtually 100% curable [6, 7]. In contrast, the surveillance relapse disease model of retroperitoneum plus lungs is more difficult to detect early and is not curable universally [8], presumably on the basis of delayed diagnosis and resultant higher volume and multiple sites disease in some.

With the development of effective chemotherapy, there has been considerable interest by medical oncologists in extending its original application in clinical stage C disease to clinical stage B disease as well. Primary chemotherapy is effective initial treatment to treat bulky or advanced disease, and there is an argument for extending this approach to early stage B on the basis that abdominal surgery would be unnecessary if chemotherapy achieved a lasting complete remission. This can be accomplished in approximately two-thirds of stage B cases [9].

The aim of this study was to review the Indiana experience with primary RPLND in clinical stage B testis cancer. From 1965 to 1989, 1180 patients have undergone RPLND at Indiana University, U.S.A., and all patients' data are computerised. Previous reports on primary surgery have been based on surgical pathological staging, and these data are not comparable with results of conservative management which are based on *clinical* staging methods. This report is based on *clinical* staging of disease prior to surgery, and provides a unique opportunity for comparative analyses with other series using clinical staging for therapeutic decisions.

## PATIENTS AND METHODS

In the 25 year period 1965–1989, 1180 patients underwent RPLND at Indiana University, U.S.A. This series can be divided into those having a postchemotherapy resection ($n$ = 542) and the remainder who underwent primary RPLND ($n$ = 638). In those having primary RPLND, 174 patients were considered stage B by clinical staging methods before surgery, the specific subgroup under study in this paper. Clinical staging after referral included CT scan in 86% of patients; the remainder had lymphangiography, ultrasound or intravenous pyelogram (IVP) in the early years of this series. Chest CT and/or lung tomography were routinely performed. Pre-operative serum markers, alpha fetoprotein (AFP) and beta human choriogonadotropin (HCG) were assayed in 89% of patients because this series spans 1965–1989. Clinical staging revealed 67% of patients ($n$ = 117) had clinical stage B1 disease (defined as nodes <2.5 cm diameter and/or <5 nodes), 26% of cases ($n$ = 46) had clinical stage B2 (2.5–10 cm diameter or >5 nodes), 2% of cases ($n$ = 4) had clinical stage B3 disease (> than 10 cm diameter). A further 4% of patients ($n$ = 7) had no radiological evidence of metastases, but had persistent elevation of serum markers HCG and/or AFP after orchiectomy.

CT scans were performed on a variety of scanners with a beam collimation of 10 mm, a reconstruction increment of 10 mm and generally a tube rotation time of 2 s or less. Oral contrast was administered in all patients. Intravenous (i.v.) contrast was given to most patients, except in the situation of decreased renal function. Patients were classified as clinical stage B if retroperitoneal node transverse diameter was 1.0 cm or greater. All scans were reviewed by the Radiology Department at Indiana University, U.S.A.

Four surgeons performed 99% of RPLND operations, including 64% ($n$ = 112) by one surgeon (JPD). There have been developments in surgical technique during this 25 year period including a downscaling of the resection template based on improved knowledge of the sites of nodal metastases [1]. Nerve-sparing techniques were also introduced in an effort to preserve ejaculatory function [10]. However, these technical modifications are recent, and were initially applied to patients with negative nodes at exploration; 83% of patients in this study underwent a full bilateral RPLND below the level of the renal vessels. Sixty-three per cent of patients ($n$ = 109) had their dissection extended into the suprahilar region either unilaterally or bilaterally. This trend reflects the historic bias of cephalad extension of the dissection template in all stage B cases, particularly in earlier years. Therefore, only 17% of patients ($n$ = 29) had a modified unilateral RPLND. Only 12% of patients ($n$ = 21) had prospective nerve-sparing of the lumbar sympathetics during RPLND; this technique was developed in the 1980s and applied relatively later in this series. From 1990 to 1994, over 300 nerve-sparing RPLNDs were done without change in relapse or survival. These are not included in this report. A midline transperitoneal abdominal approach was routinely used and no case had a thoracoabdominal incision. Additional procedures during RPLND included caval resection (1%, $n$ = 2) and nephrectomy (1%, $n$ = 2); these were performed early in the series in cases with bulky disease. Further additional procedures included inguinal dissection (2%, $n$ = 3), hemiscrotectomy (3%, $n$ = 5), testis prosthesis (1%), and gastrostomy (1%). The practice of routine appendectomy (21%, $n$ = 36) was abandoned in 1983.

For analysis, patients were divided into two categories dependent on their year of surgery; 1965–1978 ($n$ = 34), and 1979–1989 ($n$ = 140). This division of patients was chosen because clinical staging became more consistent with routine CT scans and serum tumour markers after 1978. Also, effective combination platinum chemotherapy was widely available from 1979 onwards, which makes this series comparable with other modern series using alternative approaches which include platinum-based chemotherapy programmes. The duration of follow-up in these patients treated over 25 years is wide-ranging (61–331 months). Mean follow-up varies from 229 months for cases treated before 1979 to 132 months for those treated since 1979.

## RESULTS

### 1965–1978

Between 1965 and 1978, 34 patients with clinical stage B disease underwent primary RPLND. Pre-operative clinical/radiological assessment of disease extent was: stage B1 = 56% ($n$ = 19), stage B2 = 26% ($n$ = 9), bulky stage B3 = 12% ($n$ = 4); 2 patients had persistent tumour marker elevation without radiological evidence of metastases. Surgical pathological staging confirmed stage B1 =29% ($n$ = 10), stage B2 = 24% ($n$ = 8), and stage B3 = 21% ($n$ = 7). Surgery revealed that 26% of patients ($n$ = 9) had no cancerous nodes (pathological stage A), and this figure highlights the inaccuracy of clinical staging methods during this time. No relapse was subsequently seen in the 9% of patients with pathological stage A disease (Table 1). The relapse rate among the pathological stage B patients ($n$ = 25) was 48% ($n$ = 12). Sites of relapse included the

*Table 1. Primary RPLND in clinical stage B: early results (1965–1978)*

| Disease extent | Patients n (%) | Relapse n (%) | Survival % | Deaths n |
|---|---|---|---|---|
| Path. A | 9 (26) | 0 | 100 | 0 |
| Path. B No Adj. | 5 (15) | 1 (20) | 100 | 0 |
| Path. B + "Adj Rx" | 20 (59) | 11 (55) | 75 | 4 |
| All cases | 34 | 12 (35) | 88 | 4 |

Adj, adjuvant therapy; Path, pathological stage, Adj Rx, postoperative adjuvant therapy.

lungs ($n$ = 8) with mediastinum/neck ($n$ = 2), hepatic ($n$ = 1), multiple sites ($n$ = 2); 1 patient alone suffered abdominal retroperitoneal relapse. Adjuvant therapy was poorly developed at this time and included regimens such as actinomycin D and/or irradiation and later vinblastine and bleomycin. In 1975, platinum was added to vinblastine and bleomycin for stage III disease. The decision to give postoperative adjuvant therapy to those with positive nodes was, therefore, empirical, and treatment was usually restricted to high risk cases with sizeable metastases or adverse histology. Based on these criteria, five pathological stage B patients (15%) received no further treatment after RPLND. 4 of these patients remain in complete remission and one who relapsed was salvaged by chemotherapy available at that time. 20 patients with pathological stage B disease (59%) received postoperative adjuvant treatment and the relapse rate was higher (55%, $n$ = 11). Salvage treatment, including various non-platinum based cytotoxic regimes and/or surgery and/or irradiation, was effective in 7 of the 11 patients who relapsed, and survival was 75% in this group. The overall relapse rate among 34 clinical stage B patients undergoing primary RPLND (1965–1978) was 35% and survival was 88% (Table 1). There were four cancer deaths. This indicates RPLND surgery alone was the major therapeutic weapon in pathological stage B disease.

1979–1989

The majority of patients in this series were treated between 1979 and 1989 ($n$ = 140). Results are shown in Table 2. Effective chemotherapy had become widely available and there was a move away from primary RPLND in patients with moderate or extensive retroperitoneal disease. Pre-operative disease stage in this subgroup was, therefore, biased towards lower volume disease compared to the previous patients undergoing primary RPLND. Pre-operative clinical disease stage was: stage B1 = 70% ($n$ = 98), stage B2 = 26% ($n$ = 37). No patients had stage B3 disease, while 4% ($n$ = 5) had persistent significant elevated serum markers with no radiological evidence of disease. Surgical pathological staging confirmed: stage B1 = 36% ($n$ = 50), stage B2 = 39% ($n$ = 54), stage B3 = 3% ($n$ = 4), all underestimated clinically, and stage A = 23% ($n$ = 32), thus overestimated by clinical staging methods. These surgical results show that inaccuracy of clinical staging still remains.

*Table 2. Primary RPLND in clinical stage B: results (1979–1989)*

| Disease extent | Patients n (%) | Relapse n (%) | Survival % | Deaths n |
|---|---|---|---|---|
| Path. A | 32 (23) | 2 (6) | 100 | 0 |
| Path. B No Adj. | 49 (35) | 18 (37) | 96 | 2 |
| Path. B + "Adj Rx" | 59 (42) | 0 | 98.3 | 1 |
| All cases | 140 | 20 (14) | 98 | 3 |

3 deaths: 1 cancer, 1 postoperative, 1 chemotherapy-related. For abbreviations see Table 1.

The relapse rate in pathological stage A patients ($n$ = 32) was 6% ($n$ = 2). Relapse was pulmonary ($n$ = 1) or pulmonary plus mediastinum ($n$ = 1) and survival was 100% with salvage platinum chemotherapy ($n$ = 2) and further surgery ($n$ = 1). The relapse rate in cases with pathological stage B disease without adjuvant therapy was 37% ($n$ = 18). The decision of whether or not to give post RPLND adjuvant chemotherapy (two courses of platinum, in combination) in pathological stage B was governed by a co-operative group randomised clinical trial in operation during most of this period [11]. No patient receiving adjuvant chemotherapy ($n$ = 59) suffered relapse, although one case early on in the series died of septic complications during adjuvant chemotherapy in another institution. In contrast, 37% ($n$ = 18) of the 49 pathological stage B patients who had no adjuvant chemotherapy went on to relapse. Sites included lung ($n$ = 9), with or without mediastinal or hepatic sites ($n$ = 2), mediastinum alone ($n$ = 2), multiple sites ($n$ = 2), and 5 patients relapsed with marker elevation alone. Relapse was treated by combination chemotherapy ($n$ = 14) with further surgery ($n$ = 4), surgery alone ($n$ = 1), or surgery plus irradiation ($n$ = 1). There was one death from cancer in this group. Among relapsing pathological stage B cases (none received adjuvant chemotherapy), the relapse rate in stage B1 ($n$ = 27) was 26% ($n$ = 7). In stage B2 disease ($n$ = 20) the relapse rate was 55% ($n$ = 11). Another 2 patients had stage B3 disease but interestingly neither relapsed. Overall, 3 of the 140 cases treated died, one from cancer, one postoperative death and one death related to chemotherapy complications. 2 patients developed new tumours in the contralateral testis during follow-up. Pathological stage at previous RPLND had been stage A ($n$ = 1) and stage B1 without adjuvant chemotherapy ($n$ = 1). Neither case had clinical evidence of metastases at the time of detection of second testis tumour, and both remain well after orchiectomy alone.

*All cases*

Overall, 7 patients (4%) died out of the 174 clinical stage B cases treated by primary RPLND over 25 years. There were five deaths due to cancer, one postoperative death and one death related to complications of chemotherapy. The average duration of hospital stay after RPLND was 9 days (median = 8 days, range 5–36 days), but these figures are lower for the modern 1979–1989 series (mean = 7.5 days, median = 7 days, range = 5–18 days). From 1989 to 1992, the median length of hospital stay after primary RPLND was 5 days. General postoperative complications included pneumonitis and pleural effusion (4%, $n$ = 7) and haematoma (1%, $n$ = 2). Prolonged ileus (3%, $n$ = 5) and transient pancreatitis (1%, $n$ = 2) were a feature of extensive bowel mobilisation, particularly in the past when a suprahilar dissection was routinely performed. 2 cases (1%) had retroperitoneal lymphoceles detected during follow-up despite

infarction ($n$ = 1), and femoral neuropraxia ($n$ = 1). In more recent years, there were fewer than 6% complications, all minor (e.g. phlebitis, brief ileus, etc.) which resulted in the average length of hospital stay after RPLND remaining at 5 days.

For the patient, a major concern after RPLND was reproductive status. Eighty-six per cent of the group with full bilateral dissection are reportedly anejaculatory. However, introduction of modified templates of dissection has changed the ejaculation rate from 75% here [10] to as high as 90% [12].Prospective isolation and preservation of postganglionic lumbar sympathetic fibres (joining the hypogastric plexus over the lower aorta) within these right or left modified templates can virtually ensure postoperative ejaculation [10]. Nevertheless, application of this technique remains a matter of clinical judgment and operator experience. For low volume clinical stage B disease, either standard en bloc dissection within modified right or left sided templates or prospective bilateral nerve-sparing RPLND techniques are considered an appropriate standard of care for this level of disease.

## DISCUSSION

The discovery of more effective chemotherapy was the single most important factor in causing the improvement in cure rates in NSGC testis cancer in the early 1980s [2]. The impact of cisplatinum was especially far-reaching in centres that previously relied on radiotherapy as the mainstay of treatment. The inability of irradiation to secure long-term complete remission for many patients with retroperitoneal metastases was well known, and primary chemotherapy was readily adopted in lieu of radiotherapy [13]. Routine prophylactic abdominal irradiation in cases without overt evidence of metastases (clinical stage A) was also abandoned. Instead, such cases were put on surveillance after orchiectomy, and received combination chemotherapy only when relapse was seen later [14]. The previous standard modality of treatment for NSGC tumours was, therefore, almost totally replaced by chemotherapy postorchiectomy.

These major alterations in the management of low clinical stages were less quickly adopted in centres long committed to the surgical management of testis cancer postorchiectomy. Primary chemotherapy had been successfully introduced for cases with advanced, *disseminated* disease. Based on this experience, there was a transition away from primary surgery for bulky abdominal disease to a regimen of primary chemotherapy followed by resection of residual masses. However, most U.S. surgical centres continued with routine primary RPLND in low volume (clinical stage A or B) settings for quicker staging and therapeutic considerations. Chemotherapy was also considered as an adjuvant for pathological stage B cases, and was prospectively studied in a randomised trial in this context [11]. This was based on the premise that primary RPLND was, *per se*, an effective therapeutic procedure in node-positive disease, and could safely be compared to a combined surgical and chemotherapeutic approach. The outcome analysis of this study and our present report confirms a similar survival in both arms of the study (RPLND alone versus RPLND plus adjuvant chemotherapy).

*The early series*: 1965–1978

The early results from 1965 to 1978 provide a direct comparison between primary RPLND and primary abdominal irradiation in clinical stage B. Although of historic interest and subject to overinterpretation, these surgical data based on *clinical* staging have not been previously available (Table 1).

Relapse in this surgical series was primarily supradiaphragmatic (10/12); this was easy to detect by simple chest X-ray. In the radiotherapy series, relapse was more commonly abdominal (12/15 who relapsed); these were difficult to detect at the time unless metastases were sizeable. Pulmonary relapse in this series was often curable even with the limited cytotoxics available, sometimes combined with surgery (of special interest, in the radiotherapy series, there was also a successful salvage of the only patient with lung relapse alone). In contrast, retroperitoneal relapse with or without other sites in the radiotherapy series was generally unresponsive (10/12 deaths). Even during this time, it was becoming obvious that the disease model of chest alone was more favourable than retroperitoneum with or without other sites.

While there must be other factors influencing outcome in irradiated patients as well (e.g., bone marrow depression, etc.), the obvious difference in clinical presentation at relapse suggests the possible negative influence of both greater volume and multiple sites of disease as potential contributing factors in the poorer outcome of the radiated cohort. Of course, pathological stage B cancer was diagnosed earlier in the surgical series; two-thirds of this cohort remained cured with surgery alone. Also, those who relapsed did so early (usually within 2 years), and were easily cured with chemotherapy. The outcome of this cohort was determined earlier (2–4 years). Therefore, the surgical approach forces the issue of discovery, and provides earlier treatment which is always a favourable factor in cancer treatment.

*The modern series*: 1978–1988

Based on the favourable early experience, routine primary RPLND was continued. Between 1979 and 1989, 140 patients were referred for surgery for clinical stage B NSGC tumours. The staging error by clinical methods remained just over 20% non-specific (23%), despite improved quality of routine CT and marker evaluation. The inaccuracy of CT is due to its inability to detect abnormalities in internal nodal architecture whereas it readily detects abnormalities in nodal size [15]. Lymphography (LAG) has not been practised as a diagnostic routine in equivocal cases because it would not alter the therapeutic decision in a planned surgical approach. Also, it is widely acknowledged that the insensitivity and non-specificity of LAG ranges from 20 to 40%. Today, this false positive staging error becomes important because in primary chemotherapy series, an estimated 20% of these patients without metastases will receive unnecessary primary treatment with chemotherapy based on falsely positive clinical staging. The long-term toxicity of this primary chemotherapy is well known, but not well documented. For example, the long-term impact of chemotherapy in clinical stage B NSGC tumours on the return of fertility remains essentially unreported despite many queries about this in recent years [3, 16]. For node-negative patients to suffer this toxicity would be particularly inappropriate. This opens a new and very real question of risk–benefit when considering pre-emptive primary chemotherapy in clinical stage B disease or "high risk" clinical stage A disease. In addition, this experience with primary RPLND surgery for clinical stage B NSGC tumours affords the opportunity to study cost–benefit considerations. We are currently preparing cost figures for 100 cases treated by primary RPLND in a 5 year time period. We are also calculating the total cost of care for 100 cases similarly stratified for clinical stage treated with primary chemotherapy. For each group, the cost of additional treatment will be included (e.g. chemotherapy for failures post-

RPLND and, conversely, surgery for partial remissions after primary chemotherapy). After 5 years, our locally based figures in clinical stage A disease indicate no significant difference between the two approaches in clinical stage A disease. In clinical stage B disease, however, the primary RPLND approach has been found to be relatively cost and risk beneficial *vis à vis* primary chemotherapy. This is the subject of separate reports [17, 18].

Two-thirds of cases with cancerous nodes are cured by surgery alone. Longstanding "complete remission" was achieved in 3–4 h by surgery and, we believe, with acceptable morbidity that is well documented [19]. The therapeutic benefit of RPLND is proven beyond doubt. Further, the absence of relapse in pathological stage B given only two courses of postoperative adjuvant platinum chemotherapy emphasises the efficacy of two cycles of adjuvant chemotherapy when linked to primary surgery. The results indicate that a combination of the therapeutic modalities, surgery plus chemotherapy, can virtually guarantee cure in pathological stage B disease. This regimen appears suitable and cost-effective at the present time, especially if the patient is pathological stage B2 and more likely to relapse.

Further analysis of pathological stage B series not given adjuvant therapy reveals a lower relapse of 10–26% in stage B1 compared with 40–55% relapse in bulky pathological stage B2 disease [12]. The argument for adjuvant postoperative chemotherapy (i.e., double therapy) in pathological stage B2 disease is, therefore, very appealing [11]. In this B2 subset, there may be little to choose between the primary surgical or medical approach insofar as double therapy is likely in either programme. In pathological stage B1 after surgery alone, those who relapsed (25%) were invariably cured by chemotherapy; so it is reasonable to permit withholding routine adjuvant chemotherapy in these patients provided there are facilities and the will for intensive follow-up. RPLND as monotherapy for pathological B1 promises a cost saving for most (75%).

The present survival rate of 98% among 140 patients treated between 1978 and 1989 compares favourably with even more recent early results using primary chemotherapy (96%) for small volume disease [20]. The overall relapse rates are not suitable for comparison because relapse in the surgical population was influenced by whether adjuvant chemotherapy was administered. Similarly, in Peckham's earlier chemotherapy series, 37% of cases required a postchemotherapy resection of residual masses [20]. More recent Medical Research Council (MRC) experience still indicates approximately one-third (32%) will need postchemotherapy RPLND [9].

A promising avenue of clinical research is the study of risk factors in the histology of the primary testis tumour. Just as the MRC group has shown risk factors for relapse postorchiectomy in clinical stage I, work from many units has suggested responsiveness to primary chemotherapy in advanced disease is also related to the histology of the primary tumour. Possibly those with pure embryonal cancer (MTU) will be most responsive to primary chemotherapy and those with teratoma (MTI) less so, and therefore, more suitable for primary RPLND.

Primary RPLND and/or primary chemotherapy for clinical stage B NSGC tumours are very effective when used in concert with one another. That is to say, neither primary treatment as monotherapy is sufficient for all cases. Approximately one-third in each group will require additional treatment (Tables 3–4). Chemotherapy will rescue those who relapse after surgery, and surgery will rescue most of the chemotherapy failures (partial remissions). On balance, our view remains that primary surgery for clinical stage B NSGCT is appropriate because it is both cost-effective and risk-beneficial. Further, it offers at least some theoretical strategic advantages already mentioned. We plan to study further risk factors in low volume NSGC tumours and offer nerve-sparing RPLND techniques in this context. We are encouraged by our retrospective study [21] of primary testis tumour histology and proliferative parameters, which may permit us to define more accurately risk and select candidates for primary surgery (or primary chemotherapy as in the U.K.) versus expectant management (surveillance). The choice of primary therapy options in clinical stage B will remain influenced by institutional resources and expertise.

*Table 3. Comparison of primary therapy: clinical stage B NSGCT*

| | Primary RPLND | Primary chemotherapy |
|---|---|---|
| Curative (as monotherapy) | 67% | 67% |
| Failure rate as monotherapy (range) | 33% (10–49%) | 33% (20–40%) |
| Overall survival including secondary therapy | 98% | 96% |
| Late relapses | <1% | >3% |
| Long-term toxicity | 0–10% | Unreported est. 10–30% |

*Table 4. Risk–benefit analysis of primary therapy (clinical stage B NSGCT testis cancer)*

| | Primary RPLND surgery | Primary chemotherapy |
|---|---|---|
| Failure rate (Need for 2 Rx) | 33% | 33% |
| Death rate | 2% | 4% |
| Late relapses (>2 years) | 0–1% | 3–5% |
| Long-term toxicity | 1–10% (Anejaculation) | 40–55% (Infertility) |
| Overtreatment (clinical staging error) | 20% | Unreported est. 20% |

Ideally, the patient should have a choice and be well informed. For example, a young man with fertility concerns may opt for the nerve-sparing RPLND approach in the hope of avoiding long-term toxicity of chemotherapy to germ cell reproductive function. Alternatively, a married man with family and no fertility concerns may choose primary chemotherapy in the hope of achieving a durable complete remission with chemotherapy alone, knowing that postchemotherapy surgery is available for the one-third who do not obtain a complete remission.

In conclusion, in stage B NSGCT, neither surgery nor chemotherapy are entirely sufficient as monotherapy. Approximately one-third of cases for each approach need the other for salvage of clinical failure. Until now, local customs and expertise have been the overriding factors in assignment of therapy. Further study of risk–benefit, cost–benefit and quality of life issues will assist the patient (and physician) to individualise the choice of therapy according to the patient's own needs and circumstances.

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