

# Assessing complications from retroperitoneal lymph node dissection for testicular cancer in North America

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## ABSTRACT

**INTRODUCTION:** Retroperitoneal lymph node dissection (RPLND) is a procedure of significant therapeutic and diagnostic value in the management of testicular cancer. This study aimed to conduct a contemporary review of surgical outcomes following RPLND procedures performed in North America over the last decade.

**METHODS:** We queried the National Surgical Quality Improvement Program (NSQIP) database from 2012–2022 (n=9 857 040) to identify patients who underwent RPLND and were diagnosed with testicular cancer. The primary outcome was 30-day morbidity. Secondary outcomes included time-to-complication analysis, rate of additional organ resection, hospital length of stay (LOS), and readmission rates. Binomial logistic regression and a generalized linear model were used to identify risk factors associated with 30-day morbidity and LOS.

**RESULTS:** A total of 513 RPLND procedures met the inclusion criteria. The median age was 30 years (interquartile range [IQR] 24–36.50) with a body mass index of 27.9 kg/m<sup>2</sup> (IQR 24.5–32.0). There were no deaths within 30 days. The overall 30-day morbidity rate was 17% (n=86). Bleeding/transfusion postoperatively (12%), return to the operating room (3%), and superficial surgical-site infection (2%) were the three most common complications. Factors associated with increased 30-day morbidity included: history of smoking (odds ratio [OR] 2.5, 95% confidence interval [CI] 1.35–4.68) and concurrent vascular repair/reconstruction (OR 4.1, 95% CI 1.12–15.46). The median LOS was four days (IQR 3–6) and the 30-day readmission rate was 7.0%.

**CONCLUSIONS:** This study underscores that approximately one in six patients experience complications following RPLND in North America. Identifying the timing of and risk factors for these complications can improve physician-patient communication and overall care.

## INTRODUCTION

Testicular cancer represents 1% of adult neoplasms and is the most common solid malignancy in young men.<sup>1,2</sup> At diagnosis, approximately 90% of cases are germ cell tumors (GCT), categorized as either seminomatous (SGCT) (55–60%) or non-seminomatous (NSGCT) types (40–45%).<sup>3</sup> Patients with testicular cancer can expect to have excellent outcomes, with five-year survival rates ranging from 99%, 96%, and 73% in localized (clinical stage I), regional (clinical stage II), and distant disease (clinical stage III).<sup>4</sup>

The primary landing zone for metastatic spread of testicular cancer is the retroperitoneal lymph nodes. Retroperitoneal lymph node dissection (RPLND) is an important component of multimodal treatment and has significant diagnostic and therapeutic value.<sup>5</sup> For example, primary RPLND is indicated following orchiectomy in clinical stage (CS) I NSGCT, with cure rates of approximately 90%.<sup>2,6,7</sup> In CSII NSGCT, RPLND is performed for residual retroperitoneal masses following chemotherapy, if tumor markers have normalized and there is suspicion of residual teratoma and/or other germ cell elements or as a desperation procedure for tumors that are not responding to chemotherapy.<sup>2,7,8</sup> Furthermore, RPLND is gaining popularity as an alternative to chemotherapy or radiotherapy for low-volume CSII SGCT due to concerns about long-term treatment-related toxicities, such as cardiovascular disease and secondary cancers.<sup>9-11</sup>

## KEY MESSAGES

- RPLND is a procedure of significant therapeutic and diagnostic value in the management of testicular cancer.
- The 30-day complication rate following RPLND in North America is approximately 16%.
- Risk factors associated with 30-day morbidity include smoking, longer operation times, and concurrent vascular repair.

RPLND is recognized as a technically challenging surgery, with morbidity rates ranging from 10–30% and mortality rates below 1%.<sup>12–17</sup> While much of the existing literature is based on center-specific data, two studies have provided national outcome figures. Wells et al reported 30-day complication rates in 162 men who underwent RPLND in the U.K., demonstrating a 10% morbidity rate, 0% mortality, 11% risk of synchronous nephrectomy, a 25% blood transfusion rate, and a median hospital stay of 5–6 days.<sup>13</sup> Additionally, the Swedish and Norwegian Testicular Cancer Group, which included 318 men undergoing post-chemotherapy NSGCT RPLND, reported a 30-day morbidity rate of 30%, a mortality rate of 0.3%, and a concurrent nephrectomy rate of 1.9%.<sup>12</sup> To date, there are no other international studies published on RPLND outcomes. This study, therefore, aimed to provide a contemporary analysis of morbidity and mortality with RPLND performed in North America.

## METHODS

### Study design

We performed a retrospective cohort study of patients 18 years and older who underwent RPLND for testicular cancer in North America from January 2012 to December 2022, using data from the American College of Surgeons' National Quality Improvement Program (ACS-NSQIP) database.

### NSQIP database

The ACS-NSQIP database, established in 2004 as an extension of the National Veterans Affairs Surgical Risk Study, prospectively collects data from several hundred participating institutions (range 300–700) on over 100

clinical variables, including patient demographics, disease characteristics, operative details, and 30-day postoperative morbidity. Each hospital submits approximately an average of 1600 major operations per year into the NSQIP database. A site's trained and certified surgical clinical reviewer (SCR) captures these data using a variety of methods, including medical chart abstraction. To ensure the data collected are of the highest quality, the ACS-NSQIP has developed a host of different training mechanisms for the SCRs and conducts an inter-rater reliability (IRR) audit of selected participating sites, with disagreement rates of >5% excluded from the database.

### Patient selection

The participant user file of the ACS-NSQIP database was queried for RPLND using current procedural terminology (CPT) codes 38562, 38564, 38570, 38572, 38747, 38780, 49203, 49204, 49205. The inclusion criteria were further filtered to include male patients who underwent surgery with a urologic speciality and had ICD diagnoses of testicular cancer and spermatic cord (included ICD-9 codes and I0 codes for testicular cancer were 186, 186.9, C62, C63, D40.11, and Z85.47, respectively)

### Covariates

Baseline patient characteristics were collected, including age, body mass index (BMI), race, and medical history of comorbid conditions such as diabetes, smoking, dyspnea, chronic obstructive pulmonary disease, congestive heart failure, hypertension, bleeding disorders, and steroid use. BMI was categorized based on World Health Organization criteria: <18.5, 18.5–25, 25–30, and >30 (kg/m<sup>2</sup>). The NSQIP database defines “disseminated malignancy” as cancer that has spread to at least one other site and in patients who have received treatment within one year before the procedure or the extent of disease is first appreciated at the time of the surgical procedure in question.<sup>18</sup>

Operative details were collected, including the American Society of Anaesthesiologists (ASA) score, operative time, and any concurrent procedures/organ resections. Data on 30-day outcomes were collected, including morbidity, mortality, length of stay (LOS), and readmission rates. Complications were categorized into nine groups: 1) overall mortality; 2) overall complications (including mortality); 3) cardiac complications; 4) postoperative pneumonia; 5) re-intubations required within 48 hours of surgery (and those beyond 48 hours); 6) unplanned intubations; 7) pulmonary embo-

lism and venous thrombosis; 8) renal dysfunction; and 9) surgical-site infections, including superficial, fascia, and deep infections.

## Outcomes

The primary outcome studied was 30-day overall complication rate. Secondary outcomes included specific components of the primary outcome, time-to-complication analysis, rate of additional organ resection, LOS, and readmission rates. NSQIP does not provide detailed information on the severity of complications at the individual patient level, making it impossible to grade their severity.

## Statistical analysis

Demographic and case-based characteristics of patients undergoing urologic procedures were reported as frequencies and percentages. Binomial logistic regression was performed to identify risk factors associated with 30-day morbidity, with adjustment for demographic and clinical characteristics. Models were adjusted for year, age, BMI, race, smoking status, disseminated cancer, diabetes status, ASA class, operative time, concurrent orchidectomy, and additional organ resection. Similarly, a generalized linear model (Poisson loglinear, main effects) was used to determine risk factors for prolonged LOS. Patients with missing data were excluded from the regression analyses. Regression analyses are presented as odds ratios (OR) with 95% confidence intervals (CIs). All statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 28.

## RESULTS

From 9 856 500 procedures recorded in the ACS-NSQIP database from 2012–2022, 513 RPLND procedures were analyzed. Baseline clinical and demographic characteristics are described in Table 1. The median age was 30 years (IQR 24–36.50) with a BMI of 27.9 kg/m<sup>2</sup> (IQR 24.5–32.0); 18% of patients were recorded as disseminated cancer. There were approximately 50 RPLNDs recorded in the NSQIP database per year (except for 2013 and 2019).

## Morbidity and mortality

There were no deaths reported within 30 days. The overall 30-day morbidity rate was 17% (Table 2). Perioperative bleeding/transfusion (12%), return to the operating room (3%), and superficial surgical-site infection (S-SSI) (2%) were the three most common complications. All complications are described in Table 2.

**Table 1. Clinical and demographic characteristics of the study population (n=513)**

Variable	Value
Age, years, median (IQR)	30 (24–36.5)
BMI, kg/m <sup>2</sup> , n (%)	
≤18.5	2 (0.4)
18.5–24.9	137 (26.8)
25–29.9	187 (36.6)
≥30	185 (36.2)
Race, n (%)	
White	404 (78.8)
Black	9 (1.8)
Other	19 (3.7)
Missing	81 (15.8)
Smoker, n (%)	94 (18.3)
Hypertension, n (%)	41 (8)
Diabetes, n (%)	17 (3.4)
Disseminated cancer, n (%)	94 (18.3)
Year of RPLND, n (%)	
2012	48 (9.4)
2013	30 (5.8)
2014	46 (9.0)
2015	29 (5.7)
2016	56 (10.9)
2017	59 (11.5)
2018	48 (9.4)
2019	38 (7.4)
2020	52 (10.1)
2021	62 (12.1)
2022	45 (8.8)
ASA class, n (%)	
I	18 (3.5)
II	288 (56.1)
III	195 (38.0)
IV	12 (2.3)
Operation time, minutes (median, IQR)	300 (245–374.5)
Concurrent procedures, n (%)	
Orchidectomy	42 (8.2)
Vascular repair/reconstruction	19 (3.7)
Ureteric stent	11 (2.1)
Ureteric reimplantation	6 (1.2)
Multivisceral resection, n (%)	
Nephrectomy	10 (1.9)
Bowel	4 (0.8)
Pancreas	1 (0.2)
Liver	1 (0.2)

ASA: American Society of Anaesthesiologists; BMI: body mass index; IQR: interquartile range; RPLND: retroperitoneal lymph node dissection.

The median number of blood transfusions administered postoperatively was two (IQR 1–4).

The median time to first reoperation was eight days (IQR 4–12). Reasons for reoperation included

**Table 2. Characteristics of RPLND complications at 30 days**

Type of complication	n (%)	Median time to complication, days (IQR)
<b>Skin</b>		
Surgical site infection		
Superficial (S-SSI)	12 (2.3)	12 (8–19.75)
Deep (D-SSI)	1 (0.2)	8
Organ (O-SSI)	6 (1.2)	9.5 (4.75–19.75)
Wound dehiscence	3 (0.6)	12 (11–12)
<b>Hematology</b>		
Transfusion	61 (11.9)	–
Deep vein thrombosis	7 (1.4)	9 (3–16)
Pulmonary embolism	2 (0.4)	18.5
<b>Infection</b>		
Pneumonia	5 (1.0)	5 (2.5–9.5)
Urinary tract infection	3 (0.6)	5 (5–5)
Sepsis	6 (1.2)	6.5 (2.75–11.25)
Septic shock	2 (0.4)	15
<b>Renal</b>		
Progressive insufficiency/renal failure requiring dialysis	6 (1.2)	1 (0.5–1.5)
<b>Cardiac</b>		
Myocardial infarction	–	–
Arrest	–	–
<b>Return to operating room</b>	13 (2.5)	8 (4–12)

RPLND: retroperitoneal lymph node dissection.

unknown (n=3), hemoperitoneum (n=2), and injury to the ureter (n=2).

The median LOS post-RPLND was four days (IQR 3–6). Two patients were still in hospital at 30 days (0.4%).

### Readmission

The 30-day readmission rate was 7.0%. The median time to readmission was 12 days (IQR 7–18). The three most common reasons for readmission included nausea or vomiting (n=4), infection (organ SSI, n=1; sepsis of unknown origin, n=1; septic shock, n=1), and intestinal obstruction (n=3).

### Independent predictors of morbidity and LOS

Factors associated with increased 30-day morbidity included a history of smoking (OR 2.5, 95% CI 1.35–4.68) and concurrent vascular repair/reconstruction (OR 4.1, 95% CI 1.12–15.46).

Factors associated with prolonged LOS included black ethnicity (OR 20.1, 95% CI 2.02–199.31), disseminated cancer (OR 2.93, 95% CI 1.32–6.5), and any comorbid illness (OR 41.6, 95% CI 17.5–100).

## DISCUSSION

This is the first reported study of RPLND outcomes for testicular cancer in North America over 11 years (2012–2022). The quality of RPLND surgery in North America appears satisfactory, with no reported mortality within 30 days. Compared to the U.K., 30-day morbidity rates in North America are higher (16.8% vs. 10%), while transfusion rates (11.9% vs. 25%) and median LOS (4 vs. 5.5 days) are lower.<sup>13</sup>

The U.K. has implemented a centralization strategy for cancer care, resulting in urologists performing a median of six RPLNDs/year, compared to approximately one RPLND/year in America.<sup>13,19,20</sup> Hospitals with higher patient volumes may experience fewer complications but often incur higher hospitalization costs.<sup>21</sup> Although this study does not directly assess surgeon or hospital volume, it suggests that surgical quality for RPLND is comparable to that in the U.K. Data from Sweden and Norway show a notably higher complication rate of around 30%, likely because these studies focused exclusively on post-chemotherapy NSGCT patients.<sup>12</sup>

The surgical complexity of RPLND can often necessitate additional organ resection during the operation. In the U.K. series, concurrent nephrectomy was performed in 11% of cases and vascular procedures in 5%.<sup>13</sup> Our study found these rates to be lower, at 2% and 4%, respectively. One possible hypothesis could be differences in surgical practices and case selection between European and North American urologists. For instance, the European Association of Urology (EAU) guidelines recommend RPLND mainly for CS II non-seminoma disease, while the National Comprehensive Cancer Network (NCCN) guidelines suggest RPLND as a viable option alongside chemotherapy and radiotherapy for both CS I and II seminoma and non-seminoma diseases.<sup>27</sup> Approximately 18% of the study population had “disseminated disease,” suggesting that many patients who underwent RPLND in North America may have had localized disease (CS I). RPLND performed in the primary setting (CS I) are of lower-risk profile, with a reduced likelihood of vascular and local organ involvement.

The baseline characteristics of this cohort are noteworthy, with 8% of patients undergoing synchronous (delayed) orchidectomy at the time of RPLND. Delayed orchidectomy is performed in patients with advanced GCTs (typically CS III), where first-line systemic chemotherapy can yield excellent outcomes (overall survival 70–90%), particularly in those with life-threatening metastases (e.g., back pain, shortness

of breath).<sup>27</sup> Patients undergoing RPLND and delayed orchidectomy suggest that some patients in this cohort may have received chemotherapy before confirming histology, which is not consistent with international guidelines.

Specific risk factors that increase the complexity of RPLND are currently not well-defined and published data are often too small to draw clinically significant conclusions. Our study identified that smoking and the requirement of adjuvant vascular procedures increased the risk of postoperative complications. Smoking has been demonstrated with adverse postoperative outcomes irrespective of surgical specialty, and therefore, strong cessation advice should be provided to patients before surgery.<sup>22,23</sup>

Black ethnicity was identified as a risk factor for a prolonged LOS (median of seven days). Black patients were demonstrated to have a prolonged LOS in 10 of the 16 oncologic and non-oncologic surgical procedures in the U.S.<sup>24</sup> Several unmeasured confounders could contribute to the observed disparity seen in our study, such as the severity of comorbidities and type of hospital (academic or community).<sup>25</sup>

### Strengths and limitations

Several strengths of the NSQIP database increase the validity of our findings. First, the large sample size offered by NSQIP by evaluating national practices over 10 years increases the statistical power needed to identify significant differences in complication rates. Second, as noted previously, complications in NSQIP are manually abstracted by SCRs using standardized definitions, not based on insurance claims or self-reported by surgeons, and are therefore more likely to represent true postoperative complications. Third, NSQIP captures all complications occurring within 30 days of surgery, including those occurring after hospital discharge, which other data sources may miss.

Our study has several limitations. First, we acknowledge that NSQIP has approximately 700 participating institutions (approximately 13% of all U.S. hospitals) and coding complexity for RPLND remains challenging, which is likely to underestimate the true nature of events in North America. Second, the NSQIP database does not capture all complications (e.g., complications after 30 days, ileus, lymphocele) but is based on pre-existing variables, and therefore, the complication rate is likely to be underestimated in this study.

Additionally, while NSQIP provides information on the presence or absence of medical comorbidities, it lacks data on the severity of these conditions, limiting

our ability to adjust for risk accurately. Furthermore, disease- and procedure-specific factors, such as tumor histology (seminoma vs. non-seminoma), tumor stage, exposure to perioperative chemotherapy or radiotherapy, type of RPLND dissection template (unilateral, bilateral, nerve-sparing), and the surgical approach (open or minimally invasive) are not included, which can significantly impact the technical difficulty of the surgery.

### CONCLUSIONS

Notwithstanding the limitations, we have reported on complications and perioperative outcomes for RPLNDs performed in North America and identified important predictors of complications. Surgical outcomes compare favorably to other international series. This study offers up-to-date outcomes for urologic oncologists to discuss with patients, helping them understand the inherent risks of RPLND surgery.

**COMPETING INTERESTS:** Dr. Huynh has participated in advisory boards for Astellas and Knight Therapeutics; and received compensation for travel expenses for NSUAU 2024 from Pfizer. Dr. Inman has participated in advisory boards for Abbvie, Combat Medical, Johnson & Johnson, Seattle Genetics, and TerSera; has received honoraria from the National Institutes of Health, Department of Defense, TerSera, and Tolmar; and has participated in clinical trials supported by CG Oncology, FKD Therapies, Genentech-Roche, Janssen, Medtronic, Profound Medical, Seattle Genetics, and Theralase. The remaining authors do not report any competing personal or financial interests related to this work.

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