Clinical and Radiographic Predictors of Great Vessel Resection or Reconstruction During Retroperitoneal Lymph Node Dissection for Testicular Cancer

Scott C. Johnson, Zachary L. Smith, Charles Nottingham, Zeyad R. Schwen, Stephen Thomas, Elliot K. Fishman, Nam Ju Lee, Philip M. Pierorazio, and Scott E. Eggener

OBJECTIVE To evaluate whether specific clinical or radiographic factors predict inferior vena cava (IVC) or abdominal aortic (AA) resection or reconstruction (RoR) at the time of postchemotherapy retroperitoneal lymph node dissection (RPLND) for germ cell tumors of the testicle.

MATERIALS AND METHODS Two hundred seventy-seven patients undergoing postchemotherapy RPLND at two institutions between 2005 and 2015 were identified. Preoperative imaging was reviewed with radiologists blinded to operative details. Univariable and multivariable logistic regressions were performed, and a model was created to predict the need for great vessel RoR using radiographic and clinical factors.

RESULTS Of 97 patients with preoperative imaging and clinical data available, 16 (17%) underwent RoR at RPLND. On univariable analysis dominant mass size, degree of circumferential vessel involvement, and vessel deformity were associated with RoR (all $P < .05$). No patients with clinical stage IIA or IIB disease at diagnosis required RoR. In the multivariable model, mass involvement of the IVC >135° (odds ratio 65.5, 7.8-548, $P < .01$) and involvement of the AA >330° (odds ratio 29.0, 3.44-245, $P < .01$) were predictive for RoR. These thresholds yielded a PPV of 48% and 50% and a NPV of 92% and 97% for IVC and AA RoR, respectively.

CONCLUSION Degree of circumferential involvement of the great vessels is an independent predictor for resection or reconstruction of the IVC or AA at postchemotherapy RPLND. Patients at high risk of great vessel reconstruction should be informed accordingly and have the proper teams available for complex vascular reconstruction. UROLOGY 123: 186−190, 2019.

Standard initial treatment for bulky metastatic germ cell tumor (GCT) is cisplatin-based chemotherapy. Following chemotherapy, approximately one-third of patients have residual retroperitoneal disease.[1] Depending on size and primary tumor histology, these residual masses may require surgical resection via retroperitoneal lymph node dissection (RPLND). In the setting of nonseminomatous GCT, these masses contain teratoma, viable GCT, or both in more than half of all cases.[1] Multiple studies have shown completeness of RPLND to be associated with a favorable long-term clinical outcome.[2]

From the University of Chicago, Department of Surgery, Section of Urology, Chicago, IL; and the James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, Baltimore, MD

Address correspondence to: Scott C. Johnson, M.D., Medical College of Wisconsin, Department of Urology, 8701 W Watertown Plan Rd. Milwaukee, WI 53226. E-mail: charlesjohnsonscott@gmail.com

Submitted: May 29, 2018, accepted (with revisions): August 22, 2018

Residual masses involving or adjacent to the great vessels inferior vena cava (IVC) or abdominal aorta (AA) can represent a significant technical challenge. In 5%-12% of RPLNDs, resection and/or reconstruction of the AA or IVC will be required to achieve a complete resection.[3-5] These vascular procedures can add significant technical complexity while increasing the risk of morbidity and mortality.[4,6] Preoperative identification of patients who may be at high risk for requiring vascular reconstruction would aid in preoperative planning and patient counseling.

In an analysis of 339 patients undergoing postchemotherapy (PC) RPLND, International Germ Cell Cancer Collaborative Group (IGCCCG) classification and residual tumor size greater than 5 cm were predictive of requiring caval resection or reconstruction (RoR), but found no predictors of aortic RoR.[5] While this study showed residual tumor size to be associated with caval RoR, no further tumor characteristics were investigated. Conceptually,

 https://doi.org/10.1016/j.urology.2018.08.028
0090-4295

residual tumors which abut or encase the great vessels may be more likely to require vascular intervention. However, to our knowledge no data exists to quantify or support such an association. The goal of our study was to evaluate several radiographic and clinical factors in an attempt to identify predictors for those who ultimately require major vascular intervention during PC-RPLND.

MATERIALS AND METHODS

Patients

After obtaining institutional review board approval at each facility, we retrospectively identified 277 patients who underwent PC-RPLND for GCT from 2005 to 2015 at 2 academic medical centers. Only patients with available preoperative cross-sectional imaging and complete clinical information were included. Patients with elevated tumor markers or patients undergoing so-called “desperation RPLND” were excluded. In total, 97 patients were identified for inclusion.

Clinical and Radiographic Features

Preoperative clinical information included age, body mass index, location of primary tumor, histology of primary tumor, stage, IGCCCG classification, number of chemotherapy cycles, and history of salvage chemotherapy.

The immediate preoperative cross-sectional imaging, either contrast-enhanced computed tomography or magnetic resonance imaging in both axial and coronal planes was reviewed at each respective institution by a radiologist specializing in abdominal imaging. The radiologists were blinded to surgical details. Imaging studies were evaluated for number of discrete retroperitoneal masses, maximum axial, and craniocaudal dimensions of the dominant mass, attenuation of dominant mass (measured centrally, Hounsfield units), maximum diameter of the IVC, diameter of the IVC at the level of the dominant mass, degrees of circumferential contact of the dominant mass with the IVC, deformation of the IVC (defined as >5 mm inward bowing of the IVC), maximum diameter of the AA, diameter of the AA at the level of the dominant mass, degrees of circumferential contact of the dominant mass with the AA, and deformation of the AA (defined as >5mm inward bowing of the aortic wall). These radiographic factors were selected a priori by consensus agreement among the investigators.

Surgical Technique and Outcomes of Interest

All patients underwent open, bilateral template RPLND via a midline approach with nerve-sparing when possible. In all cases, the main objective was complete resection of macroscopic disease. Small perforations along the AA were overseen with polypropylene suture. In cases where involvement of the mass with the AA wall required en bloc AA resection, a prosthetic aortic graft replacement was used. In situations requiring partial wall excision, patch angioplasty was performed to repair the aortic defect. In cases in which the IVC was grossly involved, resection of the IVC was undertaken as necessary. If the IVC lumen remained adequate after wall resection ($>50\%$ luminal diameter), it was closed primarily with a running polypropylene suture. Conversely, if the lumen was compromised, the IVC was reconstructed with bovine patch grafts. If complete resection of the IVC was necessary it was ligated proximally and left in discontinuity.

The primary outcome of interest was need for RoR of the IVC or AA. This was defined as resection of the AA requiring replacement or patch angioplasty. Regarding the IVC, intentional partial wall resection with or without patch angioplasty or en bloc removal were included. Primary closure of small AA or IVC defects were not included.

Statistical Methods

Continuous variables are presented as median and interquartile range and compared between groups using two-sample t test or Wilcoxon rank-sum test. Categorical variables are presented as frequency and percentages and compared between groups using chi-squared or Fischer’s exact test. Associations with the need for RoR were assessed with univariable logistic regression and presented with odds ratios (OR) and 95% confidence intervals (CI).

Using features found to be significant on univariable logistic regression, a multivariable model was created for prediction of IVC RoR and AA RoR using stepwise selection, with a threshold of $P<.05$ used to be included in the model. Thresholds for continuous features in the model were determined by maximizing the chi-squared statistic for comparisons of those requiring RoR.

All statistical analyses were performed using Stata, version 14.2 (StataCorp, College Station, TX). All hypotheses testing was two-sided and P values of $<.05$ were considered statistically significant.

RESULTS

Of 97 patients, 16 (16.5%) required AA or IVC RoR. There were 13 (13%) and 5 (5%) IVC and AA RoR, respectively, with 2 patients requiring RoR of both great vessels. Of those who required IVC RoR, 10 (77%) underwent resection of the IVC with primary repair, 2 (15%) underwent resection and patch angioplasty, and 1 (8%) underwent complete resection. Of patients who required AA RoR, 3 (60%) required aortic replacement and 2 (40%) underwent patch angioplasty. The 2 patients who required concurrent AA and IVC RoR both underwent resection and primary repair of the IVC, with one requiring aortic replacement and the other requiring patch angioplasty of the AA.

Patients requiring RoR tended to have more right-sided primary tumors (81% vs 43%, $P<.01$) and were more likely to have an advanced stage at diagnosis (81% vs 49% with stage III disease, $P=.04$; Table 1). No patients with less than clinical stage IIC required RoR. There were otherwise no significant differences in age, body mass index, dominant histologic component of primary tumor, IGCCCG risk group, chemotherapy cycles, or salvage chemotherapy between those requiring and not requiring RoR.

In those who required RoR, the dominant mass tended to be larger by axial dimension, craniocaudal dimension, and estimated volume. The median size of the dominant mass requiring RoR was 4.8 cm axially, 8.6 cm craniocaudally, with a volume of 77.5 cm3. The median size of the dominant mass in which no RoR was required was significantly smaller, 2.6 cm axially, 3.6 cm craniocaudally, with a volume of 9.9 cm^3 (Table 2). Patients who required IVC RoR had significantly more circumferential involvement of the IVC (median 215° vs 0°, $P<.01$), and RoR of the IVC was not required in any patient who had no contact between the mass and IVC. Deformation of the IVC

Table 1. Patient characteristics with and without great vessel reconstruction at postchemotherapy RPLND

	Reconstruction	No Reconstruction	*P* Value
Patients, n	16	81	
Age, median (IQR)	26 (23,36)	28 (22,35)	.94
BMI, median (IQR)	24.0 (21.7,26.6)	26.3 (24.0,29.7)	.05
Laterality of primary, n (%)			
Right	13 (81.3)	34 (42.5)	< .01
Dominant component of primary, n (%)			
Embryonal	7 (46.7)	37 (49.3)	.89
Teratoma	4 (26.7)	18 (24.0)	
Seminoma	3 (20.0)	10 (13.3)	
Yolk Sac	1 (6.7)	7 (9.3)	
Choriocarcinoma	0 (0)	3 (4.0)	
Stage, n (%)			
IIA	0 (0)	14 (17.3)	.04
IIB	0 (0)	14 (17.3)	
IIC	3 (18.8)	13 (16.1)	
III	13 (81.2)	40 (49.4)	
IGCCCG risk group, n (%)			
Good	5 (31.3)	49 (61.2)	.08
Intermediate	4 (25.0)	13 (16.3)	
Poor	7 (43.7)	18 (22.5)	
Chemotherapy cycles, median (IQR)	4 (4,4)	4 (3,4)	.07
Salvage chemotherapy, n (%)	4 (25.0)	9 (11.1)	.14

IGCCCG, International Germ Cell Cancer Collaborative Group; IQR, interquartile range; RPLND, retroperitoneal lymph node dissection.

was also more likely in patients who required IVC RoR (92% vs 30%, $P < .01$). Diameter of the IVC was not different between patients who did and did not require IVC RoR.

Extent of circumferential involvement of the AA wall was significantly higher in those who required RoR (330° vs 90°, $P < .01$), and RoR of the AA was not required in any patient lacking contact between the mass and AA. Deformation of the AA was less common than deformation of the IVC, however, patients who required AA RoR were still more likely to have aortic deformation (40% vs 9%, $P = .03$).

Right-sided primary as well as greater axial and craniocaudal measurements were associated with increased odds for needing either IVC or AA RoR (Table 3). The need for IVC RoR was positively associated with degrees of circumferential tumor involvement of the IVC (OR 1.83 per 45° of involvement, 95% CI 1.39-2.43, $P < .01$), as well as IVC deformation (OR 28.3, 95% CI 3.49-230, $P < .01$). Similarly, the need for AA RoR was also positively associated with degree of circumferential tumor involvement with the AA (OR 1.99 per 45° of involvement, 95% CI 1.28-3.10, $P < .01$) and aortic deformation (OR 7.0, 95% CI 1.02-48.3, $P = .04$).

Since lack of mass contact with either the IVC or AA precluded any need for RoR, only patients with vessel involvement were used to create a multivariable predictive model for the need for AA and IVC RoR. For continuous variables, thresholds were determined to be used in the model. For IVC RoR, vessel involvement greater than 135°, dominant mass axial long axis greater than or equal to 6.8 cm, and dominant mass craniocaudal

Table 2. Radiologic characteristics of patients with and without great vessel reconstruction at postchemotherapy RPLND

	Reconstruction	No Reconstruction	*P* Value
Number of masses, median (IQR)	3 (1,5)	2 (1,3)	.43
Dominant mass			
Long axis - axial (cm), median (IQR)	4.8 (3.1,8.2)	2.6 (1.6,3.7)	< .01
Craniocaudal (cm), median (IQR)	8.6 (6.8,9.8)	3.6 (2.5,6.0)	< .01
Volume (cm^3), median (IQR)	77.5 (15.3,250)	9.9 (2.5,31.4)	< .01
Attenuation (Hounsfield), median (IQR)	37 (22.0,48.0)	41.0 (26.0, 52.0)	.36
IVC (stratified by IVC reconstruction)			
n (%)	13 (13.4)	84 (86.6)	
Max diameter (cm), median (IQR)	2.4 (2.0,2.8)	2.4 (2.1,2.6)	.75
Diameter at dominant mass (cm), median (IQR)	2.4 (2.1,2.7)	2.4 (2.1,2.6)	.94
Circumferential involvement of mass (°), median (IQR)	215 (180,320)	0 (0,90)	< .01
IVC deformed, n (%)	12 (92.3)	25 (29.8)	< .01
Aorta (stratified by aorta reconstruction)			
n (%)	5 (5.2)	92 (94.9)	
Max diameter (cm), median (IQR)	1.6 (1.5,1.7)	1.6 (1.5,1.7)	.64
Diameter at dominant mass (cm), median (IQR)	1.6 (1.5,1.7)	1.6 (1.5,1.7)	.74
Circumferential involvement of mass (°), median (IQR)	330 (180,360)	90 (0,180)	< .01
Aorta deformed, n (%)	2 (40)	8 (8.7)	.03

cm, centimeters; cm^3, cubic centimeters IVC, inferior vena cava.

Table 3. Clinical and radiologic associations with great vessel reconstruction at postchemotherapy RPLND

	Odds Ratio (95% CI)	*P* Value	c Index
Age (per year)	1.01 (0.96-1.06)	.81	0.50
BMI (per kg/m^2)	0.91 (0.81-1.03)	.09	0.65
Laterality (reference left)			
Right	5.86 (1.55-22.2)	**<.01**	0.69
Dominant component of primary			
Embryonal	1.0 (Ref)		0.55
Teratoma	1.17 (0.30-4.54)	.82	
Seminoma	1.59 (0.35-7.27)	.55	
Yolk Sac	0.76 (0.08-7.13)	.81	
Stage			
IIC	1.0 (Ref)		0.53
III	1.41 (0.35-5.73)	.63	
IGCCCG risk group			
Good	1.0 (Ref)		0.66
Intermediate	3.02 (0.71-12.9)	.14	
Poor	3.81 (1.07-13.6)	.04	
Salvage chemotherapy	2.67 (0.71-10.1)	.15	0.57
Number of masses (per mass)	1.06 (0.89-1.26)	.52	0.57
Dominant mass			
Long axis - axial (per cm)	1.28 (1.08-1.52)	**<.01**	0.78
Craniocaudal (per cm)	1.21 (1.07-1.38)	**<.01**	0.79
Volume (per cm^3)	1.00 (0.99-1.01)	.06	0.78
Attenuation (per HU)	0.99 (0.96-1.02)	.39	0.57
IVC (stratified by IVC RoR)			
Max diameter (cm)	0.79 (0.23-2.68)	.71	0.47
Diameter at dominant mass (cm)	0.78 (0.26-2.31)	.65	0.51
Circumferential involvement (per 45°)	1.83 (1.39-2.43)	**<.01**	0.91
IVC deformed	28.3 (3.49-230)	**<.01**	0.81
Aorta (stratified by aorta RoR)			
Max diameter (cm)	6.17 (0.56-68.5)	.14	0.56
Diameter at dominant mass (cm)	8.76 (0.55-140)	.13	0.54
Circumferential involvement (per 45°)	1.99 (1.28-3.10)	**<.01**	0.89
Aorta deformed	7.00 (1.02-48.3)	.04	0.66

Bold indicates statistical significance ($P < 0.05$)
BMI, body mass index; RoR, resection or reconstruction.

measuring greater than or equal to 9.1 cm maximized the chi-squared statistic. Similarly, for AA RoR, vessel involvement greater than 330°, dominant mass axial long axis greater than or equal to 4.3 cm, and dominant mass craniocaudal measuring greater than or equal to 6.7 cm were most predictive.

Stepwise selection of variables found significant on univariable logistic regression (laterality of primary, axial long axis measurement, craniocaudal measurement, deformation, and degree of vessel involvement) were used to create a multivariable prediction model for both IVC and aorta RoR. Ultimately, degree of circumferential great vessel involvement was the only selected feature in each model, with no significant predictive ability gained by inclusion of additional features. Degree of tumor involvement of the IVC >135° was associated with need for IVC RoR (OR 65.5, 95% CI 7.84-548, $P < .01$). Likewise, tumor involvement of the aorta >330° was associated with requiring aorta RoR (OR 29.0, 95% CI 3.44-245, $P < .01$). Among patients with any circumferential involvement of the IVC, the positive predictive value (PPV) for the 135° threshold was 48% and negative predictive value (NPV) was 92% . Similarly, among patients with any vascular involvement, the 330° threshold yields a PPV of 50% and NPV of 97%.

DISCUSSION

We identified the extent of vascular involvement on imaging as predictors of RoR of the great vessels during PC-RPLND. RoR was required in 16% of PC resections in our series, with the majority involving the IVC, likely due to predominantly right-sided primary tumors in the RoR group (81.3%), consistent with previous reports.[3,4,6,7]

While most caval procedures involved primary repair or patch angioplasty, one patient required complete transection of the IVC. This technique, without restoring continuity to the IVC, is generally well-tolerated.[4,7] If significant compromise of the IVC lumen occurs (or ligation), collateral venous return from the lower extremities occurs via the internal iliac veins, ascending lumbar veins, and portal venous system. In many patients, the obstructive component of the tumor has been gradual and chronic, allowing for further collateralization to develop over time. Chronic lower extremity edema is very rare in this scenario (<5%), with its occurrence likely related to resection of collaterals in complex cases, and not the IVC itself.[7] The decision to perform resection, reconstruction, or ligation can be subjective, with benefits and drawbacks to each approach. Our approach was to only reconstruct the IVC if the luminal diameter was compromised 50% or more. This has been the approach of others and has resulted in excellent long-term patency.[8]

Previously identified predictors of IVC RoR were IGCCCG classification and PC tumor size >5 cm.[5] While tumor size was used in their predictive model, no other tumor features were investigated. We chose to further explore the characteristics of residual masses in an effort to identify patients at high risk for vascular intervention. Using detailed radiographic review, we created a predictive model or AA and IVC RoR. Though many factors were significant on univariable analysis, the only predictive feature in both IVC and AA models was extent of vessel encasement by tumor. Expectedly, lack of contact with either the IVC or the AA essentially eliminated the need for RoR. Furthermore, we found vessel involvement was the strongest predictor of RoR and additional clinical or radiographic features provided no additional predictive power. Based on the PPV and NPV, patients with tumor contacting one of the great vessels, vessel involvement of at least 135° for the IVC and 330° for the AA, ~50% of patients require RoR of the respective vessel with < 10% requiring RoR under the given threshold.

The clinical factors identified in our study may potentially aid urologists in preoperative identification of patients at high risk for requiring vascular intervention, allowing for preoperative consultation of additional surgical services, through patient counseling, and referral to high-volume centers if appropriate.

There are important limitations to our study. The decision to perform RoR can be subjective and affected by surgeon experience and comfort level with vascular surgical procedures. That being said, we do think that these objective findings on preoperative imaging may help identify patients at high risk for needing these adjunct vascular procedures. Further, our findings are based on the results of 2 institutions only and due to the low event rate, we were not able to externally validate the model but encourage others to do so.

CONCLUSION

The degree of circumferential tumor involvement of the aorta (>330°) and IVC (>135°) is highly associated with the need for RoR during PC RPLND, irrespective of other clinical or radiographic findings. All patients undergoing RPLND should be counseled on possible need for vascular intervention, however patients with these tumor characteristics on preoperative imaging should be considered at high risk and planned for accordingly.

References

1. Daneshmand S, Albers P, Fosså SD, et al. Contemporary management of postchemotherapy testis cancer. *Eur Urol*. 2012;62:867–876.
2. Fizazi K, Tjulandin S, Salvioni R, et al. Viable malignant cells after primary chemotherapy for disseminated nonseminomatous germ cell tumors: prognostic factors and role of postsurgery chemotherapy. *J Clin Oncol*. 2001;19:2647–2657.
3. Ehrlich Y, Kedar D, Zelikovski A, Konichezky M, Baniel J. Vena caval reconstruction during postchemotherapy retroperitoneal lymph node dissection for metastatic germ cell tumor. *Urology*. 2009;73. 442.e17-442.e19.
4. Spitz A, Wilson TG, Kawachi MH, et al. Vena caval resection for bulky metastatic germ cell tumors: an 18-year experience. *J Urol*. 1997;158:1813–1818.
5. Winter C, Pfister D, Busch J, et al. Residual tumor size and IGCCCG risk classification predict additional vascular procedures in patients with germ cell tumors and residual tumor resection: a multicenter analysis of the German Testicular Cancer Study Group. *Eur Urol*. 2012;61:403–409.
6. Christmas TJ, Smith GL, Kooner R. Vascular interventions during post-chemotherapy retroperitoneal lymph-node dissection for metastatic testis cancer. *Eur J Surg Oncol*. 1998.
7. Beck SDW, Lalka SG. surgery JPD-JOV, 1998. *Long-Term Results After Inferior Vena Caval Resection During Retroperitoneal Lymphadenectomy for Metastatic Germ Cell Cancer*. Elsevier; 1998.
8. Sarkar R, Eilber FR, Gelabert HA, Quinones-Baldrich WJ. Prosthetic replacement of the inferior vena cava for malignancy. *J Vasc Surg*. 1998;28:75–83.

EDITORIAL COMMENT

This is a paper which attempts to use radiologic criteria to predict which post chemotherapy retroperitoneal lymph node dissection (RPLND) patients will require vascular grafts or patches at surgery. Desperation RPLND patients (those who have exhausted all chemotherapy options and have obvious localized cancer remaining) were excluded. Thus, the presumption is that most of these patients had teratoma or necrosis at surgery is reasonable.

I clearly agree that the preoperative CT scan is important. However, the decision to do vascular replacement or patching is really an intraoperative decision. With normal HCG and AFP, the question becomes: what is being resected? If it seems to be teratoma or necrosis, the split and roll technique works because cutting across teratoma or necrosis does not affect the prognosis.

So the decision relies upon the clinical history, the potential morbidity of RPLND with or without vascular replacement/reconstruction and thus is dependent upon the judgment of an experienced testis cancer surgeon.

I think it is nice that these authors have tried to demonstrate that some easily measurable preoperative criteria may be helpful. Ultimately, however, the clinical scenario and intraoperative judgment are the factors which are most important. I wish it were more objective; unfortunately it is not.

Richard Foster, M.D., Barnhill drive, Indianapolis, IN

https://doi.org/10.1016/j.urology.2018.08.033
UROLOGY 123: 190, 2019.