Chapter 4
Urology

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4.1 Frequency of Urological Tumors

Urological tumors are a diverse group of oncological diseases which are relatively frequent among all general tumors. Prostate cancer is the second most frequent diagnosed cancer in men, leading to 15% of all cancers diagnosed [1], being by far the type that most collaborate for the frequency of urological tumors in population.

Other important tumors in frequency are bladder cancer, the seventh most commonly diagnosed in men and the eleventh considering both genders [2], and adrenal tumors, which affect 3–10% of general population, the majority of them being benign nonfunctional adrenocortical adenomas and the minority adrenocortical carcinomas [3].

Other less prevalent, but not less important, due to their morbidity and lethality are renal cell cancer, representing 2–3% of all cancers [4], testicular cancer, which includes 1% of all male tumors and 5% of urological tumors [5], and penile cancer, which is uncommon in developed countries, but in some parts of the world, such as, South America, South East Asia, and Africa, it represents 1–2% of malignant tumors in men [6].

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4.2 Urological Tumors Related to Vascular Complications

4.2.1 Kidney Cancer

4.2.1.1 Diagnosis

Patients with kidney tumors frequently present asymptomatic or with unspecified symptoms. Hematuria and flank pain can be present and just in fewer cases the classical triad with hematuria, flank pain, and flank mass can be found. In case of a metastatic disease, bone pain, adenopathy, and pulmonary symptoms are added as manifestations.

Physical examination is of fundamental importance as well as a complete medical history. Laboratory evaluations necessary are blood cell account, serum corrected calcium, kidney function, liver function, and urinalysis.

The frequency of incidentally diagnosed renal cell cancer has increased while imaging methods have been accessible worldwide. CT of abdomen and chest X-ray are the primary exams necessary for first evaluation. Chest CT is more accurate than X-ray to identify metastatic lung disease. In cases of allergy or moderate renal insufficiency, MRI of abdomen could be used in place of CT. Specially to evaluate vena cava condition, MRI has particular importance. Bone scan is necessary when alkaline phosphatase is elevated or when the patient presents bone pain, as well as CT or MRI of the brain in case of neurological signs and symptoms.

Needle biopsy is not generally necessary. The indications for biopsy remain in active surveillance, before ablation therapies or in cases of metastatic disease for guiding systemic treatment or suspicion of lymphoma.

PET CT or MRI is not standard method of diagnosis for renal cell carcinoma [4, 7, 8].

4.2.1.2 Staging

The classification is based on Tumor Node Metastasis (TNM) system (Table 4.1).

Specially for renal cancer, specific anatomic classification is important for decision of most appropriate treatment. Several classification systems are available such as Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification system, the R.E.N.A.L. nephrometry score, the C-index, and others.

4.2.1.3 Prognosis

The prognostic evaluation is based on anatomical factors – tumor size, venous invasion, extrarenal invasion, adrenal involvement, lymph node disease, and metastasis; histological factors – tumor grade, RCC subtype, and some findings such as sarcomatoid features, microvascular invasion, necrosis, and invasion of the collecting

Table 4.1 TNM system for kidney cancer

T – Primary tumor		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
T1	Tumor ≤7 cm or less in greatest dimension, limited to the kidney	
	T1a	Tumor ≤4 cm or less
	T1b	Tumor >4 cm but ≤7 cm
T2	Tumor >7 cm in greatest dimension, limited to the kidney	
	T2a	Tumor >7 cm but ≤10 cm
	T2b	Tumors >10 cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia	
	T3a	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumor invades perirenal and/or renal sinus fat (peripelvic fat), but not beyond Gerota fascia
	T3b	Tumor grossly extends into the vena cava below diaphragm
	T3c	Tumor grossly extends into vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)	
N – Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in regional lymph node(s)	
M – Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

Extracted from European Association of Urology Guidelines 2022 edition (https://uroweb.org/guidelines/prostatecancer)

system; clinical factors – performance status, symptoms related to disease, and metastasis; and molecular factors – expression of the BAP1 and PBRM1 genes and others needing external validation.

In general, prognosis is worse in higher stages of TNM and with higher grades. The overall survival in 5 years for all types of Renal Cell Carcinoma is 49%. The cancer-specific survival in 5 years of surgically treated RCC for each type is 71% for clear cell, 91% for papillary, and 88% for chromophobe [8].

4.2.1.4 Surgical Treatment

Surgical treatment is the first-line therapy to achieve cure in localized renal cell cancer. For T1 tumors, partial nephrectomy is the preferred technique, with oncological outcome equal to radical nephrectomy and with the advantage of saving nephrons. For other tumors where partial nephrectomy is not an option, radical nephrectomy is indicated. Both surgeries can be performed by open access,

laparoscopic surgery, and robotic surgery. Laparoscopic radical nephrectomy has lower morbidity than open nephrectomy. Adrenalectomy associated with the nephrectomy is not indicated if there is no involvement of the gland. Lymphadenectomy is not indicated for localized disease without lymph node involvement, being reserved for cases with adverse clinical features (large diameter of the tumor for example). If enlarged lymph nodes are present, it does not prove the survival benefit of lymphadenectomy, but it helps in staging the disease.

It is important to consider that active surveillance is an option for T1 tumors due to its low growth and rare progression to metastatic disease. For patients with comorbidities and elderly who are not fit for surgery and local therapy is indicated, cryoablation and radiofrequency ablation are other options for treatment.

In case of metastatic disease, cytoreductive nephrectomy is an option in selected patients with good performance status and when oligometastases can be treated.

4.2.1.5 Systemic Treatment

Adjuvant therapy in localized kidney cancer does not add benefit in survival after nephrectomy, and for this reason, is not indicated in this case. The main importance of systemic treatment in Renal Cell Cancer consists in cases of metastatic disease. Cytoreductive nephrectomy followed by sunitinib is non-inferior to sunitinib alone in metastatic cases. Systemic treatment can be performed associated with nephrectomy or alone, depending on the performance status of the patient and tumor conditions. In resume, for favorable-risk disease patients (by IMDC criteria), the first-line systemic therapy for metastatic renal cancer is sunitinib or pazopanib, and for intermediate and poor-risk patients, ipilimumab or nivolumab (with cabozantinib, sunitinib as other options, with no strong recommendations, and pazopanib an option only for intermediate risk) [8].

4.2.1.6 Vascular Lesions Related to Surgical Treatment

Radical or partial nephrectomy can be performed using conventional, laparoscopic, or robotic techniques.

The vascularization of the kidney is very important, irrigation being performed by the renal artery and venous drainage performed by the renal vein that flows directly into the vena cava and through the lumbar veins as well.

The renal hilum has a large number of anatomical variations and may have multiple arteries and/or multiple veins (Fig. 4.1).

As much as in partial nephrectomy and radical nephrectomy, a careful and rigorous dissection of the renal hilum must be performed, with the isolation of the arteries and veins, being watchful with lumbar veins to avoid lesions (Fig. 4.2).

In general, lumbar veins are located posterior to the renal vein and can be damaged during its dissection. The control of this type of bleeding is extremely complex because of the following:

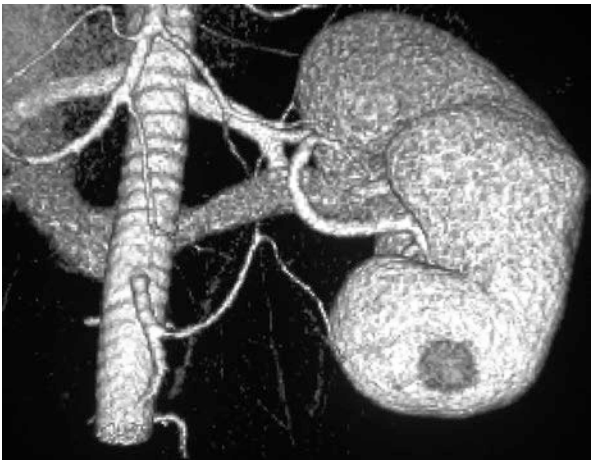

Fig. 4.1 Angiotomography demonstrating vascularization complexity of renal hilum

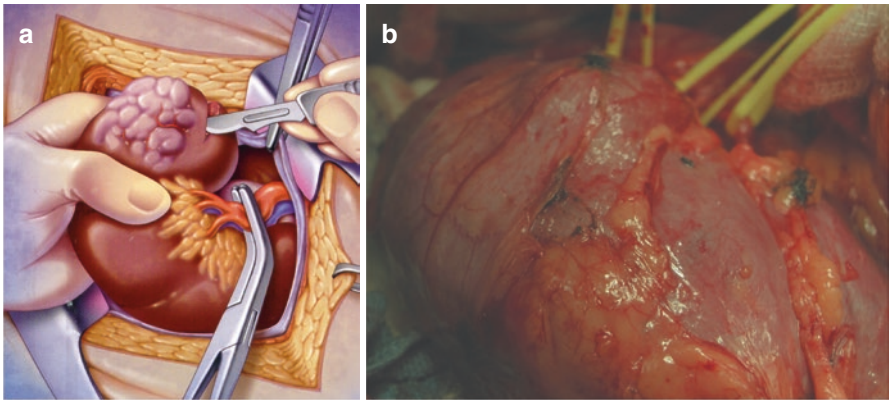

Fig. 4.2 Clamping of vascular hilum. (**a**) Clamping en bloc during open procedure. (**b**) Hilum vessels isolated and prepared for clamping

1. Difficulty to identify bleeding site due to its localization
2. Retraction of the vessel, making identification difficult

For those reasons, in some cases when it is not possible to adequately control lumbar vein bleeding, it can be necessary to quickly ligate renal vein and artery and remove the organ allowing adequate visualization for bleeding control.

These maneuvers are of high complexity and the surgeon must be prepared to perform quickly independently of the surgery access. In cases of minimally invasive surgery, the need for conversion to conventional technique (open) should be considered.

Another very relevant point is inadvertent lesions of the renal vein and vena cava. Sometimes during a partial nephrectomy and isolation of the vessels for clamping, an injury may occur. In these cases, we recommend compression maneuvers for the

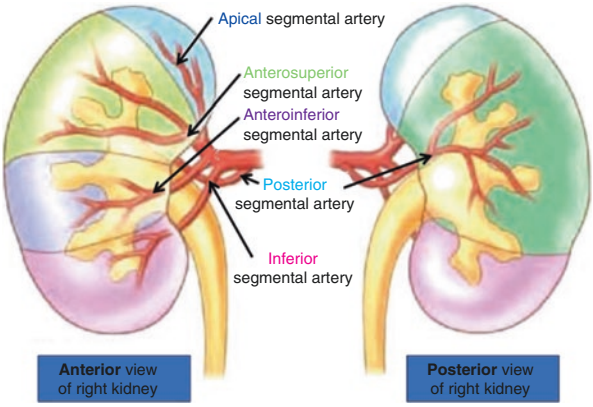

Fig. 4.3 Segmental renal arteries and irrigation areas. (From: https://www.memorangapp.com/flashcards/49859/Kidney+and+Suprarenal+Gland/)

team to prepare. After everything is prepared, a continuous suture or "x" suture must be performed with a prolene thread. It is important to remember that, in special situations, it is possible to ligate the renal vein, as the lumbar and collateral vessels are enough to maintain organ function.

Lesions of the renal artery are rare; however, it can happen in cases of anatomical variations. We must keep in mind that the renal artery ligation is directly related to function loss of the renal parenchyma irrigated by that vessel. It is common to find polar vessels that irrigate only particular segments of the kidney (Fig. 4.3).

During a kidney surgery, it is important to be attentive all the time to rigid and pulsating structures. Ligation and placement of a hem-o-lock must only be performed when the structure is well identified.

In cases of ligation of arteries, we should try to remove the ligature or clip as soon as possible and thereby allowing the flow to be reestablished. In cases where the artery has been sectioned, we must consider the possibility of reconstruction through a termino-terminal anastomosis, mainly in large vessels and trunk arteries. If this is not possible, nephrectomy should be considered or even an autotransplant with vascular graft.

The best way to avoid these types of problems is an adequate study of vascular anatomy through imaging exams before starting kidney surgery. With this, it is possible to foresee eventual difficulties and to determine factors of major attention that must be remembered during the surgery. Robotic and laparoscopic surgeons must be trained to have clearly the concepts of conversion in case of accidents. We recommend that before converting to open surgery, maneuvers to contain bleeding must be performed and we suggest the following steps:

1. Increase in pneumoperitoneum and placement of swabs for compression. This saves time for the anesthesiologist and the surgical team to be prepared.
2. "Gibson" incision in the flank region as a "hand-assistance" portal. With that, one of the surgeons places his hand and swabs to assist bleeding control, while the team makes the main incision to perform the nephrectomy.

3. Rapid dissection of the hilum or even in bloc ligation of the renal hilum. With this, it is possible to remove the kidney with reduced bleeding and open the field to work on identifying the focus of the bleeding.
4. Identification of the bleeding focus and control with suture with 4 or 5-0 prolene thread.

Direct conversion, without proper precautions and preparations, can compromise the result due to intense bleeding during opening in the absence of pneumoperitoneum and compressive maneuvers.

In summary, the renal hilum vessels are large and are high flow structures, so any type of injury can represent massive bleeding with risk of death to the patient. The surgeon must have adequate training and be prepared for these situations when indicating an access route. A careful preoperative analysis of imaging exams and vascular anatomical variations is of fundamental importance. In cases with lesions that invade or present a high risk of vessel involvement, having a vascular surgeon in the operating room is of fundamental importance.

4.2.2 Adrenal Cancer

4.2.2.1 Diagnosis

In 10–15% of the cases, adrenal cancer is found as an incidentaloma in imaging for other purposes. This number is increasing over the years due to the increasing access to CT and MRI in public and private health system. The majority of the cases is presented with hormone excess production (50–60%), such as hypercortisolism and virilizing syndromes. Other 30–40% of the cases may present with abdominal mass symptoms, which are nonspecific.

All patients with suspicion for adrenal cancer must be evaluated with complete medical history, clinical examination for symptoms, and signs of adrenal hormone excess. Hormone screening is necessary to identify if there is excess of glucocorticoids, sex hormones, and mineralo and adrenocortical steroids hormone precursors. Pheochromocytoma must be excluded.

Chest CT and abdominal-pelvic cross-sectional imaging with CT or MRI are recommended. Bone and brain imaging are reserved for symptomatic cases. Adrenal biopsy is not recommended, saved in cases of metastatic disease where histopathological findings are necessary to guide systemic treatment.

4.2.2.2 Staging

Staging at diagnosis is performed by the European Network for the Study of Adrenal Tumours (ENSAT) staging classification. Tumor stage, resection status, Ki67 index, and cortisol secretion are important keys to assess prognosis and define treatment. The Table 4.2 below shows ENSAT staging classification [9].

Table 4.2 ENSAT staging classification

ENSAT stage	Definition
I	T1, N0, M0
II	T2, N0, M0
III	T1–T2, N1, M0T3–T4, N0–N1, M0
IV	T1–T4, N0–N1, M1

T1 tumor ≤5 cm, *T2* tumor >5 cm, *T3* infiltration into surrounding tissue, *T4* tumor invasion into adjacent organs or venous tumor thrombus in vena cava or renal vein, *N0* no positive lymph node, *N1* positive lymph node, *M0* no distant metastases, *M1* presence of distant metastases

4.2.2.3 Prognosis

The prognosis is in general poor. The median survival is about 3–4 years. Five-year survival depends on the tumor staging: for locally disease, the range is about 60–80%, for locally advanced disease, 35–50%, and for metastatic disease, as low as 0–28%. The complete surgical resection is the only way for achieving the cure.

4.2.2.4 Surgical Treatment

Adrenalectomy is the only therapy option that can achieve the cure for Adrenal Cancer. If there is a suspicious or confirmed adrenal cancer, a complete *en bloc* resection is recommended. The resection should involve the adrenal, peritumoral, and periadrenal fat. It is not recommended as gold standard option enucleation of the tumor or partial adrenalectomy. If locally advanced, involved sites must be *resected en bloc* with the primary tumor. Nephrectomy is not indicated unless if involved by the tumor. Open surgery is the standard technique for adrenalectomy, but, for experient surgeons, when the tumor size is less than 6 cm and without local invasion, laparoscopic surgery is an option. Associated lymphadenectomy is recommended, including periadrenal, renal hilum, and enlarged nodes.

4.2.2.5 Systemic Treatment

Adjuvant therapy is not recommended for all cases. The use of adjuvant therapy with mitotane is recommended to be considered in patients without macroscopic residual tumors (R0) with high risk of recurrence. For cases with low and moderate risk of recurrence, the indication should be individualized. When indicated, the prescription of mitotane should ideally start within 6 weeks from surgery. There is no consensus about radiation therapy being reserved associated to mitotane in R1 or Rx resection or Stage III. In cases of advanced adrenal cancer, mitotane is the drug of choice [9].

4.2.2.6 Vascular Lesions Related to Surgical Treatment

Adrenalectomy may be performed by conventional, laparoscopic, or robotic open route. The choice of the access route takes into consideration tumor features and also surgeon experience, who must choose the access route according to his expertise and training to control any type of inadvertent injury or even tactical resection of vascular segments.

The vascularization of the adrenal gland is well-known and has few variations. Irrigation is performed by superior suprarenal artery (branch from inferior phrenic artery), middle suprarenal artery (branch from abdominal aorta), and inferior suprarenal (branch from renal artery). Venous drainage is performed through the adrenal vein that flows into the left renal vein and directly into the right vena cava. Collateral and lumbar veins are also present (Fig. 4.4).

In adrenalectomy, the first step is the identification of the adrenal vein and its ligation. Some tumors are producers of substances that can cause patient hemodynamic instability during adrenal manipulation. As the adrenal is situated immediately above the kidney, it may be necessary to dissect the renal hilum and the vena cava to identify the adrenal vein. This can lead to renal hilum damage and should be managed as described above in kidney cancer section.

Right adrenalectomy is always more complex and challenging because we must keep away the liver properly for a good exposure and the renal vein is usually very cranial and very close to the hepatic veins. Therefore, any injury in this location is extremely difficult to control because, in general, liver rotation maneuvers are necessary for its exposure.

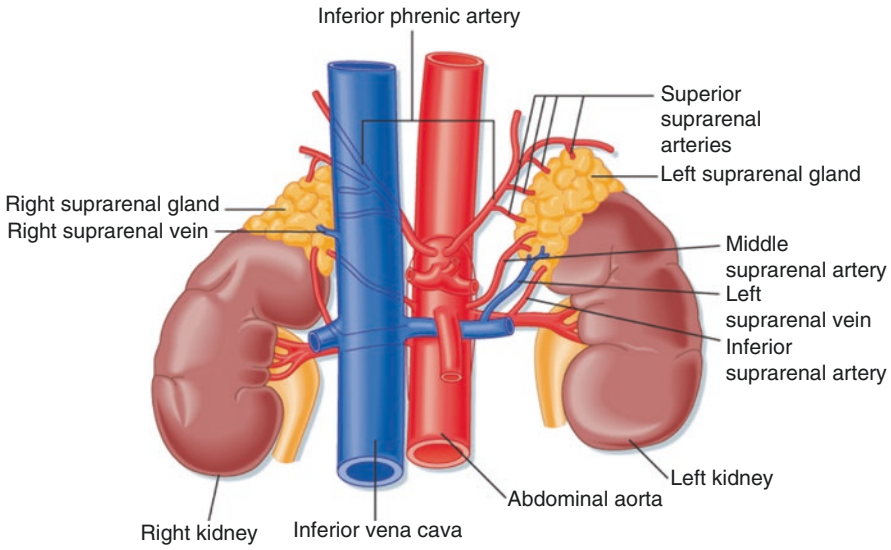

Fig. 4.4 Irrigation and venous drainage of adrenal glands

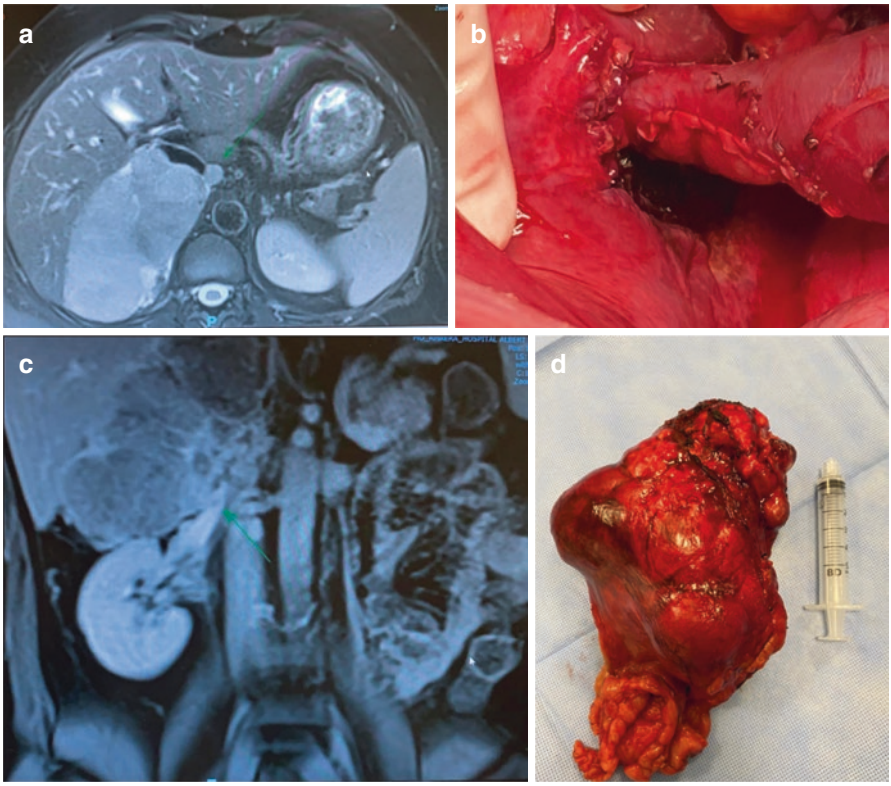

Fig. 4.5 Large adrenal tumor with direct contact with the liver and vena cava. (**a**) Axial image of MRI. (**b**) Area after resection and reconstruction of vena cava with bovine pericardium patch. (**c**) Coronal image of MRI. (**d**) Removed tumor

Adrenal carcinoma has the characteristic of being aggressive and infiltrative. In advanced cases, it usually involves invasion of the liver and also the vena cava (Fig. 4.5). In these cases, it is of fundamental importance to perform a procedure with a multidisciplinary team in which the urology team accesses and dissects the kidney and hilum, the liver team dissects the liver allowing its rotation and perform a cranial and caudal vascular control of the cava, and the vascular surgery team performs the clamping and resection of the vena cava wall with reconstruction using a bovine pericardium patch or prosthesis.

In cases of need for conversion of minimally invasive surgery to conventional surgery, the surgeon must use the same technique suggested in the nephrectomy section and must also be able to dissect and perform a liver rotation maneuver and in some cases chest opening and supra-diaphragmatic control.

4.2.3 Testicular Cancer

4.2.3.1 Diagnosis

The clinical presentation of testicular cancer is a scrotal mass, generally painless, but in up to 27% of cases, pain may be present as well. In 10% of cases, the diagnosis is delayed due to testicular cancer be confound to orchioepididymitis. In cases of suspicion, an ultrasound of the testis must be done. Other clinical features may be gynecomastia – in up to 7% of cases – and symptoms of metastasis such as abdominal mass, abdominal, and flank pain.

Ultrasound must be done in young patients with retroperitoneal mass, visceral mass, elevated human chorionic gonadotropin (hCG) or alpha-fetoprotein (AFP), or with fertility problems, even with no testicular masses.

As an option for the ultrasound, MRI of the testis can be performed, with higher sensitivity and specificity than US but with elevated costs, what is not worthy to be considered the method of choice.

Serum tumor markers must be performed at diagnosis to contribute for diagnosis and for staging as well. The time for assessment must be before orchiectomy and 5–7 days after. The three tumor markers are AFP, hCG, and lactate dehydrogenase (LDH).

4.2.3.2 Staging

Staging for testicular cancer is based on serum tumor markers as listed above (AFP, hCG, and LDH) after orchiectomy, abdominopelvic CT, testis ultrasound, bone scan or MRI column (in case of symptoms), and brain scan (in case of symptoms or metastatic disease in both lungs or high hCG values).

The recommended system is TNM. An extra classification is based on Serum tumor markers, as S0, S1, S2, and S3 (Table 4.3).

4.2.3.3 Prognosis

Prognostic staging is divided into three groups:

(a) Good prognosis: It consists of 56% of non-seminoma and 90% of seminoma tumors. The patient must have no non-pulmonary visceral metastasis and for non-seminoma cancer, AFP <1000 ng/ml, hCG <5000 iU/l, and LDH <1.5 × normal limit value. For this group, 5-year progression-free survival (PFS) is 89% and 5-year survival 92% for non-seminoma cancers and 82% and 86%, respectively, for seminoma cancers.
(b) Intermediate prognosis: It consists of 28% of non-seminoma and 10% of seminoma tumors. For non-seminoma cancer, the patient must have no non-

Table 4.3 TNM system for testicular cancer

pT – Primary tumor			
pTX	Primary tumor cannot be assessed (see note 1)		
pT0	No evidence of primary tumor (e.g., histological scar in testis)		
pTis	Intratubular germ cell neoplasia (carcinoma in situ)		
pT1	Tumor limited to testis and epididymis without vascular/lymphatic invasion; tumor may invade tunica albuginea but not tunica vaginalis[a]		
pT2	Tumor limited to testis and epididymis with vascular/lymphatic invasion, or tumor extending through tunica albuginea with involvement of tunica vaginalis		
pT3	Tumor invades spermatic cord with or without vascular/lymphatic invasion		
pT4	Tumor invades scrotum with or without vascular/lymphatic invasion		
N – Regional lymph nodes – clinical			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 2 cm in greatest dimension		
N2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumor		
N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
Pn – Regionat lymph nodes – pathological			
pNX	Regional lymph nodes cannot be assessed		
pN0	No regional lymph node metastasis		
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension		
pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence or extranodal extension of tumor		
pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
M – Distant metastasis			
MX	Distant metastasis cannot be assessed		
M0	No distant metastasis		
M1	Distant metastasis		
	M1a Non-regional lymph node(s) or lung metastasis		
	M1b Distant metastasis other than non-regional lymph nodes and lung		
S – Serum tumor markers (prechemotherapy)			
SX	Serum marker studies not available or not performed		
S0	Serum marker study levels within normal limits		
S1	*LDH (U/I)*	*hCG (mIU/mL)*	*AFP (ng/mL)*
S2	<1.5 × N and	<5000 and	<1000
S3	1.5–10 × N or	5000–50,000 or	1000–10,000
	>10 × N or	>50,000 or	>10,000

[a]Extracted from European Association of Urology Guidelines 2022 edition (https://uroweb.org/guidelines/testicular-cancer)

pulmonary visceral metastasis and AFP between 1000 and 10,000 ng/ml, hCG between 5000 and 50,000 IU/l, or LDH between 1.5× and 10× normal limit value. For the seminoma group, any condition that does not fit for good prognosis classifies the patient in the intermediate-prognosis group. Five-year PFS is 75% and 5-year survival 80% for non-seminoma and 67% and 72% for seminoma, respectively.

(c) Poor prognosis: No seminoma cancer is classified as poor-prognosis. For non-seminoma, if mediastinal primary tumor, non-pulmonary visceral metastasis, AFP >10,000 ng/ml, hCG >50,000 IU /l, or LDH >10 × normal limit value are present (only one is enough for this classification). The patient is classified as a poor-prognosis case (16% of cases). 5-year PFS is 41% and 5-year survival 48%.

Another prognostic evaluation is based on the risk for metastatic relapse in clinical stage I. The risk factors for occult metastatic disease in this stage are, for seminoma, tumor size >4 cm and invasion of rete testis; and for non-seminoma, vascular or lymphatic or peritumoral invasion, proliferation rate >70% and percentage of embryonal carcinoma >50%.

4.2.3.4 Surgical Treatment

Orchiectomy is the first step in case of testicular tumors. The procedure is performed when a testicular cancer is suspicious or confirmed, and in case of doubt, a frozen biopsy is taken during the procedure. The procedure starts with an inguinal exploration with exteriorization of the testis and, then, spermatic cord is divided, at the internal inguinal ring level.

Retroperitoneal lymphadenectomy is useful in particular cases. For residual tumors, in seminomas, after systemic treatment, when PET-CT shows residual mass larger than 3 cm, lymphadenectomy is an option instead of new chemotherapy. For non-seminomas, retroperitoneal lymphadenectomy is indicated as an option for Stage I, IIA, and B (if lymph nodes <2 cm and pure teratoma) and in cases of residual tumors, if the residual mass is larger than 1 cm.

4.2.3.5 Systemic Treatment

Systemic treatment in testicular cancer consists of chemotherapy and radiotherapy and its indications are guided by staging. Stage I is defined as tumor restricted to the testis. Stage II consists of cases with retroperitoneal lymph node metastasis. This stage is subdivided as IIA, up to 2 cm, IIB with 2–5 cm, and IIC for masses >5 cm. Stage III is defined as tumor with other metastasis.

The decision of treatment differs between seminoma and non-seminoma. For seminomas, in Stage I, if invasion of rete testis or mass >4 cm, adjuvant chemotherapy is indicated (1 or 2 cycles of carboplatin). In Stage II A or B, options for systemic treatment are radiotherapy (2 Gy × 15, total 30Gy, in paraaortic and iliac

ipsilateral field, if IIB, add 6 Gy in major lymph nodes) or chemotherapy with 3 cycles of BEP – bleomycin, etoposide, and cisplatinum (4 cycles of EP if bleomycin contraindicated). Finally, in Stage IIC or III, the indication of systemic therapy consists of 3 or 4 cycles of BEP (3 cycles if good prognosis). For residual masses, larger than 3 cm, chemotherapy is again an option (lymphadenectomy is the other option as cited above).

For non-seminomas, in Stage I, if lymphovascular invasion, the option is cycle of BEP (retroperitoneal lymphadenectomy is an option as cited above, surveillance is another option). For Stage IIA or B, 3 or 4 cycles of BEP (3 if good prognosis). In cases with lymph nodes <2 cm and pure teratoma, surveillance or lymphadenectomy is the option. Finally, for Stage IIC and III, 4 cycles of BEP are indicated. Residual masses larger than 1 cm are treated with retroperitoneal lymphadenectomy and if, after resection, viable tumor is found, chemotherapy has an important role [10, 11].

4.2.3.6 Vascular Lesions Related to Surgical Treatment

Retroperitoneal lymphadenectomy (RL) is performed as a form of recurrence prophylaxis or in cases of recurrence after chemotherapy. RL can be performed by conventional, laparoscopic, or robotic open route; however, it is known that minimally invasive techniques are more complex and should only be performed by surgeons with experience.

RL can be performed by distinct techniques and steps, but a recommended technique is the "split and roll" technique which can start with dissection at 12 o'clock of the aorta, right inferior to the left renal vein, and continue caudally, taking care in identifying inferior mesentery artery. The left para-aortic packet is dissected laterally aorta, being necessary to ligate gonadal vein and to identify left ureter and protect it from lesions. Dissection continues caudally until position of ureter above left common iliac artery. The lymphatic tissue is rolled laterally from aorta and left common iliac artery and then, inferiorly from left renal vein. The lateral limit consists of dissection of the lower pole of the kidney and left ureter. In this procedure, lumbar arteries on the left side of aorta must be ligated. Left genitofemoral nerve and sympathetic trunk must be identified and preserved when possible. Vena cava split is performed with dissection from renal hilum to the right common iliac artery, until position of ureter above this artery. Right gonadal vein is ligated and divided. The lymph node tissues are rolled medially. Lymphatic dissection from interaortocaval packet is completed with rolling medially the packet from aorta. Control of lumbar arteries must be done, as well as lumbar veins. The right paracaval packet is smaller because of the position of the right kidney and ureter near to the inferior vena cava. The lymphatic tissue is rolled laterally and superiorly from the right common iliac artery until ureter position over the artery. The dissection continues superiorly until renal hilum and crus of the diaphragm.

During the procedure, there is constant contact with the aorta, vena cava, and lumbar vessels; therefore, a careful dissection is of fundamental importance and that the surgeon may be able to perform vascular sutures.

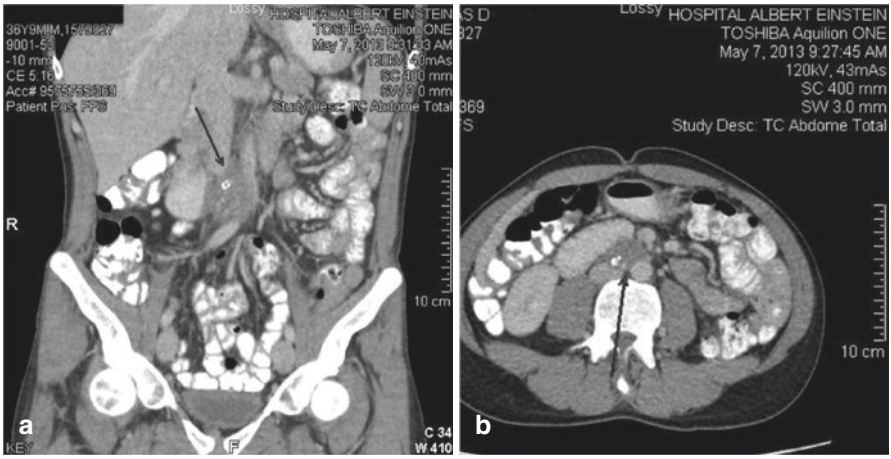

Fig. 4.6 Retroperitoneal refractory seminomatous tumor. Images of computed tomography showing retroperitoenal refractory seminomatous tumor, (**a**) coronal plane (**b**) axial plase (Personal gallery)

RL of larger tumors and refractory to chemotherapy are even more complex, being the mass, in general, in close contact with the vessels and with firm adhesions, increasing the risk of dissection (Fig. 4.6). In this type of surgery, it is of fundamental oncological importance to remove the tumor completely, and in some cases, it is necessary to resect the vessel wall and reconstruct it.

In cases of refractory seminomatous tumors, chemotherapy is even more complex, even in minor lesions. Chemotherapy has an effect on vascular structures with a reduction in the outer layer of the arteries, making the arteries more fragile and easier to damage. In these cases, we strongly recommend always having a vascular team available in the operating room in case of accidents, for reconstructing procedures [12] (Fig. 4.7).

In non-seminomatous tumors, we do not find this type of vascular changes and the surgery is usually easier; however, in cases with suspected vascular invasion, extra care must be taken.

4.2.4 Prostate Cancer

4.2.4.1 Diagnosis

Diagnosis of prostate cancer is achieved by prostate biopsy (transperineal or transrectal). A multiparametric MRI may be performed before prostate biopsy if possible to guide the procedure and increase sensitivity by adding fragments of suspicious areas. Indication of prostate biopsy consists of altered screening exams or clinical suspicious of prostate cancer. An increase of PSA is one of indications, as other

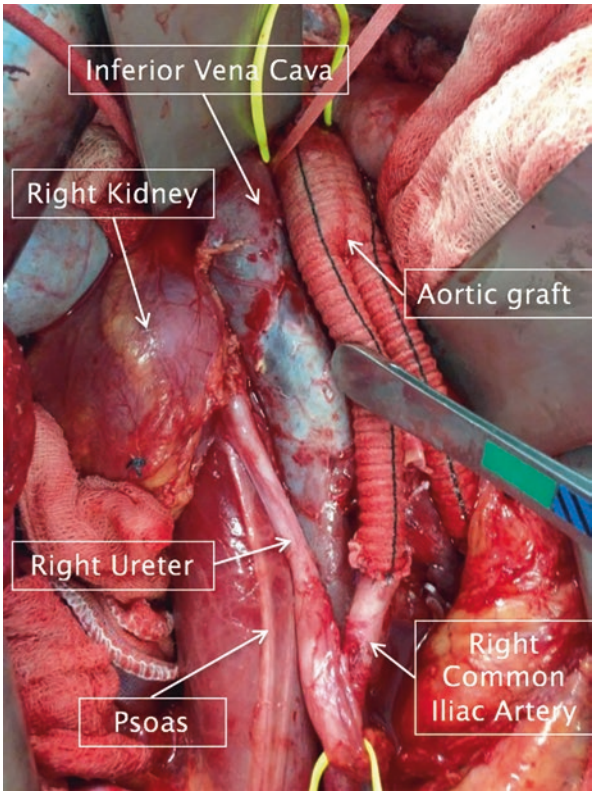

Fig. 4.7 Bilateral aortoiliac bypass. (Personal gallery)

situations may elevate PSA; alternatives for evaluation of PSA levels are options to increase specificity of the exam, such as, PSA density and free/total PSA ratio. Another absolute indication of biopsy is altered rectal digital exam (palpable nodule, induration mass).

Diagnosis is given by pathologist, by type of tumor (most Adenocarcinomas) and Gleason/ISUP grade, which helps in staging and prognostic evaluation.

4.2.4.2 Staging

Tumor staging is defined with TNM classification (Table 4.4). For this evaluation, when low risk with localized disease and when favorable intermediate risk, no complementary image is necessary. For unfavorable intermediate-risk and for high-risk cases, abdominopelvic imaging (CT or MRI) and bone scan are necessary. For local imaging assessment, MRI of the prostate is the best imaging exam and first option for this reason.

Table 4.4 TNM system for prostate cancer

T – Primary tumor (stage based on digital rectal examination [DRE] only)		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
T1	Clinically inapparent tumor that is not palpable	
	T1a	Tumor incidental histological finding in 5% or less of tissue resected
	T1b	Tumor incidental histological finding in more than 5% of tissue resected
	T1c	Tumor identified by needle biopsy (e.g., because of elevated prostate-specific antigen [PSA])
T2	Tumor that is palpable and confined within the prostate	
	T2a	Tumor involves one half of one lobe or less
	T2b	Tumor involves more than half of one lobe, but not both lobes
	T2c	Tumor involves both lobes
T3	Tumor extends through the prostatic capsule	
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
N – Regional (pelvic) lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	
M – Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	
	M1a Non-regional lymph node(s)	
	M1b Bone(s)	
	M1c Other site(s)	

Extracted from European Association of Urology Guidelines 2022 edition (https://uroweb.org/guidelines/prostate-cancer)

4.2.4.3 Prognosis

Prognostic assessment of prostate cancer is defined by biopsy results primarily. Considering only ISUP grade, there is a correlation with biochemical progression-free survival. For ISUP 1, this rate is about 97% in 5 years, while for ISUP 4, this rate lowers to 64% and 49% in ISUP 5.

D'Amico stratification risk is globally used to classify prostate cancer in three groups:

(a) Low-risk group: PSA <10 ng/ml, ISUP 1, T2a clinical stage.
(b) Intermediate-risk group: PSA between 10 and 20 ng/ml, ISUP 2 or 3, T2b clinical stage.
(c) High-risk group: PSA >10 ng/ml, ISUP 4 or 5, T2c clinical stage.

This stratification is important to evaluate recurrence risk in 5 years. For low-risk group, recurrence risk in 5 years is less than 25%, for intermediate risk, between 25% and 50%, and for high-risk group, this rate is above 50%.

4.2.4.4 Surgical Treatment

Before detailing surgical treatment, it is important to consider that non all of prostate cancers must be actively treated at diagnosis. Active surveillance is a good option in low-risk cancers, reducing the risk and comorbidities added by surgical treatment or radiotherapy and hormonal blockage without compromising oncological outcomes when well-delineated and conducted.

Another consideration is that surgical treatment and radiotherapy (with or without antiandrogen deprivation therapy – ADT) are both options for active treatment, with similar oncological outcomes in general. The decision between both options must be done individually, respecting patient desire, expectations, and considering individual medical features.

Radical prostatectomy can be performed by open, laparoscopic, or robotic surgery. All of the 3 options can be performed, with similar oncological outcomes, but robotic surgery has shown lower admissions, lower blood loss, and faster functional recovery.

Extended pelvic lymphadenectomy is not indicated for low-risk patients. Its indication is reserved for intermediate-risk group when the risk of lymph node involvement is considerable (e.g., higher than 5% for MSKCC nomogram) and for high-risk group and for locally advanced cases when prostatectomy is performed. Extended templated of pelvic lymphadenectomy consists of lymph nodes above external iliac vessels, in the obturatory fossa, and lateral and medial to internal iliac vessels.

4.2.4.5 Systemic Treatment

For localized disease, systemic treatment consists of androgen deprivation therapy (ADT) associated to radiotherapy in intermediate-risk patients, for 6 months, and in high-risk patients for 2–3 years. In cases of locally advanced disease (T3, T4, and N1), ADT as monotherapy may be indicated when surgery or radiotherapy is not an option and PSA doubling time is <12 months, PSA >50 ng/ml or tumor is low differentiated.

After surgery, ADT may be indicated if lymph node involvement, associated or not with radiotherapy.

For metastatic disease, first-line therapy consists of ADT. ADT can be achieved by bilateral orchiectomy or LHRH agonists or antagonists. Antiandrogens as monotherapy are not indicated. Both protocols can be used in M1 cases, depending on patient conditions: ADT plus Abiraterone plus Prednisone OR ADT plus Docetaxel. In cases of resistant castration prostate cancer, for M0 patients, Apalutamide and

Enzalutamide are options of treatment, and for M1 patients, Abiraterone, Docetaxel, Enzalutamide, Radium 223, and Sipuleucel T are available options [13–16].

4.2.4.6 Vascular Lesions Related to Surgical Treatment

Radical prostatectomy (RP) may be or may not be accompanied by pelvic lymphadenectomy. It can be performed by open, laparoscopic, or robotic surgical access. Prostatectomy itself does not usually take major vascular risks. Only in minimally invasive techniques, special attention must be given to the epigastric arteries during puncture of the trocars. Always a surgery is finished, the trocars must be removed under vision in order to assess any bleeding from the site. The control of epigastric artery lesions can be performed by clipping a hem-o-lock clip under vision or through a transcutaneous suture with a "Carter-Thomason" needle.

Primary or salvage pelvic lymphadenectomy (Fig. 4.8) consists of removing the lymph nodes from the template composed of these limits:

- Cranial = crossing of the ureter over iliac vessels
- Caudal = inguinal canal
- Lateral = genitofemoral nerve
- Medial = bladder wall

With that, the entire external iliac lymph node chain, as well as obturator, internal iliac, and part of the common iliac chains are removed (and eventually also from the sacral region). During this procedure, lesions of arteries with large blood flow can occur and the surgeon must be prepared for a vascular suture.

We recommend special care with the internal and external iliac veins as it can be difficult to identify its limits and its conformation may be altered with the surgical presentation.

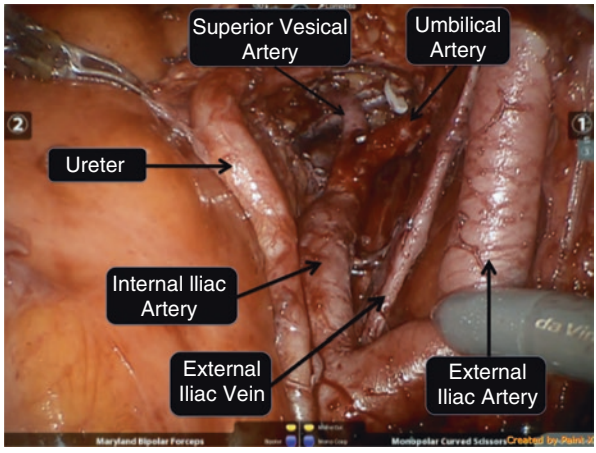

Fig. 4.8 Extended pelvic lymphadenectomy

The first anterior branch of the internal iliac artery is the obliterated umbilical artery. In general, we use this artery for presentation and do not ligate it. However, it can be connected without any impact to the patient. The first posterior branch of the internal iliac is the gluteal artery and its ligation can cause lameness to the patient.

The external iliac artery becomes the femoral artery and is responsible for irrigating the lower limbs. Its ligation can impact the loss of the limb and flow should be reestablished as soon as possible. The internal iliac artery is responsible for the irrigation of the pelvic floor and due to vast vascularity in this region; if necessary, it can be ligated, both the artery and the vein.

4.2.5 Bladder Cancer

4.2.5.1 Diagnosis

The most common clinical feature is hematuria, and when macroscopic, is associated with higher stage of disease. Carcinoma in situ may present with lower urinary tract symptoms and irritative voiding.

Cystoscopy is vital for diagnosis of bladder cancer and cannot be replaced by ultrasound, CT, or cytology. During cystoscopy, resection of the suspicious tumor can be performed and taken to analysis. If not possible to complete resection, partial resection or biopsy can be performed. During initial work-up, renal and bladder ultrasound and/or computed tomography-intravenous urography (CT-IVU) may be performed. Absolute indications for CT urography are tumors located in the trigone and multiple or high-risk tumors, for the risk of concomitant upper tract urothelial carcinoma. In cases of high-grade tumors, urine cytology is a complementary exam to cystoscopy for detection.

4.2.5.2 Staging

Bladder cancer staging is defined by TNM classification, as shown in Table 4.5.

A risk stratification needs to be performed to guide treatment decision. Tumors can be classified in one of three groups:

(a) Low-risk group: All TaG1 less than 3 cm, primary and solitary (all of them present).
(b) High-risk group: All tumors which present with one of these features: T1, G3 (high grade), Cis. Or, if the tumor is TaG1G2 and multiple, recurrent, and larger than 3 cm (all of them present). A subgroup is the highest-risk group, that is defined as T1G3 tumors with Cis, or, multiple or larger than 3 cm, or high-grade recurrent, or with lymphovascular invasion or urothelial carcinoma variants.
(c) Intermediate-risk group: those tumors which do not fit in low or high-risk groups.

Table 4.5 TNM system for bladder cancer

T – Primary tumor		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
Ta	Non-invasive papillary carcinoma	
Tis	Carcinoma in situ "flat tumor"	
T1	Tumor invades subepithelial connective tissue	
T2	Tumor invades muscle	
	T2a	Tumor invades superficial muscle (inner half)
	T2b	Tumor invades deep muscle (outer half)
T3	Tumor invades perivesical tissue	
	T3a	Microscopically
	T3b	Macroscopically (extravesical mass)
T4	Tumor invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall	
	T4a	Tumor invades prostate stroma, seminal vesicles, uterus, or vagina
	T4b	Tumor invades pelvic wall or abdominal wall
N – Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed tissue	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N2	Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N3	Metastasis in common iliac lymph node(s)	
M – Distant metastasis		
M0	No distant metastasis	
	M1a	Non-regional lymph nodes
	M1b	Other distant metastases

Extracted from European Association of Urology Guidelines 2022 edition (https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer)

4.2.5.3 Prognosis

Prognostic evaluation is based on EORTC Genito-Urinary Cancer Group scoring system and risk tables. This score reflects probability of recurrence and progression at 1 and 5 years.

4.2.5.4 Surgical Treatment

Surgical treatment is initially based on Transurethral Resection of the Bladder tumor (TURBT). This procedure is diagnostic and potentially therapeutic at the same time. If TURBT is incomplete or with no muscle sample, or consists of T1 or

high-grade, second TURBT is indicated within 2–6 weeks. Conditions that do not indicate second TURBT are complete TURBT in Ta low-grade tumors, or in cases of primary Cis.

Cystectomy is indicated for muscle-invasive tumors. Cystectomy can be performed by open, laparoscopic, or robotic surgery. Robotic surgery has longer operative time, higher costs, but, otherwise, lower hospital stay and lower blood loss. These procedures include removal of regional pelvic lymph nodes and extended pelvic lymphadenectomy has better outcomes in survival rates than limited lymphadenectomy. Cystectomy must be performed within 3 months from diagnosis, under risk of progression and cancer-specific mortality if performed more than 3 months after diagnosis.

Another role of cystectomy includes in metastatic tumors, for symptoms control. TURBT can be performed as part of a multimodal therapy associated with radiotherapy and chemotherapy in this group of tumors.

An important step in cystectomy is urinary diversion. It is important to consider that no oncological or quality of life outcomes is proved to be superior comparing different urinary diversions each other. Options of diversion are cutaneous ureterostomy, ileal conduct (Bricker), orthotopic bladder, and others.

4.2.5.5 Systemic Treatment

Neoadjuvant therapy has a consolidated role in cases of muscle-invasive bladder cancer. Neoadjuvant chemotherapy with cisplatin combination improves overall survival in 5–8% in 5 years. Recommendation from guidelines consists of indicate neoadjuvant chemotherapy with gemcitabine plus cisplatin (GC) OR methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) for T2 to T4a tumors, N0M0.

Adjuvant therapy is indicated for T3 or T4 tumors or N+ if neoadjuvant chemotherapy was not performed.

Considering metastatic disease, options for treatment are GC OR MVAC or HD-MVAC, paclitaxel, cisplatin, and gemcitabine (PCG). If not eligible for cisplatin (such as performance status 2 or glomerular filtration rate <60), options are pembrolizumab (if PD-L1 positive), atezolizumab (if PD-L1 positive), or carboplatin plus gemcitabine (if PD-L1 negative) [17–19].

4.2.5.6 Vascular Lesions Related to Surgical Treatment

Radical cystectomy consists of similar vascular risks as prostatectomy, being extended pelvic lymphadenectomy the major risk for greater vascular lesions. Care must be taken as exposed in vascular lesions session of the prostate cancer. Internal iliac and external iliac vessels must be carefully manipulated and lymph nodes templates carefully dissected.

Editors Comments

The relationship between urological tumors and the circulatory system occurs in several ways. In general, cancer patients are at higher risk for venous thromboembolic events (VTE), although malignant neoplasms such as prostate cancer are less related to thrombotic events than those of the pancreas and stomach, for example. However, oncological surgeries of the abdomen and pelvis, such as those of the genitourinary tract, are among those that are most associated with the occurrence of deep venous thrombosis and pulmonary embolism.

In addition to being exposed to an increased risk of thrombosis and recurrence of thrombosis, individuals with cancer also have a higher bleeding rate due to anticoagulant treatment. These hemorrhagic events occur more frequently in the digestive and genitourinary tracts, mainly from neoplastic lesions [20, 21].

Renal dysfunction also increases the risk of thrombosis by causing an increase in serum levels of coagulation factors, such as plasminogen activator inhibitor (PAI1) and von Willebrand factor, among others. Renal failure also provides a higher risk of bleeding once it is also characterized by disorders of the coagulation cascade and activation of the fibrinolytic system, decreased platelet activity, and impaired vessel–wall–platelet interactions [22]. The increased risk of bleeding in individuals with renal failure may also be due to the increased plasma concentration of anticoagulants used in VTE treatment. Low molecular weight heparins have almost exclusively renal elimination, whereas direct oral anticoagulants have different degrees of renal excretion – dabigatran 80%, edoxaban 50%, rivaroxaban 33%, and apixaban 27%. Warfarin is a medication with almost total elimination via the liver. However, warfarin increases the risk of bleeding as renal dysfunction worsens. Patients with creatinine clearance <30 mL/min have an almost five times greater risk of bleeding than an individual with preserved renal function. This can be attributed in part to the platelet dysfunction caused by uremia. There are animal studies that also show a negative regulation in the metabolism of some liver enzymes, such as cytochrome P-450, in the presence of renal failure [23, 24].

The intimate relationship between the genitourinary tract organs and large vessels makes the resection of urological tumors challenging, especially tumors of the kidney and adrenal gland. The dissection of the renal hilum can be quite laborious and, due to frequent anatomical variation, requires careful evaluation with imaging tests such as computed tomography in the preoperative planning. Inadvertent lesions of arterial and venous lumbar branches, in addition to the aorta and inferior vena cava, are a concern due to the difficulty in controlling the resulting bleeding, especially when the tumor has not yet been removed, making it challenging to identify and treat the injured vessel.

When there is an invasion of large vessels or visceral branches, such as the renal ones, en bloc resection of the tumor with the vascular structures brings the need for revascularization. The aorta and vena cava are, as a rule, reconstructed with synthetic vascular prostheses, whereas, in the renal vessels, autologous substitutes, such as the internal saphenous vein, may be an option. The renal vein may

eventually be disconnected with less repercussion, preferably as distally to the hilum as possible, despite our preference for reconstructing it.

Pelvic tumors, such as prostate and bladder tumors, rarely require vascular intervention. Testicular cancer, in turn, can spread through the retroperitoneal lymphatic chain, which has an intimate relationship with the great vessels of the abdomen and pelvis, and lumbar branches. Retroperitoneal lymphadenectomy can be too laborious and, in cases of more extensive involvement and greater adherence, require en bloc resection with vascular reconstruction.

A rare complication already described by our group was the occurrence of an aortic pseudoaneurysm in a patient with a retroperitoneal mass originating from an embryonic testicular carcinoma (Fig. 4.9). After eight cycles of chemotherapy, control tomography showed a 50% reduction in mass and a pseudoaneurysm of the aorta in the segment surrounded by the tumor. This patient was operated on with en bloc resection involving the tumor and the aorta with the pseudoaneurysm, with aorto-biiliac reconstruction with a bifurcated Dacron prosthesis [25].

Vascular tumors, such as inferior vena cava sarcomas, are a differential diagnosis with primary kidney neoplasms. Frequently, the diagnosis ends up being made during the surgical procedure.

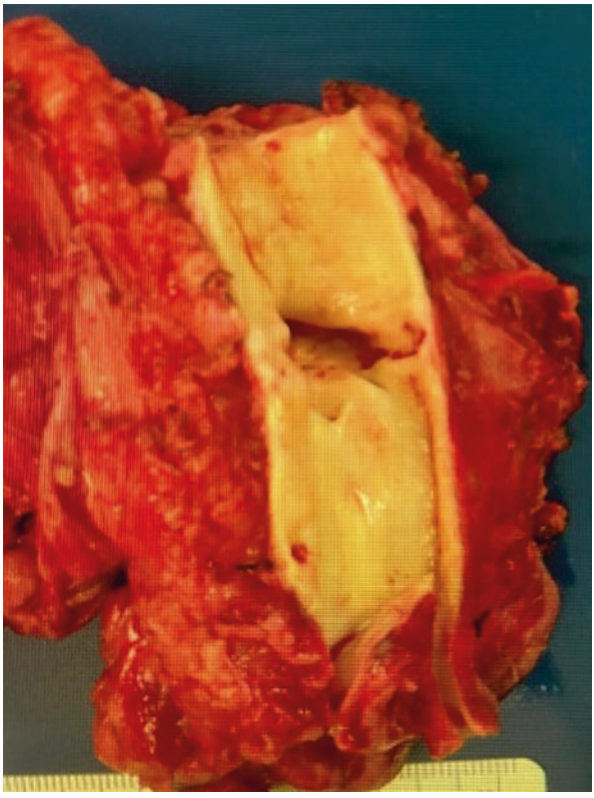

Fig. 4.9 Longitudinal section of the aorta resected en bloc with the tumor. In the center of the image, notice the rupture of the artery wall

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