

**USEFUL INFORMATION FOR PATIENTS  
THAT HAVE BEEN DIAGNOSED WITH  
BLADDER CANCER AND ARE ELIGIBLE FOR  
ROBOTIC ASSISTED RADICAL CYSTECTOMY  
(Robot-assisted radical cystectomy with DaVinci system)**

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Dear Patient,

After a careful evaluation of your case, you have been deemed eligible for robotic radical cystectomy.

We are glad that, for your surgery, you have chosen our Department. We are here to offer you the best surgery and assistance, thanks to our strong experience in this field. Our unit, in fact, performs yearly approximately 80 robot-assisted radical cystectomies per year (out of a total of 120 radical cystectomies). We are one of the urological units with the highest volume of surgical procedures in Italy and Europe, with over 30 years of experience in the treatment of bladder cancer.

Additionally, in our research hospital we have conducted many studies (and many are ongoing) on what are the major determinants of postoperative outcomes.

In a holistic approach, we have developed a path that begins before surgery and continues after.

We hope that this reinforces your trust in our Department and our Team and that these aspects reassure you.

In this document, we summarize essential information that will help to make your hospital stay, and subsequent complete recovery, as short as possible.

Bladder cancer is an insidious but curable disease! We are here to fight it with you.

*"You never know how strong you are until being strong is the only choice you have"*

*Cayla Mills*

## PRE-SURGICAL ASSESSMENT

Before surgery, your overall health status will be carefully evaluated and, in general, the following examinations will be performed or ordered:

- **Laboratory blood tests**
- **Electrocardiogram and cardiological examination**
- **Anesthesiologic assessment**, during which:
  1. The suitability for surgery is ascertained
  2. Additional exams or other physician evaluations may be ordered
  3. Any changes in, or suspensions of, chronic therapies are agreed upon
- **Chest x-ray** (if the patient has not recently undergone a chest CT scan)
- **Optical exam with visual field**: this will be required only if the patient has severe myopia, has had a recent eye trauma or has uncontrolled glaucoma in the months before surgery.

These assessments are performed either in our hospital before admission or upon admission on the surgical ward.

We are glad to inform you that the need for blood transfusions is nowadays extremely low thanks to robotic surgery.

**Yet, it is extremely important to inform us whether you are taking any anti-platelet or anti-coagulant (“blood thinners”) medication. The suspension and/or replacement with other medications must be determined by your physician or by the anesthesiologist before surgery. These medications might increase the risk of intraoperative bleeding and their suspension or titration have to be carefully examined before surgery.**

In some cases, it may be necessary to replace oral anti-coagulants (“blood thinners”) with low molecular weight heparin (injections). The anesthesiologist or coagulation specialist from our hospital will advise you in this regard.

If you do not inform us on time about these medications and they are subsequently not interrupted on time, the surgical procedure will have to be postponed, thus wasting precious time for your health!

A cardiological evaluation, in the 30 days prior to surgery is required.

### *Pre-surgical evaluation: "The radical cystectomy clinic"*

Considering the impact that radical cystectomy has on patients' quality of life, our urology unit has activated a dedicated **cystectomy clinic** available to all patients who are going to receive this type of surgery; patients are entitled to a free visit before hospitalization. Unlike the pre-operative tests, this meeting aims to prepare patients for surgery, providing practical advice and explanations regarding surgery itself, the post-operative course and post-operative home rehabilitation. This visit also gives relatives, or any person involved in patient care, the opportunity to receive indications, explanations and clarifications regarding patient management and assistance in the pre- and post-operative period. For example, information regarding the management of uro-stoma, ureteral or bladder catheters and post-operative therapies is provided. In addition, the potential complications related to urinary continence and sexual activity are discussed with patient and family members. This clinic will then become the reference clinic for each patient after surgery and discharge from the hospital, as well as for subsequent visits and check-ups to monitor patient's health during the follow-up.

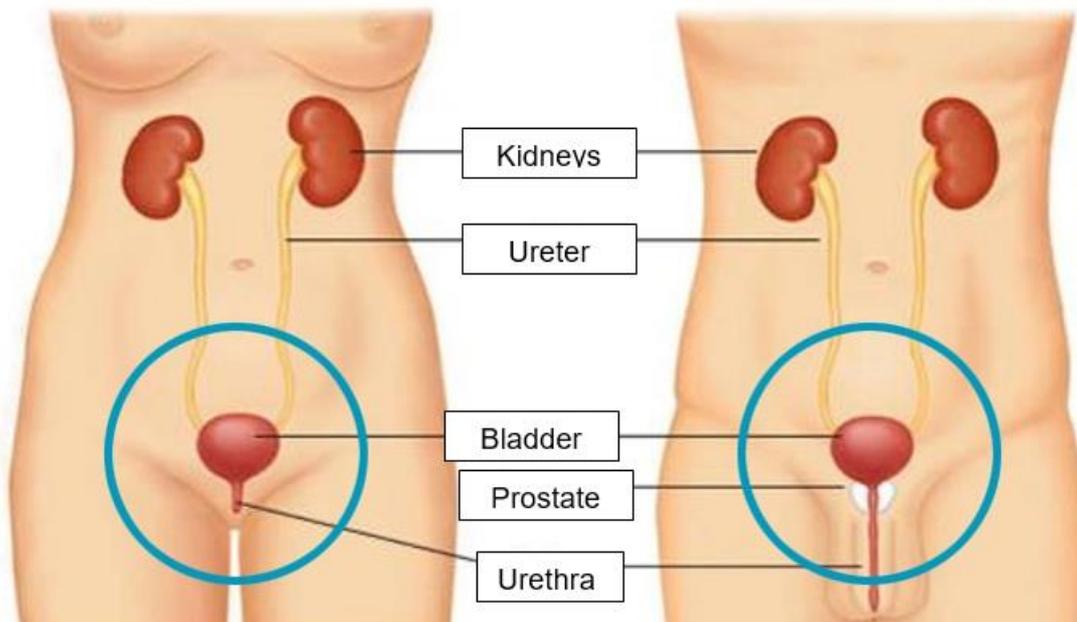
The telephone number for organizing visits in the cystectomy clinic is:

- 02.2643.6764 (Dr. Giusy Burgio)

## BLADDER ANATOMY AND BLADDER TUMOR

### The bladder

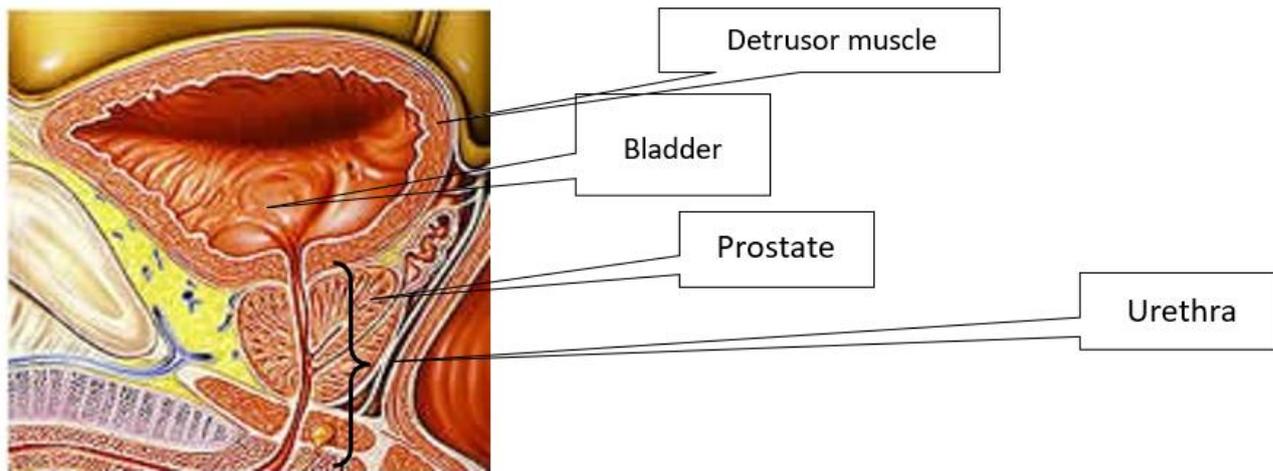
The urinary bladder is a hollow organ located in the pelvis, responsible for the collection of urine produced by the kidneys. The urine reaches the bladder through the ureters. From the bladder, urine is periodically expelled externally through the urethra (Fig. 1)



**Fig 1.** Urinary tract anatomy

The muscle that forms the bladder wall is called the “detrusor muscle”, a smooth muscle whose activity is regulated by nerve fibres, which perceive the bladder filling up and communicate this information to the central nervous system.

The urethra runs through the urogenital diaphragm, which consists of a striated muscle subjected to voluntary control, called the external sphincter. Micturition leads to the periodic emptying of the urinary bladder by an automatic reflex of the spinal cord, mediated by the central nervous system (Fig.2).



**Fig. 2** Urinary tract structures involved in urination

### Bladder cancer

Bladder cancer is the world's ninth most common cancer. Currently, there are about 430,000 new cases per year. Bladder cancer is also characterized by a high mortality rate, ranking thirteenth among the causes of death for cancer. This tumour affects men more often than women, with a ratio ranging from 6:1 to 2:1, depending on the geographical areas. However, mortality is higher in women due to a more aggressive biology, along with a more frequent diagnostic delay. The risk of developing bladder cancer generally increases with age and more frequently affects people over 50 years old.

Cigarette smoking is undoubtedly the most important risk factor associated with bladder cancer, linked to approximately 50% of bladder cancer cases. In addition to smoking, some occupational agents are responsible for an increased risk of bladder cancer. These include aromatic amines and nitrosamine (frequent in workers in the textile, dyes, rubber, and leather industries), toluene, polyaromatic hydrocarbons, chloro-ethylene, dichloromethane, diesel and fuels derivatives. Some classes of workers, such as those in the industries of tobacco, chemical dyes and metals, are at a higher risk of developing bladder cancer because of their exposure to the chemical agents mentioned above.

**If you fall into one of these risk classes, you MUST ABSOLUTELY INFORM US AT THE TIME OF THE UROLOGICAL VISIT!!! In fact, exposure to these agents must be stopped immediately as it could favour the development of a second tumour in a different location, such as the kidneys or ureters.**

Bladder cancer can occur in several histological forms. The most common type of bladder cancer is the transitional cell carcinoma or urothelial carcinoma, that is, the tumour that originates from the transitional epithelium. These tumours represent about 90% of all bladder neoplasms. The remaining 10% consists of squamous cell carcinomas (squamous cells), adenocarcinomas, small cell carcinomas, sarcomas, and mixed forms where multiple histology patterns are present.

Tumours are usually located on the lateral walls of the bladder (Fig. 3): in most cases (75%) they have a papillary shape (i.e. like a small growth) or a flat or nodular shape (carcinoma in situ, CIS).



**Fig. 3** Ultrasound allows the physician to identify a suspected bladder cancer

Bladder cancer symptoms are common to other diseases that affect the urinary tract: presence of blood in the urine and clot formation, a burning sensation in the bladder when compressing the abdomen, difficulty in and pain while urinating, greater susceptibility in getting infections. These symptoms become more and more prevalent as the disease progresses.

There are currently no reliable screening programs or early diagnostic methods, so it is necessary to take preventative measures regarding lifestyle such as quitting smoking and eating healthy and balanced meals.

### Indications for radical cystectomy

Radical cystectomy is indicated in patients with a high risk of progression, particularly when:

- The bladder cancer invades the bladder muscle (T2);
- The tumour occupies a large bladder surface with concomitant Carcinoma in Situ (CIS);
- There are frequent recurrences, despite intra-vesical therapy with chemotherapy drugs or BCG and TURB;
- The tumour involves the prostatic urethra.

## PREPARING FOR SURGERY: TOWARD YOUR IDEAL WEIGHT

In order to facilitate the execution of the surgical procedure and to optimize outcomes in terms of complete removal of the tumor while preserving the anatomical structures responsible for urinary continence and erectile function, it is imperative that you reach a body weight that is as close as possible to your ideal one.

In the modern society, almost all patients are more or less overweight at baseline. A patient's weight category can be understood by his Body Mass Index (BMI).

**If You have a BMI greater than 24.9 kg/m<sup>2</sup>, it is advisable to schedule a nutritional consultation to set up a dietary plan ultimately aimed at reaching your ideal weight. Weight loss will determine greater technical ease in performing surgery, ultimately affecting both the short- and long-term outcomes!**

Please, keep in mind that nutritional evaluations and treatments MUST always be personalized. Below is an example of an ideal low-calorie balanced diet for a 65-year-old patient who is 1.75 m tall and overweight.

<b>Breakfast, about 15% of daily kcals</b>	
Oat milk	150g
A cup of tea/coffee	60g/200g
Whole grain cereal	40g
Fruit jam without added sugars	25g
Fruit	150g
<b>Snack, about 10% of daily kcals</b>	
Walnuts or almonds	10g
Fruit	150g
<b>Lunch, about 35% of daily kcals</b>	
Pasta, rice or cereal	80g
Extra virgin olive oil	10g
Parmesan cheese	10g

Vegetables	200g
Extra virgin olive oil	10g
<b>Snack, about 10% of daily kcals</b>	
Fruit	150g
Crackers, breadsticks, or whole grain croutons	25g
<b>Dinner, about 30% of daily kcals</b>	
White meat/fish	150g/200g
Potatoes	150g
Extra virgin olive oil	5g
Vegetables	200g
Extra virgin olive oil	10g
Whole wheat bread	50g

We also recommend that you exercise regularly and, in particular, that you engage in at least 40 minutes of moderate aerobic physical activity every day.

Consult your physician relative to this dietary advice, particularly if you suffer from diabetes or any cardiovascular disease.

**A consultation with a Registered Dietitian (RD) is an integral part of our program for preparing patients for robotic surgery. This consultation must take place as soon as possible.**

## **ANESTHESIA**

The day before surgery, you must lead a normal life and eat as usual until the evening.

Robotic radical cystectomy is performed under general anesthesia. Pre-anesthesia medications will be administered before you are taken to the operating room, allowing the patient to feel calm and serene.

Simultaneously, intravenous administration of analgesic drugs (preventive analgesia) is started and will be continued through the post-operative setting for approximately 24 hours. Pain control at this point is generally optimal, allowing patients to quickly overcome the surgical trauma. The pain associated with robotic-assisted surgery is usually minimal, thanks to the absence of muscle incisions. In the postoperative setting, a slight muscle and joint pain may be felt due to the patient's position on the operating table, a problem easily resolved with analgesic drugs and early mobilization.

Rarely, in the first twenty-four hours after surgery, localized pain may arise in the shoulder blades. This pain is transitory and bears no consequences. It is generally due to presence of carbon dioxide, used to create the intra-operative pneumoperitoneum, in the pleural space.

A prophylaxis for nausea and vomiting is also administered during surgery to prevent any post-surgical discomfort. Yet, nausea and vomiting are rare after this type of minimally-invasive procedure.

The minimal invasiveness of this surgical technique usually allows patients to start drinking, eating and moving on the evening following surgery.

The prevention of thrombotic and thromboembolic phenomena is carried out with the use of elastic stockings placed on the lower limbs before surgery, by subcutaneous administration of low molecular weight heparin starting on the evening following surgery, and by early mobilization of the patient. Each of these procedures allow for the rapid recovery of patient's physical and mental status, minimizing the consequences of surgical stress. The appropriateness of low molecular weight heparin injections is evaluated case-by-case according to the present guidelines for thromboprophylaxis.

**The Consultation with our anesthesiology team is an important part of our pre-operative assessment and it must take place as soon as possible. It will be organized for you by our Urology admission office at San Raffaele Hospital.**

*Immunotherapy and its possible adverse effects*

Medications such as Pembrolizumab, have improved patient survival rates. In the last 5 years, the urology department of San Raffaele hospital, thanks to its collaboration with internationally renowned oncologists like Dr. Andrea Necchi, has activated numerous therapeutic protocols to facilitate access to immunotherapy treatments in patients with bladder cancer.

Our greatest experience derives from patients receiving pre-cystectomy immunotherapy, according to the active therapeutic protocol at San Raffaele hospital (PURE-01). Immunotherapy works by stimulating the recipient's immune system against cancer cells. It could facilitate the onset of autoimmune reactions on various organs such as the thyroid, pancreas, intestine, stomach, or even the lungs. These autoimmune reactions occur in about 40% of patients but are mostly asymptomatic and without consequences. In fact, most of the time they cause only a slight increase in inflammatory markers and body temperature or changes in hormones such as TSH or insulin. These reactions induced by immunotherapy can also occur several weeks or months after the administration of the medication, and – as frequently occurs – in the days after cystectomy. It is important to know how to recognize these adverse reactions because they are usually harmless and can be managed conservatively or with anti-inflammatory drugs; it is also important to distinguish them from the most dangerous bacterial infections that require antibiotic treatments.

## **SURGICAL TECHNIQUE**

The first surgical step consists in the creation of the pneumoperitoneum: the abdominal cavity must be filled with carbon dioxide to create a working chamber for the robotic surgical instruments.

An incision about 2 cm above the umbilicus allows for the placement of the first robotic trocar, which is done under direct vision, and serves to insert the small camera that the surgeon will use to operate. Other five operative trocars are then inserted into the abdominal cavity. Three of them are typically managed by the first surgeon and two by the surgical assistant.

Although it is an extremely rare occurrence, it is possible that the robotic trocars cannot be positioned due to the presence of numerous and tenacious intestinal adhesions and it is therefore necessary to change surgical approach, converting from robotic to open surgery.

It is important to understand that the robotic technique provides the surgeon with a visual magnification of up to 20 times and a 3-dimensional vision. This allows the operator to appreciate the depth of the surgical field, which is not possible with the classic laparoscopic technique. The intraoperative robot-assisted vision helps the surgeon to see even the smallest anatomical detail and therefore to perform surgery with a significantly higher accuracy than the classical open or laparoscopic approaches.

In males, the first step involves the isolation of the seminal vesicles. Then, the surgeon accesses to the pelvic space where the bladder and prostate are located (in men). In women, the first step is the incision of the Douglas space up to the isolation of the vaginal arches.

The pelvic lymph nodes (lymphadenectomy) are then bilaterally removed, because during the process of carcinogenesis, it is possible for some neoplastic cells to migrate and be captured by the nearest lymph nodes. For this reason, in radical cystectomy, the removal of the lymph nodes is performed for its possible therapeutic value and to obtain a more precise disease staging.

Once lymphadenectomy is completed, the ureters are isolated and disconnected from the bladder. The surgical margins of the resected ureters are immediately sent for pathological examination to ensure the absence of neoplastic disease in the terminal tract. Subsequently, the bladder and prostate (in men) or the uterus, ovaries, and a portion of the anterior wall of the vagina (in women) are removed with an anterograde technique.

Once the prostate is removed, the patient will no longer be able to ejaculate and therefore will not be able to have children. Even female patients, in case of removal of the uterus, will no longer be able to have children. If the surgeon removes part of the vagina, the quality of sexual intercourse may be affected as well.

Depending on the tumor characteristics and the patient's age, isolation and section of the vesical and prostatic (in men) or vaginal and uterine (in women) vascular peduncles is carried out with the utmost attention in safeguarding the nerves involved in sexual activity, when this is oncologically safe.

In men, the removal of the prostate along with the bladder is preceded by the section of the venous plexus of Santorini and its subsequent hemostatic suture with stitches placed under direct vision. In women this step is not necessary. To allow the detachment of the bladder, the urethra is dissected at the level of the prostate apex (or bladder neck in the woman) and then the completely freed anatomical specimen is placed in a special bag (Endobag).

In case of extension of the tumor to the urethra, a urethrectomy may be performed. In this case, the only possible urinary derivation would be the non-continent one (no neobladder!).

In men, the removal of the urethra requires a further skin incision on the pelvic floor at the level of the penis glans; the duration of the surgery is extended by 1 hour in this case.

The removal of the bladder implies the need for the creation of a urinary diversion. Each of the urinary derivations here reported has peculiar benefits, disadvantages, and possible complications. The surgery lasts 3-6 hours depending on the surgical technique used and the anatomical conditions of the patient.

Your Urologist will advise you on the more appropriate urinary derivation according to your general condition. It depends on local bladder tumor extension as well as the possible implications for your quality of life after surgery.

We present the different possibilities of urinary derivations realized with robotic technique at our center:

1. Orthotopic ileal neobladder
2. Ileal conduit (BRICKER)
3. Ureterocutaneostomy (UCS)

## **1) ORTHOTOPIC ILEAL NEOBLADDER**

If the patient is generally healthy and the disease, during surgery, is found to be confined to the bladder without involvement of the urethra and ureters, the most frequent urinary derivation is an orthotopic ileal neobladder. It consists in the reconstruction of a new bladder using a segment of about 40-60 cm of ileal intestine, shaped as a spheroidal cavity to which the ureters are anastomosed. After taking the intestinal segment to create the new bladder, the surgeon will restore the continuity of the intestine loops using a mechanical stapler. The neobladder is placed in the pelvic space and anastomosed, to the remaining part of the urethra. The neobladder will function as a reservoir for urine and should be emptied periodically. The patient must also be aware of the need for and motivated to participate in rehabilitation sessions to learn the new way of urinating. In fact, the micturition stimulus will be perceived as a feeling of fullness or vague pubic pain. Urination will occur through the compression of the neobladder after releasing the muscles of the perineal floor and will occur by increasing the abdominal pressure or using manual abdominal wall compression. During the first months, it may be necessary to periodically use catheters during the day to empty this new reservoir. Our physicians and nursing staff will be happy to teach you this maneuver that is both easy to learn and to execute. Partial urinary incontinence is not unlikely in this scenario, especially during night hours.

## **2) ILEAL CONDUIT (BRICKER)**

Neobladder urine derivations is contraindicated in the following cases:

- Local advanced bladder cancer
- Neoplastic involvement of the urethra
- Neoplastic involvement of ureters
- General frailty of the patient
- Need for assistance by the patient
- Preoperative urinary incontinence
- Previous radiation therapy
- Kidney function failure
- Intestinal diseases (Rectal ulcer syndrome, Chron's disease, malabsorption pathologies, previous intestinal neoplasms, previous intestinal surgery)
- Anatomical conformation of the patient in which the advantages of the neobladder may be lost.

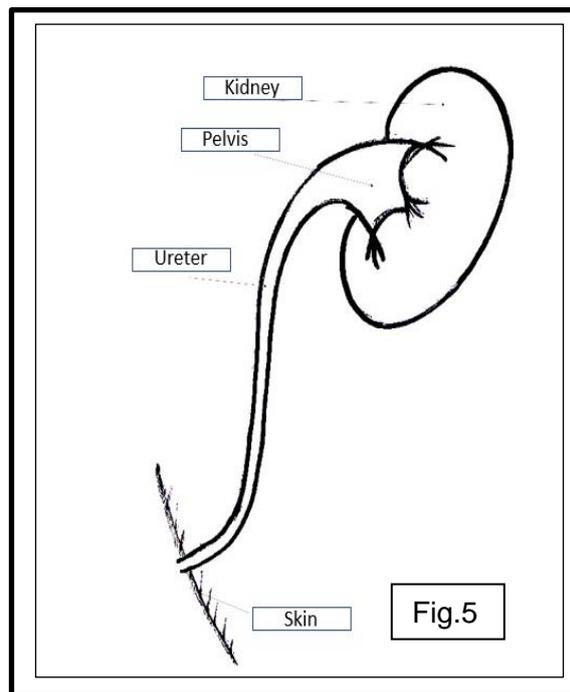
In these cases, another type of urinary derivation called Bricker's ileal conduit will be chosen. A segment of 10-15 cm of intestine (ileum) is isolated from the rest of the intestine and it is connected with the ureters. After restoring the intestinal continuity, the collected segment will be anastomosed to the skin.

This is certainly the most common technique. The urine, which continuously flows out through the ureters and the ileal conduit, is collected in a bag attached with an adhesive around the cutaneous stoma. The bag is provided with an outlet by which it can be emptied periodically. The care of the urine collection bag is easy, and the patient is properly trained to do so. The presence of the stoma, although generally difficult to accept, does not irreparably compromise the patient's quality of life.

### 3) SINGLE OR BILATERAL URETEROCUTANEOSTOMY (UCS)

It consists of connecting the ureters directly to the outside on the skin, in order to collect urine in two bags (bilateral UCS), or in one bag (mono-lateral UCS), which should be changed on alternate days, similar to those already described for the ileal conduit. The UCS can offer a definitive solution for adjuvant radiotherapy or in cases where bowels cannot be used. A ureteral stent is also placed inside each ureter to avoid the narrowing of the stoma, which will be periodically replaced every 3-6 months.

**Fig. 5** The ureter is connected directly to the skin



## **RISK OF CONVERSION TO OPEN TECHNIQUE**

During robot-assisted radical cystectomy, some clinical situations, which are difficult to predict through pre-operative diagnostic tests, can occur. In certain scenarios, the surgeon will have to change the surgical approach from robotic to the traditional "open" procedure. This is not unlikely in patients with a history of prior abdominal surgeries as the presence of internal adhesions can make the positioning of the robotic trocars markedly complex. In very rare cases, an adequate workspace for robotic surgery is not possible and therefore conversion to open surgery is necessary. Further indications for a conversion to open technique are major complications that cannot be managed robotically or laparoscopically. According to our case studies, less than 5% of the robot-assisted surgeries required an open conversion, and in the vast majority, it took place to maintain the pre-operative programmed urinary derivation (especially for neobladder creation). Conversely, the conversion rate in our cohort of patients is much lower when considering Bricker or UCS urinary derivation (<1%).

## **ERAS PROTOCOL**

In our hospital, multimodal and interdisciplinary patient care programs have been implemented with the ultimate goal of improving surgical outcomes, reducing the effects of physiological and psychological stress induced by surgery, reducing post-operative complication rates, and improving the normal patient's return to daily activities.

The ERAS protocol was first introduced for colorectal surgery in the 90s and has been implemented in several surgical fields including urology.

The new advanced post-operative recovery program (ERAS) has ensured faster and higher quality recovery in patients undergoing radical cystectomy. It reduces post-operative hospitalization time and allows for a significantly faster recovery of intestinal function, resulting in a more rapid return to the patient's normal dietary habits. Patients reported a more rapid recovery of bowel movement, reduction of sleep disturbances and above all an important reduction in post-operative pain. Furthermore, it was observed that ERAS patients had a significantly lower rate of post-operative complications such as intestinal obstruction or anemia.

Early hospital discharge was not associated with an increased 30-day post-surgery readmission rate, thus confirming the safety and efficacy of ERAS protocol even in the most complex patients. In addition, a faster discharge from the hospital brings multiple benefits, such as a more rapid access to adjuvant therapies if necessary.

## **POST-OPERATIVE COURSE**

Patients normally get out of bed on the first postoperative day and are gradually mobilized as they recover energy. This promotes the recovery of normal blood flow, aids in avoiding the formation of thrombi ("clots") in the veins of the lower limbs and facilitates the resumption of intestinal activity.

### **AS A GENERAL RULE, THE PATIENT MUST BE BEDRIDDEN FOR THE SHORTEST AMOUNT OF TIME!!!**

During surgery, the following devices can be placed:

- A nasogastric tube, which is usually removed directly in the operating room at the end of surgery, or in complex cases can be kept in place until the intestinal canalization is resumed;
- Abdominal drainage tube, which is usually placed only in patients with a neobladder reconstruction. This is subsequently removed on the first post-operative day;
- Two ureteral stents, which in case of neobladder are removed on between the tenth and twelfth day. In case of other urinary diversions, the stents remain for about 3 months and then removed (Bricker) or periodically changed (UCS);
- In case of orthotopic ileal neobladder, a bladder catheter is also placed during surgery. This is kept in place for a period usually varying from 14 to 21 days, depending on the local intra-operative conditions and the post-operative course. In rare occasions, it may be necessary to keep the bladder catheter for an extended period of time, but generally not more than 1 month. When a neobladder is created, the patient usually leaves the hospital with the bladder catheter still in place and returns to our clinic to remove the latter later.

The patient can begin to drink and eat gradually from the day after surgery, according to the resumption of intestinal activity. Successively,

homogenized fruit, meat, yogurt, ice cream and solid foods are introduced. Feeding must resume gradually, prudently and only if the patient feels comfortable.

The hospital stay varies between 6 and 15 days if no complications arise. This range depends on the urinary derivation created and, on the patient's general clinical conditions. Please keep in mind that patients with neobladder often have longer hospital stays, which can be aggravated by complications more frequently than other urinary derivations.

**HOSPITALIZATION ON THE WARD MUST BE LIMITED TO THE MINIMUM LENGTH OF TIME IN ORDER TO REDUCE AS MUCH AS POSSIBLE THE RISK FOR PATIENTS TO CONTRACT A NOSOCOMIAL INFECTION!!**

**THIS MEANS THAT, STARTING FROM THE SECOND POSTOPERATIVE DAY, AS SOON AS THE GENERAL CONDITIONS ALLOW IT, PATIENTS ARE DISCHARGED FROM THE HOSPITAL EVEN IF THE BLADDER CATHETER OR URETERAL STENTS ARE STILL IN PLACE!**

If the patient who has undergone radical cystectomy with neobladder still has the bladder catheter after hospital discharge, he/she will receive an appointment to return after a few days to our clinics to remove it.

**After the bladder catheter is removed, it is appropriate to stay in Milan for at least 24 hours.** This is due to the fact that in this period of time an inability to resume urination spontaneously or a painful abdominal syndrome due to urine leakage in the peritoneal cavity may arise.

**INFORMATION ABOUT HOTELS LOCATED NEAR THE HOSPITAL WHERE THE PATIENT (AFTER BEING DISCHARGED) AND HIS FAMILY CAN STAY WILL BE PROVIDED BY OUR OFFICES. THE CLOSEST ONES ARE:**

- 1. Hotel Rafael Via Olgettina, 60 - 20132 Milan Tel. +39 02 21765.1 - Fax. +39 02 21765888 - inside the San Raffaele campus - [rafaelhotel.it](http://rafaelhotel.it)**
- 2. NH Hotel in Milan 2 Via Fratelli Cervi - Milan 2, Segrate (MI) Tel. 022175 - mail: [nhmilano2@nh-hotels.com](mailto:nhmilano2@nh-hotels.com)**

## **POST-OPERATIVE COMPLICATIONS**

Robot-assisted radical cystectomy is characterized by a high rate of both intra- and post-operative complications due to the fact that this type of surgery is one of the most complex abdominal surgeries.

A recent European study found that almost all (99%) patients undergoing radical cystectomy present at least one or more post-operative complications. Of these complications, approximately 90% are considered mild or minor. Only 6% and 4% of the patients were respectively re-operated or hospitalized after hospital discharging.

From our most recent experience in patients who underwent radical cystectomy and had been previously treated with neoadjuvant immunotherapy, we found that about 77% of our patients developed a complication, of which about 30% required additional treatment(s).

Clearly, the complication rate changes according to the different types of urinary derivation and the hospital where the surgery is performed. It has been shown that centers with greater surgical experience, such as our department, show lower post-operative complication rates than the so-called "low volume" centers.

According to the data obtained from the surgeries carried out at our center in the last 3 years (about 200 treated patients), the most frequent complications include:

- Infections causing fever and requiring antibiotic therapy (50% of cases);
- Delay of intestinal canalization and impossibility or difficulty in evacuating stool, which requires medical therapy or enemas or intestinal transits with osmotic solutions to help bowel motility (30% of cases);
- Pain in the wound site, controlled with analgesic drugs (20% of cases);
- Anemia (drop in hemoglobin blood values) that requires blood transfusions (18%);

- Hydronephrosis (dilations of the renal cavities) or urinary fistulas (slow healing of the anastomosis) such as to require the positioning of a nephrostomy or ureteral stent; patients with a neobladder may have to keep the bladder catheter in place for an extended period of time, or have it re-placed (15% of the cases);
- Lymphorrhagia or pelvic lymphocele (lymph collection) with possible need for percutaneous drainage (7% of cases);
- Pelvic hematomas (blood collections) (6% of cases);
- Surgical wound infections or dehiscence (2% of cases);
- Different cardiorespiratory complications that require specific specialist medical therapies (<2% of cases);
- Post-operative delirium with the need for drugs and neurological evaluations (<1% of cases).

As mentioned above, rare and more serious complications include:

- Acute renal failure;
- Accidental intestine injury or dehiscence of intestinal anastomosis;
- Deep vein thrombosis, variable depending on the use of heparin, elastic stockings, and early mobilization.

In our experience, the percentage of complications observed during robot-assisted radical cystectomy surgery and during hospitalization is significantly lower than those observed in open surgical technique.

## **MORTALITY RISK**

Radical cystectomy surgery carries a risk of post-operative mortality ranging from 1.2% to 3.2% at 30 days after surgery and it varies from 2.3 to 8.0% at 90 days. In highly specialized centers this risk is reduced from 0.5% to 2%, according to the patient's clinical characteristics and the urinary derivation. Based on a cohort of 68 patients who underwent radical cystectomy in 2018 in our center, the mortality rate at 90 days was 0%. When considering all the patients treated in the last 5 years, the perioperative mortality at 90 days was less than 1%.

## **LATE POST-OPERATIVE COMPLICATIONS**

**A scheduled follow-up is important in order to prevent possible complications that may arise in the months or years following the surgery.**

**The patient will be monitored at our “cystectomy clinic” quarterly in the year after surgery and at least once a year in the following 2 years.**

**Among the most common late complications, which only affect patients with the neobladder urinary derivation, the following data have been gathered:**

**-Metabolic acidosis:** this is linked to ammonium absorption ( $\text{NH}_4^+$ ) by the gastrointestinal tract used to create the neobladder. It is a frequent but easy-to-manage complication. Patients need to perform frequent systemic acidity tests by venous blood gas analysis and to correct it by taking bicarbonate tablets depending on the amount of acidosis (from 2 to 6 pills per day). This complication usually decreases over time.

For the general metabolic management of the patient with neobladder derivation, the urologist may refer the patient to a nephrologist.

- **Hypersecretion of mucus:** patients in whom a neobladder is created may find mucus in the urine in the first few months after surgery. This phenomenon is normal since the intestine has been transformed into a bladder and its contact with acidic urine results in mucus production. After few months, the mucus tends to decrease and will disappear, as the intestine adapts to the new function. We recommend taking bicarbonate tablets together with abundant hydration.

- **Urinary incontinence:** it is a common and expected occurrence in the early postoperative period. It can be diurnal and nocturnal or only nocturnal. If it occurs in a mild form, it does not require causal treatment and tends to resolve itself over time. In our experience, urinary incontinence tends to decrease after the first 3 months, with a subsequent improvement up to 1 year after surgery. If it occurs in a serious form, it is necessary to carry out further evaluations to establish its mechanisms and causes in order to decide on the best treatment, either rehabilitation training or surgery. All patients with neobladder urinary derivation can refer to our pelvic floor rehabilitation specialists to improve urinary continence recovery.

- **Stones in the neobladder (1-5%):** their formation depends on the post-urination residue in the neobladder and can cause urinary infections. Stones can usually be treated endoscopically, and rarely require open surgery. They are easily diagnosed by an ultrasound or a CT-scan.

- **Rupture of the neobladder:** a very rare event, according to our experience of the last 200 cases treated. It occurs in poorly vascularized areas of the neobladder wall which can be resolved by a percutaneous drainage tube placement or it may require surgical repair of the new bladder.

- **Over-continence:** an event more common in female patients after the creation of a continent urinary diversion. It is characterized by the impossibility of completely emptying the bladder, usually treated with intermittent self-catheterization. It

may be due to a narrowing of urethra-neobladder anastomosis. In these cases, a small endoscopic surgery may be necessary.

To prevent over-contenance and associated complications such as urinary tract infections and the weakening of the bladder walls, there is an educational path designed to teach patient the self-catheterization. During hospitalization, a dedicated nurse teaches patients self-catheterization and provides single-use catheters to perform it. In this way, the patient will be autonomous in emptying the new bladder in the first months after surgery, avoiding urine accumulation or excessive neobladder stretching.

### **Late common complications regardless of urinary derivation are:**

- **Lymphedema** (lymph stasis and consequent swelling of the tissues) usually of the genitals and/or lower limbs. Quite frequent in the immediate post-operative period, it is usually transient and reversible within a couple of months. The patient could use jockstrap or tight-fitting underpants to reduce the swelling and prevent recurrence. As for edema in the lower limbs, the use of elastic stockings or lymphatic drainage massages are recommended. However, it should be remembered that, in rare cases, it can be a permanent and irreversible consequence.

- **Sediment in the urine:** The urine generally remains reddish for at least 1 month after surgery. Abundant hydration will help to make the urine clear again.

- **Chronic ureteral obstruction (10%) with consequent hydroureteronephrosis:** it is mainly caused by ischemia of the terminal part of the ureter. It can occur in all types of urinary derivation, usually in the anastomosis between the ureter and the neobladder, between the ureter and the intestinal loop in an ileal conduit, and between the ureter and the skin in an ureterocutaneostomy. It can occur within a variable time after surgery and may also be related to a possible tumour recurrence in the anastomosis. If bilaterally present, it can cause kidney

failure. The treatment consists of a first percutaneous drainage treatment, with the positioning of a nephrostomy catheter, which allows on one hand renal function recovery, while on the other a detailed evaluation of the cause of the obstruction. This treatment can therefore be performed endoscopically, by dilating or by cutting the stricture. If this procedure fails, a surgical treatment of the anastomosis must be performed. If the cause of the obstruction is a neoplastic recurrence, other types of surgery may be necessary.

- **Abdominal wall hernia (5-10%):** even in case of minimally invasive surgery, small incisions are made for the introduction of the robotic instruments. In some cases, these incisions can stimulate the development of a hernia. These situations are asymptomatic in most cases. However, in some rare exceptions, herniated tissue can become incarcerated and subsequently ischemic. In these cases, surgery is needed.

- **Stoma complications,** in case of urinary derivation such as ileal conduit (Bricker) or ureterocutaneostomy (UCS). They can affect up to 25% of patients and are represented by:

- Narrowing of the skin stoma, which can be treated with repeated dilatations;
- Parastomal hernia, which must be corrected surgically especially if it is large and annoying;
- Inflammatory alterations of the stoma mucosa, which must be treated by topical application of creams;
- Bleeding of small peristomal vessels, which may require the application of hemostasis stitches.

**A dedicated stoma nurse teaches stoma care to patients who will undergo radical cystectomy. You will meet the nurse during the pre-surgical clinic evaluation at the cystectomy clinic, during the hospital stay, and after post-operative follow-up.**

## **Final pathology report**

The definitive histological examination of the bladder, lymph nodes, and other organs that may have been removed during the surgical procedure usually are available in about 30 days after surgery. The final histological examination clarifies the extent and aggressiveness of the bladder tumor. In particular, the parameters considered are: 1. Histological type and presence of histological variants; 2. Extension and degree of tumor infiltration into the bladder wall; 3. Aggressiveness of the tumor; 4. Tumor volume and size 5. Tumor spread: contained within or outside the bladder; 6. Tumor involving the adjacent structures (prostate, uterus, annexes, etc.) or the removed lymph nodes.

The definitive histological examination is an essential element to decide whether the patient should receive additional treatments, such as chemotherapy, immunotherapy, or radiotherapy.

### **ADVICE AT DISCHARGE AFTER RADICAL CYSTECTOMY**

**It is absolutely forbidden to drive any type of vehicle or motorcycle, or to ride a bicycle for at least 10 days after the hospital discharge or the bladder catheter removal. Moreover, it is recommended to avoid physical exertion for the following 4 weeks after surgery.**

## **Eating**

Unlike the "natural" bladder, the neobladder promotes water and electrolytes loss, especially in the post-operative period. For this reason, it is important to maintain a correct daily intake of liquids (2-3 liters per day) and electrolytes. You do not have to abstain completely from alcohol intake, such as wine and beer, but it is suggested just a moderated consumption. In some cases, it may be useful to take sodium bicarbonate, iron, foline, B12 vitamin, etc.

It is particularly important to vary the diet by enriching it with cooked and fresh fruit and vegetables, to avoid constipation. As a target, the patient should try to have a bowel movement once a day, in order to avoid the formation of hard stools. Do not use enemas or pearls for the first 4 weeks after surgery: in fact, during this period the walls of the rectum are very thin, and you could therefore cause damage.

Frequently, the urine contains variable amounts of mucus produced by the intestine used to create a new bladder. To reduce mucus production, in addition to a greater intake of liquids, the use of products containing bilberry extract is useful. If you have one or two uro-bags, there are no special dietary limitations.

## **Physical activity**

After hospital discharge, you can gradually resume your physical activity. You can go walking and go up and down the stairs. Driving the car can generally be resumed 2 weeks after surgery.

**Remember, however, to avoid excessive physical efforts, such as lifting heavy objects or performing intense exercise (gymnastics, golf, tennis, running), during the first 3 weeks after surgery. It is also important to avoid bicycle or motorcycle use during the same period.**

In fact, it is the time required for adequate scar tissue development in the treated areas. If you undertake strenuous physical activities earlier than necessary, you could damage the delicate suture that connects the bladder to the urethra. This could lead to long-term problems related to continence and could even cause a wound hernia.

## **Emptying of the neobladder**

It is important to know that urination will be felt differently than before surgery. This means, for example, that you will no longer feel the normal urge to urinate, but distention and abdominal swelling, especially above the pubis, in relation to the degree of neobladder distention. In the period immediately following the surgery, it is advisable to empty your neobladder every two hours (constantly) even

in the absence of an urgent sensation. It is important to learn to urinate while sitting, contracting the abdominal muscles, trying to relax the anal sphincter at the same time. After few months you can increase the time interval between one urination and another (every 3-4 hours). This means that even during the night some neobladder emptying must be carried out. Defining the need, frequency and duration of the intermittent catheterization will be the task of the urologist who will teach you how to carry out such maneuvers.

### **Management of the uro-stoma**

In case of ileal conduit or bilateral UCS the patient will have one or two bags for urine collection. Especially in the early post-operative period, the patient may have difficulty in managing the stoma. You will be directed to specific clinics where dedicated nurses teach you how to change the bag and explain to both the patient and family members how to manage it. Usually, in a few weeks the patient, properly educated, reaches independence in his stoma management.

## **RESUMPTION OF URINARY CONTINENCE IN PATIENTS WITH NEOBLADDER**

The removal of the bladder is followed by the subsequent reconstruction of the urinary tract by the anastomosis between the neobladder and the residual urethral segment. This obviously guarantees urine outflow but does not allow adequate compensation for the loss of the closure mechanism guaranteed by the inner bladder sphincter, which is removed during of the surgery.

The anatomical structures that are usually not involved (unless the patient has had radiation therapy) are the muscles of the perineum which is the muscular, lozenge-shaped area that is placed on the saddle when riding a bicycle and which supports the bladder and the last portion of the urethra.

Therefore, after surgery, continence is determined only by the function of the external sphincter with the support of the muscles of the pelvic floor. The rehabilitation treatment has as its objective the strengthening of these muscles.

To favor a more rapid and gradual recovery of any post-surgical dysfunctions, pre-operative physiotherapy sessions, started at least twenty days before surgery, can help the patients. According to the patient's condition, different techniques might be used:

- **Behavioral or bladder training:** advice related to an appropriate lifestyle and an adequate daily fluid intake. These tips are personalized and based on a bladder diary kept by the patient himself for at least two consecutive days, where the liquid intake, urination and any urine leaks must be carefully noted.

- **Kinesiotherapy:** for the strengthening of the pelvic floor. A series of exercises to improve the perineal musculature, between the anus and the scrotum, around the penis. Depending on the recovery, these exercises might become increasingly demanding, until they are performed with the telemetry biofeedback technique (with anal manometry probe) during the execution of more strenuous physical activity (jumping and running).

Biofeedback allows visualizing the muscular activity on a computer screen in order to identify and correct the errors of execution of physical exercises.

- In particular situations **Functional Electrical Stimulation** is used. Its objective is not only the reinforcement of the pelvic muscles, but also the awareness of the perineal floor with subsequent inhibition on the contraction which is responsible for the emptying of the bladder. In addition to the usual technique that involves the use of ring electrodes, the most recent SANS technique is preferred, which provides for posterior tibial nerve stimulation of the lower limb in case of urge-incontinence symptoms.

Rehabilitation treatment supports the pharmacological treatment in addressing post-operative problems and represents an effective way to improve patient's quality of life in the first months after surgery, accelerating the recovery of bladder function.

## RESUMPTION OF SEXUAL ACTIVITY

The fundamental requirement for satisfactory sexual activity is the preservation, during surgery, of the nerves involved in the erection mechanism in men and lubrication and sensitivity in women.

As explained before the surgery, the resumption of sexual activity depends on age, pre-operative sex drive and on the extent of the tumor, which is the key parameter in determining the surgical approach.

The primary purpose of bladder cancer surgery is the complete eradication of the tumor. A partial or non-radical eradication of the tumor could result in an impairment of patients' survival.

The possibility of sparing the nerves and vascular structures essential for sexual function will be discussed pre-operatively and re-evaluated at the time of surgery according to the local tumor extension.

As a rule, after surgery, do not be afraid to experience sexual activity as soon as you feel fit. The radical cystectomy surgery has two important consequences:

- **In men**, the removal of the prostate leads to the disappearance of ejaculation and therefore, after surgery, the patient becomes sterile. If the patient is interested in having children, it is important to perform the cryopreservation of the semen before entering the hospital in order to proceed with any Assisted Reproductive Technologies (ART).

Some practical tips to resume your sexual activity as fully and as quickly as possible:

- Lubrication of the penis and vagina before sexual intercourse with any ad hoc gel is very useful.
- Standing or kneeling during sexual intercourse improves erections.
- Once an erection is obtained, you can put a normal elastic band at the base of the penis, which facilitates blood entrapment inside the penis.

- Don't wait for the "perfect erection" before having sex. Try to have sexual intercourse even if the erection is partial. Sexual activity facilitates the recovery!  
It is important to understand that sex is not penetrative in the first phase since the necessary penile stiffness returns after a few months. In the early days after surgery, sex is therefore mechanical, but equally pleasant! It is important to practice masturbation frequently (at least 3 times a week) because this represents the most effective form of penile rehabilitation.
- You should know that you would be able to have an orgasm even without an erection. Remember, however, that the release of seminal fluid will not follow orgasm, as the seminal vesicles and the prostate were removed during surgery. A condition of permanent sterility was therefore created.
- It is always useful to completely empty the bladder before each sexual act to avoid the phenomenon of urinary incontinence at the time of orgasm.

There are people who do not resume good sexual potency until 2 years after surgery. Erections, if they return, will gradually recover and their quality will improve month after month. Visual and psychogenic stimuli will be less intense, while tactile stimuli will be more intense in the first period. Do not be afraid to experience sexual activity as soon as you feel fit. The first favorable sign is to see an enlargement of the penis during maximum sexual arousal, even in the absence of rigidity.

In my personal experience, every patient interested in regaining normal erections needs to stimulate the penis using dedicated drugs, both those that improve blood circulation inside the penis and microinjections that promote the blood flow to the penis.

We also believe that it is very useful to take a 5-phosphodiesterase inhibitors drug before sexual intercourse and not in association with intra-cavernous injections.

Patients with chronic NITRATES therapy (medicines useful in some cases of angina - ischemic heart disease) CANNOT take the drugs listed above.

In women, the need to remove the uterus leads to total infertility. In addition, any rearrangement of the vagina walls can affect the quality of sexual intercourse and requires adequate sexual rehabilitation through dilations and the use of lubricants during intercourse.

Some practical tips to resume your sexual activity as fully and as quickly as possible:

- Lubrication of the penis and vagina prior to sexual intercourse with any petroleum-based gel or oil is very useful. It may be necessary to repeat the lubrication during sexual intercourse.
- Initially, (first 3 months) sex should be without intercourse in order to avoid defects in vaginal tissue repair.
- It is always useful to completely empty the neobladder before each sexual intercourse to avoid the phenomenon of urinary incontinence during orgasm.
- Use of antiseptic and protective vaginal lavages for the vaginal mucosa.
- During the first sexual intercourse you may feel slight pain and have some blood loss. Take B complex vitamins for a more complete sensitivity recovery.

## **POST-OPERATIVE AND ONCOLOGICAL FOLLOW-UP**

At the end of the hospital stay, you will receive a discharge letter with the indications follow-up.

Based on the histological report, your urologist of reference will schedule the follow-up visits, and may decide, based on the extent of the tumor, the possible need to perform a further specialist assessment with the oncologist or the radiotherapist.

Our Urology unit has begun a close collaboration with Dr. Andrea Necchi. If necessary, it will be our concern to suggest a visit with Dr. Necchi before and/or after surgery. Otherwise, at your discretion you can choose to be followed by Oncologist specialists from other hospitals. The same document can also be used for the radiotherapist and any radiotherapy consultation. If you wish, you can refer to the radiotherapy operative unit of this institute (ref. Prof. Nadia Di Muzio and Dr. Cesare Cozzarini).

If the tumor is limited to the bladder, you will be candidate for surveillance, involving periodic blood tests and instrumental tests (ultrasound, CT scan, chest radiograms). If you wish, you can refer to our Uro-Oncology Clinic: in this case, we will provide you with a detailed clinical report, after hospital discharge, with all the necessary details for the correct scheduling of the surveillance, which lasts at least 10 years after surgery. As for future checks, we recommend to carefully follow all the indications that have been written in your **discharge letter**.

It is a great pleasure for me to have the chance to treat you. I hope you will always consider our entire medical staff as both doctors and friends. While remaining at your complete disposal for any further clarification, I take this opportunity to offer you my best regards.

**Prof. Francesco Montorsi**

**Professor and Chairman  
Department of Urology  
Program Director  
Vita Salute San Raffaele University - Milan**