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NewYork-Presbyterian Urology Ranks #9 in the Nation

Laparoscopic Donor Nephrectomy: Continuing Refinements in the Standard of Care

In kidney transplantation, laparoscopic donor nephrectomy is now the standard of care for living donors, a technique not widely available until the late 1990s. "The first live kidney donation, performed in 1954 in Boston, represented a significant advancement in transplant surgery, but required a large open incision," says **Joseph J. Del Pizzo, MD**, Director of Laparoscopic and Robotic Surgery for the Department of Urology at NewYork-Presbyterian/Weill Cornell Medical Center. "Although this allowed family members to donate to loved ones in need if they proved to be a match, there was also a disincentive. Live donor nephrectomy was associated with a significant amount of pain and prolonged recovery time. As a result, the use of deceased donor kidneys was more common for several decades."

With the development and refinement of laparoscopic techniques came significant advantages for donors, including lower risk of complications, reduced pain after surgery, and shorter recovery time and return to all regular activities. Today, donors who undergo laparoscopic nephrectomy are generally hospitalized for one to two nights following surgery and can return to work two to three weeks later; open nephrectomy donors usually remain in the hospital for three to five nights and do not return to work for an average of 8 to 12 weeks, or longer.

Dr. Joseph J. Del Pizzo

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Current Perspectives in the Treatment of Bladder Cancer

Today, there are more options for the treatment of bladder cancer than ever before. **Christopher B. Anderson, MD, MPH**, and **G. Joel DeCastro, MD, MPH**, urologic oncologists in the Department of Urology at NewYork-Presbyterian/Columbia University Irving Medical Center, are established experts in both robotic and laparoscopic techniques for the treatment of urologic tumors, specifically bladder, kidney, prostate, and testicular cancer. Following, they offer insights into a few of the novel approaches to preserving the bladder in difficult-to-treat patient populations, as well as advances in imaging and robotic technology.

Strategies in Bladder Preservation

Muscle Invasive Cancer Most patients with aggressive cancer invading the deep muscular layer of the bladder wall are recommended to have intravenous chemotherapy and bladder removal. "However, there is a very select group of patients for whom perhaps we can salvage the bladder," says Dr. Anderson. "These are patients who were told that they needed to have their bladder removed, and they say, 'I hear what you're saying, but I don't want that. I want you to do something less aggressive.' After counseling them extensively, we can sometimes create treatment plans to preserve the bladder."

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Laparoscopic Donor Nephrectomy: Continuing Refinements in the Standard of Care (continued from page 1)

"The biggest difference we see is in return to normal activity," says Dr. Del Pizzo, who has performed some 2,500 kidney transplants since joining Weill Cornell in 2000. "Ninety-five percent of laparoscopic donors achieve this benchmark in 28 days, while those who undergo open donor nephrectomy may take up to four months to achieve full return to normal activity."

The reduction in obstacles to live kidney donation via laparoscopic surgery is complemented by the development of more effective immune therapy, making it possible to match more live donors to recipients. In the early days of laparoscopic surgery in the mid-1990s, 65 percent of kidneys were from deceased donors and 35 percent from live donors. Today, those numbers are reversed.

"The less the donor has to go through, the more incentive there will be to donate," continues Dr. Del Pizzo. "Complete strangers now donate to one another, or genetic strangers, such as husband and wife – currently one of the more common transplants we do now. If you combine the improvement in immune therapy and the technological advancements of the donor operation – increased safety, less scarring, improved cosmesis, faster recovery and return to normal activity – most large centers like ours and those around the country are performing living donor transplants at a higher percentage because more people are willing to do it."

On the recipient side, live donation also confers benefits. "Typically, more kidneys procured from living donors will function immediately and for a longer time than those from a deceased donor where the kidney may be out of the donor's body for a day or longer looking for a match," Dr. Del Pizzo says. "With live donors, the kidney is removed, put on ice, and then within 30 minutes can be transplanted into the recipient. There's a higher three-year function rate of living kidneys compared to cadaveric kidneys, so we prefer a living kidney."

While all laparoscopic nephrectomies offer these benefits to living kidney donors, Dr. Del Pizzo often employs a surgical technique that represents another advance in the past five years: laparoendoscopic single site (LESS) surgery. "The standard laparoscopic technique involves three or four small incisions in addition to the two-to-three-inch incision needed to remove the kidney. In many cases, with single-site laparoscopy we're able to operate through the two-to-three-inch incision only," he explains. Results of a randomized prospective analysis conducted at the hospital showed not only a slightly reduced recovery time, but also better cosmesis and increased patient satisfaction.

Dr. Del Pizzo has also evaluated the use of robotic technology for live donor nephrectomy but has found that it does not offer an added benefit to standard laparoscopic surgery. "In my opinion the robot is better utilized for reconstructive urologic surgery, for example, when we take part of a kidney out due to a tumor and are then left with a defect in the remaining part of the kidney. The robot can be used to close that defect," he says.

With any laparoscopic nephrectomy, donors need to remain aware that if complications develop, such as bleeding, an open nephrectomy may become necessary. However, this is rare – occurring in fewer than one percent of cases. A finding of excessive scar tissue in the patient's abdomen may also dictate the need for an open surgery. "This can occur when a patient has had previous intra-abdominal surgery," says Dr. Del Pizzo.

The possibility of complications occurring underscores the need for new surgeons to be trained in both procedures, notes Dr. Del Pizzo. "I'm a firm believer that you really can't do laparoscopic surgery effectively if you're not trained in open surgery. When I trained, we did mostly open surgeries, but we were pioneers in laparoscopic surgery. Now laparoscopic surgery is part of most resident training programs, and there is typically a higher volume of minimally invasive surgery compared to open surgery. This can present a challenge when teaching our future leaders in surgery. Fortunately at Weill Cornell Medicine, our residents get extensive training in open surgery for more complex cases. In addition, they rotate through Memorial Sloan Kettering Cancer Center, where they do a lot of open surgery, and therefore are exposed to the gamut of urologic procedures."

Addressing a Growing Need Nationally

End-stage renal disease is on the rise, contributing to a long waiting list for kidney donors. Patients waiting for a kidney must often rely on dialysis for prolonged periods, increasing both the cost of care and associated morbidity. Efforts to encourage live donation include promotion of donor exchanges in which pairs of family members or spouses are matched with other such pairs for a "swap." The Kidney Transplant Program at Weill Cornell has helped facilitate such exchanges.

In recent years a number of altruistic donors have come forward – those without any direct relationship with the recipient and in some cases this has initiated a "transplant chain" leading to a series of successful transplants. Once the chain is initiated by an altruistic donor, someone in that individual's life then donates to another person in need thus continuing the donor-recipient chain. One of Dr. Del Pizzo's former patients, the father of a transplant recipient, became involved in this cause and established the National Kidney Registry after he was unable to donate to his daughter at the time of her transplant but was willing to donate to someone else in need in order to help her.

"Every time that happens, multiple people come off the list," says Dr. Del Pizzo. "It's a win-win."

Reference Article
Aull MJ, Afaneh C, Charlton M, Serur D, Douglas M, Christos PJ, Kapur S, Del Pizzo JJ. A randomized, prospective, parallel group study of laparoscopic versus laparoendoscopic single site donor nephrectomy for kidney donation. *American Journal of Transplantation.* 2014 Jul;14(7):1630-37.

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Current Perspectives in the Treatment of Bladder Cancer (continued from page 1)

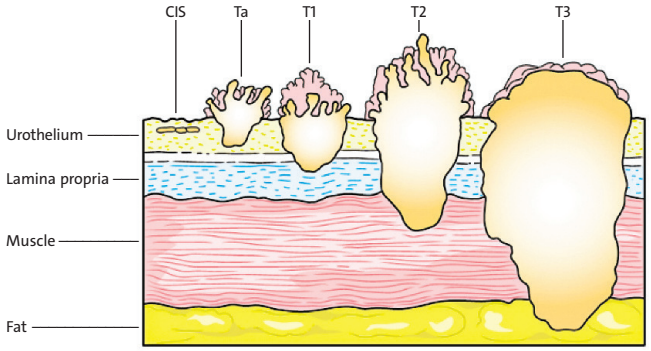
As Dr. Anderson explains, "We have described in a recent paper that if you're really good at selecting patients for bladder preservation, you have an excellent multidisciplinary team, and if the patients respond very well to chemotherapy, then it may be reasonable to consider not removing the bladder."

In a multicenter study, the Columbia urology team retrospectively reviewed the records of 148 patients with muscle invasive bladder cancer who elected surveillance following a clinically complete response to cystoscopic bladder resection and neoadjuvant chemotherapy from 2001 to 2017. These patients were advised to have a radical cystectomy but elected to preserve their bladders instead. A clinically complete response was defined as absent tumor on post-chemotherapy transurethral resection, negative cytology, and normal cross-sectional imaging. The researchers observed high rates of overall and disease specific survival in patients who achieved a clinically complete response to neoadjuvant chemotherapy, and few patients required bladder removal for a subsequent recurrence.

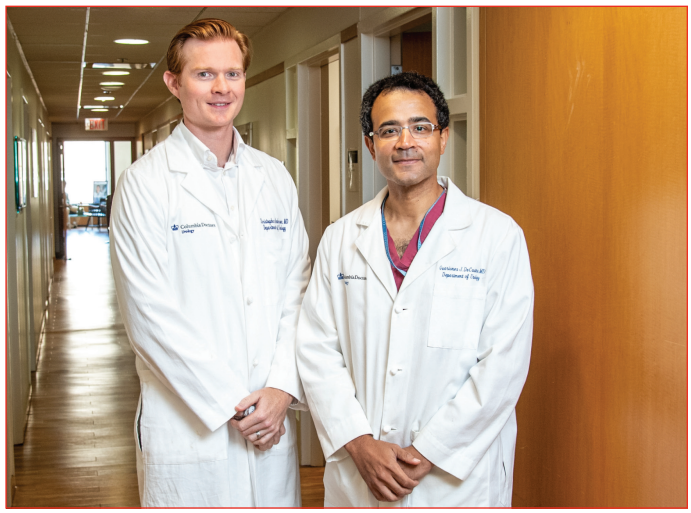
"At the very least, this is a controversial treatment, but there is considerable patient interest in bladder preservation," says Dr. Anderson. "Patients who are more likely to succeed with this approach have smaller tumors, a solitary tumor, tumors that are not blocking the kidney, and tumors that don't have any associated carcinoma *in situ*."

The trade-off with bladder preservation for patients that have a complete response to chemotherapy is a small increased risk of cancer death that may have been avoidable with an immediate surgery. However, this risk must be weighed against the risks of the surgery itself, which include major complications and even death. The Columbia researchers concluded that future studies are needed to improve patient selection for bladder preservation by identifying biomarkers predicting invasive relapse and developing novel imaging methods of early detection.

Bladder Cancer Staging



CIS: carcinoma *in situ*
Ta: non-invasive papillary carcinoma
T1: tumor invades lamina propria
T2: tumor invades muscularis propria
T3: tumor invades perivesical soft tissue
T4: tumor invades adjacent organs/structures



Dr. Christopher B. Anderson and Dr. G. Joel DeCastro

Non-Muscle Invasive Cancer Bacillus Calmette-Guerin or BCG is the most common intravesical immunotherapy for treating urothelial carcinoma of the bladder. "Historically, bladder-infused immunotherapy for cancer that has not invaded into the muscle reduces the chance that the cancer will progress to worse disease or recur," says Dr. DeCastro, noting that patients with cancers that are high grade and just shy of invading the muscle can also undergo BCG therapy.

> "Removing a bladder and doing a urinary diversion is a major undertaking. There's a subset of patients that we can actually prevent from having to undergo that surgery and that's very exciting."
>
> – Dr. G. Joel DeCastro

"Cystectomy is the standard of care for muscle invasive disease, as well as the standard of care for patients with non-muscle invasive disease that has recurred after getting BCG," continues Dr. DeCastro. "For patients who have BCG refractory bladder cancer and who refuse or can't tolerate cystectomy, we can offer a novel multidrug intravesical regimen consisting of cabazitaxel, gemcitabine, and cisplatin – CGC."

Dr. DeCastro and his colleagues, who just completed a five-year phase 1 clinical trial of CGC with 18 patients, are reporting very good results. "The underlying enthusiasm for CGC is that while we can perform cystectomy robotically with fewer incisions and less pain, it is still a major and life-changing surgery. Additional studies are necessary, but we're very excited about helping this BCG-unresponsive population. If we can actually prevent these patients from having to undergo major surgery, that is a big deal."

While the Columbia investigators believe this to be a promising new treatment, they note that it is yet to be fully investigated and that additional studies are needed. "We hope to be starting phase 1b/2 of the study this year," says Dr. DeCastro.

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Current Perspectives in the Treatment of Bladder Cancer (continued from page 3)

MRI versus CT for Greater Accuracy

The tools used to determine how aggressive and the extent of bladder cancer include cystoscopy and computed tomography. "The issue is that our ability to accurately stage the disease or estimate the extent of disease is somewhat limited because CT scans are not perfect," says Dr. Anderson. "A possible solution or improvement would be the use of MRI. The question is can MRI do a better job than CT of characterizing the extent or stage of disease to estimate risk and direct treatment? We're exploring that now – as are other investigators around the world – and have made some promising early observations."

Increasing Role of Robotics

Radical cystectomy is the surgical standard for invasive bladder cancer. At Columbia, Dr. Anderson and Dr. DeCastro are increasingly offering patients robot-assisted cystectomy. "We have found in our experience that patients do very well – they recover faster, the blood loss is less, and the pain after surgery is less," says Dr. DeCastro.

"Evidence now suggests that robotic surgery benefits patients in numerous ways," agrees Dr. Anderson. "There's a huge patient demand for it depending on the type of surgery, for example, with prostate cancer and kidney cancer. Given our expertise, we've been able to push the envelope and offer it to patients who might not be offered it elsewhere."

Both physicians emphasize that the robot is only a tool, but when used appropriately it does offer many advantages. "However, it's considered on a case-by-case basis," says Dr. DeCastro. "Some patients are not eligible for robotic surgery, and we may not recommend it. But that's part of the discussion we have in the clinic, and part of the difficult decisions we have to make."

Reference Article

Mazza P, Moran GW, Li G, Robins DJ, Matulay JT, Herr HW, DeCastro GJ, McKiernan JM, Anderson CB. Conservative management following complete clinical response to neoadjuvant chemotherapy of muscle invasive bladder cancer: Contemporary outcomes of a multi-institutional cohort study. *Journal of Urology*. 2018 Nov;200(5):1005-13.

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