

Upper Tract Urothelial Carcinomas (UTUCs)

Part II: UTUC Treatment Options

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Dr. Shabsigh: This is Ahmad Shabsigh, it's an honor to be on the panel, and thank you to Dr. Chamie for the beautiful, nice, introduction summarizing epidemiology and symptoms of upper tract urothelial carcinoma. In the next few minutes I'm gonna try to just give an overview of the treatment options for this rare, and sometimes difficult, disease.

So in general we can split the treatment for upper tract urothelial carcinomas in three different categories. Number one is what I tend to call nephron sparing or conservative management. We try to save the entire kidney, or part of the kidney, and try to preserve kidney function as much as possible, and for that we use the ureteroscopic technique that Dr. Chamie mentioned, and we try to ablate and destroy the tumor. Sometimes we give chemotherapy or immunotherapy in the pelvis or the ureter, and even in some cases, depending on the location of the tumor, we remove part of the ureter to get rid of the cancer.

Treatment Options

- Nephron sparing or conservative management (saving part or the entire kidney)
 - Ureteroscopic ablation
 - Intracavity therapy
 - Removal of the segment involved with cancer
- Radical nephroureterectomy (removing the kidney and the entire ureter)
- Systemic Chemotherapy

The second category of treatments is for more advanced disease, locally advanced disease, and in these cases we have to remove the kidney and the ureter. And in some more metastatic disease and locally even more aggressive disease we need to use chemotherapy.

How to Choose

- Location:
 - Kidney pelvis
 - Ureter (upper, mid, lower)
 - One side or both
 - Solitary kidney
- Size and number of tumors
- Pathology
 - Type
 - High grade vs low grade
 - Invasive
 - CIS
- Number of recurrences
- Imaging (invasive, hydronephrosis, metastasis)
- Kidney function and Other medical problems

So how do we decide? How does your doctor decide what to do? Well that depends on a lot of different factors. For example, the location of the tumor. Is it in the pelvis or the kidney? Is it at the beginning of the ureter, at the bottom part of the ureter? Is it on one side? Is it on both sides, both kidneys? Do you have one kidney, or do you have more than ... do you have two, more than one tumor? Sometimes the pathologist, when we do a biopsy, will tell us that you have a high grade disease, or invasive disease, and that can push us to do more aggressive treatment to

get rid of the cancer. Another factor is the number of times that the cancer came back. These cancers tend to come back after first treatment, and if this happens multiple times, or the recurrence is high volume disease, sometimes we cannot do anything but take the kidney and the ureter out. And for some patients with kidney function, you know, poor kidney function, we have to do conservative treatment to preserve kidney function and prevent the patient from moving to chemo dialysis.

So first conservative treatments. So, in general, and in a simple way, this is doing anything that ... using anything that we have to achieve cancer control while preserving the kidney. And for that we can do uteroscopy, just like what Dr. Chamie mentioned, go with the scope all the way through the urethra all the way up. Or, if that's not a good option, in some cases we have to go the other way round where we actually make a small incision in the back and we go into the kidney, and then we pass the scope all the way down from the kidney to the ureter, and get to the tumor and try to ablate it with laser and other techniques. And if we're able to achieve that for patients with more aggressive disease, especially high grade and where we have to preserve the kidney, we can use chemotherapy or immunotherapy inside the renal pelvis and the ureter, with some controversial results regarding this treatment.

Finally, we can consider part of conservative treatment is taking part of the ureter, where this is actually a major operation, however, because we are preserving the kidney itself, and taking part of the ureter, which is usually at the bottom of the ureter, if you have a tumor at the bottom you take it out and then you connect the ureter back to the bladder. This way we have the kidney preserved.

To achieve control endoscopically with the ureter scope we use different techniques. We can use biopsy, we can use basket, we can use laser to ablate and burn the tumor and we can use electricity. In some cases if we go in through the skin to the kidney we can use an instrument called a resectoscope, where we can resect and remove the tumor and preserve the kidney.

So again, regarding segmental resection, or trying to remove part of the ureter that is involved with cancer. This is usually preserved for very specific situations, for example, if the tumor is at the bottom of the ureter, and in some cases we do it for tumors in the middle. Very rare to do it for tumors in the pelvis or the kidney. Again, we will remove that part of the ureter and reconnect the ureter back to the bladder.

Segmental Resection

- Mostly for polyps/tumors in the lower part of the ureter
- Removal of part of the ureter and reconnecting
- Remove of part of the ureter and reimplant to the bladder
- Open or robotic surgery

So after you do the first treatment, what do we have to do? Well, we have to follow up to make sure that the cancer doesn't come back, and for that we use urine cytology, genetic testings of the urine, and then we do uteroscopy where we go up and look again in the kidney and the ureter using the ureter scope, and that can be done mostly in the operative room under general anesthesia and sometimes it can be done in the office. We also utilize the same imaging studies that we used for diagnosis of upper tract urothelial carcinoma to rule out recurrence, so we use CT urograms, MRIs and retrograde pyeloureterogram.

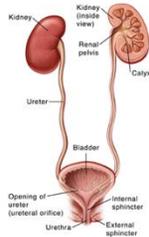
So when do we consider conservative therapy? Well mostly for patients with low grade disease, non-invasive disease, and low volume disease, and patients who have disease of, you know, lower part of the ureter. Sometimes, although it's rare, the disease can happen on both sides, and because we don't want to lose both kidneys we do our best to do conservative treatment, at least the side where there is less aggressive disease. Some patients cannot tolerate major surgery to remove the kidney, and in these patients with a lot of medical problems we also tend to do more conservative therapy, similarly to patients who have poor kidney function.

So one of the things that I get asked all the time, "So doctor, you told me that you had two small tumors, you know, very small tumors less than quarter of an inch. Why do you have to take the entire kidney and ureter? Why can't you use a ureter scope and destroy them?" Well that's related to the nature of the disease. The ureter has a very small narrow lumen, and going up with the scope and being able to guarantee complete staging and accurate staging, in addition to destruction of all the tumors, is not very reliable. So even though sometimes we have small tumors we are pushed to do more aggressive treatment by removing the kidney and the ureter. For patients who are well selected, doing conservative therapy achieves good cancer control almost similar to the cancer control that we see for patients who had their kidney and ureter removed.

So what about more aggressive disease if you have stage 2 or 3 upper tract urothelial carcinoma? That's when we use radical surgery with or without chemotherapy. What does it mean for nephroureterectomy? Well that means removing the kidney, removing the entire ureter all the way to part of the bladder. In addition to that, sometimes we remove the lymph nodes around the ureter and the kidney to make sure that the disease did not spread to the lymph nodes and, hopefully, control the

Nephroureterectomy

- Removal of the entire kidney and the ureter with or without regional lymph nodes



cancer. There are a few ways we can do this. We can do open surgery, where you have one incision which extends from the ribcage all the way down to the lower part of the abdomen, or it can be more than one incision. We can also use minimally invasive surgery, laparoscopic surgery or robotic surgery, where you have smaller incisions. Of note, the robot doesn't do anything by itself, the surgeon is in control and uses the robot to put instrument inside the abdomen, and these are used to remove the kidney, and the ureter, and the lymph nodes.

What should you expect after surgery? Well, it depends on the technique. Most patients will stay in the hospital for one to five days. Most of them will be able to eat the same day or the next day. Usually the surgeon will leave a catheter to drain the bladder and to give the bladder a chance to heal for a few days after surgery in addition to a drain, and I would say the vast majority of patients will go back to almost normal function within three to six weeks after radical nephroureterectomy.

Finally, we'll talk about systemic chemotherapy. So patients who have metastatic upper tract urothelial carcinoma usually need to get chemotherapy before surgery. There are multiple studies in the last few years that showed there is benefit to doing that before we remove the kidney. This is an analysis that combined two of the studies that showed that giving chemotherapy prior to surgery is beneficial. This is a follow up chart also showing the same thing.

Dr. Steinberg: Have there been any randomized studies to show that? Or is this pretty much looking at a number of smaller series and reviews?

Dr. Shabsigh: Dr. Steinberg's absolutely correct. So there are, as far as I know, no good randomized clinical trials showing the benefit of giving chemotherapy in advance. This is the best we have right now and, hopefully, in the near future, I know of one clinical trial that is looking at this. Hopefully we'll have that in the next couple of years.

So why chemotherapy? It may improve survival. If there is locally advanced disease sometimes giving the chemotherapy before removing the kidney can shrink the tumor and improve the chance of resection, depends on the stage of the disease and if there is metastatic distant spread of the disease. The chemotherapy can go between two to six months.

Stephanie: Thank you for that really nice overview of the treatment options. Certainly they're very dramatic treatment options and now, Dr. Steinberg, we're gonna talk a little bit about what's on the horizon, right? A little bit about where we're going with clinical trials and how we're trying to improve care for patients with upper tract urothelial carcinoma.

Dr. Steinberg: Yes. That was an excellent talk and I'm sure there's going to be a lot of questions, specifically on treatment, because while Dr. Shabsigh made it seem very straight forward and simple, there are a lot of different nuances and controversies and patients sometimes, as we know, are really quite confused as to what is the best treatment for them for their upper tract disease. So I'm sure there are gonna be a lot of questions for Dr. Shabsigh and Dr. Linehan.

