

Introduction: The aim was to evaluate ChatGPT generated responses to patient-important questions regarding upper tract urothelial carcinoma (UTUC).

Material and methods: Fifteen common inquiries asked by patients regarding UTUC were assigned to 4 categories: general information; symptoms and diagnosis; treatment; and prognosis. These questions were entered into ChatGPT and its responses were recorded. In every answer 5 criteria (adequate length, comprehensible language, precision in addressing the question, compliance with European Association of Urology guidelines and safety of the response for the patient) were assessed by the urologists using a numerical scale of 1–5 (a score of 5 being the best).

Results: Sixteen questionnaires were included. A score of five was assigned 336 times (28.0%); 4 – 527 times, (43.9%); 3 – 268 times (22.3%); 2 – 53 times (4.4%); and 1 – 16 times (1.3%). The average overall score was 3.93. Responses to each question received average scores within the range 3.34–4.18. Answers regarding “general information” were graded the highest – mean score 4.14. Artificial intelligence scored the lowest in the “treatment” category – mean score 3.68. A mean score of 4.02 was given for the safety of the response. However, a few urologists considered several answers as unsafe for the patient, by grading them 1 or 2 in this criterion.

Conclusions: ChatGPT does not provide fully adequate information on UTUC, and inquiries regarding treatment can be misleading for the patients. In particular cases, patients might receive potentially unsafe answers. However, ChatGPT can be used with caution to provide basic information regarding epidemiology and risk factors of UTUC.

Key words: AI, artificial intelligence, upper tract urothelial carcinoma, urologic oncology, ChatGPT, UTUC.

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Performance of ChatGPT in providing patient information about upper tract urothelial carcinoma

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Introduction

Upper-tract urothelial carcinoma (UTUC) is a relatively rare malignancy, which accounts for 5–10% of all urothelial cancers; however, its incidence has risen in the last decades [1, 2]. It has been suggested that the increase is caused by the ageing of the population and the development of diagnostic measures, including high resolution imaging, novel biomarkers and flexible ureterorenoscopes [1, 3, 4].

Globalisation and the widespread availability of the internet have led to a shift in the default source for seeking medical advice. According to the literature, the main sources of medical information utilised by the patients are print materials, the internet (especially internet forums), TV and family, as well as physicians' consultations [5, 6].

Unfortunately, the rarity of UTUC may hinder the patients' access to reliable information on the disease. Internet websites and forums often provide faulty data, which may be potentially harmful for the patients. Crucially, even healthcare professionals may be unfamiliar with the disease, causing patients' anxiety. As UTUC is characterised by poor survival outcomes, it is important to provide reliable and understandable information in order to ensure psychological comfort and improve the compliance with treatment and follow-up protocols [7].

Nonetheless, within the last few years, a new possible information source has arisen. Large language models (LLMs), such as ChatGPT, powered by artificial intelligence (AI), are dynamically growing in popularity in the medical field. Even though AI is expected to assist with multiple tasks, LLMs can have limitations in medicine, as they can spread misinformation and reproduce authors' bias [8]. Nowadays, AI chatbots are widely accessible, but patients might not be able to verify the correctness of LLMs' responses.

This study aimed to evaluate the ChatGPT generated responses to patient-important questions regarding UTUC.

Material and methods

We searched for common questions asked by patients regarding UTUC. Websites, internet fora, and social media were analysed. Additionally, patients admitted to our department for UTUC were interviewed and their questions were recorded. Then, the 15 most relevant and often repeated inquiries were selected and assigned to 4 categories: general information; symptoms and diagnosis; treatment; and prognosis (Fig. 1, Table 1).

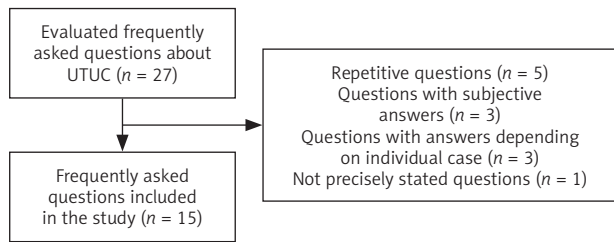


Fig. 1. Flowchart of the question selection process

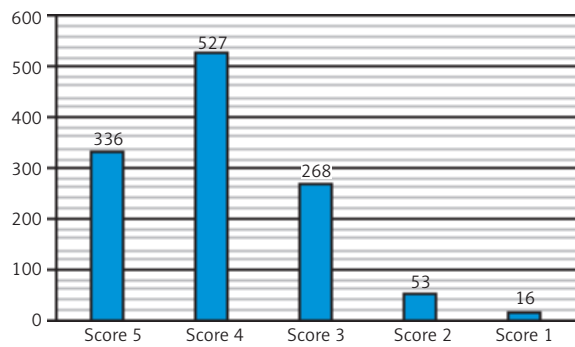


Fig. 2. Collective score distribution graph

These questions were entered into the AI chatbot ChatGPT 3.5 (OpenAI) in English language on the 5th of March 2024 and its responses were recorded without alterations. Each question was asked only once.

In order to evaluate the responses, a questionnaire was created. It included the 15 questions with ChatGPT responses and the marking areas. In every answer 5 criteria (adequate length, use of language comprehensible for the patient, precision in addressing the question, compliance with European Association of Urology (EAU) guidelines and safety of the response for the patient) were assessed using a numerical scale of 1–5 (with 5 as the best score). Moreover, the respondents were asked about their gender, age and experience in the field of urology.

Urologists with vast experience in urothelial cancer treatment were invited to anonymously and independently provide their scores for the ChatGPT answers.

A descriptive statistical analysis was conducted using Excel Version 16 (Microsoft Corporation, USA).

Results

Sixteen correctly filled questionnaires were included in the study. Thirteen of the respondents were attending urologists, while 3 were urology residents. 81.3% of the participants were male.

In the collective score distribution analysis, the following results were observed: a score of 5 was assigned 336 times (28.0%); a score of 4 – 527 times (43.9%); a score of 3 – 268 times (22.3%); a score of 2 – 53 times (4.4%); and a score of 1 – 16 times (1.3%) (Fig. 2).

Table 2. Mean scores of the answers to the questions

Question	All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Mean score (standard deviation)	3.93 (0.89)	4.15 (0.68)	4.15 (0.80)	4.18 (0.95)	4.08 (0.77)	4.06 (0.75)	4.08 (0.80)	3.84 (0.89)	3.71 (1.15)	3.93 (0.80)	3.34 (1.18)	3.78 (0.74)	3.90 (0.84)	3.89 (0.84)	3.93 (0.85)	3.94 (0.84)

Table 1. List of included questions concerning upper tract urothelial carcinoma

General information
What is UTUC?
How common is UTUC?
What are the risk factors of UTUC?
What is the difference between UTUC, bladder cancer and kidney cancer?
Symptoms and diagnosis
What are the symptoms of UTUC?
How to diagnose UTUC?
What are the stages of UTUC?
What is the difference between low- and high-risk UTUC?
Treatment
How is UTUC treated?
Is it possible to cure UTUC without surgery?
How to treat bilateral UTUC?
Prognosis
What are the complications of UTUC?
How long will I live with UTUC?
What is the probability of UTUC recurrence?
What are the complications of UTUC treatment?

UTUC – upper tract urothelial carcinoma

The average overall score was 3.93 (SD = 0.89). ChatGPT responses to each question received average scores ranging from 3.34 (SD = 1.18) to 4.18 (SD = 0.95) (Table 2). The question “Is it possible to cure UTUC without surgery?” received the lowest mean score. On the other hand, AI scored the highest on the question “What are the risk factors of UTUC?”

Mean scores considering the division of the questions into 4 categories are presented in Table 3. ChatGPT responses regarding “general information” were graded the highest, with a mean score of 4.14 (SD = 0.80). “Symptoms and diagnosis”, as well as “prognosis” categories received average scores of 3.92 (SD = 0.93) and 3.91 (SD = 0.84) respectively. AI scored the lowest in the “treatment” category with a mean score of 3.68 (SD = 0.96).

Average scores of the 5 assessed criteria are presented in Table 4. A mean score of 4.02 (SD = 0.83) was given for the use of comprehensible language and 4.02 (SD = 0.93) for the safety of the response for the patient. However, a few urologists considered several answers as unsafe for the patient, by scoring them 1 or 2 for this criterion. Regarding adequate length, compliance with EAU guidelines and precision in addressing the question, ChatGPT averaged 3.99 (SD = 0.86), 3.89 (SD = 0.84) and 3.72 (SD = 0.97), respectively.

Discussion

In this study we carried out a preliminary non-comparative analysis of the performance of ChatGPT in answering the questions regarding UTUC. Sixteen experienced physicians who specialise in UTUC subjectively marked the answers on a scale of 1–5 (5 being the best score). To date there is no published research on this particular topic. Nevertheless, the performance of AI in oncologic urology has recently been evaluated by a number of studies on different neoplasms, including renal cell carcinoma, bladder, prostate and testicular cancer [9–12].

Chatbot's answers were most commonly graded 4, which does not deviate from the overall mean. However, scores of 1, 2 and 3 were given to 28.1% of the responses, showing suboptimal performance of ChatGPT.

In the present study the mean overall score of ChatGPT's answers was 3.93. Therefore, it is clear that under no circumstances can ChatGPT substitute a medical professional as a primary source of knowledge on UTUC. Nevertheless, the score indicates that AI can provide patients with some basic information of mediocre quality.

The 15 responses of AI received scores of 3.34–4.18. The highest score was given to the question about risk factors of UTUC. This result is encouraging, as ChatGPT seems to address the public health and prophylaxis issue properly. Therefore, people who might not have urological cancer and do not visit a urologist might receive true information from the chatbot. On the other hand, the question whether it is possible to cure UTUC without surgery obtained the lowest score. It is worth noting that patients diagnosed with UTUC might use ChatGPT to look for alternative treatment methods and unverified cures for their disease, which can be extremely harmful.

The performance of ChatGPT varied between different categories of the questions. According to this study, patients would receive the best information on general knowledge about UTUC. In contrast, the worst performance of AI was recorded in the "treatment" category. Scores on symptoms, diagnosis and prognosis answers were very close to the overall mean. Therefore, ChatGPT might serve as a tool that explains the basics of UTUC to the patients. However, it should not be a primary resource in more advanced topics, especially regarding treatment of UTUC.

Finally, various aspects of the answers were assessed by the respondents based on 5 criteria: length, language, precision, compliance with EAU guidelines and safety. The most favourable scores were given for comprehensible language and the safety of the response for the patient. Nevertheless, we cannot classify ChatGPT as a safe tool, due to several 1 and 2 scores for this criterion. In order to avoid dangerous scenarios for the patient, information from ChatGPT should always be verified by a healthcare professional. Also, urologists thought that the chatbot's answers were not precise enough, giving it the lowest score of all criteria.

Flaws in ChatGPT generated responses might be caused by the rarity of UTUC with scarce data on the disease and frequently changing guidelines that vary significantly de-

Table 3. Mean scores of each question category

Question category	Mean score (standard deviation)
General information	4.14 (0.80)
Symptoms and diagnosis	3.92 (0.93)
Treatment	3.68 (0.96)
Prognosis	3.91 (0.84)

Table 4. Mean scores of each of the 5 assessed criteria

Assessed criterion	Mean score (standard deviation)
Adequate length	3.99 (0.86)
Use of language comprehensible for the patient	4.02 (0.83)
Precision in addressing the question	3.72 (0.97)
Compliance with EAU guidelines	3.89 (0.84)
Safety of the response for the patient	4.02 (0.93)

UTUC – upper tract urothelial carcinoma

pending on the publishing scientific association. Moreover, ChatGPT's 3.5 database was last updated in January 2022, and it does not have access to real-time information. Therefore, it is not able to provide truly up-to-date responses on UTUC.

In the literature, similar articles about oncologic urology may be found. Ozgor *et al.* evaluated ChatGPT's answers to frequently asked questions in topics regarding prostate, bladder, kidney and testicular cancers. The mean scores in this study were 4.4–4.5 out of 5. Moreover, in each cancer, 5 was the most commonly given score and the authors stated that ChatGPT is a valuable tool in addressing general questions on urological cancers. However, these answers were evaluated only by 3 physicians [9]. In another study on ChatGPT in prostate cancer, 2 urologists marked the answers 3.62 out of 5 on average [10]. Caglar *et al.* found that AI generated completely correct responses to 94.2% of the questions regarding prostate cancer [11]. However, only 76.2% of the questions prepared according to the strong recommendations of the EAU guideline were answered fully correctly [11]. Lastly, 70.8% of urologists thought that ChatGPT could not replace a urologist in answering questions regarding renal-cell carcinoma [12].

There is no consensus regarding ChatGPT's accuracy in answering questions on various topics. Many studies presented more encouraging results than our research. Chatbot's responses were completely accurate in 92%, 94.6% and 97.9% of the questions on paediatric urology, urolithiasis and andrology, respectively [13–15]. Moreover, AI was accurate in 96.9% of the inquiries about common cancer myths and misconceptions [16]. Ozgor *et al.* found that ChatGPT answered 91.4% of the questions about endometriosis correctly, with the worst performance in the "treatment" category [17]. On the other hand, AI's responses regarding vaccination myths and misconceptions were

accurate (85.4%), but one question was misinterpreted [18]. In addition, one study reported that 25% of ChatGPT's responses on liver cancer were inaccurate and it did not provide reliable information on the topic [19]. Finally, Ali found that LLMs' answers on lacrimal drainage disorders were suboptimal, with 40%, 35% and 25% graded as correct, partially correct and incorrect, respectively [20].

It is worth noting that all the analysed studies had heterogeneous methodologies with different numbers of questions and evaluators, as well as a variety of assessment scales. What is more, inquiries were not uniform in terms of difficulty. Finally, the results of the studies depended solely on the opinions of various experts. Therefore, it is not possible to compare these reports accurately.

Nonetheless, AI-based medical technologies are being rapidly developed and have the potential to improve multiple medical fields. Prostate cancer is an excellent example of the potential implementation of AI in urology. Numerous projects have been created where AI was able to facilitate pathological and radiological analysis in prostate cancer. Moreover, AI was used in genetic analysis and optimised radiotherapy of the carcinoma [21]. Certainly, in the future dedicated AI technologies will be invented for urological patients. We are sure that a chatbot trained specifically on verified data would provide excellent medical information for patients.

This study has some limitations that need to be disclosed. Firstly, the assessment of the questions was subjective and the number of respondents was low. Secondly, the study was non-comparative. Finally, potential variation in the structure of the questions and the version of ChatGPT might influence the quality of the responses.

Conclusions

ChatGPT does not provide fully adequate information on UTUC and inquiries regarding UTUC treatment can be misleading for the patients. What is more, in particular cases, patients might receive answers that are potentially unsafe.

However, ChatGPT can be used with caution to provide basic information regarding epidemiology and risk factors of the disease.

Disclosures

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2. Assistance with the article: None.
3. Financial support and sponsorship: None
4. Conflicts of interest: None.

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Appendix

GENERAL INFORMATION

1. What is UTUC?

UTUC stands for Upper Tract Urothelial Carcinoma. It is a type of cancer that originates in the lining of the upper urinary tract, which includes the renal pelvis (where the kidney connects to the ureter) and the ureter (the tube that carries urine from the kidney to the bladder). UTUC is relatively rare compared to other types of urothelial carcinoma, such as bladder cancer, but it can be aggressive and potentially life-threatening if not diagnosed and treated early.

The most common symptom of UTUC is blood in the urine (hematuria), which may be visible to the naked eye or detected microscopically. Other symptoms can include flank pain, abdominal pain, a palpable mass in the abdomen, and urinary tract infections. However, UTUC can also be asymptomatic, especially in the early stages, making it challenging to detect.

Diagnosis of UTUC typically involves imaging tests such as CT scans or MRIs, as well as endoscopic procedures such as ureteroscopy or retrograde pyelography. A biopsy is usually performed to confirm the presence of cancerous cells.

Treatment options for UTUC may include surgery (such as nephroureterectomy, which involves removing the affected kidney and ureter), chemotherapy, radiation therapy, and immunotherapy. The choice of treatment depends on various factors, including the stage and grade of the cancer, the patient's overall health, and their preferences.

Regular follow-up care is essential for individuals diagnosed with UTUC to monitor for any recurrence or progression of the disease. Early detection and prompt treatment can improve outcomes and prognosis for patients with UTUC.

2. How common is UTUC?

Upper tract urothelial carcinoma (UTUC) is a relatively rare type of cancer compared to other urothelial carcinomas that occur in the bladder. However, its incidence has been increasing over the past few decades. The exact prevalence can vary depending on factors such as geographic location, age, gender, and risk factors such as smoking and occupational exposures to chemicals.

In general, UTUC accounts for about 5-10% of all urothelial carcinomas. It's more common in certain regions with a higher prevalence of risk factors such as tobacco use and exposure to certain chemicals. Additionally, the incidence tends to increase with age, with most cases diagnosed in people over 60 years old.

While UTUC is relatively rare compared to bladder cancer, it's important to be aware of its existence and risk factors, especially for individuals with a family history of urothelial carcinoma or those who have been exposed to known carcinogens. Early detection and treatment are crucial for better outcomes in UTUC cases.

3. What are the risk factors of UTUC?

Upper tract urothelial carcinoma (UTUC) is a cancer that occurs in the lining of the urinary tract system, primarily in

the renal pelvis and ureter. Several risk factors have been identified for the development of UTUC:

1. **Smoking**: Tobacco smoke contains carcinogens that can increase the risk of developing UTUC.

2. **Exposure to Chemicals**: Occupational exposure to certain chemicals such as aromatic amines and polycyclic aromatic hydrocarbons (found in certain industries like dye, textile, and rubber manufacturing) has been associated with an increased risk of UTUC.

3. **Age**: UTUC is more common in older adults, with the risk increasing with age.

4. **Gender**: Men are at a higher risk of developing UTUC compared to women.

5. **Chronic Kidney Disease (CKD)**: Individuals with CKD, especially those on dialysis, are at an increased risk of UTUC.

6. **Bladder Cancer History**: Individuals with a history of bladder cancer have an increased risk of developing UTUC, possibly due to shared risk factors and genetic predisposition.

7. **Hereditary Conditions**: Rare hereditary conditions such as hereditary nonpolyposis colorectal cancer (HNP-CC) or Lynch syndrome and certain genetic mutations (e.g., mutations in the BRCA1 and BRCA2 genes) increase the risk of UTUC.

8. **Arsenic Exposure**: Chronic exposure to high levels of arsenic in drinking water has been associated with an increased risk of UTUC.

9. **Cyclophosphamide Exposure**: Long-term use of cyclophosphamide, a chemotherapy drug used to treat various conditions including cancer and autoimmune diseases, has been linked to an increased risk of UTUC.

10. **Chronic Inflammation**: Chronic inflammation of the urinary tract, possibly due to conditions such as urinary stones, chronic urinary tract infections, or certain inflammatory disorders, may increase the risk of UTUC.

11. **Analgesic Abuse**: Prolonged and excessive use of certain analgesics, particularly phenacetin-containing compounds, has been associated with an increased risk of UTUC.

12. **Hydronephrosis**: Chronic obstruction and dilation of the upper urinary tract (hydronephrosis) may increase the risk of UTUC.

It's important to note that while these factors may increase the likelihood of developing UTUC, not everyone with these risk factors will develop the disease, and individuals without these risk factors can still develop UTUC. Regular medical check-ups and screenings are important for early detection and management of UTUC, especially in individuals with known risk factors.

4. What is the difference between UTUC, bladder cancer and kidney cancer?

UTUC (Upper Tract Urothelial Carcinoma), bladder cancer, and kidney cancer are all types of cancers that can affect the urinary system, but they originate in different parts of the urinary tract and have distinct characteristics:

1. UTUC (Upper Tract Urothelial Carcinoma):

– UTUC develops in the lining of the upper urinary tract, which includes the renal pelvis (where the kidney collects urine before it moves to the ureter) and the ureter (the tube that carries urine from the kidney to the bladder).

– Risk factors for UTUC include smoking, exposure to certain chemicals, chronic kidney inflammation, hereditary factors, and certain genetic conditions.

– Common symptoms of UTUC may include blood in the urine (hematuria), flank pain, and urinary tract infections.

– Diagnosis is typically made through imaging tests (such as CT scans or MRI) and endoscopic procedures (such as ureteroscopy) to visualize the upper urinary tract and obtain tissue samples for biopsy.

– Treatment options for UTUC may include surgery (such as nephroureterectomy to remove the affected kidney and ureter), chemotherapy, radiation therapy, and immunotherapy.

2. Bladder Cancer:

– Bladder cancer originates in the bladder, which is a hollow organ located in the pelvis that stores urine before it is eliminated from the body.

– Risk factors for bladder cancer include smoking, exposure to certain chemicals (such as those found in tobacco smoke and industrial chemicals), chronic bladder inflammation, older age, male gender, and a family history of bladder cancer.

– Common symptoms of bladder cancer may include blood in the urine, changes in urinary habits (such as increased frequency or urgency), pelvic pain, and back pain.

– Diagnosis is typically made through cystoscopy (a procedure to visualize the inside of the bladder) and biopsy of suspicious areas.

– Treatment options for bladder cancer may include surgery (such as transurethral resection of the bladder tumor or radical cystectomy), chemotherapy, radiation therapy, and immunotherapy.

3. Kidney Cancer (Renal Cell Carcinoma):

– Kidney cancer originates in the kidney, which is responsible for filtering waste products from the blood to form urine.

– The most common type of kidney cancer is renal cell carcinoma (RCC), which accounts for the majority of kidney cancer cases.

– Risk factors for kidney cancer include smoking, obesity, high blood pressure, certain genetic conditions (such as von Hippel-Lindau syndrome), and exposure to certain chemicals.

– Common symptoms of kidney cancer may include blood in the urine, flank pain, a palpable mass or lump in the abdomen or side, and unintentional weight loss.

– Diagnosis is typically made through imaging tests (such as CT scans or MRI) and biopsy of suspicious kidney lesions.

– Treatment options for kidney cancer may include surgery (such as nephrectomy to remove part or all of the affected kidney), targeted therapy, immunotherapy, and radiation therapy.

In summary, while UTUC, bladder cancer, and kidney cancer all involve malignancies of the urinary system, they

differ in terms of their location of origin, risk factors, symptoms, diagnostic approaches, and treatment strategies. It's essential for individuals to be aware of the differences between these types of cancers and to seek prompt medical attention if they experience any concerning symptoms.

SYMPTOMS AND DIAGNOSIS

5. What are the symptoms of UTUC?

The symptoms of upper tract urothelial carcinoma (UTUC) can vary depending on the location and stage of the cancer. Some common symptoms associated with UTUC include:

1. ****Blood in the Urine (Hematuria)**:** This is one of the most common symptoms of UTUC. Blood in the urine can range from being microscopic (not visible to the naked eye) to gross hematuria, where blood is visible in the urine.

2. ****Flank Pain**:** Pain or discomfort in the side of the body (flank) where the affected kidney is located. This pain may be persistent or intermittent and can vary in intensity.

3. ****Abdominal Pain or Mass**:** Some individuals may experience abdominal pain or feel a mass in the abdominal area. This can occur as the tumor grows and may be associated with the involvement of nearby structures.

4. ****Changes in Urinary Habits**:** UTUC may cause changes in urinary habits, such as increased frequency of urination, urgency, or difficulty urinating.

5. ****Unexplained Weight Loss**:** Weight loss that occurs without dieting or changes in activity level may be a symptom of advanced UTUC or metastasis (spread) to other parts of the body.

6. ****Fatigue**:** Generalized fatigue or weakness may occur as a result of the cancer's effects on the body, including anemia or metabolic changes.

7. ****Swelling in the Legs**:** In some cases, UTUC can cause blockage of the urinary tract, leading to swelling in the legs due to fluid buildup (edema).

It's important to note that these symptoms are not specific to UTUC and can also be caused by other conditions such as urinary tract infections, kidney stones, or benign kidney tumors. However, if any of these symptoms persist or are accompanied by other concerning signs, it's essential to consult a healthcare professional for further evaluation and diagnosis. Early detection and treatment can improve outcomes for individuals with UTUC.

6. How to diagnose UTUC?

Diagnosing upper tract urothelial carcinoma (UTUC) typically involves a combination of medical history review, physical examination, imaging studies, and diagnostic procedures. Here are the steps commonly involved in diagnosing UTUC:

1. ****Medical History and Physical Examination**:** The healthcare provider will review the patient's medical history and conduct a physical examination. They will inquire about symptoms such as blood in the urine (hematuria), flank pain, or changes in urinary habits.

2. ****Urinalysis**:** A urinalysis may be performed to check for the presence of blood, abnormal cells, or other signs of urinary tract abnormalities.

3. **Imaging Studies**:

– **Ultrasound**: Ultrasound imaging may be used initially to evaluate the kidneys and urinary tract. It can help identify abnormalities such as tumors or kidney stones.

– **Computed Tomography (CT) Scan**: CT scans provide detailed images of the urinary tract and surrounding structures. They can help detect tumors, assess their size and extent, and identify any spread to nearby lymph nodes or other organs.

– **Magnetic Resonance Imaging (MRI)**: MRI may be used in some cases to further evaluate UTUC, especially if there are concerns about radiation exposure or if additional information is needed beyond what a CT scan provides.

4. **Ureteroscopy**: Ureteroscopy involves passing a thin, flexible tube with a camera (ureteroscope) through the urethra and into the ureter and kidney. This allows direct visualization of the inside of the urinary tract, including any abnormalities such as tumors. During ureteroscopy, biopsies may also be taken for further evaluation.

5. **Biopsy**: Tissue samples (biopsies) may be obtained during ureteroscopy or other procedures for histological examination. Biopsy results confirm the presence of cancer and provide information about the cancer's grade and stage.

6. **Cystoscopy**: In some cases, a cystoscopy may be performed to evaluate the bladder for signs of cancer. This involves inserting a thin, flexible tube with a camera (cystoscope) through the urethra and into the bladder.

7. **Staging**: Once UTUC is diagnosed, further staging tests may be performed to determine the extent of the cancer and whether it has spread to other parts of the body. This may include additional imaging studies such as chest X-rays, bone scans, or positron emission tomography (PET) scans.

Diagnosing UTUC requires a comprehensive approach involving multiple diagnostic modalities to accurately assess the extent of the disease and plan appropriate treatment. Early detection and diagnosis are crucial for optimizing treatment outcomes and prognosis.

7. What are the stages of UTUC?

The staging of Upper Tract Urothelial Carcinoma (UTUC) is typically based on the TNM staging system, which assesses the extent of the primary tumor (T), the involvement of regional lymph nodes (N), and the presence of distant metastasis (M). The stages range from stage 0 to stage IV, with lower stages indicating cancer that is confined to the urinary tract and higher stages indicating more advanced disease. Here's a brief overview of the stages:

1. **Stage 0 (Ta and Tis)**: Also known as carcinoma in situ (CIS) or non-invasive papillary carcinoma, this stage involves cancer cells confined to the inner lining of the renal pelvis or ureter. It has not invaded the deeper layers of the urinary tract wall.

2. **Stage I**: Cancer has invaded the connective tissue beneath the lining of the renal pelvis or ureter but has not spread beyond the urinary tract.

3. **Stage II**: Cancer has invaded the muscle layer of the renal pelvis or ureter but is still confined to the urinary tract.

4. **Stage III**: At this stage, cancer has spread beyond the renal pelvis or ureter to nearby tissues, organs, or lymph nodes but has not reached distant sites.

5. **Stage IV**: Cancer has metastasized to distant organs or tissues, such as the liver, lungs, bones, or other distant lymph nodes.

Staging helps guide treatment decisions and provides information about prognosis. Early-stage UTUC (stages 0, I, and II) is often treated with surgery to remove the affected kidney and ureter (nephroureterectomy) or with kidney-sparing procedures for select cases. Advanced-stage UTUC (stages III and IV) may require a combination of surgery, chemotherapy, radiation therapy, and/or immunotherapy.

It's important to note that staging is determined based on various factors, including imaging studies, biopsies, and surgical findings, and it may vary for each individual case. Treatment plans are often tailored to the specific characteristics of the cancer and the patient's overall health.

8. What is the difference between low- and high-risk UTUC?

In upper tract urothelial carcinoma (UTUC), tumors are often classified into low- and high-risk categories based on various factors, including tumor characteristics, stage, grade, and likelihood of disease recurrence or progression. Here's how low- and high-risk UTUC differ:

1. **Low-Risk UTUC**:

– **Low-grade tumors**: Tumors with low-grade urothelial carcinoma cells are considered low-risk. Low-grade tumors tend to have less aggressive behavior and are associated with a lower likelihood of progression or recurrence.

– **Non-invasive tumors**: Low-risk UTUC tumors are typically confined to the mucosa (inner lining) of the urinary tract and have not invaded deeper layers of tissue.

– **Small tumor size**: Low-risk UTUC tumors are often smaller in size, which may indicate a lower risk of spreading or metastasis.

– **Absence of lymphovascular invasion**: Lymphovascular invasion refers to the presence of cancer cells within blood vessels or lymphatic channels. Low-risk UTUC tumors typically lack lymphovascular invasion.

– **Favorable location**: Tumors located in the distal ureter (closer to the bladder) or renal pelvis may be considered low-risk due to easier surgical access and lower risk of recurrence.

2. **High-Risk UTUC**:

– **High-grade tumors**: Tumors with high-grade urothelial carcinoma cells are considered high-risk. High-grade tumors are more aggressive and have a higher likelihood of progression or recurrence.

– **Invasive tumors**: High-risk UTUC tumors have invaded deeper layers of the urinary tract, such as the muscularis propria or surrounding tissues.

– **Large tumor size**: High-risk UTUC tumors are often larger in size, which may indicate a greater potential for spread or metastasis.

– **Presence of lymphovascular invasion**: High-risk UTUC tumors may exhibit lymphovascular invasion, indicating a higher risk of metastasis to lymph nodes or distant organs.

– Unfavorable location: Tumors located in the proximal ureter (closer to the kidney) or involving the renal pelvis may be considered high-risk due to challenges in surgical management and higher risk of recurrence.

Overall, the distinction between low- and high-risk UTUC helps guide treatment decisions and prognosis. Low-risk tumors may be managed with less aggressive approaches such as endoscopic resection or partial nephroureterectomy, while high-risk tumors may require radical nephroureterectomy and adjuvant therapies such as chemotherapy or immunotherapy to reduce the risk of recurrence and progression.

TREATMENT

9. How is UTUC treated?

Treatment for upper tract urothelial carcinoma (UTUC) depends on several factors, including the stage and grade of the cancer, the location of the tumor, the patient's overall health and preferences, and the expertise of the medical team. The main treatment modalities for UTUC include:

1. **Surgery**:

– **Nephroureterectomy**: The primary treatment for UTUC involves surgical removal of the affected kidney and ureter, a procedure known as nephroureterectomy. This may involve either a partial nephroureterectomy (removal of a portion of the kidney and ureter) or a radical nephroureterectomy (removal of the entire kidney, ureter, and surrounding tissue). In some cases, a bladder cuff may also be removed to reduce the risk of cancer recurrence.

– **Minimally Invasive Surgery**: Laparoscopic or robotic-assisted techniques may be used to perform nephroureterectomy, offering benefits such as shorter hospital stays, faster recovery times, and reduced postoperative pain compared to traditional open surgery.

2. **Endoscopic Treatment**:

– **Ureteroscopy with Laser Ablation or Resection**: Small, low-grade UTUC tumors confined to the lining of the ureter may be treated endoscopically using a ureteroscope equipped with a laser or resection tools. This approach preserves the affected kidney and ureter, but it requires careful surveillance due to the risk of recurrence.

3. **Adjuvant Therapy**:

– **Intravesical Therapy**: After nephroureterectomy, some patients may receive intravesical chemotherapy or immunotherapy directly into the bladder to reduce the risk of bladder cancer recurrence.

– **Systemic Therapy**: In cases where UTUC is high-grade, invasive, or metastatic, systemic chemotherapy or immunotherapy may be recommended to target cancer cells throughout the body. Targeted therapies and clinical trials may also be considered for advanced UTUC.

4. **Radiation Therapy**: External beam radiation therapy (EBRT) or brachytherapy (internal radiation therapy) may be used as part of the treatment for UTUC in select cases, particularly for patients who are not candidates for surgery or have unresectable tumors.

5. **Palliative Care**: For patients with advanced or metastatic UTUC, palliative care focuses on symptom management, pain relief, and improving quality of life.

Treatment decisions are typically made by a multidisciplinary team of healthcare professionals, including urologists, medical oncologists, radiation oncologists, and pathologists, in collaboration with the patient. The goal of treatment is to achieve optimal cancer control while preserving renal function and maximizing quality of life.

10. Is it possible to cure UTUC without surgery?

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Staging helps guide treatment decisions and provides information about prognosis. Early-stage UTUC (stages 0, I, and II) is often treated with surgery to remove the affected kidney and ureter (nephroureterectomy) or with kidney-sparing procedures for select cases. Advanced-stage UTUC (stages III and IV) may require a combination of surgery, chemotherapy, radiation therapy, and/or immunotherapy.

It's important to note that staging is determined based on various factors, including imaging studies, biopsies, and surgical findings, and it may vary for each individual case. Treatment plans are often tailored to the specific characteristics of the cancer and the patient's overall health.

11. How to treat bilateral UTUC?

Bilateral UTUC (Upper Tract Urothelial Carcinoma), where cancer is present in both kidneys or ureters, presents a complex treatment challenge. Treatment typically depends on various factors including the stage of the cancer, the patient's overall health, and their treatment preferences. Here's an overview of treatment options for bilateral UTUC:

1. **Surgery**: Surgery is often the primary treatment for UTUC. For bilateral UTUC, the extent and type of surgery may vary. Options may include:

– **Nephroureterectomy**: This involves removing both kidneys and ureters. After this surgery, patients will require dialysis or a kidney transplant for renal function.

– Kidney-sparing surgery: In select cases, where the tumors are small and limited, kidney-sparing surgery may be an option. This involves removing only the tumors while preserving kidney function.

2. **Chemotherapy**: Chemotherapy may be recommended before or after surgery to shrink tumors, kill cancer cells, or prevent recurrence. Chemotherapy can be systemic (given orally or intravenously) or delivered directly into the bladder (intravesical chemotherapy).

3. **Radiation Therapy**: Radiation therapy may be used in some cases, particularly when surgery is not an option or to complement surgical treatment. It uses high-energy beams to kill cancer cells.

4. **Immunotherapy**: Immunotherapy drugs such as pembrolizumab, atezolizumab, or nivolumab may be used in advanced cases or in patients who are not candidates for surgery. These drugs work by enhancing the body's immune response against cancer cells.

5. **Clinical Trials**: Participation in clinical trials may be an option for some patients, especially those with advanced or recurrent UTUC. Clinical trials test new treatments or combinations of treatments to determine their effectiveness and safety.

6. **Supportive Care**: Palliative care and supportive measures focus on relieving symptoms, managing side effects of treatment, and improving quality of life. This may include pain management, dietary support, and psychological support.

Treatment decisions for bilateral UTUC should be made in consultation with a multidisciplinary team of healthcare professionals, including urologists, medical oncologists, radiation oncologists, and other specialists. The treatment plan will be tailored to the individual patient's needs and circumstances.

PROGNOSIS

12. What are the complications of UTUC?

Upper tract urothelial carcinoma (UTUC) and its treatment can lead to various complications, which may vary depending on factors such as the stage of the cancer, the type of treatment received, and the individual's overall health. Some potential complications of UTUC include:

1. **Urinary Tract Obstruction**: UTUC tumors can obstruct the urinary tract, causing urinary retention, hydronephrosis (fluid buildup in the kidney), and kidney damage. This obstruction can lead to symptoms such as flank pain, urinary frequency, urgency, and difficulty urinating.

2. **Kidney Dysfunction**: In cases where UTUC affects kidney function or leads to kidney removal (nephroureterectomy), individuals may experience decreased kidney function or renal insufficiency. This can result in symptoms such as fatigue, fluid retention (edema), electrolyte imbalances, and impaired waste excretion.

3. **Hydronephrosis**: Hydronephrosis occurs when urine accumulates in the kidneys due to blockage or obstruction of the urinary tract. It can lead to pain, urinary tract infections (UTIs), and kidney damage if left untreated.

4. **Urinary Tract Infections (UTIs)**: UTUC and its treatment can increase the risk of urinary tract infections, which can cause symptoms such as urinary urgency, fre-

quency, burning with urination, and fever. UTIs may require antibiotic treatment to resolve and prevent complications.

5. **Hematuria**: Blood in the urine (hematuria) is a common symptom of UTUC, but it can also occur as a complication of the cancer or its treatment. Hematuria may range from microscopic (not visible to the naked eye) to gross (visible blood in the urine) and can indicate disease progression or treatment-related side effects.

6. **Recurrence and Progression**: Despite treatment, UTUC can recur or progress to more advanced stages over time. Close surveillance is essential to monitor for recurrence, progression, and the development of metastases.

7. **Metastasis**: Advanced UTUC can spread (metastasize) to distant organs or tissues, such as the lungs, liver, bones, or lymph nodes, leading to more serious complications and poorer outcomes.

8. **Treatment Side Effects**: Treatments for UTUC, such as surgery, chemotherapy, immunotherapy, and radiation therapy, can cause side effects and complications. These may include surgical complications, infection, pain, fatigue, nausea, vomiting, hair loss, and immunotherapy-related adverse events.

It's important for individuals with UTUC to discuss potential complications and management strategies with their healthcare team. Close monitoring, symptom management, and supportive care can help minimize complications and improve quality of life for patients undergoing treatment for UTUC.

13. How long will I live with UTUC?

The prognosis for individuals diagnosed with upper tract urothelial carcinoma (UTUC) can vary widely depending on several factors, including the stage of the cancer at diagnosis, the grade of the tumor, whether it has spread to other parts of the body, the individual's overall health, and their response to treatment.

In general, earlier-stage UTUC that is localized to the kidney or ureter and has not spread to other organs tends to have a better prognosis. Treatment options such as surgery, chemotherapy, and radiation therapy may be effective in controlling the disease and improving survival rates.

However, UTUC that is diagnosed at a later stage or has spread to other organs may have a poorer prognosis. In these cases, the goal of treatment may shift towards managing symptoms and improving quality of life rather than curing the cancer.

It's important to discuss prognosis and treatment options with your healthcare provider, as they can provide personalized information based on your specific situation and help you make informed decisions about your care. Additionally, joining support groups or seeking counseling can provide emotional support and help you cope with the challenges of living with UTUC.

14. What is the probability of UTUC recurrence?

The probability of upper tract urothelial carcinoma (UTUC) recurrence varies depending on several factors, including the stage and grade of the cancer, the extent of surgical resection, the presence of lymphovascular invasion, the adequacy of follow-up surveillance, and the in-

dividual's overall health and response to treatment. While many patients with UTUC experience successful treatment without recurrence, others may face the risk of cancer returning (recurrence) after initial treatment. Here are some general factors that influence the probability of UTUC recurrence:

1. **Stage and Grade of the Cancer**: Higher stage (e.g., stage III or IV) and higher grade (e.g., high-grade) UTUC are associated with an increased risk of recurrence compared to lower stage and grade disease. Tumors with more aggressive characteristics are more likely to recur after treatment.

2. **Surgical Margins**: The completeness of surgical resection (e.g., whether all cancerous tissue was removed) during nephroureterectomy or other surgical procedures can affect the risk of recurrence. Positive surgical margins (presence of cancer cells at the surgical margin) increase the likelihood of local recurrence.

3. **Lymphovascular Invasion**: The presence of lymphovascular invasion (cancer cells invading lymphatic or blood vessels) in the tumor specimen is associated with a higher risk of recurrence and metastasis.

4. **Tumor Size and Multifocality**: Larger tumor size and multifocal tumors (presence of multiple tumor sites) are associated with an increased risk of recurrence.

5. **Tumor Location**: Tumors located in certain areas of the upper urinary tract, such as the renal pelvis, may have a higher risk of recurrence compared to tumors located in the distal ureter.

6. **Treatment Response**: The effectiveness of treatment in eradicating cancer cells and preventing recurrence is a critical factor. Patients who achieve a complete response to treatment and have no evidence of residual disease after initial therapy have a lower risk of recurrence.

7. **Follow-Up Surveillance**: Regular surveillance and follow-up monitoring are essential to detect any signs of recurrence early. Patients who undergo frequent follow-up visits, imaging studies (e.g., CT scans), and urine cytology tests are more likely to detect recurrence at an earlier, potentially more treatable stage.

While UTUC recurrence can occur, it's important to note that not all patients will experience recurrence, and the probability of recurrence varies from person to person. Close collaboration with a healthcare team experienced in managing UTUC and adherence to surveillance protocols can help minimize the risk of recurrence and improve outcomes for patients with UTUC.

15. What are the complications of UTUC treatment?

The treatment for upper tract urothelial carcinoma (UTUC) can involve various interventions, including surgery, chemotherapy, radiation therapy, and immunother-

apy. While these treatments can be effective in managing the cancer, they can also lead to certain complications. Some potential complications of UTUC treatment include:

1. **Surgical complications**: Surgery, such as nephroureterectomy (removal of the affected kidney and ureter) or ureteroscopy (endoscopic removal of the tumor), can carry risks such as bleeding, infection, blood clots, damage to surrounding organs or structures, and complications related to anesthesia.

2. **Urinary tract complications**: Following surgery or other treatments, patients may experience urinary tract complications such as urinary tract infections, urinary incontinence, urinary retention, or narrowing (strictures) of the urinary tract.

3. **Kidney function impairment**: Removal of a kidney (nephroureterectomy) can lead to a decrease in kidney function, particularly if the remaining kidney is already compromised or if there are complications during surgery.

4. **Sexual dysfunction**: Surgery and certain treatments may lead to sexual dysfunction in both men and women. This can include erectile dysfunction in men or vaginal dryness and discomfort in women.

5. **Lymphedema**: Removal of lymph nodes during surgery can sometimes lead to lymphedema, which is swelling due to a buildup of lymph fluid. This typically occurs in the legs or genital area.

6. **Chemotherapy and radiation side effects**: Chemotherapy and radiation therapy can cause side effects such as nausea, vomiting, fatigue, hair loss, skin irritation, and increased risk of infections due to weakened immune function.

7. **Long-term complications**: Some treatments for UTUC can have long-term effects on overall health, including increased risk of secondary cancers, cardiovascular disease, or other chronic health conditions.

It's essential for patients to discuss potential complications and side effects with their healthcare team before starting treatment. Additionally, healthcare providers will monitor patients closely during and after treatment to manage any complications that may arise and optimize the patient's quality of life.

– After completing treatment, you will need regular follow-up appointments and surveillance tests to monitor for any signs of recurrence or complications. It's important to attend these appointments and communicate any concerns or symptoms to your healthcare team promptly.

Overall, while UTUC treatment may bring about temporary changes and challenges, many people are able to adapt and maintain a fulfilling lifestyle with appropriate support, self-care, and adjustments. It's essential to communicate openly with your healthcare team about your concerns, needs, and goals throughout your treatment journey.