

Transitional Cell Carcinoma

What is transitional cell carcinoma?

Transitional cell carcinoma (TCC), arising from the transitional cells that line the urinary tract, is the most common tumor of the urinary bladder in dogs and is most frequently located in the trigone region of the urinary bladder (exit of the bladder into the urethra). TCC can affect other portions of the lower urinary tract including the urethra and the prostate (in males). Risk factors that have been described that may increase the risk of developing TCC include sex predisposition (females are at higher risk than males), breed predisposition (Scottish Terriers, Shetland Sheepdogs, Beagles, West Highland White Terriers are overrepresented), obesity, exposure to insecticides and herbicides, and exposure to environmental carcinogens (ie smoking, urban areas).

What are the clinical signs?

Clinical signs associated with TCC resemble those of other lower urinary tract diseases. Most owners first notice that their pet has been straining to urinate, urinating more frequently, having bloody urine, and having accidents in the house. The development of frequently recurrent urinary tract infections may also be noted. These clinical signs may be present for weeks to months, and may temporarily resolve with antibiotics, but often recur once the antibiotic is discontinued. Straining to defecate can also occur if the mass or associated lymph nodes enlarge and compress the colon. In some cases, life-threatening complications can occur quickly, related to partial/complete obstruction of the urethra (passage between the urinary bladder to the outside) and can result in non-productive urination characterized by dribbling or an inability to pass urine. Metastatic disease, usually to the regional lymph nodes first and then to the liver, lungs, and bone is typically found in about 15% of cases at the time of diagnosis; however, the anticipated metastatic rate of this tumor is estimated to be about 50% over time.

How is TCC diagnosed and staged?

The diagnosis of TCC is typically made by the initial discovery of a mass effect in the urinary bladder/proximal urethra on abdominal ultrasound. While this provides information that can be sufficient for a presumptive diagnosis, biopsy, either using traumatic catheterization or transurethral cystoscopy, is the most common means of obtaining a definitive diagnosis and information about grade. If biopsy is not elected, urine sediment cytology looking for the presence of abnormal transitional cells can also be used to support a diagnosis of TCC. A bladder antigen test for canine TCC has been proposed but unfortunately can be falsely positive in urinary tract infections or in the presence of other benign inflammatory conditions.

In addition to tumor sampling, a thorough staging evaluation is recommended including a physical examination, bloodwork, urinalysis, and thoracic/abdominal imaging. A physical examination is recommended to evaluate the urethra, prostate, and regional sublumbar lymph nodes as well as to determine if other concerning changes are present. Bloodwork, including a CBC, serum biochemical profile, and urinalysis is also recommended. Additional imaging, including thoracic radiographs and abdominal imaging (typically using abdominal ultrasound), are used to help identify evidence of regional or distant disease spread (metastasis) as well as to assess for urinary tract obstruction affecting the kidneys and ureters.

Urinary bladder TCC is staged using the Tumor, Node, Metastasis WHO Classification:

T= Primary Tumor: T0= No evidence of cancer (typically achieved after surgical resection if possible), Tis= Carcinoma in situ, T1= Superficial papillary tumor, T2*= Tumor invading the urinary bladder wall, T3*= Tumor invading into adjacent organs

*most primary tumor presentations of canine TCC are T2 or T3

N= Node: N0= No evidence of regional lymph node metastasis, N1= Regional lymph node involvement, N2= Regional and juxta-regional lymph node involvement

M= Metastasis: M0= No metastasis, M1= Evidence of distant metastasis

How is TCC treated?

- **Surgical Options:** Surgical treatment for TCC is regarded as a palliative option or part of a multi-modal treatment approach to TCC. As most urinary TCC primary tumors in dogs are invasive into the bladder wall/adjacent tissue (T2 or T3 presentations) and are primarily located in the urinary bladder trigone or into the urethra, surgical excision is typically not a feasible treatment option without radical approaches (ie removal of entire urinary bladder). In rare cases, surgical excision is plausible (ie apical tumors) however a high risk of local recurrence exists due to a phenomenon called the field effect (locally seeding of the tumor). Instead, surgical techniques involving laser debulking or endoscopically placed urethral stenting are primarily used to palliate the primary tumor and to help immediately address clinical signs associated with lower urinary tract obstruction.
- **Radiation Therapy:** As a single treatment modality, radiation therapy provides poor local tumor control. However, external beam radiation therapy can be used primarily in a palliative setting especially in cases with acute urinary obstruction.
- **Oral NSAIDs:** Non-steroidal anti-inflammatory drugs (NSAIDs), including piroxicam (Feldene) and deracoxib (Deramaxx), have been investigated as single agent therapy for TCC and result in good disease/clinical sign control. These drugs are associated with a ~15-20% response rate, ~80% disease stabilization, a median disease free progression of approximately 5-7 months and are frequently used in combination with chemotherapy.
- **Chemotherapy:** Systemic chemotherapy is the preferred treatment of choice for the management of canine TCC. It addresses both the local disease as well as helps reduce the risk of/prolong the time to development of metastatic disease. Mitoxantrone with piroxicam has been associated with a 35% response rate, ~80% disease stabilization, median survival times ranging from 8.5 to 11.5 months and is our first line of therapy for these tumors. Other chemotherapeutics that have shown efficacy include the use of doxorubicin, platinum drugs (Cisplatin), gemcitabine, vinblastine, and oral metronomic Leukeran.
- **Other Options:** Photodynamic therapy (PDT) has been used primarily in an academic, investigational setting for the management of canine TCC (particularly for prostatic presentations). Unfortunately, this treatment option is not readily available. Intra-arterial chemoembolization/tumor embolization has been proposed as a possible treatment option for canine TCC however this has not been evaluated in dogs.
- **Investigational/Clinical Trial Opportunities:** Investigational options and/or clinical trials may be considered if available and if patients are eligible for inclusion.

What is the prognosis associated with a canine TCC?

Prognostic factors associated with canine TCC include:

1. Sex (Spayed females are found to have a better survival than castrated males)
2. Location and extent of tumor (Poorer prognosis associated with urethral or prostatic presentations or with patients presenting initially with complete urinary obstruction)
3. Histologic grade
4. Clinical stage (Degree of primary tumor invasiveness and presence of metastasis)
5. The use of chemotherapy and type of chemotherapy used (anthracycline antibiotics associated with better outcomes than platinum chemotherapeutics)