Mammary tumours are the most common neoplasm in intact female dogs and account for approximately half of all neoplasms in the bitch. In contrast, mammary neoplasms are rare in male dogs, accounting for less than 1% of these types of tumours. The incidence of mammary tumours is higher in dogs than any other domesticated animal and is three times the incidence in humans. Approximately half of the tumours are malignant, and half of these have metastasized by the time they are initially diagnosed. Sex hormones certainly play a role in development of mammary tumours in the bitch. Intact females have a seven-fold increased risk of developing mammary cancer compared to neutered females. The age at which ovariohysterectomy takes place is directly proportional to the risk of developing mammary cancer. Data clearly indicate the preventive role of ovariectomy prior to the second estrus. Interestingly, when only the dogs that had 2 or more estrus cycles before spaying are considered, there is still a benefit to earlier spaying. If they were spayed before 2.5 years of age, then the risk was 6% of those dogs not spayed at all; (that approximates to the 8% quoted for 1 estrus cycle). If they were older than 2.5 years, the risk was 40% of unspeyed dogs, but that difference was not significant. Essentially the greatest reduction in risk comes if you spay before the first heat, but then as long as you spay before 2.5 years, the risk is very low. Counter to all current thought one group reviewed the statistics in all the literature regarding the risk of neutering and found the data weak. We continue to recommend speying at an early age.

Two studies showed that after a malignant mammary tumour develops, there is no effect of ovariectomy on tumour progression. In contrast a recent study showed increases in survival time for dogs that were ovariectomized within 2 years before mammary tumour surgery. Obesity may be a factor in mammary neoplasia in dogs. In one case-controlled study, the risk of mammary carcinoma among ovariectomized dogs was significantly reduced (by 40%) in dogs that had been thin at 9 to 12 months of age. Among intact dogs that were thin at 9 to 12 months, however, risk of mammary cancer was not reduced. In contrast another study, showed obesity at 1 year of age almost trebled the incidence of mammary cancer in intact dogs. In that study, dogs with a higher intake of red meat in their diet were also at higher risk for developing mammary cancer. Interestingly, feeding of a high fat diet, and obesity in the year before being diagnosed with a mammary cancer had no influence of tumour development. Caregivers should be counseled to ovariectomize their dogs before the first estrus, and to ensure weight control is practiced in at least the first year of life. Ovariectomies performed later in life, while not as protective, should not be discouraged.
Staging and Diagnosis
The two most common sites of metastases are lungs and regional lymph nodes. Therefore, staging should include a minimum database of thoracic radiographs, complete blood count (CBC), biochemical profile, urinalysis, and an evaluation of regional lymph nodes (axillary and inguinal) by palpation, fine-needle aspiration cytology, and (if indicated) biopsy.

Prognostic Factors
Somewhat surprisingly, the prognosis for dogs with mammary cancer is not influenced by either tumour location or number of tumours.\textsuperscript{4,7} Other factors that are not prognostic are number of pregnancies, age at first pregnancy and occurrence of pseudopregnancies. The following are prognostic factors that have been shown in studies to predict survival or disease-free interval.

Stage
Dogs with stage 1 tumours were more likely to survive longer than dogs with any other stage tumour.\textsuperscript{7} This effect of tumour stage was similar in other studies and is detailed in the following tables.\textsuperscript{8,9}

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent alive 1 year after surgery</th>
<th>Percent alive 2 years after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>97.9</td>
<td>97.9</td>
</tr>
<tr>
<td>3</td>
<td>75.8</td>
<td>66.4</td>
</tr>
<tr>
<td>4</td>
<td>13.6</td>
<td>13.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effect of tumour stage on survival.\textsuperscript{9}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

Tumour Size
This is probably one of the most important prognostic factors for a dog with a mammary mass. Dogs with mammary tumours less than 3 cm in diameter have a significantly better prognosis than dogs with larger tumours. In another study, dogs with tumours larger than 5cm in diameter were more likely to develop metastases than dogs with smaller tumours and were 7 times more likely to die in the first 2 years after surgery.\textsuperscript{10}

Metastasis
Metastases to regional lymph nodes has been associated with an increased risk for tumour recurrence and for decreased overall survival. The presence of distant metastases was found to be prognostically important in other studies.\textsuperscript{8,9} Those dogs with no metastases were more than 3 times as likely to survive one year from diagnosis.\textsuperscript{7}

Age
Older dogs have a worse prognosis in some studies. It is unclear if this is due to tumour related factors or competing risks.
Diet and Body Weight
In one study, the effect of diet in the year prior to diagnosis on survival after surgery showed that dietary fat and dietary protein together influenced outcome. When dogs were categorized by the percent of total calories they derived from fat and protein, the median survival time for dogs fed a low fat diet (< 39%) with protein greater than 27%, 23-27%, and less than 23% was 3 years, 1.2 years, and 6 months, respectively. For dogs fed a high fat diet (> 39%), there was no difference in survival for the different intake levels of dietary protein. In addition, body conformation 1 year prior to diagnosis affected survival.

Degree of Invasion and Ulceration
Dogs with tumours that ulcerate overlying skin have a worse prognosis (shorter overall survival times) than dogs with tumours without ulceration. Rapid and invasive growth correlates with a worse prognosis, which may be recognized as fixation of the tumour to the underlying skin. Vascular or lymphatic invasion is a poor prognostic factor; dogs with histologic evidence of invasion have a shorter median survival.

Histopathology
Several histologic grading schemes are of prognostic significance. Important factors include histologic classification, degree of nuclear differentiation, and the presence of lymphoid accumulation. In general, the more highly differentiated the tumour, the better the prognosis. Poorly differentiated tumours are much more likely to recur than well-differentiated tumours. The chance of recurrence for poorly differentiated canine mammary tumours is 90%; for moderately differentiated tumours, 68%; and for well-differentiated tumours, 24%. Dogs that have mammary cancer but no evidence of lymphoid cellular reactivity at the time of initial mastectomy have a threefold increased risk of developing recurrence within two years compared to those with such reactivity. Dogs with inflammatory carcinomas also have a poor prognosis.

When reviewing a histopathology report, the clinician should look for information regarding completeness of the surgical excision; invasion into lymphatics or blood vessels, and differentiation of the tumour. Dogs with tumours that showed a high proportion of Ki-67 staining (which is an immunohistochemical marker for cellular proliferation) were more likely to develop metastases in studies. Additionally Ki-67 staining was inversely related to survival time.

Hormone-Receptor Activity
Dogs with tumours that are estrogen- and/or progesterone-receptor positive have a better prognosis than dogs with tumours that do not have receptors, with longer disease-free and overall survival times. Receptor-positive tumours are likely to be benign. While presence of estrogen and progesterone receptors were predictive for disease-free survival after surgery in one study, on multivariate analysis the effects of tumour size and histologic grade overpowered that effect.

Ovariectomy Status
In one study dogs that were intact at the time of surgery for a mammary carcinoma survived a shorter time (median survival 9.5 months) compared to dogs ovariectomized within the 2 years before surgery (median survival 25 months). Dogs ovariectomized more than 2 years before mammary tumour surgery did not benefit to the same extent. In addition, dogs that were intact had a higher proportion of solid and anaplastic carcinomas than either group of ovariectomized dogs (80% solid carcinomas in intact dogs compared to 20% (<2 years) and 7% (> 2 years)). In another study dogs that were not entire at the time of diagnosis were 2.5 times more likely to survive 2 years after surgical excision of the mammary malignancy. In contrast
ovariohysterectomy at the time of tumour removal had no effect on survival in another study with approximately 60% of dogs with malignant tumours dying within 2 years of surgery whether they were spayed at the time or not.  

**Duration of tumour presence**

Dogs that had a mammary malignancy present for longer than 6 months were more likely to develop metastases than dogs with tumours removed soon after diagnosis.  

**Treatment**

**Extent of Surgery**

The extent of surgery influences neither survival nor disease-free interval but rather the histologic completeness of surgical margins as assessed by histopathology has been shown to be prognostic for survival so the best surgery to achieve complete margins is the surgery that should be offered.

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Number of dogs</th>
<th>Number alive at 2 years</th>
<th>2-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass removal</td>
<td>56</td>
<td>52</td>
<td>92.9%</td>
</tr>
<tr>
<td>Mammectomy</td>
<td>64</td>
<td>56</td>
<td>87.5%</td>
</tr>
<tr>
<td>Ipsilateral mastectomy</td>
<td>25</td>
<td>21</td>
<td>84.0%</td>
</tr>
<tr>
<td>Bilateral mammectomy</td>
<td>24</td>
<td>21</td>
<td>87.5%</td>
</tr>
</tbody>
</table>

**Adjuvant chemotherapy**

Dogs with large, invasive or metastatic mammary tumours may benefit from systemic chemotherapy. Appropriate clinical studies are essential to document the efficacy of chemotherapy, but have not yet been reported. There are indications of activity for different chemotherapy agents from *in vitro* studies but there is a huge leap from these studies to clinical efficacy. Drugs shown to have *in vitro* activity or potential clinical efficacy include 5-fluorouracil, cyclophosphamide, doxorubicin, carboplatin, mitoxantrone, paclitaxel and docetaxel.

The finding that normal mammary tissue has no evidence of cyclo-oxygenase-2 (*cox-2*) expression, and that 24% of benign and 56% of malignant mammary tumours do express *cox-2* had led to speculation that non-steroidal inhibitors of *cox-2* may play a role in the treatment of mammary carcinoma, and possibly the prevention of new lesions. In two other studies, mammary carcinomas that were more anaplastic had higher levels of *cox-2* expression. In an early evaluation of piroxicam (a non-steroidal anti-inflammatory drug) in the treatment of cancer in dogs, one of 3 dogs with mammary carcinoma had a partial response to therapy. Piroxicam has been shown in some studies (although not in others) to improve survival in dogs with inflammatory mammary carcinomas.

A very recent study found that dogs receiving carboplatin and *cox-2* inhibitor had longer survivals than comparable patients treated by surgery alone.

---


