

Retrospective Study Of Canine Mammary Tumor Recurrence After Mastectomy (2015~2020)

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Abstract:

The most prevalent tumors in female dogs are mammary gland tumors, with approximately 50% being malignant. Surgical resection is the preferred treatment; however, the high risk of post-operative recurrence and metastasis leading to death or euthanasia poses a significant challenge. This study aims to comprehensively analyze and assess the clinical outcomes of 105 cases of canine mammary tumors, examining associated risk factors for recurrence within a 2-year period. Factors such as tumor size, surgical method, location, weight, age, and lymph node invasion were considered. Our findings revealed a higher recurrence rate in the older group compared to the median group ($P=0.005$), and dogs with lymphatic invasion exhibit a significantly higher recurrence rate than those without invasion ($P < 0.001$). In conclusion, this study identified patient neuter status, lymph node invasion by mammary tumors, and patient age as critical factors influencing the recurrence of mammary gland tumors.

Key Word: Canine mammary gland tumor; Recurrence; Age; Lymphatic invasion.

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I. Introduction

Mammary gland tumors are the most common neoplasms affecting female dogs; approximately 50% of these tumors are malignant [1-3]. Clinical presentations of mammary tumors vary from asymptomatic to the presence of lumps, changes in skin color, swelling, and pain.

Treatment options for mammary gland tumors in dogs include chemotherapy, hormone therapy, radiation therapy, and surgical resection, with the latter being the most preferred [4]. The choice of surgical method depends on factors such as the size, location, and density of the tumor, the patient's physical condition and age, as well as the surgeon's preference. Available surgical methods include lumpectomy, simple mastectomy, regional mastectomy, and chain mastectomy [5].

Despite surgical resection of mammary gland tumors, a favorable prognosis in dogs is not guaranteed. Up to 48% of dogs treated with surgery either died or were euthanized within 1 year after surgery due to tumor recurrence or metastasis [6,7]. Similar to studies in human medicine [8], canine mammary tumors are known to have a high recurrence rate within 2 years after surgical resection [3,9]. Dogs with invasive mammary tumors within 2 years after surgical resection were found to have a 13-fold increased risk of recurrence compared to dogs with non-invasive mammary tumors [9].

The follow-up period for human breast cancer is typically 5 or 10 years [10], equivalent to 2 years in dogs [11]. Therefore, this study conducted a follow-up up to 2 years after surgery and evaluated the recurrence rate.

Factors affecting the prognosis after surgical resection of a mammary tumor include age, tumor size, lymph node invasion, histological classification, and whether the tumor recurs. Since the quality of life varies depending on the recurrence of tumors after surgery, determining the recurrence risk becomes an important indicator for patient counseling.

Therefore, this study was aimed to provide patients with preliminary information about the surgery and assist clinical veterinarians in selecting the most appropriate surgical method after diagnosing patients with mammary gland tumors.

II. Material And Methods

Case Selection Criteria:

The medical records of canine mammary gland tumor cases at a primary care hospital in Korea between January 2015 and December 2020 were retrospectively reviewed. A total of 105 female dogs that underwent surgical resection for mammary gland tumors were included in the study.

Breed Distribution:

Breed distribution was as follows: one Bichon Frise, three Cocker Spaniels, three Dachshunds, one Italian Greyhound, one Jindo, 31 Maltese, 15 Mixed breeds, five Pomeranians, 17 Poodles, five Schnauzers, 11 Shih Tzus, one Siberian Husky, one Spitz, one White Terrier, and nine Yorkshire Terriers (Table no 1).

Table no 1: The breed distribution with Canine mammary gland tumor in this study.

Breed	Tumors	
	Dogs (n=105)	%
Bichon Frise	1	1.0
Cocker Spaniel	3	2.8
Dachshund	3	2.8
Italian Greyhound	1	1.0
Jindo	1	1.0
Maltese	31	29.5
Mixed	15	14.2
Pomeranian	5	4.7
Poodle	17	16.4
Schnauzer	5	4.7
Shih tzu	11	10.4
Siberian Husky	1	1.0
Spitz	1	1.0
White Terrier	1	1.0
Yorkshire Terrier	9	8.5

Pre-treatment Evaluation:

Prior to surgical resection, a physical examination was conducted to assess the size, number, and involvement of mammary glands, adhesions with the abdominal wall, and enlargement of lymph nodes. The examinations encompassed thoracic and abdominal radiographs, a complete blood count, serum biochemistry, ultrasound, fine needle aspiration, and computed tomography.

Histological Evaluation:

The final diagnosis relied on biopsy results obtained after surgical resection. The excised mammary tumors were fixed in 10% formalin and processed using standard histological techniques. Histological evaluation followed the World Health Organization classification system [13], utilizing hematoxylin and eosin (HE) stained tissue sections. In instances of multiple tumors, classification was based on the highest malignancy, and the size and number of tumors were determined based on the largest values.

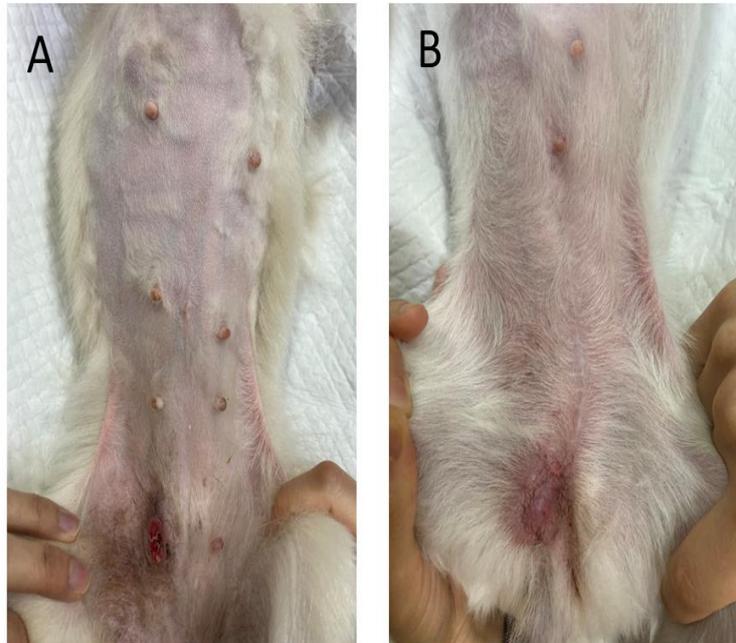
Surgical Treatment:

Lumpectomy, simple mastectomy, regional mastectomy, and chain mastectomy were selectively performed, taking into account factors such as tumor size, location, number, and the patient's physical condition. In cases where two or more surgical methods were employed, classification was based on the method with a broader resection range.

Risk of Tumor Recurrence:

The recurrence risk was assessed when the tumor reappeared in the original location and its surrounding area (Figure no 1). Histological features mirrored those of the primary tumors [14,15]. The occurrence of recurrence and lymphatic invasion was determined through radiography, computed tomography, fine needle aspiration, and biopsy.

Figure no 1: Photos of Canine mammary gland tumor in this study: (A) Mammary gland tumor with right side of cranial and caudal sites; (B) Recurrence mammary tumor with right caudal site in the same patient.



Follow-up:

Throughout the study, dogs underwent examinations every 3 months for a period of 2 years post-surgery. These examinations included a physical examination, complete blood count, thoracic and abdominal radiographs, and abdominal ultrasound. Data collection encompassed instances of recurrence and tumor-related deaths, in which dogs either died spontaneously or were euthanized.

Statistical Analysis:

Pearson's Chi-square and Fisher's exact tests were employed to assess recurrence based on factors such as size, surgical methods, breed, age group, tumor site, and lymph node invasion. The Kaplan-Meier method and log-rank test were utilized to estimate the 2-year survival time for dogs with lymphatic invasion and recurrence after surgery. Statistical significance was defined as $P < 0.05$. IBM SPSS Statistics ver. 19.0 software was used for statistical analysis.

III. Result

Age Distribution:

The mean age of the dogs was 10.3 ± 2.75 years at the time when owners initially identified the tumor (Range, 4 to 18 years). When categorized into median and older age groups, 63 cases were under 11 years (median group), and 42 cases were over 12 years (older group). Recurrence was observed in five cases from the median age group and 12 cases from the older age group (Table no 2).

Table no 2: Recurrence rate based on the age.

Age	Total	Recurrent case	Recurrence rate*
	n	n	%
≤ 11 years	63	5	7.9
> 12 years	42	12	28.5

* Recurrence rate between median and older group: Chi-Squared test $P=0.005$

The Neuter Status Incidence:

The incidence of neuter status with mammary gland tumors was also examined. Among dogs with mammary tumors, 95 were intact females (90%), and 10 were spayed females (10%). All 95 intact females underwent concurrent ovariohysterectomy during mammary tumor surgery.

Histopathologic Tumor Classification:

Among the 105 cases with mammary tumors, 69 were benign and 36 were malignant. The benign tumors included 46 cases of adenoma and 23 cases of benign mixed tumors. Malignant tumors comprised 34 cases of carcinoma and 2 cases of sarcoma (Table no 3). In this study, all recurrent tumor types (n=17) were identified as carcinoma.

Table no 3: Histological type of Mammary gland tumor after surgery.

Tumor type		n	%
Benign	Adenoma*	46	43.8
	Benign mixed tumor	23	21.9
Malignant	Carcinoma ^o	34	23.8
	Sarcoma	2	1.9

* Includes the tumor types: cystic, complex

^o Includes the tumor types: complex, tubular, solid, anaplastic

Tumor Size:

As a result of classification according to the maximum diameter of mammary tumors, 91 cases of canine mammary tumors were less than 3 cm, nine cases of mammary tumors were 3-5 cm, and five cases of mammary gland tumors were more than 5 cm. Recurrence risk based on the size of the tumor was as follows: 15 cases were 3 cm or less in size, one case was 3-5 cm, and one case was 5 cm or more (Table no 4).

Table no 4: Recurrence rate based on the tumor size.

Tumor size	Total	Recurrent case	Recurrence rate*
	n	n	%
< 3cm	91	15	16.4
3~5cm	9	1	11.1
> 5cm	5	1	20.0

* Recurrence rate based on the tumor size: Chi-Squared test P=0.199

Surgical Method:

Based on the classification according to the surgical method, lumpectomy was performed in five cases, simple mastectomy in 17 cases, regional mastectomy in 47 cases, and chain mastectomy in 36 cases (Table no 5). Recurrence risk based on the type of surgical methods was as follows: one case of lumpectomy, 11 cases of regional mastectomy, two cases of simple mastectomy, and three cases of chain mastectomy.

Table no 5: Recurrence rate based on the type of surgical methods.

Surgical method	Total	Recurrent case	Recurrence rate*
	n	n	%
Lumpectomy	5	1	20.0
Regional mastectomy	47	11	23.4
Simple mastectomy	17	2	11.7
Chain mastectomy	36	3	8.3

* Recurrence rate based on the surgical methods: Chi-Squared test P=0.291

Breed Distribution:

When tumor recurrence was classified into small breed dogs and others, 87 cases of small breeds under 10 kg and 18 cases of others showed recurrence. Recurrence was observed in 15 cases of small breeds and two cases of others (Table no 6).

Table no 6: Recurrence rate based on the age.

Breed	Total	Recurrent case	Recurrence rate*
	n	n	%
Small breed dogs (<10kg)	87	15	17.2

Others	18	2	11.1
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* Recurrence rate based on the breed distribution: Fisher's Exact test P=0.520

Tumor Site:

When the tumors were classified by site, there were 28 cranial and 36 caudal cases, and 41 cases of both. Three cases of cranial, nine cases of caudal, and five cases of both showed recurrence (Table no 7).

Table no 7: Recurrence rate based on the tumor site.

Tumor site	Total	Recurrent case	Recurrence rate*
	n	n	%
Cranial (gland 1,2 and 3)	28	3	10.7
Caudal (gland 4 and 5)	36	9	25.0
Both	41	5	12.1

* Recurrence rate based on the tumor site: Chi-Squared test P=0.194

Lymph node Invasion:

When classified into cases with lymph node invasion, there were eight cases with metastasis (Figure no 2) and 97 cases without invasion. Six cases of lymph node invasion and 11 cases of non-invasion showed recurrence (Table no 8). The 2-year survival rate for dogs with lymphatic invasion was 12.5%, with a mean survival time of 12.87 ± 2.87 months. In contrast, for cases with non-invasion, the survival rate was 96.9%, with a mean survival time of 23.62 ± 0.32 months (Figure no 3). None of the dogs with lymph node invasion and recurrence survived within 2 years after surgery.

Figure no 2: Histopathology of dogs with mammary gland tumor. Lymphatic vessels around the periphery of the tumor contain clusters of tumor cells (Hematoxylin & Eosin stain, X100). Black arrows indicate lymphatic invasion.

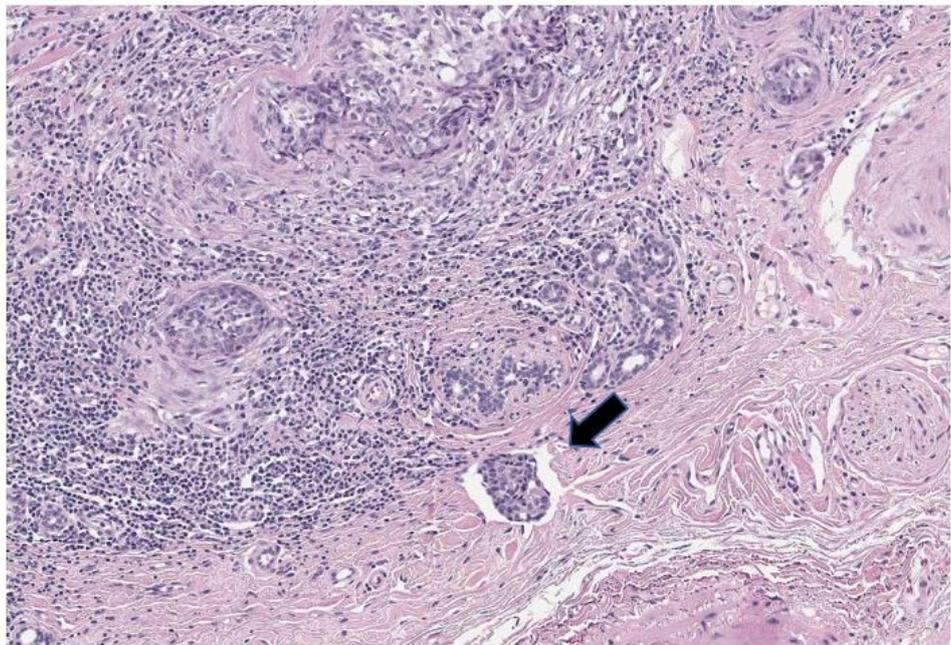
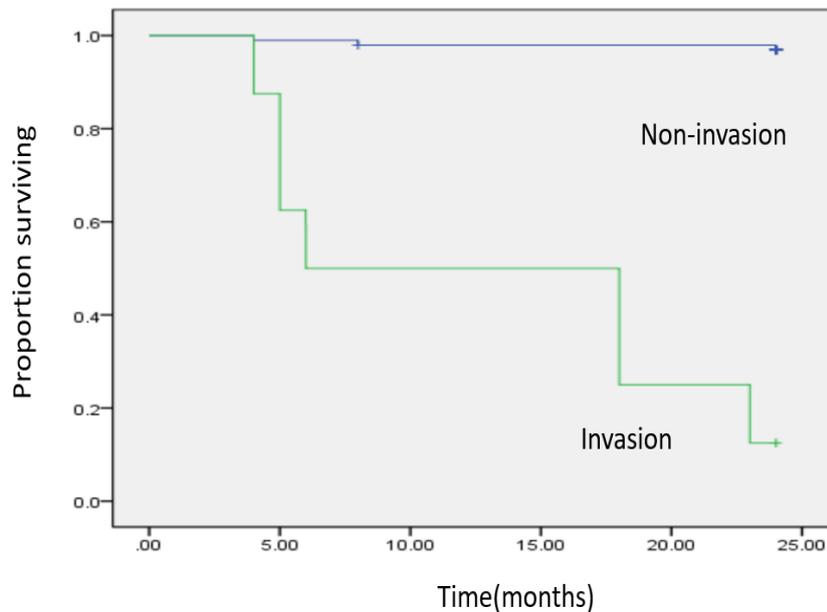


Table no 8: Recurrence rate based on whether lymph node invasion has occurred.

Lymph node	Total	Recurrent case	Recurrence rate*
	n	n	%
Invasion	8	6	75.0
Non-invasion	97	11	11.3

* Recurrence rate based on the lymph node invasion: Chi-Squared test P<0.001

Figure no 3: Kaplan-Meier survival curves following surgical removal of mammary gland tumor for 105 dogs grouped basis on lymphatic invasion.



IV. Discussion

According to previous studies, the reported incidence of malignant tumors among mammary tumors varies from 30% to 67% [16,17]. In this study, 67% of the subjects had benign tumors, while 33% had malignant tumors. These findings align with the results of previous studies; however, in the case of malignant tumors, the outcomes may have been influenced by numerous instances of refusal to treat mammary gland tumors or cases in which tumors were surgically removed before reaching a significant size.

The mean age of the dogs was 10.3 ± 2.75 years when the owners first identified the tumor (range, 4–18 years), which is consistent with ages reported in previous studies [17-19]. In line with a previous study, both human and canine mammary tumor cases showed similar age distributions throughout life [11]. The median age for human breast cancer was reported as 58 years, roughly equivalent to 11 years in a dog's life. Dogs were classified into two groups: median (≤ 11 years) and older (> 12 years) groups. Canine mammary gland tumors recurred more frequently in the older group than in the median group ($P = 0.005$), consistent with previous studies indicating worse prognosis in older dogs [20].

Similar to previous studies, more mammary tumors were observed in female dogs that were not spayed or neutered in this study. These results suggest that ovariohysterectomy significantly reduces the risk of developing mammary gland tumors in dogs [21]. All 95 cases of mammary tumors in intact females underwent neutering surgery together, but the correlation between recurrence rate and mastectomy with ovariohysterectomy could not be confirmed due to variations in hormone exposure time for each case.

According to a study related to tumor size, dogs with tumors larger than 3.4 cm had significantly worse outcomes in remission and survival than those with smaller tumors [22]. In another study, however, tumor size was not significant in dogs with regional lymph node invasion [3]. This study confirmed that there was no significant difference in recurrence risk even with a tumor size ≤ 3 cm compared to that with a size ≥ 3 cm ($P = 0.199$).

Regional mastectomy was the most frequently applied surgical method for each tumor, followed by chain mastectomy, simple mastectomy, and lumpectomy. Similar to previous studies, in female dogs, the types of surgery do not seem to affect the prognosis and recurrence as long as complete excision is achieved [12,19,22].

The incidence of mammary gland tumors in small dogs weighing < 10 kg was higher than in other breeds. This is interpreted as reflecting the characteristics of Korea, where many small dogs are raised. The risk of recurrence according to breeds did not show any significant results [23].

In the classification according to tumor location, a large number of mammary glands, including caudal abdominal and inguinal, showed no significance recurrence. This is consistent with a previous study stating that tumor location was not related to prognosis [12].

As in several studies, lymph node invasion was closely related to the risk of recurrence of canine mammary tumors [17,19,20,24]. There was a 23.45-fold increase in the risk of tumor recurrence in the lymphatic

invasion group compared to the non-lymphatic invasion group in this study (OR=23.45, 95% CI: 4.204-130.848, $p < 0.001$).

In this study, significant factors influencing the postoperative recurrence rate of mammary tumors in dogs were identified as neuter status, age, and lymph node invasion. However, tumor location, number of tumors, surgical method, and concurrent neuter surgery did not show a significant impact on the postoperative recurrence rate.

V. Conclusion

In conclusion, this study suggests that a 2-year follow-up period post-mammary gland excision is effective in assessing the prognosis of canine mammary tumors. The presence of lymph node invasion and age over 12 years has been confirmed as significant factors for recurrence, providing valuable insights for the clinical diagnosis and prognostic assessment of canine mammary gland tumors.

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