UNIVERSITI PUTRA MALAYSIA

RETROSPECTIVE STUDY ON IMPACT OF SURGICAL TECHNIQUES ON CLINICAL OUTCOME OF FELINE AND CANINE MAMMARY GLAND TUMOUR FROM 2013 TO 2022 IN UNIVERSITY VETERINARY HOSPITAL (UVH)

SOH QIAN HUI

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SOH QIAN HUI

A project paper submitted to the
Faculty of Veterinary Medicine, Universiti Putra Malaysia
In partial fulfilment of the requirement for the
DEGREE OF DOCTOR OF VETERINARY MEDICINE
Universiti Putra Malaysia
Serdang, Selangor Darul Ehsan.

DECEMBER 2023

CERTIFICATION

It is hereby certified that I have read this project paper entitled "Retrospective Study on Impact of Surgical Techniques on Clinical Outcome of Feline and Canine Mammary Gland Tumours from 2013 to 2022 in University Veterinary Hospital (UVH)" by Soh Qian Hui and in my opinion it is satisfactory in terms of scope, quality and presentation as partial fulfilment of the requirement for the course VPD4999 – Final Year Project.

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ACKNOWLEDGEMENT

First of all, I would like to express my deep and sincere gratitude to my supervisor, Dr. Ong Siew Mei for mentoring me as her FYP student and providing invaluable guidance throughout this project. Her patience, encouragement and enthusiasm in guiding me along this journey made this project to be completed perfectly.

Besides, my sincere thanks also go to the staffs in University Veterinary Hospital for their assistance in case file retrieval and data collection. Without their assistance, this project could not have been accomplished smoothly.

Also, I would like to take this opportunity to thank my FYP mate, Yen Dee, who have been working together with me throughout this project and always provided me with support and encouragement. Not forgetting my housemates and friends who were willing to spend time listening to my presentation and providing me with honest feedback to improve my project.

Last but not least, I am extremely grateful to my family for their love, caring and unending emotional and spiritual support towards the completion of this project.

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LIST OF ABBREVIATIONS

MGT Mammary Gland Tumour

ST Survival Time

DFI Disease-Free Interval

ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar, Universiti Putra Malaysia untuk memenuhi sebahagian daripada keperluan VPD4999-Projek Tahun Akhir.

KAJIAN RETROSPEKTIF MENGENAI IMPAK TEKNIK PEMBEDAHAN TERHADAP HASIL KLINIKAL TUMOR PAYUDARA KUCING DAN ANJING DARI 2013 HINGGA 2022 DI HOSPITAL VETERINAR UNIVERSITI (HVU)

Oleh

Soh Qian Hui

2023

Penyelia: Dr Ong Siew Mei

Tumor payudara atau tumor kelenjar mamari merupakan tumor yang paling kerap didiagnosis pada anjing betina dan neoplasma ketiga yang paling biasa pada kucing betina. Walaupun pembedahan merupakan pilihan rawatan utama untuk tumor payudara, bukti mengenai teknik pembedahan yang paling berkesan untuk pengurusan tumor payudara pada anjing dan kucing masih kekurangan. Tujuan kajian ini adalah untuk menilai pengaruh pendekatan pembedahan yang berbeza terhadap hasil klinikal pada kucing dan anjing dengan tumor payudara dan untuk menentukan faktor-faktor yang mempengaruhi kelangsungan hidup dalam kalangan pesakit-pesakit ini. Rekod perubatan 80 anjing dan 46 kucing menghadapi tumor payudara yang dirawat dengan pembedahan antara tahun 2013 dan 2022 di Hospital Veterinar Universiti, Universiti Putra Malaysia telah dikaji semula. Data pesakit dan maklumat pengikutan direkodkan dan dianalisis menggunakan SPSS. Semua kucing dan anjing adalah betina. Purata umur didiagnosis bagi anjing dan kucing adalah 9.6 tahun (± 2.05) dan 11.22 tahun (± 3.57) masing-masing. Di antara keseluruhan kes, 54 (76.0%) anjing dan 43 (98.0%) kucing mempunyai tumor malignan. Baka anjing yang paling biasa adalah mongrel, campuran dan Shih Tzu (9.1%), dan kucing domestic berambut pendek (65.2%). Purata jangka hidup bagi anjing dengan tumor malignan dan tumor benigna adalah 20.91 (± 23.96) dan 42.55 (± 20.98) bulan masing-masing; manakala bagi kucing, 7.33 (± 7.33) bulan untuk tumor malignan. Pada anjing dengan tumor malignan, mastektomi unilateral dan serantau berkaitan dengan jangka hidup yang lebih panjang ($p < 0.05$); bagaimanapun, tiada perkaitan yang signifikan antara teknik pembedahan dan jangka hidup pada kucing. Dalam anjing, saiz baka kecil adalah faktor prognostik yang vital. Manakala dalam kucing, kebanyakan faktor tidak signifikan secara prognostik kecuali status pemandulan di mana kucing yang dimandulkan sebelum 2 tahun atau sebelum mastektomi mempunyai selang waktu bebas penyakit yang lebih panjang ($p < 0.05$). Secara kesimpulannya, pendekatan pembedahan yang berbeza mempengaruhi hasil klinikal anjing dengan tumor payudara malignan tetapi tidak pada kucing.

Kata kunci: anjing, kucing, tumor payudara, mastektomi, prognosis

ABSTRACT

An abstract of the project paper presented to Faculty of Veterinary Medicine in partial fulfilment of the above course VPD4999- Final Year Project.

RETROSPECTIVE STUDY ON IMPACT OF SURGICAL TECHNIQUES ON CLINICAL OUTCOME OF FELINE AND CANINE MAMMARY GLAND TUMOURS FROM 2013 TO 2022 IN UNIVERSITY VETERINARY HOSPITAL (UVH)

By

Soh Qian Hui

2023

Supervisor: Dr Ong Siew Mei

Mammary gland tumour (MGT) is the most commonly diagnosed tumour in female dogs and the third most common tumour in female cats. While surgical excision is the primary treatment options for mammary gland tumours, there is still lack of evidence on the most effective surgical techniques for the management of canine and feline MGT. The aims of this study were to evaluate the influence of different surgical approach on clinical outcomes in cats and dogs with MGT and to determine the factors influencing survival in these patients. Medical records of 80 surgically treated dogs and 46 cats with MGT between 2013 and 2022 in University Veterinary Hospital, Universiti Putra Malaysia were reviewed. Patient data and follow up information were recorded and analysed using SPSS. All the cats and dogs are female. The mean diagnosis age for dogs and cats were 9.6 years (± 2.05) and 11.22 years (± 3.57), respectively. Among all the cases, 54 (76.0%) dogs and 43 (98.0%) cats had malignant tumours. The most common breeds were mongrel, mixed breed and Shih Tzu (9.1%) and domestic shorthair cat (65.2%). The mean survival times in dogs for malignant and benign tumour were 20.91 (± 23.96) and 42.55 (± 20.98) months respectively; while in cats, 7.33 (± 7.33) months for malignant tumour. In dogs with malignant tumour, unilateral and regional mastectomy was associated with longer survival time ($p < 0.05$); however, there was no significant association between surgical techniques and survival time in cats. In dogs, small breed size was significant prognostic factor. While in cats, most of the factors were not prognostically significant except neuter status where cat neutered before 2 years old or before mastectomy had longer disease-free interval ($p < 0.05$). In conclusion, different surgical approaches affect the clinical outcomes of dogs with malignant mammary tumour but not the feline counterparts.

Keywords: canine, feline, mammary gland tumour, mastectomy, prognosis

1.0 INTRODUCTION

Mammary gland tumour (MGT) is the most commonly diagnosed neoplasm in bitches (Pastor *et al.*, 2018) and third most common in queens (Jemal *et al.*, 2003), but is infrequent in male dogs (Misdorp, 2008) and tomcats (Hayes *et al.*, 1981). About half of the canine MGT are malignant (Evans *et al.*, 2021) while malignancy in feline MGT is approximately 85% (Morris, 2013).

The increased occurrence of MGT in dogs and cats is associated with various risk factors. Middle to old-aged dogs and cats are the most commonly affected where the peak incidence for dogs is 9 to 12 years old (Salas *et al.*, 2015) and 10 to 12 years old for cats (Morris, 2013). Shih Tzu, German Shepherd, Dachshund, Poodle, Cocker Spaniel and Yorkshire Terrier are the most affected breeds (Salas *et al.*, 2015),while in cats, Siamese is most commonly affected breed (Sorenmo *et al.*, 2013). Besides, ovarian hormones such as oestrogen and progesterone play a role in promoting mammary tumourigenesis. In dogs, the risk of developing MGT is as low as 0.5% when spayed before their first heat cycle. The risk gradually rises to 8% if spaying occurs before the second heat cycle and further increases to 26% before the third heat cycle (Sonnenschein *et al.*, 1991). While in cats, spaying before 6 months old and 1 year old will reduce risk of getting MGT by 91% and 86%, respectively (Lana *et al.*, 2007). Diet is also one of the risk factors. However, this factor is only proved to affect dogs but not cats, where homemade diet and red meat cause higher risk of developing MGT (Alenza *et al.*, 1998).

There are various treatment modalities for MGT, such as chemotherapy, immunotherapy and radiation therapy; however, surgical excision is still the primary treatment option (Papazoglou *et al.*, 2014). The decision on the surgical techniques, such as lumpectomy, mammectomy, regional, unilateral or bilateral mastectomy, is dependent on the size, location, number of tumours as well as owner's expectations

(Misdorp, 2008). However, the most effective surgical techniques for the management of canine and feline MGT remains debatable.

The objectives of this study were to evaluate the influence of different surgical approaches on clinical outcomes in cats and dogs with MGT and to determine the factors that influence the survival time and disease-free interval. This study aims to offer insights into the surgical approach that leads to the most favourable clinical outcomes in patients with canine and feline MGT and identify key prognostic factors that influence the quality of life of the patients. This study hypothesised that there is a significant relationship between different surgical approaches and clinical outcomes in cats and dogs with MGT.

2.0 LITERATURE REVIEW

2.1 Anatomical structure

Most dogs possess five pairs of mammary glands, which consist of two thoracic (M1 and M2), two abdominal (M3 and M4) and one inguinal (M5) mammary glands. M4 and M5 are most commonly affected glands (Goldschmidt *et al.*, 2016). For the lymph drainage, M1 and M2 drain to axillary and sternal lymph nodes; M3 drains to axillary, medial iliac and superficial inguinal lymph nodes; M4 drains to axillary and superficial inguinal lymph nodes while M5 drains to superficial inguinal lymph nodes (Patsikas *et al.*, 2006). Cats have four pairs of mammary glands, namely cranial (T1) and caudal (T2) thoracic, and cranial (A1) and caudal (A2) abdominal glands (Goldschmidt *et al.*, 2016). T1 drains to axillary lymph nodes; T2 and A1 drains to axillary or superficial inguinal lymph nodes and A2 drains superficial inguinal lymph nodes (Raharison *et al*., 2006). A study reported that the abdominal mammary glands (A1 and A2) are most frequently affected (De Campos *et al.*, 2014), but Hayden and Nielsen suggested that the cranial glands were more frequently affected (Hayden *et al.*,1971). Meanwhile, Viste *et al.* (2002) described a high incidence in both cranial and caudal mammary glands.

2.2 Clinical presentation

It is common for dogs and cats with mammary tumours to exhibit multiple tumours instead of single tumour. In dogs, small masses have a high chance to be benign and large tumours are more likely to be malignant (Sorenmo *et al.*, 2009), size of mammary gland tumours in cats is not indicative of their biological behaviour where nodules may exhibit malignancy (Goldschmidt *et al*., 2016). According to Bergman (2007), dogs with multiple MGT typically exhibit multiple masses in different locations while cats are more likely to have multiple tumours in a single mammary gland. The entire mammary chain either unilateral or bilateral may be affected in cats, which suggests that neoplastic cells metastasise through the lymphatic system rather than the presence of multiple simultaneous primary tumours (Moore, 2006). About 25% of the affected cats have ulcerated tumours due to extensive tumour necrosis (Novosad *et al.*, 2006); while in dogs, ulceration may be observed notably over large masses that had undergone traumatisation. Most dogs with MGT do not show systemic signs but cachexia and breathing difficulty may be present if the tumours metastasise to lung (Goldschmidt *et al*., 2016). However, systemic signs are apparent in dogs with inflammatory mammary carcinomas (Marconato *et al.*, 2009). Meanwhile cats with benign MGT can exhibit systemic signs such as fever, decreased appetite and lethargy (Görlinger *et al.*, 2002).

2.3 Diagnosis

A detailed history taking is important which emphasises on the patient's age, breed, neuter status, use of hormonal contraceptives, number of births, clinical signs and progress of mammary mass (Wypij *et al*., 2006; Ferreira *et al*., 2003). Complete physical examination including palpation of mammary glands and regional lymph nodes should be performed. Mammary tumours are highly suggested if single or multiple mammary nodules or masses are palpated (Zappulli *et al.*, 2015) while enlargement of regional lymph nodes may indicate presence of metastasis (Sorenmo, 2003). Thoracic radiograph (ventrodorsal, right and left lateral views) and abdominal ultrasound should be performed to evaluate local and distant metastasis (Novosad, 2003; Sorenmo, 2003). Fine needle aspiration cytology is useful to rule out other differential diagnoses such as mast cell tumours and lipomas (Misdorp *et al*., 1999) and to differentiate mammary tumour from fibroadenomatous hyperplasia (Gimenez *et al.*, 2010). Excisional biopsy and histopathological examination are normally performed to confirm the diagnosis (Gimenez *et al.*, 2010).

2.4 Surgical techniques

Treatment options for canine and feline MGT include surgery, chemotherapy, radiation therapy and immunotherapy (Ferguson, 1985; Cassali et al, 2014). However, surgical excision remains the favoured intervention method (Misdorp, 2002; Sorenmo, 2013;). There are five types of surgical techniques available, namely lumpectomy, mammectomy, regional mastectomy, unilateral and bilateral mastectomy (Chang *et al.*, 2005).

Lumpectomy involves removal of small non-adherent benign masses that do not exceed 1 cm in diameter, while mammectomy is the removal of a mammary gland with a single large mass. Regional mastectomy is performed when mammary tumours are identified in consecutive glands or situated in between two glands. In dogs, the M1 to M3 or M3 to M5 are removed as a unit as they share the same lymphatic and venous drainage. Unilateral mastectomy involves the removal of all mammary glands on one side. It is indicated when multiple masses are found in several mammary glands of a single chain whereas bilateral mastectomy is performed when there are multiple masses in both mammary chains (Chang *et al.*, 2005; Patsikas *et al.*, 2006; Van Nimwegen, 2012). Bilateral mastectomy can be performed in one or two stages with at least two-weeks interval between the surgeries (Novosad *et al.*, 2006). Staged bilateral mastectomy is usually recommended especially in deep-chested dogs as removal of both mammary glands at once will cause higher tension which may lead to higher risk of complications (Stone, 2000).

In contrast to dogs, where the extent or type of surgery depends on the clinical stage, lymphatic drainage, size and location of lesions (Sorenmo, 2013), radical mastectomy is recommended in most cats regardless of the tumour size (McNeill *et al.*, 2009). Prophylactic removal of unaffected glands which cause better prognosis is usually done in cats (Mac Ewen *et al.*, 1984). However, such aggressive measure has not been shown to be associated with positive outcome in dogs (MacEwen *et al.*, 1985; Horta *et al.*, 2014).

Lymphadenectomy is recommended during mastectomy for staging purposes as lymph node metastasis affects the prognosis. Superficial inguinal lymph node is removed with the affected caudal mammary glands as it is embedded within the subcutaneous tissue adjacent to the caudal mammary glands while axillary lymph nodes are not routinely removed unless they are enlarged or suspicious for metastasis (Gimenez *et al.*, 2010; Papazoglou *et al.*, 2014).

2.5 Postoperative complications

The common complications associated with post-mastectomy include seroma, hindlimb oedema, wound dehiscence, infection, necrosis of surgical site, haematoma, and tumour regrowth (Papazoglou *et al.*, 2014). Animals that underwent bilateral mastectomy were shown to have higher risk of postoperative complications (Gemignani *et al.*, 2018; Evans *et al.*, 2021). Hindlimb oedema is characterised by the accumulation of lymph fluid in the hindlimb due to obstruction in the lymphatic system at the inguinal region after removal of the inguinal lymph nodes. Seroma formation is commonly observed when there is inadequate dead space elimination or because of lymphatic drainage disruption (Coveney *et al.*, 1993).

2.6 Prognosis / Prognostic factors

Prognostic factors in canine and feline MGT include age at diagnosis, tumour size, tumour subtype and grade of tumour (Sorenmo, 2003; Zappulli *et al.*, 2005;

Goldschmidt *et al.*, 2016). Older patients exhibit poorer prognosis because of the higher anaesthetic risk as they are usually presented with various co-morbidities which make anaesthetic management challenging (Alenza *et al.*, 1997). A smaller tumour size is associated with better prognosis where patients with tumours smaller than 3 cm have longer disease-free intervals. Lymph node status also plays a vital role in determining the prognosis of patients with MGT where the survival time is significantly shorter once lymph node invasion is present. Besides, those with high grade mammary tumours have a poor prognosis compared to those with low grade tumours (Sorenmo, 2003; Zappulli *et al*., 2005; Goldschmidt *et al.*, 2016). According to Alenza (2000), adenocarcinoma and carcinoma in situ offer better prognosis while sarcoma confers the worst prognosis due to its aggressive biological behaviour. In addition, Wakui (2001) reported that mutation of the P53 gene, which is a tumour suppressor gene, is associated with a shortened survival and disease-free interval. In contrast to dogs, where the type of surgery does not affect the survival rate (Allen, 1989), cats that had underwent radical mastectomy has a significantly longer disease-free interval (Ito *et al.*, 1996).

3.0 MATERIALS AND METHODS

The primary data source was derived from the surgery case logbook of University Veterinary Hospital (UVH), Universiti Putra Malaysia. Dogs and cats that were diagnosed with mammary gland tumour and had undergone surgery from 2013 to 2022 in UVH were included in this study. Medical records, surgical reports and histopathology reports of these patients were reviewed.

For each patient, detailed information such as age, sex, breed, body weight, neuter status, details of masses (location and number, radiographs, histologic classification of tumour, type of surgery performed, presence of post-operative complications and follow-up evaluation were obtained. Phone interviews with the owners were conducted to obtain missing information and latest updates about the patients.

All the data was organised in Microsoft Excel spreadsheet. All cases fulfilling the criteria was included in the statistical analysis, with omission of cases without histopathological report. All the statistical analyses were performed using SPSS, version 27 (SPSS Inc., Chicago, IL, USA). Pearson's Chi-square test was performed to analyse the association among groups (neuter status and nature of tumour, surgical technique and presence of post-operative complication). Survival time (ST) for each individual is defined as the time from surgery until death due to MGT while disease-free interval (DFI) is the time frame between surgery until presence of local recurrence or distant metastasis. Kaplan-Meier method was used to describe the overall ST and DFI, and statistical significance was confirmed by comparing differences in survival distribution using a log-rank test. A significance level of 0.05 was chosen, and any *p*-value below this threshold was considered statistically significant. Only individual that died due to MGT was included in Kaplan Meier analysis. Those that lost to follow-up or died due to reasons other than MGT were excluded from Kaplan Meier analysis.

4.0 RESULTS

4.1 Signalment

All patients were female, with 80% (n=64) of the dogs and 48% (n=22) of the cats were intact and the remaining 20% (n=16) of the dogs and 52% (n=24) of the cats were neutered. The mean age at diagnosis for dogs was 9.6 years (range 5 – 14 years) with peak incidence of 10 years old (Figure 1). While in cats, the mean age at diagnosis was 11.22 years (range 3 – 19 years) and the peak incidence was at 15 years old (Figure 2). Mongrel, mixed breed and Shih Tzu (n=9, 9.1%) were the most common breeds, followed by Golden Retriever (n=8, 8.1%), German Shepherd and Rottweiler (n=7, 7.1%) (Figure 3). Meanwhile, Domestic shorthair cat was the most commonly affected breed (n=30, 65.2%), followed by Persian (n=9, 19.6%) and domestic longhair cat (n=3, 6.5%) (Figure 4).

4.2 Nature of tumour

Majority of the tumours in dogs were malignant (n=54, 76%), while benign cases only made up 24% (n=17). The most common MGT subtypes diagnosed in dogs were adenocarcinoma (n=16, 16.2%), followed by simple carcinoma (n=9, 9.1%) and then mixed carcinoma (n=8, 8.1%) (Figure 5). The median ST and DFI of dogs with benign mammary tumours were 41.72 months (range 12.39 – 75.73 months) and 35.02 months (range 0.62 – 75.73 months), respectively; while for dogs with malignant mammary tumours, the median ST and median DFI was 12.94 months (range 2.00 – 101.32 months) and 8.69 months (range 0.20 – 66.76 months), respectively (Tables 1 and 2). The survival rate for dogs with benign masses in first year was 100% and declined slightly to 85.71% in the second year. Meanwhile, the one-year and two-year survival rate was significantly lower for malignant MGT, which were only 60% and 28.57% respectively (Table 3 and 4).

Nearly all the cats diagnosed with MGT had malignant tumours (n=43, 98%) and only a minority of the cases was benign in nature (n=1, 2%). Similar to dog, three of the most common MGT subtypes diagnosed in cats were adenocarcinoma (n=21, 47.7%), simple carcinoma (n=8, 18.2%) and mixed carcinoma (n=5, 11.4%) (Figure 6). The median ST for cats with malignant mammary tumours was 4.50 months (range 1.30 – 30.00 months) while the DFI for malignant cases was 3.00 months (range 0.80 – 21.00 months) (Tables 5 and 6). The benign cases cannot be included in the analysis as there was only one sample in this category which may cause bias in the result. In comparison with dogs with malignant mammary tumours, cats with malignant mammary tumour had notably lower survival rate, with only 23.33% (n=7) of them surviving the first year, and only 10% (n=3) reached the two-year mark (Tables 7 and 8). There was a lack of association between neuter status and the nature of tumour in both dogs and cats (Figures 7 and 8).

4.3 Clinical presentation

Thirty-five dogs (43.8%) and twenty cats (51.3%) had only a single mass, while 45 dogs (56.2%) and 19 cats (48.7%) had multiple masses at the time of evaluation. Most mammary tumours involved caudal mammary glands, where in dogs, inguinal mammary glands were the most frequently affected (n=37, 28.7%) followed by caudal abdominal mammary glands (n=36, 27.9%). While in cats, cranial abdominal mammary glands had the highest frequency (n=22, 34.9%) followed by caudal abdominal mammary glands (n=16, 25.4%). Meanwhile, cranial thoracic mammary glands had the lowest incidence in both dogs and cats, with frequency of 10% (n=13) in dogs and 17.5% (n=11) in cats (Figure 9 and 10).

4.4 Surgical techniques and Postoperative complications

In dogs, regional mastectomy was most commonly performed (n=29, 36.7%), followed by bilateral mastectomy (n=22, 27.8%) and unilateral mastectomy (n=26, 20.3%) (Figure 11). Complications were observed in 31.3% (n=25) of the dogs that underwent surgical treatment. The complications observed include seroma (28.7%, n=25), suture breakdown (23%, n=20), swelling (18.4%, n=16), infection (11.5%, n=10), hindlimb oedema (8.0%, n=7), bruising (5.8%, n=5) and necrosis (4.6%, n=4) (Figure 12). There was no significant association between type of surgical techniques and presence of postoperative complications. However, there was a high chance of complications after bilateral mastectomy (n=18, 81.8%) (Figure 13).

In cats, bilateral mastectomy was the most performed surgical approach (n=18, 39.1%), followed by unilateral mastectomy (n=11, 23.9%). Lumpectomy was the least common surgical approach practised (n=4, 8.7%) (Figure 14). In cats, the highest incidence of postoperative complications observed was swelling (n=10, 26.3%) followed by bruising, seroma and suture breakdown (n=6, 16.7%). Besides, four cats (11.1%) experienced hindlimb oedema and three cats (8.3%) had infection. Skin necrosis was observed in only one cat (2.8%) (Figure 15). There was no significant association between type of surgical techniques and presence of postoperative complications. However, from Figure 16, we can observe that lumpectomy caused 100% (n=4) postoperative complications, followed by bilateral mastectomy (72.2%, n=13).

4.5 Prognostic factors

There was no significant difference in ST and DFI with dogs that experienced different surgical techniques (Figure 17). However, when only looking at the malignant cases, dogs that underwent unilateral and regional mastectomy had longer DFI (p =

0.046) (Figure 18). Besides, the breed size was significantly associated with prolonged survival time (p = 0.005), where small breed dogs had longer survival time (Figure 19).

In cats, the type of surgery performed was not significantly associated with the ST and DFI (Figures 20 and 21). Besides, the neuter age (p = 0.025) and neuter timing (ovariohysterectomy performed before, during or after mastectomy) (p = 0.029) were significantly associated with prolonged DFI. Cats that were neutered before 2 years old had longer DFI than those neutered after 2 years old (Figure 22). Furthermore, spaying done before mastectomy had the longest DFI, followed by spaying performed during and after mastectomy (Figure 23).

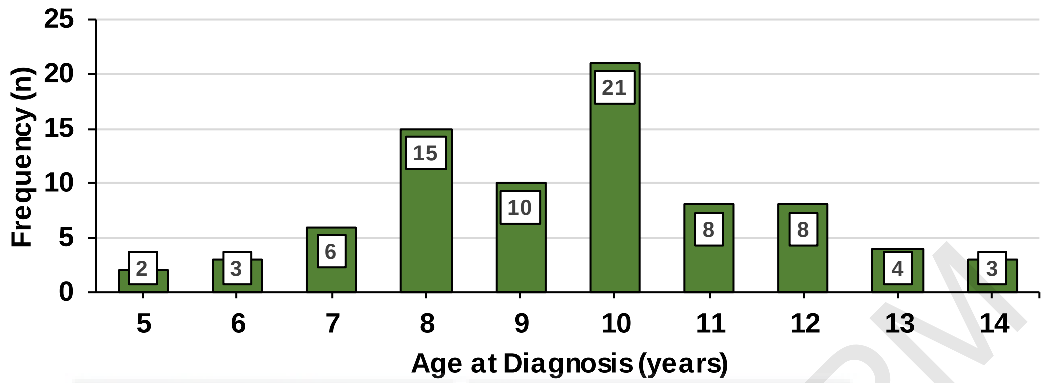

Figure 1 Age distribution of dogs diagnosed with mammary gland tumour.

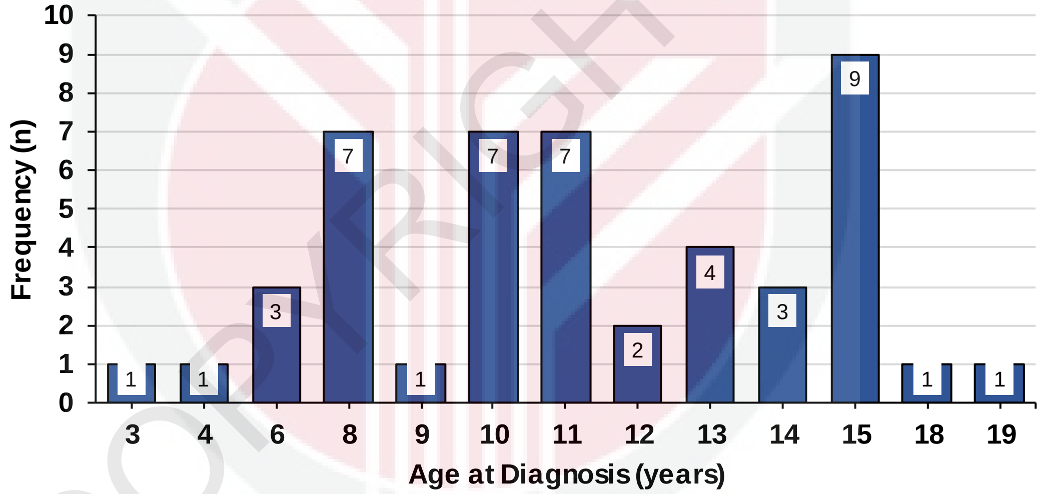

Figure 2 Age distribution of cats diagnosed with mammary gland tumour.

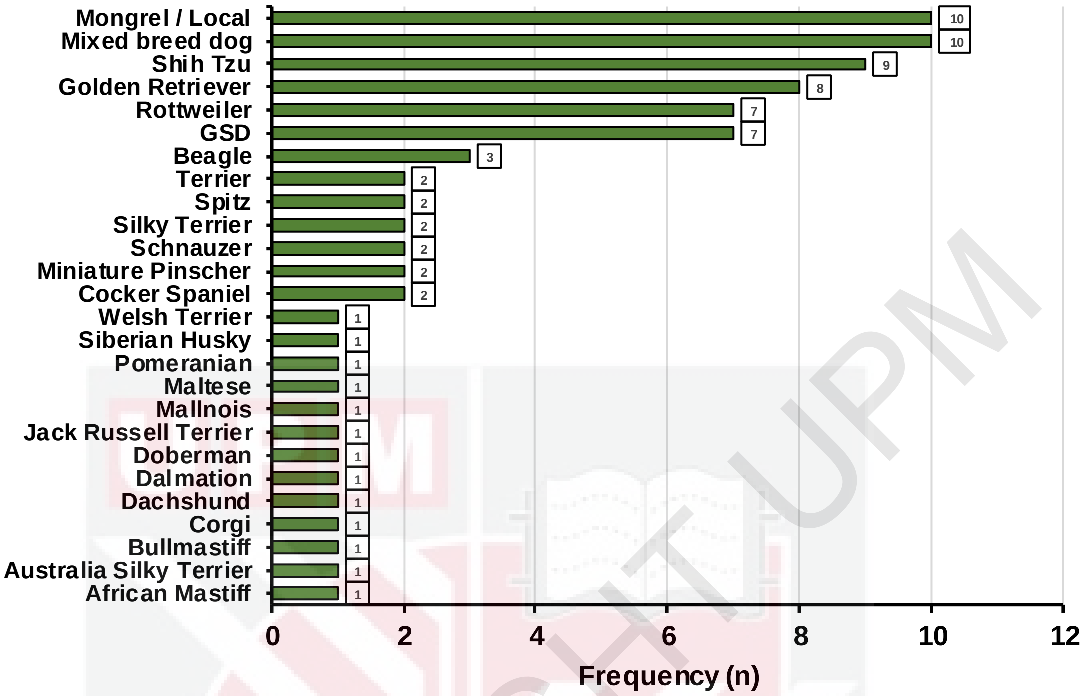

Figure 3 Breed distribution of dogs diagnosed with mammary gland tumour.

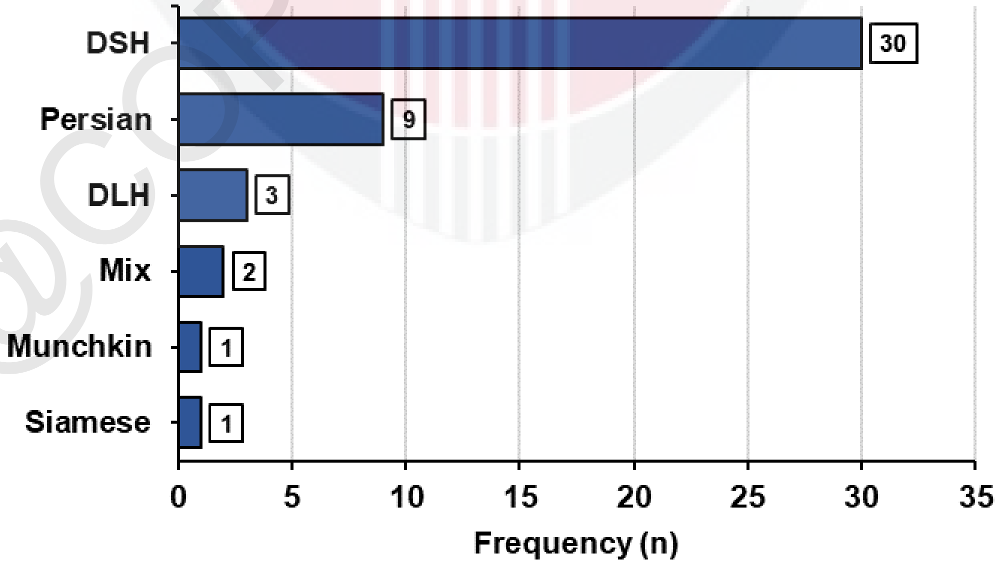

Figure 4 Breed distribution of cats diagnosed with mammary gland tumour.

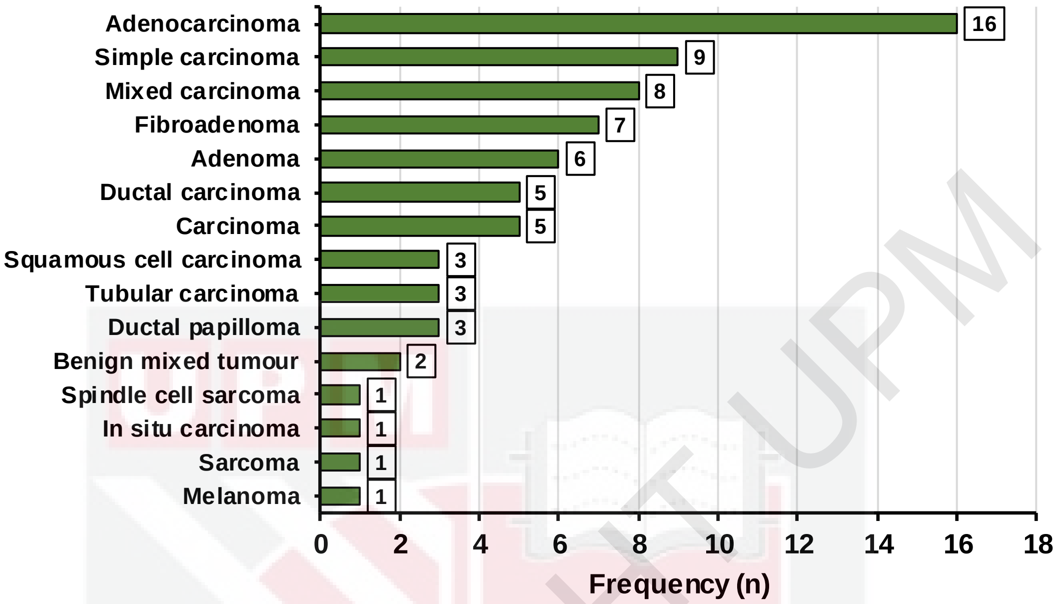

Figure 5 Histologic subtype distribution of dogs diagnosed with mammary gland tumour.

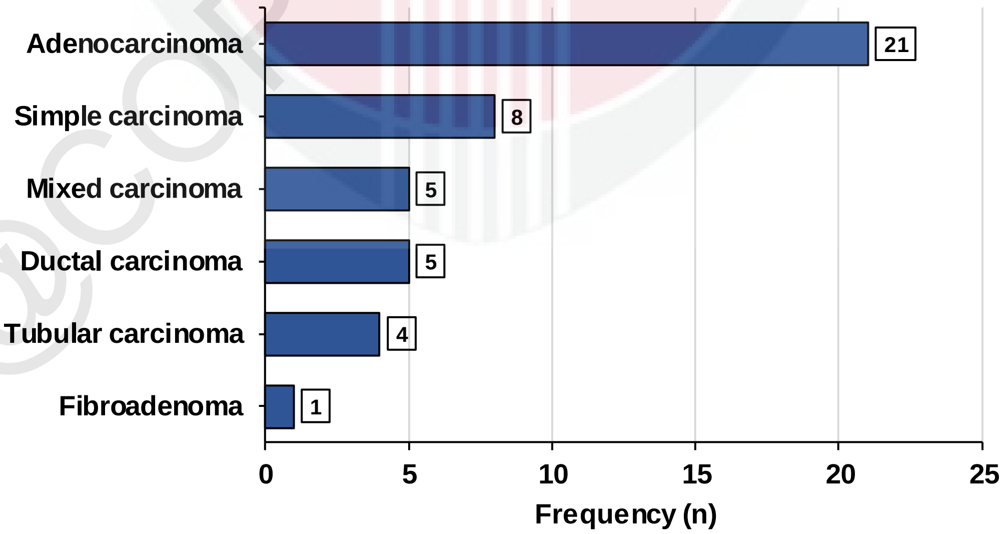

Figure 6 Histologic subtype distribution of cats diagnosed with mammary gland tumour.

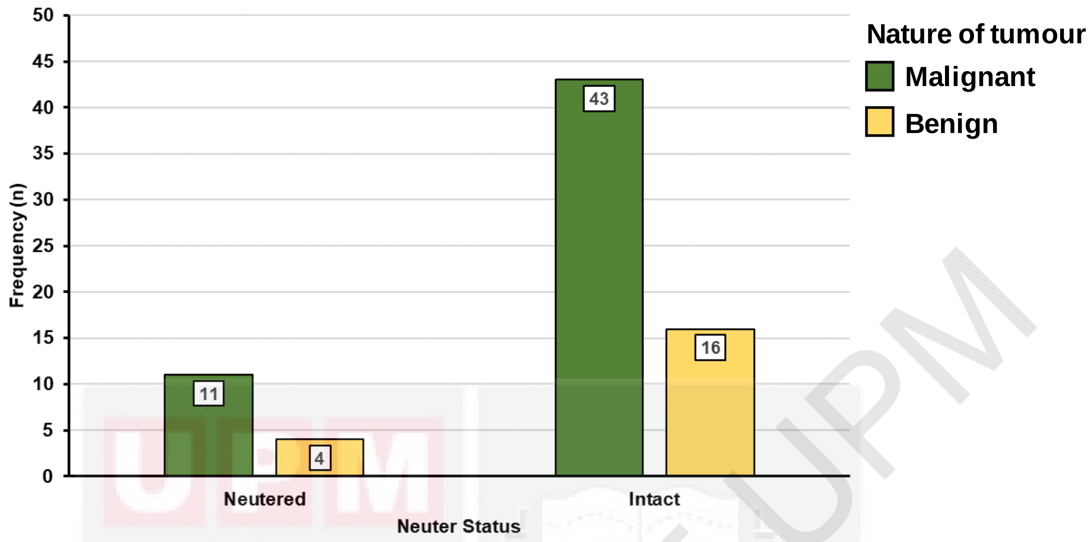

Figure 7 Cross tabulation of neuter status and nature of tumour in dogs with mammary gland tumours. (*p*=0.781)

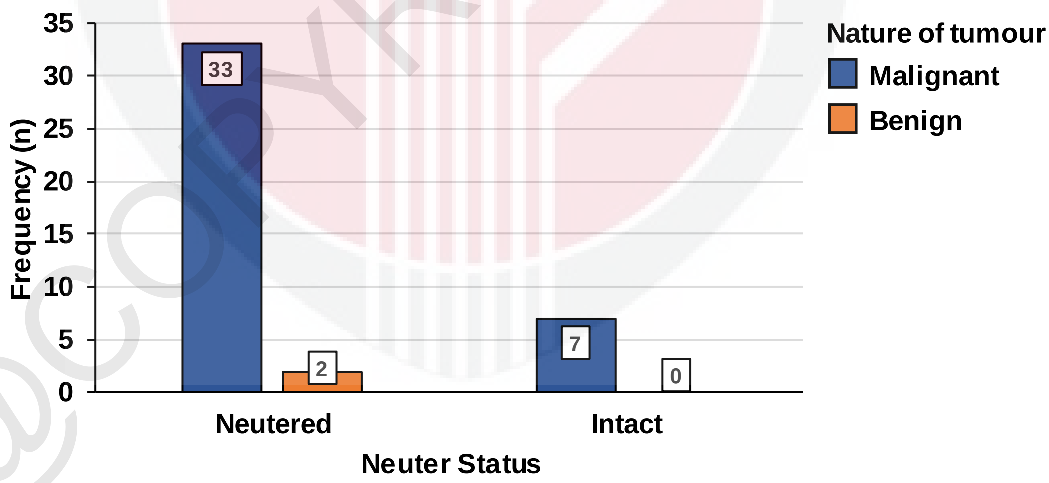

Figure 8 Cross tabulation of neuter status and nature of tumour in cats with mammary gland tumours. (*p*=0.356)

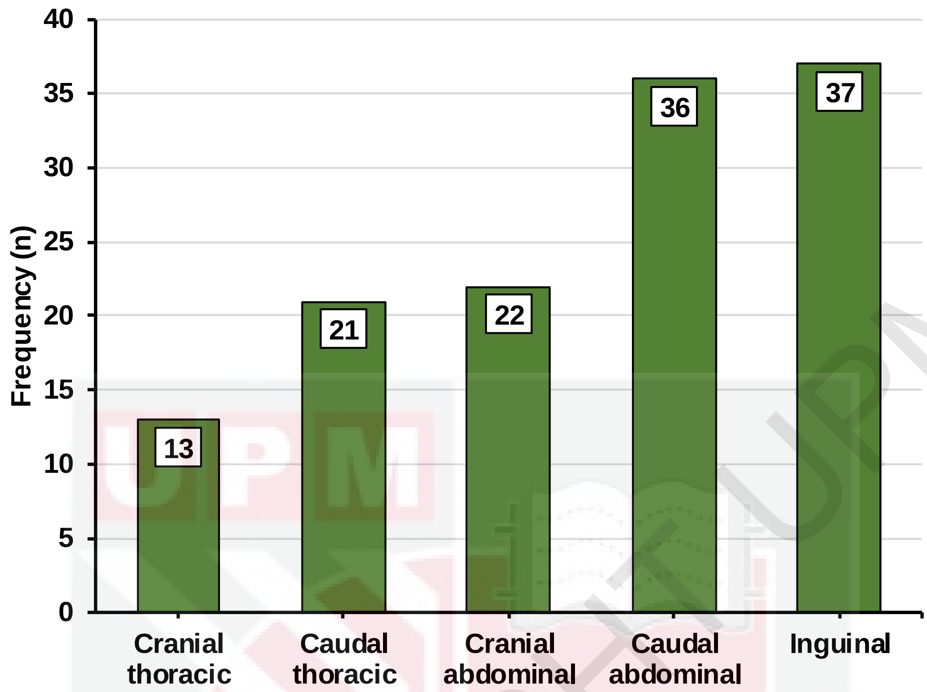

Figure 9 Mammary tumour localisation in dogs that underwent surgery.

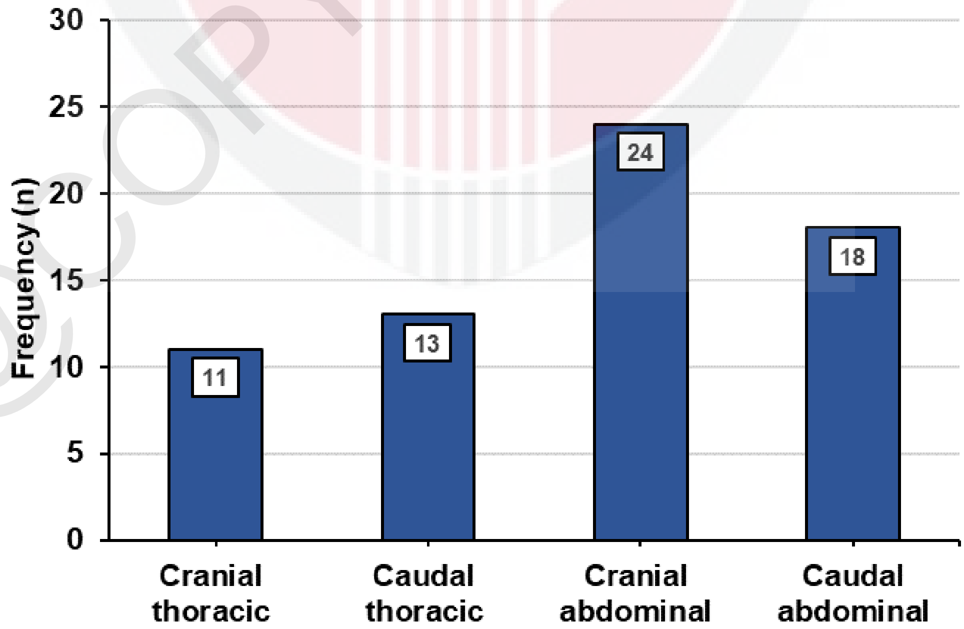

Figure 10 Mammary tumour localisation in cats that underwent surgery.

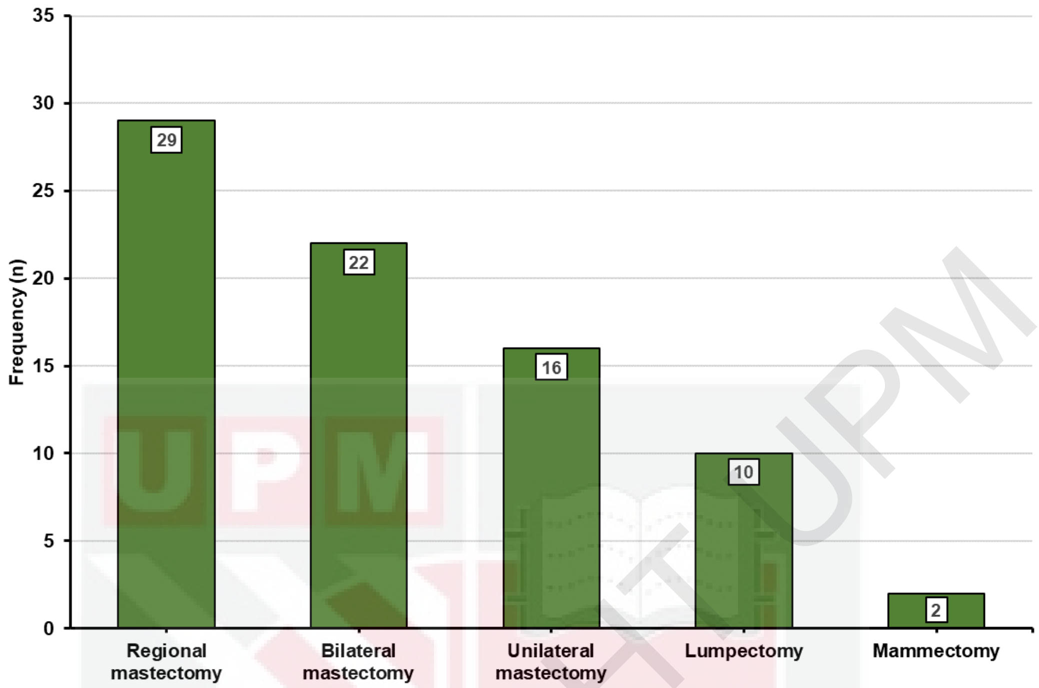

Figure 11 Frequency of surgical techniques performed on dogs with mammary tumours.

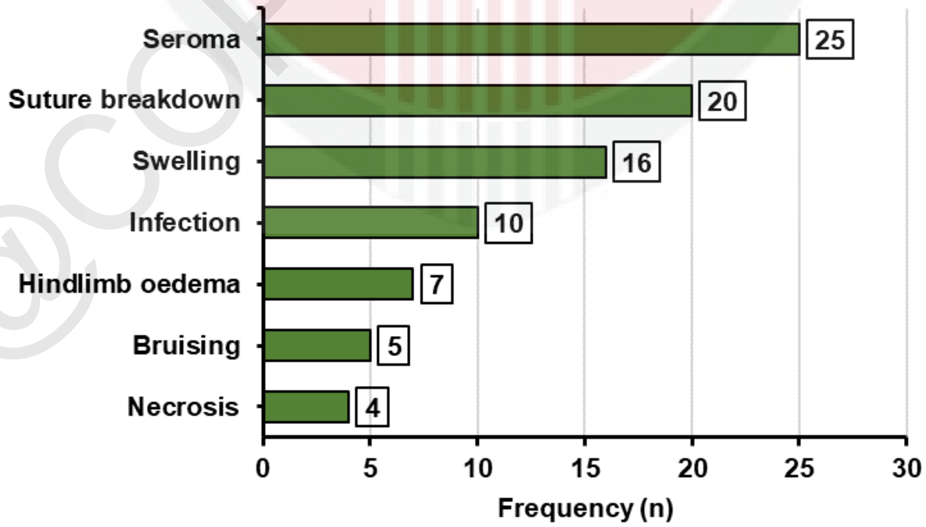

Figure 12 Post-operative complications observed in dogs with mammary gland tumours.

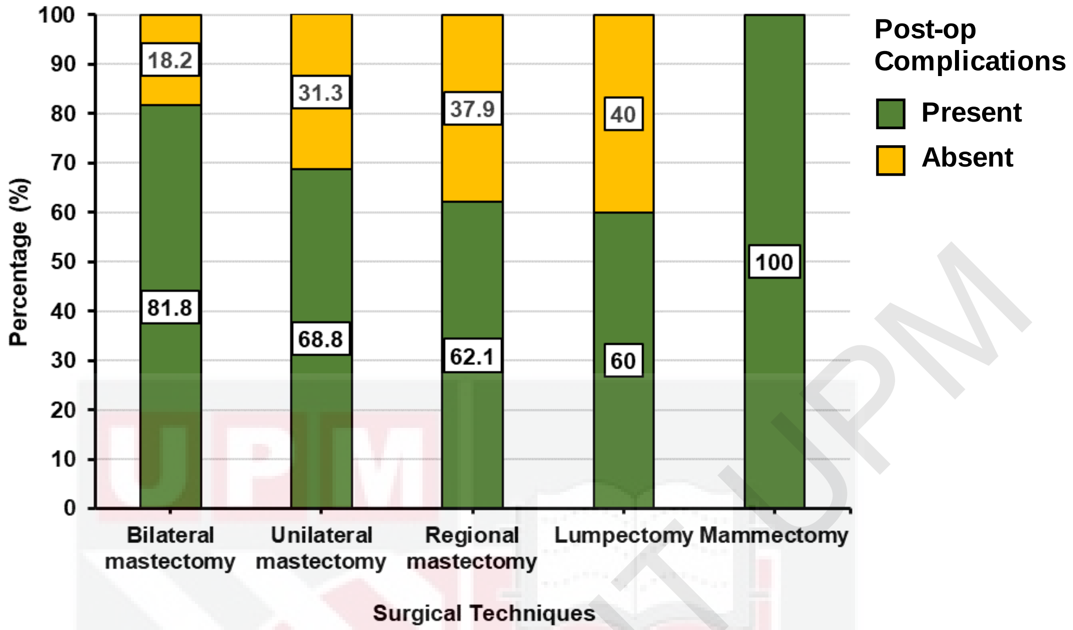

Figure 13 Cross tabulation of surgical techniques and postoperative complications in dogs. (p=0.493)

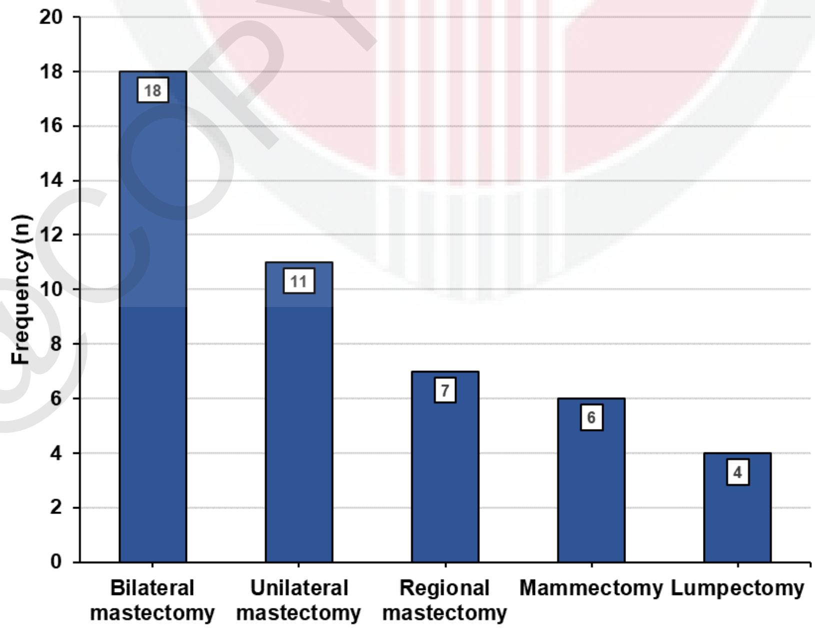

Figure 14 Frequency of surgical techniques performed on cats with mammary tumours.

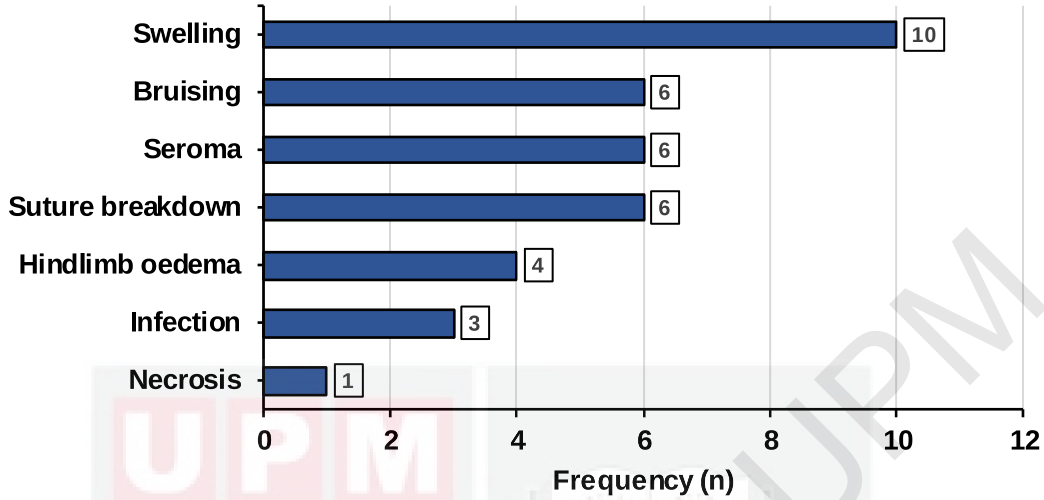

Figure 15 Post-operative complications observed in cats with mammary gland tumours.

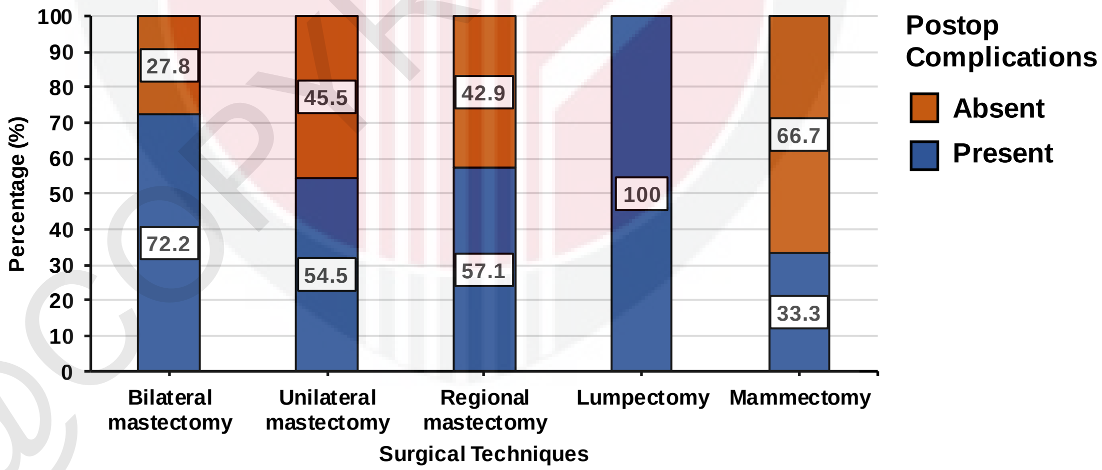

Figure 16 Cross tabulation of surgical techniques and postoperative complications in cats. (p=0.222)

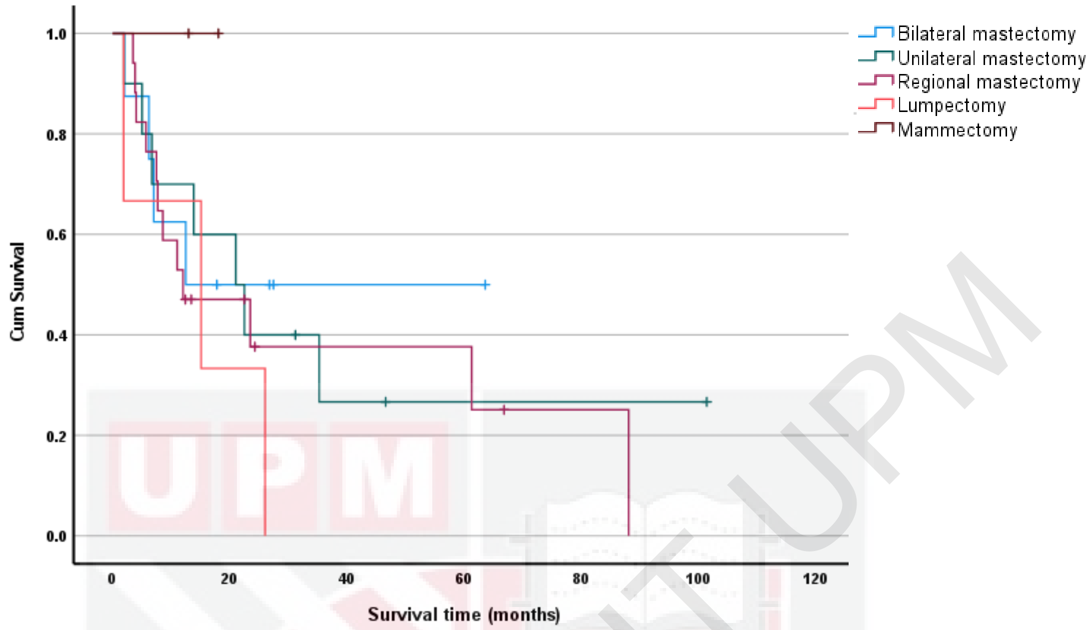

Figure 17 Kaplan Meier survival curves (*p*=0.059) of dogs after surgical removal of mammary tumours, sub-grouped by types of surgical techniques used.

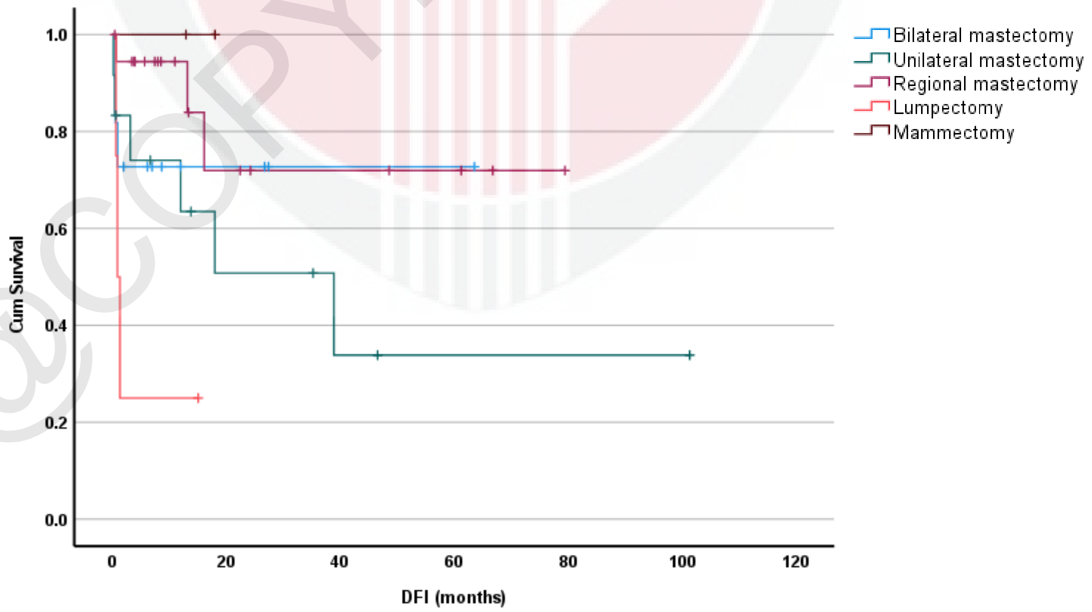

Figure 18 Kaplan Meier disease-free interval curves (*p*=0.046) of dogs after surgical removal of malignant mammary tumours, sub-grouped by types of surgical techniques used.

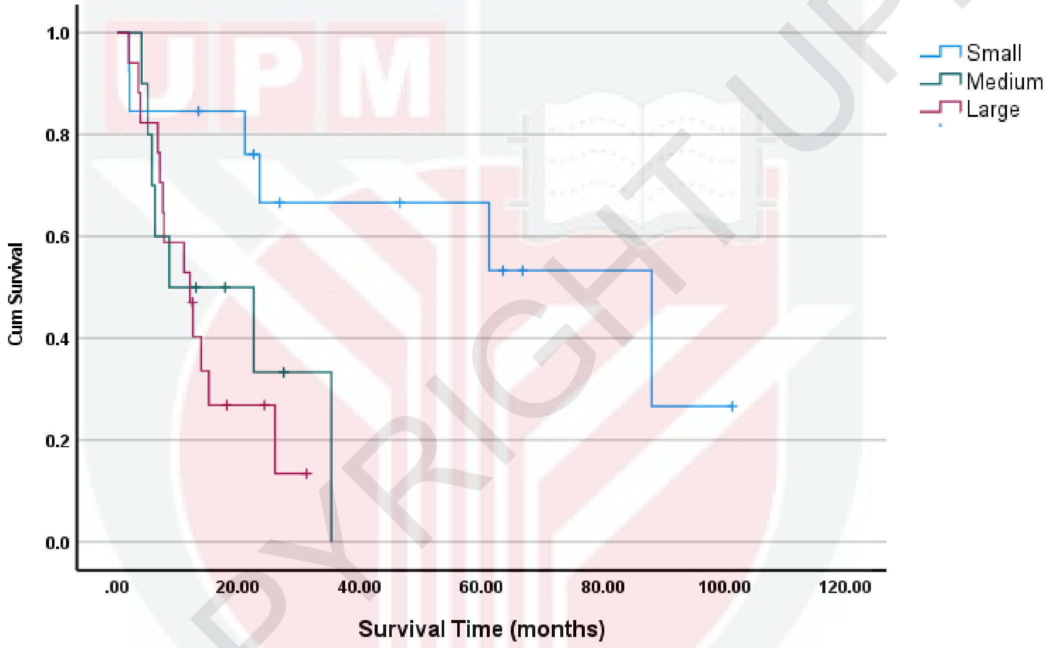

Figure 19 Kaplan Meier survival time curves (*p*=0.005) of dogs after surgical removal of mammary tumours, sub-grouped by breed size of dogs.

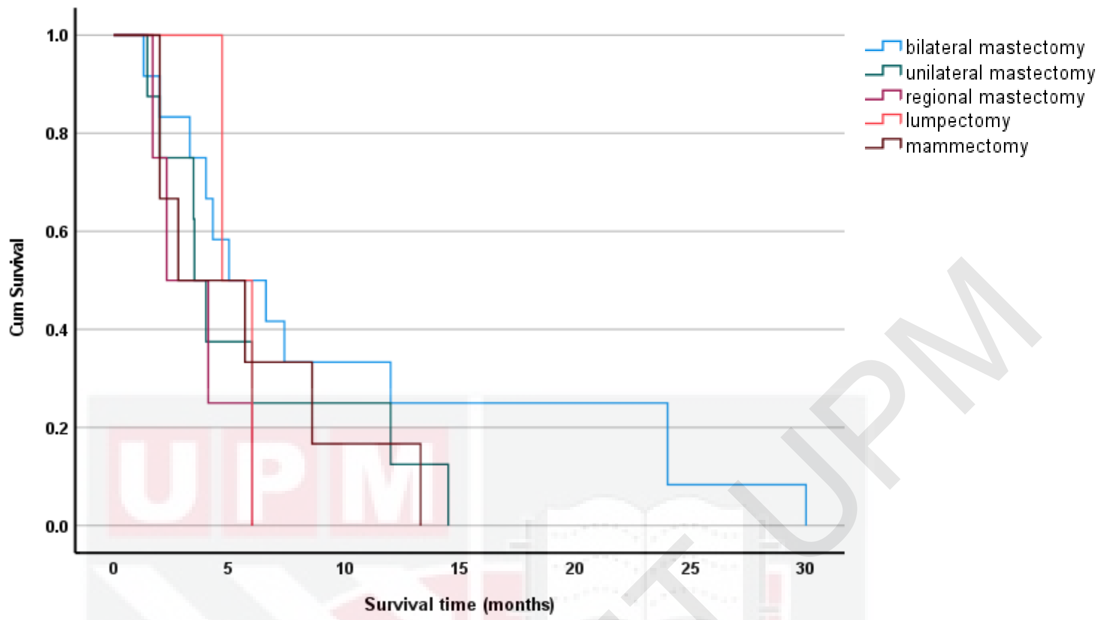

Figure 20 Kaplan Meier survival curves (*p*=0.537) of cats after surgical removal of malignant mammary tumours, sub-grouped by types of surgical techniques used.

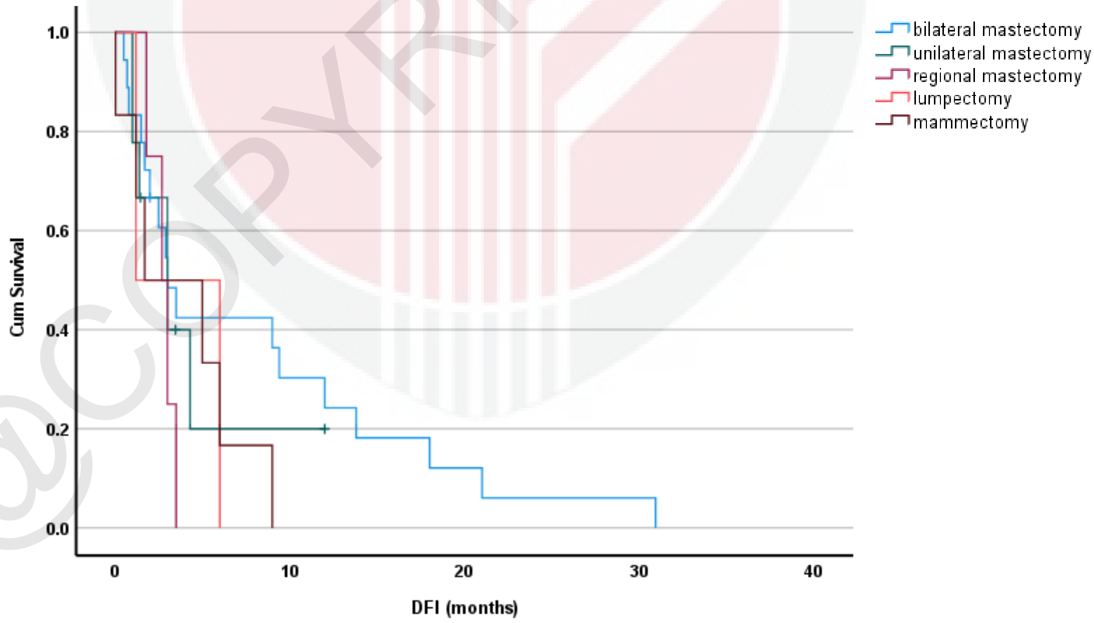

Figure 21 Kaplan Meier disease-free interval curves (*p*=0.648) of cats after surgical removal of malignant mammary tumours, sub-grouped by types of surgical techniques used.

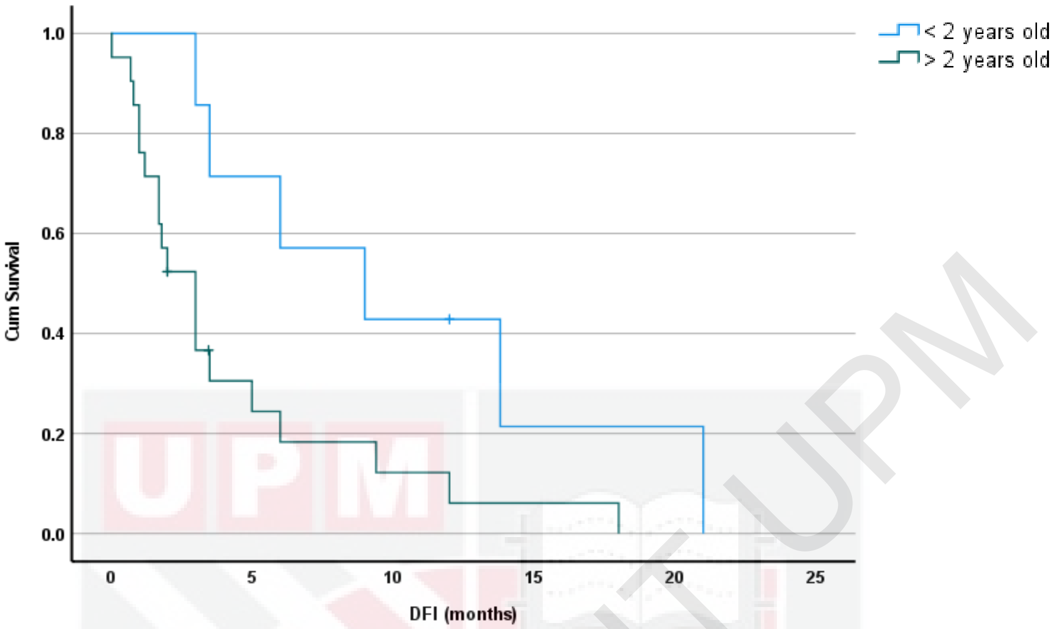

Figure 22 Kaplan Meier disease-free interval curves (p=0.025) of cats after surgical removal of malignant mammary tumours, sub-grouped by neuter age.

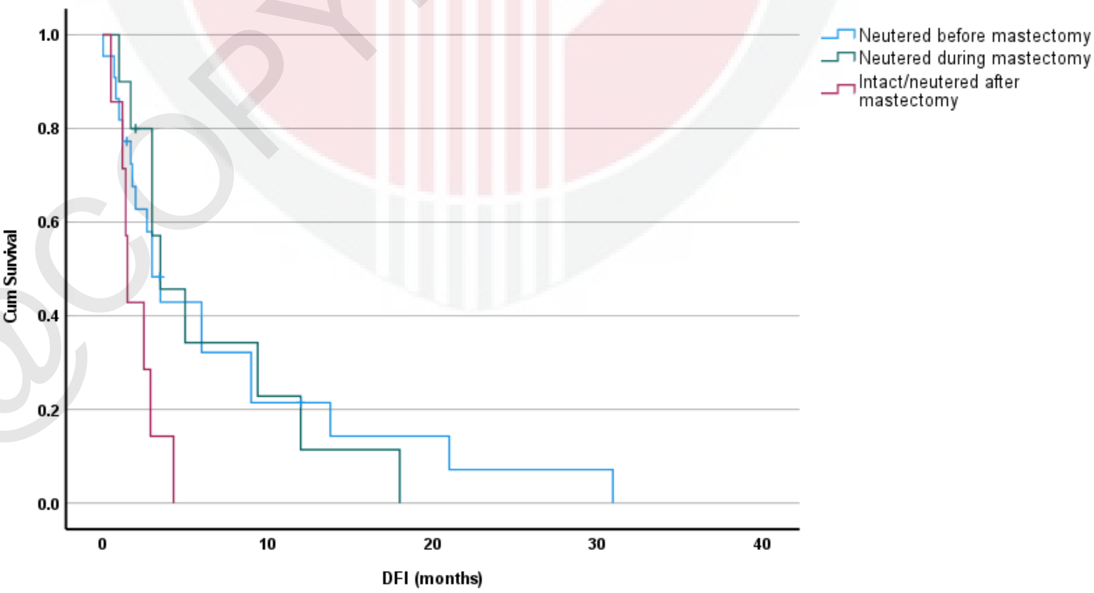

Figure 23 Kaplan Meier disease-free interval curves (p=0.029) of cats after surgical removal of malignant mammary tumours, sub-grouped by neuter timing.

Nature of Tumour	Range (months)	Mean (months)	Median (months)	Standard Deviation
Malignant	0.20 – 66.76	17.84	8.69	23.03
Benign	0.62 – 75.73	36.98	35.02	25.80

Table 1 Postoperative disease-free interval for dogs with mammary tumours.

Nature of Tumour	Range (months)	Mean (months)	Median (months)	Standard Deviation
Malignant	2.00 – 101.32	20.91	12.94	23.96
Benign	12.39 – 75.73	42.55	41.73	20.98

Table 2 Postoperative survival time for dogs with mammary tumours.

Nature of Tumour	Total	Survived	Died	Survival Rate
Overall	42	28	14	66.67%
Malignant	35	21	14	60.00%
Benign	7	7	0	100.00%

Table 3 One-year survival rate for dogs with mammary tumours that underwent surgery.

Nature of Tumour	Total	Survived	Died	Survival Rate
Overall	42	16	26	38.10%
Malignant	35	10	25	28.57%
Benign	7	6	1	85.71%

Table 4 Two-year survival rate for dogs with mammary tumours that underwent surgery.

Nature of Tumour	Range (months)	Mean (months)	Median (months)	Standard Deviation	N
Malignant	0.80 – 21.00	5.40	3.00	6.63	37
Benign	0.80	0.80	0.80	-	1

Table 5 Postoperative disease-free interval for cats with mammary tumours.

Nature of Tumour	Range (months)	Mean (months)	Median (months)	Standard Deviation	N
Malignant	1.20 – 30.00	7.33	4.50	7.33	30
Benign	-	-	-	-	0

Table 6 Postoperative survival time for cats with mammary tumours.

Nature of Tumour	Total	Survived	Died	Survival Rate
Overall	31	7	24	22.58%
Malignant	30	7	23	23.33%
Benign	1	0	1	0.00%

Table 7 One-year survival rate for cats with mammary tumours that underwent surgery.

Nature of Tumour	Total	Survived	Died	Survival Rate
Overall	31	3	28	9.68%
Malignant	30	3	27	10.00%
Benign	1	0	1	0.00%

Table 8 Two-year survival rate for cats with mammary tumours that underwent surgery.

5.0 DISCUSSION

In this study, all the dogs and cats diagnosed with MGT were female, indicating a higher risk of developing MGT in bitches and queens. Bitches and queens are exposed repeatedly to ovarian hormones during the oestrus cycle in their early life. Ovarian hormones such as progesterone and oestrogen promote mammary tumourigenesis. Progesterone upregulates growth hormone production which promotes proliferation of mammary epithelium, leading to development of mammary neoplasm. Oestrogen binds to oestrogen receptors in the normal mammary gland, and changes in the expression pattern of ER in mammary gland have been reported in the course of neoplastic transformation and progression (Sorenmo *et al.*, 2019; Torres *et al.*, 2021).

We observed that dogs aged 10 years had the highest incidence, which is consistent with a previous study suggesting that the peak incidence of MGT in dogs was between 9 to 12 years old (Salas *et al.*, 2015). In contrast to Morris (2013) who reported the peak incidence of feline MGT was at 10 to 12 years of age, the highest incidence in our study population was at 15 years old. Besides, the highest frequency was observed in mongrel, mixed breed dogs and Shih Tzu. This is due to the reason that mongrel is the most common dog breed in Malaysia while Shih Tzu has strong overexpression of BRCA1. BRCA1 is a tumour suppressor gene, but when it undergoes mutation, it loses its function, causing disruption of normal mammary tissue development and increases the risk of malignant transformation (Im *et al.*, 2013). Meanwhile, domestic short hair cat is over-represented because it is the most common breed in Malaysia.

Unlike the previous study, where approximately 50% of the MGT cases in dogs and 80 – 96% of feline MGT were malignant (Moulten, 1978; Gimenez *et la*., 2010; Morris, 2013; Evans *et al.*, 2021), the present study found a higher proportion of malignancy in both dogs (76%) and cats (98%). As UVH is a referral veterinary hospital, most patients probably had more advanced disease which is more likely to be associated with cancer. We also observed that the inguinal and caudal abdominal mammary glands were the most affected glands in dogs. According to Gupta (2012), caudal mammary glands have higher glandular tissue content and tend to retain secretary abilities longer than other glands. In accordance with previous study which suggested that abdominal mammary glands are the most commonly affected in cats with MGT (De Campos et al., 2014), this study showed that mammary tumour mostly occurred at the cranial abdominal mammary gland, followed by caudal abdominal mammary gland.

Regional mastectomy was the most commonly practised surgical approach in dogs in UVH because radical mastectomy has been shown to not provide clinical advantage in dogs with MGT (Horta et al., 2015). Mammectomy was the least preferred surgical technique as more than half of the dogs (56%, n=45) presented had more than one mass. While in cats, bilateral mastectomy was the most frequently performed, as most of the cases in UVH were malignant and radical mastectomy is the choice of malignant MGT (Mcneill *et al*., 2009). The highest postoperative complications noted in dogs was seroma, which could be due to inadequate dead space elimination or disruption of lymphatic drainage (Coveney *et al.*, 1993). A high number of the canine patients had wound dehiscence particularly after regional mastectomy which could be associated with high skin tension. While in cats, swelling had the highest frequency, followed by bruising. This is due to the fact that cats have delicate skin and are prone to swelling and bruising as a result of excessive tissue handling. Although there was no significant association between the type of surgical techniques and the presence of postoperative complications, we observed a higher tendency of wound dehiscence post-bilateral mastectomy in both dogs and cats. Large amounts of mammary tissue were resected during bilateral mastectomy, leading to excessive tension at the incision site. In cats, lumpectomy caused 100% post-operative complications because the surgery involved resection of multiple masses.

Dogs that underwent unilateral and regional mastectomy had longer DFI but not overall ST. This is consistent with a study which suggested that lumpectomy of malignant masses often leads to tumour recurrence so should be avoided (Allen *et al.*, 1989) In this study, 56% of the dog population had multiple mammary masses and required a more radical surgical approach. The same study also mentioned that the type of surgery does not influence survival as long as the entire tumour is removed with clean histologic margins, which is consistent with this study. While in cats, there was no significant difference found in both ST and DFI curves, However, we observed that bilateral mastectomy provided the longest ST (30 months) in comparison with other types of surgical approach, which is consistent with the findings of Novosad et al., (2006).

Contrary with previous study, where adenocarcinoma and carcinoma in situ provide better prognosis (Alenza *et al.*, 2000) to the dog patients, in the present study showed that tubular carcinoma and fibroadenoma provide longer DFI to the patients. Besides, cats neutered before 2 years old had longer DFI than those neutered after that. However, performing ovariohysterectomy after 2 years of age only reported to not provide significant benefit in preventing MGT but not affecting the ST or DFI (Lana *et al.*, 2007). Also, neuter timing was one of the prognosticators in feline MGT but not in canine. From the Kaplan-Meier plot, we can notice that cats neutered before mastectomy had longer disease-free intervals than those neutered after mastectomy. However, similar study about neuter timing and prognosis of MGT only reported in dogs but not in cats, where there was no significant difference between ST in different groups with different neuter timing in dogs (Yamagami *et al.*, 1996).

6.0 CONCLUSION

In conclusion, unilateral and regional mastectomy were associated with longer DFI in dogs with malignant mammary tumour. Cats that were neutered before 2 years old or at time of diagnosis had longer DFI, but not the ST. Number of mass, age at diagnosis and postoperative complication were not prognostically significant in both dogs and cats.

7.0 RECOMMENDATIONS

Larger sample size is required for future studies to provide better representative of the population. A computerised recording system should be used in UVH for better data accessibility. In addition, separating data from new and experienced surgeons can help reduce variation in the surgical outcome. Other prognostic factors such as suture material for closure, post-operative care and staging of the MGT should be further investigated.

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9.0 APPENDICES

Appendix 1: Chi-square test result

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.077[a]	1	.781		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.076	1	.783		
Fisher's Exact Test				.745	.510
Linear-by-Linear Association	.076	1	.782		
N of Valid Cases	71				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.59.

b. Computed only for a 2x2 table

a. Association between neuter status and nature of tumour in dogs

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.853[a]	1	.356		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	1.232	1	.267		
Fisher's Exact Test				1.000	.545
Linear-by-Linear Association	.833	1	.361		
N of Valid Cases	44				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .45.

b. Computed only for a 2x2 table

b. Association between neuter status and nature of tumour in cats

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	19.444[a]	20	.493
Likelihood Ratio	19.222	20	.507
Linear-by-Linear Association	.276	1	.600
N of Valid Cases	79		

a. 24 cells (80.0%) have expected count less than 5. The minimum expected count is .10.

c. Association between surgical techniques and presence of postoperative complications in dogs

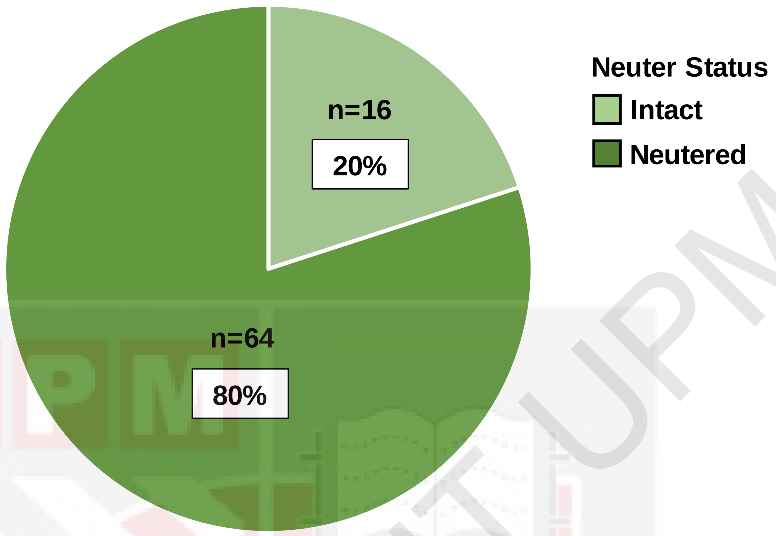
Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	5.714[a]	4	.222
Likelihood Ratio	6.975	4	.137
Linear-by-Linear Association	.925	1	.336
N of Valid Cases	46		

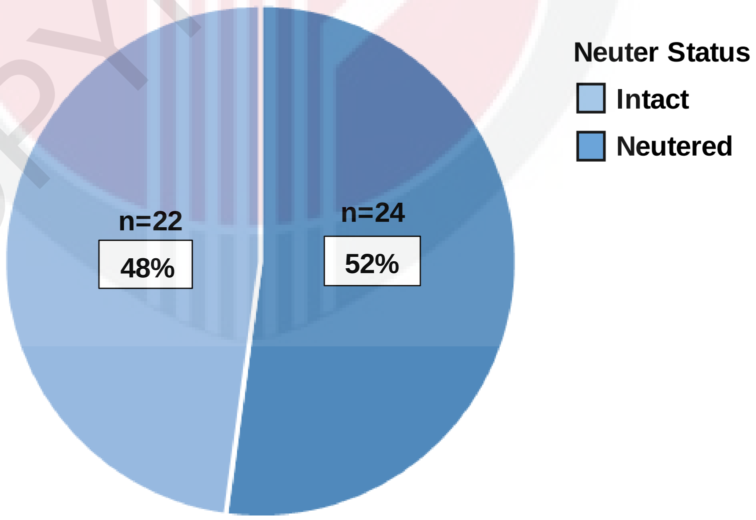
a. 7 cells (70.0%) have expected count less than 5. The minimum expected count is 1.48.

d. Association between surgical techniques and presence of postoperative complications in cats

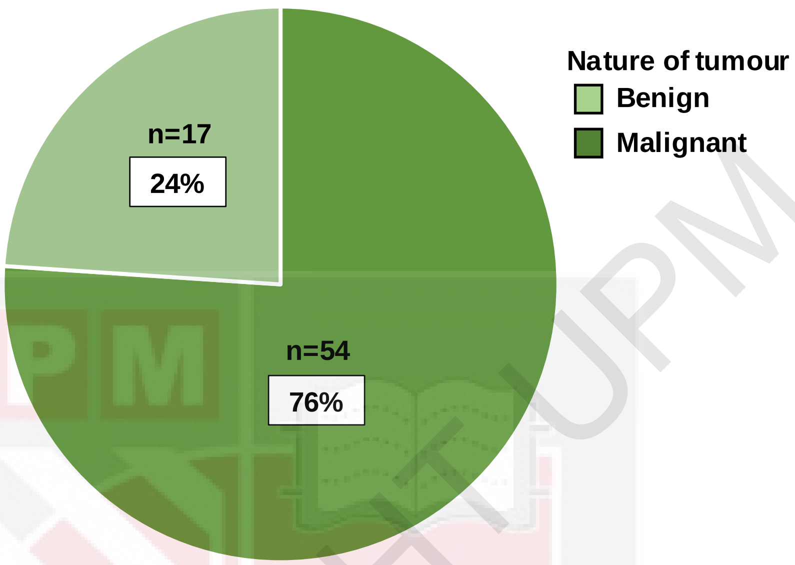
Appendix 2: Neuter status of dogs diagnosed with mammary gland tumour



Appendix 3: Neuter status of cats diagnosed with mammary gland tumour



Appendix 4: Nature of tumour in dogs diagnosed with mammary gland tumour



Appendix 5: Neuter status of cats diagnosed with mammary gland tumour