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Research Article

Surgical Management of Interscapular Feline Injection-Site Sarcomas (FISS): A Case Series of 43 Cats

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Abstract

Evaluate surgical treatment efficacy for feline injection-site sarcomas (FISS) in the interscapular region by assessing complications, local recurrence, and long-term clinical and questionnaire findings. Forty-three cats with interscapular swelling and confirmed FISS were included. Surgery indication followed the 3-2-1 rule (mass ≥3 months, size ≥2 cm, growth within 1 month). Wide excision was performed under general anesthesia with ~5 cm lateral margins and ≥2 fascial planes depth. Flap reconstruction was done if primary closure was impossible. Postoperative follow-up assessed complications, disease-free interval (DFI), overall survival (OS), and pain-related behavior via caregiver questionnaires at 0, 3, 6, 9, and 12 months. Thoracic radiographs evaluated metastasis. Kaplan–Meier and log-rank tests analyzed data. The most frequent complication was incision dehiscence in 28/43 cats (65,1%); secondary infection in 3/43 (7,0%). Complications did not significantly affect OS or DFI ($p>0.05$). Local recurrence occurred in 18/43 cats (41,9%). Median OS exceeded 10 months in cats undergoing revision surgery, versus ~6 months in those refusing further surgery ($p = 0.03$). Suspicious thoracic lesions appeared in 2 cats; metastasis was not confirmed. Caregiver questionnaires showed significant improvement at 3 months ($p < 0.01$), with scores rising between 6 and 12 months in cats with recurrence ($p < 0.001$). FISS is surgically challenging due to high local invasiveness and recurrence despite low metastatic potential. Wide margins and flap reconstruction reduce tension and complications, improving outcomes. Vaccines and injections in extremities or tail, with regular monitoring, may aid early diagnosis and treatment success.

Keywords: Cat, chronic pain, flap reconstruction, injection site sarcoma, local recurrence

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Introduction

Feline injection site sarcomas (FISS) in cats are malignant mesenchymal tumors that have been described since the 1990s and are now considered a significant clinical problem (Saba 2017). Although a strong association with vaccination practices has been demonstrated, long-acting drug injections, suture materials, implants, and microchips may also play a role in their etiology. Initially thought to be solely caused by vaccines, later studies revealed that any injectable material causing local inflammation could be involved in carcinogenesis (Morrison and Starr 2001). Additionally, adjuvants such as aluminum have been proposed as causal factors (Hendrick et al 1992). However, despite extensive research into the pathogenesis of these sarcomas, no definitive causal relationship or direct link with vaccination has been established to explain their development. The most widely accepted hypothesis suggests that a chronic inflammatory response at the injection site serves as a trigger for subsequent malignant transformation (Tasker et al 2023). Although FISS has a low metastatic potential (10-28%), its rapid growth and locally invasive behavior are key features that complicate management in veterinary oncology (Hartmann et al 2023, Ruger et al 2023). Due to their aggressive biological behavior, many pathologists consider FISS to be high-grade sarcomas regardless of histological features. Nevertheless, some authors have attempted to identify factors associated with survival,

metastatic spread, and local tumor recurrence in both low- and high-risk groups (Kobayashi et al 2002, Nieto et al 2003, Hershey et al 2005).

The primary approach to treat these tumors is wide or radical surgical excision. However, their often anatomical location in the scapular region or proximal limbs makes it difficult to achieve clear surgical margins. In cases treated with surgery alone, local recurrence rates are high (30-70%), and recurrences typically occur within a few months post-operation, with recurrent cases becoming increasingly difficult to manage. Therefore, surgical treatment is frequently supplemented with adjuvant therapies such as radiotherapy. Nonetheless, the margins obtained during the initial surgery are considered critical determinants of the disease's prognosis (Bloch et al 2020). Achieving complete surgical excision can be challenging in many anatomical locations; current recommendations, based on positive outcomes reported in the publication by Phelps et al (2011), suggest obtaining 5 cm lateral margins and two fascial planes for deep margins. Major surgical complications have been reported in 11% of cats, with wound dehiscence being the most common complication. However, the recurrence rate in these cases is approximately 14% (Phelps et al 2011). The use of muscle flaps (e.g., latissimus dorsi) to close scapular region defects after wide surgical excision can contribute to stable healing by promoting extensive vascularization and preserving the tissue's natural anatomy, thereby reducing postoperative pain and complication risks (SOJr et al 2001). Although recent reports indicate promising results from adjuvant therapies such as immunotherapy and chemotherapy in FISS treatment, surgical excision remains the primary treatment option given current clinical experience and accessibility, especially when these therapies are used adjunctively or in the early stages. Therefore, the importance of surgical excision in the management of FISS continues to be emphasized, with the width of surgical margins and the success of the initial procedure being among the most critical prognostic factors (Cohen et al 2015, Hartmann et al 2023).

The purpose of this study is to evaluate the outcomes of surgical excisions performed on 43 cats with pathologically confirmed FISS, focusing on survival time, recurrence rate, complications, and behavioral changes related to pain, as assessed through owner questionnaires.

Material and Methods

This study protocol was approved by the Dicle University Health Sciences Application and Research Center Animal Experiments Local Ethics Committee (Approval number: 28/08/2025-08-09).

Animals

The study included a total of 43 cats with a clinical and histopathological diagnosis of FISS. The cats' ages ranged from 18 months to 5 years (mean ± SD; 3.4 ± 1.2 years). Their body weights varied between 4.12 and 5.76 kg (mean ± SD; 4.8 ± 0.6 kg). Of these, 19 were males (44.2%) and 24 were females (55.8%). Among the male cats, 16 (84.2%) were neutered, and among the females, 23 (95.8%) were neutered. Regarding breed distribution, 8 males were Scottish Fold, 3 were Tekir, and 8 were mixed; for females, 15 were Scottish Fold and 9 were mixed. All tumors were localized in the interscapular region across all cases.

Inclusion and Exclusion Criteria

All cats suspected of having FISS during clinical examination and deemed suitable for surgical excision were included in the study. The inclusion criterion was a histopathological confirmation of FISS diagnosis. Clinically, cases were classified according to the '3-2-1 rule' described by Hendrick et al (1992) that is, masses in the injection area lasting longer than 3 months, larger than 2 cm, and showing growth within the last month were considered for biopsy/excision. Tumor sizes were measured with calipers, and anamnesis data were obtained from the pet owners. Cats suspected of systemic problems underwent further diagnostics. Preoperative thoracic radiographs were performed in all cases to evaluate for metastatic disease.

Pain and Behavioral Assessment

To evaluate the effects of tumor-related pain on the behaviors of the cats, a standardized questionnaire was administered to the pet owners preoperatively (before surgery) and at 3, 6, 9, and 12 months postoperatively. The questionnaire included questions about the cats' daily activities (mobility, jumping, playfulness, climbing stairs) and behavioral attitudes (appetite, social interactions, bathroom habits). These questionnaires were adapted from the previously validated Feline Musculoskeletal Pain Index (FMPI) and Client-Specific Outcome Measures (CSOM) scales, used for assessing chronic pain in cats (Lascelles et al 2007, Enomoto et al 2022).

Anesthesia Protocol

All surgeries were performed under a standardized general anesthesia protocol. Cats were fasted for 8 hours prior to the procedure, and an intravenous catheter was placed. Premedication was administered using a combination of medetomidine (10–20 µg/kg IM; Domitor®, Orion Pharma, Finland) and butorphanol (0.2–0.4 mg/kg SC; Butomidor®, Richter Pharma AG, Austria). Induction was achieved with propofol (4–6 mg/kg IV; Propofol-

Lipuro® 1%, B. Braun Melsungen AG, Germany), followed by endotracheal intubation and transition to inhalation anesthesia. Maintenance anesthesia was provided using isoflurane (1.5–2%; Forane®, AbbVie Inc., USA).

Throughout the operation, heart rate, respiratory rate, oxygen saturation (SpO_2), end-tidal CO_2 ($EtCO_2$), non-invasive blood pressure, and body temperature were continuously monitored. Intraoperative fluid support was provided with 0.9% NaCl solution at a rate of 5 ml/kg/hour IV. For analgesia, meloxicam (0.2 mg/kg SC preoperatively; continued at 0.05 mg/kg/day orally; Metacam®, Boehringer Ingelheim, Germany) was used. Prophylactic antibiotic treatment consisted of cefazolin (20 mg/kg IV; Cefazolin Sandoz®, Novartis, Switzerland), administered preoperatively and continued for 5 days.

Surgical Preparation and Excision Technique

The surgical area was shaved to encompass at least a 10 cm margin around the tumor and disinfected with 10% povidone-iodine and 2% chlorhexidine gluconate. Skin incisions were planned to be approximately 5 cm lateral from the tumor, involving at least two fascial planes in depth. Tumors were excised en bloc, removing the surrounding tissues as a single piece. Hemostasis during dissection was achieved using electrocautery or ligatures. For large tissue defects post-excision, particularly in interscapular regions where primary closure was not feasible, reconstruction was performed using latissimus dorsi muscle flaps or rotation flaps, as previously described (Nicoll et al 1996). The subcutaneous tissue was closed with absorbable continuous sutures, and the skin was closed with simple interrupted or intradermal continuous sutures. No surgical drains were used (Figure 1).

Histopathological Examination

Biopsy samples obtained from cats, measuring approximately 2 × 3 × 2 cm and 3 × 3 × 2 cm, were submitted to the Research Laboratory of the Department of Pathology, Faculty of Veterinary Medicine, Dicle University. The tissues were fixed in 10% formalin solution. Following standard tissue processing protocols, the samples were passed through graded alcohol and xylene series and then embedded in paraffin blocks. Sections of 4 µm thickness were obtained from the paraffin blocks using a rotary microtome (Leica Microtome RM2235) and mounted onto glass slides. The prepared slides were stained using the Hematoxylin and Eosin (H&E) staining method, examined under a light microscope (Bioblue 1153-PLI), and photographed.

Histopathological examination of the biopsy samples revealed marked hyperplasia of the epidermal layer, accompanied by pronounced rete ridge formation extending into the dermis and evident parakeratosis. The collagen fibers located beneath the epidermis exhibited an irregular and disorganized distribution. In the subepithelial region, inflammatory cell infiltration composed predominantly of lymphocytes and plasma cells was observed around blood vessels and between adipocytes. This infiltration continued within fibrotic areas between collagen fibers, and some blood vessels showed marked congestion. In the subepithelial area, granuloma structures consisting of macrophages were observed, accompanied by a surrounding mononuclear cell infiltrate and a few neutrophils. Within the granulomas, foamy macrophages

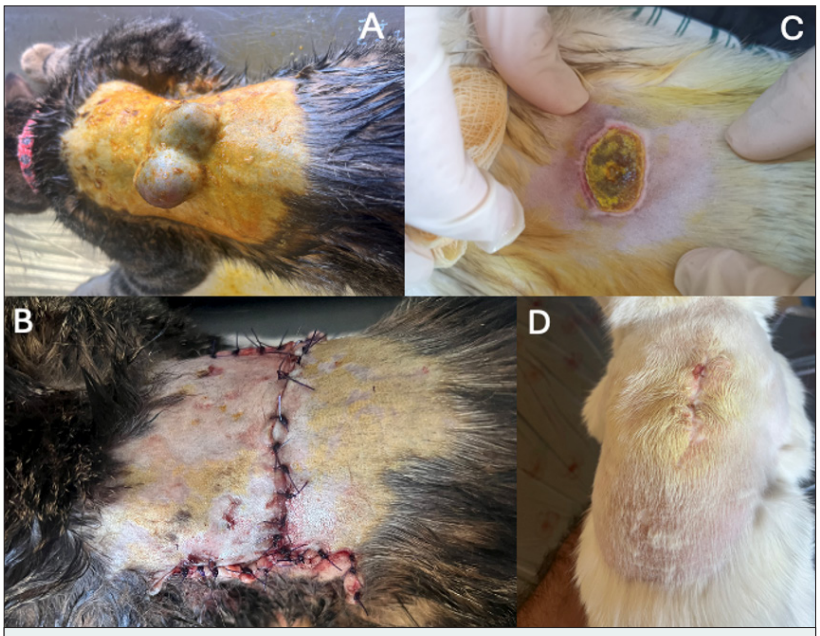

Figure 1. Images of certain cases in the study. A. Preoperative images showing two FISS cases; B. Flap image taken during the postoperative period; C. Unhealed open wound observed in a case after surgery; D. Another case with an incompletely closed wound after surgery

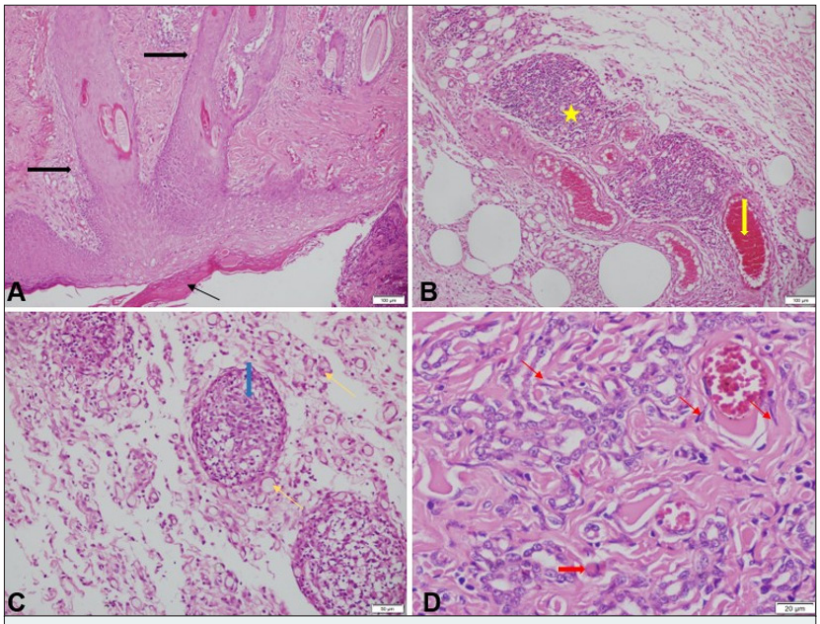

Figure 2. Microscopic image of the H&E-stained lesion in the study. A. Parakeratosis (thin black arrow) accompanied by rete ridge formations extending into the dermis (thick black arrow); B. Lymphoplasmacytic infiltration (yellow star) observed in the subepithelial area, along with vascular congestion (thick yellow arrow); C. Granuloma formation (blue arrow) and foamy macrophages (thin yellow arrow) in the subepithelial region; D. Spindle-shaped cells (thin red arrow) and a mitotic figure (thick red arrow) are present within the tissue.

characterized by lipid-laden cytoplasm exhibiting a vacuolated appearance were prominent. Additionally, numerous lipid vacuoles of varying sizes were observed in the subepithelial area, particularly surrounding the granulomas. Alongside macrophages of different sizes, multinucleated giant cells and spindle-shaped fibroblast-like cells were also identified. No significant nuclear atypia was noted in the cells, and mitotic activity appeared to be low. The histopathological findings were consistent with a chronic inflammatory reaction associated with vaccine administration. However, fibroblastic proliferation observed in certain areas and the cellular characteristics raised the possibility of a low-grade injection-site sarcoma (Figure 2).

Follow-up and Monitoring Protocol

All cats were monitored for at least 12 months postoperatively. Regular clinical examinations were performed during the first 6 months; subsequent follow-ups were supplemented with information obtained from the pet owners. Clinical assessments included inspection and palpation of the surgical area, and additional imaging modalities were used in cases where recurrence was suspected. Additionally, thoracic radiographs were obtained preoperatively and during follow-up to investigate for metastatic spread.

Statistical Analysis

Data were analyzed using SPSS Statistics v.26.0 (IBM Corp., Armonk, NY, USA). The normal distribution of continuous variables was assessed with the Shapiro–Wilk test. Data following a normal distribution were expressed as mean ± standard deviation (SD), while those not fitting a normal distribution were presented as median

Table 1. Demographic characteristics of cats with histopathologically confirmed FISS (n=43)

Variable	Category	n	%	Mean ± SD (Range)
Age (years)	-	–	–	3.4 ± 1.2 (1.5–5)
Body weight (kg)	-	–	–	4.8 ± 0.6 (4.12–5.76)
Sex	Male	19	44.2	–
	Female	24	55.8	–
Neutering status	Neutered males	16	84.2*	–
	Neutered females	23	95.8*	–
Breed	Scottish Fold	23	53.5	–
	Domestic shorthair	3	7.0	–
	Crossbred	17	39.5	–

Demographic characteristics of 43 cats with histopathologically confirmed feline injection-site sarcoma (FISS). * Neutering percentages are calculated within sex groups.

Table 2. Recurrence and survival outcomes in cats with FISS (n=43)				
Parameter	n	%	Time frame (months)	Notes
Recurrence (overall)	18	41.9	3–11	8 euthanized (3–7 mo), 10 later (8–11 mo)
Second revision surgery	5	11.6	8–11	Performed after re-recurrence
Euthanasia due to recurrence/no surgery	8	18.6	3–7	Owners declined further intervention
Median DFI (days)	–	–	–	196 (90–360)
Median OS (days)	–	–	–	274 (120–380)

Recurrence and survival outcomes following wide excision of interscapular FISS in 43 cats.

(minimum–maximum) values. Categorical variables were summarized as counts (n) and percentages (%).

Local recurrence, disease-free interval (DFI), and overall survival (OS) were calculated using the Kaplan–Meier method; differences between groups were compared with the log-rank test. A p-value of less than 0.05 was considered statistically significant (Figure 3).

Results

The included 43 cats had a mean age of 3.4 ± 1.2 years, and the average body weight was 4.8 ± 0.6 kg. Of these, 19 (44.2%) were males and 24 (55.8%) were females. Among the males, 16 (84.2%) were neutered, and among the females, 23 (95.8%) were neutered. Regarding breed distribution, the majority of cases were Scottish Fold (53.5%) and mixed breeds (39.5%), with only 3 cats (7.0%) of the Tekir breed (Table 1).

Tumor sizes measured with calipers showed that only 8 cats (18.6%) had tumors smaller than 2 cm in diameter, while 35 cats (81.4%) had masses larger than 2 cm. Based on owner-reported histories, 19 cats (44.2%) noticed the masses within the first 10–20 days, 9 cats (20.9%) had a previous surgical history at different centers, and the remaining 15 cats (34.9%) had masses that had been present for longer than 3 months.

All cats underwent planned wide or radical excision. The most frequently observed postoperative complication was wound dehiscence, detected in 28 of the 43 cats (65.1%). Of these cases, 17 were males and 11 were females. Most wound dehiscence cases occurred within the first 10 days following surgery. Secondary wound infection was recorded in 3 cats (7.0%). While revision surgery was performed in 2 of these cats, the remaining cases were successfully managed with conservative methods (secondary intention healing, local wound care, and medical treatment). There was no statistically significant relationship between surgical complications and local recurrence (p>0.05).

During the follow-up period, 18 cats (41.9%) developed local recurrence. Eight of these recurrences were observed between the 3rd and 7th months post-surgery, and due to owners declining secondary surgery, euthanasia was performed. The remaining 10 cats experienced recurrences between the 8th and 11th months; of these, 5 underwent revision surgery, while the other 5 owners declined additional surgical intervention. The median survival time for cats that underwent revision surgery was over 10 months, whereas for those that did not, it was approximately 6 months. This difference was statistically significant according to the log-rank test (p=0.03).

Overall survival (OS) and disease-free interval (DFI), evaluated using Kaplan–Meier analysis, exhibited a rapid decline in the early period (first 6 months), followed by a plateau in subsequent months (Figure 3, Table 2).

Thoracic radiographs revealed suspicious lesions in the lungs of only two cats; however, these findings could not be definitively confirmed as metastases. Both cases involved cats that were followed for an extended period and underwent revision surgery.

Table 3. Owner-based pain and behavior assessment scores at different follow-up times (mean ± SD)			
Time (months)	Non-recurrence group (n=25)	Recurrence group (n=18)	p-value (between groups)
Pre-op (0)	7.8 ± 1.2	8.1 ± 1.4	0.412
3	3.2 ± 0.9	3.5 ± 1.0	0.537
6	3.4 ± 1.1	6.8 ± 1.5	<0.01*
9	3.6 ± 1.2	7.2 ± 1.6	<0.01*
12	3.5 ± 1.0	7.5 ± 1.7	<0.01*

* Statistically significant difference (p<0.05). Owner-assessed pain and behavior scores in cats with FISS before surgery and at 3, 6, 9, and 12 months postoperatively. Scores increased significantly in recurrence group from the 6th month onward.

Owner questionnaire results indicated that all cats exhibited significant behavioral changes related to pain before surgery (month 0), including decreased activity, reduced playfulness, loss of appetite, and diminished social interactions. A significant improvement in these parameters was observed at 3 months postoperatively ($p<0.01$). However, from the 6th month onward, particularly in cases with recurrence, scores increased again, reaching statistically significant higher levels between 9 and 12 months ($p<0.05$). Repeated measures analysis demonstrated that the changes in pain scores over time were statistically significant ($p<0.001$). In cats without recurrence, low scores were maintained up to 12 months, while in cases with recurrence, scores increased from 6 months onward, indicating a direct association between recurrence and chronic pain (Table 3).

Discussion

This study evaluated the outcomes of surgical excision performed on 43 cats with localized FISS in the interscapular region. Surgical wound dehiscence was observed in 65.1% of cases; however, these complications did not have a statistically significant effect on local recurrence rates or survival times. The local recurrence rate was determined to be 41.9%, which is consistent with previously reported rates ranging from 26% to 59% in the literature (Hershey et al 2005, Phelps et al 2011). Notably, cats that underwent revision surgery had a significantly longer median survival time, supporting the notion that the success of the surgical outcome is largely dependent on the quality of the initial excision.

In our study, early and mid-term recurrences (3–7 months) mostly resulted in euthanasia due to owners declining additional surgery, whereas some late recurrences (8–11 months) could be managed with revision surgery. This finding aligns with the view reported by Phelps et al (2011) that "the long-term outcomes are determined by the radicality of the initial excision". Similarly, Martano et al (2011) reported that wide surgical margins offer better local control but increase the need for reconstruction and the risk of complications.

Owner questionnaire results demonstrated that FISS causes chronic pain in cats, leading to behavioral changes. Significant improvement was observed in these symptoms during the early postoperative period; however, scores increased again in cases with recurrence. This finding indicates that FISS is not only an oncological issue but also a significant clinical problem affecting behavior and quality of life. As previously reported by Bray et al (2014), chronic pain is closely associated with behavioral changes in cats and can lead to a substantial decline in quality of life.

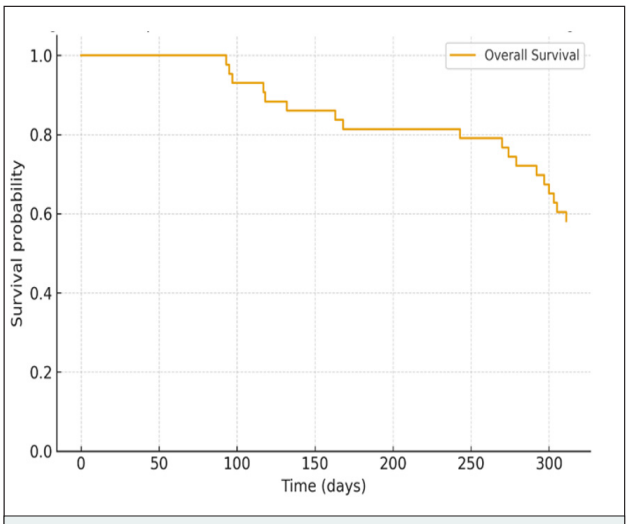

Figure 2. Kaplan–Meier survival curve for 43 cats with feline injection-site sarcoma (FISS) undergoing surgical excision. The curve illustrates overall survival (OS) following primary surgery. A rapid decline in survival probability was observed within the first 6 months due to early recurrences and euthanasia. Afterward, the curve plateaued, reflecting the survival of cats with either revision surgery or no recurrence during the follow-up period.

The high rate of wound dehiscence observed in our study (65.1%) may be associated with the extensive surgical excision in the interscapular region. Literature reports indicate that major postoperative complication rates following FISS surgery range between 10% and 30% (Bray and Polton 2016). This discrepancy can be explained by the fact that all cases in our study involved tumors localized to the interscapular area, where primary closure is challenging due to the defect size. In cases where wide surgical margins are achieved, the use of flaps and grafts can reduce wound tension and facilitate healing (Cantatore et al 2014). Studies utilizing latissimus dorsi or trapezius muscle flaps have reported decreased complication rates and improved postoperative pain management, owing to well-preserved vascularization (Giudice et al 2010). As noted in the literature, all cases in our study involved flap application to reduce wound tension. However, the formation of large wound defects likely contributed to an increased incidence of wound dehiscence at the incision site.

In our study, metastasis was suspected in only two cases but could not be confirmed definitively. Literature reports metastasis rates in FISS cases generally range between 10% and 28% (Phelps et al 2011, Bray and Polton 2016). The observation of low metastasis rates in our study may be related to the short follow-up duration. However, the detection of suspicious lung lesions in cases followed long-term and subjected to revision surgery suggests that metastasis could develop over time in these cases. We believe that the true metastasis rate can only be determined through longer-term prospective studies.

All cases in our study were localized to the interscapular region. However, the literature reports that administering

injections to distal limbs or the tail can facilitate more straightforward and radical surgical excisions in potential FISS cases, and this approach has been associated with improved prognosis (Shaw et al 2009, Stone et al 2020). Considering the results of our current study, we believe that performing surgery in the interscapular area is quite challenging and that, as suggested in previous research, vaccinations in the distal limbs and tail could help prevent such difficult cases. Therefore, it is very important for veterinary practitioners to be more cautious about vaccination sites and for pet owners to regularly monitor injection areas.

A significant limitation of our study is that none of the cases received adjuvant radiotherapy or chemotherapy. Literature indicates that multimodal treatment protocols (surgery + radiotherapy ± chemotherapy) significantly reduce recurrence rates compared to surgery alone and prolong disease-free survival (Martano et al 2011, Bray and Polton 2016). Therefore, the high recurrence rate observed in our study (41.9%) may be primarily related to the absence of adjuvant therapies. Additionally, the common refusal of revision surgeries by owners and the early euthanasia of cases with recurrence contributed to the high euthanasia rate. These findings underscore the importance of multimodal treatment approaches in FISS management and highlight the limitations of solely surgery-based protocols in achieving long-term prognosis.

Conclusion

While surgery remains the primary treatment option for cats with FISS, early diagnosis and multimodal approaches (surgery + radiotherapy ± immunotherapy) should not be overlooked. Preference for limb injections during vaccination, regular monitoring of injection sites by pet owners, and prompt veterinary consultation in suspicious swellings play a critical role in enabling early detection. Early diagnosis followed by wide surgical excision combined with adjuvant therapies can improve the prognosis of affected cases. Additionally, limiting vaccinations to necessary situations, veterinarians being more cautious during injection procedures, and informing pet owners about the risks of FISS are key strategies to reduce the incidence of these tumors. We believe that a conscious approach by veterinarians regarding vaccination and injection practices, along with early owner observation, can help lessen the clinical burden of FISS.

Our study results indicate that, particularly when performed early, radical surgical excision can achieve higher success and somewhat longer survival times—even with limited access to adjuvant therapies—compared to cases diagnosed at later stages. Therefore, in managing FISS, preventive strategies, early diagnosis, and a multimodal approach (surgery + radiotherapy ± immunotherapy), when possible, are of great importance and should be considered together to optimize outcomes.

Declarations

Competing Interests
The authors declare no conflict of interest.

Funding
This research received no external funding.

Availability of Data and Materials
The data that support the findings of this study are available on request from the corresponding author.

Ethical Statement
This study protocol was approved by the Dicle University Health Sciences Application and Research Center Animal Experiments Local Ethics Committee (Approval number: 25/09/2025-06-10).

Author Contributions
Motivation/Concept: SY, NS; Design: NS, BEK, SY, EC; Data Collection and Processing: NS, BEK, EC; Analysis and Interpretation: NS, SY, BT, EE; Literature Review: NS, EC, BEK, SY, BO, Writing the Article: SY, NS; Critical Review: SY, NS

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