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CLINICAL RESEARCH

Outcomes of dogs with apocrine gland anal sac adenocarcinoma treated via modified closed anal sacculectomy (2015–2022)

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Abstract

Objective: To evaluate the postoperative complication rate and local recurrence rate of apocrine gland anal sac adenocarcinoma (AGASACA) in dogs surgically treated with a modified closed anal sacculectomy technique between 2015 and 2022.

Study design: Observational clinical retrospective study.

Animal population: Forty-seven client-owned dogs histologically diagnosed with AGASACA.

Methods: Medical records were evaluated for patient demographics and history, physical examination findings, diagnostic imaging, incidence of concurrent neoplasia, postoperative complications, and incidence and time to local recurrence. Dogs with at least 150 days of follow-up were included in evaluation of local recurrence.

Results: Two dogs were euthanized at 4 and 11 days after surgery. Forty-five dogs were included for long-term local recurrence evaluation, with a median of 364 days of follow-up (range 156–2156 days). Only one dog (2.2%) developed local recurrence with a time to recurrence of 90 days. Postoperative complications were reported in 15 dogs (31.9%) and were considered minor in 14 dogs (93.3%) and major in one dog (6.7%). Mean survival time for the 20 dogs that were deceased as of November 1, 2022 was 521 days (range 156–1409 days) and the median survival time was 388 days.

Conclusion: The modified closed anal sacculectomy technique resulted in a lower AGASACA local recurrence rate than previously reported in the veterinary literature with a comparable postoperative complication rate.

Clinical significance: Given the low recurrence rate found in this study, the modified closed anal sacculectomy technique may reduce the need for adjuvant radiation therapy and potentially chemotherapy in AGASACA patients.

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1 | INTRODUCTION

Apocrine gland anal sac adenocarcinoma (AGASACA) is an epithelial neoplasm responsible for approximately 2% of canine skin tumors and approximately 17% of perianal malignancies.[1,2] The most common clinical signs at the time of diagnosis, in addition to a palpable mass, are tenesmus, perianal swelling polyuria and polydipsia, dyschezia, and abnormal pelvic limb gait, although 38.6%–81% of tumors are diagnosed with no clinical signs present.[1,2] Hypercalcemia of malignancy has been reported in 25%–90% of AGASACA cases.[3–5] These tumors are typically very locally aggressive with a high rate of metastasis.[4–6] In previous studies, 50%–90% of dogs had metastasis present at the time of diagnosis.[4,6–8] Metastasis occurs primarily to the regional lymph nodes, but distant metastasis to the liver, spleen, and lungs can occur later in the disease process and is seen in 2%–18% of cases.[2,4,5,8] Metastasis to the regional lymph nodes or distant organs has repeatedly been associated with a shorter disease-free interval (DFI) after surgical excision and shorter median survival time (MST).[1,4,6,9,10] Extirpation of lymph nodes that are metastatic has been shown to increase DFI and MST in dogs.[9–11] Reported MST for surgery alone varies widely in the literature and has been reported as 182–1237 days.[12–14] Reported median survival time is 540 days for surgery with adjunctive chemotherapy and 742–956 days for surgery with both radiation therapy and chemotherapy.[2] Potanas et al. reported that completeness of the surgical excision was not associated with differences in DFI or MST.[10]

Standard of care for surgical excision of AGASACA tumors includes both excision of the primary tumor and anal sacculectomy of the affected side(s), as well as extirpation of any metastatic regional lymph nodes.[1,5,6] The two main techniques for removal of the anal sac in the non-neoplastic setting are the open technique and the closed technique, while the closed technique is almost exclusively used in cases of suspected neoplasia due to the potential for increased contamination of the surrounding tissue using the open technique. The open technique has also been associated with a higher incidence of incisional complications.[15,16]

Local recurrence, even despite histologically clean margins, is relatively common in dogs with AGASACA. Sterman et al. reported local recurrence in 18% of cases with an average DFI of 374 days after primary tumor removal with or without lymphadenectomy.[1,17] Other studies have reported local recurrence rates of 20%–50% with surgery alone.[3,14] Tanis et al. found that the average time to documented progression after anal sacculectomy and lymph node extirpation was 196 days.[2] Other postoperative complications such as incision dehiscence, fistula formation, and fecal incontinence may result in delayed healing time and increase the postoperative recovery burden on owners.

The modified closed technique was performed in the dogs in this study because it is the preferred technique of the surgeon (CP) who performed the anal sacculectomy surgeries and because of concern that normal anal gland secretions in a dog with AGASACA may seed the entire duct with neoplastic cells. This concern forms the basis of our hypothesis that complete excision of the sac and duct, which does not occur in the traditional closed technique, would result in a lower local recurrence rate. The authors are unaware of any previous AGASACA literature examining outcomes of surgery via the open technique or a modified closed technique; most previous reports on the topic of surgical treatment of AGASACA do not describe the specific surgical technique used.

The goal of this study was to examine the postoperative complication and local recurrence rates in dogs with AGASACA who underwent primary tumor excision and anal sacculectomy via a modified closed technique. We hypothesized that included dogs would show a higher postoperative complication rate but lower local recurrence rate than was previously reported in the literature for this disease.

2 | MATERIALS AND METHODS

Records were reviewed from two specialty referral hospitals for dogs undergoing anal sacculectomy between June 1, 2015 and June 1, 2022. Records of dogs undergoing anal sacculectomy, regardless of etiology, were identified by searching for patients with invoices that included "sacculectomy" or "anal sacculectomy". All surgeries were performed by a single board-certified surgeon who had completed a fellowship in surgical oncology (CP). Dogs were included in this study if they underwent anal sacculectomy for an anal gland tumor (either unilateral or bilateral) via the modified closed technique, histopathology of the mass confirmed a diagnosis of AGASACA, complete medical records were available, and follow-up was available for at least 150 days (either at the study institutions or through the primary care veterinarian). A medical record was considered complete if it included the history, physical examination, digital rectal examination, details of the surgical procedure, details of postoperative treatments and postoperative complications, a discharge report, and follow-up. Dogs were excluded if the histopathology reported a diagnosis other than AGASACA, if no histopathology report was available, or if the medical record was incomplete.

Demographic variables reviewed included breed, age, sex, weight, clinical signs, and incidence of previous or concurrent neoplasia. Other factors assessed included known duration of tumor presence before surgery, whether preoperative cytology was performed on the anal sac mass, preoperative staging (thoracic radiographs, abdominal ultrasound, and/or computed tomography [CT] scan), preoperative lymph node aspiration, index of suspicion for metastasis at the time of surgery, incidence of surgical or anesthetic complications, incidence of local recurrence, postoperative complications, and whether adjunctive therapy was pursued. Complete records were available for 47 dogs. Two dogs were euthanized within 2 weeks after surgery and were included in analysis of postoperative complication rates but not in analysis of local recurrence rates ($n = 45$).

All surgeries were performed via a modified closed technique with the goal of marginally removing all anal sac tissue en bloc. In the modified closed technique, a circular incision was made around the anal sac duct, then extended in a caudolateral direction overlying the anal sac. The subcutaneous tissues were dissected away from the sac and duct, and the tumor, sac, and duct were excised en bloc in their entirety. The external anal sphincter was then reconstructed, and the subcutaneous tissues and skin were sutured closed (Figure 1). In cases of a large anal mass where removal of the mass created a significant amount of dead space, a 7 French spiral drain (MILA International, Inc., Florence, Kentucky) connected to a closed suction reservoir grenade was placed for 3–5 days after surgery to minimize the risk of seroma formation. If evidence of lymph node metastasis was present at the time of surgery based on abdominal imaging, the affected lymph nodes were removed under the same anesthetic episode.

Individual anesthetic protocols were based on the preferences of the attending anesthesiologist, which

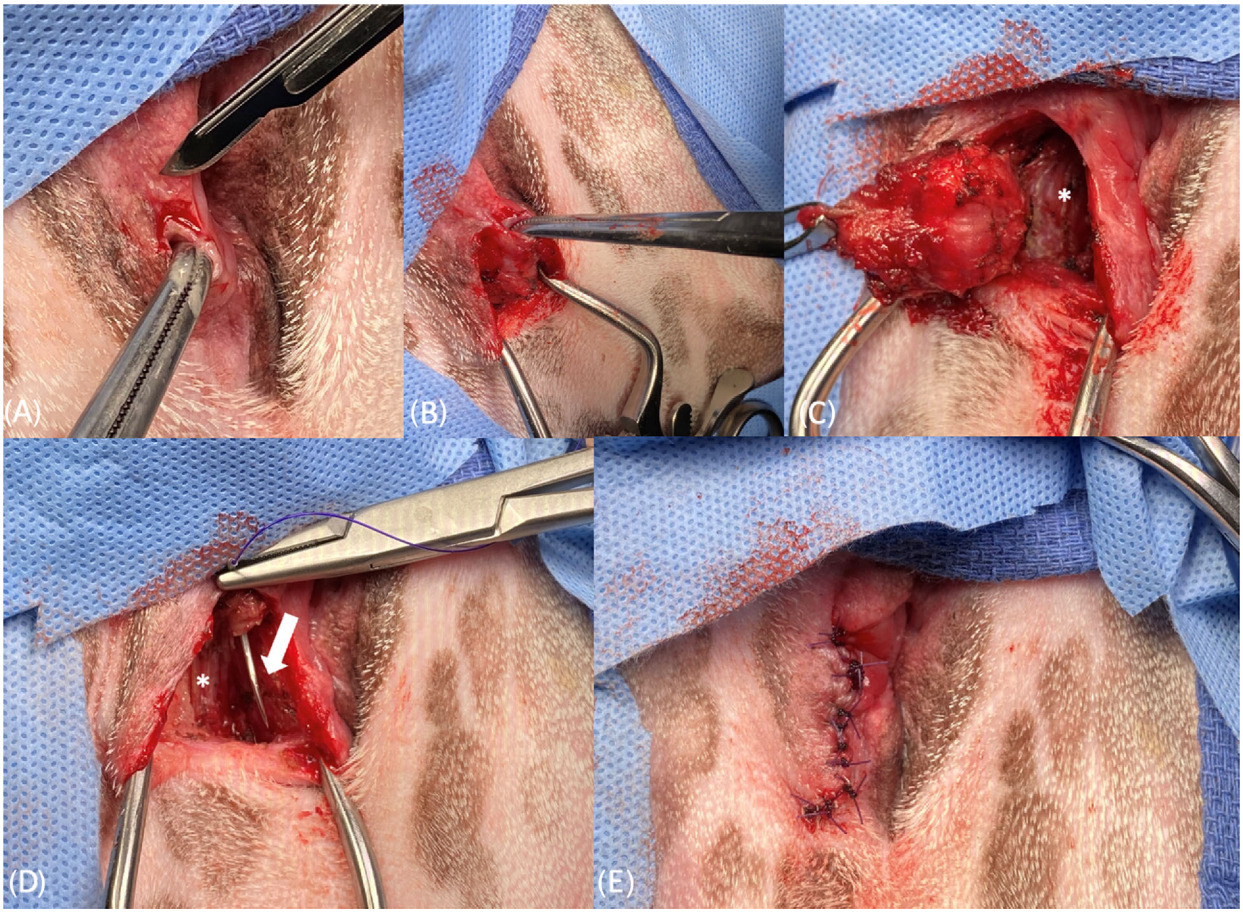

FIGURE 1 Anal sacculectomy via the modified closed technique. (A) Right angle forceps are placed into the duct of the left anal sac, and a scalpel blade is used to create a skin incision circumferentially around the duct. (B) Right angle forceps are maintained within the duct opening while the subcutaneous tissues are dissected away from the anal sac and associated mass. (C) Further dissection of the anal sac and associated mass. The external anal sphincter is identified by the asterisk. (D) Reconstruction of the anal sphincter after excision of the anal sac and associated mass. The external anal sphincter is indicated by the asterisk. The internal anal sphincter is indicated by the arrow. (E) Closure of the subcutis and skin, with placement of interrupted cruciate skin sutures using absorbable suture.

generally included preanesthetic medication with an opioid and benzodiazepine, induction with propofol or alfaxalone, and maintenance on inhalant anesthetic gas. All dogs received intraoperative antibiotic prophylaxis with cefazolin 22 mg/kg IV every 90 min. All dogs were discharged with sedative medication to be given as needed, antibiotics (most frequently amoxicillin-clavulanic acid for 7–14 days), and pain medication, typically a combination of a nonsteroidal anti-inflammatory and gabapentin.

Postoperative complications were recorded, and details were noted. Complications were defined as any undesirable outcome related to the surgery. Postoperative complications recorded included incision dehiscence, infection, changes in defecation or stool quality, significant inflammation, and seroma formation. A major complication was defined as a complication resulting in euthanasia or requiring revision surgery, while a minor complication was defined as a complication that was self-limiting or managed medically. This classification method was modified from the Clavien-Dindo classification of surgical complications, which comprehensively defined and categorized postoperative complications.[18]

Histopathology reports for each AGASACA tumor were reviewed. Data were collected for all of the following, when reported: histopathological margins, mitotic count, evidence and degree of necrosis, evidence of lymphatic and/or vascular invasion, detail of any other invaded tissues, evidence of lymph node metastasis, when applicable, and tumor node metastasis (TNM) classification.

3 | RESULTS

Out of 47 dogs, 29 (61.7%) were castrated males, four (8.5%) were intact males, 14 (29.8%) were spayed females, and there were no intact females. The median age of the dogs at the time of surgery was 10.0 years (range 5.0–13.6 years) and the median weight was 29.8 kg (range 4.0–55.9 kg). The majority of dogs in the study population were mixed breed ($n = 25$). Other breeds represented included the Golden Retriever ($n = 6$), Labrador Retriever ($n = 6$), Australian Cattle Dog ($n = 2$), Pomeranian ($n = 1$), Husky ($n = 1$), Havanese ($n = 1$), Dutch Shepherd ($n = 1$), German Shepherd ($n = 1$), Border Collie ($n = 1$), Basset Hound ($n = 1$), Alaskan Malamute ($n = 1$) and Rhodesian Ridgeback ($n = 1$).

There was a high incidence of neoplastic comorbidity in the dogs in this study. Seventeen dogs (36.2%) were diagnosed with an additional neoplastic disease either previously ($n = 8$) or at the same time ($n = 9$) as their anal sac mass, including two dogs with two different previous tumor types. These neoplasias included mast cell tumor ($n = 4$), osteosarcoma ($n = 3$), melanoma ($n = 1$), hemangiosarcoma ($n = 1$), hepatocellular carcinoma ($n = 1$), mammary carcinoma ($n = 1$), soft tissue sarcoma ($n = 1$), peripheral nerve sheath tumor ($n = 1$), thyroid carcinoma ($n = 1$), parathyroid adenoma ($n = 1$), rectoanal carcinoma ($n = 1$), mandibular fibroma ($n = 1$), clitoral papilloma ($n = 1$), and testicular Leydig cell tumor ($n = 1$).

Approximately half of dogs presented for an anal sac mass ($n = 27$, 57.4%) had no clinical signs and the mass was found incidentally on physical examination. Of dogs that had a related clinical sign present when the anal mass was discovered, the most common complaint was licking of the perineal area, which was reported in six dogs (12.8%). Other clinical signs were scooting ($n = 2$, 4.3%), perineal swelling ($n = 2$, 4.3%), hematochezia ($n = 2$, 4.3%), lethargy ($n = 2$, 4.3%), weight loss ($n = 2$, 4.3%), polyuria/polydipsia ($n = 2$, 4.3%), abnormal gait ($n = 2$, 4.3%), diarrhea ($n = 1$, 2.1%), and hesitation to sit ($n = 1$, 2.1%). Forty-six of the dogs had a unilateral anal sac mass and one dog had bilateral disease.

Preoperative staging, consisting of bloodwork, thoracic radiographs or CT scan, and abdominal ultrasound or CT scan was performed in the majority of patients. Complete staging was performed in 38 dogs (80.9%) while partial staging (imaging of only one body cavity) was performed in six dogs (12.8%). Thirty-six dogs (76.6%) had thoracic radiographs while three dogs (6.4%) had a thoracic CT scan performed, including one dog (2.1%) who underwent both thoracic imaging modalities. Thirty-four dogs (72.3%) had an abdominal ultrasound, including one who then underwent a pelvic CT scan, and seven dogs (14.9%) had an abdominal CT scan. Based on these staging tests, one dog out of 47 (2.1%) was diagnosed with suspected pulmonary metastasis and 11 of 47 (23.4%) dogs were diagnosed with suspected abdominal lymph node metastasis (including the dog with suspected pulmonary metastasis).

Two dogs (4.3%) were noted to have intraoperative complications. One dog had bradycardia and hypotension that were treated with a fluid bolus, a 0.02 mg/kg dose of IV atropine, and initiation of a norepinephrine constant rate infusion at 2 mcg/kg/min. The other dog experienced bradycardia that was treated with two doses of 0.02 mg/kg intravenous atropine.

All 47 dogs included in the study were diagnosed with AGASACA based on histopathology. Invasion of other structures, such as skeletal muscle and lymphatic tissue, was noted at the time of surgery in 11 dogs (23.4%). A mitotic count was reported in histopathology reports in 44 dogs and the median mitotic count was 15 per 10 high power fields, with a range of 2 to >60. Necrosis was present in 39 masses (83.0%), although the majority of histopathology reports did not quantify the extent of

necrosis. Vascular invasion was documented in four dogs (8.5%) while lymphatic invasion was documented in 15 dogs (31.9%). Complete histological margins were reported in 21 dogs (44.7%). Abdominal lymph node extirpation was performed in five dogs (10.6%), and four (8.5%) of these lymph nodes were confirmed as metastatic based on histopathology. The non-metastatic lymph node, as determined based on histopathology, was a medial iliac lymph node. All the lymph nodes confirmed to be metastatic on histopathology were medial iliac lymph nodes. In four dogs with suspect lymph node metastasis, lymph node extirpation was not performed due to the presence of pulmonary metastasis ($n = 1$) or aggressive concurrent neoplasia ($n = 3$), and anal sacculectomy was performed as a palliative measure. In the remaining two dogs, there was insufficient information in the medical record to determine why lymph node extirpation was not performed given the suspicion of metastasis.

Full data to perform TNM staging based on the World Health Organization classification system (Table 1) was available for 30 patients.[19] Thirteen dogs were classified as stage T_1, 13 as stage T_2, five as stage T_3, and one as stage T_4. Twenty-five dogs were classified as stage N_0, one as stage N_{1a}, two as stage N_{1b}, and two as stage N_{2b}. Twenty-six were classified as stage M_0 and four as stage M_1.

TABLE 1 World Health Organization tumor node metastasis (TNM) classification for canine tumors of epidermal or dermal origin (excluding mastocytoma and lymphosarcoma).

T: Primary tumor
T_{is} = preinvasive carcinoma (carcinoma in situ)
T_0 = no evidence of tumor
T_1 = tumor <2 cm in maximum diameter, superficial or exophytic
T_2 = tumor 2–5 cm in maximum diameter, or with minimal invasion irrespective of size
T_3 = tumor >5 cm in maximum diameter, or with invasion of the subcutis, irrespective of size
T_4 = tumor invading other structures such as bone, cartilage, fascia, or muscle
N: Regional lymph nodes
N_0 = no evidence of regional lymph node involvement
N_1 = movable ipsilateral nodes
N_{1a} = nodes not considered to contain growth
N_{1b} = nodes considered to contain growth
N_2 = movable contralateral or bilateral nodes
N_{2a} = nodes not considered to contain growth
N_{2b} = nodes considered to contain growth
N_3 = fixed nodes
M: Distant metastasis
M_0 = no evidence of distant metastasis
M_1 = distant metastasis detected

Fifteen dogs (31.9%) experienced postoperative complications (Table 2). Of the 21 postoperative complications reported, 18 (85.7%) were considered minor and 3 (14.3%) were considered major. The most common complication reported was incisional dehiscence ($n = 11$, 23.4%), occurring in one dog 4 days postoperatively due to self-trauma of the incision site, and in one dog that was noted by the owner to scoot frequently after surgery. All dehisced incisions were managed as an open wound except for two, one of which was surgically revised 7 days after the initial surgery. The second dog was euthanized 4 days after surgery due to concerns regarding dehiscence and infection that would have required a revision surgery. Dehisced incisions that were managed medically were treated via dilute povidone-iodine solution flushed into the wound bed by the owner, and the wounds were allowed to heal via second intention. Other post-operative complications reported were infection ($n = 7$, 14.9%), which was based on clinical suspicion, transient fecal incontinence ($n = 1$, 2.1%), and diarrhea ($n = 1$, 2.1%). One dog, which was diagnosed with suspect splenic metastasis during initial staging tests, underwent anal sacculectomy to palliatively treat difficulty defecating. This dog was euthanized 11 days after surgery due to guarded prognosis and quality of life concerns related to an existing peripheral nerve sheath tumor. Out of the 45 dogs available for follow-up for at least 150 days, one dog (2.2%) had local recurrence of AGASACA reported. The time to recurrence for this dog was 90 days.

Sixteen dogs (34.0%) underwent adjunctive chemotherapy to treat their AGASACA after surgery. Adjunctive

TABLE 2 Severity and types of postoperative complications associated with the modified closed anal sacculectomy technique for treatment of apocrine gland anal sac adenocarcinoma (AGASACA) in 47 dogs.

Type of complication	Level of complication	Number of cases
Dehiscence without revision	Minor	9/47 (19.1%)
Infection	Minor	7/47 (14.9%)
Diarrhea	Minor	1/47 (2.1%)
Transient fecal incontinence	Minor	1/47 (2.1%)
Dehiscence requiring revision	Major	2/47 (4.3%)
Local recurrence	Major	1/45 (2.2%)

Note: Local recurrence was only calculated for dogs with at least 150 days of follow-up ($n = 45$).

chemotherapy most commonly consisted of four doses of carboplatin ($n = 13$) while three dogs received mitoxantrone. Follow-up examination and restaging were recommended to be performed every 3 months for all dogs. As of November 1, 2022, 20 (42.6%) of the original 47 dogs were still alive, 22 (46.8%) dogs were deceased, and information regarding survival status was unavailable for three dogs (6.4%). Survival time data was available for all deceased dogs. For the 20 deceased patients, excluding the two dogs who were euthanized 4 and 11 days after surgery, the mean survival time was 521 days (range 156–1409 days) and the median survival time was 388 days.

4 | DISCUSSION

The incidence of postoperative complications in this study was 31.9%. This is comparable to the 32.3% postoperative complication rate in dogs undergoing closed technique anal sacculectomy reported by Charlesworth.[20] Similarly, in dogs undergoing both anal sacculectomy and lymphadenectomy, Tanis et al. found a 38.6% postoperative complication rate relating specifically to the anal sacculectomy surgery, although the method of anal sac removal was not reported.[2] Hill and Smeak reported a 21.4% rate of incisional fistula formation in dogs undergoing anal sacculectomy for non-neoplastic disease.[15] However, the postoperative complication rate in the present study is notably higher than the 7.1% rate reported by Potanas et al. and the 17% rate reported by Sterman et al.[1,10] The differences in the complication rates reported in the literature may be due to differences in reporting and classification of complications, as well as level of follow-up. Additionally, the modified closed technique described herein requires a circumferential incision around the anal sac duct and subsequent repair of the anal sphincter once the mass is excised. This may cause a higher complication rate, particularly regarding incision dehiscence, than other studies in which a single linear skin incision is performed without involvement of the anal sphincter. Overall, the modified closed technique described in the present study was associated with a complication rate that is consistent with rates found in the existing anal sacculectomy literature. Given that the vast majority of complications in the present study were mild and self-limiting, the notably lower recurrence rate found with the modified closed technique may provide a clinical benefit over the traditional closed technique.

The local recurrence rate in this study was 2.2%. One dog experienced progression of disease 146 days after surgery. This patient was considered to have progression rather than recurrence because there was gross tumor left behind during the initial anal sacculectomy surgery due to the large size (5.0 × 6.0 cm) and deep extent of the tumor. Regardless, this recurrence rate was notably lower than has been previously reported in the literature.[1,13,14,17] Reducing the local recurrence rate may also reduce the need for adjuvant radiation therapy or chemotherapy.[14] In addition to the previously described side effects, adjuvant radiation therapy incurs significant additional financial burden to the owner and requires multiple anesthetic events for the patient.[13] While the modified closed technique may incur more self-limiting or medically manageable complications in the short-term, reducing the need for adjuvant radiation therapy reduces the risk of serious side effects of that treatment, such as bowel stricture and perforation.[3,13]

It is important to note that the majority of dogs in this study ($n = 27$, 57.4%) had a mass that was identified on routine rectal examination with no other clinical signs or behavioral changes present. Interestingly, tenesmus and dyschezia were only reported in one dog at the time of diagnosis in this study population. This highlights the importance of performing a digital rectal examination as part of every physical examination, including wellness examinations, to identify an anal sac mass as early as possible.

There are several limitations to this study. The retrospective nature of this study may limit the ability to achieve short and long-term follow-up, and there was no control group included as part of the study. Similarly, it is possible that the postoperative complication and local recurrence rates are underreported as some patients may present to their primary care vet for follow-up care rather than return to a specialty hospital. Third, although having all procedures performed by a single surgeon aids with consistency in technique and skill, postoperative complications and incomplete margins could be more common in novice surgeons or surgeons with less oncologic training. Assessment of preoperative calcium levels, a known prognostic factor, was not possible given that they were only sporadically reported in the medical records.[3–5] Finally, due to the retrospective nature of this study, postoperative adjunctive therapy was not standardized. Differences in postoperative treatment and monitoring may have influenced the mean survival time and ability to detect local recurrence. Future studies regarding anal sacculectomy technique for the treatment of AGASACA should directly compare the traditional and modified closed techniques and ideally include a longer follow-up period.

In dogs undergoing anal sacculectomy for the treatment of AGASACA, excision of the tumor and anal sac via the modified closed technique was associated with a comparable postoperative complication rate but a lower

local recurrence rate than has been previously reported in the literature.

AUTHOR CONTRIBUTIONS

Davey E., DVM: Identified suitable medical records, recorded demographic information, compiled and interpreted all data, and drafted and revised the manuscript. Prpich C., BVSc, MANZCVS, DACVS (Small Animal), ACVS Fellow (Surgical Oncology): Responsible for surgical management of the cases, provided intraoperative photographs, and revision of the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors did not receive any financial support for this study and do not declare any conflicts of interest.

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