CVJ CLUJ VETERINARY JOURNAL

Review Article

Early Cancer Screening in Companion Animals: Combining Traditional Diagnostics with Emerging Methods

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Abstract: Early tumor screening in companion animals (dogs and cats) integrates traditional and emerging diagnostic techniques to identify malignant lesions at the preclinical stage, enabling timely intervention and improved prognosis. Early-stage tumors in dogs and cats often lack specific clinical signs, frequently presenting only as palpable subcutaneous masses or nonspecific weight loss, which commonly leads to diagnostic delay. While histopathological examination remains the gold standard for tumor diagnosis, its invasive nature limits application in large-scale screening. Emerging non-invasive or minimally invasive methods including liquid biopsy (detection of circulating tumor DNA, circulating tumor cells, and exosomes), serum tumor marker analysis, and exhaled volatile organic compound testing complement traditional strategies and enable earlier, more precise tumor detection. For localized tumors detected at an early stage, radical surgical resection remains the cornerstone of treatment; emerging interventions such as tyrosine kinase inhibitors and immune checkpoint blockade further improve clinical outcomes, and their success is highly dependent on early diagnosis via screening. This review summarizes current advances in early tumor screening for companion animals, focusing on combined strategies of traditional diagnostics and emerging technologies, and highlights their translational potential to enhance diagnostic efficacy and optimize clinical management pathways.

Keywords: Early cancer screening; Dogs; Cats; Liquid biopsy; Circulating tumor DNA; Serum tumor markers; Histopathology; Immunotherapy; Metabolomics

Received: 08.06.2026
Accepted: 14.07.2026
Published: 28.07.2026

DOI:10.52331/v31i3q253



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1. Introduction

Early tumor screening employs physical examinations, laboratory tests, imaging, and molecular biology techniques to detect malignant lesions in companion animals (dogs and cats) before overt clinical symptoms appear, with the goal of enabling timely intervention and improving prognosis [1,2]. In veterinary practice, the boundary between "screening" and "diagnosis" remains debated: some frameworks categorize early detection as a component of preventive health care, while others restrict screening to the detection of preclinical tumors in entirely asymptomatic animals [3]. For the purposes of this review, "early tumor screening" refers to all testing strategies employed before the onset of overt tumor-specific clinical signs, or when only nonspecific clinical manifestations are present.

Cancer is a leading cause of death in senior dogs and cats. Approximately 47% of deaths in dogs over 10 years of age are attributed to malignant tumors, and the corresponding proportion in cats exceeds 30% [4,5]. Cancer incidence increases with age, and can occur across all ages, sexes, and breeds [6]. However, breed-specific predispositions are well documented: Boxers, Golden Retrievers, Bernese Mountain Dogs, and Labrador Retrievers consistently show higher rates of lymphoma, mast cell tumors, osteosarcoma, and histiocytic sarcoma across epidemiological studies [7,8]. In cats, Siamese cats have been associated with elevated risk of lymphoma and mammary tumors, though most supporting data come from older, small-scale studies that require validation in larger cohorts [9,10].

Traditional early screening methods include systematic physical examination (including palpation of superficial lymph nodes and assessment of cutaneous/subcutaneous masses), basic hematology and serum biochemistry, thoracic and abdominal radiography

and ultrasonography, and fine-needle aspiration cytology [11]. Molecular biomarkers are increasingly entering clinical practice: in dogs, serum thymidine kinase 1 (TK1) activity and C-reactive protein (CRP) levels serve as adjunctive screening markers for lymphoma and select solid tumors [12]; in cats, serum thymidine kinase and specific microRNA profiles have shown preliminary utility as early tumor markers [13,14]. Liquid biopsy technologies, which detect tumor-derived nucleic acids, proteins, and circulating cells in peripheral blood, may identify tumor signals before masses are visible on conventional imaging [15].

The biological feasibility of early screening stems from nucleic acids, proteins, and metabolites released into peripheral blood by developing tumor cells, as well as associated epigenetic and immune microenvironment changes [16]. Genetic susceptibility, chronic inflammation, immunosenescence, and epigenetic reprogramming all contribute to companion animal tumorigenesis, and these molecular events provide detectable targets for early detection [17]. Advances in multi-omics research have further established that effective screening requires integration of multi-dimensional data including genomic, transcriptomic, proteomic, and metabolomic abnormalities rather than reliance on a single biomarker [18].

Early diagnosis remains challenging. While histopathology is the diagnostic gold standard, its invasiveness and sampling requirements limit its use as a first-line screening tool [2,19]. However, tumors detected at an early, localized stage are typically amenable to curative surgical resection, with significantly improved prognosis [20,21].

This review synthesizes literature retrieved from PubMed and Scopus (including reference list mining), covering publications through 2026. It summarizes established diagnostic techniques and emerging detection methods for early tumor screening in dogs and cats, and explores their translational potential to optimize clinical management and long-term prognosis.

2. Clinical Signs and Physical Examination Findings

Preclinical tumors in dogs and cats may produce only nonspecific findings, or no detectable abnormalities at all [1,22]. Cancer anorexia (reduced food intake secondary to neoplasia) and cancer cachexia (weight loss and metabolic dysfunction despite adequate nutrition) are the most prevalent and impactful paraneoplastic syndromes in companion animal oncology [23]. In dogs, approximately 14% lose 5–10% of body weight in the 12 months before diagnosis, and 23% lose more than 10%. In cats, 45–55% of patients with lymphoma or solid tumors present with a body condition score (BCS) ≤5/9 at diagnosis; 93% exhibit muscle wasting, including 72% with BCS in the adequate range (≥5) [24,25]. Pre-diagnostic weight loss is a negative prognostic indicator in both species, with more pronounced effects in cats.

Palpable superficial masses or subcutaneous nodules are among the most notable early physical findings. According to the 2026 AAHA Oncology Guidelines, mast cell tumors are the most common canine skin tumor (16–21% of all skin neoplasms), while lymphoma is one of the most prevalent malignant tumors in cats [26,27]. Canine multicentric lymphoma typically presents with painless, elastic generalized lymphadenopathy affecting submandibular, prescapular, and popliteal nodes, with or without hepatosplenomegaly [28]. Feline lymphoma most commonly presents as the gastrointestinal form, which does not cause generalized lymphadenopathy and produces nonspecific signs (anorexia, weight loss) that are easily confused with pancreatitis, renal failure, or other chronic conditions [29]. Osteosarcoma, the most common primary canine bone tumor (85% of canine bone neoplasms), presents as persistent lameness and localized swelling, with strong predisposition in large breeds [30].

Non-healing wounds or ulcers are key warning signs for cutaneous and oral tumors. Feline cutaneous squamous cell carcinoma occurs most frequently on sparsely haired, lightly pigmented sites (ear tips, nasal planum, eyelids), presenting as red, ulcerated, crusted lesions with alopecia or pink discoloration [31]. Feline oral squamous cell carcinoma is highly aggressive, with early signs including oral ulcers, ptyalism, weight loss, halitosis, and loose teeth that are often misattributed to dental disease [32].

Lymph node evaluation is a core component of tumor screening. Using histopathology as the reference standard, Langenbac et al. (2001) assessed the diagnostic performance of palpation, fine-needle aspiration, and core needle biopsy for regional lymph node metastasis in dogs and cats with solid tumors [33]. The 2026 AAHA guidelines emphasize systematic regional lymph node assessment, with follow-up imaging, cytology, or histopathology as indicated. Importantly, lymphadenopathy may stem from metastatic disease or non-neoplastic causes (infection, inflammation), and size assessment via palpation alone is unreliable [34]. Monthly at-home full-body palpation is recommended as an adjunctive measure to detect hidden masses and facilitate early referral.

Recognition of paraneoplastic syndromes can provide early clues to occult tumors. Hypercalcemia is the most common paraneoplastic syndrome in companion animals. In dogs, the most common associated malignancies are T-cell lymphoma (35–55% of cases), anal sac adenocarcinoma, multiple myeloma, and thymoma; in cats, it is most frequently linked to oral squamous cell carcinoma [35,36]. Clinical signs include polyuria/polydipsia, vomiting, anorexia, bradycardia, and muscle weakness; in cats, anorexia and lethargy predominate, with less frequent gastrointestinal and urinary signs [37]. Paraneoplastic hypoglycemia occurs primarily in canine insulinomas, caused by aberrant insulin secretion from pancreatic β-cells, and presents as muscle weakness, collapse, ataxia, and seizures; it is rare in cats [38,39]. Additional notable paraneoplastic manifestations include cancer cachexia, fever of unknown origin, non-regenerative anemia, thrombocytopenia, and cutaneous paraneoplastic syndromes (e.g., feline paraneoplastic alopecia, canine superficial necrolytic dermatitis) [40,41,42].

Common clinical and physical examination findings are summarized in Table 1.

3. Diagnosis

3.1. Integrated Strategies Combining Traditional and Emerging Screening Methods

No single gold-standard method exists for universal early cancer screening in dogs and cats; the combination of physical examination, basic imaging (radiography, ultrasonography), and cytology forms the core of traditional screening protocols [2,43]. In recent years, liquid biopsy, circulating tumor DNA (ctDNA) testing, metabolomics, and AI-assisted image interpretation have expanded screening capabilities, though these remain supplementary to traditional methods rather than replacements, pending broader clinical validation.

All screening protocols begin with a thorough history and physical examination, with prioritization of senior animals (generally dogs ≥7 years, cats ≥10 years), high-risk breeds (e.g., Golden Retrievers, Boxers, Siamese cats), and individuals with known genetic predispositions [45,46]. Baseline hematology and serum biochemistry help rule out non-neoplastic causes of clinical signs and assess organ function [47].

Traditional imaging (thoracic and abdominal radiography, abdominal ultrasonography) is accessible and cost-effective, with good sensitivity for mass-forming solid tumors (e.g., splenic hemangiosarcoma, hepatic tumors, bladder transitional cell carcinoma). However, it has limited ability to detect micrometastases <3–5 mm in diameter or early carcinoma in situ [1,48]. Liquid biopsy, by contrast, detects tumor-derived nucleic acids, proteins, or circulating cells in peripheral blood, and shows preliminary potential to identify tumor signals before masses are radiologically visible [2]. A prospective study of canine lymphoma and hemangiosarcoma reported that ctDNA point mutation-based liquid biopsy achieved 62% and 71% sensitivity for early detection of these two tumor types, respectively, with >95% specificity [49]. Sensitivity is lower (30–50%) for non-hematologic solid tumors such as osteosarcoma and lung cancer [15].

Fine-needle aspiration cytology is low-cost and rapid, and can distinguish benign from malignant lesions. However, its accuracy is highly operator- and pathologist-dependent, and it cannot provide molecular subtype information [50,51]. Emerging tools including flow cytometry, immunocytochemistry, and machine learning-based image analysis can improve cytologic interpretation consistency, but require specialized equipment and sample processing that are not widely available in most veterinary diagnostic laboratories [52].

Screening strategies should be tiered based on individual risk factors, owner financial capacity, and clinical utility (i.e., whether early intervention improves prognosis) [45]. For high-risk animals (senior patients, high-incidence breeds), abdominal ultrasound and thoracic radiography may be added to annual wellness examinations; liquid biopsy may be added as a supplementary test when feasible [53]. The high specificity of liquid biopsy corresponds to low false-positive rates, but its limited sensitivity means a negative result does not rule out early-stage tumors [15]. Positive results from any emerging screening method require confirmation via conventional imaging or cytology, and negative results do not justify discontinuing clinical follow-up.

Combined modalities improve performance over single tests. For example, combining liquid biopsy with abdominal ultrasound increases sensitivity for canine splenic and hepatic solid tumors from ~50–70% (single modality) to >85% [54,55]. Similarly, AI-assisted imaging interpretation paired with cytology reduces inter-observer variability and improves detection of pulmonary nodules and small abdominal masses [56]

Table 1. Common clinical signs and physical examination findings in dogs and cats with tumors

Clinical sign / Finding	Associated tumor type/condition	Key features or incidence	References
Weight loss and muscle wasting (cancer cachexia)	Various tumors, especially lymphoma and solid tumors	Dogs: 14% lose 5–10% body weight pre-diagnosis, 23% lose >10%; Cats: 45–55% have BCS ≤5/9, 93% have muscle wasting (72% even with BCS ≥5)	[24,25]
Palpable superficial mass / subcutaneous nodule	Most common skin tumors: mast cell tumor (dog); lymphoma (cat)	Dogs: MCT accounts for 16-21% of all skin tumors; Cats: lymphoma is one of the most common malignant tumors	[26,27]
Generalized lymphadenopathy (painless, elastic)	Multicentric lymphoma (dog)	Submandibular, prescapular, popliteal nodes; with/without hepatosplenomegaly	[28]
Non-specific gastrointestinal signs (anorexia, weight loss)	Feline gastrointestinal lymphoma	No generalized lymphadenopathy; easily confused with pancreatitis, renal failure	[29]
Persistent lameness + localized limb swelling	Osteosarcoma (dog)	Most common primary bone tumor (85% of canine bone tumors); large breeds predisposed	[30]
Red, ulcerated, crusted lesions on sparsely haired/lightly pigmented areas (ear tips, nasal planum, eyelids)	Cutaneous squamous cell carcinoma (cat)	May present with alopecia or pink appearance	[31]
Oral ulceration, drooling, halitosis, loose teeth	Oral squamous cell carcinoma (cat)	Highly aggressive; early stage often mistaken for dental disease	[32]
Lymphadenopathy (unreliable by palpation alone)	Regional lymph node metastasis	Palpation alone has low sensitivity (60%) and specificity (72%); cytology/histopathology required	[33,34]
Hypercalcemia	Most common paraneoplastic syndrome; in dogs: T-cell lymphoma (35–55%), anal sac adenocarcinoma, multiple myeloma, thymoma; in cats: oral SCC	Clinical signs: polyuria/polydipsia, vomiting, anorexia, bradycardia, muscle weakness	[35,36,37]
Hypoglycemia (muscle weakness, collapse, ataxia, seizures)	Insulinoma (dog)	Caused by abnormal insulin secretion from pancreatic β-cells; rare in cats	[38,39]
Fever of unknown origin, non-regenerative anemia, thrombocytopenia	Various paraneoplastic syndromes	Important and noteworthy manifestations	[40,42]
Cutaneous paraneoplastic syndromes	Feline paraneoplastic alopecia; Canine superficial necrolytic dermatitis	May precede diagnosis of underlying neoplasia	[41]

Owner awareness and compliance are key determinants of screening effectiveness [57]. Veterinarians should communicate the benefits and limitations of each method clearly, and develop individualized screening plans. For animals undergoing liquid biopsy or other emerging tests, follow-up testing every 6–12 months is recommended to monitor biomarker trends.

If initial screening is negative but nonspecific tumor-associated signs persist (unexplained weight loss, anorexia, chronic gastrointestinal signs, persistent fever), re-evaluation after 2–3 months with additional modalities (e.g., PET/CT at referral centers, metabolomic serum testing) is advised [1,58,59]. Interpretation of screening markers is more complex in animals with concurrent chronic inflammatory disease (e.g., inflammatory bowel disease, chronic kidney disease), as these conditions can independently elevate inflammation-related cytokines and metabolites [60].

Asymptomatic high-risk animals may undergo routine screening (physical exam + baseline blood work + imaging) without pharmacologic intervention [1]. Short-acting sedation may be administered as needed before invasive procedures (e.g., ultrasound-guided biopsy) to reduce patient stress and procedural risk [61].

Histopathological examination remains the reference standard for definitive diagnosis of clinically actionable lesions; imaging and liquid biopsy results indicate high suspicion but cannot confirm malignancy independently [62]. Following mass detection on imaging, cytologic or histologic confirmation via fine-needle aspiration or core needle biopsy is mandatory to avoid overtreatment [51].

When liquid biopsy is positive but no lesion is identified on initial imaging, targeted imaging follow-up with biopsy attempt is indicated; if biopsy is negative but clinical suspicion remains high, combined imaging and liquid biopsy re-evaluation after 3–6 months is recommended to detect progressive lesions [15,16]. No evidence-based standard exists for optimal follow-up intervals after a positive liquid biopsy result, and decisions should be individualized based on patient risk level.

Analogous to cross-reactivity in food allergy diagnosis, some circulating biomarkers (e.g., TK1) may be elevated across multiple tumor types, and may also produce false positives in non-neoplastic proliferative conditions (e.g., splenic extramedullary hematopoiesis, reactive lymphoid hyperplasia) [63,64]. No single biomarker elevation is sufficient for definitive diagnosis; all abnormal results require correlation with imaging and cytologic findings.

A core challenge of screening programs is balancing early intervention against overdiagnosis [65]. Not all screen-detected tumors—particularly indolent neoplasms or low-grade mast cell tumors in geriatric patients—will become clinically relevant within the patient's lifespan. Decisions regarding immediate invasive treatment should integrate tumor type, grade, location, overall patient health, and owner preferences.

If initial screening is negative but clinical suspicion remains high, advanced imaging (whole-body CT or MRI) or repeat liquid biopsy on an alternative platform may be considered to reduce false-negative risk [66,67]. In patients with multiple comorbidities, alternative etiologies must be excluded before attributing abnormal screening results to neoplasia.

While no single standard confirms screening efficacy, the most reliable approach is histopathologic confirmation combined with ≥12 months of clinical follow-up to assess negative predictive value. For screen-positive patients, excisional biopsy with histopathology serves both therapeutic and diagnostic purposes.

3.2. Additional Diagnostic Methods

A range of additional in vivo and in vitro diagnostic approaches have been investigated for early tumor screening, but none are validated as standalone screening tools. Their utility ranges from diagnostic support to risk stratification, and none replace traditional screening protocols combined with histopathologic confirmation.

3.2.1. Serum Biomarkers and Conventional Auxiliary Assays

Multiple serum tumor markers are commercially available, including thymidine kinase 1 (TK1), vascular endothelial growth factor (VEGF), and carcinoembryonic antigens (e.g., CEA, CA15-4). However, current evidence indicates single-marker testing lacks sufficient sensitivity and specificity for early cancer screening in dogs and cats [68–71]. Flory et al. (2021) reported that combining serum TK1 with abdominal ultrasound improves detection of occult splenic and hepatic tumors compared to annual physical examination alone, but cannot reliably distinguish malignant tumors from benign proliferative lesions [15].

Detection of specific metabolites or DNA methylation markers in feces, urine, or oral swabs is not currently recommended for independent tumor screening. While non-invasive sampling is convenient for owners, most supporting studies involve small cohorts or specific tumor types (e.g., bladder transitional cell carcinoma), and performance across breeds, ages, and tumor stages remains unvalidated [72]. Overreliance

on these non-specific markers carries risks of false positives (leading to unnecessary invasive testing and owner anxiety) and false negatives (delaying diagnosis) [67].

Serum TK1 activity is markedly elevated in canine lymphoma and hemangiosarcoma, but shows minimal or no increase in other solid tumors such as osteosarcoma and thyroid cancer; this heterogeneity likely reflects differences in tumor proliferative activity [15,68,69]. TK1 reference ranges vary by assay platform (ELISA, chemiluminescence) and laboratory, with divergent diagnostic thresholds across studies, which contributes to inconsistent reported performance [73,74]. Additional confounders include age-related baseline changes and non-specific elevations associated with concurrent inflammation or infection, which complicate establishment of a universal clinical cutoff [63].

Similarly, ELISA-based detection of serum matrix metalloproteinases (MMPs), endostatin, and other cytokines is not validated for early tumor screening. In a small single-center cohort of 26 dogs with mammary tumors and 26 healthy controls, Khaki et al. (2023) measured serum MMP-2 and MMP-9 levels via gelatinase zymography. The study found that the presence of active MMP-9 was associated with elevated risk of tumor metastasis and recurrence, but the assay had limited capacity to distinguish benign from malignant mammary lesions. The previously included remark regarding a "diagnostic AUC of 0.68" was an erroneous leftover note from internal fact-checking that was incorrectly retained in the manuscript. Given the small sample size and limited discriminative performance, this method is not currently suitable for standalone early cancer screening [75].

3.2.2. Emerging Molecular and Liquid Biopsy Tools

Proteomic and metabolomic fingerprinting methods, while still in the research phase, have shown utility in specific scenarios such as differentiating benign from malignant pleural or peritoneal effusions. Ko et al. (2025) applied machine learning to analyze cell-free DNA fragment size and copy number variations, achieving an average AUC of 0.93 in 10-fold cross-validation for distinguishing canine hemangiosarcoma from healthy controls [76]. However, these methods require specialized mass spectrometry equipment and standardized sample processing, limiting current use to research settings.

Circulating tumor cell (CTC) enumeration has demonstrated higher specificity than traditional serum biomarkers in preliminary studies of canine mammary and lung adenocarcinoma. In a small pilot investigation, Marconato et al. used the automated CellSearch platform to test 27 dogs with metastatic mammary tumors, detecting CTCs in 44.4% (12/27) of malignant cases and no CTCs in 5 healthy control dogs. As these findings are limited by small sample size and the absence of a benign lesion control group, they should be interpreted as preliminary. A separate ctDNA analysis of 48 dogs demonstrated significantly higher ctDNA fractions in malignant splenic tumors (11.2%) compared to benign lesions (3.2%) and healthy dogs (1.4%), supporting the differential diagnostic value of circulating tumor markers [77].

Proliferative or metastatic tumors may shed CTCs early in disease progression, suggesting CTC testing could detect hematogenous dissemination before radiologically visible micrometastases [78]. A prospective analysis of 57 histologically confirmed canine soft tissue sarcomas detected CTCs in 28.1% (16/57) of peripheral blood samples, even in cases without imaging evidence of metastasis. CTC detection was significantly associated with higher tumor proliferative activity (high histologic grade) and predicted postoperative recurrence risk [79]. This dissociation between radiologic metastasis timing and CTC positivity suggests CTC testing can provide prognostic information independent of imaging.

Kanayama et al. (2024) developed a polymer-based microfluidic "CTC Chip" that can be conjugated with anti-EpCAM or anti-cell surface vimentin antibodies to capture epithelial or mesenchymal tumor cells, respectively. As a proof-of-concept using in vitro spiked tumor cell lines, the EpCAM chip achieved 99.4% capture efficiency for epithelial (PC9) cells and 88.8–90.8% for intermediate-type cells, but only 13.4% for mesenchymal (A549) cells. The CSV chip achieved 88.4% capture efficiency for mesenchymal cells at 100 μg/ml antibody concentration [80]. These performance data are derived from laboratory-based cell line experiments and have not yet been validated in clinical patient samples. A key conceptual advantage is that the platform does not rely on tumor-specific mutation profiles; in theory, switching antibody panels can adapt it to different tissue origins. While multicenter, large-scale prospective clinical validation is still required, CTC detection shows preliminary promise as a complement to traditional imaging, particularly for tumor types at high risk of micrometastatic spread.

Flory et al. (2024) reported a liquid biopsy assay integrating cfDNA quantification with NGS for canine cancer screening. In a clinical validation study across seven predefined cancer types, the assay achieved 71.3% overall sensitivity (95% CI: 62.9–78.5%) in 122 dogs with cancer and 98.7% specificity (95% CI: 97.0–

99.3%) in 473 healthy dogs, using multi-dimensional cfDNA features including copy number variations and fragmentomics [49]. Ko et al. (2025) further confirmed the utility of cfDNA fragmentomics for canine hemangiosarcoma detection via whole-genome sequencing and machine learning, with an AUC of 0.93 [76].

Quantitative PCR (qPCR) targeting specific ctDNA hotspot mutations, such as BRAF V595E for canine bladder transitional cell carcinoma, shows auxiliary diagnostic utility for specific tumor types. However, performance is dependent on the tumor's mutational status, making these assays unsuitable for tumors with low or no characteristic mutations, including most soft tissue sarcomas and lymphoma subtypes [81–85]. They are best applied as risk stratification tools for high-risk breeds (e.g., bladder cancer screening in Scottish Terriers and West Highland White Terriers) rather than universal screening modalities.

Despite promising preliminary results, most emerging diagnostic methods suffer from small sample sizes, lack of independent external validation, and methodological heterogeneity. Most studies are single-center or laboratory-based, limiting reproducibility and clinical applicability. Some commercial kits also lack multicenter prospective validation, carrying risk of result overinterpretation or false positives. These tools provide supplementary information and risk stratification value but cannot replace the traditional diagnostic workflow of physical examination, imaging screening, and histopathologic confirmation. Figure 1 summarizes a practical screening strategy prioritizing validated traditional tools, with adjunctive and emerging methods incorporated as clinically appropriate.

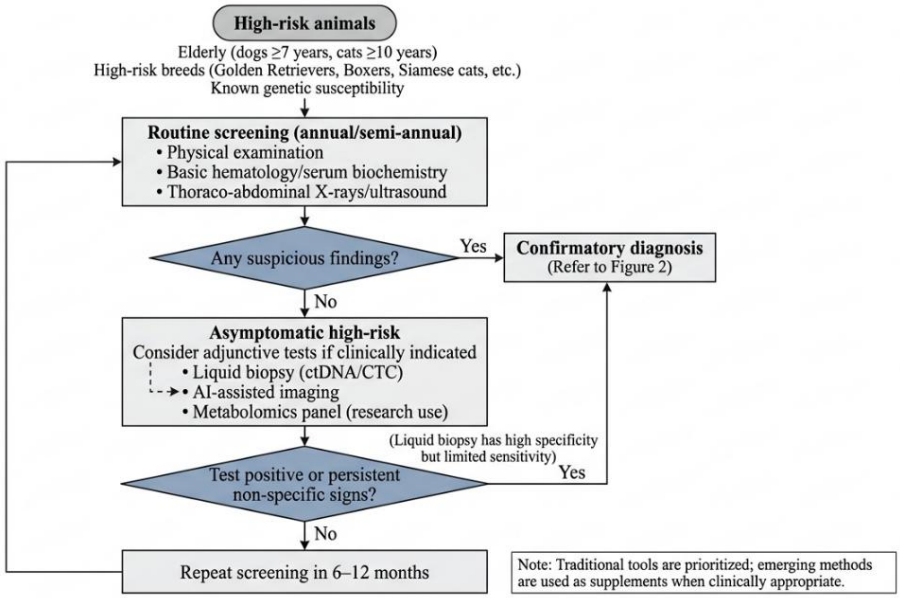


Figure 1. Practical screening strategy for early cancer detection in dogs and cats

4. Management Strategies Following a Positive Screening Result

The primary goal of post-screening management is to obtain a definitive diagnosis via confirmatory testing (e.g., histopathology) while minimizing overdiagnosis and overtreatment, and to develop an appropriate monitoring or intervention plan based on tumor type, stage, and patient characteristics. No screening result alone should be used to initiate treatment; all cases require confirmatory diagnostic follow-up.

4.1. Confirmatory Diagnosis and Staging Assessment

For animals with screen-positive findings on imaging or liquid biopsy, cytologic or histopathologic specimens should be obtained via fine-needle aspiration (FNA) or core needle biopsy to confirm tumor nature (benign/malignant) and histologic type [51]. If screening shows only elevated hematologic biomarkers (e.g., TK1, ctDNA fragmentomic abnormalities) with no definitive mass on imaging, recheck of biomarkers and repeat imaging after 2–3 months is recommended to avoid unnecessary invasive procedures.

Following malignant tumor diagnosis, clinical staging is performed based on anatomic location, local invasion extent, and regional lymph node or distant metastasis status. For suspected metastatic cases, thoracic CT, triphasic contrast-enhanced abdominal CT, or whole-body 18F-FDG PET-CT are recommended [86,87,88]. Staging accuracy directly impacts treatment decisions (surgery alone vs. surgery with adjuvant chemotherapy) and prognostic assessment.

Treatment and monitoring plans should integrate patient age, body condition score, vital organ function (particularly hepatic and renal), comorbidities (chronic kidney disease, heart disease, diabetes), and owner financial capacity and treatment willingness. For geriatric patients or those with severe comorbidities, palliative supportive care with regular follow-up may be appropriate even for confirmed malignant tumors, if life expectancy is limited or surgical risk is prohibitive.

4.2. Surgical and Medical Interventions

For confirmed malignant tumors where intervention provides clear survival benefit, complete surgical resection with adequate margins remains first-line treatment for most solid tumors (mast cell tumors, soft tissue sarcomas, mammary tumors, splenic hemangiosarcoma) [89]. Preoperative evaluation includes baseline hematology, coagulation testing, and cardiac function assessment; transfusion preparation is evaluated for large, deep-seated tumors.

When complete resection is not feasible (e.g., tumors adjacent to major vessels or nerves), multiple metastases are present, or owners decline surgery, alternative options are selected based on histologic type: chemotherapy (e.g., multi-agent protocols for lymphoma, NSAIDs combined with chemotherapy for transitional cell carcinoma), targeted therapy (e.g., toceranib for mast cell tumors with c-Kit mutations), or palliative radiation therapy [90–94]. All pharmacologic interventions should be guided by a veterinary oncologist, with close monitoring for adverse effects including myelosuppression, gastrointestinal toxicity, and cardiotoxicity.

While awaiting biopsy results or when definitive treatment cannot be initiated immediately, symptomatic and supportive medications may be used to alleviate clinical signs: NSAIDs (e.g., meloxicam, carprofen) for tumor-related inflammation and mild pain; opioids for moderate to severe pain; glucocorticoids to reduce peritumoral edema or for temporary control of select lymphoproliferative diseases [95,96]. Such symptomatic treatment does not replace or delay etiologic treatment.

All treatment decisions (including decision to forego treatment and monitor) should be made after histopathologic confirmation. Attending veterinarians should fully discuss expected benefits, risks, costs, and alternatives with owners, with written documentation of the discussion.

4.3. Adjuvant and Emerging Treatment Strategies

Adjuvant strategies include immunotherapy, molecular biomarker-guided personalized treatment, and nutritional and microbiome support. Most remain in clinical evaluation and should be administered at specialized referral centers or within clinical trial frameworks.

Immunotherapy: The xenogeneic DNA vaccine (Oncept®) for canine malignant melanoma has been shown to prolong disease-free survival, but is only indicated for surgically resected early-stage (II–III) cases and must be used with an adjuvant [97,98,99]. A heat shock protein-based vaccine for bladder transitional cell carcinoma has shown preliminary safety in small studies, but efficacy requires further validation [100].

Tyrosine kinase inhibitors: Toceranib and masitinib may be used for canine mast cell tumors carrying c-Kit mutations; c-Kit genotyping is recommended prior to use to predict treatment response [101]. Response rates are significantly lower for mast cell tumors without these mutations, and routine use is not recommended.

Minimal residual disease (MRD) monitoring: ctDNA- or CTC-based MRD monitoring has shown ability to detect recurrence 2–4 months earlier than imaging in preliminary studies of canine lymphoma and mammary carcinoma. However, use to guide treatment adjustments remains experimental and is not standard of care [102,103].

Nutritional and microbiome support: Dogs with cancer frequently experience reduced appetite, muscle wasting, and gut dysbiosis. Prospective studies indicate prebiotic (e.g., fructooligosaccharides) and omega-3 polyunsaturated fatty acid supplementation can improve body weight and inflammatory status, but randomized controlled trials confirming direct effects on tumor progression or survival are lacking [104]. These interventions are recommended as components of holistic supportive care, not as substitutes for anti-tumor therapy.

Table 2. Summary of management strategies following a positive screening result

Category	Specific strategy	Indication / notes	References
Staging assessment	Chest CT, triphasic contrast-enhanced abdominal CT, or whole-body 18F-FDG PET-CT	Suspected metastasis; influences treatment planning	[86,87,88]
Treatment decision factors	Age, body condition score, organ function (liver/kidney), comorbidities, owner's financial capacity and willingness	Comprehensive evaluation needed	[45,46]
First-line treatment (solid tumors)	Surgical resection with complete margins	Mast cell tumor, soft tissue sarcoma, mammary tumor, splenic hemangiosarcoma	[89]
Alternative therapies (when surgery not feasible or refused)	Chemotherapy (e.g., CHOP for lymphoma; NSAID + chemo for TCC); Targeted therapy (toceranib/masitinib for c-Kit+ MCT); Palliative radiotherapy	Based on tumor histology	[90–94]
Symptomatic/supportive care while awaiting definitive diagnosis	NSAIDs (meloxicam, carprofen) for mild pain/inflammation; Opioids for moderate-severe pain; Glucocorticoids for peritumoral edema or temporary control of lymphoproliferative diseases	Improves quality of life; does not replace etiological treatment	[95,96]
Immunotherapy (adjunctive)	Xenogeneic DNA vaccine (Oncept®) for canine oral malignant melanoma	Only for surgically resected stage II–III cases; use with adjuvant	[97,98,99]
	Heat-shock-protein-based vaccine for bladder TCC (investigational)	Small study; safe but efficacy needs validation	[100]
Tyrosine kinase inhibitors	Toceranib or masitinib for canine mast cell tumors with c-Kit mutations	c-Kit genotyping recommended prior to use to predict response	[101]
Minimal residual disease monitoring	ctDNA or CTC-based monitoring	In canine lymphoma/mammary carcinoma; may detect recurrence 2–4 months earlier than imaging; still experimental	[102,103]

For screen-positive patients with negative biopsy results (false-positive screening) or benign lesions, individualized follow-up plans are indicated: benign nodules (e.g., splenic nodules, hepatic cysts) may be monitored with imaging every 6–12 months; suspicious atypical hyperplastic lesions require shorter 3–6 month intervals with repeat biopsy as needed [105,106]. For rare cases with positive liquid biopsy and negative conventional workup, no evidence-based guidelines exist; repeat liquid biopsy with whole-body diffusion-weighted MRI after 3 months may be considered, but long-term repeated testing is discouraged to avoid owner anxiety and unnecessary costs.

Key management strategies are summarized in Table 2, and Figure 2 illustrates the recommended workflow from positive screening to final decision-making.

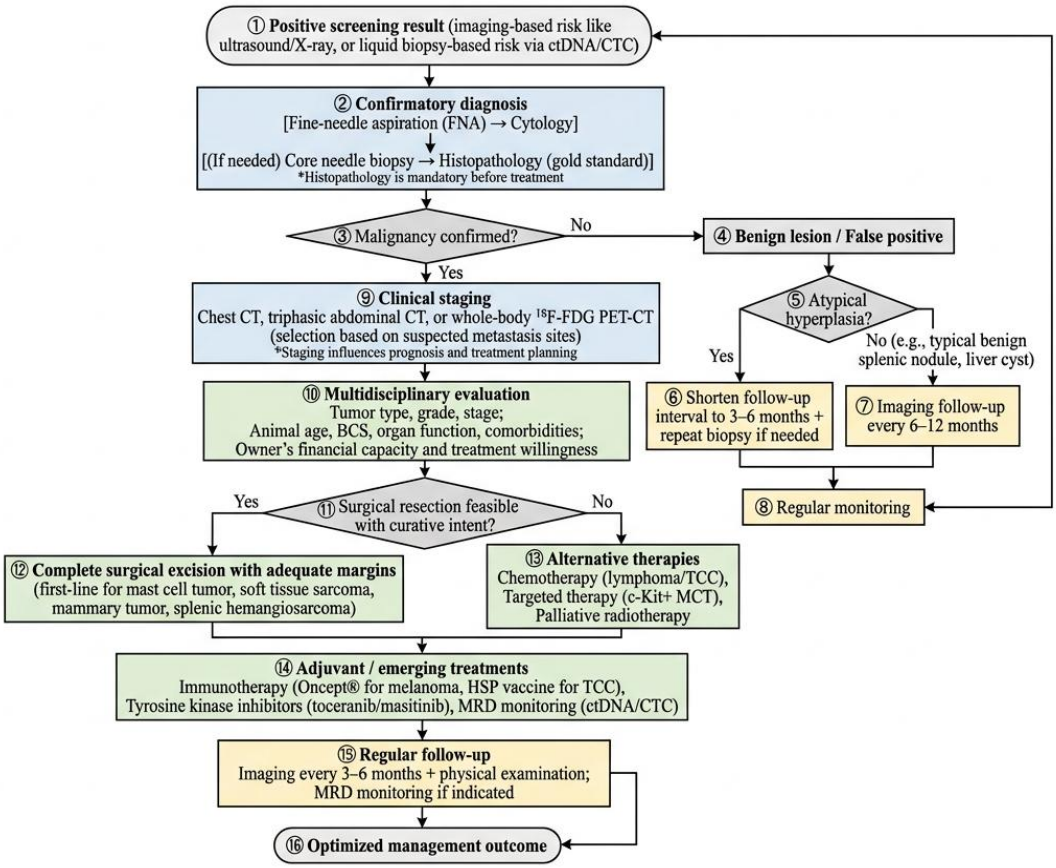


Figure 2. Recommended workflow following a positive cancer screening result

5. Conclusion

Early cancer screening in dogs and cats remains clinically challenging, primarily due to a lack of large-scale validated early biomarkers with robust sensitivity and specificity. Traditional screening methods (physical examination, imaging, cytology) have limited ability to detect micrometastases, early carcinoma in situ, and occult lesions, and are time- and operator-dependent. However, ongoing technological advances are progressively addressing these gaps.

Liquid biopsy technologies (ctDNA testing, metabolomic analysis, CTC enumeration) and AI-assisted image interpretation enable detection of peripheral blood molecular abnormalities before radiologically visible lesions appear, providing pathways for earlier, more precise screening and risk stratification. Quantitative ctDNA mutation detection (e.g., BRAF V595E for canine bladder cancer), multi-omics discriminative models, and machine learning-enhanced cytomorphologic analysis can complement traditional cytologic and histopathologic diagnoses, supporting clinical decision-making and reducing unnecessary invasive procedures.

The future of companion animal early cancer screening lies in the seamless integration of traditional clinical methods with emerging molecular diagnostics, AI-assisted image analysis, and multi-panel

biomarker testing. Realizing this potential requires large-scale, multicenter, prospective clinical validation studies to define diagnostic accuracy, clinical utility, and cost-effectiveness, and to establish standardized operating procedures and result interpretation criteria. The ultimate goal is to deliver efficient, precise, quality-of-life-aligned early screening tailored to individual patient risk profiles, ensuring timely diagnosis for cases that benefit from early intervention while avoiding excessive medical intervention.

Author Contributions: Conceptualization, Z.Z. and G.M.L.; methodology, Z.Z.; software, Z.Z.; validation, Z.Z., L.S.H. and M.B.H.; formal analysis, Z.Z.; investigation, Z.Z.; resources, G.M.L.; data curation, L.S.H., M.B.H. and C.X.; writing—original draft preparation, Z.Z.; writing—review and editing, Z.Z., L.S.H., M.B.H., C.X. and G.M.L.; visualization, Z.Z.; supervision, G.M.L.; project administration, G.M.L.; funding acquisition, L.L.R. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the Xinjiang Production and Construction Corps Funding Project (Grant No. 2018CB037)

Institutional Review Board Statement: Not applicable. This review article does not involve any animal or human studies performed by any of the authors.

Data Availability Statement: No datasets were generated or analysed during the current study.

Acknowledgments: In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest: The authors declare no competing interests.

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