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Faculty of Veterinary Medicine – Final degree project, June 2019

Introduction

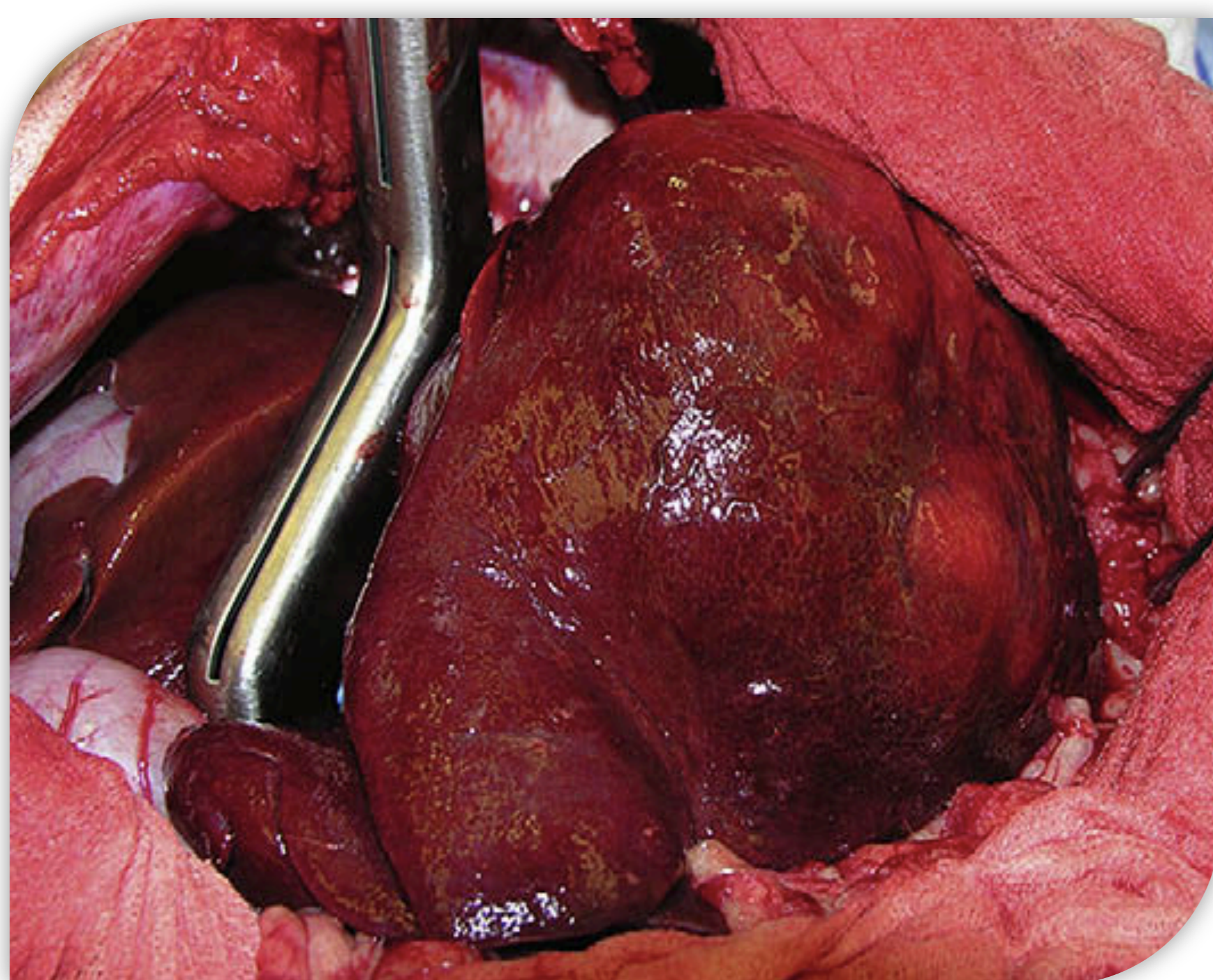
- Hepatobiliary neoplasia is uncommon in dogs. Frequently are malignant and secondary tumors from spleen, gastrointestinal tract and pancreas that metastasize to the liver. The majority of dogs diagnosed are older than 10 years of age and show nonspecific clinical signs.
- Hepatocellular carcinoma accounts for > 50% of primary liver tumors. Early detection is difficult and only enables a complete surgical resection of massive morphology appearance without metastases.

Objectives

- Make a current bibliographic review of canine liver tumors.
- Research on current and future therapies for management of unresectable human hepatocellular carcinoma and discuss the advantages and contraindications to assess which of them could be good therapeutic strategy for this neoplasia in dogs.

Semiology and physical examination

- Approximately 25% of affected dogs show no clinical signs.
- Clinical signs are nonspecific (normally associated with gastrointestinal tract).
- Hepatomegaly or cranial abdominal mass is the most common physical examination abnormality.



Hepatocellular carcinoma in a dog. (Balkman 2009)

Diagnosis

CBC/ Serum biochemistry

changes are common but not specific for liver tumour

		Incidence
Hematocrit	Decrease	(27% to 50%)
Leukocytes	Increase	(54% to 73%)
Platelets.	Increase	(50% hepatocellular carcinoma)
ALT	Increase	(44% to 75%)
ALP, GGT	Increase	(> 61% and 39% respectively)
Glucose	Decrease	Occasionally
Albumin	Decrease	(52% to 83%); increase occasionally
Bile acids.	Increase	(50% to 75%)
Total bilirubin	Decrease	(18% to 33%)

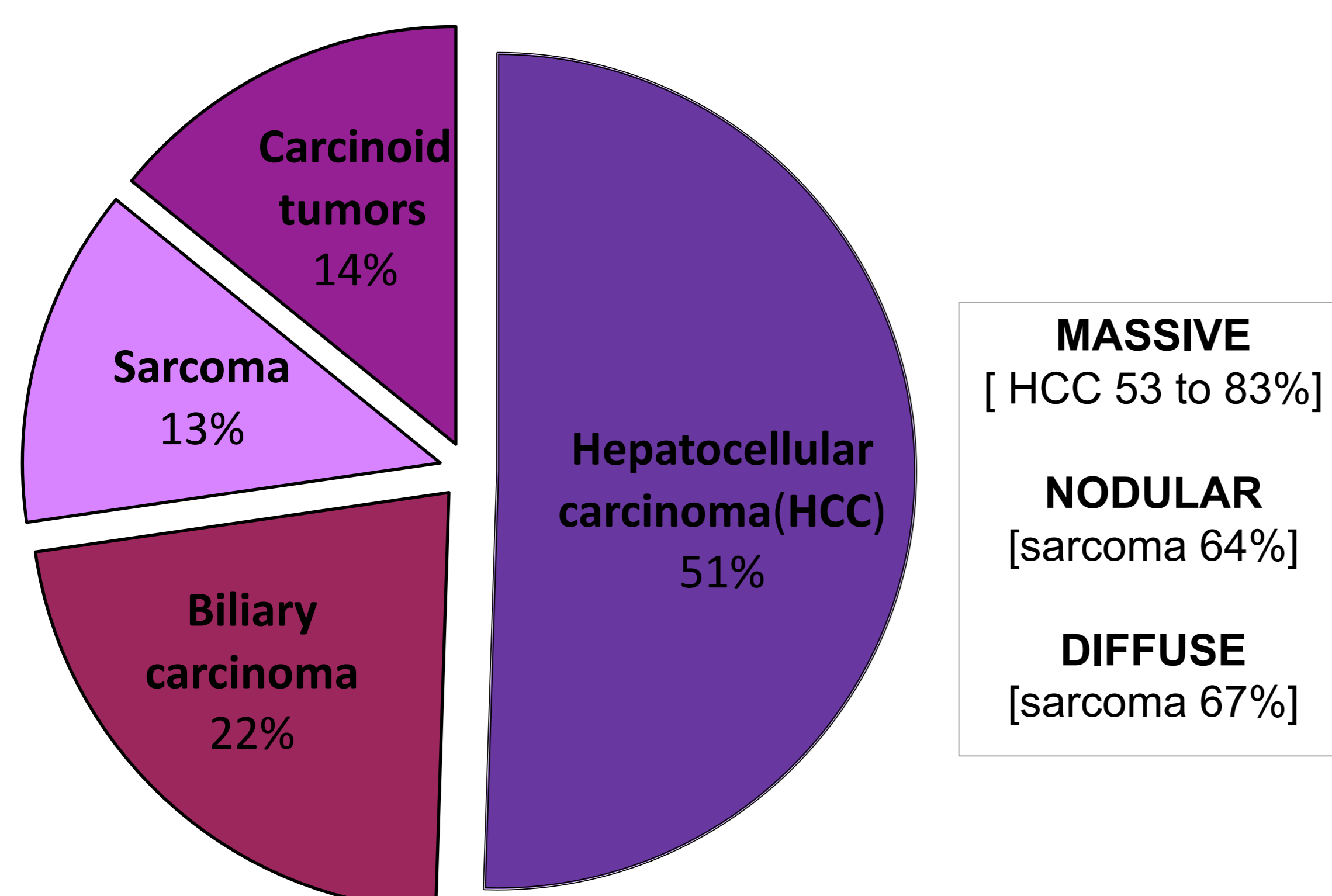
Imaging

- **Abdominal RX:** often reveal a cranial abdominal mass with caudal and lateral displacement of the stomach.
- **Abdominal US:** determine morphology, size and location of tumors and its relationship with adjacent structures (cava vein, gallbladder). Metastases and tumor vascularization (Doppler).
- **CT / RMI:** diagnosis and staging liver tumors. MRI has more sensitivity (100%) and specificity (90%) for differentiation of malignant and benign masses.

FNA / Biopsy

- Cytology and /or histology → Definitive diagnosis.
- A correct diagnosis is obtained in > 60% of hepatic aspirates and 90% of biopsies.

Primary malignant hepatic tumors



Incidence of primary malignant liver tumors. (Pastor and Planellas 2013)

Treatment approach of canine hepatocellular carcinoma (HCC)

Pattern	Treatment	Notes
MASSIVE	Surgical resection	Election. Rare recurrences (0-13%). Median overall survival (OS) > 4 years. Not recommend for metastatic tumour. May not be possible if HCC involves the cava vein.
	Chemoembolization (CE)	<ul style="list-style-type: none"> • Indicated if surgical resection is not possible. It has been reported with moderate success in the palliation of four dogs with HCC.
NODULAR and DIFFUSE	CE	
	Multi-kinase inhibitors	<ul style="list-style-type: none"> • Toleranib showed a clinical benefit. Are required more studies to validate which usefulness.

Futures therapeutic strategies (?)

- Radiofrequency ablation**
 - Complete responses in > 90% of human HCC <0.3 cm.
 - Combination with CE (size, recurrence).
- Immune- checkpoint inhibitors (anti PD-1)**
 - Nivolumab showed antitumor activity and tolerated safety in advanced human HCC.

Conclusions

- HCC may progress silently in dogs with sufficient liver function and escape early diagnosis due to vague complaints and non-specific symptom.
- Prognosis and therapy options depends to the combination of histological and morphological pattern.
- Liver lobectomy is the gold standard for dogs with massive HCC but tumours with such risk factors should be poor prognostic.
- RFA seems to be a good future curative strategy for canine HCC.
- Multikinase inhibitors and anti-PD1 are offering hopeful results as future individualized strategy for HCC treatment.

References

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