HYPERCALCEMIA OF MALIGNANCY IN THE DOG
Final degree project- June 2022
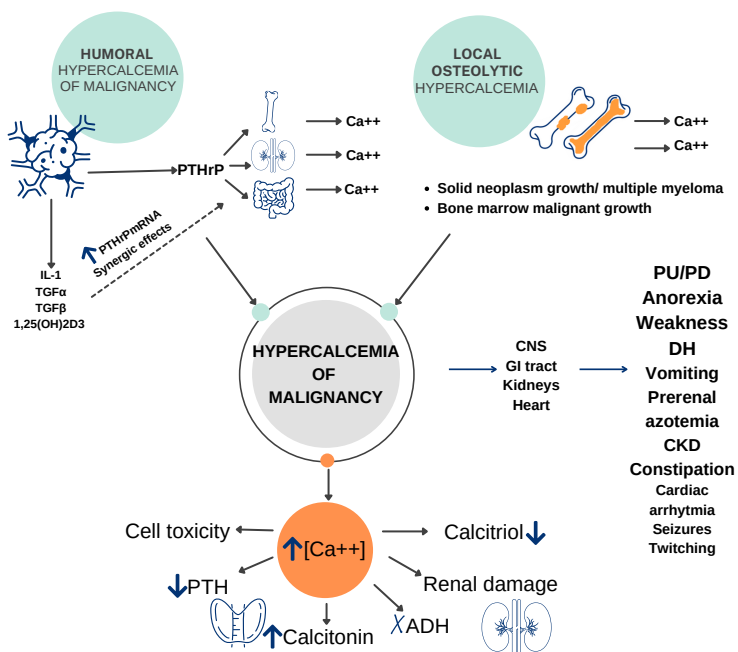Clàudia Pedescoll Aguilar

INTRODUCTION

Hypercalcemia of malignancy (HM) is the most common cause of hypercalcemia in the dog. It has an incidence of 12,9%. Its importance in veterinary and human medicine, has encouraged scientific investigations in the field.

The highest prevalence of HM is found in lymphoma, followed by apocrine gland anal sac adenocarcinoma (AGASACA), carcinoma, bone neoplasia, sarcoma, multiple myeloma (MM), leukemia and thymoma.

PICO QUESTION: In dogs suffering from neoplastic processes **(P)** how does hypercalcemia of malignancy **(I)** compared to the absence of this paraneoplastic syndrome **(C)** influence **prognosis (O)**?

Studies regarding the prognostic value in T-cell lymphoma, AGASACA, MM and thymoma are ambiguous. The administered **treatment**, tumor **phenotype** and the effect of **other** prognostic **variables**, may affect the obtained results.

OBJECTIVES

1. Review published information and identify areas which need further exploration.
2. Develop research questions in a PICO format, including population (P), intervention (I), comparison (C), and outcome (O).
3. Facilitate the search for scientific information.
4. Identify gaps in knowledge.

PICO QUESTION: In dogs suffering from neoplastic processes **(P)** how beneficial are ionized calcium (iCa) and predicted ionized calcium (piCa) measurements **(I)**, compared with total (tCa) or adjusted calcium determinations **(C)** in **diagnosing** hypercalcemia of malignancy **(O)**?

High tCa elevation and normophosphatemia favor the prediction of iCa. Still, hypercalcemia can remain **not detected** when **tCa or adjusted calcium** is measured. **piCa** calculation should be considered as an alternative method in case iCa cannot be determined. **iCa** remains the **gold standard** for calcium status assessment.

PICO QUESTION: Are tumor-bearing dogs **(P)**, who have high **parathyroid hormone-related protein** (PTHrP) concentrations **(I)** compared with those with lower PTHrP levels or without PTHrP elevation, **(C)** more likely to present high calcium elevations **(O)**?

HM development depends on **specific synergic mechanisms** that are characteristic of every neoplastic process in each patient. **Analogous PTHrP and calcium** concentration values are **uncommon**. Thus, PTHrP measurement cannot entirely explain the process causing HM. PTHrP concentration, PTH/PTHrP receptor, cytokine and growing factor profile, and laboratory reference intervals must be considered.

Pathophysiology and clinical consequences of hypercalcemia of malignancy. Interleukin-1 (IL-1), Transforming Growth Factor α (TGF- α), Transforming Growth Factor β (TGF- β), 1,25 dihydroxyvitamin D3 (1,25(OH)2D3), Parathyroid hormone-related protein (PTHrP), calcium (Ca++), Central Nervous System (CNS), Gastrointestinal tract (GI tract), Polyuria/polydipsia (PU/PD), dehydration (DH), Chronic Kidney Disease (CKD), Parathyroid hormone (PTH), Antidiuretic hormone (ADH)

CONCLUSIONS

- **Deeper tumor characterization** is needed to determine the impact hypercalcemia of malignancy has on prognosis.
- **Ionized calcium** is the only precise parameter to evaluate calcium status in a patient.
- The emerging use of **predicted ionized calcium** provides valuable information on clinical situation of hypercalcemic dogs.
- PTHrP **effects on calcium concentration** depend on cytokine and growing factor expression, extracellular matrix components, PTH/PTHrP receptor and synthetized protein viability.
- PTHrP synthesis does **not always** prompt calcium **elevation**.