

Cushing's syndrome in Flanders and the Netherlands: an owner survey

*Syndroom van Cushing bij honden in België en Nederland:
een enquête bij de eigenaars*

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ABSTRACT

Cushing's syndrome is a common chronic condition, with daily impact on the owner's and dog's life. The owners' perception and quality of life are essential, as any negative impact could lead to cessation of medical care or decision of euthanasia. The present survey aimed at collecting the perception of Flemish and Dutch owners of dogs affected by Cushing's syndrome on medical, practical, financial and emotional aspects. In total, the questionnaires of 218 respondents were available for analysis, highlighting owners' expectations, quality of life, understanding of the disease and encountered difficulties, and identifying weak and strong points regarding owner-veterinary interactions, together with providing several demographic data related to canine Cushing's syndrome in Flanders and the Netherlands.

SAMENVATTING

Het syndroom van Cushing is een veelvoorkomende chronische aandoening, met een dagelijkse impact op het leven van de eigenaar en de hond. De perceptie van de eigenaren en de kwaliteit van leven zijn essentieel, aangezien elke negatieve impact kan leiden tot stopzetting van medische zorg of de beslissing tot euthanasie. Het voorliggende onderzoek was gericht op het verzamelen van de perceptie van Vlaamse en Nederlandse eigenaren van honden met het syndroom van Cushing over de medische, praktische, financiële en emotionele aspecten van de aandoening. In totaal waren 218 vragenlijsten beschikbaar voor analyse, waarbij de verwachtingen van eigenaren, kwaliteit van leven, begrip van de ziekte en ervaren moeilijkheden werden benadrukt. Tevens werden zwakke en sterke punten geïdentificeerd met betrekking tot de interactie tussen eigenaar en dierenarts. Tot slot werden verschillende demografische gegevens over honden met het Cushingsyndroom in Vlaanderen en in Nederland verzameld.

INTRODUCTION

Hypercortisolism (HC) is a relatively common endocrine disorder in older dogs, with a prevalence of 0.20-0.28% in dogs attending primary-care veterinary practices (O'Neill et al., 2016; Carotenuto et al., 2019). Dogs often exhibit chronic clinical signs. Diagnosis, treatment and monitoring of Cushing's syndrome can be challenging. Moreover, medical therapy is required lifelong and treatment is expensive. All

these factors impact an owner's daily life on different levels (financial, practical and emotional). Recently, a health-related quality-of-life tool for dogs with Cushing's syndrome has been developed, based on answers provided by dog's owners. In the study performed to elaborate that tool, the authors considered the financial and emotional strain of Cushing's syndrome to the owner. Indeed, a negative impact of disease and/or therapy on the owner could lead to cessation of treatment or euthanasia (Schofield et al., 2019). The

aim of the present survey was to collect the opinion of owners of dogs suffering from HC in Flanders and the Netherlands about their perception and understanding of Cushing's syndrome, from the diagnosis until the treatment, focusing on the impact on their own daily life, and the relationship with their veterinarian.

MATERIAL AND METHODS

In May 2021, owners of dogs with HC living in Flanders and the Netherlands were contacted. A message was posted on social media groups related to canine Cushing's syndrome. People owning, or who had recently owned, a dog with HC, were asked to answer an online questionnaire. The questionnaire was uploaded to an online survey tool (SurveyMonkey, San Mateo, California). The questionnaire was available only in Dutch, and counted 45 questions (38 multiple choice and seven open questions), divided in six categories: general information, dog and owner characteristics, diagnosis, treatment and veterinarian-related information. The estimated time to complete the survey was ten minutes. The questionnaire was available during ten days. If the diagnosis of Cushing's syndrome was not made by a veterinarian, the results of the questionnaire were excluded.

RESULTS

In total, 228 questionnaires were completed (180/228 from the Netherlands, 48/228 from Flanders). Ten questionnaires were excluded. In 9/10, the diagnosis of Cushing's syndrome was not confirmed by a veterinarian and one questionnaire was filled-out by the owner of a cat with Cushing's syndrome.

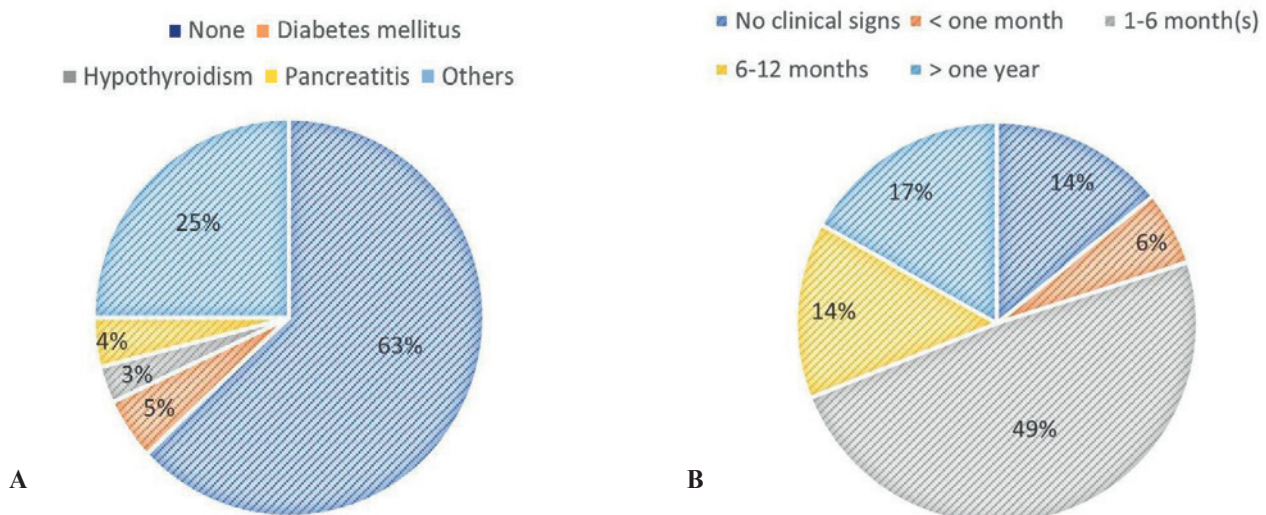
Of the 218 included questionnaires, 135 were from owners of dogs alive at the moment of the survey. The

median age of these dogs was eleven years (range: 4-18 years). The median age of all dogs at the moment of the diagnosis was nine years (range: 2-17 years). Thirty-seven percent of the dogs (81/218) had at least one comorbidity and, for most cases (107/218, 49%), clinical signs related to HC had been present for one to six month(s) before diagnosis (Figures 1A and B).

In 96/218 (44%) cases, the owners suspected Cushing's syndrome themselves. Seventy-seven percent of the dogs (169/218) had a general blood test, and 185/218 (85%) urinalysis, performed during work-up, while 196/218 (90%) underwent more specific tests for HC. Screening tests for HC were realized in 190/218 (87%) cases. The urine cortisol:creatinine ratio (UCCR) was the most commonly used screening test, followed by the ACTH-stimulation test and the low-dose dexamethasone suppression test (LDDST) (Figure 2). Imaging was performed in a total of 115/218 (53%) dogs, before or after (up to two years later) diagnosis. Seventy-four percent (85/115 dogs) underwent abdominal ultrasound, 39/115 (34%) CT scan or MRI.

To most owners 179/218, (82%), the differentiation of Cushing's syndrome in their pet was clear: 137/179 (77%) pituitary-dependent hypercortisolism (PDH), 30/179 (17%) adrenal-dependent hypercortisolism (ADH), 10/179 (6%) both pituitary- and adrenal-dependent hypercortisolism and 2/179 (1%) iatrogenic Cushing's syndrome.

In 121/218 (55%) cases, the primary veterinarian was the only person involved in the diagnosis, treatment and follow-up, but 70/218 (32%) owners consulted several veterinary practices before reaching the diagnosis, and 81/218 (37%) took a second opinion after diagnosis. For 57/81 (70%) respondents, the second opinion included a consultation with a specialist in internal medicine. In total, a specialist was consulted at least one time by 65/218 (30%) participants. The dog's usual, primary veterinarian was not consulted at all in eight cases.



Figures 1A and B. Prevalence of comorbidities and duration of clinical signs related to HC before diagnosis, n=218 dogs.

Most owners (152/218, 70%) found the explanation of their veterinarian about the disease at the moment of diagnosis satisfying but 29/218 (13%) evaluated the quality of the information given as insufficient. These data, together with the satisfaction levels regarding the explanation of the veterinarian about the different modalities of treatment, can be found in Figure 3.

The dogs had been treated for a broad variety of time (less than one month to more than one year) at the moment of the survey, or before they died. Most dogs in both groups had been treated for more than one year (72/135, (53%) in the alive group, 43/83 (52%) in the deceased group). Three percent of the dogs (4/135) in the alive group and 7/83 (8%) in the deceased group did not receive medication. The majority of dogs 191/218, (88%) were treated with trilostane (Vetoryl®, Dechra Limited, North Yorkshire, UK), at one of the following frequencies: 2/191 (1%) once every other day, 83/191 (43%) once a day, 102/191 (53%) two times a day and 14/191 (7%) three times a day. Eight percent of the owners (18/218) mentioned using alternative therapy (holistic, homeopathic, energetic, natural products or Chinese herbs), alone (n=7) or in combination with classical treatment (n=11). Only 9/218 (4%; 2% adrenalectomy and 2% hypophysectomy) dogs were treated surgically. More than half (123/209, 59%) of the owners noticed clinical improvement with treatment, 60/209 (29%) judged the evolution as being highly variable and fluctuating, while 26/209 (12%) did not see any changes with therapy. Trilostane was mainly bought at the local veterinary practice (152/208 responses). Other provided answers were: at the pharmacy (31/208, 15%), online/second-hand/abroad (Italy, Spain and United Kingdom before Brexit) (25/208, 12%), by another veterinarian (42/208, 20%). As Vetoryl is only available at few different dosages, it was sometimes (n=11) reformulated into a more convenient dosage by the pharmacy. Three respondents opened and divided the capsules themselves.

The care of a dog with Cushing's syndrome was evaluated as costly by 120/218 (55%) of respondents, while costs were acceptable for 55/218 (25%) and not a problem at all for 43/218 (20%). Only 25/218 (11%) dogs were insured, and a major part of the costs was covered by the insurance in 19 of these 25 dogs (76%). The median extra time per day that owners had to put into the care of their dog was 30 minutes (range; 1-300 minute(s)). The administration of the medication was difficult in 14/209 (7%), average in 28/209 (13%) and easy in 167/209 (80%) medically treated dogs. Only 7/209 (3%) owners found the reorganization of their daily routine difficult, while 173/209 (83%) evaluated it as easy. The global care needed for a dog suffering from HC was underestimated and overestimated by 52/201 (26%) and 4/201 (2%) participants, respectively.

To improve their knowledge of the disease,

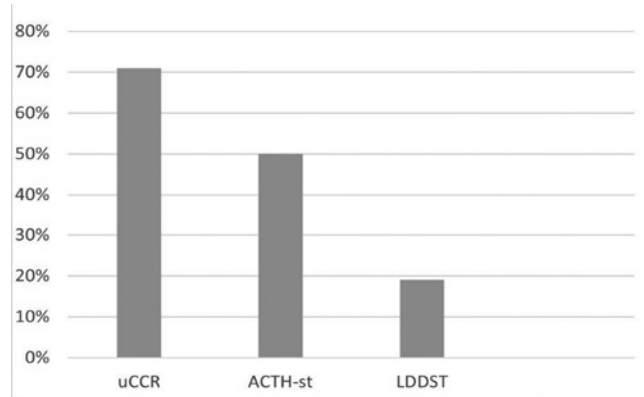


Figure 2. Percentages of the different screening tests performed in a total of 190 dogs.

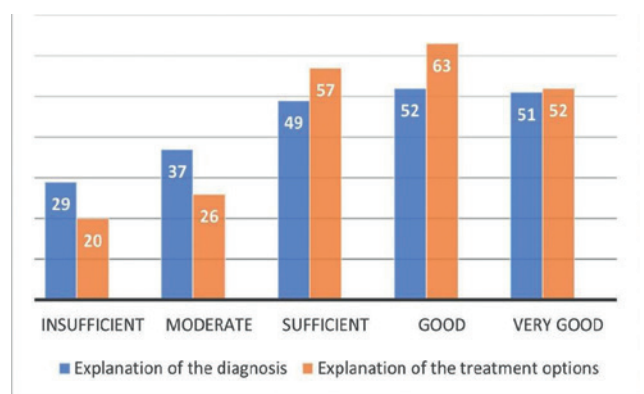


Figure 3. Levels of satisfaction regarding communication with the veterinarian, n=218.

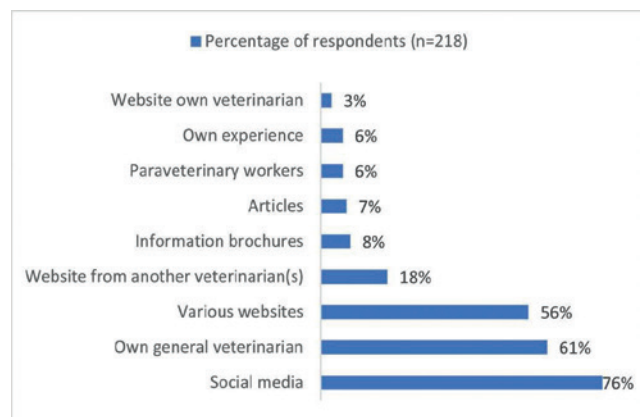


Figure 4. Sources of information about canine Cushing's syndrome, n=218.

164/218 (75%) respondents spent more than five hours (on top of the veterinary consultations) looking for information. The different sources of information are illustrated in Figure 4. Nevertheless, 81/218 (37%) owners felt like they still did not know enough about their pet's disease.

The pet-owner relationship did not change after the dog's diagnosis for 142 (65%), improved for 65 (30%) and deteriorated for 11/218 (5%) respondents. Most participants (185/218, 85%) could assess the

other ones, and may have wrongly thought that this test was also the one used for diagnosis. More than half of the dogs in present survey underwent imaging (abdominal ultrasound and/or CT scan/MRI), and the delay between diagnosis and imaging varied greatly. This delay may be due to the evolution of the clinical signs, such as appearance of neurological signs in case of pituitary macroadenoma, or to insufficient improvement despite therapy. Imaging in dogs with HC is especially important to determine the best treatment option for individual cases, by discriminating between ADH and PDH and evaluating the presence of metastasis, or to plan surgery/radiotherapy (Feldman et al., 2015).

Consultation with one or more other veterinarian(s) before reaching diagnosis, or for a second opinion, was very common. A significant percentage of respondents evaluated the explanation of their primary veterinarian regarding diagnosis and treatment of Cushing’s syndrome as insufficient, with the most commonly mentioned weakness being a lack of knowledge of the practitioner. A possible explication is that many general veterinarians in Belgium and in the Netherlands, according to the authors’ estimation, only encounter one to two dog(s) with HC per year. Another possible contributing factor for dissatisfaction is that, nowadays, clients have access to a lot of online information. Consequently, the owners will easily find content about canine Cushing’s syndrome and could have the feeling, while coming up with specific questions, that the veterinarian was unable to answer them or to provide new elements. Access to the internet could also, at least partially, explain the high number of owners who raised the initial suspicion of HC themselves. Four respondents specifically added in the free text area that they googled the clinical signs of their pet, and found Cushing’s syndrome as a possible diagnosis. Others already had owned a dog with Cushing’s

syndrome and recognized the clinical picture. However, it is difficult to believe that almost half of the respondents suggested the diagnosis to their veterinarian. It is possible that the question was not fully understood by the participants. Interestingly, 14% of the respondents answered that their pet had no clear clinical signs of HC. None of the currently available adrenal function tests are totally reliable and, when a population without high clinical suspicion is tested, some patients could be misdiagnosed and started on unnecessary therapy, placing them in a potentially life-threatening situation. In order to keep the number of false-positive results as low as possible, a compatible history and physical examination findings remain the main indication to test for HC (Behrend et al., 2013). Based on these data, it is not impossible that some dogs in the present study were misdiagnosed with Cushing’s syndrome.

Participants to this survey had a clear preference for direct personal contact with their veterinarian regarding communication, mainly through consultations or over the phone. Nowadays, pet owners wish tailored communication based on their needs and expect partnership and shared decision-making with their veterinarian (Janke et al., 2021). Extra communication via mails or phone calls could be beneficial for both the patient and his owner. However, it might be challenging to add these (often free) services to the already heavy workload of most veterinarians. The pet respondents’ preference for a quarterly consultation during long-term follow-up is in agreement with the classical recommendation of three to six months monitoring after having reached a stable dose of trilostane (Ramsey, 2010).

Eight percent of the respondents indicated using alternative therapies, alone (7/18) or alongside (11/18) conventional treatment. There is a raising interna-

Table 1. Short- and long-term follow-up options, preferences of 218 respondents.

Short-term follow-up (218 respondents, several answers possible)	Contact with veterinarian n=254	<ul style="list-style-type: none"> • Consultations n=133 • Phone calls n=99 • Emails n=22
	Contact with paraveterinary staff n=27	
	Others n=50	<ul style="list-style-type: none"> • Information brochures n=15 • Summary on paper n=35
Long-term follow-up (218 respondents, several answers possible)	Contact with veterinarian n=185	<ul style="list-style-type: none"> • 6-months consultations n=74 • 3-months consultations n=31 • Monthly consultations n=42 • Emails n=34 • Phone calls n=4
	Contact with paraveterinary staff n=79	<ul style="list-style-type: none"> • While picking up medication n=65 • 3-months contact n=5 • Monthly contact n=6 • Emails n=3
	Others n=23	Daily diary

tional interest in veterinary naturopathy and complementary medicine, from both veterinarians and pets' owners. In a recent survey among German small animal medicine veterinary practitioners, 85.4% of the participants used naturopathy and complementary medicine. The owners' demand for naturopathy and complementary treatments over the last five years was rated as growing by 57.9% of the respondents (Stanossek and Wehrend, 2022). There is currently a lack of evidence-based data regarding the effectiveness, safety and mechanism of action of these alternative therapies. If given without conventional treatment, they could lead to disease progression.

Only 4% of the dogs in this survey were treated surgically. Surgery allows the removal of the source of hormones excess. Adrenalectomy is recommended for dogs with uni- or bilateral adrenocortical tumor, and hypophysectomy is especially interesting in cases of pituitary macroadenoma (Sanders et al., 2018). Four owners added in the questionnaire that they were not informed by their veterinarian about surgical options. No specific question was asked in this survey as whether the respondents knew about the possibility of adrenalectomy or hypophysectomy. Consequently, more owners could have been unaware of these treatment options. Other possible explanations for the low number of surgeries mentioned in the survey are the high initial costs and the fear of severe peri-operative complications. The most frequently used treatment was trilostane. Vetoryl is registered for the medical treatment of canine PDH and ADH. There is a broad variation in the optimal dose. Some dogs may benefit from three-times-a-day medication (Feldman, 2011; Vaughan et al., 2008), but 3/14 owners in that situation found this schema complex. Giving trilostane every other day, as done by two respondents, is not recommended. Worryingly, a few owners opened the capsules of trilostane. Trilostane is a hazardous substance (may be harmful by inhalation, ingestion, or skin absorption: skin corrosion/irritation, serious eye damage/eye irritation, toxic to reproduction, may be irritating to the mucous membranes and respiratory tract), and the capsules should never be opened without the required experienced and equipment (Dechra, 2017). Veterinarians should be aware of this and strongly discourage owners who wish to compound trilostane themselves.

One owner out of four underestimated the care required for a dog with Cushing's syndrome, which reinforces the importance of clear communication and explanation at the moment of the diagnosis. The veterinarian should make sure that all treatment options, with their associated benefits and risks, have been discussed with the owner, and provide a long-term plan. However, based on the results, multiple weaknesses seem to exist in this regard. Likely, veterinarians do not always have sufficient time during a consultation to inform the clients thoroughly. If unexperienced with Cushing's syndrome, the general practitioner could offer referral.

More than one third of the respondents assessed their quality of life as being negatively impacted by their pet's disease. In a study by Schofield et al. (2019), the most important questions reported by pet owners were those that explored whether Cushing's syndrome affects the bond with their animal and how much they worry about their dog's future health. In the present survey, 30% of the respondents answered that the pet-owner relationship after diagnosis improved. This could be due to the extra time spent with a diseased pet, because of both medical and 'tender loving' care. Tender loving care was, actually, often mentioned as an 'extra' treatment by the respondents in the free text area. A small percentage of participants found, on the contrary, that the bond with their dog deteriorated. Frustration, stress, fear, linked to the administration of the medication itself, or to other factors, can have a negative impact on the owner-pet bond. Not to underestimate is the impact of interrupted night sleep because of nocturia.

The present study has several limitations. First, only owners from the Netherlands and Flanders could participate. Geographical variations in owners' perception are likely (cultural, economic and availability of local professional skills). A study assessing differences between patients from the USA and the Netherlands in how the Cushing QoL (widely used disease-specific questionnaire to assess quality of life in humans with Cushing's syndrome) is interpreted, showed that 3/12 items on the questionnaire were interpreted differently, concluding that the results' interpretation requires consideration of the country of residence (Winter et al., 2018). As the questionnaire was available online and was posted in specific Facebook groups only, there is likely a bias in the selected population, especially as 92% of the participants were members of the same Facebook group. Indeed, members of a discussion group are more likely to be strongly involved in their pet's medical condition and treatment. This, together with the aforementioned cultural and financial differences, suggest that the results of the present survey cannot be extrapolated to the totality of the pet owners population worldwide. However, the authors believe that the findings are still very relevant in a large part of the world, and indicate points of attention and areas of possible improvement in relation to canine hypercortisolism.

CONCLUSION

The present survey provides a valuable insight from the owner's point of view into canine Cushing's syndrome in the Netherlands and Flanders. For the majority of respondents, the quality of life was not impacted negatively by their dog's medical condition. Many owners were highly-motivated and ready to involve themselves in terms of finances and time, in the medical care of their pet. Several weak points related to diagnosis were identified, with no screening tests

performed to confirm HC in more than 10% of the dogs, and with only half of the present study population undergoing medical imaging. Consequently, a significant proportion of dogs in this survey was treated without a proper diagnosis. These findings highlight the importance of veterinary education about Cushing's syndrome. Information regarding potential owner's exposure to trilostane is mandatory.

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