

Decision of Diagnostic Criteria of Feline Obesity Disease

Summary of Doctoral Thesis

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The incidence of obesity has increased in developing countries as well as in developed countries in these years. According to a report from World Health Organization (WHO), the incidence of obesity has nearly tripled since 1975, with 39% of the world's adults being overweight and 13% being obese in 2016. Obesity is one of the most widespread social problems facing our society health problem. The incidence of obesity in dogs and cats has increased, and it has been reported over 40% of adult dogs and cats were overweight or obese in the United States. Obesity is a risk factor for metabolic syndromes, so prevention of obesity is very important for the health maintenance of dogs and cats. In human medicine, pathological obesity with health problems based on visceral fat accumulation is defined as 'obesity disease' differing from simple obesity. In this study, we settled the diagnostic criteria for obesity disease for cats based on visceral fat accumulation investigated by computed tomography (CT) images and biochemical markers.

#### 1. Incidence of obesity in cats and its characterization

The incidence of obesity has increased in cats as in humans. We investigated body condition scores (BCS) of clinically healthy dogs and cats, which went to the hospital for health examination at two animal hospitals in Tokyo metropolitan for the past three years. Measurement of BCS was done with a 5-points scales system (BCS3, idea; BCS4, overweight; BCS5, obese), which is widespread in Japan. Over 40% of cats were diagnosed as overweight or obese, and its proportion was higher than that of dogs. This result was thought to be owing to the cat's characterization of energy metabolism such as lower glycolytic activity and tend to be insulin resistant than dogs. In obese individuals, excessively accumulated visceral fat secretes free fatty acids (FFA) and some inflammatory cytokines and induces chronic systemic inflammatory. These changes are called lipotoxicity. Similar changes seem to be induced in obese cats, and visceral fat accumulation should be studied.

## 2. Investigation of subcutaneous and visceral fat accumulation using computer tomography (CT) in obese cats

Japan Society for the Study of Obesity (JASSO) defined pathological obesity, which needed medical treatment, as ‘obesity disease’ in ‘Guidelines for the management of obesity disease 2016’. Obesity disease is diagnosed based on a mass of accumulated visceral fat measured by CT or MRI, and early diagnosis of obesity disease is useful for the prevention of metabolic syndrome. So early and accurate diagnosis of obesity disease needs measurements of mass and distribution of accumulated body fat in animals. We divided examinee cats into three groups with different BCS values, BCS 5, BCS 6~7, and BCS 8~9, and measured their plasma metabolites and hormone concentrations, and mass and distribution of subcutaneous and visceral fat (visceral fat /subcutaneous fat ratio, VS ratio) by CT. Plasma triglyceride and FFA concentrations increased accompanying the increase of BCS, adiponectin concentrations were changed among three groups. Plasma SAA concentrations increased with visceral fat accumulation, but BCS did not always reflect changes in the mass of visceral fat. There was no correlation between VS ratio and plasma adiponectin and SAA concentrations. There was a higher correlation between plasma SAA concentrations and visceral fat accumulation observed by CT. However, as VS ratio was changed at photograph positions of CT, VS ratio was not an appropriate marker for the decision of obesity condition, and there was no clear correlation between VS ratio and plasma adiponectin concentrations. Remodeling (enlargement) of adipose tissue induced decreased adiponectin concentrations and increased inflammatory cytokine concentrations in plasma of obese animals. Such an obese condition is thought to be pathological obesity differing from simple obesity without health problems. Simple obesity (overweight without health problems) is not classified as a disease. Therefore, pathological obesity cannot be decided by only BCS values. CT pictures could detect increases in fat mass (quantitative change), but could not detect enlargement of adipocytes (qualitative change) in animals. We need appropriate blood markers to decide the differences between simple or pathological obesity of animals.

### 3. Establishment of new diagnostic criteria for feline obesity disease

Simple obesity is not always classified as a disease. JASSO defined pathological obesity which needed medical treatment as ‘obesity disease’. Feline obesity should be classified into simple and pathological obesity referring to the criteria for human medicine. Obesity is classified into primary and secondary obesity. Primary obesity is of our interest and is further divided into simple and pathological obesity based on obesity-associated symptoms like glucose intolerance, lipidemia, fatty liver, and others. Simple obesity is defined as without any health problems. Pathological obesity is further divided into with and without visceral fat accumulation. And obesity disease may be diagnosed if overweight cats with BCS  $>7/9$  show two or more of the following, low adiponectin, hypertriglyceridemia, and high SAA values. Obesity disease cats according to these criteria showed significantly higher plasma triglyceride and SAA concentrations and lower adiponectin concentrations than the control (ideal weight) cats. These criteria may be useful for the detection of early-stage of inflammation and prevention of progression of obesity disease.

### 4. Application of the new criteria for feline obesity disease for prevention of diseases

In Japan as a super-aging society, non-communicable diseases (NCD) such as obesity, diabetes mellitus, kidney injury, and cancer, become social problems in recent years. In dogs and cats kept at home, the number of aged animals over 15 years old like a man’s over 75 years old has increased and the prevalence of their NCD has increased with aging recently. On the other hand, the population ratio of young animals under one-year-old is 4 to 5%, so the declining birthrate and aging population are progressing and the prevalence of NCD is increasing in veterinary medicine as in human medicine. Prevention is the most effective treatment for the suppression of obesity. In veterinary medicine for dogs and cats, prevention for NCD will become increasingly important in the future.

Obesity is categorized as chronic systemic inflammation induced by aberrant secretion of inflammatory cytokines from increased visceral fat accumulation. Settlement of appropriate diagnostic markers at each stage of obesity is needed to suppress obesity

disease. The new criteria for feline obesity disease proposed by our present research may be a useful tool for progressing preventive medicine for dogs and cats.

Clients of aged animals seek a better quality of life than cure of illness and increasing healthy life expectancy. The treatment system for the prevention of diseases and making a better quality of life is expected for veterinary medicine. Early diagnosis and early treatment are the best measures to prevent NCD. The treatment concept of 'measures to prevent illness rather than cure it' should be promoted in veterinary science.