腹腔鏡を用いた犬及び猫の肥満診断法の開発に関する研究

(Studies on development of new diagnostic system with laparoscopy for obesity in dogs and cats)

学位論文の内容の要約（英語）

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Summary

As in human, prevalence of overweight and obesity has increased remarkably in dogs and cats recently. In particular, cats tend to become obese compared to dogs due to their characters in glucose and lipid metabolism. Obesity is described as the state of excessive triglyceride accumulation in the adipose tissue, and although it is not diagnosed as a disease, since it can lead to a variety of health issues, human medicine defines the state of needing weight reduction as "Obesity disease" . Metabolic syndrome (MS) is considered to be rapidly emerged as a result of a change in our lifestyle, including our everyday diet. As described in the MS guideline, there exists a definite standard for evaluating obesity in human, which uses the body mass index (BMI) as an objective parameter. However, in veterinary medicine, there are no criteria for early diagnosis of obesity, and veterinarians must assess each animals using a subjective parameter, the 5-point body condition score (BCS). Improvement in lifestyle and environment are critical in weight management of animals; thus it is necessary for each owner to realize and understand their pets' weight condition.

In human medicine, the "Guideline for diagnosis of obesity disease" is published every 5 years, and each statement, supplemented with level of evidence, is given a suggested grading score. By referring to the human obesity classification flowchart, a counterpart for cats with BCS 4 or 5 was designed. First, "Primary Obesity" and "Secondary Obesity" was defined. The primary obesity was then divided into those with or without health issues, and the former was termed pathological obesity (obesity disease), the later was termed simple obesity. Pathological obesity (obesity disease) was further divided into subcutaneous fat obesity and visceral fat obesity or metabolic syndrome.

In Chapter 1, we described that the history of application of laparoscopy to medicine to clarify the necessity of laparoscopy to visualize obesity state in veterinary medicine. In particular in human medicine, laparoscopy is used as not only surgical technique but also diagnostic method for metabolic disorders in recent years.

In Chapter 2, we discussed the possibility of laparoscopy as diagnostic method for metabolic disorders in dogs and cats. Invasiveness by operation was compared and discussed between laparoscopy and open surgery for contraception operation in dogs. Plasma concentrations of cortisol after operation was significantly lower with laparoscopy than with open surgery. Plasma cortisol concentration is considered as stress marker after the surgery. Laparotomy has many advantages that surgical area is small and recovery after the operation is quick etc., compared to open surgery. As reported previously, adipose tissue's main purpose is to store energy, and its part as an endocrine organ has been recently recognized. The many cytokines that are released from the adipose tissue include adiponectin and leptin, which are both secreted from small fat cells, while TNF-α, IL-6, and insulin resistance factor, all of which are also knows as inflammatory cytokines, are released from enlarged fat cells. Previous reports have suggested that the release of adipokines from adipose tissues decreases in laparoscopic surgery compared to an open surgery owing to its low level of surgical stress. Additionally, because the levels of MDA, INS, ADN, and COR were lower in dogs that underwent laparoscopic ovariohysterectomy compared with dogs that had an open surgery, it was suggested that laparoscopic surgery enables the observation of abdominal organs such as the liver and kidney possibly effected by metabolic disease under minimum surgical stress.

In Chapter 3, tissue sample sampling from cat with BCS5 suffering from lipidosis was done. Lipidosis is considered as the latest stage of visceral fat

accumulation. Vacuolation was observed in most of liver cells, and M/L ratio as marker of energy production ability was significantly decreased. These results suggest that the ATP generating ability of feline liver cell with adipose degeneration deteriorates. This suggested that the hypermetabolism of the reserved adipose tissue exceeds the liver's metabolism, causing the accumulation of fat and ultimately leading to liver lipidosis. Unlike human medicine, veterinary medicine depends on each veterinarian's subjective analysis using the BCS system for diagnosing obesity, and there were no reports that has measured or directly observed the aberrant fat accumulation in cats according to the respective BCS scores to this day.

In Chapter 4, we performed a laparoscopic surgery and a CT scan in cats with a BCS of 3, 4, or 5, which enabled a direct observation of the state of aberrant peritoneal fat accumulation as well as a biopsy of adipose and liver tissue. As BCS increased, the level of blood serum ADN decreased, while the increase in peritoneal fat accumulation was evident. Seeing that cats with BCS 4 already had aberrant fat accumulation on the liver and other intraperitoneal organs, as well as decreased blood serum ADN level, it was suggested that even in cats with BCS 4, the small fat cells would start to evolve into enlarged fat cells which release insulin resistance hormone.

When managing obesity, it is necessary to build a treatment strategy based upon an accurate evaluation of the current body weight status. This would require development of a biochemical marker and a quantitative scaling system for each corresponding stage of the disease. The metabolome markers deemed appropriate were malate dehydrogenase / lactate dehydrogenase activation ratio which reflects energy metabolism, HDL / LDL ratio reflecting the lipid metabolism, and triglyceride concentration. In addition, the change in blood concentration levels of insulin and adiponectin are also indispensable as a diagnostic marker. Blood concentrations of ALT and AST are useful indication for changes in liver enzymes. High-sensitivity CRP,

TNF-α, MCP-1, and interleukin are inflammatory marker, whereas MDA concentration as lipid peroxide marker, SOD and GSHpx activities as antioxidant enzyme marker are also effective for diagnosing obesity.

Those with simple obesity and even those with a moderate physical impairment without visceral adipose accumulation, will benefit from physical exercise and dietary enhancement. By using laparoscopy, we were able to accurately and safely take samples not only from intrabdominal organs, but also from the dorsal peritoneal wall and the falciform mesenteriolum. This allowed for an understanding of the severity of aberrant fat accumulation in obese animals. By performing more of the same procedure and increasing the number of data, we aim to establish the obesity diagnostic criteria in dogs and cats.