INTRODUCTION:
Steroid-induced osteonecrosis (ON) is known to occur in patients who received corticosteroids for the treatment of such underlying diseases as systemic lupus erythematosus, nephrotic syndrome, and after renal transplantation. Gender gap is present in systemic lupus erythematosus and other collagen diseases, which may affect the prevalence of ON. Several animal models of osteonecrosis have been reported (1-3), however, the sex of the animals has been different. In addition, the gender gap in the development of osteonecrosis has not been reported. A single injection of high-dose corticosteroids is known to be capable to induce osteonecrosis in male rabbits (3).

In this study, we investigated the gender gap in the development of steroid-induced ON in rabbits.

MATERIALS AND METHODS:
This experiment was reviewed by the Committee of the Ethics on Animal Experiment in Faculty of Medicine, Kyushu University.

Fourteen adult male Japanese rabbits, weighing 3.6-4.0 kg, and fifteen adult female Japanese rabbits weighing 3.2-3.6 kg, were intramuscularly injected once with 20 mg/kg of methylprednisolone acetate into the right gluteus medius muscle.

Two weeks after the corticosteroid injection, both femora and humeri were histopathologically examined for the presence of ON.

Blood samples were collected from all rabbits equally through the auricular arteries in a fasting state in the early morning immediately before the corticosteroid injection (0-weeks), and 1 and 2 weeks after the steroid injection.

RESULTS:
The incidence of ON in the male rabbits was 9/14 (64%), while that in the female rabbits was 4/15 (27%) (Figure 1). The incidence of ON in the female rabbits was significantly lower than that in the male rabbits (p < 0.05).

Histopathologically, ON lesions demonstrated an accumulation of bone marrow debris, where the bone trabeculae showed the empty lacunae (Figure 2). These findings were consistent for all ON positive rabbits regardless of the gender.

The levels of total cholesterol in the male rabbits were significantly lower (p < 0.05) than those in the female rabbits throughout the experimental period (Figure 3A). The high-density lipoprotein-cholesterol (HDL-cho) levels in the male rabbits remained lower levels than those in the female rabbits at all the time points tested (p < 0.05, Figure 3B).

Other plasma lipid levels (VLDL, triglycerides) did not show any differences between the male and female rabbits.

DISCUSSION AND CONCLUSION:
In a recent animal study about the gender gap, basal release of nitric oxide from aortic rings has been reported to be greater in the female rabbits than that in the male rabbits (4). Another study showed that female rabbits develop less-expensive diet-induced atherosclerosis than male rabbits (5). Therefore we speculate that the gender gap may affect the development of steroid-induced osteonecrosis, presumably by influencing the differences in the lipid metabolism and the basal expression of eNOS.

In summary, our current study showed that the incidence of ON in rabbits was different between the male and female rabbits.

REFERENCES: