Oral Presentation (PCS-16)

Determaining Surgical Method by Meniscectomy Induction on Garut sheep (*Ovis aries*) for early stage of Osteoarthritis

Handina Rakhmawati[1*], Adrian Situmeang[2], Nurhidayat[1], Andri Maruli Tua Lubis[2], Harry Murti[3], Arief Boediono [1]

[1] Department of Anatomy physiology and Pharmacology, Faculty of Veterinary Medicine, Bogor Agricultural University, Dramaga Campus, Bogor 16680, Indonesia.
[2]Department of Orthopaedy and Traumatology, Faculty of Medicine, University of Indonesia Dr. CiptoMangunkusumo General Hospital, Jakarta, Indonesia.
[3]Division of Stem Cell, Stem Cell and Cancer Institute, PT. Kalbe Farma, Tbk, Jl. Jend. Ahmad Yani No.2 Pulo Mas, Jakarta 13210, Indonesia.

*Author for correspondence (handina.rakhmawati@gmail.com)

Keywords: early, meniscectomy, osteoarthritis, sheep, stage, surgical.

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease that cause of pain and disability by various factors such as advanced age, obesity, trauma, and arthritis disease. These factors affect by degeneration of the cartilage surface, leading to loss of matrix include proteoglycan osteophyte formation, subcondral and synovial membrane affected. In the healthy joint, meniscus, articular cartilage, subchondral bone, and synovial membrane provide support to the joint. The meniscus is an important load bearing structure and has nutritive as well as lubricating properties in the knee joint as well (Little *et al*. 2010).

Animal models are research materials that can be used in studying potential pathogenesis and therapy in various diseases in humans. Sheep are commonly large animal model of OA because of the availability, ease of handling, and have a similarities with humans in size and structure of joint. In the development of science, sheep can be used as an animal model in studying the pathogenesis of diseases in human orthopedics studies such as joints, ligaments, and bones. Garut sheep is an Indonesian germplasm indigenous that has the structure, density, and size of joint anatomy that are similar in human joints rather than other small animals. This is the basis of the utilization of Garut sheep as an animal model in human orthopaedic. (Little *et al*. 2010; Gregory *et al.* 2012).

The aim of this study was to identify and analyze the determining surgical method by meniscectomy induction on Garut sheep with 8 weeks post meniscectomy observation for early stage of OA.

MATERIALS AND METHODS

This study used 4 Garut sheep (*Ovis aries*) aged 4 years old, female, 35-40 kg, healthy, and has acclimatized for 2 weeks. Sheep are divided into 2 groups: the group one is unilateral meniscectomy of total lateral meniscus (n=2) and the group two is unilateral meniscectomy of total lateral meniscus and partial medial meniscus (n=2). The procedures used for this study was approved by the animal ethics committee of Bogor Agricultural University (No: 8-2016 RSHP FKH IPB).

The induction technique is accompanied by an exercise as far as ± 150 m daily for 3 weeks, followed by addition of 4 weeks observation. The parameters measured were radiological assessment of OA in femorotibial joint using Kellgren Lawrence grading score refers to Schiphof *et al*. (2008). A macroscopic evaluation was performed on the articular surface from lateral condyle referred to Osteoarthritis Research Society International (OARSI) recommendations (Little *et al*., 2010). The data of radiography and macroscopic were analyzed descriptively and quantitatively on 8 weeks post meniscectomy observation.

RESULT AND DISCUSSION

The use of sheep as animal model of OA is supported by anatomical similarity of the femorotibial joint in humans, making easier to induce and observe the pathological effects of OA. Sheep presented the disadvantage of not prone to spontaneous arthritis, so induction is needed first to create the condition of OA (Gregory et al. 2012). The method of induction of femorotibial joint OA with meniscectomy in this study was chosen because it can cause femorotibial contact stress, so that the cartilage of the lateral condyle of the

tibia gains a greater proportion of the load received by the body.

Radiological result at 8 weeks post meniscectomy in both groups showed narrowing of the joint of the femorotibial lateral (Figure 1). In the medial condyle of group two there is a moderate level joint space compared to group one. In addition, severe osteophytes were found on the edges of the lateral condyle, increased density and severe sclerosis in the subchondral bone in both groups (Figure 1). The presence of osteophytes in the lateral condyle is an effort to improve joint degeneration and is a physiological response to overloaded joints by increasing of joint edges (Schiphof *et al*. 2008).

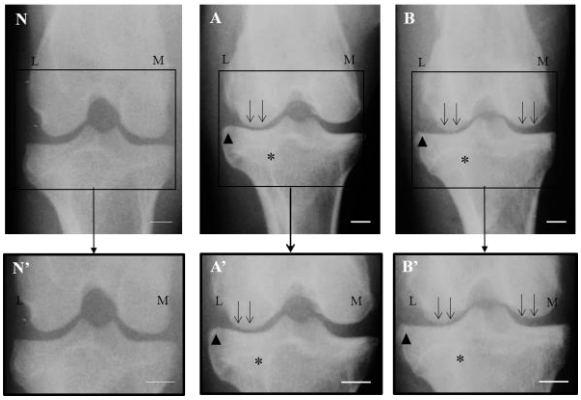

Figure 1 Radiography of the femorotibial joint on right hind limb on 8 weeks post meniscectomy.
The (A, A') group one and (B, B') second group showed an osteophytes formation on the condyle edges (head arrow), joint space narrowing (arrow), and subcondral sclerosis (star) on the lateral condyle compared to (N, N") negative control. On the medial condyle (B, B') group two showed joint space narrowing (arrow) compared to (A, A') group one. Bar: 1 cm.

At 8 weeks, all sheep in group one present of yellow fibrillation in the articular surface that focused on the cranial to the caudal of the lateral condyle. Furthermore, were seen in group two, the location of fibrillation was only found in the lateral cranial condyle and in the cranial part of the medial condyle (Figure 2). In the macroscopic terms found the existence of fibrillation of development of worse OA by yellow to brown color, damage to the articular surface causes loss of matrix to subchondral bone. In addition to fibrillation, severe osteophytic formation was found in group one compared to group two. This occurs because of the increased contact stress of the lateral condyle of the tibia which results in the joints directly forming osteophytes on the edge of the lateral condyle as joint efforts of load distribution (Beveridge *et al*. 2011).

Based on radiological and macroscopic results on 8 weeks post meniscectomy, it was identified that unilateral induction of meniscus total lateral meniscectomy results in progresive damage focused on the lateral condyle compared to unilateral induction of meniscus lateral meniscectomy and partial medial meniscus.

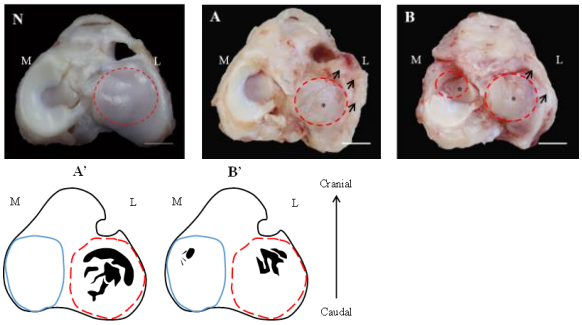

Figure 2 Macroscopic analysis of articular surface from a lateral condyle of tibia in the right hind limb on 8 weeks post meniscectomy.
The (A, A') group one showed a yellow fibrillation (star) on the cranial to caudal of faciesarticularis from lateralis condyle and osteophyte (arrow) on the edge of the condyle. The (B. B") group two showed a yellow fibrillation (star) on the cranial lateralis condyle and osteophyte (arrow) on the edge of the condyle also showed erosion on the cranial of medial condyle compared (N, N') negative control. Note: (L) lateral and (M) medial. Bar: 1 cm.

According to Beveridge *et al*. (2011) that lateral meniscectomy can provide more progressive damage to joint cartilage compared to medial meniscectomy. According to the macroscopic results it is known that in both groups the final stage of OA event is present. This causes the animal model with 8 weeks post meniscectomy procedure is impossible to use as a model in OA therapy.

CONCLUSION

The results showed that induction with unilateral meniscectomy of total lateral meniscus with followed by exercise is possible to produce progresive damage focused on the articular lateral condyle and it becomes the determining surgical method of meniscectomy induction on Garut sheep (*Ovis aries*). The progressive damage in 8 weeks post meniscectomy observation is impossible to used, because it is on the final stage of OA. Therefore, for the further study must decrease time of post meniscectomy observation for showed the early stage of OA.

ACKNOWLEDGMENTS

The authors would like to thank dr. Boenjamin Setiawan, Ph.D for support research funding and Indra Bachtiar, Ph.D for advice in the proposal research preparation. A word of appreciation is expressed to Drh. Mawar Subangkit, M.Si, Drh. Elpita Tarigan for advice on this study, Drh. Tri Isyani Tungga Dewi from Animal Hospital of Faculty of Veterinary Medicine IPB and UPHL FKH IPB staff for the contributions of this research.

REFERENCES

[1] Beveridge JE, Shrive NG, Frank CB. 2011. Meniscectomy causes significant in vivo kinematic changes and mechanically induced focal chondral lesions in a sheep model. *Journal of Orthopaedic Research*. 29: 1397-1405.

[2] Gregory MH, Capito N, Kuroki K, Stoker AM, Cook JL, Sherman SL. 2012. A review of translational animal models for knee osteoartritis. *Arthritis*. 14 (12): 1-14.

[3] Little CB, MM Smith, MA Cake, RA Read, MJ Murphy, FP Barry. 2010. The OARSI Histopathology initiative-recommendations for histological assesments of osteoarthritis in sheep and goats. *Osteoarthritis and Cartilage*. 18: S80-S92.

[4] Schiphof D, Boers M, Bierma-Zeinstra SMA. 2008. Differences in descriptions of Kellgren and lawrence grades of knee osteoarthritis. *Annals of the Rheumatic Diseases.* 67:1034-1036.