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ORIGINAL ARTICLE

Optimising femoral-head osteochondral allograft transplantation in a preclinical model

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Summary *Background/Objective:* Osteochondral autografting and allografting of the femoral head have been described as treatments for avascular necrosis without segmental collapse, fracture, osteochondritis dissecans, and tumours. One long-term study reported that 80% of nonsteroid-treated patients had successful outcomes. Most data are compiled from small case reports or series. Although these results are encouraging, to the authors' knowledge, there is no basic scientific evidence regarding optimal graft source or technique reported in the peer-reviewed literature. The objective of this study was to create a translational canine model to compare femoral-head osteochondral autografts and allografts with respect to safety and efficacy.

Methods: With Institutional Animal Care and Use Committee approval, skeletally mature hound-mix dogs ($n = 6$) weighing >20 kg underwent aseptic surgical implantation of osteochondral grafts using a craniolateral approach to the hip, without dislocation. Three graft options were evaluated: small auto ($n = 3$), 6-mm-diameter autograft from the trochlear ridge of the ipsilateral knee; small allo ($n = 3$), 6-mm-diameter fresh (21-day storage) allograft from a size-matched canine femoral head; or large allo ($n = 3$), 14-mm-diameter fresh (21-day storage) allograft from a size-matched canine femoral head. Small grafts were implanted into the same femoral head of three dogs, and large grafts were implanted alone in the other three dogs. The dogs were allowed unrestricted activity in their runs, and were walked on a leash for 15 minutes 5 times/wk. The outcome measures included functional, radiographic, and arthroscopic assessments at 8 weeks, and functional, chondrocyte viability, and histologic assessments at 6 months after surgery. The pre- and postoperative data were compared for

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statistically significant ($p < 0.05$) differences. Based on data from the canine study, four human patients underwent fresh (<28-day storage) osteochondral allografting using large (>30-mm diameter) size-matched femoral-head grafts. The radiographic, quality of life, and functional assessments were captured postoperatively.

Results: All grafts had >80% chondrocyte viability at the time of implantation. All grafts showed radiographic evidence for integration into host bone. Small auto and small allo showed significant ($p < 0.05$) loss in range of motion, chondrocyte viability, and articular-cartilage integrity 8 weeks after implantation, whereas large allo maintained viability and structural integrity throughout the study period. The large-allo dogs maintained full hip range of motion and hindlimb function. A similar type of large allograft (>30 mm) was performed in the four human patients. Due to the defect size, three out of the four human patients required two large allografts at the time of implantation. At the time of this manuscript's acceptance, patient follow-up ranged from 4 months to 18 months. All human patients were full weight-bearing without an assistive device, and showed no evidence of graft failure or progressive arthrosis.

Conclusion: These data provide initial translational and clinical evidence for large osteochondral allografts as a potential option for functional resurfacing of full-thickness cartilage defects of the femoral head.

Introduction

Femoral-head defects resulting from trauma or disease processes pose significant management challenges, especially when they are large and/or occur in young patients where total joint arthroplasty is not ideal and other treatment options are limited. Osteochondral allograft (OCA) transplantation has been extensively used and studied for the treatment of large articular defects of the human knee with good to excellent long-term results reported [1—3]. OCA transplantation for the treatment of femoral-head defects in human patients has also been described, but only in the form of case reports or small case series [4—7]. The largest case series in the peer-reviewed literature is from 1985, and reported that OCA transplantation of the femoral head for the treatment of post-traumatic femoral-head defects, avascular necrosis without segmental collapse, osteochondritis dissecans, and tumours to be associated with an 80% long-term success rate in patients who did not have a steroid-related aetiology [7]. However, numerous questions remain regarding optimal graft size and source and implantation technique.

The chondrocyte viability in OCAs at the time of transplantation has been reported to be critically important to the clinical success of the surgery [1,8—11]. As such, different storage methods and implantation techniques have been investigated to try to maintain chondrocyte viability in implanted OCAs above minimal acceptable levels (typically considered to be 70% viable cells) [8,12—16]. To address these factors, the Missouri Osteochondral Allograft Preservation System, a serum-free tissue-preservation method (Cook JL, Hung CT, Lima E, Stoker A, inventors. Tissue preservation system. United States patent application #US 2012/0177615 A1. 2012 Jul 12; claims pending 2015 Jun.) that has prolonged the time for maintenance of acceptable levels of chondrocyte viability in osteochondral tissues to more than twice as long the current standard-of-care based on *in vitro* and *in vivo* assessments [8,14,15], and an instrumentation system for creating tapered grafts that can be implanted such that chondrocyte viability is better preserved compared to standard cylindrical grafts [17], were developed.

Dogs were selected for this large animal model based on their extensive use in cartilage-repair research, the similar anatomy, pathologic conditions, treatment options in dogs' hips in comparison to humans, and successful use of OCAs in dogs [8,18—20]. In addition, dogs are one of the large animal species designated by the Food and Drug Administration and American Society for Testing and Materials guidelines as acceptable for preclinical studies designed to test the safety and efficacy of cartilage-repair techniques for clinical use [21,22].

The purpose of this study was to use a preclinical canine model to determine the effects of graft size and source and implantation technique on outcomes for femoral-head osteochondral transplantation with respect to safety and efficacy for clinical application in human patients.

Materials and methods

All procedures were approved by the University of Missouri's Animal Care and Use Committee. Six skeletally mature (age range 2—4 years) hound-mix (mean body weight = 28.2 kg; range 26.7—31.4 kg) purpose-bred research dogs (Marshall Farms BioResources, North Rose, NY, USA; US Department of Agriculture #21-A-008) were used. Complete orthopaedic examination and radiographs of both hips and both stifles (knees) were performed to ensure no musculoskeletal pathology was evident in any dog prior to enrolment in the study.