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Effect of Donor Age on Bone Mineral Density in Irradiated Bone–Patellar Tendon–Bone Allografts of the Anterior Cruciate Ligament

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Background: Allograft tissue remains a valuable alternative for anterior cruciate ligament reconstruction. No study to date has correlated the effect of donor age to bone mineral density (BMD) in a large series of irradiated bone–patellar tendon–bone (BPTB) allograft tissue.

Hypothesis/Purpose: The authors attempted to correlate donor age with BMD in a large group of BPTB allograft specimens treated with low-dose gamma irradiation (1.0-1.3 Mrad) collected over a 4-year period. They hypothesized there would be no effect of donor age on the BMD of irradiated BPTB allografts.

Study Design: Descriptive laboratory study.

Methods: A total of 110 BPTB allograft specimens from 44 male and 66 female donors with a mean age of 46 years (range, 21-58 years) were analyzed. Bone mineral density data were obtained from both the patellar and tibial bone plugs of the BPTB complex. Statistical analyses were conducted using linear regression for correlations and 2-tailed Student *t* tests for comparisons between groups.

Results: The mean BMD of the patellar bone plug (0.471 g/cm^2) was significantly greater than the mean BMD of the tibial bone plug (0.328 g/cm^2) ($P < .001$). No correlation was identified between donor age and BMD for either the patella or tibial bone plugs (R^2 = .014 and .011, respectively). Both patellar and tibial BMD was significantly greater for the male grafts than the female ones.

Conclusion: No correlation was found between donor age and BMD for irradiated BPTB allograft tissue. The patellar bone plugs were noted to have a greater BMD than the tibial bone plugs. Allograft tissue from male donors had higher BMD values than that harvested from female donors.

Keywords: allograft; anterior cruciate ligament reconstruction; bone mineral density

Each year in the United States an estimated 250 000 anterior cruciate ligament (ACL) injuries occur, most commonly associated with participation in athletic activities.[27] For active patients, surgical reconstruction of the ACL after rupture is recommended. This intervention will help restore knee stability and kinematics, leading to an improvement in function and a return to play. Although reconstruction with bone–patellar tendon–bone (BPTB) autograft has remained the gold standard, there has been an increasing trend toward the use of allograft tissue for selected cases. Recent estimates have reported that 20% to 30% of ACL reconstructions currently being performed utilize allograft tissue.[7,8,13]

With increased availability and improved screening and procurement protocols, the use of allogeneic musculoskeletal tissue in orthopaedic surgery has more than doubled in the past decade.[26] While concerns over the potential for disease transmission, cost, and issues with graft incorporation exist, advantages of allograft use for ACL reconstruction include a lack of donor-site morbidity, decreased surgical time, decreased postoperative pain, improved cosmesis, and faster rehabilitation.[5,7,19,20,27] A number of clinical studies, including a recent systematic review, have demonstrated no significant difference in subjective or objective outcomes between autograft and allograft ACL reconstructions.[†]

Based on the idea that harvested tissue from older donors would be inadequate for use in a young, athletic patient population, the early experience with allograft ACL reconstruction was limited to donors younger than 40 years of age.

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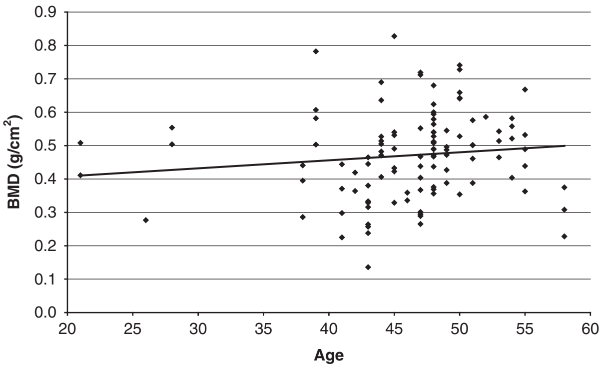

Figure 1. Correlation of age and bone mineral density for patellar bone plugs. No significant correlation was noted (R^2 = .014).

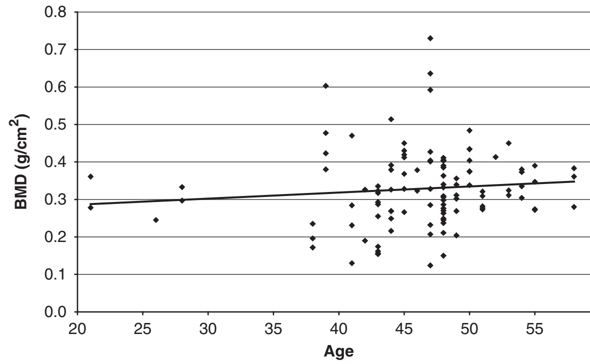

Figure 2. Correlation of age and bone mineral density for tibial bone plugs. No significant correlation was noted (R^2 = .011).

However, with increasing demand and biomechanical studies indicating no correlation between donor age and graft tensile strength, the spectrum of donor age has expanded, creating the potential for a large disparity in age between the tissue donor and recipient.[19] An additional concern regarding allograft use in ACL reconstruction is the effect sterilization techniques have on the graft's biomechanical properties. In an effort to eliminate microorganisms without substantially weakening the allograft's collagen ultrastructure, most tissue banks employ a low-dose (1.0-2.0 Mrad) gamma irradiation sterilization protocol.[7]

Although the effects of donor age and the method of graft sterilization on the quality and biomechanical properties of allograft tissues used in ACL reconstruction have been evaluated separately within the orthopaedic surgery literature,[3,4,9,11-13,25,28] no study to date has correlated the effect of donor age with bone mineral density (BMD) in a large series of irradiated BPTB allografts. Therefore, in this controlled laboratory study, we attempted to correlate donor age with BMD in a large group of BPTB allograft specimens treated with low-dose gamma irradiation (1.0-1.3 Mrad) collected over a 4-year period. We hypothesized that there would be no effect of donor age on the BMD of irradiated BPTB allografts.

MATERIALS AND METHODS

A total of 110 BPTB allograft specimens from 44 male and 66 female donors with a mean age of 46 years (range, 21-58 years) were evaluated. These specimens were obtained from the same allograft processing company (AlloSource, Centennial, Colorado) and underwent a consistent low-dose gamma irradiation protocol (1.0-1.3 Mrad). Once the middle third of the grafts were used for clinical purposes, the medial and lateral aspects were used for the purposes of our study. Only grafts with patellar tendon widths $\geq$10 mm and stable bony attachment sites were included in the study.

A Lunar Prodigy dual-energy x-ray absorptiometry (DXA) scanner device (GE Healthcare, Madison, Wisconsin) was used to obtain bone density images for each specimen. These images were then processed using Encore 2007 software to obtain BMD data from both the patellar and tibial bone plugs of the BPTB complex. Regions of interest were identified for the BMD analysis. These regions were defined as the bony attachment sites for the tendons. The average region of interest areas were 2.9 cm^2 (standard deviation [SD] 1.1 cm^2) and 3.5 cm^2 (SD 1.2 cm^2) for the patellar and tibial regions, respectively.

Statistical analyses were conducted using linear regression for correlations and 2-tailed Student *t* tests for comparisons between groups. A power analysis, with a power of 0.8, was used to qualify the statistical validity of our sample sizes. More specifically, with a power of 0.8, a sample size of N = 20 in each group was needed to detect a difference in BMD of 0.1 g/cm^2 between the tibial and patellar bone plugs.

RESULTS

The mean BMD of the patellar bone plug (0.471 g/cm^2) was significantly greater than the mean BMD of the tibial bone plug (0.328 g/cm^2) ($P < .001$). No correlation was identified between donor age and BMD for either the patellar or tibial bone plug (R^2 = .014 and .011, respectively) (Figures 1 and 2).

A gender difference was noted in the allograft specimens, with the mean BMD of the male patellar bone plug (0.506 g/cm^2) significantly greater than the mean BMD of the female patellar bone plug (0.447 g/cm^2) ($P < .03$). A similar significant difference was found between the mean BMD of the male tibial bone plug (0.372 g/cm^2) and the mean BMD of the female tibial bone plug (0.300 g/cm^2) ($P < .001$). No correlation was noted between donor age and BMD within each gender group.

DISCUSSION

In our evaluation of 110 irradiated BPTB allograft specimens harvested from a donor cohort with a mean age of 46 years, we found no significant correlation between donor age and BMD for either the patellar or tibial bone plug. Overall, the BMD of the patellar bone plugs was found to be significantly greater than that seen in the tibial bone plugs. As expected, grafts harvested from male donors had mean BMD values that were significantly greater than those harvested from female donors for both the patellar and tibial bone plugs.

Secondary to concerns that allograft tissue harvested from older donors would not be capable of withstanding the functional loads seen in a young, athletic patient population, most early allograft ACL reconstructions were performed with tissue obtained from donors younger than 40 years of age. This theory was supported by several studies in the orthopaedic surgery literature, which reported an inverse relationship between specimen age and the strength of the femur-ACL-tibia complex.[13,21,28] However, with clinical success leading to increasing demand and more recent biomechanical studies indicating no correlation between donor age and graft strength, the spectrum of donor age has expanded, creating the potential for a large disparity in age between the tissue donor and recipient.

In an evaluation of BPTB complexes harvested from donors 18 to 55 years of age, Flahiff et al[11] found no significant effect of donor age on force at failure, tensile stress, modulus of elasticity, and percent elongation. On the basis of their data, they concluded that patellar tendon allografts from donors up to age 55 years have similar mechanical properties. In a similar biomechanical study, Blevins et al[4] reported no correlation between donor age and the tensile strength of 82 fresh-frozen BPTB allografts harvested from 25 donors with an age range of 17 to 54 years. A wider spectrum of donor age was evaluated by Bianchi et al[3] in their testing of 142 BPTB allografts from donors aged 18 to 96 years. The authors found that while tissue from donors younger than 35 years of age had significantly higher maximum loads to failure and that from donors older than 66 years had significantly lower maximum loads to failure, BPTB allografts from donors in the 35- to 65-year age range had similar overall strength and stiffness. From the available data, it appears that with respect to the biomechanical properties of BPTB allografts, allogeneic tissue from donors up to the age of 65 years appears suitable for use in ACL reconstruction.

Although the risk is small, the potential for disease transmission is a significant and frequently cited disadvantage of using allograft tissue for ACL reconstruction. In addition to graft harvesting with aseptic technique, many tissue banks employ secondary sterilization protocols to provide an added level of safety for allograft use. Gamma irradiation is 1 such sterilization technique that has been shown to effectively reduce the risk of microorganism transmission. However, a dose-dependent deleterious effect on the biomechanical properties and function of allograft tissues with the use of gamma irradiation exists.[7,13] In a goat model, Gibbons et al[12] reported that while gamma irradiation with 2 Mrad did not affect the structural properties of BPTB grafts, doses higher than 3 Mrad reduced the tissue's maximum stress, maximum strain, and strain energy to maximum force by up to 40%. In a similar caprine model, Schwartz et al[25] found that at 6 months postoperatively, allografts irradiated with 4 Mrad showed lower stiffness and maximum force compared with nonirradiated controls. Curran et al[9] evaluated the effect of low-dose gamma irradiation (2 Mrad) on the biomechanical properties of BPTB allografts obtained from 13 donors with a mean age of 51 years. The authors found that the irradiated allografts had significantly larger elongation with cyclic loading (27% greater) and a significantly lower load to failure (1965 N versus 2457 N) compared with their nonirradiated, paired controls. On the basis of their data, the authors concluded that surgeons should consider the use of nonirradiated allografts as an alternative to irradiated grafts for ACL reconstruction.

Although the effects of donor age and the method of graft sterilization on the quality and biomechanical properties of allografts used in ACL reconstruction have been evaluated separately within the orthopaedic surgery literature, there is only 1 published study evaluating the combination of donor age and low-dose irradiation on allograft tissue. Greaves et al[13] tested 126 fresh-frozen anterior and posterior tibialis tendon allografts harvested from 37 donors with an age range of 20 to 65 years. The authors divided their specimens into 3 groups based on donor age, with their younger cohort comprising tissue obtained from donors younger than 45 years; middle, from donors 46 to 55 years; and older, for grafts harvested from donors 55 to 65 years of age. Biomechanical testing demonstrated that donor age up to 65 years did not significantly affect initial load to failure, stiffness, or displacement at failure. Interestingly, the authors noted an age-related decrease in failure stress among their nonirradiated specimens that was not observed in the grafts treated with 1.46 to 1.80 Mrad of gamma irradiation.

The current study is the first to attempt to correlate donor age with BMD in a large group of BPTB allograft specimens treated with low-dose gamma irradiation (1.0-1.3 Mrad). Our data support our initial hypothesis that there would be no effect of donor age on the BMD of irradiated BPTB allografts. Whether BPTB autograft or allograft is used for ACL reconstruction, graft fixation relies primarily on bone-to-bone healing within the femoral and tibial tunnels. Studies have demonstrated that subsequent to implantation, the bone plugs proceed through a healing process, starting with osteonecrosis and followed by a rapid incorporation of surrounding host bone into the graft.[14,22] Papageorgiou et al[22] showed in a goat model of ACL reconstruction that by 6 weeks postoperatively, the femoral bone plug had complete incorporation within the cancellous femoral tunnel. Other investigators have demonstrated that the bone plugs from allograft BPTB ACL reconstructions proceed through the same healing process as BPTB autografts, albeit at a slower rate secondary to a prolonged inflammatory response to the foreign tissue.[7,14,16,17] Harris et al[16] found in a goat model of ACL reconstruction that BPTB allografts required 18 weeks to achieve complete incorporation into the host tibial tunnel.

The fact that the BMD of the patellar bone plug was consistently greater than that of the allograft tibial bone plug supports the idea of implanting the patellar bone plug into the tibial tunnel, as this is the more common location of early fixation failure.[29] The gender difference noted in bone plug BMD is another interesting finding of our study. Where initial fixation strength may be of concern with the lower BMD of grafts obtained from female donors, it is possible that this difference allows for more rapid host incorporation into the cancellous femoral and tibial tunnels postimplantation. These issues will be addressed in future studies from our institution.

Limitations of the current study include its observational nature without a nonirradiated control group for comparison. Additionally, as the specimens were retained from excess tissue left over medial and lateral to the 10-mm BPTB graft used clinically, it is possible that there is some variability with respect to BMD in the tested tissue compared with the central 10 mm used for allograft ACL reconstruction. Finally, the current study did not incorporate any biomechanical, biochemical, or histologic evaluation of the tested specimens. We intend to continue our analysis of this large series of irradiated BPTB allografts, investigating each of these parameters.

SUMMARY

Clinical success after allograft ACL reconstruction has increased the demand for acceptable donors of allogeneic musculoskeletal tissue. Secondary to the increased demand, the spectrum of donor age has increased, creating the potential for a disparity between the age of the tissue donor and the recipient. The current study demonstrated 3 main findings: (1) there is no correlation between donor age and the BMD of BPTB allografts treated with low-dose gamma irradiation, within the age range we studied, (2) the patellar bone plug was found to have a higher mean BMD than the tibial bone plug, and (3) specimens from male donors were found to have higher BMD than those obtained from female donors.

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