Achilles Tendon Allograft Incorporated with Autologous Mesenchymal Stem Cells: an Animal Model
Zijun Zhang, MD, Michael Aynardi, MD, Talal Zahoor, MD, Lew Schon, MD

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Introduction/Purpose: Achilles tendinopathy and rupture are common and generally can heal without aggressive intervention. When a large defect of Achilles tendon is left by trauma or severe tendinopathy, however, it is a challenge to restore the function of Achilles tendon, because of the size of the tendon and the limitation in Achilles autograft. In contrast, allograft of Achilles tendon does not have restrain of supply. The biology, biomechanics and function of the transplanted Achilles allograft, however, are unknown. Particularly, the revitalization of Achilles allograft is a concern. Mesenchymal stem cells (MSCs) are known for their capability of multi-lineage differentiation and regenerative potentials.

Methods: Achilles allografts were harvested from donor rats (approved by Institutional Animal Care and Usage Committee) and kept at -80°C before transplantation. Subcutaneous adipose tissue was harvested from the would-be allograft recipient rats for isolation of MSCs. MSCs were cultured expanded and characterized. On the day of allograft transplantation, adipose tissue derived MSCs were collected and applied onto allografts (1x10^5 per allograft). Achilles tendon was resected from the left hind limb of the adipose tissue donor rats. Achilles allograft, with or without autologous MSCs, was implanted and sutured with calf muscles proximately and calcaneus distally. Animal gait was recorded in the week prior to Achilles allograft transplantation (week 0) and every week postoperatively, using a CatWalk system. The transplanted Achilles allografts, with or without MSC incorporation, as well as the normal Achilles tendon in the opposite limbs were harvested at 4 weeks for biomechanical testing and histology.

Results: The operated limbs altered gait significantly. By week 4, the recoveries of stand index (speed at which the paw loses contact with ground) and duty cycle (percentage of the stance phase in a step cycle) of the reconstructed limbs were not statistically different between the Achilles allograft group and Achilles allograft+MSCs group. Maximum load of failure among Achilles allograft group (27.2±11.5 N), Achilles allograft+MSCs group (27.6±6.4 N) and normal Achilles tendon group (19.9±9.9 N) was not significantly different. On histology, cellularity was generally higher in Achilles allograft+MSCs group than Achilles allograft group (average cellularity grade 2.7±0.5 vs 1.7±0.5). Type III collagen staining was more intense in the Achilles allograft+MSCs group than in the Achilles allograft group.

Conclusion: In this pilot study, the allograft incorporated with autologous MSCs demonstrated no significant differences from Achilles allograft alone in maximum failure load and gait analysis. Supplementation of MSCs increased the cellularity and led to more active matrix remodeling in the allograft but these biological improvements did not translate into rat gait and the strength of the implanted allograft. It may be necessary to follow up the animals for an extended period because the remodeling of Achilles allograft takes longer than 4 weeks. In addition, the small size of the rat Achilles allograft might falsely show an accelerated revitalization.