INTRODUCTION

Osteoarthritis (OA), characterized by articular cartilage loss and thickening of subchondral bone, affects 27 million Americans\(^1\) and is a frequent cause of pain and disability among older adults. The metabolic pathway Mammalian Target of Rapamycin (mTOR) is upregulated and AMP-Activated Protein Kinase (AMPK) is downregulated in OA and play a causal role in disease progression\(^2\). The drug rapamycin can inhibit mTOR and metformin can stimulate AMPK and have been shown to be protective against secondary (injury-induced) OA in young mice\(^3,4\). However, there are distinct differences in mouse and human joint anatomy that limit these findings to aging adults. Therefore there is a need to determine if rapamycin and/or metformin can delay the onset of primary (age-related) OA, the type of OA most seen in humans.

AIM

The goal of our research study was to test if rapamycin and metformin could delay the onset or slow the progression of primary, age-related OA in the Dunkin-Hartley guinea pig.

METHODS

Beginning at 5 months of age, guinea pigs were randomized to a control diet or diets enriched with rapamycin (14ppm), metformin (1000ppm), or rapamycin + metformin for 3 months. Upon sacrifice, right hind limbs were collected for analysis and measured for cortical bone thickness as the knee joint and histological samples were given OA scores using the OARSI guideline.