

The Association Between Plasma Leptin and Diaphyseal Femur Fracture Healing: A Pilot Study

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INTRODUCTION: Fracture healing is an intricate process that is dependent on stability and biology. Pre-clinical animal studies have shown that leptin, a hormone that aids in regulating energy storage may play a role in fracture healing. Furthermore, leptin is thought to be related to the heterotopic ossification and faster fracture healing observed in patients with traumatic brain injury. The goal of this pilot study is to determine the relationship between plasma leptin levels and radiographic fracture healing in the setting of adult patients with femur fractures. We hypothesize that patients with higher plasma leptin will exhibit faster fracture healing.

METHODS: This is a prospective, single-centre cohort study of patients with operatively treated diaphyseal femur fractures. This study was approved by an institutional research ethics board. Orthogonal radiographs were taken 2- and 6-weeks following intramedullary fixation of femur fractures. Plasma was acquired at 2- and 6-week post-operative follow-up and leptin levels were measured using a single-analyte immunoassay electrochemiluminescence measurement (MESO QuickPlex SQ 120MM, Meso Scale Diagnostics). Radiographs were classified as “healed”, “partially healed,” or “not healed” and were also scored according to the Radiographic Union Score for Tibial fractures (RUST) by two independent reviewers. We defined “healed” as bridging of 4 cortices, “partially healed” as bridging of ≥ 2 cortices, and “not healed” as bridging of ≤ 1 cortex. A paired t-test was used to compare leptin levels at the 2-week and 6-week follow-up, and a linear regression analysis was used to evaluate the relationship between leptin levels and RUST scores.

RESULTS: Eighteen patients with operatively treated diaphyseal femur fractures were included, with a mean age of 50.9 years (SD=22.87). 67% of patients were male and the mean body mass index (BMI) was 25.6 (SD=4.2). At the 2-week follow-up, none of the patients achieved partial or complete radiographic union or a RUST score greater than five. At the 6-week follow-up, 38% of patients had achieved partial union, with the remainder being unhealed. There was a significant increase in RUST score between 2-week (mean=4.10; SD=0.31) and 6-week follow-up (mean=6.44; SD=1.39; $p < 0.0001$). Mean leptin levels were greater at the 6-week follow-up (mean=9717; SD=14,009) compared to the 2-week follow-up (mean=7236; SD=9115); however, this was not statistically significant ($p=0.078$). There was no difference in leptin levels at the 6-week follow-up between patients who had achieved partial union versus those who were unhealed ($p=0.442$). The linear regression analysis did not demonstrate a significant correlation between leptin levels and RUST scores in this pilot cohort.

DISCUSSION: This pilot study did not demonstrate a significant association between plasma leptin levels and radiographic fracture healing; however, the short duration of follow up and the small sample size likely contributed to this finding. We did observe an insignificant trend of increasing plasma leptin levels that paralleled fracture healing, which warrants further investigation. Executing this study has facilitated us learning techniques for measuring biomarkers of interest and will facilitate future studies with larger sample sizes.

CLINICAL RELEVANCE: Although we did not demonstrate a significant relationship between serial leptin levels and fracture healing over time, future studies with a larger sample size and longer follow-up are still warranted and this study has informed longer planned follow-up.

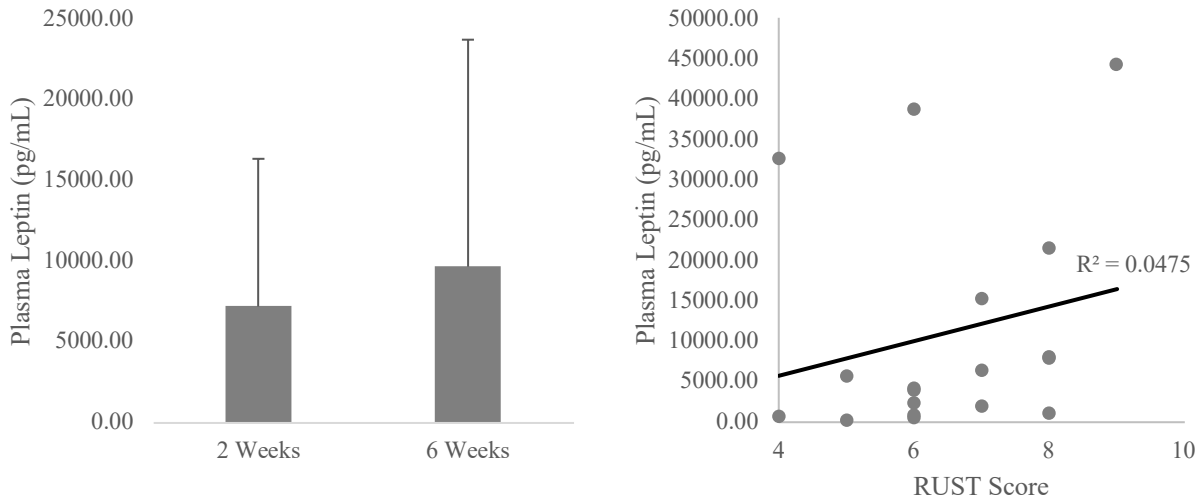


Figure 1: (a) Comparison of plasma leptin levels between 2 and 6 weeks ($p=0.079$). (b) Regression analysis comparing plasma leptin levels and RUST scores at six-week follow-up in patients with operatively treated femur fractures ($R^2 = 0.0475$).