

Towards an understanding of inter-patient variability in marrow progenitor populations.

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INTRODUCTION: Currently, cell therapy using bone marrow derived cells is being investigated in a diverse range of disciplines from nephrology and cardiology to orthopaedics. But the degree of inter-patient variability in the growth and differentiation of these cells means that the therapeutic potential of cell therapy for individual patients may become a lottery. In a study using concentrated bone marrow as an intervention for tibial non-unions, the degree of healing was correlated to the number of progenitor cells harvested from each patient's marrow¹. Although several studies have investigated the effect of patient age on progenitor number in bone marrow, there has been little investigation into other patient predictors. This study examined changes in osteogenic capacity of human bone marrow cells as a function of patient related parameters.

METHODS: Bone marrow samples were obtained with consent from patients undergoing elective primary hip replacement at Musgrave Park Hospital. 6mls bone marrow aspirate was collected from the femoral canal during surgery. Outcome measures were - total nucleated cell count, colony forming efficiency at d14 and alkaline phosphatase expression.

RESULTS: Body Mass Index (BMI) had a significant positive relationship with colony number and area in males alone (fig 1). Regression analysis demonstrated that changes in BMI accounted for 60% of the variation in mean colony area in the male study population. The number of colonies and the percentage of those colonies expressing alkaline phosphatase was also related to the type of statin, if any, prescribed to the patient (fig 2). Atorvastatin reduced the colony no. and the percentage that were AP+ve, while simvastatin increased both and pravastatin increased the percentage of AP+ve colonies but had no affect on the overall number. There was no significant effect of age, smoking, alcohol intake or NSAIDS.

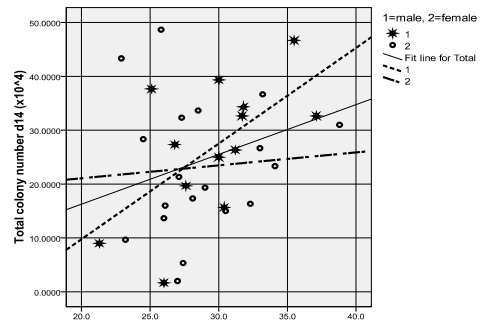


Fig. 1: Relationship of body mass index to CFU-F number. $r = 0.598$, $p = 0.031$ in males

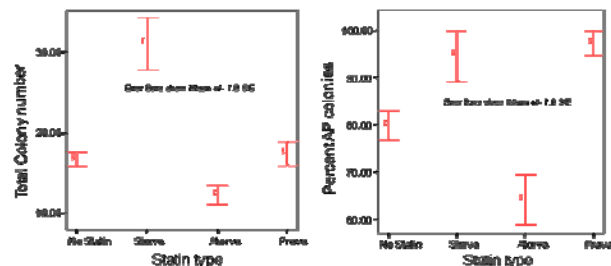


Fig.2 Effect of statins on CFU-F number (left) and percentage of colonies expressing alkaline phosphatase (right).

DISCUSSION & CONCLUSIONS: This study found that colony forming efficiency was related to statin-use and there was a gender-specific correlation with BMI. BMI was highly predictive of CFU-F area measurements for males, suggesting an increase in the stem cell population in bone marrow for this gender. Other studies have found similar gender differences^{1, 2}. The results of this study suggest a broader investigation into patient factors that affect the progenitor population of bone marrow is warranted. These results will have implications for the selection of patients suitable for autologous cell based therapies.

REFERENCES: ¹ Hernigou et al. JBJS-Am, 2005, 87-A:1430-1437. ² Muschler et al., J Orthop Res. 2001, 19:117-125.