RACP
Specialists. Together
EDUCATE ADVOCATE INNOVATE

RACP Foundation Research Awards

FINAL REPORT

Project Title		The relationship between osteoporosis and diabetes: exploring the bone-metabolism interface
Name		Dr Angela Sheu
Award Received		2017 Osteoporosis Australia RACP Research Entry Scholarship
Report Date		6 December 2018
Chief Investigator / Supervisor		Jacqueline Center
Administering Institution		Garvan Institute of Medical Research
Funding Period	Start Date:	1 December 2017
	Finish Date:	30 November 2018

PROJECT SUMMARY

Osteoporosis and diabetes are two common conditions that affect many Australians. Despite having relatively normal bone density, paradoxically diabetes patients may experience more fractures. However, the underlying mechanisms that account for this increased fracture risk is unknown. There have been few studies examining both bone and diabetes-related characteristics within the same person.

In a unique collaboration between bone and diabetes researchers, this study will explore the factors that link bone and metabolic health. The clinical goal is a greater understanding of how these processes interact, in order to identify which patients are at high risk for fractures, and to minimise the serious and costly complications of each of these diseases. Understanding mechanistic interactions between bone and glucose metabolism allows the potential for future therapies to be developed to specifically target bone health in these patients.

PROJECT AIMS / OBJECTIVES

1. To determine the fracture risk and post-fracture mortality in those with type 2 diabetes mellitus (T2DM).

Prospective analysis of the Dubbo Osteoporosis Epidemiology Study (DOES), the longest-running population-based osteoporosis study internationally.

2. To determine the relationship between bone turnover markers (BTM), BMD and body composition in insulin-sensitive lean (IS-L), insulin-sensitive overweight (IS-0), insulin resistant (IR) and T2DM subjects.

Cross-sectional analysis of a subset of the DOES where concurrent whole body scans and fasting plasma samples were analysed for bone and metabolic parameters.

SIGNIFICANCE AND OUTCOMES

Results 1:

At baseline, those with T2DM had higher BMI and BMD compared to those without. Women with T2DM had higher prevalent fractures, but overall, there was no increase in incident fracture risk in T2DM women or men, suggesting that bone fragility may affect a subset of T2DM patients. Within those with T2DM, BMD was lower in those with incident fracture, and remains an independent predictor for incident fracture in men.

Both T2DM and fracture alone were associated with increased mortality, and the combination of both was associated with the highest mortality. Post fracture mortality was increased in T2DM after all fracture types, especially in those with T2DM for >5 years duration.

Thus, early identification of T2DM patients at risk for fracture is imperative, given the severe mortality consequences. Future studies examining risk factors for fracture within T2DM and potential effects of diabetes treatments on bone health are underway.

Results 2:

In this study, subjects were divided into 4 groups based on obesity and insulin sensitivity. The insulin sensitive lean group had the lowest BMD. Fat mass, especially visceral fat, progressively increased from the insulin-sensitive lean (IS-L}, insulin-sensitive overweight (IS-0), insulin resistant (IR) and T2DM subjects. However, bone turnover markers were lowest only in T2DM.

When all body composition parameters were included in predictive modelling, visceral fat remained an independent negative predictor for all bone turnover markers. Insulin resistance was an independent predictor, and a stronger predictor than visceral fat, of only c-terminal telopeptide (a marker of bone resorption).

Thus, the higher BMD seen in T2DM is likely due to obesity. Visceral fat and insulin resistance, not total body fat, is associated with low bone turnover. Visceral fat may impair bone formation while insulin resistance may preferentially impair bone resorption. Therefore, in spite of higher BMD, bone quality may be specifically affected in T2DM due to reduced bone turnover and may contribute to fracture risk. Future studies examining specific metabolic effects on bone quality and fracture are required.

PUBLICATIONS / PRESENTATIONS

Study 1 presented at:

- Oral presentation at Australasian Diabetes Congress Scientific Meeting. Finalist for ADS President's Young Investigator Award.
- Oral presentation at St Vincent's Campus Research Week. Winner of Chair's Choice Award for Fast Forward Oral Presentation.
- Poster presentation at Australian/New Zealand Bone and Mineral Society Annual Scientific Meeting. Awarded ANZBMS Travel Grant.
- Poster presentation at International Osteoporosis Foundation Regional meeting.
- Poster presentation at St Vincent's Campus Research Symposium. Awarded Poster Award (runner up).

Study 2 presented at:

- Oral presentation at Australasian Diabetes Congress Scientific Meeting. Awarded ADS Travel Grant.
- Poster presentation at Australian/New Zealand Bone and Mineral Society Annual Scientific Meeting. Awarded ANZBMS Travel Grant.
- Poster presentation at International Osteoporosis Foundation Regional meeting.
- Oral presentation at St Vincent's Campus Research Symposium.