ORIGINAL ARTICLE

Can the use of triglyceride to glucose and triglyceride to high density lipoprotein ratios indicate metabolic syndrome in the spinal cord injured male?

Lynnette M Jones and Michael Legge

ABSTRACT

Aim: To determine whether the use of triglyceride to glucose (TyG:G) and triglyceride to high density lipoprotein (TyG:HDL) indices can indicate the onset of metabolic syndrome in spinal cord injured (SCI) males.

Methods: Fasting plasma from 20, age, BMI, and physical parameters matched controls and 20 spinal cord injured males was analysed for triglycerides, glucose and insulin. In addition to the analyte values HOMA-IR was calculated for both groups. **Results**: Significant differences were identified between spinal cord injured complete and incomplete injuries for the TyG:G (p=0.042) and TyG:HDL (p=0.037) when compared with matched controls. Complete spinal cord injured were significantly different for TyG:G (p=0.039) and TyG:HDL (p=0.001). Those with incomplete lesions were not significantly different from the matched controls TyG:G (p=0.871) and TyG:HDL (p=0353).

Conclusion: Those with complete spinal cord injuries demonstrated outcomes consistent with metabolic syndrome, whereas those with incomplete spinal cord injuries did not differ from the able-bodied controls. It is concluded that the level of de-innervation has a significant role in the onset of metabolic syndrome in the spinal cord injured.

Keywords: spinal cord injured (SCI)

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INTRODUCTION

Spinal cord injury (SCI) resulting in paralysis causes significant change in body composition below the lesion. The resultant loss of motor function leads to significant skeletal muscle wasting and a fat mass increase at both above and below the lesion (1,2). This significant change in body composition initiates major metabolic changes (3) that has been strongly associated with the development of cardiovascular disease (4). In addition, the development of glucose intolerance, hyperinsulinaemia, insulin resistance and dyslipidaemia are all contributing factors associated with the metabolic syndrome, which is frequently identified in SCI (3,5).

Our previous research using biochemical parameters and factor analysis in SCI identified a strong association with markers of metabolic syndrome (6). Subsequently, we identified using fatty acid analysis that desaturase and elongase activity was significantly different in SCI when compared with matched able-bodied controls (7), confirming a disruption of lipid metabolism. More recently we reported significantly elevated fasting plasma free fatty acids and glycerol in the SCI when compared to the matched controls (8).

In this current work we have investigated the use of the triglyceride: glucose index (TyG:G ratio) in SCI as a potential inexpensive surrogate marker for insulin resistance (9). In addition, we compare the TyG:G ratio to other potential biochemical markers of cardiovascular disease – the triglyceride to HDL ratio (TyG:HDL) and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (10,11,12).

MATERIAL AND METHODS

Participants and outcomes

The present study was undertaken using plasma from SCI and control individuals from our previous study (7). All data relating to biophysical information, spinal injury classification, dual energy x-ray absorptiometry (DEXA) results and physical activity have been previously published (6). In brief, there were 20 participants in each group (SCI and controls) who were male and matched for age, height, weight, BMI and physical activity. There were no significant differences between all these parameters and between the groups (7). Ethical approval was obtained from both the Regional Health Funding Authority and the Canterbury Ethics Committee.

Biochemical data

Triglyceride (TyG) levels were determined enzymatically, while high density lipoproteins (HDL) were determined using the direct assay method. Both analytes were determined using the Aeroset system (Abbott Laboratories Diagnostics Division, Illinois, USA). Glucose was analysed using the Ultimate 5 glucose kit (Roche Diagnostics Corporation, Indianapolis, USA). And insulin was analysed by radioimmunoassay using the Coat-A-Count assay (Diagnostic Products, Los Angeles, USA). Analysis was undertaken on a Cobas Mira Plus auto-analyser (Roche Diagnostics Corporation, Indianapolis, USA).

Statistical analysis

All data were normally distributed and variances for the groups were the same. The TyG index was log transformed. The tests were two-sided independent t-tests. While able bodied and spinal injured men were similar in height, weight and age, they were independent groups. The t-tests were used primarily as an exploratory procedure to ascertain statistical differences between the controls and the SCI with complete and incomplete spinal injury, and a one-way ANOVA was performed to compare the TyG:G ratio, HOMA-IR and TyG:HDL ratio between the groups. All statistical analyses were undertaken using Statistical Packages for Social Sciences (SPSSv25), (IBM Statistics, Armonk, USA).

RESULTS

The initial exploratory between group t-test revealed a significant difference in the TyG:G ratio between the SCI men with complete lesions and those with incomplete lesions, p=0.042 and for the TyG:HDL ratio p=0.037. Significant differences were also found for comparisons between men with complete lesions and their matched controls, TyG:G p=0.039 and TG:HDL, p=0.001. Results for men with incomplete lesions and controls were not significant for either TyG:G or the TyG:HDL indices, p=0.871 and p=0.325 respectively.

The one-way ANOVA revealed that there was no statistical difference between the groups for TyG:G and HOMA-IR ($F(2,7)=2.858$, p=0.07 and $F(2,37)=0.087$, p=0.92 respectively. However, the TG:HDL ratio was significant ($F(2,37)=7.163$, p=0.02. Post hoc tests for multiple comparisons found significant differences between SCI with complete lesions and incomplete spinal lesions (p=0.037, 95% CI=0.056,2.10) and between complete spinal lesions and controls (p=0.02, 95% CI=4.496, 2.319). There was no statistically significant difference for TyG:HDL between the SCI with incomplete injuries and controls (p=0.614)

DISCUSSION

The purpose of this study was to investigate whether routine biochemical indices could identify at risk SCI for diabetes and cardiovascular disease, namely the use of triglycerides, glucose and HDL. The TyG:G ratio has been previously shown to correlate with insulin resistance (13,14) and with cardiovascular disease (9) in able bodied populations. Similarly, the TyG:HDL ratio has been found to be a suitable marker to identify insulin resistance in the able-bodied population (11.12). Given that SCI are at higher risk for developing both type 2 diabetes and cardiovascular disease (4,15) it was considered that there was a potential to use these indices to identify SCI at risk using routine relatively inexpensive biochemistry tests. More sophisticated non-invasive testing such as ultrasound for local arterial stiffness can provide diagnostic information, however this and related techniques required access to ultrasound and an experienced operator.

The results from this limited small study have identified an interesting relationship between complete and incomplete SCI. Briefly, complete SCI is considered to be where nerve damage is sufficiently severe that nerve impulses cannot be transmitted, whereas incomplete SCI does not have total nerve damage. However, the relationship between nerve damage and function in the incomplete SCI may depend on the level of the spinal cord injury (16). The result from the current investigation clearly indicates an outcome which could be related to the level of nerve damage i.e. completes vs incomplete. There were significant differences for TyG:G and TyG:HDL ratios between the complete and the incomplete SCI. Additionally, TG:HDL ratios from the complete SCI were also significantly different from the matched controls, whereas the incomplete SCI showed no significant difference with controls. We consider that this may well reflect the retention of some muscle innervation in the incomplete SCI thereby providing sufficient metabolic signalling to retain some muscle metabolic activity. Whether this would ultimately be sufficient to prevent metabolic syndrome is outside of the scope of this current work. However, we have previously identified significant changes in individual free fatty acids which are associated with insulin resistance and metabolic syndrome in all SCI (7). Additionally, we have demonstrated significant elevation in total free fatty acids and glycerol in both SCI groups compared to controls (7). This would indicate an overall shift from normal skeletal muscle metabolism below the injury to fat deposition and lipolysis. Although the BMI between the controls and SCI groups has been shown to be not significant, there was a 47% increase in the fat mass and a 16% decrease in lean tissue mass below the lesion (15). This was consistent with subsequent investigations identifying that while the BMI remained within normal limits, the SCI group demonstrated metabolic variables consistent with metabolic syndrome (6). This indicates an overall shift from normal skeletal muscle metabolism below the injury to fat deposition and lipolysis. Although we did not identify a significant difference in the TyG:G index, and no significant difference with HOMA-IR, we consider that the sample size may well be a limitation of this work rather than the overall predictive value of the ratio.

Skeletal muscle is a major body organ involved in both glucose and fatty acid metabolism (17) and a loss of this metabolic activity will ultimately give rise to disruption of the interaction of energy substrates i.e. the loss of the ability to metabolise glucose. Typically, with the loss of the ability to metabolise glucose, insulin resistance will develop and is a precursor to metabolic syndrome and diabetes (18,19). While we accept the limitations of this study, it is clear that the transformation from lean tissue mass to fat mass below the lesion following denervation disrupts the normal metabolic function of skeletal muscle. The possibility of using simple biomarker ratios may help in the early detection of insulin resistance and metabolic syndrome in SCI individuals.

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