ISRCTN18419418 Preliminary results

Three manuscripts reporting the first results of the RISKMet study have been submitted for peer review.

The first is a cross-sectional analysis of 101 adults with schizophrenia spectrum disorder or bipolar I/II disorder treated with second-generation antipsychotics (SGAs), recruited at the Brescia and Palermo sites. It found that metabolic risk is graded rather than all-or-nothing. Two-hour post-load glucose (75 g OGTT) rose as the number of metabolic syndrome (MetS) components increased, starting from a single component (+28.7 mg/dL vs. no components; $p = 0.027$). Among participants below the diagnostic threshold, each additional component was linked to an increase of about 26 mg/dL. This held after adjusting for fasting glucose, after excluding the glycaemic criterion, and when the analysis was limited to normoglycaemic, untreated participants. In contrast, fasting-based markers (HbA1c, fasting insulin, HOMA-IR, C-peptide) rose only from three components onward. These findings suggest that counting MetS components could help decide which SGA-treated patients need post-load glucose testing and closer cardiometabolic monitoring.

The second study compared cardiometabolic biomarker profiles in 101 adults and 49 paediatric patients treated with SGAs. In both age groups, MetS (in adults) or metabolic dysfunction (in children and adolescents) was associated with higher insulin, C-peptide, leptin and zonulin. Adults also showed changes in HbA1c and adiponectin. Most of these differences became weaker after adjusting for BMI, which points to adiposity as a major shared driver. The study also developed RISKMet-Bio, a composite biomarker score of metabolic dysregulation. It discriminated well between patients with and without MetS or metabolic dysfunction (AUC 0.83; 0.79–0.80 after internal validation). It also flagged some participants who did not meet the categorical criteria but had high scores. RISKMet-Bio is a candidate tool for the early identification of cardiometabolic risk and needs prospective validation.

The third study measured physical activity objectively, using a wrist accelerometer worn for 7 days, in 96 patients and 51 age- and sex-matched healthy controls. Patients repeated the measurement after 3 months. Physical activity was lower in patients who met more MetS criteria, and differences persisted at follow-up between patients meeting no criteria and those meeting 3–5. Patients with no MetS criteria were still less active than controls. This suggests that psychiatric illness and metabolic comorbidity may add up as separate burdens, and supports promoting physical activity early, before MetS develops.