standardization and harmonization of insulin assays limit the clinical use of insulin-based surrogate indexes of insulin resistance. The lipoprotein insulin resistance (LPIR) score, a metabolomic marker, reflects the lipoprotein abnormalities observed in insulin-resistant states. The reliability of the LPIR score to predict IR in South Asians is currently unknown. In this study, we aimed to evaluate the predictive accuracy of LPIR compared to other fasting-based surrogate indices in SA.

In a cross-sectional study of 59 non-diabetic SA subjects (age 36 ± 8 years, BMI 26.5 ± 5.2 kg/m^2), we used calibration model analysis to assess the ability of the LPIR score and other simple surrogate indices [homeostasis model assessment (HOMA-IR), quantitative insulin sensitivity check index (QUICKI) and Adipose tissue insulin sensitivity (Adipo-SI)] to predict insulin sensitivity derived from the reference frequently sampled intravenous glucose tolerance test (FSIVGTT) and Minimal Model analysis (SiMM). LPIR scores were calculated using six lipoprotein particle concentrations and sizes measured by nuclear magnetic resonance (NMR) spectroscopy. Further, quantitative predictive accuracy and index comparisons were determined by root mean squared error (RMSE) of prediction and leave-one-out cross-validation-type RMSE of prediction (CVPE). Receiver operating characteristic (ROC) curve analysis was performed to determine how well LPIR distinguished insulin resistant individuals, categorized as an SiMM < 3.

As determined by calibration model analysis, Adipo-SI, HOMA-IR, and QUICKI showed moderate correlations with for SiMM (Adipo-SI: r = 0.66; HOMA-IR: r = 0.60; QUICKI: r = 0.57, p = <0.0001). No significant differences were noted among CVPE or RMSE from any of the routinely used surrogate indices when compared with LPIR. The ROC area under the curve was 0.76 (95% CI 0.64–0.87) suggesting that LPIR performed well in identifying insulin resistant subjects. The optimal cut-off in IR individuals was LPIR >46 (sensitivity: 75.9 %, specificity: 70.0%). We conclude that NMR-derived LPIR may be an appropriate index to assess insulin resistance in South Asians.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Can Histology Predict the Presence of KCNJ5 Somatic Mutation in Aldosterone-Producing Adenomas?

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Aldosterone-producing adenoma (APA) is well known to harbor marked intratumoral heterogeneity in terms of morphology and CYP11B2 (aldosterone synthase) localization. In histology, APA is generally characterized by two distinct cell subtypes, namely “clear cells” and “compact cells”. Clear tumor cells harbor abundant lipid droplets in their cytoplasms and compact tumor cells generally featuring small round shape have abundant intracytoplasmic organelles including mitochondria.

Relatively close correlation between these histological characteristics (morphology and CYP11B2 immunohistochemistry) and genotypes of aldosterone-driver gene somatic mutation has been reported. Among them, *KCNJ5*-mutated APAs have been reported to harbor clear cell predominant features, while APAs with other rare somatic mutations including *ATP1A1*, *ATP2B3* and *CACNA1D* harbor heterogenous or relatively compact cell predominant morphometry. However, these previous evaluation were based on eyeball analysis with relatively low reproducibility. Therefore, we developed the more quantitative methods using digital image software in order to analyze the widespread area, which can reflect intratumoral heterogeneity, with high reproducibility to analyze the further detailed correlation between histopathological characteristics and genotype in APA. We explored the utility of immunohistochemistry including CYP11B2 and KCNJ5. We further attempted to propose histopathological scoring system to predict the presence of *KCNJ5* somatic mutation in APAs.

Results of our present study revealed that KCNJ5 was predominantly immunolocalized in zona glomerulosa among adrenal cortex (vs. ZF, P=0.0002, vs. ZR, P=0.0002), furthermore, predominantly in APCCs than in non-APCCs (P=0.0019). Among the tumors, KCNJ5 immunoreactivity was significantly higher in *KCNJ5*-wild type APAs than in mutated ones (P=0.0037). *KCNJ5*-mutated APAs had significantly lower nuclear / cytoplasm ratio and abundant clear cell components than those with wild type, harboring large tumor size. In conclusion, we firstly proposed a novel histopathological predicting scoring system for the presence of *KCNJ5* somatic mutation, including the following histopathological findings; N/C ratio, clear cell (%), tumor size, CYP11B2 immunoreactivity and KCNJ5 immunoreactivity. It is true that no single histological factors above could precisely predict the presence of *KCNJ5* somatic mutation but this newly developed combined histopathological predicting scoring system could provide relatively high accuracy to predict *KCNJ5* somatic mutation in APAs (AUC=96%, sensitivity:100%, specificity:90%, 4 points or more). However, further prospective validation by large number of cases is required for clarification.

Adrenal

ADRENAL CASE REPORTS I

Primary Adrenal Lymphoma Presenting with Symptomatic Hypercalcaemia

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