Dr. Bekir Tanriover

Abstract:
The first living kidney transplantation performed in 1954; however, data on long-term safety of living donation is sparse and limited to single center reports due to lack of donor registry. One third of living kidney donors are obese and without health insurance coverage at the time of nephrectomy. Knowledge on metabolic state and insulin sensitivity in living kidney donors is also scarce. Reduction in glomerular filtration rate (GFR) following nephrectomy surgery (25-30 ml/min in average) in overweight and obese donors may lead to increased plasma insulin levels and insulin resistance, which is a strong predictor of metabolic syndrome, diabetes and cardiovascular disease. In this proposal, we plan to utilize sequential dynamic metabolic testing, the mixed meal tolerance test (MMTT), to assess beta cell function and insulin sensitivity before and after donor nephrectomy. The MMTT is a practical physiological test to stimulate first phase insulin surge (beta cell function/reserve) in response to a standard oral mixed meal formula (the Boost). Insulin sensitivity is computed from serial timed (total 2 hours) blood collections for c-peptide area under curve (AUC) calculation following the Boost administration based on Cobelli minimal model. Our objectives are: (1) to compare sequential measures of metabolic state including fasting (glucose, insulin, and c-peptide), dynamic (the MMTT), HbA1C (hemoglobin A1C, integrated measure of metabolic control), and metabolic phenotype (metabolic syndrome criteria and family history of diabetes) in the assessment of beta cell function and insulin sensitivity before and after donor nephrectomy; (2) to evaluate the predictors of insulin resistance and metabolic syndrome. We will be conducting a prospective cohort study (for 3 months period). The subjects will be their own controls (baseline results compared to post-nephrectomy values). We will recruit living kidney donors from the Renal Transplantation Program at the Columbia University Medical Center (CUMC) and enroll total 60 patients from different BMI, race and gender groups. The MMTT and iothalamate plasma clearance (kidney function assessment) will be performed pre donor nephrectomy and post-op at 3 months. While the research will be led by an early-stage investigator (Dr. B Tanriover, a nephrologist who has successfully competed for an NIH funded K-Award), the research team has the necessary experience. We will be collaborating with Dr. Lauren Golden (our expert scientist on diabetes and the MMTT) in the Naomi Berrie Diabetes Center at the Columbia University, New York and Dr. Claudio Cobelli at the Department of Electronics and Informatics, University of Padova, Italy (the prominent investigator who developed a software for beta cell function and c-peptide AUC calculations).

Beta cell function and insulin sensitivity assessment before and after donor nephrectomy procedure will improve our understanding changes in metabolic state in response to decrease in GFR and will establish the normal acceptable ranges for different gender, BMI and race groups. It may help to define adverse metabolic consequences resulting from living kidney donation and enhance our informed decision making process, especially in potential donors who have body mass index (BMI) greater than 25 kg/m^2 and lack health insurance at the time of evaluation.