THE LANCET Diabetes & Endocrinology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Diabetes Surgery Study Appendix

Diabetes Surgery Study Eligibility Requirements

Inclusion criteria

1. Age 30 to 67 years at eligibility visit.

2. Diagnosed with T2DM at least 6 months prior to enrollment, under the active care of a doctor for at least the six months prior to enrollment, HbA1c ≥ 8.0 % and HbA1c ≤ 14.0%.

3. Body Mass Index (BMI) ≥ 30.0 kg/m^2 and ≤ 39.9 kg/m^2 at eligibility visit.

4. Willingness to accept random assignment to either treatment group.

5. Expect to live or work within approximately one hour's traveling time from the study clinic for the duration of the two-year trial.

6. Willingness to comply with the follow-up protocol and successful completion of the run-in (described below).

7. Written informed consent.

Exclusion criteria

1. Cardiovascular event (myocardial infarction, acute coronary syndrome, coronary artery angioplasty or bypass, stroke) in the past six months.

2. Current evidence of congestive heart failure, angina pectoris, or symptomatic peripheral vascular disease.

3. Cardiac stress test indicating that surgery or IMM would not be safe.

4. Pulmonary embolus or thrombophlebitis in the past six months.

5. Cancer of any kind (except basal cell skin cancer or cancer in situ) unless documented to be disease-free for five years.

6. Significant anemia (hemoglobin 1.0 g/dL or more below normal range) or history of coagulopathy.

7. Serum creatinine greater than 1.5 mg/dl.

8. Serum total bilirubin greater than the upper limit of normal in the absence of Gilbert's

syndrome, or alkaline phosphatase or ALT greater than twice the upper limit of normal.

9. History of stomach surgery, bile duct surgery, pancreatic surgery, splenectomy, or colon resection.

10. Gastric or duodenal ulcer in the past six months.

11. History of intra-abdominal sepsis (except for uncomplicated appendicitis or diverticulitis more than six months prior to enrollment).

12. Previous organ transplantation.

13. Self-reported HIV-positive status, active tuberculosis, active malaria, chronic hepatitis B or C, cirrhosis, or inflammatory bowel disease.

14. Currently pregnant or nursing, or planning to become pregnant in the next two years.

15. History of alcohol or drug dependency (excluding caffeine and nicotine) in the past five years.

16. Active psychosocial or psychiatric problem that is likely to interferer with adherence to the protocol.

17. Depression: A score of 17 or higher may be used to disqualify a participant. At the clinic's discretion, participants with a CES-D score of 17 or higher may be referred to a licensed psychologist or psychiatrist for a formal psychological evaluation. In that case, the formal psychological evaluation and recommendation will be important factors in the determination of eligibility by the eligibility committee. If this evaluation clearly indicates potential risks associated with depression, the participant may not be randomized. If the evaluation is equivocal or unclear, the eligibility committee must take this into account in rendering their decision

18. Current participation in a conflicting research protocol.

19. Presence of any chronic or debilitating disease that would make adherence to the protocol difficult.

20. 12-lead EKG indicating that surgery would not be safe.

21. Serum c-peptide less than 1.0 ng/ml 90 minutes post-challenge.

22. Exclusions may also be made at the discretion of the attending physician or the eligibility committee.

Diabetes Surgery Study Measurements

Blood pressure and pulse

Blood pressure and pulse were measured three times, one minute apart. The participant was to have been seated for at least five minutes before the first reading. The participant's feet were to have been flat on the floor. There were to be no disturbances in the area. There was to be no clothing between the cuff and the upper arm. The same arm was used at every visit unless there is a problem with that arm. If the blood pressure was being measured using a standard sphygmomanometer, then the following additional rules applied (source: Pickering, J. Hall, L. Appel, B.Falkner, J. Graves, M. Hill, D. Jones, T, Kurtz, S. Sheps, E. Roccella, "Recommendations for blood pressure measurement in humans and experimental animals, Part 1: Blood pressure measurements in humans" Circulation, 2005; 111: 697- 716.):

- Select appropriate cuff size. The "ideal" cuff should have a bladder length that is 80% and a width that is at least 40% of arm circumference (a length: width ratio of 2:1). The same size cuff should be used throughout the study unless the arm circumference changes to another size.
- For arm circumference of 27-34 cm, use "adult" size: 16x30cm.
- For arm circumference of 35-44 cm, use "large adult": 16x36cm.
- Palpate the brachial artery in the antecubital fossa and place the midline of the bladder of the cuff (commonly marked on the cuff by the manufacturer) so that it is over the arterial pulsation over the participant's bare upper arm. The participant's sleeve should not be rolled up such that it has a tourniquet effect above the blood pressure cuff. The lower end of the cuff should be 2-3 cm above the antecubital fossa to allow room for placement of the stethoscope.
- Place stethoscope bell below the antecubital space over the brachial artery.
- Inflatecuffpressuretoatleast30mmHgabovethepointatwhichtheradialpulse disappears.
- Slowly release pressure at a rate equal to2-3mmHg/sec noting first Korotkoff sound (systolic blood pressure).
- Continue releasing pressure, noting where sound disappears (5th phase diastolic blood pressure).
- Record values to the nearest 2mmHg where the first and last sounds are observed.
- Each patient uses the same type of device throughout the trial.

Weight

The participants in Minneapolis were weighed on electronic scales, which were fully serviced and calibrated annually. Before being weighted, participants removed shoes, heavy outer clothing (sweaters and coats), and any heavy objects in their pockets or on their person, including loose change and keychains. Participants were asked to empty their bladder before weighing. Weights were measured to the nearest 0.1 of a kg. The scales were checked for proper resets to "0" before and after each participant weight.

Height

To measure height, participant were asked to stand with their back against the stadiometer scale, heels together, heels touching or very close to the stadiometer, with buttocks in contact with the stadiometer. If possible, the upper back (scapula) was also be in contact with the

stadiometer. Participant were to be standing erect (not slouching) and looking straight ahead. The headboard would be lowered firmly onto the head, without a lot of hair between the headboard and scalp, and kept parallel to the floor. Height was measured to the nearest cm just before the participant exhaled.

Laboratory Analyses

The lab values to be assessed at each visit were described in form DSS-lab and in the "Scheduled medical visits and labs" section of the Manual of Procedures. Eligibility visit 1 and the randomization visit were the only visits where lab tests were done but fasting was not required. Laboratory testing was done in each institutions fully accredited clinical laboratory.

All lab values were retained in the participant's chart, and used by the attending physician in providing medical care. Complete form DSS-lab was completed and sent to the Data Coordinating Center (DCC).

At Eligibility Visit 2 and months 3, 6, 12 and 24, Columbia University in New York, NY and Mayo Clinic in Rochester, MN shipped samples to the University of Minnesota for analysis of HbA1c. This was to assure consistency in lab technique at key visits. International biological specimen shipping rules precluded shipping calibration samples from Taiwan.

Additional lab tests could be requested by the attending physician, in response to patient symptoms. The unscheduled tests were for providing patient care, and were not reported to the DCC except as part of an adverse event report (if necessary). The clinic coordinator worked directly with Covidien regarding financial reimbursement.

LDL was estimated using the other lipid fractions. In some cases, however (for instance, if triglycerides are over 400) this was not possible. In this case, the lab was asked to measure LDL directly. Most labs will keep some reserve sample for a few days, to accommodate requests such as this. LDL was one of the study's primary endpoints, and it was important to get a lab result.

Sometimes, a patient was delayed during the screening process. If any of the following tests were more than 2 months old, they were repeated shortly before randomization: HbA1c, fasting glucose, and fasting lipids. The new values would be submitted as error corrections to the original values. If the new HbA1c was not within the allowable range, then the patient was excluded.