ORIGINAL ARTICLE

Effects of Metabolic Surgery on Diabetic Kidney Disease and Diabetic Retinopathy Among Obese Asian Indians with Type 2 Diabetes

Sundaramoorthy Chandru[1,2*], Rajendra Pradeepa[1], Veerasundar Palanichamy Poonkodi[1], Thyparambil Aravindakshan Pramodkumar[1], Madhanagopal Sathish Kumar[1], Mangesh Tiwaskar[3], Kuppan Gokulakrishnan[4], Ranjit Mohan Anjana[1], Viswanathan Mohan[1], Ramachandran Rajalakshmi[1]

Abstract

Introduction: To evaluate the effect of metabolic surgery on microvascular changes associated with diabetic retinopathy (DR) and diabetic kidney disease (DKD) in obese Asian Indians with type 2 diabetes (T2DM), one year after metabolic surgery.

Methods: This is a follow up study in 21 obese Asian Indians with T2DM who underwent metabolic surgery (MS). Diabetic microvascular complications were assessed before and one-year post surgery using urinary albumin, protein creatinine ratio, eGFR, retinal colour photography and Optical coherence tomography (OCT).

Results: Microalbuminuria (54±26 vs 28±16 vs 21±6 µg/mg, p<0.001) and protein creatinine ratio (0.4±0.1 vs 0.2±0.03 vs 0.1±0.02, p<0.05) reduced significantly 6 months and one year after Metabolic surgery (MS) respectively compared to baseline values. Estimated Glomerular Filtration (eGFR) rate and creatinine was stable and there was no decline in renal function one year after MS. DR was present in eight individuals at baseline. After metabolic surgery, 12 % of individuals achieved regression of DR and 12% individuals showed a one step regression from severe to moderate non proliferative DR while 12 % individuals progressed from moderate to severe non proliferative DR. Of the 14 (53.8%) individuals who had micro or macroalbuminuria at baseline, 43% individuals reverted back to normoalbuminuria. There was also a reduction in the usage of anti- hypertensive medications after MS.

Conclusion: In obese Asian Indians with T2DM, metabolic surgery reduced urinary microalbuminuria and protein creatinine ratios at one-year post MS. MS resulted in stable D. Retionpathy status one-year post surgery. MS may help to improve in stabilisation of the microvascular complications in obese patients with T2DM.

Introduction

Diabetes related microvascular changes in the retina, glomerulus and peripheral nerve are caused by chronic hyperglycaemia. Hyperglycaemia affects the vascular endothelium leading to endothelial dysfunction, an impairment in vasodilatation, fibrinolysis, and anti-aggregation[1] and also impaired nitric oxide derived vasodilatation.[2,3] The two major randomized clinical trials, the Diabetes Control and Complication Trial (DCCT)[4] and the United Kingdom Prospective Diabetes Study (UKPDS)[5] have clearly shown the role of intensive diabetes control in substantial decrease in the microvascular complications in individuals with type 1 diabetes (T1DM) and T2DM respectively which are the leading causes of morbidity.[6]

In both type 1 diabetes (T1DM) and T2DM, diabetic retinopathy (DR) is a very specific complication which include damage to the nerve and capillaries (neurovascular) and its prevalence is strongly associated with the degree of glycemic control and duration of diabetes. A meta-analysis which included 35 studies from different countries around the world between 1980 to 2008 reported prevalence of any DR to be 35.4% while that of prevalence of proliferative diabetic retinopathy (PDR) was 7.5%.[7] The Discover study[8] done in T2DM with mean duration of 4.1 year from 38 countries showed the prevalence of micro and macrovascular complications to be 18.8% and 12.7% respectively. Asian Indians are known to be more prone to develop T2DM a decade earlier compared to European individuals.[9] The Chennai Urban Rural Epidemiology Study (CURES) has reported the overall prevalence of diabetic retinopathy to be 17.6%, neuropathy (25.7%), overt nephropathy (2.2%) and microalbuminuria (26.9%) in a representative population in Chennai, South India.[10] Both DKD and DR have common risk factors like long duration of diabetes, poor glycemic control and hypertension. Obesity is an important risk factor associated with DR and DKD.

Bariatric surgery done for weight loss has been shown to be effective in terms of diabetes remission and improvement in diabetes status with several changes in metabolic parameters which led to the use of term ‘metabolic surgery’ (MS) instead of ‘bariatric surgery’.[11] The American Diabetes Association (ADA) and the International Diabetes

[1]Madras Diabetes Research Foundation and Dr Mohan’s Diabetes Specialities Centre, Chennai, Tamil Nadu; [2]Ph.D. Scholar, University of Madras, Chennai, Tamil Nadu; [3]Shilpa Medical Research Centre, Mumbai, Maharashtra; [4]National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka; [*]Corresponding Author
Received: 25.02.2021; Accepted: 15.09.2021

Federation (IDF) have recommended consideration of bariatric surgery for control of T2DM in obese T2DM individuals who were not able to attain desired glycemic control with optimal lifestyle measures or medications.[12] Observational studies and randomized, controlled trials have shown that MS significantly improves glycemic control, reduces cardiovascular risk factors and mortality and favourably reduces both micro and macrovascular complications of T2DM and enhances quality of life.[13,14] O` Brien[15] conducted a retrospective matched cohort study to compare the incident microvascular complication between patient who underwent bariatric surgery and nonsurgical measures and reported that bariatric surgery was associated with significantly lower incident microvascular complications compared to patients treated with non-surgical treatment methods. Coleman et al[16] have shown the evidence for the 'legacy effects' of surgery as there was 29% lower incidence of microvascular disease in patients who achieved diabetic remission than non-remitters, and also a microvascular risk reduction by 19% in those patients who experienced relapse after diabetes remission compared with the patients who never had a diabetes remission.

There are virtually no studies in Asian Indians regarding the impact of metabolic surgery on the microvascular complications. This study was carried out at a tertiary diabetic centre to evaluate the effects of MS on diabetic microvascular complications outcomes, specifically in the eye and kidney among obese Asian Indians with T2DM one year post surgery.

Methods

This is a short term observational study of obese Asian Indian (South India) individuals with T2DM who underwent MS from November 2013 to March 2019. 36 individuals underwent bariatric surgery at a tertiary care diabetes centre in Chennai, south India of whom 30 individuals consented to take part in the study and come for regular follow up for one year. Preoperative evaluation was done in all the patients with a multi-disciplinary bariatric surgical team which includes bariatric surgeon, physician, anaesthetist, psychologist and dietician, a detailed history of diabetes, hypertension, lipid disorder, thyroid disorder, diabetes complications, including duration co-morbidities and diabetes medications, lipid lowering medication, antihypertensive medications were collected. Of the 30 patients who underwent metabolic surgery, 26 individuals had T2DM and 4 patients had prediabetes. A subset of 21 T2DM patients who had data on DR were included in the present study. Informed consent was obtained from all participants and the study was approved by the Ethics Committee of the Madras Diabetes Research Foundation (MDRF) (MDRF/NCT/07-02/2014).

Clinical and Biochemical Assessments

Measurements of weight, height, and waist circumference were obtained using standardized techniques. Blood pressure was measured using a sphygmomanometer and was recorded in the sitting position in the right arm. Two readings were taken 5 minutes apart and the mean of the two was recorded as the blood pressure. Body mass index (BMI) was calculated using the following formula: weight (kg)/ height (m^2). A fasting venous blood sample and urine sample was collected after an overnight fast of at least 10 hours for the estimation of fasting glucose and a 2hour postprandial sample was obtained for postprandial plasma glucose estimation. Analysis of plasma glucose levels was done by hexokinase method, serum cholesterol by cholesterol oxidase peroxidise amidopyrine method, serum triglyceride by the glycerol phosphate oxidase- peroxidase amidopyrine method, high density lipoprotein(HDL) cholesterol by direct method- immunoinhibition, creatinine by Jaffe method, urea by GLDH Kinetic method, uric acid by Uricase UV, urine protein by pyrogallol red method, urine creatinine by Jaffe kinetic method, microalbumin by immunoturbidometric assay method using a Beckman Coulter AU680 autoanalyser (Beckman kits). Friedewald formula was used to calculate Low-density lipoprotein (LDL) cholesterol.[17] HbA1c was measured by high performance liquid chromatography using the Variant II Turbo (Bio-Rad, Hercules, CA, USA). The intra and inter-assay coefficients of variation for the biochemical assays ranged between 3.1 and 7.6%.

Retinal Examinations

A comprehensive ophthalmic evaluation was performed prior to the metabolic surgery in the Department of Ophthalmology at Dr Mohan's Diabetes Specialities Centre, Chennai, south India. The eye examination included (i) visual acuity testing by illuminated Snellen vision chart (ii) intra-ocular pressure (IOP) measurement by non-contact tonometry (NCT) and (iii) slit lamp examination of the anterior segment of the eye to assess the depth of anterior chamber, the angles and presence of media opacities like cataract was performed. The eyes were dilated for a detailed fundus examination by the retina specialist. Retinal colour photography of both eyes was taken using a digital retinal camera (Zeiss FF450 plus fundus camera, Carl Zeiss Meditec, Jena, Germany) as previously described.[18]

Optical coherence tomography (OCT) scans of both eyes were performed by the optometrist using Cirrus HD-OCT 500 (Carl Zeiss Meditec, Jena, Germany) for a sub sect of individuals (n=11). The central sub-foveal thickness (CFT), central macular thickness (CMT), macular volume (MV) and retinal nerve fibre layer (RNFL) thickness of both eyes were assessed. The individuals who underwent metabolic surgery underwent a follow up complete ophthalmic evaluation including OCT between 1 year after metabolic surgery.

Surgical techniques

Recently metabolic surgeries have been classified as restrictive procedures (RP), which dramatically reduce the volume of the stomach to limit gastric capacity and promote early satiety but do not alter intestinal anatomy and gastrointestinal diversionary procedures (DP), which bypass segments of the small bowel.[24] Biliopancreatic diversion (BPD) is a more extensive surgical procedure that includes a partial gastrectomy and bypasses a longer segment of the small bowel to induce significant malabsorption.[24] Single Anastomosis Duodenoileal Bypass with Sleeve (SADI S) and Sleeve Gastrectomy with Loop Gastroileal Bypass (SG LGIB) were Modified procedure of Biliopancreatic Diversion with Duodenal Switch (BPD DS). Of the 26 individuals operated, 11 underwent Restrictive procedure (SG) (11) and 15 underwent Gastrointestinal

Table 1: Clinical characteristics of study individuals before and after metabolic surgery

Variables	Preoperative n=21 (%)	Post-Operative 6 months (n=21) (%)	12 months (n=21) (%)
Age at bariatric surgery	47.1±11.2	NA	NA
Duration of Diabetes mellitus (years)	9.9 ±5.4	NA	NA
Male (%)	33	NA	NA
Weight (kg)	103±17	**82±16***	**78±15***
BMI (kg/m²)	41±6.8	**32±5.9***	**30±5.7***
Waist (cm)	125±14	**109±13***	**105±13***
Hip (cm)	127±15	**114±15***	**108±13***
Systolic blood pressure (mmHg)	128±16	**118±14***	**112±15***
Diastolic blood pressure (mmHg)	80±9	74±7**	73±8**
Fasting blood sugar (mg/dl)	172±56	**114±30***	**107±27***
Postprandial blood sugar (mg/dl)	228±85	**139±42***	**125±47***
HbA1c(%)	8.9±1.7	**6.4±0.8***	**6.3±0.8***
Total Cholesterol (mg/dl)	146±34	143±35	148±23
Triglyceride (mg/dl)	166±75	**115±35***	**118±54***
HDL-Cholesterol (mg/dl)	35±7	**42±9***	44±12*
LDL-Cholesterol (mg/dl)	77±29	86±30	85±20
Total Cholesterol/HDL-C ratio (mg/dl)	4.2±1	3.7±1	3.6±1.1
Urea (mg/dl)	23±6	23±5	24±6
Creatinine (mg/dl)	0.7±0.1	0.7±0.2	0.7±0.2
eGFR (mL/min/1.73m²)	107±15	105±19	105±18
Uric acid (mg/dl)	4.6±1.2	4.1±1.4	4.2±1.3

**<0.05 Compared to baseline, *<0.001 Compared to baseline.

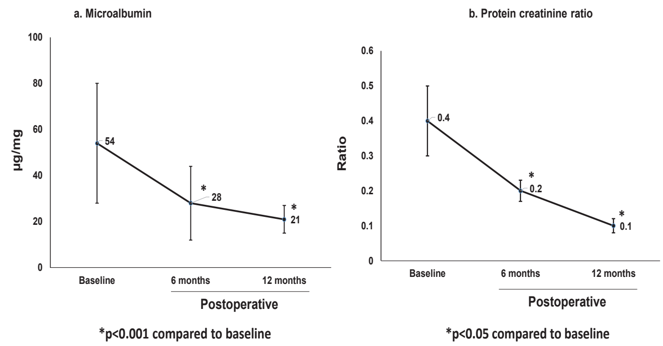

Fig. 1: Microalbuminuria and protein creatinine ratio before and after metabolic surgery

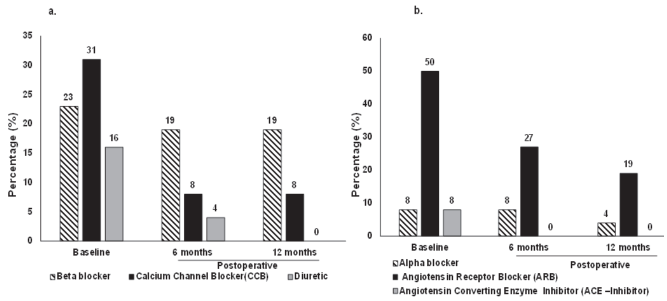

Fig. 2: Use of different classes of hypertensive medications before and after metabolic surgery

Table 2: Diabetic retinopathy grading in individuals with T2DM before and post metabolic surgery

Variables	Pre-operative retinopathy status (n=21)	Post-operative retinopathy status (n=21)
No diabetic retinopathy n (%)	13 (62.0)	14 (66.8)
Mild non-proliferative diabetic retinopathy n (%)	2 (9.5)	1 (4.7)
Moderate non-proliferative diabetic retinopathy n (%)	3 (14.3)	3 (14.3)
Severe non-proliferative diabetic retinopathy n (%)	2 (9.5)	2 (9.5)
Proliferative diabetic retinopathy n (%)	1 (4.7)	1(4.7)

diversionary procedures(DP) RYGB(12), SADI S(2) and (SG LGIB) (1). The type of surgery was decided by the bariatric surgeon based on the duration of diabetes, the desired weight loss and other comorbid conditions of the patient at baseline.

Definitions

Estimated Glomerular Filtration Rate (eGFR)

eGFR is estimated abbreviated MDRD equation :186 x $(Creatinine/88.4)^{-1.154}$ x $(age)^{-0.203}$ x (0.742 if female) x (1.210 if black).[19]

Table 3: Intra ocular pressure, Ocular Coherence Tomography (OCT) parameters in individuals with T2DM

Variables	Pre-operative	Post-operative	p value
Intraocular pressure (IOP) mm Hg (NCT) (n=21)	16 ± 2	17 ± 2.3	0.9643
Central sub-foveal thickness (CFT) microns (n=11)	234± 36	252± 26	0.0344
Central Macular Thickness (CMT) microns (n=11)	245±51	274± 12	0.4744
Macular Volume (n=11) cu.mm	9±2	10± 1	0.0074
Retinal Nerve Fiber Layer (RNFL) thickness microns (n=11)	94± 13	90 ± 8	<.0001

Diabetic retinopathy

The grading of DR was done by the retina specialist based on the International Clinical Diabetic Retinopathy (ICDR) severity scale.[20,21] The ICDR severity scales provides a classification of five stages of DR as follows: (1) no apparent retinopathy (No DR) (2) mild non-proliferative DR (NPDR) (3) moderate NPDR (4) severe NPDR (5) proliferative DR (PDR). The final diagnosis for each patient was determined from the level of DR of the worse eye using ICDR scale. Worsening (progression) was defined as a two-step change in the ETDRS Early Treatment of Diabetic Retinopathy Study or appearance or worsening of macular edema[21] DR regression was defined as the decrease of DR severity from grades 1-4 to grade 0 in atleast one eye and no DR worsening in the other eye.[22]

Microalbuminuria

Microalbuminuria was diagnosed if the albumin excretion was between 30 and 299 μg/mg of creatinine.[23] Macroalbuminuria was diagnosed if albumin excretion was ≥300 μg/mg of creatinine.

Statistical analysis

All statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA). Continuous data are expressed as mean ± standard deviation while categorical data are presented as proportions. To compare characteristics between the two groups, independent t tests was used to compare means. Shapiro-Wilks test was performed to find the normal distribution and Spearman correlation was used to compare OCT parameters. Fisher Exact test was used to compare the proportions of those with DR and STDR. For all statistical tests, p value of <0.05 was considered statistically significant.

Results

The study group consisted of 21 T2DM individuals (males n=7, females n=14) who underwent MS and had both retinal and renal studies done. **Table 1** presents the clinical characteristics and biochemical parameters of the study individuals. There is a significant reduction in weight (p<0.001), BMI (p<0.001), waist (p<0.001), Hip circumference (p<0.001), systolic blood pressure (p<0.001), diastolic blood pressure (<0.05), fasting plasma glucose (p<0.001), postprandial plasma glucose (p<0.001), HbA1c (p<0.001), serum triglyceride (p<0.001), and significant increase in serum HDL-Cholesterol (p<0.001) after MS.

Table 2 presents DR status before and after surgery. Eight individuals had DR at baseline (38%), of whom seven individuals had stable DR during post-metabolic surgery follow up while one individual achieved complete DR regression. In one individual DR progressed (one step progression) from moderate to severe NPDR and in one individual there was a decrease in grading of DR (one step regression) from severe to moderate NPDR.

Table 3 presents the OCT parameters, the central macular thickness (CMT), central sub-foveal thickness (CFT), the macular volume (MV) and retinal nerve fibre layer (RNFL) thickness which showed the changes after metabolic surgery. The pre-operative OCT parameters; mean CFT (234 ± 36 μ), mean CMT (246 ± 51μ) and the mean MV (9 ± 2cu.mm) increased post-operatively to 252 ± 26μ (p=0.0344), 274 ± 13 μ (p=0.4744) and 9.9 ±1 cu.mm (p=0.0074) respectively. There was also a significant decrease in the RNFL thickness from 94 ± 13μ to 90 ± 8μ (p<0.001) post metabolic surgery.

Figures 1 a. and b. shows urine microalbuminuria and protein creatinine ratio in individuals before and after MS. Microalbuminuria (54±26 vs 28±16 vs 21±6 μg/mg, p<0.001) and protein creatinine ratio (0.4±0.1 vs 0.2±0.03 vs 0.1±0.02, p<0.05) significantly reduced at 6 and 12 months post surgery compared to baseline.

Significant reduction in blood pressure was observed post metabolic surgery as shown in Table 1. There was a reduction in the use of different classes of antihypertensive medications after surgery. **Figures 2a and b** presents the use of anti-hypertensive medications before and after surgery. Compared to baseline, use of beta blockers (23% vs 19%vs 19%) and calcium channel blockers (31% vs 8% vs 8%) significantly reduced at 6 and12 months post-operatively. Diuretics were taken by 16% of participants at baseline which decreased to 4% at 6 months and were discontinued 12 months post-surgery. Angiotensin Receptor Blocker (ARB) use reduced from 50% at baseline to 27% and 19% at 6 and 12 months, respectively while the use of Angiotensin-Converting Enzyme Inhibitor (ACE-I) were discontinued post-surgery.

Discussion

This study has evaluated the impact of metabolic surgery on diabetic microvascular complications particularly renal and retinal changes as well as the usage of antihypertensive medications one year after MS in obese Asian Indians with T2DM. The important observations are as follows: Firstly, there is a significant reduction in the microalbuminuria levels 12 months' post surgery, estimated Glomerular Filtration (eGFR) rate was stable and there was no decline renal function one year post surgery. Secondly, diabetic retinopathy status was stable in most of the patients and DR regression was observed in 12 % individuals. Thirdly, the use of different classes of antihypertensive medications were reduced significantly one year post MS.

During End Stage Renal disease (ESRD) there is interstitial fibrosis in the kidney that leads to a decline in Glomerular Filtration Rate (GFR) results in Uremia.[26] In our study, there is no change in the creatinine and eGFR levels at 6 and 12 months post surgery compared to baseline and these data suggest that renal function is stable one year after metabolic surgery. Afshinnia et al[27] conducted a meta-analysis involving 13 trials with 522 patients and evaluated different methods of weight loss and showed that there is a 1.1 mg decrease in albumin excretion for every 1 kg decrease in body weight. Amor et al[28] conducted an observational study in 96 T2DM patients who underwent bariatric surgery. Before bariatric surgery, the albumin/creatinine ratio (ACR) was 85.7 ± 17 mg/g with an ACR > 30 mg/g (microalbuminuria) present in 45.7% of patients, which was reduced to 42.2 ± 14.8 mg/g and the number of patients with microalbuminuria decreased by 50% at 1 year after bariatric surgery. Brethauer et al[29] conducted a study in 217 T2DM patients and showed 53% improvement in diabetic nephropathy after bariatric surgery. In our study, there was regression of microalbuminuria to normalbumiuria in 23% of individuals one year post MS.

The systemic review done by Kim et al has shown that bariatric surgery has beneficial effects on DR progression.[30] Our study has also shown that the DR remained clinically stable one year after metabolic surgery. There was no new incidence of DR during the follow-up. One step progression of DR was observed only in 12% individuals one year post MS. This is the first study from India that has looked at the effect of metabolic surgery on DR substantiated further with OCT changes in people with T2DM. The stabilization of DR was achieved could attributed to sustained improvement of HbA1C levels, reduced blood pressure, improved kidney function and lower lipid levels due to multifactorial reduction in oxidative stress at the cellular level seemingly superior to refractory medical management in obese individuals with T2DM. Whether the sustained reduction in HbA1c observed after metabolic surgery translates to an improvement in the DR needs to be determined by long term follow-up of a large sample size of individuals.

The present study has assessed 1 year follow up and there is no new onset DR among 13 patients without DR. One patient showed regression another patient showed improvement and one patient showed progression of DR. Further long-term follow-up after metabolic surgery will help in assessment of the long-term effect of metabolic surgery on microvascular complications like DR. Hence we would like to conclude that metabolic surgery virtually intended just as a weight-loss procedure has been found to be effective not only for superior glycemic control in morbidly obese individuals with T2D but also with beneficial effects on microvascular changes after metabolic c surgery.[31-32]

Studies by Brynskov et al[33] showed that patients with T2DM who underwent bariatric surgery had clinically stable DR in the first postoperative year and had a clinically negligible increase in foveal thickening 6 months postoperatively. Studies by Dogan et al[33] showed an increase in the CMT, CFT and MV during the 6 month follow-up post bariatric surgery. The possible explanation given by Dogan et al[34] that the adipose tissues could compete with the retina for uptake of Lutein and Zeaxanthin (highest concentration found in the macula) thus resulting in decreased macular pigment optical density(MPOD) in obese individuals.

We have earlier reported that there is an improvement in multiple parameters like HbA1c, triglycerides, systolic and diastolic blood pressure (obesity and central obesity) one year after bariatric surgery.[35] Apart from the aforementioned improvements in multiple parameters there is also significant reduction in the waist circumference (decrease in central obesity) in our patients. Some studies have shown central obesity leading to increase in intra-abdominal pressure, the decrease in central obesity in our study patients could have reduced the intra-abdominal pressure leading to decrease in glomerular pressure with subsequent reduction in urinary albumin excretion. There was also significant reduction in the antihypertensive medication one-year post surgery which shows that metabolic surgery is effective in reducing blood pressure due to improvement in multiple metabolic parameters following after metabolic surgery.[36]

To our knowledge, this is the first study from India to assess the effect of metabolic surgery on both DKD and DR. However, being a single-center study with a relatively small sample size, further long-term follow-up studies with large sample size is required to investigate the relationship of the metabolic surgery to microvascular complications of diabetes.

In summary, metabolic surgery resulted in significant reduction in weight, hypertension and improvement in glycemic control, which stabilized the diabetic retinal complications and decreased urinary microalbuminuria and stabilized glomerular function one year post surgery.

References

1. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes* 2005; 54:1615-25.
2. Meza CA, La Favor JD, Kim DH, Hickner RC. Endothelial Dysfunction: Is There a Hyperglycemia-Induced Imbalance of NOX and NOS? *Int J Mol Sci* 2019; 20:3775.
3. Creager MA, Lüscher TF, Cosentino F, Beckman JA. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: Part I. *Circulation* 2003; 108:1527-32.
4. Nathan DM; DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. *Diabetes Care* 2014; 37:9-16.
5. American Diabetes Association. Implications of the United Kingdom Prospective Diabetes Study. *Diabetes Care* 2000; 23 Suppl 1:S27-31.
6. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. *Phys Ther* 2008; 88:1322-35.
7. Yau JWY, Rogers SL, Kawasaki R, et al. MetaAnalysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care* 2012; 35:556–564.
8. Kosiborod M, Gomes MB, Nicolucci A, Pocock S, Rathmann W, Shestakova MV, Watada H, Shimomura I, Chen H, Cid-Ruzafa J, Fenici P, Hammar N, Surmont F, Tang F, Khunti K; DISCOVER investigators. Vascular complications in patients with type 2 diabetes: prevalence and associated factors in 38 countries (the DISCOVER study program). *Cardiovasc Diabetol* 2018; 17:150.
9. Nag T, Ghosh A. Cardiovascular disease risk factors in Asian Indian population: A systematic review. *J Cardiovasc Dis Res* 2013; 4:222-8 .
10. Pradeepa R, Anjana RM, Unnikrishnan R, Ganesan A, Mohan V, Rema M. Risk factors for microvascular complications of diabetes among South Indian subjects with type 2 diabetes--the Chennai Urban Rural Epidemiology Study (CURES) Eye Study-5. *Diabetes Technol Ther* 2010; 12:755-761.
11. Singh AK, Singh R, Kota SK. Bariatric surgery and diabetes remission: Who would have thought it? *Indian J Endocrinol Metab* 2015; 19:563-76. doi: 10.4103/2230-8210.163113.
12. Dixon JB, Zimmet P, Alberti KG, Rubino F. International Diabetes Federation Taskforce on Epidemiology and Prevention. Bariatric surgery: an IDF statement for obese Type 2 diabetes. *Diabet Med* 2011; 28:628-42.
13. Tsilingiris D, Koliaki C, Kokkinos A. Remission of Type 2 Diabetes Mellitus after Bariatric Surgery: Fact or Fiction? *Int J Environ Res Public Health* 2019; 16:3171
14. Solomon SD, Chew E, Duh EJ, Sobrin L, Sun JK, VanderBeek BL, Wykoff CC, Gardner TW. Diabetic Retinopathy: A Position Statement by the American Diabetes Association. *Diabetes Care* 2017; 40:412-418.
15. O'Brien R, Johnson E, Haneuse S, et al. Microvascular Outcomes in Patients With Diabetes After Bariatric Surgery Versus Usual Care: A Matched Cohort Study. *Ann Intern Med* 2018; 169:300-310. doi:10.7326/M17-2383.
16. Coleman KJ, Haneuse S, Johnson E, Bogart A, Fisher D, O'Connor PJ, Sherwood NE, Sidney S, Theis MK, Anau J, Schroeder EB, O'Brien R, Arterburn D. Long-term Microvascular Disease Outcomes in Patients with Type 2 Diabetes After Bariatric Surgery: Evidence for the Legacy Effect of Surgery. *Diabetes Care* 2016; 39:1400-7.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of lowdensity lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18:499–502.
18. Rajalakshmi R, Shanthirani CS, Anandakumar A, Anjana RM, Murthy GVS, Gilbert C, Mohan V. Assessment of diabetic retinopathy in type 1 diabetes in a diabetes care center in South India-Feasibility and awareness improvement study. *Indian J Ophthalmol* 2020; 68 (Suppl 1):S92-S95.
19. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med* 2013; 158:825–30.
20. Wilkinson CP, Ferris FL 3rd, Klein RE, Lee PP, Agardh CD, Davis M, et al Global

Diabetic Retinopathy Project Group. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology* 2003; 110:1677-82.

21. Wu L, Fernandez-Loaiza P, Sauma J, Hernandez-Bogantes E, Masis M. Classification of diabetic retinopathy and diabetic macular edema. *World J Diabetes* 2013; 4:290-4.
22. Jin P, Peng J, Zou H, Wang W, Fu J, Shen B, Bai X, Xu X, Zhang X. The 5-year onset and regression of diabetic retinopathy in Chinese type 2 diabetes patients. *PLoS One* 2014; 9:e113359.
23. Mohan V, Meera R, Premalatha G, Deepa R, Miranda P, Rema M: Frequency of proteinuria in type 2 diabetes mellitus seen at a diabetes centre in southern India. *Postgrad Med J* 2000; 76:569–573.
24. Quercia I, Dutia R, Kotler DP, Belsley S, Laferrère B. Gastrointestinal changes after bariatric surgery. *Diabetes Metab* 2014; 40:87-94.
25. O'Brien P. Surgical Treatment of Obesity. [Updated 2016 Jan 19]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-.
26. Vaidya SR, Aeddula NR. Chronic Renal Failure. [Updated 2020 Jul 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.
27. Afshinnia F, Wilt TJ, Duval S, Esmaeili A, Ibrahim HN. Weight loss and proteinuria: systematic review of clinical trials and comparative cohorts. *Nephrol Dial Transplant Off Publ Eur Dial Transplant Assoc Eur Renal Assoc* 2010; 25:1173– 83.
28. Amor A, Jiménez A, Moizé V, Ibarzabal A, Flores L, Lacy AM, et al. Weight loss independently predicts urinary albumin excretion normalization in morbidly obese type 2 diabetic patients undergoing bariatric surgery. *Surg Endosc* 2013; 27:2046-51. DOI: http://dx.doi.org/10.1007/s00464- 012-2708-3.
29. Brethauer SA, Aminian A, Romero-Talamás H, Batayyah E, Mackey J, Kennedy L, et al. Can diabetes be surgically cured? Long--term metabolic effects of bariatric surgery in obese patients with type 2 diabetes mellitus. *Ann Surg* 2013; 258:628-37.
30. Kim YJ, Kim BH, Choi BM, Sun HJ, Lee SJ, Choi KS. Bariatric surgery is associated with less progression of diabetic retinopathy: A systematic review and meta-analysis. *Surg Obes Relat Dis* 2017; 13:352-360.
31. Heneghan HM, Cetin D, Navaneethan SD, Orzech N, Brethauer SA, Schauer PR. Effects of bariatric surgery on diabetic nephropathy after 5 years of follow-up. *Surg Obes Relat Dis* 2013; 9:7-14.
32. Gorman DM, le Roux CW, Docherty NG. The Effect of Bariatric Surgery on Diabetic Retinopathy: Good, Bad, or Both? *Diabetes Metab J* 2016; 40:354-364.
33. Brynskov T, Laugesen CS, Svenningsen AL, Floyd AK, Sørensen TL. Monitoring of Diabetic Retinopathy in relation to Bariatric Surgery: a Prospective Observational Study. *Obes Surg* 2016; 26:1279-1286.
34. Dogan B, Dogan U, Erol MK, Habibi M, Bulbuller N. Optical Coherence Tomography Parameters in Morbidly Obese Patients Who Underwent Laparoscopic Sleeve Gastrectomy. *J Ophthalmol* 2016; 2016:5302368. doi: 10.1155/2016/5302368. Epub 2016 Jun 16.
35. Chandru S, Pramodkumar TA, Pradeepa R, Muthukumar S, Balasubramanyam M, Bhuvaneshwari R, Anjana RM, Mohan V. Outcomes of metabolic surgery in obese patients with type 2 diabetes with respect to impact on beta cell function, insulin sensitivity and diabetes remission - A study from south India. *Diabetes Metab Syndr* 2020; 14:1829-1835.
36. Kovesdy CP, Furth SL, Zoccali C; World Kidney Day Steering Committee. Obesity and Kidney Disease: Hidden Consequences of the Epidemic. *Can J Kidney Health Dis* 2017; 4:2054358117698669.