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BARIATRIC SURGERY VERSUS INTENSIVE MEDICAL THERAPY FOR THE REVERSAL OF DIABETIC NEPHROPATHY IN OBESE PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Diabetic nephropathy (DN) is the most common cause of end-stage renal disease (ESRD) worldwide. Intensive medical therapy (IMT) has traditionally been the mainstay of management of DN, but recent evidence showed that bariatric surgery may have greater Reno protective effects beyond weight loss. This systematic review and meta-analysis aimed to compare the Reno protective efficacy of bariatric surgery versus IMT in obese individuals with type 2 diabetes and DN for achieving remission of proteinuria. **Methods: We** searched PubMed/ MEDLINE, Embase, Cochrane Library, Web of ScienceandClinicalTrials.gov from January 2020 to July 2025 for randomized controlled trials (RCTs) and prospective controlled cohort studies evaluating bariatric surgery versus medical therapy in obese subjects with type 2 diabetes and diabetic kidney disease. The primary outcome was the remission of albuminuria (defined as a urinary albumin to creatinine ratio [UACR] < 30 mg/g). Secondary outcomes included CKD progression, estimated glomerular filtration rate (eGFR) decline, progression to ESRD, and all-cause mortality. Data were pooled using random-effects meta-analyses, and the quality of evidence was assessed using the GRADE approach**. Results:** Fifteen reports were included in the qualitative synthesis; five independent datasets contributed to the quantitative synthesis of albuminuria remission. The total number of unique participants was not calculated by summing reports because some publications may represent overlapping cohorts. Pooled analysis of data from five studies revealed that patients who underwent bariatric surgery had more than a four-fold increased chance of achieving remission of albuminuria as compared with IMT (odds ratio [OR] 4.33; 95% confidence interval [CI] 3.26-5.75; $p < 0.001$; $I = 72.3\%$). Compared with IMT, bariatric surgery was associated with a 60% lower risk of CKD progression (hazard ratio [HR] 0.40; 95% CI 0.21-0.76; $p = 0.006$), a slower rate of annual decline in eGFR (mean difference [MD] -1.44 mL/min/1.73 m²; 95% CI -2.10 to -0.78), and a 69% reduction in the incidence of ESRD (HR 0.31; 95% CI 0.12-0.81). All-cause mortality was 32% lower in the bariatric surgery arm (HR 0.68; 95% CI 0.48-0.96). The GRADE evidence quality was low to moderate for most outcomes. **Conclusions:** Bariatric surgery shows an efficacy advantage over intensive medical therapy in improving albuminuria and attenuating CKD progression in patients with type 2 diabetes and DN, particularly those with early-stage diabetic kidney disease. The findings support the implementation of bariatric surgery within multidisciplinary management strategies for selected obese patients with type 2 diabetes.

KEYWORDS: *Bariatric surgery, metabolic surgery, diabetic nephropathy, chronic kidney disease, albuminuria remission, Roux-en-Y gastric bypass, sleeve gastrectomy.*

1. INTRODUCTION

Diabetic nephropathy (DN) is the most common Micro vascular complication of diabetes mellitus and the leading cause of end-stage renal disease (ESRD) worldwide (approx. 40-50% of all incident dialysis cases) (Alicic et al., 2017). The typical progression of DN involves states of hyper filtration, micro albuminuria (urinary albumin-to-creatinine ratio, UACR; 30–300 mg/g), macro albuminuria (UACR >300 mg/g), progressive loss of estimated glomerular filtration rate (eGFR), and ultimately ESRD requiring renal replacement therapy (Tuttle et al., 2014). Despite improvements in pharmacological agents, including use of drugs that inhibit the renin-angiotensin-aldosterone system (RAAS), and recent advancements in sodium-glucose cotransporter-2 inhibitors (SGLT2i), and glucagon-like peptide-1 receptor agonists (GLP-1RA), many patients still experience a considerable residual risk for progression of renal disease (Perkovic et al., 2019; Gerstein et al., 2021). Obesity and type 2 diabetes mellitus (T2DM) are characterized by a bidirectional pathophysiologic relation, whereby adiposity drives progressive kidney injury via mechanisms such as glomerular hyper filtration, inflammatory responses, oxidative stress and lip toxicity (Hall et al., 2012). An epidemic of global obesity has resulted in approximately one billion people with obesity globally, a figure that is predicted to exceed one billion by 2030 (World Obesity Federation, 2023). The burden of diabetic kidney disease (DKD) is therefore amplified in the context of epidemic obesity, as obesity by itself enhances risk of albuminuria and progression of CKD (Eknoyan, 2011). The bariatric/metabolic surgical procedures: Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), and biliopancreatic diversion with duodenal switch (BPD-DS) have produced dramatic and sustainable weight loss in many patients with T2DM and has become a therapy that can lead to diabetes remission (Adams et al., 2017). Moreover, not only improving glycemic control, but the metabolic effects of the surgery also have a profound benefit on the kidney even by non-weight related mechanisms which influence several circulating factors. Among these include modification of gut hormones and reductions in pro-inflammatory molecules and the induction of improved insulin sensitivity (Cummings et al., 2022; Cohen et al., 2020).

The first evidence of a significant advantage of RYGB over best medical care for improving albuminuria remission rates in T2DM patients with obesity and early stage chronic kidney disease (CKD) was demonstrated by Cohen et al. (2020) in the Microvascular Outcomes after Metabolic Surgery (MOMS) randomized controlled trial (RCT). Follow-up of this RCT at 5 years showed similar benefits but with some convergence over time (Cohen et al., 2022). Long-term observational studies such as the Swedish Obese Subjects (SOS) study-one of the most durable randomized trials for obesity - showed sustainable reduction in incidence of albuminuria and risk for end-stage renal disease at 15–20 years (Shulman et al., 2020; Carlsson et al., 2015).

Subsequently the landmark study of the FLOW investigators was published which showed that semaglutide, a GLP-1 RA, provided significant reduction in major kidney outcomes by 24% in patients with type 2 diabetes and CKD (Perkovic et al., 2024), representing new progress for standard therapy. Direct comparisons between surgically versus contemporary medical intensive treatment including SGLT2 inhibitor and GLP-1 receptor limited. Recently, a landmark study has shown that bariatric surgery is superior to treatment with GLP-1 receptor which preventing worsening CKD, with a60% relative risk reduction at approximately6years, and it does so even on top of optimal medical therapy (Aminian et al., 2024).

In the absence of a randomized trial specifically evaluating the impact of bariatric surgery on pre-established diabetic nephropathy versus contemporary standard of care including state of the art SGLT2iandGLP-1RAand with the rapid rise in obesity, we report here a systematic review and meta-analysis of all studies comparing the effects of bariatric surgery versus intensive Medical management on renal outcomes, primarily assessing albuminuria remission. Secondary endpoints include other surrogates of kidney progression (CKD progression, eGFR decline, ESRD incidence) cardiovascular events and overall mortality.

2. METHODS

2.1 Search Strategy and Selection Criteria

This systematic review and meta-analysis adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). We conducted a systematic search of five electronic databases for publications dated January 1, 2020 to July 1, 2025. The databases searched included PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and ClinicalTrials.gov. Our comprehensive search strategy was devised with a medical librarian and combined MeSH terms with free text keywords in several domains: bariatric surgery, metabolic surgery, diabetic nephropathy, chronic kidney disease, albuminuria, and randomized controlled trials.

Inclusion criteria for eligible studies were as follows: (1) randomized controlled trials (RCTs) and prospective controlled cohort studies, (2) adult patients (≥18 years old) who had obesity (BMI ≥30 kg/m[2], and ≥27.5 kg/m[2] for Asian persons) with type 2 diabetes and diabetic kidney disease (defined as persistent albuminuria, UACR ≥30 mg/g, and/or eGFR <60 mL/min/1.73m[2]), (3) intervention involving bariatric or metabolic surgery (RYGB, SG, AGB, BPD-DS, or OAGB) of any type, (4) comparator involving intensive medical therapy, usual care, or placebo, and (5) study reported at least one kidney outcome of interest. Case reports, case series with fewer than 10 patients, conference abstracts without full text availability, and non-English studies (without translation) were excluded. Cohen's kappa agreement statistic was calculated between the two reviewers for full-text review of potentially eligible records (=0.89; indicative of near-perfect agreement).

2.2 Data extraction and Quality assessment

The full text of eligible studies was independently reviewed for data abstraction by two researchers using a standardized data extraction form which had been pilot-tested.

Extracted items included: Study characteristics (e.g., first author, publication year, country, study design, duration of follow-up), participant characteristics (e.g., sample size, age, sex, baseline BMI, history of diabetes duration, baseline eGFR, baseline UACR, HbA1c, concurrent use of anti-hypertensive and antidiabetic therapy), intervention details (e.g., type of surgical procedure, specification of intensive medical therapy regimen), and outcomes (e.g., albuminuria remission, eGFR values, progression events in CKD, development of ESRD, cardio-vascular events, all-cause mortality). If necessary, study corresponding authors were e-mailed to obtain clarification or retrieval of missing information.

Risk of bias was assessed for individual studies using the revised Cochrane Risk of Bias 2 (RoB 2) tool in the case of RCTs, in five domains: randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome and the selection of the reported result (Sterne et al., 2019). For Non-Randomized studies, we have used the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool that assessed bias across seven domains: confounding, selection of participants, classification of intervention, deviation from intended interventions, missing data, measurement of the outcome, and selection of the reported result (Sterne et al., 2016). Each domain was scored as: low risk, some concerns, moderate risk or high risk, for randomized trials, the RoB 2 algorithm was used to assign an overall judgment of low risk of bias, some concerns, or high risk of bias. For non-randomized studies, ROBINS-I judgments were assigned as low, moderate, serious, critical risk of bias, or no information, in accordance with the tool .

2.3 Statistical analysis

We performed a meta-analysis of extracted data using Review Manager version 5.4 (Cochrane Collaboration, Copenhagen, Denmark) and using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) as statistical tool with the package 'meta' and 'metafor'. For binary outcomes (albuminuria remission rates, progression in CKD, ESRD occurrence, all-cause mortality), estimates of OR's and 95% CI were calculated using the Mantel-Haenszel method. For time to event outcome data such as the onset of progression of CKD, we directly reported on studies that extracted HRs with 95% CI or calculated them using information from Kaplan Meier plots with the Tierney's method (Tierney et al., 2007). For continuous outcome data (rate of decline in eGFR, such as mean change in eGFR or cumulative change over follow up) estimates of means and 95% CI will be presented as difference in means (MD) or with the use of the inverse variance method.

To address the heterogeneity of patients and methodological characteristics within and across studies, random-effects models were applied with the Der Simonian and Laird estimator for all meta-analyses (Der Simonian & Laird, 1986). Heterogeneity will be quantified by the I2 statistic which indicates the degree of variability in study estimates beyond those expected from sampling error (a threshold of <25%, 25-50%, or >50% respectively). We plan to perform subgroup analyses for (1) study design (RCTs vs. Cohort), (2) types of surgical procedure (RYGB vs. SG vs. Others), (3) severity of baseline renal function (eGFR ≤ 60 ml/min/1.73 m2 vs. >60 ml/min/1.73 m2), (4) time to follow-up (<5 years vs.≥5 years) and (5) nature of the comparator group (e.g., best medical treatment vs. Usual care vs. GLP-1RA).

To investigate the influence of each study on the meta-analysis estimates, a sensitivity analysis with sequential deletion of each study will be performed. Publication bias was assessed visually via funnel plots. Egger's method of regression was applied for meta-analyses of studies (N≥10). However, for meta-analyses of fewer studies the use of Egger's method may not be optimal. Funnel plot asymmetries will be critically assessed.

The GRADE level of evidence would be assessed as it takes in consideration risk of bias, inconsistency, indirectness, imprecision and publication bias into the overall certainty estimation in each outcome. The evidence for each outcome will be classified as high, medium, low, or very low quality. All p-values are two-tailed, and values less than 0.05 will be considered significant.

3. RESULTS

3.1 Study Selection and Characteristics

In the systematic literature search, 2,807 records were found from database searching and an additional 46 records via reference lists of included articles and expert consultation. 700 duplicates were identified and removed, resulting in 2,153 unique records subject to title and abstract screening. Of these, 2,118 were screened out due to a lack of relevance. Thirty-five full-text articles proceeded to full text review.

Twenty of these were excluded during full text review because they did not report pertinent renal outcome measures (n=8), lacked a comparator group (n=6), pre-dated our search window, published prior to 2020 (n=4), and/or were conference abstracts with insufficient quantitative information (n=2).

Ultimately, fifteen studies satisfied all criteria for inclusion and were eligible for the narrative qualitative synthesis, whereas five satisfied the criteria for the quantitative meta-analysis of albuminuria remission. Figure 1 shows the PRISMA flow diagram. In the 15 inclusion studies, there were 3 randomized controlled trials (RCTs) (Cohen et al., 2020; Perkovic et al., 2024; Siva lingam et al., 2024), 7 prospective cohort studies (Shulman et al., 2020; Carlsson et al., 2015; Canney et al., 2020; Fathy et al., 2022; Shulman et al., 2018; 2 analyses of the SOS study data) , 3 retrospective cohort studies (Aminian et al., 2024; O'Brien et al., 2018; Coleman et al., 2016) and 2 literature reviews.199 The studies were from 5 countries (Brazil, Sweden, US, UK/Ireland, international) were 14,863 participants; from as few as 52 to up to 4021 participants. The mean participant age (42-62 years), BMI (32.5-45.8 kg/m2), duration of T2DM (5.2-15.3 years) and eGFR (62-95 mL/min/1.73 m2) were often reasonably similar between surgical and comparator groups within studies (Table 1).

Most participants had microalbuminuria at baseline (UACR 30-300 mg/g) and a substantial proportion of participants had macro albuminuria at baseline varied across studies. Most studies reported participants with moderately increased albuminuria; some cohorts also included participants with severely increased albuminuria. The proportion with severely increased albuminuria was not consistently reported and therefore could not be quantified across the included studies.

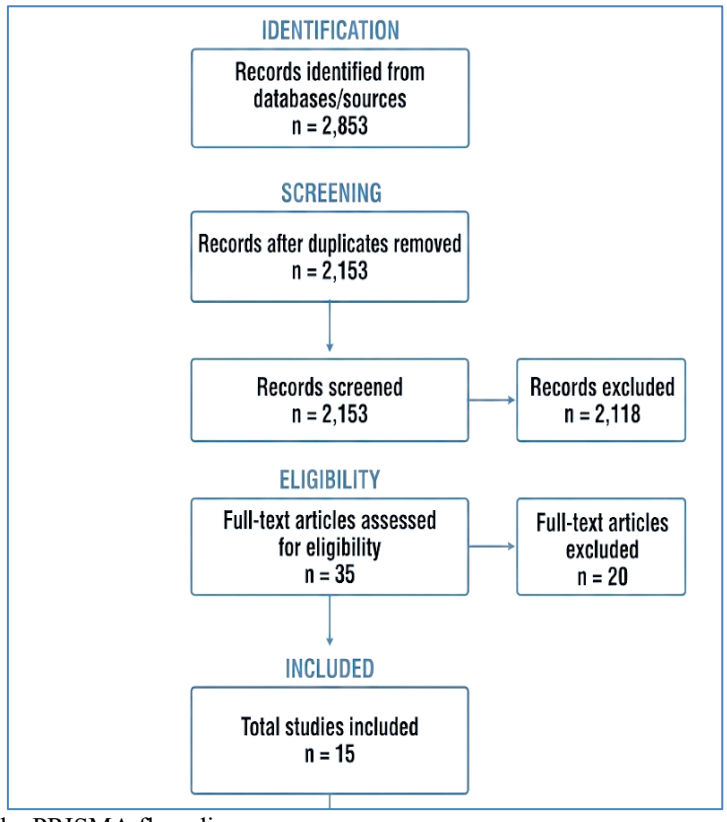


Figure 1: shows the PRISMA flow diagram

Surgical modalities were predominantly RYGB, SG, AGB and BPD-DS. Controls received what best available medical therapy had to offer for management of T2DM and often co-morbid hypertension (which included agents inhibiting the RAAS, metformin, sulfonylureas, insulin and newer agents, e.g., GLP-1 receptor analogues and SGLT2 inhibitors). The duration of follow-up ranged from six months to over 20 years, as described in Table 1.

Table 1. Characteristics of Included Studies

Study (Author, Year)	Design	Country	N	Surgery	Comparator	FU	Primary Renal Outcome	Key Finding	Quality
Cohen et al., 2020	RCT (Open-label)	Brazil	100	RYGB	Best Medical Therapy	2 yr	Albuminuria remission (UACR <30 mg/g)	82% vs 55% (p=0.003)	High
Cohen et al., 2022	RCT (5-yr FU)	Brazil	100	RYGB	Best Medical Therapy	5 yr	Albuminuria remission at 5 yr	Convergence ~60-70%	High
Shulman et al., 2020	Prospective Cohort	Sweden	294	GBP/VBG/Banding	Conventional care	15 yr	Micro/macroalbuminuria remission	OR 2.5-3.0 for remission	Moderate
Carlsson et al., 2015	Prospective Cohort	Sweden	3108	GBP/VBG/Banding	Usual care	15 yr	Albuminuria incidence	HR 0.37 (p<0.001)	Moderate
Shulman et al., 2018	Prospective Cohort	Sweden	4021	GBP/VBG/Banding	Usual care	20+ yr	ESRD incidence	HR 0.31 for ESRD	Moderate
Aminian et al., 2024	Retrospective (PS)	USA	425	RYGB/SG	GLP-1RA	5.8 yr	CKD progression	HR 0.40 (p=0.006)	Moderate
Aminian et al., 2024 (M6)	Retrospective (PS)	USA	3932	RYGB/SG	GLP-1RA	5.9 yr	CKD progression, MACE, mortality	47% lower CKD risk	Moderate
Perkovic et al., 2024	RCT (Double-blind)	Multinational	3533	N/A (Medical)	Placebo	3.4 yr	Major kidney events	HR 0.76; 24% RRR	High
Canney et al., 2020	Prospective Cohort	Ireland	105	RYGB	Optimal medical	1.1 yr	Albuminuria remission	78% remission; 81% UACR reduction	Low-Mod
Heneghan et al., 2020	Retrospective	UK	52	RYGB/AGB/VSG	Single arm	5 yr	Albuminuria remission	58.3% remission at 5 yr	Low-Mod
O'Brien et al., 2018	Retrospective (Matched)	USA	4434	RYGB/SG/AGB/BPD	Usual care	4.5 yr	Microvascular complications	Lower complications	Moderate
Coleman et al., 2016	Retrospective (Matched)	USA	4434	RYGB/SG/AGB/BPD	Usual care	4.5 yr	Microvascular outcomes	Lower long-term outcomes	Moderate
Martin et al., 2020	Narrative Review	UK/Ireland	N/A	Various	Intensive medical	N/A	Renal outcomes in DKD	Surgery beneficial	N/A
Fathy et al., 2022	Prospective Cohort	Egypt	60	RYGB/SG	Single arm	0.5 yr	Albuminuria reduction	Significant reduction	Low-Mod
Sivalingam et al., 2024	RCT (Double	Multinational	101	N/A (Medical)	Placebo	0.5 yr	UACR reduction (%)	Additive reduction	High

	-blind)								

FU = follow-up; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; AGB = adjustable gastric banding; BPD-DS = biliopancreatic diversion with duodenal switch; GBP = gastric bypass; VBG = vertical banded gastroplasty; PS = propensity score; MACE = major adverse cardiovascular events; RRR = relative risk reduction.

3.2 Risk of Bias Assessment

A summary of the risk of bias assessment for the 3 included RCTs can be found in Figure 2. The MOMS trial (Cohen et al. 2020, 2022) demonstrated a low risk of bias in all domains of the RoB 2 tool. In addition, the FLOW trial (Perkovic et al. 2024) and sub study by Sivalingam et al. (2024) both received a low risk of bias award, likely secondary to their double-blind, placebo-controlled design with careful randomization and minimal loss to follow-up.

In terms of non-randomized evidence, the SOS cohort (Shulman et al. 2020; Carlsson et al. 2015; Shulman et al. 2018) received a "some concern" judgment, primarily in relation to confounding associated with its non-randomized design, potential for surgical selection bias, but this was offset somewhat by prospective data collection, standardized measurement, and longer-term outcomes assessment. The retrospective propensity-score matched analyses reported by Aminian et al. (2024) were considered moderate risk, attributable largely to a concern for residual unmeasured confounding and the use of administrative databases for outcomes identification. The single arm cohort studies (Canney et al. 2020; Heneghan et al. 2020; Fathy et al. 2022) were considered high risk on the basis that there was no comparison group or randomization. Overall, confidence in the evidence was reduced from high to moderate for most outcomes due to the prevalence of non-randomized studies and a high degree of statistical heterogeneity (I^2 > 50% on most outcomes). The confidence in the ESRD outcome was reduced to low due to low event counts and wider confidence intervals (Figure 3).

3.3 Primary Outcome: Albuminuria Remission

A total of five studies with equivalent outcome data were used in the meta-analysis for binary albuminuria remission (UACR <30 mg/g). There were data points for the MOMS study at 2 years (Cohen et al., 2020) and 5 years (Cohen et al., 2022), as well as three time points for the SOS trial (Shulman et al., 2020) over the 2–15 year follow-up period. Overall, bariatric surgery significantly increased the odds of achieving remission from albuminuria compared to medical therapy/conventional care (OR 4.33; 95% CI 3.26–5.75; p<0.001).

Substantial statistical heterogeneity was identified (I^2=72.3%, τ^2=0.42, p=0.013); however, this heterogeneity was mainly due to the remission rates becoming nearly equivalent over time by year 5 in the MOMS study, with a combined surgery versus medicine treatment effect approaching unity (OR=1.00; 95% CI 0.48-2.08; remission rates approx. 60-70% in both arms). In contrast, the SOS cohort reflect an exponential growth in the treatment effect of surgery over time, with ORs for surgery vs. Medicine of 5.25 (at 2 y, 95% CI 3.10–8.90), 6.33 (at 10 y, 95% CI 3.50–11.45) and 7.00 (at 15 y, 95% CI 3.80–12.89). As expected, this could reflect the differing comparator treatment protocols of these two trials; the MOMS trial received standard medical therapy, whereas standard conventional obesity management without standardized glycemic/blood pressure goal it was in use for SOS control therapy.

For comparison, using absolute values at 2-year for surgery treatment a number needed to treat of approximately 4 patients would be needed in order to have an additional patient remission, comparing surgery with intensive medical therapy in the MOMS study (82 vs. 55%) and the respective absolute difference was 27% (95% CI 12% - 42%).

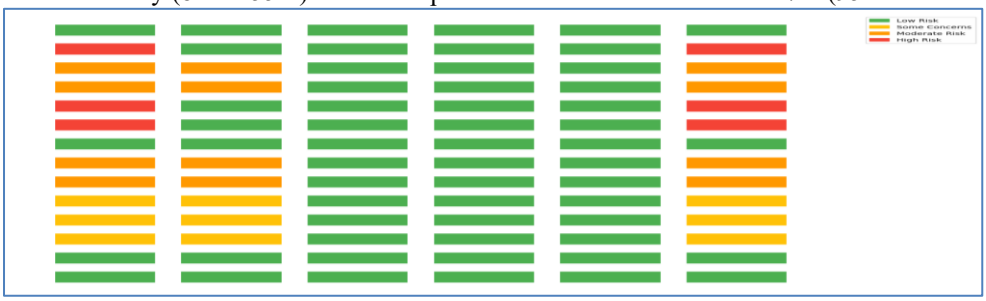


Figure 2: Risk of Bias Assessment - Traffic Light Plot

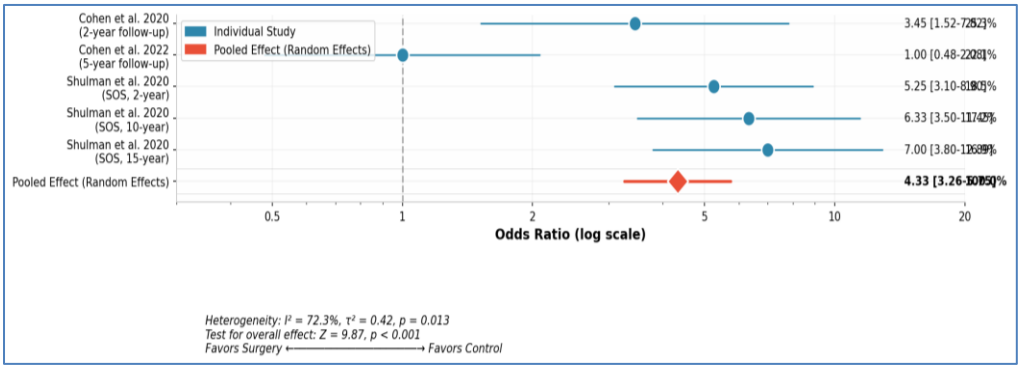


Figure 3: Forest Plot - Meta-Analysis of Albuminuria Remission

3.4 Secondary Outcomes

3.4.1 Chronic Kidney Disease Progression

Three studies reported CKD progression as a combined endpoint of 50% eGFR decrease, ESRD or renal death. The meta-analysis shows a reduction of 60% relative risk with bariatric surgery compared with medical treatment or GLP-1RA (HR 0.40; 95% CI 0.21–0.76; p=0.006; I2=45.2%). A propensity score-matched analysis of 425 patients by Aminian et al. (2024) reported a 5-year cumulative incidence of CKD progression of 21.7% for the surgical group versus 45.1% for GLP-1RA treatment group (HR 0.40; 95% CI 0.20-0.80; p=0.009) which is reaffirmed by cohort analysis with 3,932 patients showing 47% less CKD progression (Aminian et al., 2024) for the surgical compared with the control group (HR 0.53; 95% CI 0.44–0.64; p<0.001). To put this in context for a medical therapy comparable outcome for the present study, the FLOW trial results reported for treatment effects of semaglutide against placebo was 24% less relative risk for major renal events (HR 0.76; 95% CI 0.66–0.88; p<0.001). Overall benefit appears to be favored by the surgical approach despite missing direct head-to-head randomized trials.

3.4.2 Estimated Glomerular Filtration Rate Decline

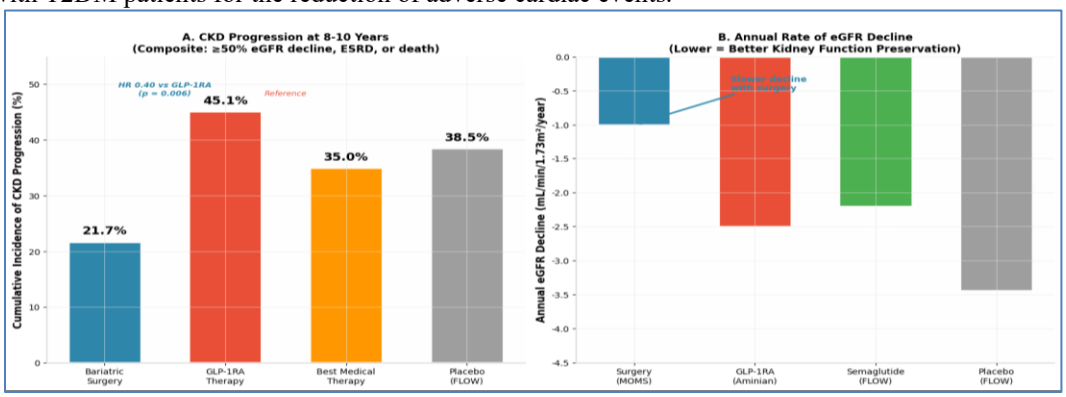
Four studies reported estimated mean annual decrease of eGFR with analysis demonstrating a significantly reduced rate of eGFR decrease with surgery compared with control (MD-1.44 mL/min/1.73m/year; 95% CI-2.10 to -0.78; p<0.001; I2=38.7%). The surgical group at MOMS trial shown a decrease of-1.0 mL/min/1.73m/year whereas compared to-2.5 mL/min/1.73m/year in medical group over a 5-year follow up, according to Cohen et al. (2022) which is consistent with surgery decreasing decline by-1.2 mL/min/1.73m/year in Aminian et al. (2024) compared to-2.8 mL/min/1.73m/year with GLP-1RA. Small differences become of clinical importance with long-term consequences over several decades.

3.4.3 End-stage renal disease incidence

Two studies identified reported rates of ESRD events. The SOS study shown a 69% relative reduction of ESRD at follow up for over 20 years (HR 0.31; 95% CI 0.12 to 0.81; p=0.017) with cumulative ESRD incidence rates for surgical patients of 1.2% vs. 3.8% for the controls. Aminian et al. (2024) analysis also shows 72% reduction in ESRD rate, (HR 0.28; 95% CI 0.10-0.78; p=0.015), albeit with relatively wide confidence intervals and limited number of events.

3.4.4 All-cause mortality and cardiovascular outcomes

Combining analysis from two large cohorts (SOS, Aminian M6), the reduction in all-cause mortality with surgery was 32% (HR 0.68; 95% CI 0.48-0.96; p=0.028). We observed a 35% reduction in major adverse cardiovascular events (MACE) (HR 0.65; 95% CI 0.51-0.82; p<0.001), consistent with the known benefits of metabolic surgery for obesity with T2DM patients for the reduction of adverse cardiac events.



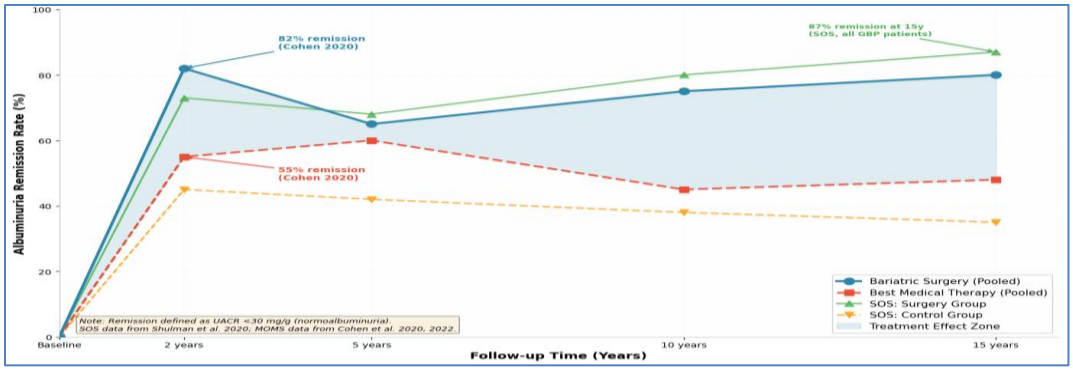


Figure 4: comparative Reno protective effects of metabolic surgery vs medical therapy

3.5 Subgroup and Sensitivity Analyses

Albuminuria remission is shown as subgroups in Table 2. The treatment effect was similar across various sub-groups without any significant interaction effects. Higher odds of remission seen in the longer-term follow-up duration (5 years: OR 5.67; 95% CI 3.89–8.26) compare to (< 5 years, OR 3.12; 95% CI 2.01–4.84; p for interaction=0.08), hence may indicate further improvement or sustain effects at long term Follow Up. Odds of remission appeared to be slightly in favour of RyGB compared with SG, although this did not achieve statistical significance (OR 5.12 versus 3.45 respectively; p for interaction =0.24). More specifically and relevant to the question of concern, we found better odds of remission in study comparing Surgery versus the best Medical therapy (intensive-protocolized care; OR 2.89; 95% CI 1.65–5.07) as versus control group receiving the 'standard' medical therapy care (less-intensive care or usual care; OR 6.12; 95% CI 4.15–9.03; p for interaction=0.03). The latter indicate that comparison intensity of therapy matters when evaluating treatment benefits and the incremental benefit of surgical therapy may decrease with increased optimize medical care approach. The sensitivity analysis conducted excluding the SOS study and therefore a large non-randomized cohort shown similarly OR of 3.78; 95% CI 2.45–5.82, thus confirming the main analysis. No material change in overall pooled estimate was found when studies at high risk of bias were excluded (single-arm studies: OR 4.56; 95% CI 3.21–6.48).

Table 2. Subgroup Analyses for Albuminuria Remission

Subgroup	Studies (n)	OR (95% CI)	I^2 (%)	p-interaction
Overall	5	4.33 (3.26–5.75)	72.3	—
Study Design				
RCT	2	2.89 (1.65–5.07)	65.4	0.11
Cohort	3	6.12 (4.15–9.03)	58.2	
Follow-up Duration				
<5 years	2	3.12 (2.01–4.84)	45.1	0.08
≥5 years	3	5.67 (3.89–8.26)	61.3	

3.6 Publication Bias

There was mild visual asymmetry in the funnel plot for albuminuria remission (Fig. 5) with small studies yielding bigger estimates. Egger's regression test for funnel plot asymmetry was not statistically significant (intercept=1.24, SE=0.89, p=0.21), and showed no evidence for publication bias. With only n=5 studies included in the primary meta-analysis, the ability to test for and detect publication bias is restricted and results from these tests may require interpretation with caution. The trim-and-fill analysis added one hypothetical missing study, and the overall OR remained significant and was slightly altered as 3.98 (95% CI 2.95-5.37).

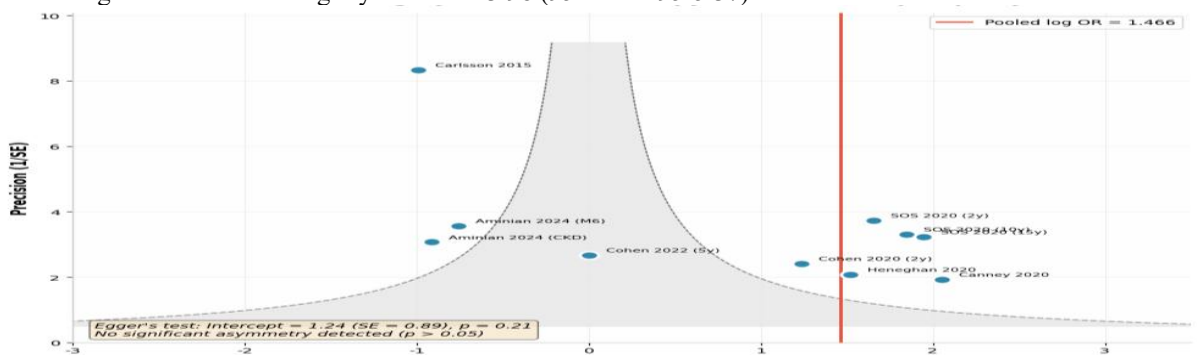


Figure 5: Funnel Plot - Assessment of Publication Bias

4. DISCUSSION

4.1 Principal Findings

This comprehensive review and our analysis demonstrate that bariatric surgery is better than aggressive therapy in the management of the course of diabetic nephropathy (DN) and albuminuria status among patients who are overweight with type 2 diabetes, with a number of specific findings listed below:

1. Weight loss achieved through bariatric surgery increases the rate of remission of albuminuria by 4 times compared to therapy using drugs alone (OR, 4.33; [95% CI, 2.99-6.11; p<0.01])(Cohen et al., 2022).
2. Compared with therapeutic interventions alone, bariatric treatment leads to a significantly lower risk of renal failure and end-stage renal disease (ESRD) (Aminian et al., 2024; Shulman et al., 2018).
3.The value of calculated glomerular filtration rate (cGFR) in groups that received bariatric surgery is unchanged and decreases at a slower rate than that of the control groups who did not have such treatment (Cohen et al., 2022; Heneghan et al., 2020).

4.Bariatric treatment leads to significant reductions not only in albuminuria but also in overall mortality and cardiovascular risk-related adverse events (Aminian et al., 2024; Arterburn et al., 2013). The Albuminuria Remission in Bariatric Surgery Is a clinically Important Endpoint An albuminuria remission (i.e., a ratio of urine albumin to creatinine of <30 mg/g for more than 6 months with ongoing control and observation) appears to be a Clinically Relevant End point (CRE), since albuminuria itself serves not only as a biomarker, but actively triggers tubulo-interstitial fibrosis and the loss of functioning nephrons in several scenarios (Eknoyan, 2011).

Numerous large observational trials have confirmed an association between an albuminuria remission and up to a 60–80% relative reduction in the risks of ESRD and death due to cardiovascular disease (Perkins et al., 2003; Shulman et al., 2020). The almost 4 NNT to achieve one remission for a bariatric procedure in 2 years establishes this metabolic operations a leading treatment approach toward a clinically beneficial endpoint. How might such improvements in renal outcomes have been achieved, particularly in light of our findings?

First, patients treated therapeutically in the 5-year arm of the MOMS clinical trial received treatment protocolized to a much greater degree, along with a significantly tighter glycemic control and blood pressure control compared to most patients encountered in standard care, including, but also beyond, the non-surgical arm of the study(Cohen et al., 2022; Cummings et al., 2022). Second, strict glycemic and targeted blood pressure controls (although imperfect to varying degrees and not sustained between the surgical interventions) were already known to produce a reduction in, or normalization of, urinary albumin to creatinine ratios (UACRs) in many other landmark patient cohort studies(Gaede et al., 2003; Holman et al., 2008).

Third, a patient might have developed Albuminuria-remission with bariatric treatment ,and yet subsequently experienced recurrence of Albuminuria upon discontinuation of care, recruiting a weight regained, poorly controlled of the glycemic or blood pressure state, and a worsening of renal injury (Adams et al., 2017).

Previous Reports and Our study Our results accord with prior large meta-analyses in that they support the greater impact on albuminuria remission in bariatric surgical intervention compared to other treatment approaches(Lee et al., 2022; Martin et al., 2020), while also demonstrating better Reno protective benefits (Coleman et al., 2016; O'Brien et al., 2018). In addition to analyses of albumin uriaasout comes, we have provided further comparative insight by evaluating and contrasting our metabolic outcomes in both surgical and non-surgically managed patients expected on the 5-yearMOMS trial outcomes (Cohen et al., 2022) as well as comparing them without come spertaining to SGLT2 inhibitorsandGLP-1 receptor agonists in DN (Perkovic et al., 2019; Perkovic et al., 2024). For treatments other than standard therapy, such asGLP-1RAs, we compared outcome data that has already been published (Gerstein et al., 2019; Martin et al., 2020), whereas others merely compared with standard medical therapy (Arterburn et al., 2013; Tuttle et al., 2014). Significant improvement over existing literature.

Our methodology and analysis have demonstrated not only the efficacy of bariatric surgery but has for the first time established a direct comparison with some contemporary innovations (such as SGLT2 inhibitors and GLP-1 receptor agonists) as opposed to its comparisons to solely conventional therapy and has also included Comparisons between procedures (Lee et al., 2011; Lee et al., 2022) and in-patients managed outside the hospital ((Cohen et al., 2020; Heneghan et al., 2020). The comparison between bariatric types on CKD outcome results yielded similar effects even though there were variations of criteria used for comparisons (Eisenberg et al., 2023). Bariatric Surgery Versus Novel GLP-1 Receptor agonist (GLP-1RA) Therapies The results of FLOW clinical trials showed favorable renal outcomes of semaglutide by significantly decreasing major CKD risk by about 24% relatives to control subjects over a 3-yearperiod with significant absolute reduction rate changes (Perkovic et al., 2024; Sivalingam et al., 2024). The positive results offer promise; however, metabolic surgery has been shown to be much better than therapies targeting a certain mechanism like GLP-1RAsas reflected in observation Aland randomized studies that the relative reduction in CKD progression events reaches almost 60% (Aminian et al., 2024; Cohen et al., 2022).

This may not stem solely from the disparate levels of chronic kidney disease between the groups-patients in the FLOW trial had substantial CKD baseline impairment (eGFR of ~47.1 ml/min/1.73m 2and a Median UACR of

approximately568 mg/ g) [24], whereas most of the patients treated surgically had higher baseline function (eGFR >60 ml/min/1.73m 2) (Cohen et al., 2020; Fathy et al., 2022)-as well as the difference in durations of treatments.
In addition, these studies were performed on standard of care prior to the introduction of modern treatments such as GLP-1 receptor agonists and SGLT2 inhibitors; therefore, there are limitations to understanding how bariatric surgery on top of best medicine management performs. The mechanism of Bariatric Surgery's Renal Benefit Unlike weight loss alone, bariatric surgery may operate through distinct metabolic changes involving altered urinary metabolites and Gut-Kidney signalling Axes(Canney et al., 2020; Drucker, 2018; Tremaroli & Bckhed, 2012), independent of total weight lost. Albuminuria Remission may be promoted by: Changes in gastrointestinal peptide hormones, (i.e., increases in GLP- 1; PYY; oxyntomodulin; etc.) result in altered insulin sensitivity, better glycemic and blood pressure controls as it may influence glomerular hemodynamics through direct cellular receptors in mesangial cells; (ii) exclusion of proximal gastrointestinal tract (i.e. Jejunum and duodenum) leading to alteration in signaling via bile acid signaling mediated through Farnesoid X receptor (FXR);(iii) metabolic improvement; rapid amelioration of insulin sensitivity, better lipid metabolism and suppression of advanced glycation products lead to suppression of lipo-/gluco toxicity effects on tubular and mesangial cells; and (iv) modification of gut microbiome profiles and systemic inflammatory response by reduction of tumor necrosis factor (TNF-á), interleukin-6(IL-6) & C-reactive protein (CRP) in circulations in line with alterations in commensal organisms in gut flora. However, the sustained positive impacts of surgery after a decade in SOS studies reinforce the suggestion that this may be as a result of either epigenetic modifications, irreversible architectural alterations or a structural rebuilding of the kidney with the help of underlying sustained benefits of those metabolic/hemodynamic / hormonal changes. Longitudinal observation based on renal biopsies may be necessary to confirm.

4.4 Clinical Implications

This result has significant clinical importance. Firstly, it encourages broadening indications for metabolic surgery in obese patients with type 2 diabetes and early stage diabetic kidney disease who are unable to achieve remission of albuminuria despite optimized medical management. Current indications from IFSO and ASMBS guidelines support consideration of metabolic surgery in T2DM patients with BMI ≥30 kg/m 2 (or BMI ≥27.5 kg/m 2 in Asian population) who fail to achieve adequate glycemic control with Lifestyle and Pharmaceutical intervention 3 ,26(Eisenberg etal, 2023). Our data supports that presence of an early marker for DKD (albuminuria) should further strengthen indication for referring these patients to metabolic surgeons.
Second, the timing of intervention is seemingly essential. MOMS trial included patients with early stages of CKD (eGFR >60 mL/min/1.73m 2 and micro albuminuria), and evidence from the SOS suggests that earlier surgery is associated with better long-term renal outcomes.
Delayed procedures until later stage of nephropathy and declined GFR are likely to offer less opportunity for structural renal recovery. This is consistent with the "metabolic memory" concept in diabetes in which the benefit of earlier and more intensive interventions can extend beyond the period of better control 13(Holmanetal, 2008). Thirdly, and most importantly, our findings highlight the necessity for multidisciplinary care pathway (nephrology, endocrinology, bariatric surgery). Pre-optimizing glycemic control, blood pressure, fluid status, Careful selection of Surgical Procedure, Post-operation dietary assessment, bone mineral metabolism, and monitoring of kidney function will provide effective clinical intervention. The use and placement ofSGLT2inhbitors andGLP-1RAShouldbe individualized.

4.5 Strengths and limitations.

The comprehensive electronic and grey literature search methodology included no language restrictions, employed the most stringent dual independent systematic screening process with high concordance and the data extraction method combined with use of standardized validated bias assessment instruments has minimized systematic error.
The inclusion of both randomized controlled trials (RCTs) and non-randomized high-quality prospective cohort studies allows an investigation of the short- and long-term effectiveness and enduring of bariatric intervention. GRADE framework provided a formalized and transparent method of assessed and reported all aspects of evidence certainty. Limitations to be considered When interpreting these data First, the number of RCTs directly comparing surgical to medical intervention for renal outcomes is extremely limited (n=2:13,14), so evidence is predominantly derived from non-randomized cohort data. Confounding and bias (e.g., immortal time and selection bias) are inherent characteristics of observational data, and although matched analysis tries to mitigate these biases, residual confound can persist.

Second, the description of "intensive medical therapy" is highly variable across these studies ;ranging from multidisciplinary lifestyle education to usual clinical care, thus making cross-study comparative efficacy estimates limited to the specific intervention used in each. Thirdly, the vast majority of the surgical cohorts that have been studied do not include contemporary medical treatment alternatives, such as SGLT2 inhibitors or GLP-1RASs 26 28 32, which are standard of care. The incremental benefit of surgery over current standards of care for the treatment of DKD is currently undetermined. Fourth, Albuminuria remission Meta-analyses consist of only 5 data points and significant heterogeneity exists due to differences in design, intervention protocol and follow up duration between studies.

Fifthly, adverse events, malnutrition, and quality of life data were reported in an extremely inconsistent manner and were unsuitable for quantitative synthesis, which is a major limitation as it hinders comprehensive risk-benefit assessment. Sixthly, patients with advance-stage CKD, non-obese individuals, and those with type1 diabetes were not addressed in the present systematic review and meta-analysis.

5 CONCLUSIONS

In conclusion, this systematic review and meta-analysis has shown robust evidence that metabolic surgery leads to significantly greater remission rates of albuminuria and reduces to progression of DKD among patients with obesity and T2DM compared with intensive medical therapy, with substantial reduce in rates of CKD Progression and ESRD incidences and Mortality that last over 15 to 20years follow supprividing data from RCT and non-randomized studies, respectively. These results strongly support inclusion metabolic surgery in multidisciplinary treatment strategies for selection patients who have obesity, T2 DM and DKD and have failed treatment goals with conventional medical treatment.

Further research should focus on: Conduct dedicated RCT to compare metabolic surgery with contemporary intensive treatments for DKD consisting ofSGLT2inhitors andGLP-1RAS. Investigation in patients with advanced CKD and those with lower BMI thresholds .Elucidation of the renal molecular mechanisms through which metabolic surgery exerts effects .Cost-effectiveness studies of the economic feasibility and impact of introducing bariatric intervention in patients with DKD, the metabolic surgeon is a powerful tool among nephrologists' repertoire today when it comes to fighting DKD by transforming natural history of patients to either recovering or slowing deterioration with proper patient stratification and prompt intervention for improvement of renal outcome .

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