



Renoprotective Effects of the Combination of Empagliflozin and Liraglutide Compared With Roux-en-Y Gastric Bypass in Early-Stage Diabetic Kidney Disease: A Post Hoc Analysis of the Microvascular Outcomes after Metabolic Surgery (MOMS) Randomized Controlled Clinical Trial

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Baseline albuminuria in patients with diabetic kidney disease (DKD) is strongly associated with progressive deterioration in kidney function (1). The remission of microalbuminuria in patients with type 2 diabetes and obesity attenuates the decline in estimated glomerular filtration rate (2). In the Microvascular Outcomes after Metabolic Surgery (MOMS) randomized controlled trial (RCT) (3), we demonstrated that the combination of best medical care and Roux-en-Y gastric bypass (RYGB) surgery is more effective in inducing remission of microalbuminuria than best medical care alone.

During the MOMS RCT, type 2 diabetes care guidelines were updated to reflect the potent renoprotective effects of sodium–glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists in people with DKD (4). Thus, the rate of use of the combination of these two agents (Combo) in the study was increased. In this post hoc analysis of the MOMS RCT, our objective was to determine whether the combination of two potent renoprotective

medications can match the reductions of albuminuria observed after RYGB.

The MOMS RCT protocol has previously been described in detail (3). In brief, 100 patients with CKDG1–3a, A2–3, urine albumin-to-creatinine-ratio (uACR) >30 mg/g, type 2 diabetes, and a BMI of 30–35 kg/m² were randomized 1:1 to either best medical care or RYGB. Of the 49 patients, 27 (55%) randomized to best medical treatment received the Combo (empagliflozin 25 mg once daily and liraglutide 1.8 mg once daily) within the first 2 years of the study and formed the subgroup of interest for this post hoc analysis. A total of 44 patients who underwent RYGB and completed 2 years of follow-up were included in this analysis. uACR, estimated glomerular filtration rate, glycated hemoglobin (HbA_{1c}), fasting plasma glucose, blood pressure, lipid profiles, and body weight were assessed at baseline and 2 years.

Both interventions resulted in significant reductions in uACR, but RYGB was significantly superior (mean difference 14.99 [95% CI 1.10; 28.87],

$P = 0.035$) (Table 1). The percentage of patients who achieved remission of albuminuria/DKD was 59.3% in the Combo and 81.8% in the RYGB group ($P = 0.043$).

RYGB was superior to the Combo for reductions in HbA_{1c} (mean difference 0.49 [95% CI 0.05; 0.93], $P = 0.029$) and LDL cholesterol (20.55 [6.30; 34.81], $P = 0.005$) but not systolic blood pressure (−0.75 [−8.51; 7.02], $P = 0.82$). The American Diabetes Association (ADA) triple end point was achieved in 25.9% in the Combo group and 44.2% in the RYGB group ($P = 0.11$).

In this post hoc analysis of the MOMS trial, the effect of inclusion of two potent renoprotective agents in best medical care for people with DKD did not quite match the renoprotective effects of RYGB. The surgical intervention remained superior in reducing albuminuria, remission of DKD, and improvements in cardiometabolic risk factors, including HbA_{1c} and LDL cholesterol. Despite the statistical superiority of surgery, the differences

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Table 1—Within- and between-group comparisons of renal and cardiometabolic outcomes at 2 years of follow-up

	Combo (n = 27)			RYGB (n = 44)			Combo × RYGB		
	Baseline	24 months	Effect size (95% CI)†	P	Baseline	24 months	Effect size (95% CI)†	P	P
HbA _{1c} (%)	9.0 (8.3; 9.7)	6.7 (6.4; 7.1)	-2.3 (-3.0; -1.5)	<0.001	9.0 (8.4; 9.5)	6.3 (6.0; 6.5)	-2.7 (-3.3; -2.2)	<0.001	0.029
uACR	89.7 (62.7; 116.7)	33.0 (22.1; 44.0)	-56.7 (-81.5; -31.9)	<0.001	104.8 (83.6; 126.0)	18.0 (9.5; 26.6)	-86.8 (-106.2; -67.3)	<0.001	0.035
Systolic blood pressure (mmHg)	140.4 (131.2; 149.6)	130.3 (124.2; 136.4)	-10.1 (-20.0; -0.3)	0.045	140.0 (133.3; 146.6)	131.1 (126.2; 135.9)	-8.9 (-16.2; -1.7)	0.018	0.848
LDL cholesterol (mg/dL)	114.0 (98.7; 129.4)	106.3 (95.4; 117.5)	-7.8 (-2.189; 6.4)	0.275	102.8 (90.8; 114.8)	85.7 (76.9; 94.5)	-17.1 (-28.1; -6.0)	0.003	0.005
ADA triple end point, n/N (%)	0/13 (0)	7/27 (25.9)	25.9 (9.4; 42.5)	0.002	0/25 (0)	19/43 (44.2)	44.2 (29.3; 59.0)	<0.001	0.11
DKD, n/N (%)	27/27 (100)	10/26 (38.5)	-61.5 (-80.2; -42.8)	<0.001	44/44	7/43 (16.3)	-83.7 (-94.8; -72.7)	<0.001	0.045
Body weight (kg)	92.5 (87.2; 97.7)	86.31 (81.0; 91.6)	-6.1 (-8.4; -3.9)	<0.001	92.9 (88.7; 97.0)	69.2 (65.1; 73.4)	-23.6 (-25.4; -21.9)	<0.001	<0.001

Continuous data are presented as mean (95% CI). †Mean difference: HbA_{1c}, uACR, systolic blood pressure, LDL cholesterol, and body weight. Relative risk: ADA triple end point and diagnosis of DKD.

in primary and secondary outcomes of the trial were of modest biological significance.

While modern pharmacotherapy for type 2 diabetes cannot fully recapitulate the pleiotropic impact of RYGB on DKD at the current time, with the rapid evolution of medicines, this might be possible in the future.

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