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INTRODUCTION

Diabetes mellitus may be originated from an autoimmune reaction towards pancreatic β -cells that altered insulin production (type-I diabetes), or because progressive deterioration of β -cells function superimposed on insulin resistance of cells in the body (type-II diabetes or T2DM).¹ Following the recommendation from American Diabetes Association (ADA), the management of diabetes is aiming to prevent complications that arise for such conditions, particularly from the cardiovascular disease.² Bariatric surgery is currently the leading procedure to serve this purpose through increased weight loss and alteration of gut hormones release. Non-invasive intervention, such as lifestyle modification, is also considered because it possesses a minimal risk of complications.³ This meta-analysis intends to evaluate clinical studies regarding remission, either partial or complete remission, of T2DM using bariatric surgery or lifestyle intervention

Research Design and Method

Selection of studies

The Eligible publication was screened independently by authors, which have inclusion criterias: 1) minimal follow up at least 1 month; 2) established control group; 3) written with English language; 4) published at least from 2008 and; 5) had completed clinical study phase 1-3. Any situation which altered endocrinologic status is an exclusion criteria.

Search strategy

Literature review was carried out using keywords: (Diabetes mellitus) AND (Remission) AND (Bariatric Surgery , RYGB) in several database of Cochrane Central Register of Controlled trials (CENTRAL), Current Controlled Trials (ISRCTN), ClinicalTrials. gov, EMBASE, Elsevier, Nature and Google Scholar.

Data Extraction and assessment

All references was reviewed using critical appraisal for clinical trials by

Remission occurred 4 months until 5 years after treatment. Mean diabetes duration is not significant statistically different from control group with p=0.94. The risk differences remission of T2DM was 0.26 (95% CI 0.23- 0.28) for fixed effect while random effect 0.45 (95% CI 0.31-0.58) by RYGB.

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identified through reco database through		records	f additional ds identified					Experimental		Control			Risk Difference	Risk Difference	
		through other sources				Study or Si	ibgroup E	vents	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	
			-				Cummings	2015	9	15	1	17	8.1%	0.54 [0.27, 0.81]	
	+						Mingrone 2	015	7	19	0	15	9.0%	0.37 [0.14, 0.60]	
	56 of record				records		Moinnes 20	117	11	27	4	28	9.1%	0.26 [0.04, 0.49]	
screened by us MESH		y using		excluded for being duplicate		Sachdev 20		14	15	14	15	0.0%	0.00 [-0.18, 0.18]		
							Dixon 2008		22	30	2	20	9.5%	0.63 [0.43, 0.84]	
				<u>(</u>			Mingrone 2		15	20	0	20	9.6%	0.75 [0.55, 0.95]	
52 of full-text articles assessed		xt	21 of full-text articles excluded,			led,	Courcoulas		16	20	0	23	9.7%		
		-	for being animal or molecular						-			0.67 [0.47, 0.86]			
	for eligibility			Lor m	ulecular		Chong 201		14	36	0	35	10.3%	0.39 [0.23, 0.55]	
	1						lkramuddin		22	60	0	59	11.0%	0.37 [0.24, 0.49]	
	31 of studie	s					Lean 2018		68	149	6	149	11.6%	0.42 [0.33, 0.50]	-
included in qualitative synthesis							Yska 2015		107	569	22	1881	12.1%	0.18 [0.14, 0.21]	+
							Total (95%	CI)		949		2247	100.0%	0.45 [0.31, 0.58]	•
10 of studies						Total event	s	291		35					
included in															
quantitative synthesis (meta-analysis)				Test for overall effect: $Z = 6.49$ (P < 0.00001)								-0.5 -0.25 0 0.25 0.5 Favours (experimental) Favours (control)			
Pre Inte			ervention Post Interver				ntion Mean Difference								Mean Difference
Study or Subgroup Mean		SD Total Mean SD				Weight	it IV, Random, 95% Cl				1	ľ	V, Random, 95% Cl		
McInnes 2017		7.1	1.4	27	6.6	0.1	27	9.2%	(D.50 (-	-0.03,	1.03	3]		
Mingrone 2012		8.51	1.24	20	7.69	0.57	20	9.1%	0.82 [0.22, 1.42]			2]		_ -	
Lean 2018		7.7	1.25	149	6.8	1.2	=	9.5%	0.90 [0.62, 1.18]]				
Dixon 2008		7.8	1.2	30	6.8	0.82		9.2%	1.00 [0.48, 1.52]				_ _		
Yska 2015		7.8	1.6	569	6.7	1	569	9.6%	1.10 [0.94, 1.26]				-		
		7.7	1	15	6.4	1.6		8.4%		1.30	• •				
Mingrone 2015		8.5	1.3	15	6.9	0.6		8.8%	1.60 [0.88, 2.32] 2.30 [1.36, 3.24]		-				
Courcoulas 2014 Ikramuddin 2016		8.7	2.2 1	24	6.4 6.7	0.82		8.4%							
Sachdev 2016		9.6 9.1	0.2	60 30	6.7 6.1	0.1	60 30	9.1% 9.6%			[2.33, [2.92,		-		•
	Chong 2017 9.		1.1	30	6.32	1.05		9.0% 9.2%			[2.92, [2.74,		-		
Total (95%	Total (95% CI)			969			969	100.0%		1.70 [[0.94,	2.46]		•
-	neity: Tau ² = /erall effect: J	•			= 10 (P <	(0.00	001); I² =	99%						-4 -2	
restion	reran enect. ,	2-4.30	(r ∼ 0.00	,01)										Favours [exper	imental] Favours [control]

Glycemic. The reduction of HbA1C (%) after follow up between group was significant as statistically 1.7 ± 0.36 for experimental, while 0.79 ± 0.69 for the control group with p= 0.0042. The mean the difference HbA1C between before and after therapy 2.45% using fixed and 1.74 (95% CI 0.94 -2.64) using random effect. HOMA-IR was decreased until 5.02 ± 0.87 ng/L for RYGB and 2.8 ± 2.7 for the control group.

Lipid Profile. Decreasement of HDL, TG and Total C and increment HDL profile were reported as a trend in all studies. HDL before therapy was $0.82 \pm 0.4 \text{ vs } 0.3 \pm 0.4$, TG $18.6 \pm 35 \text{ vs } 1.19 \pm 0.9$ and total Cholesterol $1.2 \pm 1.58 \text{ vs } 0.9 \pm 0.58 \text{ mmol/L}$.

Centre for Evidence-Based Medicine Oxford University. While risk of bias determined by Cochrane Handbook for Systematic Reviews of Interventions (PRISMA).

Statistical Analysis

Extracted literatures were entered into Review Manager 5.3 and Graph Prism 8. Mean value of HbA1c before and after treatment along with remission prevalence between treated and untreated group were compared. Data was analyzed using mean difference with fixed and random effects model to avoid heterogeneity, according with the previously published guidelines for statistical reporting and the Cochrane Handbook For Systematic Reviews of Interventions. Heterogeneity was considered significant at P<0.10

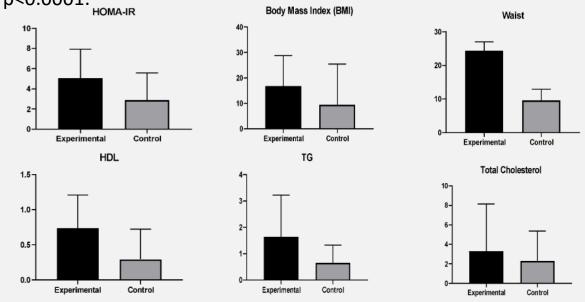
Result

Eleven studies were selected with a total 3226 participants included. The selection process algorithm as detailed in Figure 1. The mean of age for RYGB and control group were 49.92 ± 4.22 years and 50.79 ± 4.46 respectively, while DM duration for each group were 8.69 ± 3.85 and 7.59 ± 3.84 years. All studies used T2DM subjects. Diabetic status was monitored using the HbA1C level and followed from 1 month until 5 years. The control group was given standard antidiabetic therapies such as insulin and oral antibiotic, along with low-fat diet and high exercise activity. All studies included a control group vs intervention groups to compare the outcome of the therapy.

The Outcome

Prevalence of Remission. In ten studies, 229 patients of 964 in the experimental group achieved remission, while in the control group were 49 of 2262 patients.

BMI and Waist. BMI was decreased (23.4 ± 18) for RYGB, compared to control group (13.9 ± 21) Kg/m²; While for waist circumference between both group were 24.37 \pm 7.17 vs 9.56 \pm 3.8 cm with p<0.0001.



Limitation and Conclusion

This meta-analysis has limitations; 1)a very limited number of studies, which had small sample sizes and short duration of follow up; 2) inequality of duration of follow-up, This potentially affected the accuracy of the analysis and duration of follow-up were short, which couldn't evaluate the long-term effect and safety.

The findings suggest that RYGB had desirable effects on metabolic, although there are risks to be considered.

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