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MINI REVIEW

East Asian perspectives in metabolic and bariatric surgery

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ABSTRACT
The prevalence of diabetes and obesity continues to rise in East Asia. As the risk of diabetes increases at a lower body mass index (BMI) in East Asians than in Europeans, the threshold of BMI values for metabolic and bariatric surgery (MBS) is lower in East Asians. MBS is considered upon reaching a BMI of 27.5 kg/m^2 and is recommended at a BMI of ≥ 32.5 kg/m^2, depending on the status of glucose homeostasis. The most commonly performed MBS in East Asia is sleeve gastrectomy, followed by Roux-en-Y gastric bypass (RYGB). Because the incidence of gastric cancer is higher in East Asia than in other regions, concerns regarding surveillance for gastric cancer might be related to a preference for sleeve gastrectomy over RYGB in this region. Even though there is a paucity of data on direct comparisons of the efficacy of MBS among different ethnic groups, the degree of weight reduction in East Asians is not inferior to other ethnic groups. Moreover, studies suggest that the diabetes remission rate in East Asians seemed to be higher than in other ethnic groups. Future studies involving multiethnic groups are necessary to identify possible ethnic differences in diabetes remission and to determine the appropriate BMI threshold for MBS according to ethnicity.

INTRODUCTION
It is estimated that the global prevalence of diabetes will continue to increase from 9.3% in 2019 to 10.9% by 2045[1]. Due to rapid urbanization and nutrition transition, Asia has become an epicenter of the diabetes epidemic[2]. South-East Asia has the third highest world age-standardized prevalence of diabetes (11.3%) after the Middle East and North Africa (12.2%), and the Western Pacific (11.4%). At a country level, China has the world's highest number of people living with diabetes, estimated to be 166 million. The Japan National Health and Nutrition Survey (2003–2012) of individuals aged ≥ 20 years, showed that the age-standardized prevalence of diabetes was 8%[3]. Data from the Korean National Health and Nutrition Examination Survey VII (2016–2018) showed the estimated prevalence of diabetes in Korean adults (age ≥ 30 years) was 13.8%[4].

Compared with Europeans, Asians develop type 2 diabetes at a lesser degree of obesity[5]. There are several explanations for this finding, such as a relatively higher amount of visceral fat than subcutaneous fat in Asians[6], and an impairment in the compensatory increase of the insulin secretory function under insulin resistance[7]. A prospective observational study from the Korean Genome and Epidemiology Study demonstrated that reduced β-cell function and a lack of β-cell compensation for increased insulin resistance were observed in subjects who developed diabetes[8]. Regarding the higher risk of diabetes at the same BMI, the treatment algorithm for type 2 diabetes recommends that BMI thresholds for metabolic bariatric surgery (MBS) should be lowered by 2.5 kg/m^2 for Asian subjects with diabetes[9], as elaborated below.

TREATMENT GUIDELINES FOR MBS IN EAST ASIA
The 2nd Diabetes Surgery Summit (DSS-II) was held in 2015, and the indication for metabolic surgery for individuals with type 2 diabetes was updated and released in 2016[9]. The Chinese Diabetes Society was involved in the development of the DSS-II consensus statement, and the Japan Diabetes Society endorsed the guidelines in the same year. These guidelines recommend that metabolic surgery for Asians can be considered in subjects with a BMI of ≥ 27.5 kg/m^2. The Asia-Pacific Metabolic and Bariatric Surgery Society endorsed the same criteria for metabolic surgery[10]. The Korean Society for Metabolic and Bariatric Surgery (KSMBS)[11] and the Korean Society for the Study of

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Obesity[12] recommend metabolic bariatric surgery when the BMI is ≥35 kg/m^2, or ≥30 kg/m^2 with comorbidities, or ≥27.5 kg/m^2 with uncontrolled type 2 diabetes. However, the Korean Diabetes Association[13] did not adopt the decreased BMI cutoff by 2.5 kg/m^2 because of paucity of data about the long-term results of the MBS in Korean subjects with a BMI of < 30 kg/m^2. Recently, the Japanese Society for Treatment of Obesity, the Japan Diabetes Society, and the Japan Society for the Study of Obesity developed a consensus statement recommending the MBS for subjects with a BMI of ≥ 35 kg/m^2 and subjects with BMI ≥ 32 kg/m^2 if they have diabetes or have two or more non-diabetic obesity-related health disorders[14]. Table 1 shows the available guidelines for the indications of MBS in East Asian countries.

In Korea, the National Health Insurance Service has covered MBS since January 2019. Subjects with a BMI of ≥ 35 kg/m^2, or a BMI of ≥ 30 kg/m^2 with obesity-related comorbidities, can benefit from the coverage. The Japanese National Health Insurance has approved laparoscopic sleeve gastrectomy (SG) and sleeve duodenojejunal bypass (DJB) as highly advanced medical treatments since 2010 and 2018, respectively[14]. Therefore, the costs of these two procedures are partly covered by insurance. Taiwan provides only partial coverage for bariatric surgery and China does not provide any national health insurance for bariatric surgery[15].

MECHANISMS OF METABOLIC IMPROVEMENT OF MBS

The diabetes remission rate after the MBS was estimated to be around 30–63%[9], which is hardly to be expected with current medical treatment. The improvement of glucose metabolism is related to multiple factors including decreased calorie intake, weight loss, changes in gut physiology, restored beta-cell function, and improved insulin sensitivity[16]. Among these features, gut hormones such as glucagon-like peptide-1 and peptide-YY were robustly increased at a very early stage after the MBS, and play an important role in energy and glucose metabolism[17]. In addition, the exclusion of foregut (duodenum and proximal jejunum) may also contribute to the improvement of glucose metabolism after MBS[18,19]. The changes in gut derived factors were accompanied by gut adaptation[20], and this intestinal plasticity could be a major driver of the effect of MBS[21]. Interestingly, MBS could attenuate beta-cell senescence[22], which might aggravate beta-cell dysfunction, a critical pathologic mechanism of diabetes in East Asia. Besides the aforementioned mechanisms, other factors such as a redistribution of bile acids, alteration of gut microbiota, and changes of the energy set-point and taste preference have been proposed[23].

THE MBS IN SUBJECTS WITH BMI < 30 KG/M^2

The DSS-II statement[9] is based upon the consistently better glucose-lowering effects of MBS compared with medical

Table 1 | Indications for metabolic and bariatric surgery in East Asian countries

Country	Organization (Year)	Indications
South Korea	Korean Diabetes Association (2021)[13]	• T2D with BMI ≥ 35 kg/m^2 • Uncontrolled T2D with BMI ≥ 30 kg/m^2
	Korean Society for Metabolic and Bariatric Surgery (2018)[11]	• Bariatric surgery: BMI ≥ 35 kg/m^2 or comorbidities with BMI ≥ 30 kg/m^2 • Metabolic surgery: uncontrolled T2D with BMI ≥ 27.5 kg/m^2
	Korean Society for the Study of Obesity (2020)[12]	• BMI ≥ 35 kg/m^2 or comorbidities with BMI ≥ 30 kg/m^2 • Uncontrolled T2D with BMI ≥ 27.5 kg/m^2
Japan	Joint Committee in the Japanese Society for Treatment of Obesity, the Japan Diabetes Society, and the Japan Society for the Study of Obesity (2021)[46]	• BMI ≥ 35 kg/m^2 • BMI ≥ 32 kg/m^2 with diabetes or two or more non-diabetic obesity-related health disorders
China	Chinese Society for Metabolic & Bariatric Surgery, Chinese College of Surgeons, and Chinese Medical Doctor Association (2019)[47]	• BMI ≥ 37.5 kg/m^2 (strong recommendation), BMI 32.5–37.5 kg/m^2 (recommendation) • Comorbidities (≥ 2) with BMI 27.5–32.5 kg/m^2
	Chinese Diabetes Society (2019)[48]	• T2D with BMI ≥ 32.5 kg/m^2 • T2D in the presence of other cardiovascular risk factors with BMI 27.5–32.5 kg/m^2

BMI, body mass index; DJB, duodenojejunal bypass; SG, sleeve gastrectomy; T2D, type 2 diabetes.

treatment, regardless of whether the baseline BMI is above or below 35 kg/m^2. This analysis included randomized controlled trials (RCTs) that were conducted in subjects with type 2 diabetes. Therefore, there is little doubt that individuals with a BMI of < 35 kg/m^2 derive substantial benefit from MBS. However, RCTs including subjects with a lesser degree of obesity (BMI < 30 kg/m^2) are relatively scant. Ji *et al.*[24] reported the results of a meta-analysis to determine the effect of MBS on Asian subjects with type 2 diabetes with a BMI of < 30 kg/m^2. This meta-analysis included single-arm studies and, given the nature of the study design, the quality of the study was not high. Despite this limitation, the study delivered important clinical insights for MBS in Asian populations with lower BMI. The decrease of HbA1c was 2.38% at 1 year and 1.58% at 2 years, which is comparable to a previous meta-analysis[9], including only one Asian study[25] out of 15 studies. This non-Asian-dominant meta-analysis showed a median HbA1c reduction of 2.0% with an observational duration of 6–60 months. Therefore, MBS conducted in subjects with a lower BMI (<30 kg/m^2) might be as effective as that in subjects with a higher BMI in terms of HbA1c reduction. However, a higher baseline BMI is a well-known predictor for higher rates of remission of diabetes[26]. Moreover, the effect of a higher baseline BMI on the higher propensity for diabetes remission was more prominent in a meta-analysis that included Asian studies[27]. Taken together, these data suggest that we need more clinical information regarding the effect of MBS on East Asian populations with a BMI of < 30 kg/m^2. Several studies have evaluated the effect of MBS in subjects even with a normal BMI. Heo *et al.*[28] reported that six out of nine Korean subjects (mean BMI, 23.1 kg/m^2) with type 2 diabetes showed remission or improvement of diabetes after 1 year. Cui *et al.*[29] also showed that 48 out of 58 Chinese subjects (mean BMI, 23.9 kg/m^2) with type 2 diabetes discontinued antidiabetic medications and achieved a complete remission after 1 year. Despite these findings, there is still insufficient evidence to recommend a low BMI cutoff point.

TYPES OF THE MBS PERFORMED IN EAST ASIA

Standard procedures of MBS are the Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), adjustable gastric banding (AGB), and biliopancreatic diversion (Figure 1)[9]. According to a survey by the International Federation for the Surgery of Obesity and Metabolic Disorders, sleeve gastrectomy (53.6% of total MBS in 2016) and RYGB (30.1%) were the most commonly performed procedures worldwide[30]. In the Asia-Pacific region, SG accounted for 69% of MBS procedures and RYGB only 10%. The most commonly performed MBS was also SG (74.4% in 2019 and 71.9% in 2020) in the registry of the KSMBS, and the number of RYBG was much less than that of SG (15.2% in 2019 and 13.2% in 2020). The main reason why RYGB has been performed less frequently is probably because endoscopic gastric cancer screening is difficult after this procedure. However, SG seems to be less effective in diabetes remission compared with RYGB[31]; therefore, a bypass procedure is also necessary for Asian subjects who need more sustainable metabolic benefits. Resectional RYGB, a procedure that combines RYGB and stomach removal, can be applied, but this procedure is recommended only in very limited situations [32]. In fact, the occurrence of gastric cancer in the remnant stomach after RYGB is reported to be rare.[33] However, the overall disease-related mortality rate is high, as much as 33.3% in 17 cases. Therefore, the development of an effective screening tool for gastric cancer is necessary to ensure the safety of RYBG in Asians.

To overcome the limitation of gastric cancer screening and the relatively lower efficacy of simple restriction surgery, sleeve duodenojejunal bypass has been introduced and frequently performed in Taiwan and Japan[15]. Lee *et al.*[34] reported that sleeve DJB was superior to sleeve gastrectomy in subjects with type 2 diabetes in terms of excessive weight loss (EWL) (87.2 ± 14.9%

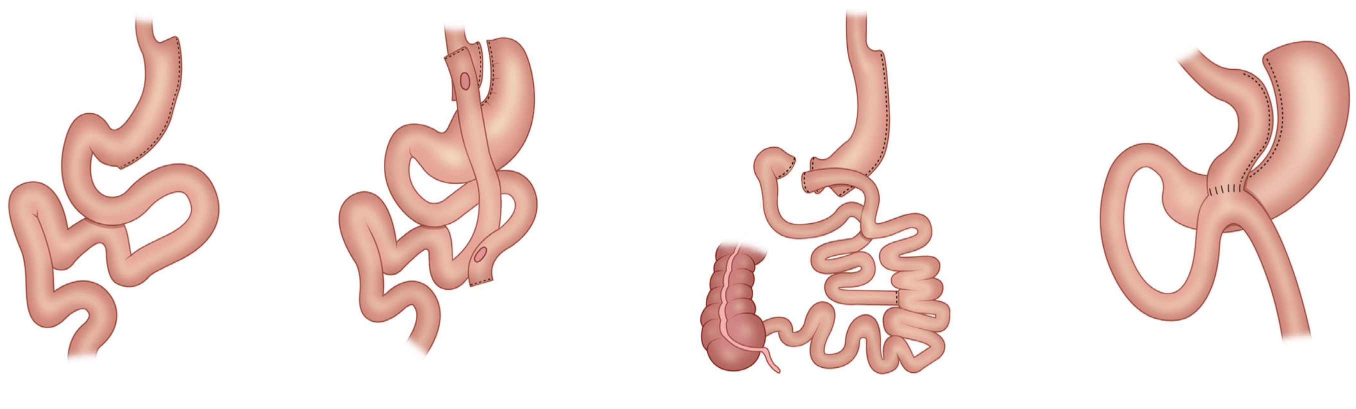

Figure 1 | Types of metabolic and bariatric surgery performed in East Asia. (a) Sleeve gastrectomy, (b) Roux-en-Y gastric bypass, (c) sleeve duodenojejunal bypass, (d) mini gastric bypass (one anastomosis gastric bypass).

in sleeve DJB vs. 67.5 ± 27.0% in SG, $P = 0.023$), and the decrease of HbA1c (2.8% vs. 2.1%, $P = 0.045$) at 1 year after surgery. However, the operation time and hospital stay were longer in sleeve DJB than in SG. Complications were also numerically higher in sleeve DJB compared with SG. Single-anastomosis DJB-SG (SADJB-SG) is a simplified technique of sleeve DJB and has the advantage of reducing operation time compared with sleeve DJB with dual anastomoses[35]. Another variation of metabolic surgery is the mini gastric bypass (one anastomosis gastric bypass). Among various procedures of metabolic surgery, one anastomosis gastric bypass exhibited significantly higher efficacy in the total body weight loss and type 2 diabetes remission at 1 year after surgery compared with other procedures (RYGB, SG, sleeve DJB, and SADJB-SG) among 1,016 patients who underwent MBS from Taiwan, Japan, and Hong Kong[36]. In this study, any type of bypass procedure was associated with better outcomes compared with SG. Therefore, application of a bypass procedure in addition to sleeve gastrectomy can be considered in selected subjects, although a large-scale study is necessary to confirm its benefit relative to risk and to reveal any long-term effects.

LONG-TERM OUTCOME OF THE MBS IN EAST ASIA

In a multicenter retrospective cohort study from Korea, 261 subjects with obesity were included between January 2008 and February 2011[37]. From this cohort, 137 subjects were followed up for more than 5 years. The total weight loss was 24.9% in the surgical group and 2.8% in the conventional treatment group[38]. A larger study[39] including East Asian patients ($n = 463$) from 5 Chinese, 9 Korean, and 10 Japanese institutes, showed 25.1 ± 11.0% of total weight loss at 3 years after surgery, and 23.7 ± 10.7% at 5 years after surgery. Excessive weight loss was 85.3 ± 116.5% and 91.9 ± 231.2% at 3 years and 5 years after surgery, respectively. The surgical procedures performed in this retrospective study were SG, RYGB, and sleeve DJB. A multi-institutional survey from Japan reported 26% and 32% weight loss after SG and sleeve DJB, respectively at 5 years[40]. Another 5-year study from a multiethnic Asian population[41], including 41.5% Chinese, showed 47.3% and 47.7% of EWL after SG and RYGB, respectively. Therefore, although the follow-up rate and individual outcome varied across these studies, the long-term outcome for weight loss looks promising.

In terms of diabetes remission, Asian-dominant studies showed a better outcome than non-Asian populations. For example, Kim *et al.*[42] reported a difference in the effects of bariatric surgery between Asian and non-Asian populations including 37 RCTs through April 2019. This meta-analysis showed a higher diabetes remission rate at 2 years in Asian populations compared with non-Asian populations (67.2% vs. 56.3%). In the aforementioned East Asian study[39], 463 subjects showed a high diabetes remission rate of 64.2% at 3 years and 51.4% at 5 years. Further studies that include diverse ethnicities may provide direct evidence for the differences in the effects of metabolic surgery between Asian and non-Asian populations.

To observe mortality data after MBS, more than 10 years of observation is needed. The Swedish Obese Subjects study is a good example that demonstrates the association between MBS and reduction in overall mortality[43]. Among East Asian countries, the Taiwan Diabesity Study (TDS) is the largest study planned to evaluate mortality and end organ damage in overweight and/or obese patients with type 2 diabetes receiving metabolic surgery compared with conventional medical treatment[44]. The Taiwan Diabesity Study enrolled 126 subjects who received MBS and 890 subjects who have been under medical treatment since March 2014. The long-term outcome from this study will provide more concrete evidence about the influence of MBS on mortality.

PREDICTION OF DIABETES REMISSION AFTER MBS

The most remarkable benefit of the MBS is a profound improvement in glycemic control, which often comes as a remission of diabetes. Therefore, a good prediction model for diabetes remission would be very helpful to select surgical candidates. Currently various diabetes remission prediction models have been developed. Among them, ABCD and Dia-Rem have been widely validated[45]. The ABCD scoring system includes age, BMI, C-peptide, and diabetes duration (therefore, the acronym ABCD was adopted) and was originally developed based on the data of Taiwanese[26] and subsequently validated mainly by Asian studies. The meta-analysis with regard to the ABCD score showed a good predictive power with an area under the receiver operating characteristic curve of 0.79 and 0.80 at 1 year and more longer-term follow up, respectively[45].

CONCLUSIONS

Metabolic bariatric surgery is a good option for the management of diabetes and obesity in East Asians. Previous studies reported that the efficacy of MBS in Asians is not inferior and sometimes even superior to that in non-Asians. However, data on which type of surgery is more appropriate in this population in terms of both efficacy and safety remain scarce. Given that a lower BMI at baseline might be associated with less effective outcomes after MBS, analysis of data on the performance of MBS in subjects with a lesser degree of obesity (BMI < 27.5 kg/m^2) is necessary. Furthermore, considering the early deterioration of β-cell function in East Asians with diabetes, the early application of MBS might be beneficial for this group. Further large-scale long-term follow-up studies should be performed to answer this question.

DISCLOSURE

The authors declare no conflict of interest.
Approval of the research protocol: N/A
Informed Consent: N/A
Approval date of Registry and the Registration No. of the study/trial: N/A
Animal Studies: N/A

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