Diabetes burden in Asia: the role of metabolic surgery

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Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Type 2 diabetes mellitus (T2DM) is one of the largest epidemics the world has ever faced. As a result of rapid economic development and urbanization, Asia has the fastest-growing population affected by T2DM worldwide due to the shift to a sedentary lifestyle and over-nutrition status. The understandings of genetic predisposition have elucidated the potential connection between obesity and T2DM in the Asian populations. On the other hand, the Asian populations tend to have android adiposity, which may further contribute to the pathogenesis of T2DM. In this article, we'll discuss the potential role of metabolic surgery in the management of T2DM in the Asian populations.

Keywords: Type 2 diabetes mellitus (T2DM); Asia; genomics; visceral adiposity

Received: 05 December 2016; Accepted: 20 December 2016; Published: 11 February 2017.
doi: 10.21037/ales.2017.01.04
View this article at: http://dx.doi.org/10.21037/ales.2017.01.04

Diabetes as a global epidemic

Diabetes mellitus (DM), characterized by clinical symptoms and signs of chronic hyperglycemia, is one of the largest and fastest-growing epidemics the world has ever faced. The non-communicable diseases (NCD) Risk Factor Collaboration stated that the number of adults with DM worldwide increased from 108 million in 1980 to 422 million in 2014 due to rise in prevalence, population growth and aging (1). According to the global estimate of International Diabetes Federation (IDF), there were 415 million people affected by DM in 2015, and the number will rise up to 642 million, which equals to a prevalence of 10% (2). DM can be categorized into several different types according to their distinctive pathophysiology. Among these various types, type 2 DM (T2DM) is the one mainly responsible for the current global epidemic, both in developed and developing countries (3). Being aware of the rapidly escalating menace of DM as a NCD, the United Nations (UN) General Assembly passed Resolution 61/225 in 2006, which stated that DM should be recognized as an international public health challenge and for each nation to target prevention and control of the emerging threat (4). In 2011, the UN General Assembly made a political declaration on the prevention and control of NCDs (5). In 2012, the World Health Organization (WHO) declared to reduce 25% of premature mortality from NCDs by 2025 (6). While the fight against T2DM has become a global issue, in this article we'll focus on the burden of T2DM and the role of metabolic surgery in Asia.

Diabetes burden in Asia

Being the most populated area around the world, Asia has the fastest-growing population affected by T2DM, with many Asian countries suffer from folds of increase in disease prevalence (1,2). In 2015, the estimated population with DM in Asia was around 232 million (2). In China, the prevalence of T2DM has increased from 0.9% in 1980 to 10.6% in 2015 (2,7). In Malaysia, the prevalence of T2DM has increased from 2.1% in 1982 to 16.1% in 2015 (2,8,9).

In Indonesia, the prevalence of T2DM has increased from 1.6% in 1981 to 5.7% in 2015 (2,9,10). In India, an astounding high prevalence of T2DM (18.2%) was noticed in the urban area (11). It is generally believed that changes in lifestyle and dietary patterns due to rapid economic and social development are the major factors associated with the rapid growth of T2DM in Asia, especially in developing countries (12). Urbanization and westernized diet have led to sedentary lifestyle and over-nutrition- both are well-established risk factors for T2DM. The healthcare cost for T2DM increases as complications gradually occur or when hospitalization, surgery, or treatment of newer medications is required. However, despite of the rapid economic growth, wealth inequality is rather common in developing countries in Asia. In the lower economic groups, up to 34% of their income might have to be spent to cover costs for the care of diabetes (13,14). Together with scarcity of adequate health-care facilities and low educational status, these phenomena have undoubtedly lay obstacles in optimizing care for T2DM.

Genetic predispositions

Genome-wide association studies (GWAS) have identified many susceptible genes for T2DM in Asian population, including *TCF7L2* (15,16), *PPARG* (17), *SLC30A8* (17), *HHEX* (17), *IGF2BP2* (17), *CDKN2A/CDKN2B* (17), *FTO* (17), *CDKAL1* (17,18), *KCNQ1* (19,20), and *KCNJ11* (21). Among these genes, *FTO* was found to be associated with the risk of T2DM and obesity in Asian populations. Genomic study performed in 3,041 patients with T2DM and 3,678 control subjects of Asian ancestry from Hong Kong and Korea identified the association between *FTO* and increased risk of T2DM. Furthermore, the A allele of rs8050136 at *FTO* was associated with increased body-mass index (BMI) (22). Chang *et al.* identified the rs9939609 A allele of *FTO* was strongly associated with obesity and BMI in the Chinese population, with each additional copy of the rs9936609 A allele was associated with a BMI increase of approximately 0.37 kg/m^2 (23). Further studies targeted on specific population groups also consistently confirmed the association of *FTO* with obesity-related traits in Chinese, Japanese, Koreans, Vietnamese, Filipino, Malay, and Asian Indian populations (24). In a meta-analysis that combined data of 96,551 individuals of Asian ancestry, each additional minor allele increases the risk of obesity by 1.25-fold, which is similar to the effect seen in European populations. Despite the increase in BMI for each additional minor allele is less than in those with European ancestry, it might reflect the differences in adiposity phenotype in Asian populations (25).

Visceral adiposity in Asian populations

Asians generally have a lower BMI than do people of many other races, with a different body composition. Abdominal obesity and adiposity is a characteristic feature in many Asian populations, especially in Southeast Asia (12). Compared to Caucasians with similar waist circumferences, Asians tend to have more visceral adipose tissue (VAT) (26). Excess VAT is known as an independent risk factor for T2DM, and is more strongly correlated to the disease states than subcutaneous adipose tissue (SAT) (27-29). Increased lipolysis originated from excess VAT leads to the elevation of non-esterified fatty acids and triglycerides in blood and skeletal muscle, which hinders muscular utilization of glucose. Excess VAT also increases insulin resistance by changing the secretion of cytokines, especially of leptin and adiponectin (30), and leads to pro-inflammatory conditions (31).

Effects of metabolic surgery on adiposity

Most studies which focused on the change of fat mass deposit found significant reductions in both VAT and SAT within the first few months after metabolic surgery. However, studies with longer post-operation follow-up durations revealed further declines in VAT instead of SAT (32). In patients who received Roux-en-Y gastric bypass, Faria *et al.* identified that the reduction of VAT served as an indicator of the remission of metabolic syndrome 1 year after the procedure, even with identical BMI and SAT area (33). Studies also demonstrated reduction of plasma leptin and elevation of plasma adiponectin levels after metabolic surgery (32), which might suggest potential improvement to the obesity-related low-grade inflammation and the associated metabolic disorders. These lines of evidence might suggest a specific role of metabolic surgery in the management of T2DM in obese Asian patients. Indeed, the IDF statement declares that metabolic surgery is an appropriate management for obese T2DM patients who fail to achieve treatment targets with medical therapies, and the BMI cut-off point for intervention should be lower in Asians populations compared to other races (*Table 1*) (34).

Table 1 Eligibility and prioritization for metabolic surgery in Asian populations not achieving optimal T2DM control with medical therapy according to the IDF statement

BMI range (kg/m^2)	Eligible for surgery	Prioritized for surgery
<27.5	No	No
27.5–32.5	Yes–conditional*	No
32.5–37.5	Yes	Yes-conditional*
>37.5	Yes	Yes

*, HbA_{1c} >7.5% despite fully optimized conventional therapy, especially if weight is increasing, or other obesity-related co-morbidities, e.g., hypertension and sleep apnea, are not achieving targets on conventional therapies. Adapted from Dixon *et al.* Bariatric surgery: an IDF statement for obese type 2 diabetes (34). T2DM, type 2 diabetes mellitus; IDF, International Diabetes Federation; BMI, body-mass index.

Conclusions

Rapid economic development and urbanization have resulted in a tremendous increase in the prevalence of T2DM in Asia over the past few decades. The genetic predisposition and distinct body composition create a unique association among obesity, adiposity and the pathogenesis of T2DM in the Asian populations. With the effects on body weight reduction as well as change of the configuration of adipose tissue, the role of metabolic surgery in the management of T2DM in the Asian populations warrants further investigation.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Wei-Jei Lee) for the series “Laparoscopic Metabolic Surgery for the Treatment of Type 2 Diabetes in Asia” published in *Annals of Laparoscopic and Endoscopic Surgery*. The article has undergone external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2017.01.04). The series “Laparoscopic Metabolic Surgery for the Treatment of Type 2 Diabetes in Asia” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/ales.2017.01.04
Cite this article as: Lin CH, Chuang LM. Diabetes burden in Asia: the role of metabolic surgery. Ann Laparosc Endosc Surg 2017;2:21.

