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REVIEW

Metabolic and bariatric surgery in an era of anti-obesity medication

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The global obesity epidemic has been well described. In South Africa (SA) in 2017, 68% of women and 31% of men were overweight or obese, defined as having a body mass index (BMI) ≥ 25 kg/m^2. Obesity is a complex, chronic, and progressive disease with severe metabolic, mechanical, and mental complications, with a clearly associated increased risk for premature cardiovascular and cancer deaths. Lifestyle and behavioural modification (diet and exercise) form the basis of weight gain prevention. However, it is a sustainable treatment option for very few patients. Metabolic and bariatric surgery (MBS) has evolved into the cornerstone for long-term, durable treatment of obesity, with robust evidence supporting its cost-effectiveness and decreased mortality. There is increasing evidence of the efficacy of anti-obesity medications (AOMs) in achieving weight-loss outcomes comparable to those of surgery. Both highly effective treatment options remain underutilised by health insurers and the National Department of Health and are mostly inaccessible to South Africans. This review examines the evolving global and local relationship between surgical and pharmacological approaches to obesity treatment.

Keywords: metabolic surgery, bariatric surgery, anti-obesity medication

The changing landscape of obesity in South Africa

Severe obesity, defined as a body mass index (BMI) ≥ 35 kg/m^2, is the fastest growing obesity class in South Africa (SA), with 30% of women and 6% of men aged 55–64 years living with severe obesity in 2017.[1] More concerning is the 13% of children under five years of age who were overweight or obese in 2017, a population now entering adolescence. With the last SA population surveys conducted nearly a decade ago, it is important to note that the known SA prevalence numbers are dated and likely a gross underestimation.

The Lancet Commission recently defined "clinical obesity" as "a chronic, systemic illness characterised by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity."[2] When tissue dysfunction becomes the focus of defining the disease, rather than weight measurements alone, the gross underestimation of disease prevalence in sub-Saharan Africa is reflected in the alarming rise in type 2 diabetes (T2D) prevalence and death due to stroke and ischaemic heart disease.[3-5]

Increased sedentary lifestyles and the availability of affordable, highly processed food are international drivers of obesity. In SA, cultural perceptions of body weight and socioeconomic determinants of health (urbanisation, the "nutrition transition", education/health literacy, and employment status) continue to play a role and remain targets for preventative strategies.[6,7] Uncovering the pathophysiological basis of obesity has shed light on the role an increased appetite plays in the inability to reduce weight once it has been gained.[8] This increase in appetite, when weight comes down, is not under conscious control and has become the main target in treatment strategies.

The direct cost of obesity to SA's public healthcare system was estimated to be approximately R33.2 million (15% of government health expenditure) in 2020 when considering medication, outpatient visits, hospitalisation, diagnostic procedures, and treatment of comorbidities in diagnosed cases (direct costs of obesity).[9] When indirect costs due to productivity losses (absenteeism and decreased productivity) are added, the cost to private health insurers in SA is estimated at R701 billion annually.[10]

The metabolic consequences of obesity (T2D, hypertension, and dyslipidaemia) are well known. However, recent cumulative evidence regarding metabolic dysfunction-associated steatotic liver disease (MASLD) and obstructive sleep apnoea among the ± 200 recognised complications of obesity makes the disease a truly multidisciplinary challenge. In sub-Saharan Africa, there is a data gap regarding MASLD, but superimposed on an already high prevalence of viral and alcoholic hepatitis, it is likely to follow international trends where MASLD has become the leading cause of liver disease.[11] With T2D recognised as an independent risk factor for MASLD, the incidence increases according to rising rates of especially childhood obesity in low- to middle-income countries.[12] The lack of awareness regarding MASLD, imprecise diagnostic methods, and ineffective preventive interventions add to significant disease and economic consequences.

Metabolic and bariatric surgery – state-of-the-art

Laparoscopic sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are the two most common metabolic and bariatric surgery (MBS) procedures, with single anastomosis duodeno-ileal bypass and one anastomosis gastric bypass recently acknowledged by the International Federation for the Surgery of Obesity (IFSO).[13,14] Although MBS is performed laparoscopically with a perioperative risk equivalent to laparoscopic

cholecystectomy, SG is associated with a 30% risk of increased gastro-oesophageal reflux disease, and RYGB is associated with a risk for long-term bowel obstruction due to internal herniation or jejunojejunal intussusception.[15] The occurrence of Barrett's oesophagus in 12% of patients after SG is now agreed to warrant postoperative endoscopic surveillance, and although hernia sites are closed at the time of RYGB, the herniation risk remains at 1% per year.[16]

Long-term outcomes after MBS confirm durable weight loss, resolution of T2D and other comorbidities, and decreased cardiovascular events, cancers, and mortality.[17-20] Current indications for MBS include individuals with a BMI > 35 kg/m^2, regardless of the presence, absence, or severity of comorbidities, and individuals with metabolic disease and a BMI of 30–34.9 kg/m^2.[21]

Access to MBS in SA is currently limited to large urban areas, mostly in Gauteng and the Western Cape. Meanwhile, insurer coverage is limited to the most comprehensive plans. Endoscopic sleeve gastroplasty is available for patients reluctant or unable to undergo surgery and intragastric balloon placement for preoperative optimisation in patients with severe obesity.[22]

Anti-obesity medications – the new frontier

The arrival of anti-obesity medications (AOMs) in SA, including glucagon-like peptide-1 (GLP-1) receptor agonists like semaglutide and GLP-1/glucose-dependent insulinotropic polypeptide (GIP) combinations like tirzepatide, draws attention to the 15–22% total body weight loss achieved with their use.[23,24] Both drugs are classified as incretins, and their mechanism of action includes appetite suppression and delayed gastric emptying. These injectable drugs are well tolerated with minimal gastrointestinal side effects, the most notable being delayed gastric emptying (nausea and vomiting), requiring consideration of a dose omission before general anaesthesia and/or upper gastrointestinal endoscopy.[25]

The only absolute contraindication to their use is a personal or family history of medullary thyroid carcinoma and/or multiple endocrine neoplasia syndrome type 2. As seen after MBS, the resolution of comorbidities following AOM initiation follows weight-loss trajectories, and their rapid, positive effect on cardiovascular risk seems to extend beyond weight loss.[24,26] Regaining up to two-thirds of lost weight after cessation implies the need for long-term treatment.[27]

Surgical versus medical obesity management

Although the effect of AOMs on weight and resolution of comorbidities is now approaching that seen after MBS, with an expected weight loss of 15–22% versus 25–35%, respectively, there are no head-to-head comparisons available.[17,23,24] The robust long-term (30-year) data supporting MBS as the most effective and sustainable current weight and comorbidity management option is still lacking for AOMs. Likewise, although the AOMs are safe and well-tolerated in available published studies, their long-term effects remain unknown. Surgery carries a higher upfront cost with a low, yet well-known, risk of long-term complications. Medications require long-term patient compliance with concern regarding long-term cost and side effects.

The goal of obesity management is shifting towards achieving health rather than chasing a target weight or BMI.[8] Because obesity is a chronic, relapsing disease, management strategies take a complementary and synergistic approach rather than a competitive one, and randomised controlled comparisons are unlikely to contribute. Furthermore, as MBS is currently funded by limited private health insurers in SA, restricted to comprehensive coverage, and available in only three government centres in SA, the task ahead is to establish patient access to healthcare providers and units knowledgeable in obesity management.

Despite the ongoing approval of AOMs by the South African Health Products Regulatory Authority (SAHPRA) for use in obesity, they are not yet covered for this indication by health insurers and are not available to government pharmacies. Thus, the challenge in SA remains one of increased awareness of the chronic disease status of obesity, the excellent outcomes achievable with multidisciplinary treatment, and the cost-effectiveness of treating the upstream driver of the multitude of obesity associated comorbidities.

Conclusion

The development of obesity guidelines in SA will allow a framework for integrated multidisciplinary clinician decision-making and personalised treatment of obesity in a resource-constrained setting. With a multitude of AOMs in the pipeline, costs are expected to decrease over time, allowing for more affordable options. Medical management may be more appropriate in patients with less severe obesity and those reluctant to undergo surgery, while MBS may be more suitable for patients with severe obesity and multiple comorbidities. The immediate challenge in SA is to prioritise obesity as a disease and understand the cost implications if left untreated. Research gaps include current disease prevalence and defining BMI correlates and treatment response for local ethnic groups.

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