Review Article :

Review on Bariatric Surgery in Human Immunodeficiency Virus Patients.

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Abstract

Bariatric surgery (BS) is a surgical intervention that aims to reduce excess body weight and improve obesity-related comorbidities. Obesity is a growing health problem among patients with human immunodeficiency virus (HIV) infection, especially with the widespread use of antiretroviral therapy (ART). However, there is limited evidence on the safety and efficacy of bariatric surgery in this population. This review summarizes the current knowledge on bariatric surgery in HIV patients, focusing on the types of procedures, the impact on HIV-related outcomes, antiretroviral considerations, concerns, and possible complications. The available data suggest that bariatric surgery is safe and well tolerated in HIV-infected individuals and does not adversely affect HIV disease progression or virologic suppression. However, bariatric surgery may increase the risk of postoperative complications such as strictures and micronutrient deficiencies and may require adjustments in ART regimens due to altered pharmacokinetics. Therefore, careful selection of candidates, multidisciplinary collaboration, and close monitoring are essential for optimal outcomes. Further studies are needed to evaluate the long-term effects of bariatric surgery in HIV patients and to compare different surgical techniques.

Keywords:
Bariatric surgery, HIV infection, Obesity, Antiretrovirals, People living with HIV.

Introduction

The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS), characterized by a compromised immune system and an increased risk of developing opportunistic infections and malignancies [1]. Since its inception, the World Health Organization (WHO) estimates that there have been 40,1 million fatalities from about 84.2 million infection cases. Recent findings in 2021 reveal that 38.4 million people were infected with HIV around the globe [2].

According to the Ministry of Health, the incidence of HIV in Saudi Arabia was

3 cases per 10,000 population in 2018, which is lower than the global average of 7.1 cases per 10,000 population. However, this number may not reflect the burden of the disease, as there may be underreporting and stigma associated with HIV testing and diagnosis [3]. More recently the World Health Organization claimed that in 2020, about 12,000 people in Saudi Arabia had HIV [4].

Since the discovery of the country's first AIDS patient in 1984, Saudi Arabia has struggled with issues related to HIV infection surveillance, prevention, and treatment [3]. Such issues include limited awareness and cultural and religious factors contributing to the stigma and misunderstanding surrounding HIV in the region [5]. In addition, the surveillance of HIV is challenging despite the availability of medical care and effective antiretroviral therapy. Furthermore, progress towards meeting the WHO's 90-90-90 goals for HIV is not being systematically monitored [5,6]. These challenges highlight the need for resilient treatment methods and preventive measures.

However, the treatment of HIV infection in Saudi Arabia has improved over the years, with the introduction of effective antiretroviral therapy (ART) that can suppress viral replication and improve survival and quality of life. The ART coverage rate was estimated to be 90% in 2018, higher than the regional average of 64% [6]. However, there are still gaps and barriers in accessing and adhering to ART, such as lack of awareness, social stigma, discrimination, fear of disclosure, and side effects.

One such side effect is the development of obesity, a condition characterized by excess body fat, clinically described as BMI ≥ 30 kg/m2 or waist circumference ≥ 102 cm or ≥ 88 cm for men and women, respectively, that can increase the risk of various chronic diseases, estimated to have a national prevalence of 24.7% in Saudi Arabia [7].

Co-infection with HIV and obesity can negatively impact individuals' health and quality of life. This is because systemic inflammation, which may be caused by differences in adipose tissue's innate and adaptive immune cell composition, is linked to HIV infection and obesity [8]. Obesity can impair the immune system and increase the susceptibility to opportunistic infections, which are common among people living with HIV. Obesity can also interfere with the pharmacokinetics and efficacy of antiretroviral therapy (ART), the mainstay of HIV treatment. Moreover, obesity can exacerbate the metabolic complications of HIV and ART, such as dyslipidemia, insulin resistance, and cardiovascular disease [9]. The increased risk of

metabolic disorders in people living with HIV (PLWH) may be due to a combination of variables, including those unique to HIV and obesity.

The treatment plan for obesity among HIV patients to reduce these adverse effects is mainly aimed at achieving weight reduction, which could include lifestyle modifications, such as dietary counseling, physical activity, and behavioural therapy [10,11]. Pharmacological interventions, such as anti-obesity drugs or bariatric surgery, may be considered for individuals who fail to achieve adequate weight loss with lifestyle modifications [12,13]. Here, we review the current understanding of the role of Bariatric surgery as a treatment option for obesity in people living with HIV.

Hiv And Obesity

In the past, HIV infection was often associated with wasting, a condition characterized by loss of body fat and muscle mass. However, with antiretroviral therapy (ART), which can suppress HIV replication and improve survival, wasting has become less common among PLWH. Instead, many PLWHs face the opposite problem: obesity [9].

The causes of obesity in PLWH are not fully understood. Still, they may involve a complex interplay of factors, such as HIV infection, Adipose tissue, ART use, genetic predisposition, lifestyle behaviors, and metabolic dysregulation [14]. HIV infection can alter the distribution and function of adipose tissue (fat), leading to ectopic fat accumulation (fat in places where it should not be) and inflammation [15]. HIV being a cause of wasting in itself, depleting subcutaneous adipose and visceral adipose tissue reserves suggests it directly affects adipose tissues and can induce metabolic disturbances [16].

According to Koethe et al.[14], the Trans-activator of transcription, Viral protein R, and Negative factor are viral proteins secreted by HIV-infected T cells and macrophages. These proteins target proximal adipocytes imposing several cellular consequences ranging from fibrosis as a result of increased extracellular matrix components production, increased production of proinflammatory cytokines (such as α-smooth muscle actin, tumor necrosis factor, CCAAT/enhancer-binding protein-α, transforming growth factor-β, peroxisome proliferator-activated receptor-γ, lipoprotein lipase, reactive oxygen species, and fatty acid binding protein [4]), as well as reduced adipogenesis, mitochondrial dysfunction, and decreased production of adiponectin and leptin. These processes are inevitable since adipose tissues with latently infected CD4+ T cells and macrophages in subcutaneous and visceral layers serve as

reservoirs for HIV and immune changes, improving tissue inflammation and insulin resistance in obesity.

Furthermore, Some ART drugs, especially older ones, can also affect fat metabolism and cause lipodystrophy. This condition involves changes in body fat distribution, such as fat loss in the limbs and face and fat gain in the abdomen and neck. Additionally, PLWH may adopt unhealthy behaviors, such as physical inactivity and poor diet, due to stigma, depression, or lack of access to resources. These behaviors can contribute to weight gain and obesity [14].

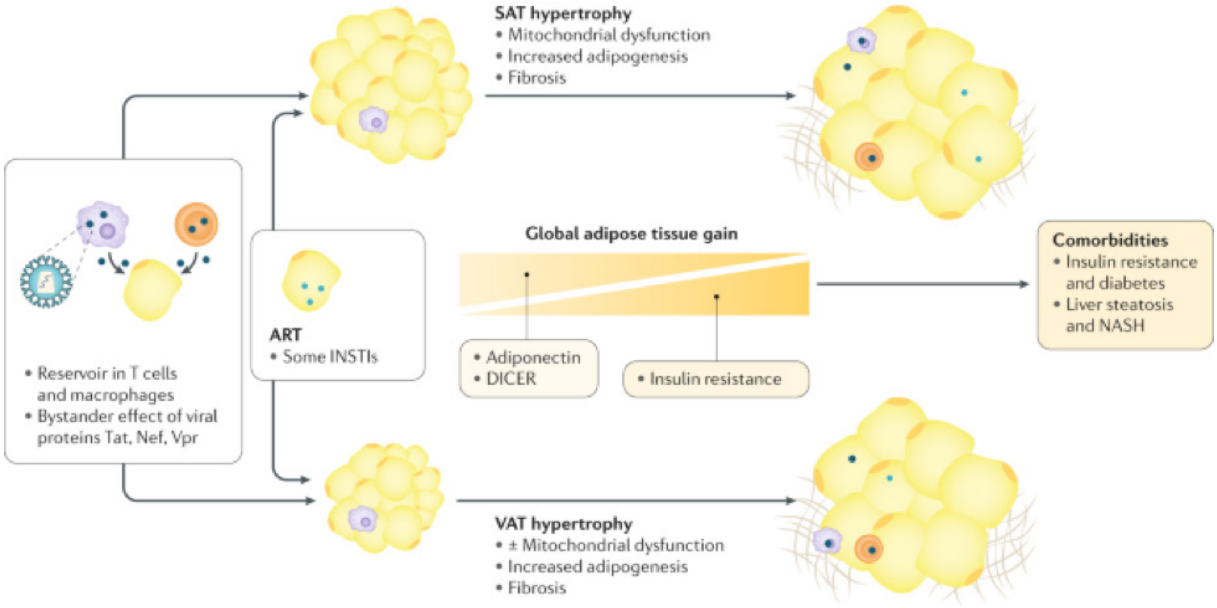


Fig 1: Etiopathogenesis of Obesity in PLWH 14

As shown in Fig 1, certain drugs known as integrase strand transfer inhibitors (INSTIs) can cause changes in fat tissue. These changes include the enlargement of fat cells (adipocyte hypertrophy), an increase in the creation of new fat cells (adipogenesis), increased fibrosis (formation of excess fibrous connective tissue), and problems with the mitochondria. These changes can lead to an overall increase in body fat, including subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT). There can also be an increase in fat in the peripheral parts of the body. As a result of these changes, the body may become less responsive to insulin (a condition known as insulin resistance), and there may be an accumulation of fat in the liver (known as liver steatosis) [14].

Obesity is a growing challenge in the era of effective ART for HIV infection. It poses significant health risks for PLWH and requires comprehensive prevention and treatment strategies. Therefore, addressing obesity in PLWH can improve their quality of life and long-term outcomes.

Bariatric Surgery

Bariatric surgery (BS) is a general term for various surgical operations performed on obese patients to facilitate weight loss and better overall health. It involves making structural and functional changes to the digestive system, most notably by decreasing the size of the stomach or rerouting some food that enters the body around the small intestine. By altering the signals and hormones that control hunger and energy expenditure, bariatric surgery reduces the quantity of food that can be eaten and absorbed [17,18].

BS is usually not a cosmetic procedure but a medical intervention that can significantly benefit people with obesity-related conditions, such as type 2 diabetes and HIV [12]. It requires a lifelong commitment to healthy eating and physical activity to lose weight and prevent complications. It also requires regular follow-up visits with a multidisciplinary team of health professionals, including surgeons, dietitians, psychologists, endocrinologists, and primary care providers [18].

Studies have shown that BS is not widely utilized by eligible patients, partly due to their perception of the risks and benefits of the procedure. One systematic review by Rajeev et al.[19] examined 41 studies that assessed patient and public perceptions of BS using various methods, such as surveys, interviews, focus groups, and vignettes. The review found that many patients and public members overestimated the risks, had unrealistic expectations, and were unfamiliar with BS outcomes. They also reported stigma, discrimination, and negative attitudes toward BS from themselves and others. The review highlighted that perceptions and motivations for BS often varied by race, ethnicity, gender, and age and suggested that patient-centered education in the prereferral stage could improve BS utilization.

In Saudi Arabia, many people have limited knowledge and awareness even though bariatric surgery has proven benefits and safety. Altaf & Abbas[20], in their cross-sectional study conducted in Jeddah between 2016 and 2017, interviewed 1,129 Saudis aged 18 and above, excluding healthcare professionals and people who have had the surgical procedure. According to the study's findings, most participants (97.7%) knew the connection between obesity and comorbidities; however, only 50% knew the appropriate indications for bariatric surgery. In addition to this, 22.7% of the participants had never heard of the operation known as bariatric surgery, and 18.9% of them believed that it was a cosmetic procedure. Additionally, 41.2% of the participants stated that they would not seek

the assistance of a bariatric surgeon even if they were diagnosed with morbid obesity. The authors concluded that the public perspective on obesity and bariatric surgery in Saudi Arabia is limited. To raise public awareness, the authors advocated effective interagency collaboration between surgeons, health educators, and other healthcare practitioners. The study also suggested further research on the barriers and facilitators of seeking bariatric surgery among the Saudi population.

Types Of Bariatric Surgery

There are different types of bariatric surgical procedures, and the commonest among them are Roux-en-Y gastric bypass (RYGB), Sleeve gastrectomy (SG), Laparoscopic adjustable gastric band (LAGB), and Biliopancreatic diversion with duodenal switch (DS). These procedures differ in their mechanisms of action, efficacy, safety, and long-term outcomes, each with advantages and disadvantages [17,21-24].

RYGB is a procedure that involves creating a small pouch from the upper part of the stomach and connecting it to a segment of the small intestine, bypassing the rest of the stomach and the duodenum. This reduces the amount of food intake and alters the hormonal and neural signals that regulate appetite and glucose metabolism. RYGB is considered the gold standard of bariatric surgery as it has been shown to achieve significant and durable weight loss, improve comorbidities, and reduce mortality [21,22].

SG is a procedure that involves removing about 80% of the stomach, leaving a narrow tube-shaped pouch. This reduces food intake and affects the secretion of ghrelin, a hormone that stimulates hunger. SG has gained popularity in recent years as it is technically simpler than RYGB, has fewer complications, and has comparable efficacy in terms of weight loss and improvement in comorbidities [23].

LAGB is a procedure that involves placing an inflatable band around the upper part of the stomach, creating a small pouch above it. The band can be adjusted by injecting or removing saline through a port under the skin. This regulates the opening size between the pouch and the rest of the stomach, controlling the amount of food intake. LAGB is less invasive than RYGB or SG, has lower perioperative risks, and can be reversed. However, LAGB has lower efficacy in weight loss and improvement in comorbidities and requires frequent follow-up visits and adjustments [17].

DS removes a large portion of the stomach and connects the remaining part to a lower segment of the small intestine, creating two separate pathways for food and digestive juices. This results in a very high

degree of malabsorption of calories and nutrients, leading to substantial weight loss and improvement in type 2 diabetes. However, DS also carries a high risk of adverse effects such as malnutrition, diarrhea, foul-smelling stools, and bone loss [24].

Bariatric surgery can be performed safely and effectively in patients with HIV infection who meet the criteria for obesity surgery. However, this population has some special considerations, such as potential interactions between antiretroviral therapy (ART) and bariatric surgery, changes in HIV disease markers such as CD4 cell count or viral load (VL), and nutritional deficiencies [25]. A literature review by Akbari and colleagues found that bariatric surgery had no adverse impact on HIV disease progression or ART absorption and did not significantly affect CD4 cell count or VL. However, they also noted that data on their topic is limited, and more studies are needed to evaluate the long-term outcomes of bariatric surgery in HIV patients [13].

Type of Surgery	Pros	Cons
Roux-en-Y Gastric Bypass (RYGB)	Effective in weight reduction by reducing volume of food, capacity to assimilate fats nutrients and calories	The procedure is technically more intricate compared to the adjustable gastric band or laparoscopic sleeve gastrectomy. It carries risks such as excessive bleeding, infection, adverse reactions to anesthesia, formation of blood clots, respiratory complications, and potential leaks in the gastrointestinal system.
Sleeve Gastrectomy (SG)	Effective in weight reduction by reducing volume of food, capacity to assimilate fats nutrients and calories Results in lower production of the appetite-regulating hormone ghrelin, which may subsequently reduce desire to eat.	It does not interfere with the absorption of calories and nutrients in the intestines. It carries risks such as excessive bleeding, infection, adverse reactions to anesthesia, formation of blood clots, respiratory complications, and potential leaks in the gastrointestinal system.
Laparoscopic Adjustable Gastric Band (LAGB)	The size of the opening between the pouch and the remainder of your stomach influences the amount of weight loss. The size can be adjusted by inflating or deflating the band through a port located beneath the skin of your abdomen.	The adjustable band results in less weight loss compared to the Roux-en-Y gastric bypass (RYGB).
Biliopancreatic Diversion with Duodenal Switch (DS)	Effective in weight reduction by reducing volume of food, capacity to assimilate fats nutrients and calories	It carries risks such as excessive bleeding, infection, adverse reactions to anesthesia, formation of blood clots, respiratory complications, and potential leaks in the gastrointestinal system.

Fig 2: Types of bariatric surgery and their pros and cons [21-24]

Bariatric Surgery In Hiv Patients

According to some studies, BS has effectively treated obesity and its related complications, such as diabetes, hypertension, and cardiovascular disease [18,21]. However, the role of BS as a treatment option for obesity in people living with HIV (PLWH) is less clear. PLWH face unique challenges and risks associated with obesity, such as increased inflammation, immune activation, and viral persistence. Moreover, BS may affect the absorption and efficacy of antiretroviral therapy (ART), which is essential for maintaining viral suppression and preventing disease progression [26].

The most common bariatric procedure for HIV patients is sleeve gastrectomy (SG), which involves removing about 80% of the stomach and creating a tubular pouch. SG has resulted in significant weight loss and resolution of comorbidities such as diabetes, hypertension, dyslipidemia, and obstructive sleep apnea in HIV patients [13,27]. SG also appears to have minimal effect on ART pharmacokinetics and HIV viral suppression as long as appropriate adjustments are made to the drug regimen and dosing [26,27]. However, some studies have reported malabsorption, nutritional deficiencies, and opportunistic infections after SG in HIV patients[28], suggesting close monitoring and supplementation.

Other bariatric procedures reported in HIV patients include RYGB, LAGB, and DS [13,27]. However, they may also result in more significant weight loss and metabolic benefits than SG. Still, available data on these procedures in HIV patients are scarce and primarily based on case reports or small case series [29].

Several positive outcomes have been recorded in using RYGB, SG, and AGB effectively in managing obesity in HIV patients. In their review study of 12 articles, Akbari et al.13 reported the successful use of SG only (N=18) in three studies, RYGB only (N=18) in six studies, and the use of mixed procedures, including SG (N=4), RYGB (N=7), and AGB (N=11) in three studies.

Similarly, in a case study reported by Cimino et al.[27], the successive use of RYGB was reported in a 48-year-old man with a history of HIV and morbid obesity (BMI 43 kg/m2) co-infection. The study revealed that the patient was on a stable antiretroviral regimen of tenofovir/emtricitabine/efavirenz before and after surgery. His CD4 cell count and viral load remained stable at 450 cells/mm3 and undetectable, respectively. He lost 45 kg in the first year after surgery and had no complications or adverse effects related to his antiretroviral therapy.

Fysekidis et al.[30] retrospectively studied 8 female patients (with mean age, preoperative BMI, duration of HIV infection, and CD4 cell count of 46 years, 42 kg/m2, 13.4 years, and 457 cells/mm3, respectively) who have undergone SG to evaluate treatment impact and outcomes on weight loss and markers of HIV. Their research showed that the operation yielded favorable results when performed, with a mean weight reduction of 37 kilograms over twenty months, an excess BMI loss of 80.8 ± 30.9%, and an excess weight loss of 81.5 ± 28.9%. There was no change in the CD4 count, and most of the patient's comorbidities vanished, significantly reducing the cardiovascular risk. The authors advised that SG should be considered an essential part of the treatment option for morbidly obese HIV patients due to its safety and effectiveness.

Alfa-Wali et al.[29] also reported a case of a 46-year-old man with a history of HIV infection since 2001 and morbid obesity (BMI 41 kg/m2) who underwent an AGB in 2012. The patient was on a stable antiretroviral regimen of raltegravir/tenofovir/emtricitabine before and after surgery, and his CD4 cell count and viral load remained stable at 350 cells/mm3 and undetectable, respectively. He lost 35 kg in the first year after surgery and had no complications or adverse effects related to his antiretroviral therapy.

In contrast however, Pucci and Batterham emphasized that although bariatric procedures are generally effective, individual outcomes can vary significantly. According to the authors, some patients may achieve excellent long-term weight loss, while others experience less favorable results in terms of health benefits [31]. Similarly, In their research on the long-term effectiveness of bariatric surgery for treating super obesity, Soong et al. [32] discovered that the group undergoing Roux-en-Y gastric bypass (RYGB) experienced more intraoperative blood loss, a longer duration of operation, and an extended hospital stay compared to the other two groups. Furthermore, the RYGB group had a higher rate of major complications within 30 days post-operation (4.8%) compared to the sleeve gastrectomy (SG) group (0.5%).

Benefits Of Bs In Hiv Patients

Some potential benefits of BS in PLWH are its ability to improve weight loss and metabolic outcomes. Among PLWH, BS has been demonstrated to enhance metabolic markers, including weight loss, blood sugar control, blood pressure, and lipid profiles. These changes can potentially lessen the likelihood that PLWH may develop cardiovascular disease, diabetes, and other complications of obesity [13,18,26].

In their retrospective study, Alfadda et al.[26] reported that BS (sleeve gastrectomy or Roux-en-Y gastric bypass) resulted in significant weight loss and improved metabolic parameters in 91 PLWH over a median follow-up of 3 years.

BS also plays an essential role in reducing inflammation and immune activation, which is beneficial to PLWH by reducing chronic inflammation and immune activation, which are associated with HIV disease progression and non-AIDS complications. BS may also enhance the response to antiretroviral therapy (ART) by increasing CD4+ T cell count and decreasing viral load. This role was further explained by the retrospective study of Sharma et al.[25], who suggested that BS may benefit HIV-related outcomes, such as inflammation, immune activation, and viral reservoirs, by reducing adipose tissue mass and improving metabolic health.

BS may improve the quality of life and psychological well-being of PLWH by alleviating obesity-related stigma, depression, anxiety, and low self-esteem [33]. It also improves adherence to ART and other medications by reducing pill burden and simplifying dosing regimens [34]. In their cross-sectional study to assess the quality of life following BS, Alotaibi et al.[33] revealed a fair to average quality of life among the 400 participants recruited for their study. According to the authors, participants' sociodemographic characteristics, including marital status, nationality, educational level, age, gender, and history of chronic disease or comorbidities significantly associated with the quality of life experienced by respondents.

Concerns And Limitations Of The Use Of Bs In Hiv Patients

One of the main concerns is the potential impact of bariatric surgery on the pharmacokinetics of antiretroviral therapy (ART), which is essential for maintaining viral suppression and preventing HIV-related complications. Bariatric surgery may alter the absorption, metabolism, distribution, and excretion of ART drugs, depending on the type of surgery and the drug class [27]. For example, RYGB and SG may reduce the absorption of protease and integrase inhibitors, requiring an acidic environment for optimal dissolution. BS may also affect the bioavailability of drugs that undergo extensive first-pass metabolisms, such as efavirenz and rilpivirine. In addition, bariatric surgery may alter the volume of distribution and clearance of highly protein-bound drugs or have a high extraction ratio, such as darunavir and atazanavir [26,34]. Therefore, ART drug levels and viral load monitoring are recommended before and after bariatric surgery in PLWH, and

dose adjustments may be necessary to ensure adequate exposure and efficacy.

Furthermore, BS may cause nutritional deficiencies and complications due to reduced food intake, malabsorption, vomiting, diarrhea, dumping syndrome, and altered food preferences. These may include anemia, osteoporosis, protein malnutrition, vitamin B12 deficiency, thiamine deficiency, and neurological disorders. Therefore, nutritional assessment and supplementation are essential after BS in PLWH [35].

BS may also have surgical complications and mortality risks similar to or higher than the general population. These may include bleeding, infection, leakage, stricture, ulceration, bowel obstruction, hernia, pulmonary embolism, and cardiovascular events. Therefore, careful selection and evaluation of candidates for BS are necessary for PLWH [36]. Another concern is how efficient and safe bariatric surgery is in PLWH compared to non-HIV-infected individuals. Although limited data are available, reports have shown that BS is safe and effective in PLWH, with no significant adverse effects on HIV disease progression or immune status. A literature review by Akbari et al.[13] found that bariatric surgery did not negatively impact CD4 cell count or viral load in PLWH, regardless of the BS type. Moreover, BS resulted in weight loss and improvement of obesity-related comorbidities in PLWH. However, these studies were mostly retrospective and had small sample sizes, so more prospective and comparative studies are needed to confirm the long-term outcomes of bariatric surgery in PLWH.

Conclusion

In conclusion, BS may offer some benefits for PLWH with morbid obesity and metabolic syndromes, such as weight loss, metabolic improvement, neuropathy relief, and possibly reduced HIV-related inflammation and viral persistence. However, BS also poses some risks and challenges for PLWH, such as altered ART pharmacokinetics and pharmacodynamics, requiring careful monitoring and adjustment of ART regimens before and after surgery.

Moreover, the long-term safety and efficacy of BS in PLWH are still uncertain due to the limited evidence available. Future research is also needed to explore the potential long-term implications of BS on patients' physical appearance. The changes can be significant and may lead to a need for subsequent cosmetic surgery. This, in turn, can have profound effects on patients' self-esteem and confidence. However, the interplay of these factors is complex and multifaceted, involving not only physical changes but also psychological and social dimensions. It is also crucial to consider

the individual patient's perspective, as the perceived need for cosmetic surgery can vary widely among patients. While this review touches upon these issues, a comprehensive exploration of these dimensions is beyond its scope.

Therefore, more research is needed to determine the optimal indications, procedures, long-term outcomes, and follow-up strategies for BS in PLWH. This will help to ensure that the benefits of BS are maximized, while the risks are minimized, for this unique patient population.

Conflict Of Interest

There is no conflict of interest.

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