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# EVALUATION OF THE GLYCEMIC PROFILE OF PATIENTS UNDERGOING BARIATRIC SURGERY: LITERATURE REVIEW

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**Abstract:** Obesity is a global epidemic that affects billions of adults, impacting on the development of various diseases such as Type 2 Diabetes Mellitus (DM2), hypertension, dyslipidemia, cancer and kidney disease. It is postulated that alterations in lipid and glucose metabolism, linked to overweight and obesity, can trigger insulin resistance, cell dysfunction and DM2. Considering the large number of overweight and obese individuals with DM2, the Federal Council of Medicine recognizes the importance of bariatric surgery for the treatment of patients with DM2. Bariatric surgery is recommended as an anti-obesity treatment for patients aged between 18 and 65 with a body mass index (BMI) of over 40 or over 35 kg/m² associated with severe comorbidities and refractory to non-pharmacological and pharmacological treatment. This literature review study aims to evaluate the effect of bariatric surgery, using the gastric *bypass* method, on fasting blood glucose and plasma glycated hemoglobin (HbA1c) concentration in patients with a previous diagnosis of diabetes. A total of 1053 individuals were analyzed, with ages ranging from 40.00 to 53.00 years and postoperative periods of 0.5, 1, 2, 3, 4 and 5 years. The mean glycemia (187.05 ± 30.90 mg/dL) and HbA1c (8.58 ± 0.92 %) values found in the pre-surgery stage, which were compatible with diabetes, decreased to the pre-diabetes range, respectively, to mean values of 109.33 mg/dL and 6.25% one year after surgery. Over the years, the reduction in glycemic parameters was smaller. In this context, it can be considered that the reduction of obesity through the *by-pass* bariatric surgery technique led to partial remission of DM2.
**Keywords:** bariatric surgery, diabetes mellitus, glycemia, HbA1c.

## INTRODUCTION

Obesity is considered a global epidemic and it is estimated that in 2035 approximately 4.0 billion adults will be overweight, an increase of 10% compared to 2020 (WOF, 2023), which increases the risk factors for the development of several important diseases such as Type 2 Diabetes Mellitus (DM2), hypertension, dyslipidemia, cancer and kidney disease. Furthermore, the greater the excess weight, the greater the severity of these diseases. According to the body mass index (BMI), an individual is considered overweight or obese with a BMI of 25 to 29.9 kg/m²; obese with a BMI of 30 to 34.9 kg/m²; obese with a BMI of 35 to 39.9 kg/m² and severely obese with a BMI of grade III³ 40.0 kg/m² (ABESO, 2016).

First and foremost, treatment for obesity advocates lifestyle changes associated with adequate calorie intake. When obesity is refractory to non-pharmacological treatment, i.e. with a BMI ≥ 30 or BMI ≥ 25 Kg/m² associated with hypertension, DM2, hyperlipidemia, sleep apnea, osteoarthritis, gout, among other risk factors, the use of anti-obesity drugs is recommended (ABESO, 2016). For those patients aged between 18 and 65, BMI > 40 or > 35 kg/m², respectively, with one or more serious comorbidities, bariatric surgery is recommended (ABESO, 2016).

## BARIATRIC SURGERY AND OBESITY

Bariatric surgery is considered a highly cost-effective alternative with repercussions on weight loss and fewer systemic consequences (FRÜHBECK G, 2015; NEOVIUS M et al., 2012).

Depending on the patient and their particularities, the surgeon can choose between different bariatric surgery techniques such as gastric *bypass*, vertical gastrectomy, duodenal *switch* and adjustable gastric banding. In this study, the technique chosen for analysis was gastric *bypass*, also known as Roux-en-Y gastroplasty with intestinal detour. This procedure can be performed robotically, laparoscopically or open, and consists of forming a gastric pouch, creating a biliopancreatic branch, performing a jejunojejunostomy and a gastrojejunostomy (MITCHELL BG, GUPTA N, 2024).

Initially, the functionality of bariatric surgery to minimize obesity was thought to be due to its mechanisms of restriction and reduced absorption. However, the mechanism of gastric *bypass* is quite complex (MITCHELL BG, GUPTA N, 2024), generating increased energy expenditure and changes in the hormonal network, intestinal microbiota and metabolic efficiency. One of the mechanisms of weight loss is the reduction in the synthesis of ghrelin, the hormone responsible for hunger and produced in the cells located in the gastric fundus, which is predominantly excluded in gastric *bypass*. In addition, evidence suggests that concomitant vagotomy in these patients may inhibit the effect of this hormone on appetite stimulation. Other hormones can be attributed to the reduction in the size of patients' postoperative meals, such as the anorexigenic hormones CCK, GLP-1, PYY and amylin (LUTZ TA, BUETER M, 2014). It has also been observed that the GLP-1 hormone, released by L cells in the terminal ileum and colon, has a considerable postprandial increase in the first few weeks after surgery. This hormone causes satiety and a reduction in food intake, as well as stimulating the secretion and increasing sensitivity to insulin, which is why it is believed to be a key player in the resolution of DM2 after gastric *bypass*.

## OBESITY AND TYPE 2 DIABETES MELLITUS

Obesity is a chronic disease evidenced by the accumulation of localized or generalized adipose tissue, resulting from an imbalance between the gain and expenditure of glyceride lipids associated with endocrinometabolic and nutritional disorders, the environment, lifestyle and emotional factors (ABESO, 2016). Triglyceride lipids are stored in adipose tissue and, when necessary, are hydrolyzed and the resulting fatty acids are used to maintain cellular energy homeostasis. The nutritional supply of glucose, which can be converted into triglycerides, and the decrease in energy expenditure lead to the accumulation of lipids in adipocytes, also enabling an increase in visceral and ectopic fat, as well as an increase in free fatty acids (MA Y et al., 2020) and pre-inflammatory cytokines in plasma.

The accumulation of free fatty acids in hypertrophied adipocytes results in hypoxia which contributes to the generation of reactive oxygen species, inflammation and fibrosis (BAYS HE, 2023). The oxidation of fatty acids produces apoptotic derivatives such as diacylglycerol and ceramides, which promote the development of inflammatory processes. The action of apoptotic derivatives and the consequent inflammatory process lead to resistance to the action of insulin and cellular glucose absorption mediated by the GLUT4 translocator, reducing the effectiveness of the insulin receptor in the membrane and the signaling cascade for glucose absorption. Therefore, the increase in free fatty acids, possibly resulting from changes in lipid and glucose metabolism, can trigger insulin resistance, cell dysfunction and DM2 (CALDAS JP et al., 2016; MA Y et al., 2020; BAYS HE, 2023).

A large proportion, around 89% of adult individuals in the United States with DM2, are overweight or obese (NATIONAL DIABETES


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STATISTICS REPORT, 2020); however, among overweight and obese individuals, only 13.8% have DM2 (OGDEN CL et al., 2015). This data raises the question of cause and effect between DM2 and obesity.

Previous studies have analyzed patients with grade II and grade III obesity and high fasting blood glucose values who underwent bariatric *bypass* surgery. After the procedure, the individuals achieved normal glycemic values (CALDAS JP et al., 2016). In 2017, the Federal Council of Medicine published resolution 2.172, which recognizes the importance of bariatric surgery for the treatment of patients with DM2 who have a BMI between 30 and 34.9 $Kg/m^2$, refractory to clinical drug therapy (CFM, 2017). In this context, it is hoped to find a regression of DM2 due to a reduction in the inflammatory effects of adipose tissue. Thus, in addition to the importance of weight loss through the reduction of adipose tissue, gastric *bypass* emerges as a valuable alternative for the treatment of obese patients with DM2.

In view of this, this literature review study aims to evaluate the effect of bariatric surgery, using the gastric *bypass* method, on fasting glycemia and the plasma concentration of glycated hemoglobin (HbA1c) in patients with a previous diagnosis of diabetes.

## METHODOLOGY

### BIBLIOGRAPHIC SURVEY

A bibliographic survey of the PubMed and Scielo databases, using the keywords "*Bariatric surgery and Diabetes*", found 272 articles published between 2012 and January 27, 2023.

### SELECTION CRITERIA

We included studies that met the following criteria: (1) complete publications, (2) randomized controlled studies, (3) studies conducted exclusively with human patients, (4) patients who had undergone bariatric *bypass* surgery and were diagnosed with DM2, (5) studies that presented glycated hemoglobin (HbA1c) and/or fasting glucose values before and after bariatric surgery.

### DATA ANALYSIS

Statistics were carried out using the R *software* (R CORE TEAM, 2022) for descriptive analysis and summary measures. Articles that did not present the mean age of the patients were assigned the term NA (*Not Assigned*) for the analysis.

## RESULTS

Of the total of 272 articles found in the databases, only 25 full articles met the selection criteria and could be used to obtain HbA1c and fasting blood glucose values in the pre- and post-operative periods of patients with DM2 undergoing bariatric surgery using the *bypass* technique. Only one article did not present a mean age, which was assigned the value "NA" (Not Assigned). The 25 articles evaluated postoperative periods of 0.5 years (n = 4), 1 year (n = 18), 2 years (n = 9), 3 years (n = 6), 4 years (n = 1) and 5 years (n = 4).

A total of 1053 individuals were analyzed, with ages ranging from 40.00 to 53.00 years. The baseline parameters of age, body mass index (BMI), glycemia and HbA1c are described in Table 1 and represent the original values (mean and standard deviation) obtained from the selected articles. The total shown in the table corresponds to the mean and standard deviation determined from the mean values of each study analyzed, and specific standard deviations were disregarded.


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| Studies/Subgroups | Individuals (n) | Age (Years) | BMI (Kg/m2) | Pre Glycemia (mg/dL) | Pre HbA1c (%) |
|---|---|---|---|---|---|
| Salminen P et al., 2018 | 49 | 48,40 (9,30) | 48,4 | 140,54 (11,71) | 7,20 (0,19) |
| Almby KE et al., 2021 | 13 | 51,00 (10,00) | 36,80 (3,90) | 149,55 (34,23) | 7,20 (1,10) |
| Khoo CM et al., 2014 | 30 | 49,60 (1,40) | 43,40 (0,80) | 155,60 (8,60) | 7,53 (0,23) |
| Petry TZ et al., 2015 | 10 | 47,00 (8,00) | 29,70 (1,90) | 203,00 (64,00) | 8,70 (1,30) |
| Astiarraga B et al., 2020 | 13 | 53,00 (7,00) | 39,30 (1,40) | 160,36 (36,94) | 7,30 (0,65) |
| Hofsø D et al., 2019 | 54 | 48,20 (8,90) | 42.40 | 210,82 (17,11) | 7,90 (0,30) |
| Kashyap SR et al., 2013 | 18 | 42,90 (9,70) | 36,10 (2,60) | 211,00 (35,50) | 9,80 (1,35) |
| Courcoulas AP et al., 2015 | 20 | 47,30 6,60) | 35,67 (0,61) | 191,50 (18,33) | 8,56 (0,46) |
| Ikramuddin S et al., 2013 | 60 | 49,00 (2,50) | 34,9 | 222,00 (19,00) | 9,60 (2,50) |
| Nemati R, et al., 2018 | 32 | 47,00 (1,20) | 40,00 (7,00) | 126,13 (39,64) | 8,20 (1,70) |
| Ikramuddin S et al., 2015 | 60 | 49,00 (9,00) | 34,90 (3,00) | 214,41 (57,66) | 9,60 (1,00) |
| Wallenius V et al., 2020 | 25 | 49,10 (9,20) | 39,30 (3,60) | 178,38 (55,86) | 7,90 (1,50) |
| Jahansouz C et al., 2019 | 34 | 51,00 (9,00) | 36,10 (2,70) | 224,00 (65,00) | 9,50 (0,90) |
| Cheng A et al., 2022 | 12 | 40,00 (NA) | 29,10 (1,60) | 227,02 (57,65) | 9,90 (1,40) |
| Sachdev S et al., 2016 | 15 | 46,90 (2,20) | 36,20 (0,70) | 229,00 (21,00) | 9,70 (0,20) |
| Nguyen KT et al., 2015 | 34 | 50,00 (1,00) | 35,80 (0,50) | 236,00 (14,00) | 9,80 (0,20) |
| Wölnerhanssen BK et al., 2021 | 229 | 45,30 (NA) | 46,40 (6,60) | 129,73 (27,93) | 7,00 (0,35) |
| Courcoulas AP et al., 2014 | 24 | 46,30 (7,20) | 35,50 (2,60) | 190,90 (78,10) | 8,70 (2,20) |
| Mingrone G et al., 2015 | 20 | 43,90 (7,57) | 44,00 (4,60) | 172,07 (60,36) | 8,56 (1,45) |
| Cohen RV et al., 2020 | 51 | 52,50 (7,60) | 32,50 (1,90) | 167,00 (22,00) | 8,80 (1,86) |
| Robert M et al., 2019 | 117 | 42,60 (10,20) | 43,90 (5,10) | 156,76 (0,00) | 7,50 (1,70) |
| Tang Q et al., 2016 | 38 | 40,40 (12,30) | 37,80 (5,60) | 162,16 (61,26) | 7,40 (1,80) |
| Yang J et al., 2015 | 27 | 41,40 (9,30) | 32,30 (2,40) | 187,39 (39,64) | 8,90 (1,30) |
| Schauer PR et al., 2014 | 48 | NA | 36,00 (3,50) | 193,00 (47,00) | 9,30 (1,40) |
| Courcoulas AP et al. 2020 | 20 | 45,40 (7,50) | 35,67 (0,61) | 191,50 (18,33) | 8,56 (0,46) |
| Total | **1053** | **46,97 (3,57)** | **36,96 (4,13)** | **187,05 (30,90)** | **8,58 (0,92)** |

Table 1: Characteristics of the baseline parameters analyzed in each article.

| Studies/Subgroups | Pre Glycemia (mg/dL) | Post Glycemia (mg/dL) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 6 months | 1 years | 2 years | 3 years | 4 years | 5 years |
| Salminen P et al., 2018 | 140,54 (11,71) | 109,91 (6,31) | 106,31 (6,31) | | 120,72 (9,01) | | 121,82 (10,00) |
| Almby KE et al., 2021 | 149,55 (34,23) | 113,51 (23,42) | | | | | |
| Khoo CM et al., 2014 | 155,60 (8,60) | 113,30 (7,30) | 113,50 (8,70) | | | | |
| Petry TZ et al., 2015 | 203,00 (64,00) | 148,00 (45,00) | 146,00 (26,00) | | | | |
| Astiarraga B et al., 2020 | 160,36 (36,94) | | 91,89 (14,41) | | | | |
| Hofsø D et al., 2019 | 210,82 (17,11) | | 102,70 (20,72) | | | | |
| Kashyap SR et al., 2013 | 211,00 (35,50) | | 93,00 (27,50) | 87,00 (15,00) | | | |
| Courcoulas AP et al., 2015 | 191,50 (18,33) | | 121,70 (8,03) | 140,90 (7,50) | 125,50 (7,39) | | |
| Ikramuddin S et al., 2013 | 222,00 (19,00) | | 111,00 (8,50) | | | | |
| Nemati R, et al., 2018 | 126,13 (39,64) | | 113,51 (18,02) | | | | |
| Ikramuddin S et al., 2015 | 214,41 (57,66) | | 113,51 (63,06) | 111,71 (52,25) | | | |
| Wallenius V et al., 2020 | 178,38 (55,86) | | 113,51 (52,25) | 111,71 (52,25) | | | |
| Jahansouz C et al., 2019 | 224,00 (65,00) | | 108,00 (0,00) | | | | |
| Cheng A et al., 2022 | 227,02 (57,65) | | 115,79 (5,94) | 134,63 (10,90) | 128,73 (6,95) | 139,85 (16,64) | 134,40 (23,18) |
| Sachdev S et al., 2016 | 229,00 (21,00) | | 116,00 (9,00) | | | | |
| Nguyen KT et al., 2015 | 236,00 (14,00) | | 117,00 (6,00) | | | | |
| Wölnerhanssen BK et al., 2021 | 129,73 (27,93) | | 95,50 (18,92) | | 108,11 (21,62) | | 109,91 (22,73) |
| Courcoulas AP et al., 2014 | 190,90 (78,10) | | 79,70 (30,30) | | | | |
| Mingrone G et al., 2015 | 172,07 (60,36) | | | 102,52 (19,28) | | | |
| Cohen RV et al., 2020 | 167,00 (22,00) | | | 104,10 (13,90) | | | |
| Robert M et al., 2019 | 156,76 (0,00) | | | 109,91 (52,25) | | | |
| Tang Q et al., 2016 | 162,16 (61,26) | | | 122,52 (48,65) | | | |
| Yang J et al., 2015 | 187,39 (39,64) | | | | 104,50 (12,61) | | |
| Schauer PR et al., 2014 | 193,00 (47,00) | | | | 100,00 (27,00) | | |
| Courcoulas AP et al. 2020 | 191,50 (18,33) | | | | | | 142,40 (15,96) |
| **Total** | **187,05 (30,90)** | **121,18 (15,55)** | **109,33 (14,16)** | **113,89 (15,66)** | **114,59 (10,90)** | **139,85 (16,64)** | **127,13 (12,57)** |

Table 2: Baseline blood glucose and after bariatric surgery.

| Studies/Subgroups | Pre HbA1c | Post HbA1c (%) | | | | | |
|---|---|---|---|---|---|---|---|
| | (%) | 6 months | 1 years | 2 years | 3 years | 4 years | 5 years |
| Salminen P et al., 2018 | 7,20 (0,19) | 6,60 (0,25) | 6,20 (0,15) | | 6,40 (0,20) | | 6,70 (0,20) |
| Almby KE et al., 2021 | 7,20 (1,10) | 5,90 (0,50) | | | | | |
| Khoo CM et al., 2014 | 7,53 (0,23) | 6,33 (0,20) | 6,33 (0,20) | | | | |
| Petry TZ et al., 2015 | 8,70 (1,30) | 7,20 (1,10) | 7,50 (1,00) | | | | |
| Astiarraga B et al., 2020 | 7,30 (0,65) | | 5,60 (0,70) | | | | |
| Hofsø D et al., 2019 | 7,90 (0,30) | | 5,90 (0,30) | | | | |
| Kashyap SR et al., 2013 | 9,80 (1,35) | | 6,30 (0,78) | 6,70 (1,28) | | | |
| Courcoulas AP et al., 2015 | 8,56 (0,46) | | 6,68 (0,11) | 7,39 (0,15) | 7,14 (0,02) | | |
| Ikramuddin S et al., 2013 | 9,60 (2,50) | | 6,30 (0,20) | | | | |
| Nemati R, et al., 2018 | 8,20 (1,70) | | 6,20 (1,00) | | | | |
| Ikramuddin S et al., 2015 | 9,60 (1,00) | | 6,40 (1,60) | 6,50 (1,60) | | | |
| Wallenius V et al., 2020 | 7,90 (1,50) | | 5,80 (1,30) | 5,90 (1,40) | | | |
| Jahansouz C et al., 2019 | 9,50 (0,90) | | 6,30 (0,00) | | | | |
| Cheng A et al., 2022 | 9,90 (1,40) | | 6,10 (0,12) | 6,71 (0,20) | 6,64 (0,25) | | 7,15 (0,36) |
| Sachdev S et al., 2016 | 9,70 (0,20) | | 6,40 (0,30) | | | | |
| Nguyen KT et al., 2015 | 9,80 (0,20) | | 6,40 (0,20) | | | 6,66 (0,34) | |
| Wölnerhanssen BK et al., 2021 | 7,00 (0,35) | | 5,80 (0,35) | | 6,10 (0,30) | | 6,10 (0,30) |
| Courcoulas AP et al., 2014 | 8,70 (2,20) | | 6,40 (0,00) | | | | |
| Mingrone G et al., 2015 | 8,56 (1,45) | | | 6,35 (1,42) | | | |
| Cohen RV et al., 2020 | 8,80 (1,86) | | | 6,18 (0,31) | | | |
| Robert M et al., 2019 | 7,50 (1,70) | | | 6,10 (0,90) | | | |
| Tang Q et al., 2016 | 7,40 (1,80) | | | 6,40 (1,60) | | | |
| Yang J et al., 2015 | 8,90 (1,30) | | | | 5,70 (0,70) | | |
| Schauer PR et al., 2014 | 9,30 (1,40) | | | | 6,70 (1,30) | | |
| Courcoulas AP et al. 2020 | 8,56 (0,46) | | | | | | 7,10 (0,39) |
| **Total** | **8,58 (0,92)** | **6,51 (0,47)** | **6,25 (0,26)** | **6,47 (0,41)** | **6,45 (0,46)** | **6,66 (0,34)** | **6,76 (0,42)** |

Table 3: HbA1c at baseline and after bariatric surgery

After surgery, at 6 months, 1, 2, 3, 4 and 5 years, there was a decrease of 35.22, 41.55, 39.11, 38.74, 25.23 and 32.03% in glycemia and 24.13, 27.16, 24.59, 24.83, 22.38 and 21.21% in HbA1c. In the same period, BMI (Kg/m2) decreased from the grade II obesity seen at baseline (36.96 ± 4.13) to grade I obesity (33.67 ± 1.16) in six months and overweight (27.52 ± 2.83, 27.01 ± 2.00, 26.82 ± 4.05, 25.69 ± 1.62 and 29.78 ± 4.69) in the years following the surgical procedure. The mean and specific values for each study analyzed, for glycemia and HbA1c, over the period from six months to five years, are shown in Tables 2 and 3, respectively.

## DISCUSSION

The blood glucose and HbA1c values indicated by the Brazilian Diabetes Society (SBD, 2023) were used as a reference: fasting normoglycemia when plasma glucose concentration is less than 100 mg/dL and HbA1c is less than 5.7%; pre-diabetes or increased risk of diabetes, with fasting glucose ≥ 100 and < 126 mg/dL and HbA-1c ≥ 5.7 and < 6.5% and established diabetes with fasting glucose ≥ 126 mg/dL and HbA-1c ≥ 6.5%. The average glycemia (187.05 ± 30.90 mg/dL) and HbA1c (8.58 ± 0.92 %) values found in the pre-surgical stage were compatible with diabetes. The greatest rate of decrease, of 41.55% for glycemia and 27.16% for HbA1c, reaching mean values of 109.33 mg/dL and 6.25%, respectively, were observed one year after surgery (Tables 2 and 3). Although the blood glucose and HbA1c values did not reach the normoglycemia range, there was a decrease ($p<0.05$) in the parameters to a range considered pre-diabetes. It is important to note that over the years, the decrease in blood glucose and HbA1c indices was smaller, with the absolute values returning to the diabetes range four years after the surgical procedure. BMI decreased over the years and followed the trend of reversion to grade I obesity five years after surgery. Figure 1A shows the behavior of blood glucose and HbA1c levels over the period analyzed and Figure 1B shows the residual percentage of blood glucose, HbA1c and BMI in relation to baseline values, considered to be 100%. The values four years after the surgical procedure were not represented in the graphs due to the low number of individuals and the impossibility of carrying out a statistical analysis.

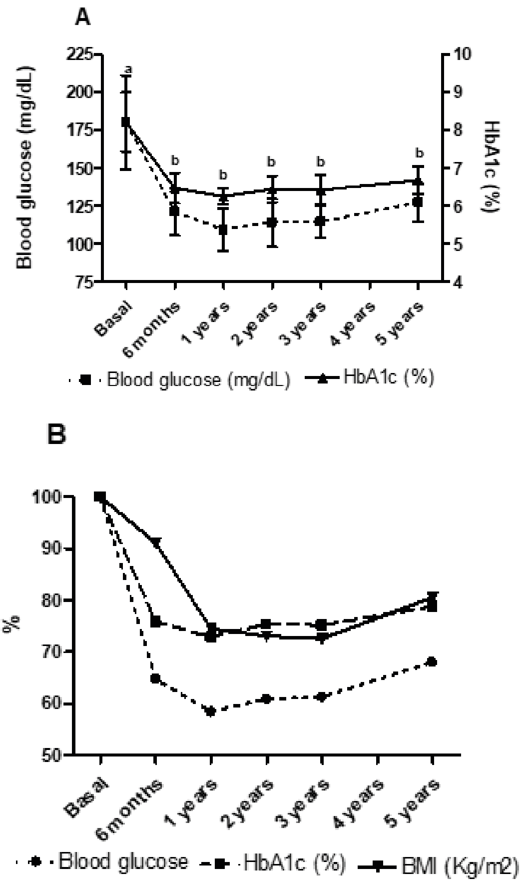


Figure 1: Variation in blood glucose, HbA1c and BMI as a function of time after bariatric surgery. a, b represent $p< 0.05$.

According to the American Diabetes Association criteria, complete remission of DM2 is considered to be HbA1c below 6.0% and fasting glucose below 100 mg/dL and partial remission is considered to be HbA1c below 6.5% and fasting glucose between 100 and 125 mg/dL, both for at least one year and in the absence of drug therapy (Wölnerhanssen BK et al., 2021). In this context, it can be considered that the reduction of obesity through the *by-pass* bariatric surgery technique led to partial remission of DM2. However, over time, multifactorial mechanisms resulting from DM2, such as hyperinsulinemia, glucose metabolism dysfunction and/or factors inherent to the individual and the environment, such as increasing age, genetic predisposition and obesogenic environments, can reverse the hyperglycemia and increase in HbA1c, as shown in the data presented in this study.

## CONCLUSION

The results indicate that bariatric *bypass* surgery is an important strategy for the treatment of DM2 in obese patients, reducing the plasma values of HbA1c and fasting glycemia from "diabetes" to "pre-diabetes", according to the diagnostic criteria established by the Brazilian Diabetes Society and considering the period of up to 3 years after surgery.

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