Long-term diabetes outcomes after bariatric surgery—managing medication withdrawal

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Abstract

Background/objectives Bariatric surgery leads to type 2 diabetes mellitus (T2DM) remission, but recurrence can ensue afterwards. However, literature provides heterogeneous remission/recurrence criteria and there is no consensus on long-term T2DM management after surgery. We aim to assess T2DM remission/recurrence rates using standardized criteria and to identify relapse predictors. We also intend to analyze the management of residual T2DM and the impact of maintaining/ withdrawing metformin in avoiding future relapse.

Subjects/methods We investigated a cohort of 110 obese patients with T2DM who underwent bariatric surgery and were followed for 5 years (Y0–Y5). Patients who ever attained remission were accounted for cumulative remission, while prevalent remission was considered for individuals who were on remission in a specific visit.

Results A complete prevalent remission of 47.3% was reached at Y1 and it remained stable till Y5 (46.4–48.2%). Complete cumulative rate was of 57.3% at Y5. Five-year T2DM recurrence rate was 15.9% and it was associated with higher pre-operative HbA1c levels (β = 1.06; p < 0.05) and a milder excess body weight loss (EBWL) (β = 0.49; p < 0.05). Glucose-lowering agents were fully stopped in 51.4% of the patients till Y1 and in 16.2% of them afterwards. Medication withdrawal was mainly attempted in patients with a lower baseline HbA1c (β = 0.54; p < 0.01) and higher first-year EBWL (β = 1.04; p < 0.01). Patients that kept metformin after reaching a HbA1c in the complete remission range (<6.0%) did not have greater odds of avoiding relapse in the next visit (OR = 0.33; p = 0.08).

Conclusions Baseline HbA1c and EBWL were the main variables driving both T2DM relapse after bariatric surgery and the attempt to withdrawal anti-diabetic medication. In our population keeping metformin once an HbA1c < 6.0% is achieved did not seem to diminish relapse but further studies on this matter are needed.

Introduction

Obesity is closely related to the development of type 2 diabetes mellitus (T2DM) and the incidence of both diseases is growing worldwide [1]. Bariatric/metabolic surgery is an effective strategy to attain diabetes remission in obese patients [2]. According to the American Diabetes Association (ADA) it should be recommended not only for adults with body mass index (BMI) ≥ 35 kg/m² but also considered in those with BMI ≥ 30 kg/m² when hyperglycemia is inadequately controlled despite lifestyle and optimal medical therapy [3].

Different authors have reported highly disparate T2DM remission rates, ranging from 26% to 83% [4, 5]. The distinct duration of the studies and the different HbA1c/fasting glucose criteria used are some of the possible explanations [6]. Only few publications on this matter distinguish complete vs. partial remission and prevalent vs. cumulative remission, which further contributes to the stated variations [7, 8]. T2DM remission after surgery is not always durable and relapse may ensue. The definition of T2DM recurrence after bariatric surgery is widely variable in literature and...
Relapse rates are underreported throughout the majority of studies [4, 9, 10]. While predictors of T2DM remission are relatively well-defined, those that can predict relapse are still under investigation as their identification requires longer follow-ups. These pitfalls can lead to patients’ reluctance in accepting a treatment with such an uncertain result and to physicians’ difficulties in choosing the appropriate bariatric procedure and in managing T2DM after it.

Consensus on post-bariatric medical management mainly focus on the peri-operative and early post-operative T2DM control and do not state how the disease should be approached on a long-term perspective [11, 12]. Several authors referred that metformin could be allowed as consistent with the remission, since this drug is now considered standard of care for T2DM prevention [3, 13]. Additionally, some authors state that it is unfair to require that patients have to be off medication in order to be classified as in remission [14]. To the best of our knowledge, there are no studies neither analyzing the impact of maintaining metformin in post-surgical glycemic outcomes nor evaluating which factors drive the management of residual T2DM. Also, anti-diabetic medication withdrawal or maintenance, mainly after reaching T2DM remission, still constitutes a challenge for most physicians that follow these patients.

The objective of this study is to assess T2DM remission and recurrence rates following bariatric surgery using standardized criteria and to identify relapse predictors. We also intend to analyze anti-diabetic medication management after surgery. Finally, we aim to understand the impact of maintaining or withdrawing metformin on the forthcoming glycemic control of these patients.

Methods

Study design and participants

This is a 5-year retrospective observational study conducted in a population of obese (BMI ≥ 35 kg/m²) patients followed by the Multidisciplinary Group for Surgical Management of Obesity at our hospital. After the first post-operative year, our follow-up protocol includes at least one yearly visit where patients are evaluated by an endocrinologist and perform blood analysis (Y0, Y1, Y2, Y3, Y4, and Y5). A total of 165 patients with T2DM diagnosis underwent bariatric surgery between January 2010 and July 2012. Among them, 110 patients remained compliant with regular follow-up and they were included in this study. Thirty-six (32.7%) of the patients underwent laparoscopic adjustable band gastroplasty (LABG), 62 (56.4%) Roux-en-Y gastric bypass (RYGB), and 12 (10.9%) sleeve gastrectomy (SG).

Clinical, anthropometric (height, weight, BMI, waist and hip circumferences), and analytic measures (HbA1C, fasting plasma glucose, C-peptide, lipid profile) were obtained in the follow-up period. Excess body weight loss (EBWL) was calculated by dividing the difference between initial BMI and final BMI by the difference between initial BMI and a target BMI of 25 kg/m². Weight regain was calculated using the formula (current weight – previous weight)/(pre-surgical weight – previous weight) and it was expressed as a percentage. Patients with previous bariatric procedures and those with severe renal or hepatic dysfunction were excluded.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients gave their consent before being enrolled.

Type 2 diabetes definition and remission/recurrence criteria

To define T2DM we used the 2018 ADA guidelines criteria: fasting plasma glucose ≥ 126 mg/dL or HbA1C ≥ 6.5% or 2-h post-load plasmatic glucose ≥ 200 mg/dL during an oral glucose tolerance test (OGTT) or use of hypoglycaemic agents [3]. Complete T2DM remission was defined as HbA1C < 6.0% and no anti-diabetic medication use and partial T2DM remission was defined as HbA1C < 6.5% and no anti-diabetic medication use [15]. Patients who ever attained remission were accounted for cumulative remission, while prevalent remission was considered only for individuals who were on remission in the evaluation moment. Besides determining these rates in accordance with the described classic definitions of remission, we have also calculated them considering a broader concept of remission in which metformin is allowed. Diabetes recurrence was defined as HbA1C ≥ 6.5% or need for anti-diabetic medication reintroduction after a remission period. Time to relapse in patients that had previously achieved remission was calculated as following: (yearly visit in which recurrence was noticed – yearly visit in which remission was not noticed) (expressed in months).

Statistical analyses

Categorical variables were expressed as frequencies and percentages and and were compared by chi-square test or Fisher’s exact test, as appropriate. Continuous variables were presented as means and standard deviations and were compared using Student’s t-test. Normal distribution was evaluated using Shapiro–Wilk test or skewness and kurtosis. We have firstly used univariate analysis to study the
association of different clinical and laboratorial parameters
with T2DM relapse, anti-diabetic medication withdrawal
and glycaemic control after the surgery. Those parameters
that achieved statistical significance in the univariate ana-
lysis (p < 0.05) were then included in binary logistic (for
dichotomous nominal variables) and linear regressions mod-
els (for continuous variables) to adjust for confounding
variables [results expressed as β and confidence intervals
(CI)]. A variance inflation factor (VIF) above 5 was used to
assume collinearity and to exclude variables for the
regression. Reported p values are two-tailed and p < 0.05
was considered significant. Analyses were performed with
the use of SPSS Statistics 25.

Results

Baseline characteristics

The mean age of the enrolled was 49.5 ± 9.02 years old.
Average weight and BMI were 113 ± 16.6 kg and 43.9 ±
5.93 kg/m², respectively. Eighty-four individuals (76.4%)
presented morbid obesity criteria (BMI ≥ 40 kg/m²). All
patients included had T2DM diagnosis with a mean pre-
operative HbA1c of 6.88 ± 1.42%. At the time of the sur-
gery, 105 (95.5%) patients were on anti-diabetic medica-
tion. Among them, 98 individuals (93.3%) were on metformin (mean dose of 1806 ± 751 mg) and 11 patients
were on insulin therapy (10.5%). Other anthropometrical
and analytic characteristics of the studied population are
summarized in Table 1.

T2DM remission and recurrence

Maximal EBWL was observed at Y1 evaluation (60.6 ±
24.5%). EBWL remained stable at Y2 (59.9 ± 24.9%; p =
0.56) but presented a significant decrease at Y3 (57.2 ±
25.8%; p < 0.05), Y4 (55.5 ± 24.7%; p < 0.01), and Y5
(53.8 ± 25.5%; p < 0.001). A significant decrease in HbA1c
levels was achieved at Y1 (5.72 ± 0.64; p < 0.001) and it
was maintained till Y5 (5.83 ± 0.63; p < 0.001) when both
were compared with pre-surgical levels.

Prevalent T2DM remission rates across the 5 years of follow-up are depicted in Fig. 1. Complete remission was
reached by 47.3% of the patients at the time of the first post-
operative visit. This rate remained relatively stable after Y1
(46.4–48.2%). When patients with a HbA1C < 6.0% and
exclusively on metformin were also considered as in com-
plete remission, yearly remission rates were on average
22.3 ± 2.4 percentage points (pp) higher. Prevalent partial
remission rates fluctuated between 50.9% and 51.8%. In
what concerns cumulative remission percentages, complete
and partial rates were of 57.3% and 63.8% at Y5,
respectively. Among patients treated with insulin before
surgery, only 1 (9.09%) attained complete remission at Y1,
and none of them was on remission at Y5.

T2DM recurrence criteria was documented in 10 out of
the 63 patients (15.9%) who ever attained complete remis-
sion. Recurrence happened 20.4 ± 9.88 months after
achieving remission. HbA1c levels at the end of the follow-
up period were still significantly lower than pre-operative
ones (mean difference of 1.02 ± 0.41%; p < 0.05) in these
patients. Binary logistic regression identified pre-operative
HbA1c levels (β = 1.06; CI 1.01–1.11; p < 0.05) and
EBWL in the first year after surgery (β = 0.49; CI 0.26–
0.95; p < 0.05) as independent predictors of recurrence. No
Table 2  Analysis of variables that influenced anti-diabetic medication withdrawal during the first post-operative year

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medication withdrawn</td>
<td>Medication not withdrawn</td>
</tr>
<tr>
<td>n (%)</td>
<td>54</td>
<td>51</td>
</tr>
<tr>
<td>Female/male sex—no.</td>
<td>45/9</td>
<td>41/10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.3 ± 9.1</td>
<td>52.1 ± 8.1</td>
</tr>
<tr>
<td>Weight at Y0 (kg)</td>
<td>116 ± 17.9</td>
<td>110 ± 15.2</td>
</tr>
<tr>
<td>BMI at Y0 (kg/m$^2$)</td>
<td>44.9 ± 7.0</td>
<td>42.8 ± 4.7</td>
</tr>
<tr>
<td>Fasting glucose at Y0 (mg/dL)</td>
<td>116 ± 30</td>
<td>137 ± 54</td>
</tr>
<tr>
<td>HbA1c at Y0 (%)</td>
<td>6.4 ± 1.0</td>
<td>7.3 ± 1.7</td>
</tr>
<tr>
<td>Pre-op C-peptide levels at Y0 (ng/mL)</td>
<td>4.7 ± 1.4</td>
<td>4.4 ± 1.9</td>
</tr>
<tr>
<td>Insulin therapy at Y0 (yes/no)—no.</td>
<td>3/51</td>
<td>8/43</td>
</tr>
<tr>
<td>First year EBWL (%)</td>
<td>70.7 ± 23.1</td>
<td>52.3 ± 22.6</td>
</tr>
</tbody>
</table>

$CI$ confidence interval, $Y0$ year zero (pre-operative evaluation), $BMI$ body mass index, $EBWL$ excess body weight loss

*Statistically significant ($p < 0.05$)

Differences were found regarding sex, age, and pre-operative BMI or use of insulin/oral anti-diabetic drugs.

Post-operative T2DM management

Anti-diabetic medication was fully withdrawn in 54 patients (51.4%) during Y1. Table 2 summarizes the variables that influenced its withdrawal. Considering univariate analysis, younger patients ($p < 0.01$), those with lower pre-operative fasting glucose ($p < 0.05$) and HbA1c ($p = 0.001$) and greater EBWL ($p < 0.01$) had higher chances of seeing their T2DM medication discontinued. Features that achieved statistical significance in univariate analysis were then included in a linear regression model. Fasting glucose levels were excluded due to its collinearity with HbA1c. Pre-operative HbA1c and EBWL remained as statistically significant variables that influenced the anti-diabetic medication withdrawal attempt. Among patients on insulin therapy before the bariatric procedure ($n = 11$), seven discontinued it in the first post-operative year (mean HbA1c at Y1 of 6.29 ± 0.70%) but only three were free of any kind of T2DM-targeted therapy.

After Y1, anti-diabetic medication was stopped in 17 additional patients (16.2%) (Fig. 2). The mean HbA1c at the visit where that decision was made was of 5.75 ± 0.62%. Conversely, medication was restarted in 16 patients (15.2%). Insulin therapy was discontinued in three additional patients with no need to be reintroduced in any of the total 10 individuals that withdrew it in the 5-year follow-up period.

Metformin maintenance after bariatric surgery

Among patients who attained a HbA1c < 6.0% at Y1, there were no differences in the chance of avoiding T2DM relapse at Y2 when those who kept metformin and those who did not were compared (OR = 0.33; $p = 0.08$). The same was seen when those with a HbA1c in the partial remission range (<6.5%) at Y1 were considered (OR = 1.91; $p = 0.32$). Similar results were obtained for the subsequent four years of follow-up ($p > 0.05$).

In order to further investigate the impact of maintaining metformin after reaching a HbA1c < 6.0% at Y1, factors that could influence subsequent glycaemic control were investigated and are depicted in Table 3. Of the 73 patients that achieved that milestone at Y1, physicians decided to continue metformin monotherapy till Y2 in 22 (30.1%) of them, while the rest ($n = 51$) were left without any anti-diabetic medication. Linear regression analysis showed that there were no differences in HbA1c in Y2–Y5 between those that kept metformin and those who did not. Higher HbA1c levels at Y1 and greater weight regain were the main predictors of HbA1c levels during the follow-up period of these individuals. Patients’ age only independently influenced HbA1c at Y2 evaluation ($p < 0.01$).
Table 3 Multivariate analysis of variables influencing follow-up glycaemic control after a HbA1c < 6.0% was attained in the first post-operative year

<table>
<thead>
<tr>
<th>Variables</th>
<th>HbA1c</th>
<th></th>
<th>Y3</th>
<th></th>
<th>Y4</th>
<th></th>
<th>Y5</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>( \beta )</td>
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<td>( \beta )</td>
<td>( p )</td>
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<td>( p )</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.24</td>
<td>&lt;0.01*</td>
<td>0.08</td>
<td>0.43</td>
<td>-0.09</td>
<td>0.42</td>
<td>-0.06</td>
<td>0.56</td>
</tr>
<tr>
<td>HbA1c at Y1 (%)</td>
<td>0.32</td>
<td>&lt;0.001*</td>
<td>0.42</td>
<td>&lt;0.001*</td>
<td>0.42</td>
<td>&lt;0.001*</td>
<td>0.28</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Weigh regain (%)</td>
<td>0.12</td>
<td>0.23</td>
<td>0.31</td>
<td>&lt;0.01*</td>
<td>0.19</td>
<td>&lt;0.05*</td>
<td>0.45</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Metformin maintained (Yes)</td>
<td>-0.03</td>
<td>0.76</td>
<td>-0.02</td>
<td>0.85</td>
<td>0.07</td>
<td>0.53</td>
<td>0.18</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Statistically significant \( p < 0.05 \)

In addition, those patients with an HbA1c < 6.0% at Y1 that maintained metformin throughout all 5-year follow-up \((n = 14)\) presented a higher HbA1c at Y5 than those that were kept free of medication in this period (mean difference of 0.32 ± 0.12; \( p = 0.01 \)). This difference was not significant after adjusting for the aforementioned confounders.

**Discussion**

In this study, we report three main findings. First, prevalent complete and partial remission rates of 47% and 51%, respectively, were reached at the end of the first post-operative year and remained relatively stable afterwards. Remission rates were on average about 20pp higher when patients exclusively taking metformin were also accounted as being in remission. Second, anti-diabetic medication was mainly withdrawn in the first post-operative year and a 5-year recurrence rate of 16% was observed. Higher pre-surgical HbA1c levels and a milder EBWL were the main factors influencing both T2DM recurrence chance and anti-diabetic medication withdrawal. Finally, keeping metformin once an HbA1c in the complete remission range was attained did not seem to have impact on avoiding future relapse.

We have found increasing cumulative remission rates throughout the 5-year follow-up to a maximum of 57%, but prevalent ones remained stable around 50% showing an even proportion of patients entering and leaving the remission group after Y1. These results picture a remission plateau after Y1 in our population that contrasts with other publications stating its attainment by the third post-diabetic year \([9, 16]\). We herein have observed a maximal EBWL at Y1 potentially explaining this precarious plateau. T2DM remission can however occur even before substantial weight loss has been reached as confirmed by improved glycaemic control as early as the first post-operative week \([17]\). Changes in gut incretins and neurotransmitters, improvement of hepatic and peripheral insulin sensitivity, altered bile acid metabolism, and gut microbiota are possible weight loss independent mechanisms of T2DM remission after bariatric surgery \([18, 19]\). Low relapse rates in our population could also have accounted for the narrow difference between prevalent and cumulative remission rates, contrasting with previous studies reporting differences of around 30% \([6]\). When we have compared partial (HbA1C < 6.5%) with complete remission (HbA1C < 6.0%), an additional proportion of 5% of the enrolled patients were considered as T2DM remittent. Other publications on this matter reported a bigger gap between the percentage of patients fitting in these two concepts (from 10pp to 30pp) \([7, 8]\).

DiGiorgi et al. was the first to describe T2DM recurrence after RYGB in a small cohort of patients \([20]\). However, an HbA1c above 6% was used to establish recurrence, contrasting with most of publications that state a 6.5% cutoff. We have found a 5-year recurrence rate of 16%. Other studies including patients that also underwent mixed surgical procedures and with a comparable follow-up time reported percentages between 19% and 53% \([7, 8, 21]\). This lower proportion of relapses is probably due to the better pre-operative glycaemic control of our population (mean HbA1c at Y0 of 6.9%). However, the lack of standardization of recurrence definitions can also account for these differences. In addition, we have found that higher pre-operative HbA1c levels and milder EBWL were independently associated with relapse. Other studies have confirmed older age, longer diabetes duration, and pre-operative use of insulin or other glucose-lowering agents as variables favoring recurrence \([7, 8, 22]\). A recent report concluded that alterations in gut microbiota may play a role in diabetes recurrence after a bariatric procedure in rats \([23]\).

Data on long-term T2DM management following bariatric surgery is scarce. Recent guidelines mainly focus on glycaemic control on the surgery day and on the subsequent 10 days. After this early post-operative period recommendations state that standard diabetes guidelines should apply \([11]\). However, physicians that assist these patients face specific challenges, namely how to balance the weaning of anti-diabetic medication as glycaemic control rapidly improves and the impending risk of T2DM recurrence. An analysis of physicians’ prescription records revealed that there appears to be a proportional de-escalation of almost
every category of anti-diabetic medication in the first year after bariatric surgery [24]. Kashyap et al. proposed an algorithm with a pharmacological approach to residual T2DM following bariatric surgery [25]. However, it was based on the physiological mechanisms of the various types of surgical procedures and anti-hyperglycemic agents and not on populational studies indicating a proven advantage of that approach. In our study, anti-diabetic medication was stopped in most of the patients in the first post-operative year, paralleling T2DM remission, with additional 16% discontinuing them from Y1 to Y5. A lower pre-operative HbA1c and a higher EBWL were independently associated with the attempt to withdraw T2DM medication. Interestingly, those were the same variables that we found to influence T2DM relapse, showing that physicians empirically perceived them as important factors in managing glucose-lowering drugs. Insulin therapy was discontinued in most of the patients, but none of them attained a HbA1c ≤ 6.5% at Y5, probably a sign of a poorer beta cell function in insulin-treated patients. This fact signals that the subset of individuals are those who should benefit from a more aggressive treatment with oral anti-diabetic drugs after insulin is withdrawn.

Halpern et al. argued that an HbA1c target that was independent of medication use would be a better study outcome in some clinical situations, as when comparing bariatric surgery T2DM outcomes with medical therapy [14]. Given its well-established role as the first-line drug in the treatment of T2DM [3, 26], other authors acknowledge that a discussion on the role of metformin in T2DM remission would be of value despite requiring new conceptualizations of remission [6]. In our study, a mean difference of 22pp in complete remission rates was found when metformin was allowed. As far as we know, only one previous publication has considered metformin as consistent with the remission status, but a comparison of remission rates with and without the drug was not provided [13]. This data poses clinicians an additional challenge: should metformin be maintained after reaching T2DM remission? In our population, keeping metformin after attaining an HbA1c < 6.0% or 6.5% did not have a significant impact in the remission/relapse status of the next visit. Besides, when we analyzed factors that could influence glycemic control after a HbA1c in the complete remission range was achieved, there were no differences in HbA1c in Y2–Y5 between those who maintained metformin and those who did not. Instead, younger age, lower HbA1c levels and less weight regain were the variables predicting a better glycemic control for patients that initially achieved that milestone.

Bariatric surgery leads to a reduction of all-cause mortality, cardiovascular events, and microvascular complications of T2DM in obese patients [27–29]. However, reports that T2DM relapse can ensue after a period of improved glycemic control raises awareness about the potential compromise in these benefits. Large clinical trials like the 10-year follow-up of United Kingdom Prospective Diabetes Study (UKPDS) and Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) proved a “legacy effect” showing long-term benefits despite the loss of glycemic differences after the conclusion of the studies [30, 31]. Only one study focused on this issue in a bariatric cohort and proved that among patients who experienced T2DM relapse the length of time spent in remission was inversely related to the risk of incident microvascular disease [32]. As so, T2DM recurrence should not be seen as a surgical failure given that transient remission can potentially bring lifelong benefits. Moreover, our results show that follow-up HbA1c levels after relapse are still lower than those before surgery. No publications have investigated post-surgical metabolic memory in cardiovascular outcomes. Future studies should continue to address the potential benefits of keeping metformin or other anti-diabetic medications not only in attaining and maintaining T2DM remission but also in preventing micro and macrovascular complications of the disease in this specific population.

Our study had a longer follow-up period than other publications on this matter, maximizing the capacity to detect recurrence and to investigate its predictors. Furthermore, we think that including patients that underwent three different bariatric surgical procedures was an important advantage since most of the studies on T2DM remission/recurrence only included RYGB patients. There is still an ongoing debate on the better surgical procedure to induce T2DM remission in different subsets of individuals, but this was not the aim of our work and we consider that discussion outside the scope of this publication [8, 33]. The retrospective design of our study precludes causal inference and that can be stated as a potential limitation. Patients lack of adherence to follow-up visits is a common problem to all bariatric studies that can potentially lead to attrition bias. However, our drop-out percentage was similar to other studies on this matter and glycemic-related variables do not seem to have an impact on this outcome [34, 35]. It should be also underlined that the enrolled patients presented a remarkably low T2DM recurrence rate limiting the statistical power to detect an advantage of keeping metformin.

In conclusion, we intend to raise awareness about the need to standardize diabetes remission/recurrence definitions. This can lead to improved clinicians’ decision-making in selecting individuals who benefit the most of surgical treatment of T2DM and to better elucidate patients on surgery expected benefits and pitfalls. The low but still significant relapse rates we have described reinforce the
need of a multidisciplinary follow-up of obesity-related comorbidities even after attaining their apparent resolution. To the best of our knowledge, this is the first publication to analyze the patterns of residual TZDM management after bariatric surgery and the impact of maintaining/withdrawing metformin in the forthcoming glycomic control. In our population, maintaining metformin in patients that reached a HbA1c lower than 6% did not seem to have a significant influence on relapse rates during their follow-up. However, metformin pleiotropic benefits go well beyond glycomic control and future studies should continue to address this subject.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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