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Predicting Weight Regain after Bariatric Surgery: Using Decision Tree and Logistic Regression

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ABBREVIATIONS

ALAT	Alanine Amino Transferase
AUC	Area under the Curve
BDI	Beck Depression Inventory
CP	Complex Parameter
DBC	Dutch: Diagnose Behandel Combinatie
EMR	Electronic Medical Records
EWL	Excess Weight loss
GGT	Gamma Glutamyle Transferase
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
NPV	Dutch: Nederladse Persoonlijkheids Vragenlijst
RIVM	Dutch: Rijksinstituut voor Volksgezondheid en Milieu
ROC	Receiver Operating Characteristics
RYGB	Roux en Y Gastric Bypass
SCL	Symptom Checklist
SG	Sleeve Gastrectomy
SQL	Standardized Query Language
TSH	Thyroid Stimulating Hormone
WHO	World Health Organization
WM	Weight Maintained
WR	Weight Regain
ZGT	Dutch: Ziekenhuis Groep Twente

Chapter 1. INTRODUCTION

Over the past decades, the prevalence of obesity has increased, becoming one of the leading causes of chronic diseases[1]. Obesity is a pandemic public health problem that is defined as abnormal or excessive fat accumulation that impairs the health of the individual[2, 3]. World Health Organization report in 2016 showed that obesity affected more than 650 million adults worldwide[3]. According to the National Institute of Public Health and Environment (RIVM) of the Netherlands, 13.9% of Dutch people aged over 18 are obese[4].

An adult is considered to be obese when the Body Mass Index (BMI) is greater than or equal to 30kg/m^2 [calculated by dividing the weight in Kg (Kilogram) by height in squared meter][5], and its cause is multifactorial including sedentary lifestyle, consumption of diets high in simple carbohydrates, and genetic factors[6]. Obese patients are classified into three grades: obesity grade I – BMI ≥30 kg/m^2 and <35 kg/m^2, obesity grade II – BMI ≥35 kg/m^2 and <40 kg/m^2 and obesity grade III (morbid) – BMI ≥40 kg/m^2.

In order to prevent obesity in individual, understanding of our body weight control mechanisms is crucial. However, established management guidelines and protocols are undeniably required for the effective control in those people that are in the state of obesity. The management of obesity ranges from behavioral and pharmacological interventions to weight loss surgeries[7]. Numerous studies have shown that such interventions are useful for two reasons: they reduce the risk of developing metabolic comorbidities such as diabetes and hypertension; they also bring health benefits by ameliorating the health conditions and enhancing positive outcomes in those with the disease[7, 8, 9].

Behavioral management, either with or without pharmacological therapy, often fail to produce satisfactory results in the treatment of obesity for several reasons. Behavioral management largely focuses on nutritional counseling and lifestyle modification approaches which involve limiting the amount of diet and calorie intake, and promotion of regular physical exercise. The main challenge encountered in this intervention is the lack of guidelines to the ideal weight loss program, which prevents the intervention from achieving and maintaining weight loss in most people over the long term period. The other type of management is pharmacological therapy, which is usually administered in conjunction with other interventions like behavioral management in order to achieve an additional weight loss or maintain the weight after achieving weight loss. Several factors impeded the development of pharmacotherapy, comprising the safety concerns to the patients and uncertainties in legal pathways in the approval of the medications[10]. Both behavioral and pharmacological interventions require a long duration of time to have an optimal impact on patients with obesity and often fail to treat morbid obesity (grade III) due to their poor weight loss outcome, which necessitates a more effective treatment for obesity[6, 7].

Weight loss surgery (bariatric surgery) is found to be the most effective intervention available for management of morbid obesity with significant long term efficacy[9] and durability in the improvement of obesity-related comorbidities such as diabetes and dyslipidemia[11]. The outcomes of the surgery have led obese patients in the ultimate improvement of quality of life[7]. As a result, bariatric surgery adjunct with other obesity management has remained a gold standard of treatment for morbid obesity[11].

Compared with other obesity treatments, bariatric surgeries have a higher cost of operation and expose patients to a risk of surgery related complications. For these reasons, the examination of the outcomes of the surgery in the long term period is crucial for providing adequate justifications as a first line treatment for morbid obesity[12]. There is no clear consensus for measuring the success or failure of the surgery[5] however it is a common practice by surgeons to define the success of the surgery outcome in terms of the amount of weight loss achieved. Surgeries that result with a loss of at least 50% of excess weight, regarded as a successful surgery (by defining the excess weight as the difference between preoperative weight and the ideal weight[14, 15, 18]). However, it is relevant for the evaluation of the outcome of the surgery to take into account not only the amount of excess weight loss but also the maintenance of the achieved weight loss over the long term[10], for purpose of enhancing a better quality of life and life expectancy[16].

In obese patients who underwent bariatric surgery, the lowest weight (nadir weight) is observed between the first and second postoperative year [17, 25] with resolutions in obesity related conditions including diabetes, hypertension, hyperlipidemia, and sleep apnea[13, 20]. Nonetheless, weight loss maintenance, which is a vital element in sustaining the resolution of comorbidities[19], is not achieved by all patients due to several surgical and non-surgical related factors encountered in the long term[17]. Weight loss maintenance is a phase of preserving the nadir weight that is achieved after bariatric surgery in long-term which eventually leads patients to greater quality of life. After the achieving intended nadir weight, the weight maintenance phase begins which has a different physiological mechanism from weight loss[7].

Studies estimated that 20-50% of patients after bariatric surgery have the difficulty of maintaining weight loss, resulting in unwanted postoperative outcome called premature weight stabilization or weight regain[21, 22]. Weight regain is one the leading cause for the surgeons and patients to require a revisional bariatric surgery that predisposes patients to risky and less productive procedure[23]. Although weight regaining is the most common indication for revisional surgery, the incidence of revisional bariatric surgery largely depends on the type of primary bariatric surgery operated. The incidence is higher among patients who had a restrictive type of bariatric surgeries such as Gastric banding with 33.4% –40% followed by Roux en Y gastric bypass (10-20%) and Sleeve Gastrectomy (5-10%) [24].

American Diabetic Association[7] stated that weight regain, in part, is attributable to normal physiological alternations in the weight maintenance phase, which are an increment in metabolic efficiency, an increment in the prominence of hunger signals, and a reduction in the salience of satiety signals due to the initial weight loss after the operation[15]. Numerous studies have shown the period of time for the occurrence of weight regain is beginning from 18-24 months postoperatively[20]. In a prospective cohort study of 1406 adults who underwent Roux-en-Y gastric bypass, which is a gold standard for treatment of morbid obesity, with a median follow-up of 6.6 years revealed that 43.4 % of patients begin to regain weight by 1 year since reaching nadir weight, with number growing over the passage of time (63.4% by 4 years)[25].

The exact drivers of weight regain are widely varied due to lack of consensus among the studies on a scientifically meaningful definition of weight regain. From the several studies of weight regain, it is likely that causes of weight regain are multifactorial, and health professionals strive to understand the related risk factors. It is possible to categorize predictors into surgical and non-surgical for explaining the risk factors of weight regain after bariatric surgery. Surgical factors are related to the anatomical and physiological changes such as the size of the gastric pouch and the dilation of the pouch and the stoma with the course of time[2, 26]. Non-surgical determinants involve making a distinction between the patient's preoperative and postoperative behavioral and demographic characteristics. Various studies have shown preoperative factors such as high baseline BMI[5, 19], younger age[15], and abnormality in physiological and metabolic set points like hyperlipidemia[25] and deficiency of iron[16] as important determinants for explaining the the occurrence of weight of regain after the surgery. Furthermore, several postoperative factors have been found in plenty of studies that contribute to the occurrence of weight regain. These include the presence of post-surgical psychological disorders such as binge eating, depression, and anxiety[26], maladaptive eating behaviors (high calorie intake and alcohol consumption), and non-adherence to the follow up[10], and time since the surgery[16]. In addition, patients who lack adequate physical exercise after having the surgery has shown a higher risk of developing weight regain[10, 27]. Therefore, the mixed results on predictors among studies urge additional researches in order to confirm what has been reported and possibly uncover vital new predictors of weight regain.

Given the variability in the results between various studies regarding the predictors that are contributing to weight regain, the primary objective of this study was to develop a predictive model for weight regain in patients who underwent bariatric surgery at Ziekenhuis Groep Twente (ZGT) hospital. The second objective of this study is to determine the prevalence of weight regain.

To achieve our primary and secondary objective, we formulated the following four research questions:

1. **What are the preoperative and postoperative factors associated with weight regain in patients who underwent bariatric surgery from 2015-2016 in ZGT hospital with a follow up of at least 24 months?**
2. **What preoperative and postoperative factors are predictors of weight regain according to the logistic regression model in patients who underwent bariatric surgery from 2015-2016 in ZGT hospital with a follow up of at least 24 months?**
3. **What preoperative and postoperative factors are used to predict weight regain using decision tree model in patients who underwent bariatric surgery from 2015-2016 in ZGT hospital with a follow up of at least 24 months?**
4. **Which predictive model performs best in predicting the occurrences of weight regain in patients who underwent bariatric surgery from 2015-2016 in ZGT hospital with a follow up of at least 24 months?**

Significance of the study

This study aims to elucidate the possible causative factors of weight regain in patients who had bariatric surgeries which help to support the decision of health care professionals in combating weight regain during the follow up period. Identifying the factors could lead to early personalized patient interventions to the conditions which eventually result in improving the health and wellbeing of patients after the surgery through diminishing the effect of the existed comorbidities and the need for revisional surgery.

Chapter 2. METHOD

2.1. Study Characteristics

The study was conducted at ZGT (ZiekenhuisGroep Twente) hospital which is located in Almelo and Hengelo, Netherlands. The ZGT obesity center provides bariatric surgery for approximately 500-600 patients per year. This study uses a retrospective cohort study design to investigate the predictors of weight regain in patients who had bariatric surgery in ZGT.

The ZGT's ethical board committee approval was requested to get access to the patients' EMR (Electronic Medical Records). Due to the retrospective nature of the study, the waiving of the patient's informed consent was necessary. After the institutional review board approval was obtained, the study was carried out on patients who had bariatric surgeries beginning from 2015-2016 by searching from the electronic patient record database.

There are different types of bariatric surgeries. The most commonly performed procedures in Ziekenhuis Groep Twente (ZGT) hospital are the Mini gastric bypass, Roux-en-Y Gastric Bypass (RYGB) and the Sleeve Gastrectomy (SG) in order of most occurrences[28]. In brief, the Mini Gastric bypass involves modification of gastrointestinal structure by making a new mini stomach and rerouting of the intestines. It is performed laparoscopically by making 4 to 6 small incisions in the abdomen. The stomach is reduced by up to 90 percent, and then it is attached approximately 6 feet down the small intestines; this allows for food to bypass the upper intestines. In RYGB, involves the creation of gastric pouch which of approximately 20cm by dividing stomach horizontally 5 cm below gastroesophageal junction and vertically along a 36F bougie. The pouch is then attached to a part of the small intestine called the Roux limb forming "Y" shape which makes the food to bypass not only the stomach but also the upper part of the small intestine. For SG, the greater curvature including the complete fundus was resected from the distal antrum (5 cm proximal to the pylorus) to the angle of His. A laparoscopic stapler, with a 60-mm cartridge (3.5-mm staple height, blue load), was used to divide the stomach alongside a 34 French bougie (placed against the lesser curvature of the stomach).

2.2. Study Population

Participants are patients who have met the eligibility criteria for bariatric surgery and have undergone either one of the commonly performed bariatric surgeries (namely RYGB, SG, and Mini gastric bypass) at the obesity center beginning from 2015 till 2016.

2.3. Inclusion/Exclusion Criteria

The inclusion criteria for patients were if they were ≥18 years of age, had one of the three common types of bariatric surgeries performed in the hospital and had a follow up of at least 24 months after surgery in the ZGT obesity center.

Patients who had undergone gastric banding were excluded from our study due to the paucity of the data and the less applicability of the procedure in the future. Moreover, patients with a history of revisional bariatric surgery were taken into account for descriptive statistics but were excluded from any statistical analyses. Patients who found to be deceased irrespective of the cause of death were excluded from our study.

2.4. Sampling

Out of the potentially 1448 patients who 18 years or more at the time of bariatric surgeries, retrieved from electronic patient's record using a data extraction tool, CTcue. 34 (2.3%) were excluded as they had revisional surgery after the primary bariatric surgery, 10 (0.69%) as they deceased after the surgery, and 167 (11.1%) due to the lack of adequate follow up beyond 24 months. The included participants had one of the three bariatric surgeries as a primary treatment for their obesity before the year 2017. In this period 882, 226 and 129 participants had RYGB, SG and Gastric mini bypass respectively. Further information is given in Figure1 at appendix1, displaying the flow diagram for finding the study cohorts using CTcue.

2.5. Data Collection

Data were extracted from electronic medical records through automated extraction using SQL (Structured Query Language) and CTcue application. Patient's records are stored in EMR in structured and unstructured form. The unstructured form of the data constitutes more than 75% of the whole data. As a result, the data extraction process comprises writing customs scripts using both automatic extraction tools to obtain the data points at pre and postoperatively and manually reading of the health professional's documentation using CTcue. Data were recorded in the consultation reports of the health professionals, in the medical assessments and patients interviews carried out by the surgeons, internists and/or nurse practitioner during the provision of medical care to patients.

The whole data collection process was carried out in collaboration with data management department of the hospital and health professionals. Health professionals and the researcher used CTcue application to extract data automatically and manually reading from source documents, while the data analytics department applied a series of scripts for each variable using SQL.

CTcue is a data extraction tool that enables users to retrieve complex and unstructured healthcare data by organizing into logical categories. The application uses rule-based technique as a means to extract the valuable textual medical information from the source database and that enables the analysis of textual medical records in order to find the intended information in the texts. In order to collect the data, the CTcue's search query interface allows primarily finding the study population and validating the outcome. Once the study population is obtained, the interface permits to collect the patient's data by setting different parameters. In the CTcue, there was no access to the patient identifiers for use in this study.

2.6. Steps in the Collection of the Data

Thus, a total of 1237 participants included for collecting of relevant medical and social history at the preoperative and postoperative time. The variables were firstly collected using CTcue and the results were checked with HiX, which is the healthcare information management software, for the reliability and consistency of the relevant data. It was possible to collect preoperative variables including the laboratory measurements and medical comorbidities. Although we were able to gather a few medical histories of the patients during the postoperative follow up, majority laboratory measurements and other psychological and behavioral determinants were not gathered due to the short data collection period and presence of missing data.

2.7. Study Variables

The following patient's preoperative medical data were collected: Age, gender, weight, height, presence of comorbidities (diabetes, hypertension, and dyslipidemia), history of smoking and alcohol consumption, laboratory results including lipid profiles (Total cholesterol and Triglyceride), presence of depression, and marital status. Postoperative independent variables collected were the type of the procedure, time since the surgery, weight, and the resolution of medical comorbidities. In addition, only two laboratory measurements namely Ferritine and ALAT (Alanine-aminotransferase) were collected at four months postoperatively.

2.7.1. Patient Characteristics

- *Age*: Recorded by the health care professionals at the time of surgery.
- *Patient Gender*: Recorded at the time of the surgery as “male” and “female”.
- *Preoperative BMI* (*kg*/m^2): Calculated from Preoperative weight and height recording found in medical assessment form at the time of surgery. Postoperative BMI also calculated in the same way as preoperative after collecting weight measurements at two data points.
  - BMI= Preoperative Weight(Kg)/ (Height(m)×Height(m))
- *Alcohol History*: Self-reported by the patient during one of the appointments with clinicians preoperatively. It was considered as “Yes” for those who claimed they drink and “No” for those who stop drinking for more than a year or who claimed they have never drink in their lifetime.
- *Smoking History*: Self-reported by the patients during one of the appointments with clinicians preoperatively. It was reported as “Yes” for those who reported as a smoker, as “No” for those who have never smoked in their lifetime and as “Stopped” for those who reported they quitted smoking for more than a year.
- *Marital Status*: Reported by patients during the preoperative assessment by clinicians. It was denoted as “Married”, “Unmarried”, “Registered Partnership”, “Divorced”, “Living together (not married), and “Widow”.
- *Comorbidities*: Recorded during preoperative and postoperative appointments with clinicians. In this study, reports of surgeons, internists, nurses, and psychiatrists were assessed to find whether the patient had the comorbidities or not.
  - *Diabetes:* defined as for those who had a diagnosis of diabetes irrespective of the type except gestational diabetes and/or were on antidiabetic medication in the documentation of health professionals. The diabetes status was checked postoperatively for those who were diagnosed with diabetes preoperatively.
  - *Hypertension:* defined as “Yes” for those who had a diagnosis of hypertension irrespective of the type and/or those who were on antihypertensive medication in the reports or forms. The hypertension status was checked postoperatively for those who were diagnosed with hypertension preoperatively.

- *Dyslipidemia*: were obtained from the laboratory measurements of lipid profiles preoperatively. If at least one of the measurements was abnormal, the patient is categorized as having dyslipidemia. Abnormal level considered when the level of LDL-cholesterol≥2.6mmol/l, HDL≤1mmol/l, Total cholesterol≥5.2mmol/l, and Triglyceride≥1.7mmol/l.
- *Depression:* Patients were identified as they have depression using the Beck Depression Inventory (BDI-II) questionnaire as well as the actual diagnosis of the condition from the history reports. In the questionnaire, those who have a higher recording in rating scale were categorized as having depression. Those who were taking any antidepressant medication before the surgery were also considered as depression patients.
- *Laboratory Findings*: TSH (Thyroid Stimulating Hormone) in mU/l, GGT (Gamma Glutamyltransferees), and Lipid profiles in mmol/l of patients such as LDL (Low density lipoprotein), HDL (High density lipoprotein), Total cholesterol, and Triglyceride were collected preoperatively. ALAT in U/l was collected both before the surgery and at 4 months after the surgery during the follow up period. Ferritine in µg/l was also extracted at 4 months after the surgery.

2.7.2. Postoperative Outcomes

- *Operative Procedure:* RYGB, Mini gastric bypass and SG were identified from the patient's records using their respective DBC codes.
- *Nadir Weight (lowest weight)*: Included the last measurement that the patients had within 2 years postoperatively.
- *Recent Weight*: The last measurement that the patient had during the follow up appointments with the Nurses and/or Internists.
- *Ideal Weight*: Calculated using the height of the patient and BMI of $25kg/m^2$. Ideal Weight = $25kg/m^2 \times Height(m)^2$
- *Time since the surgery*: defined as Date of Recent Weight measurement – Date of Operation
- *Percentage of Excess Weight Loss (%EWL):* It is calculated as [(Preoperative Weight-Nadir Weight/Recent Weight)/ (Preoperative weight-Ideal weight)] × 100
- *Weight Regain (WR):* Calculated using the nadir weight as a percentage of maximum weight loss. And It is given by:

$$([\text{Recent weight} - \text{Nadir Weight}] / [\text{Preoperative Weight} - \text{Nadir Weight}]) \times 100$$

The collection of the patient's records was conducted using two data extraction tools: CTcue and SQL. The anthropometric measurements at preoperative and postoperative time were primarily collected using CTcue. The missing data and outliers found in the measurements were screened and necessary corrections for the values were made from the actual reports of the health professionals and from the results SQL that were obtained from data management department of the hospital.

The final dataset consisted of categorical and numerical variables were checked for validation using CTcue for cross-validation of results with the EMR. Each patient was evaluated for including the necessary variables and whether the included variables met the criteria with certain confidence score according to CTcue. All of the laboratory results and weight measurements collected before and after the surgery were treated as numerical values. Also age at time of surgery was kept as a numeric values. The rest of variables considered as categorical type for all of the analysis.

2.7.3. Rationale for Measurement of Weight Loss Outcomes

In the recent study by king et.al, various measurements and threshold levels of weight regain were compared for defining weight regain according to their statistical significance and fitting of the model. The study included 1040 patients who had RYGB surgery and had a follow up to 5 years or longer. The definition given for weight regain as a percentage of maximum weight loss from nadir weight found to perform better than other alternative measurements in finding the association with clinical outcomes[25]. Nadir weight is defined as the recording of lowest weight achieved during the postoperative time. It usually happens within the first two years, between 18-24 months. This definition is applied in multiple studies, stating that the less likelihood of the value being affected by the initial weight (preoperative weight) [11, 29]. Furthermore, King et.al investigated the different cutoff levels for defining weight regaining and their impact on the model fitness. The study concludes that a 20% threshold level perform best than other dichotomous measures after adjusting the RR (relative risk).

This study applies the above calculation for percent WR and ≥20% threshold level were used to divide patients into two groups, one with weight regain (WR) and one with weight maintenance (WM) group. In addition, the EWL (excess weight loss) was calculated at two times during the follow up period, using the nadir weight and last follow up weight measurements for the comparison among the two groups.

2.8. Data Preparation

The output from CTcue and SQL were captured separately in excel file. The number of samples was determined according to the output of CTcue. Then the SQL results were combined with CTcue's output for not only to fill the missing values in each variable but also to add the laboratory finding. The combined dataset, then, was screened for outliers both for continuous and categorical variables and adjustments were given accordingly. The treatments involve manually checking in the records of the patient using CTcue or replacing them with mean values.

In the combined dataset, missing data were common in each extracted variables. Out of 1237 participants, only 46 (3.72%) patients had complete inputs in each variable. Table5 in appendix 2 shows the number and percentage of missing inputs in the combined dataset with respect to each variable.

Due to a large number of incomplete values, filling in the missing values were crucial. Missing values were treated using different imputation techniques ranging from simple methods such as replacing with mean and mode to the machine learning imputation techniques. Imputation techniques were chosen after comparing various techniques for their impact on the model according to their accuracy.

As shown in table5 in appendix 2, variables which have a missing data of more than 75% were excluded, resulting in an increasing number of patients who had complete records 165(13.3%). The excluded postoperative variables were: lipid profiles (HDL, Triglyceride, LDL, Total cholesterol) and the status of anxiety and eating disorders. All continuous variables except Nadir weight that have less than 5% of missing data were replaced with mean values. But for those which have a missing data of ≥5% and Nadir weight were imputed using regression technique. Similarly, categorical variables which have missing values of <5% were replaced with the most common value (mode) of the variable, while the missing values of ≥5% were treated with random forest algorithm[30, 31].

2.9. Statistical Analysis

Initially, descriptive analysis was conducted on patients' demographic and clinical characteristics. The results were expressed as the mean ± standard deviation for continuous variables and as frequency n (%) for categorical variables. A chi-squared test and unpaired t-test were applied to the categorical and continuous variables respectively in order to compare the demographic characteristics and bariatric surgery outcomes among the weights regained and weight maintained group. We applied two models namely logistic regression and decision tree to explore the predictors and assess the consistency of the models in identifying the predictors to the weight regain. Consequently, we build the models to make a prediction of weight regain based on the performance of models. All data preparation and statistical analyses were done using R v3.5.1.

2.9.1. Logistic regression:

A univariate analysis was performed to find predictors that had a significant association with weight regain. Variables with *p-value<0.01* were considered as statistically significant and included in the final model, multivariate logistic regression.

The multivariate logistic regression is given by:

$$P(y) = Exp \sum BiXi/(1 + Exp \sum BiXi)$$

Where, P is the probability of weight regain occurring, Bi is the regression coefficient of X and Xi is the predictor variable

Equation1. Multivariate Logistic Regression

Multivariate logistic regression was used to analyze the relationship between the target variable and only univariate significant variables ($P<0.01$) were included for final analysis. And the significance of independent variables was assessed at a threshold of significance of $P< 0.05$. Furthermore, the odds ratio (OR) was obtained for significant variables. Collinearity was assessed among the included multivariate variables and removal of the related variables from the model was necessary.

2.9.2. Decision Tree:

In addition to the multivariate logistic regression, decision trees were built in order to compare the result with the multivariate logistic regression. Prediction using decision tree is one of the most common machine learning technique that involves the construction of tree using decision nodes, branches, and leaf (terminal) nodes. The algorithm portrays specific sequences of decisions and consequences. It is situated upside down, with the root at the top of the tree where the original dataset exists. Then the tree grows to the first node based on a particular most informative input variable in order to split the population into categories. Then, for each value defined for the decision values of the best attribute, the algorithm repeats the process with additional attributes.

To choose the most informative variable, the measure of Gini index is used which basically assess the purity of the variables (see equation2). The Gini index is a measure of prediction power of variables in regression or classification, based on the principle of impurity reduction and does not rely on data belonging to a particular type of distribution. It is used to calculate the importance of the variable for prediction, explanation, or classification of an outcome variable.

The Gini index of a node n is calculated as follows:

$$\text{Gini (n)} = 1 - \sum_{j=1}^{2}(Pj)^2$$

Where Pj is the relative frequency of class j in the node n

Equation2. Gini index Calculation

For building and plotting of the decision trees “rpart” package was used. After constructing the tree, pruning was necessary to increase the accuracy of the model and ease of interpretability. It was carried out by manually manipulating the parameters of the tree including a complex parameter (Cp) and minimum splits. Complex parameter has role of saving the computing time by pruning off splits that are obviously not worthwhile. Thus any split made in the tree which does not improve the fit by Cp will likely be pruned off by cross-validation. Minimum split is specifying the number of observations that must exist in a node in order for a split to be attempted.

2.9.3. Variable Selection

In both models, variables selection was necessary to optimize the predictability of the models. In logistic regression, the predictive model was built based on statistically significant variables in the univariate analysis. All variables that had $P \leq 0.01$ were included in the final model and assessed the interaction and Collinearity among the variables. The variable selection process in decision tree involves the calculation of Gini index of all variables. The concept of variable importance is an implicit feature selection performed by the decision tree model and it is assessed by the Gini impurity criterion index. And the top ten most important variables were included to build an optimized decision tree.

2.9.4. Cross Validation of the Models

Both methods of analysis use a dataset that was randomly split into train and test set, capturing 70% and 30% of data respectively. The misclassification error rate in the prediction was calculated in the test set after training the data using the train set. Confusion matrix was computed using “caret” package in order to find the performance of the model. In the confusion matrix, various metrics such as sensitivity, specificity and the accuracy of the model were evaluated. Based on the value of metrics, optimizations of the models were needed by fixing the imbalanced class of WR in the dataset. Different methods of dealing class imbalance such as undersampling, oversampling and synthetic data generation were compared in terms of interpretability of the output and overall performance of the classification. “ROSE” package used to balance the dataset.

In addition to the computation of confusion matrix, model evaluation technique such as Receiver Operating Characteristics (ROC) curve used to visualize the tradeoffs between sensitivity and specificity. Plotting of ROC was crucial to calculate the AUC (Area under the curve) as the curve is insensitive to class imbalance. AUC (Area under the Curve) was measured to identify the degree of separability between the patients with a high risk of developing weight regain and no weight regain. The AUC of the curve used to quantify the performances of the two models in predicting the weight regain. “pROC” package used to plot the curve and calculate AUC for both models.

Chapter 3. RESULTS

3.1.Demographic characteristics

Among the 1237 patients, the average age was 44years ± 10.63 at time of the surgery, 955 (77.2%) were females and the average preoperative body weight was 129.0±19.9 kg. Most patients were married 748 (60.5%) and had a mean follow up of 38.7±11.3 months.

Weight regain was observed in 195 cases (15.8%) with an overall mean follow up time of 45.7±10.7 months. Characteristics of WR and WM groups are summarized in table1. The percentage of patients who had SG were significantly higher among the WR group compared to the WM group (*$p<0.001$*). Furthermore, patient with WR had a significantly higher level of LDL level (*$p<0.001$*) and had history of smoking (*$p=0.009$*). Measurements of BMI and weight at preoperative time showed almost the same amount the in two groups. The percentage of depression among the WM group was significantly higher (*p value*=0.008).

3.2. Postoperative Outcomes of Bariatric Surgeries across the Groups

As shown in table2, in WR group the mean nadir weight was 84.3±16.6 kg, which was almost comparable with the weight maintained group. The mean %EWL in the last follow up of patients during the postoperative period was significantly higher in the WM group with 80.1±19.3%, while in the WR group it was 55.7±22.5% (*$p<0.001$*). The average percent of weight regain after maximum weight loss in weight regain group was 32.9±17.0%. Time elapsed since the patients had the surgery was significantly higher among the WR group (*$p<0.001$*). The mean follow up was significantly higher among WR group with 45.7±10.7 months than in WM group (37.4±10.7 months). In the entire cohort, maximum weight loss (nadir weight) was recorded at 20.6 ±6.3 months and at that time the mean %EWL was 72.0±29.5. During the last follow up at the obesity center the mean %EWL was 63.6±20.4 in both groups.

Table1: Population Characteristics based on the two groups using Chi-Square and t-test.

	Weight maintained (WM) N=1042	Weight regain (WR) N=195	P value
Age mean ±SD	44.25 ±10.72	44.81±10.13	0.505
Gender: male (%)	233 (22.4%)	49(25.1%)	0.452
Preoperative Weight (mean ±SD)	129.42±19.92	126.78 ±19.78	0.090
Operation Procedure (%)			**<0.001**
Mini Gastric Bypass	125 (12.0%)	4 (2.1%)	
RYGB	745 (71.5%)	137 (70.3%)	
SG	172 (16.5%)	54 (27.7%)	
Preoperative BMI (mean± SD)	44.78 ±6.41	43.18 ±5.10	**0.001**
Smoking Status (%)			**0.009**
Stopped	191 (18.3%)	53 (27.2%)	
Yes	205 (19.7%)	41 (21.0%)	
No	646 (62.0%)	101 (51.8%)	
Alcohol Consumption: Yes (%)	378 (36.3%)	68 (34.9%)	0.769
Preoperative Diabetes: Yes (%)	297 (28.5%)	51 (26.2%)	0.560
Postoperative Diabetes: Yes (%)	90 (8.6%)	21 (10.8%)	0.412
Preoperative Hypertension: Yes (%)	450 (43.2%)	76 (39.0%)	0.311
Postoperative Hypertension: Yes (%)	180 (17.3%)	36 (18.5%)	0.766
Preoperative Depression: Yes (%)	679 (65.2%)	107 (54.9%)	**0.008**
Preoperative TSH level (mean± SD)	2.41±1.69	2.49 ±1.63	0.578
Preoperative GGT level (mean ±SD)	39.65±27.73	37.29±26.77	0.273
Preoperative ALAT level (mean ± SD)	30.78±18.57	30.79±32.10	0.996
ALAT level at 4 months postoperatively(mean± SD)	28.76±15.27	27.97±16.65	0.514
Ferritine level at 4 months postoperatively (mean± SD)	134.31±115.93	136.81±127.51	0.786
Preoperative dyslipidemia = Yes (%)	891 (85.5)	176 (90.3)	0.098
HDL (mean ±SD)	1.22±0.31	1.23±0.29	0.516
LDL (mean ±SD)	2.98±0.85	3.19±0.87	**0.001**
Triglyceride (mean ±SD)	1.85±0.98	1.78±0.90	0.387
Total cholesterol (mean ±SD)	5.05±0.99	5.22±0.97	0.024
Marital (%)			0.973
Divorced	1 (0.1%)	0	
Married	627 (60.2%)	121 (62.1%)	
Unmarried/Single	251 (24.1%)	46 (23.6%)	
Registered Partnership	8 (0.8%)	2 (1.0%)	
Living together (not married)	141 (13.5%)	23 (11.8%)	
Widowed	14 (1.3%)	3 (1.5%)	

3.3. Predictors of Weight Regain

3.3.1. Predictors according to Logistic Regression:

The univariate analysis revealed that patients who had a history of smoking and Patients who had SG and RYGB, a higher level of LDL, or a long time since the operation was associated with weight regain (*P<0.01)*. Moreover, patients who had mini gastric bypass surgery or having a greater preoperative BMI/weight were less likely to experience weight regain (*P<0.01)*, while having depression, dyslipidemia, greater cholesterol level and no history of smoking trended toward significance (*P<0.05)*. The result of obtained from the univariate analysis are summarized in table3. All other variables were not found to predict weight regain significantly.

Table2. Chi-square and t-test on the surgery outcomes between the WR and WM groups

Surgery Outcomes (mean ± SD)	**WM (N=1042)**	**WR (N=195)**	**P value**
Ideal weight	73.0±8.43	73.2±9.2	0.777
%EWL recent	80.1 ±19.3	55.7 ±22.5	**<0.001**
%EWL nadir	81.8 ±19.1	82.2±23.1	0.847
Nadir BMI (kg/m2)	29.0±4.3	28.8±4.3	0.504
Recent BMI (kg/m2)	29.3±4.4	33.4 ±5.0	**<0.001**
Nadir Weight (Kg)	84.5±14.5	84.3±16.6	0.852
Recent Weight (Kg)	85.4±14.9	97.7±19.3	**<0.001**
% Weight gain	1.7±10.7	32.9±17.0	**<0.001**
Time since operation (months)	37.4±10.7	45.7±10.7	**<0.001**

Only variables with a *P*<0.01 were included for multivariate logistic regression analysis. To avoid Collinearity between the weight measurements in Kg and BMI in the multivariate analysis, we compared the AIC level of the model by including the two measurements in a separate model. And preoperative BMI showed some improvement in the model performance by decreasing the AIC level. Thus, preoperative BMI was only included in the multivariate analysis.

The Multivariate analysis showed that longer duration since the operation, a higher level of LDL were significant predictors of the weight regain after bariatric surgery (see Table4). After controlling time since the surgery and type of bariatric surgery in the multivariate analysis, LDL remained to be a statistically significant predictor for weight regain with *P*= 0.036 (OR= 1.27, 95%CI: 1.02-1.60). Hence, for every 1mmol/L increment in LDL, the odds of weight regain in patients who had bariatric surgeries were 1.27 times the odds of those with LDL 1mmol/L lower. Moreover, odds of weight regain increased by 1.06 for every one month increment in patients after the surgery. Lower preoperative BMI was a statistically significant predictor of weight regain, where the odds of weight regain after surgery decreased by a factor of 0.99 for each increase in preoperative BMI of patients. The multivariate analysis did not show any significant associations of bariatric procedures to weight regain.

Table3. Univariate results examining the factors for a weight regain

	Estimate	**Std. Error**	**z value**	**Pr(>|z|)**		**Crude OR**
Operation procedure: Mini	-3.4340	0.5866	-5.854	4.79e-09	***	0.03
Operative procedure: RYGB	1.7453	0.5969	2.924	0.00346	**	5.69
Operative procedure: SG	2.1729	0.6179	3.516	0.00044	***	8.76
Preoperative BMI	-0.0647	0.0181	-3.572	0.00035	***	0.94
Preoperative Weight	-0.0136	0.0051	-2.682	0.00731	**	0.99
Smoking status: No	-0.5131	0.2229	-2.302	0.0213	*	0.60
Depression: Yes	-0.4532	0.1899	-2.386	0.017	*	0.64
Preoperative Dyslipidemia: Yes	0.7649	0.3447	2.219	0.0265	*	2.13
LDL	0.2837	0.1075	2.639	0.00832	**	1.32
Total cholesterol	0.1890	0.0925	2.043	0.0411	*	1.20
Time since operation	0.0658	0.0085	7.734	1.04e-14	***	1.09

*Significance codes of P-value: '***' 0.001 '**' 0.01 '*' 0.05*

Time since the surgery was the only variable found to be a confounding variable to LDL level. Bivariate analysis using two sample t-test of the two variables revealed that there was a significant relationship ($p<0.001$) between the level of LDL and time since the operation. Furthermore, Pearson chi-square test between time since the operation and weight regain showed a significant association ($X^2 = 903.14$, $P = 0.035$). However, the coefficient of the level of LDL have not shown 10% change before and after including the time since operation in the model. Thus, the likelihood ratio test (LRT) was necessary to decide the variable to be included in the model as a confounding variable. LRT was statistically significant that the model performs well with the inclusion of time since the operation.

Logistic regression was trained on 70% of the dataset using variables used in multivariate analysis. And the model performance was assessed on 30% of the test set. As seen in the confusion matrix (table 6 in appendix 3), the model performs well for those who don't have weight regain with an accuracy of 83% (see table 7). Since our focus is on those who experienced weight regain, optimizations of the model were necessary. One of the optimization areas needed was correcting the class imbalance existed in our sample. The WR group was on 16% of our sample population. As the majority of our population was in weight maintenance, it is difficult for our model to learn the occurrence of weight regain from the given variables. After adjusting the model for oversample population (Weight maintainers), the prediction in the test set shows the actual accuracy of 64.2% (95% CI: 59.2 to 68.9) with a sensitivity of 62% and specificity of 64.5%. The confusion matrix and AUC level of the model are displayed in appendix 3.

Table4. Multivariate result of logistic regression among covariates for predicting WR

	Estimate	Std. Error	z value	Pr(>|z|)		Adjusted OR
(Intercept)	-4.465886	1.024599	-4.359	1.31e-05	***	
Time since operation	0.057977	0.009010	6.435	1.24e-10	***	1.06
LDL	0.248802	0.115095	2.162	0.031	*	1.28
Operation: RYGB	1.063474	0.609796	1.744	0.081	.	2.89
Operation: Sleeve	1.160649	0.642495	1.806	0.071	.	3.19
Preoperative BMI	-0.011151	0.005411	-2.061	0.029	*	0.99

*Significance codes of P-value: '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1*

3.3.2. Predictors according to Decision Tree:

In a decision tree, we employed all variables to create the train and test set with 70% and 30% proportion respectively. Upon training the model, confusion matrix on test data showed the tree performs with an accuracy of 82% (CI=78.35%-85.12%), sensitivity=20.3% and specificity=92.8% (details found in appendix4). As our sensitivity performance was not predictive to weight regain, pruning and adjustments of the parameters were necessary. Pruning of the tree brought a negligible change in the accuracy with 82.64%. The pruned decision tree (see figure3 in appendix 4) showed time since the surgery as the most important variable to perform the classification followed by preoperative LDL, preoperative BMI and Triglyceride level. This finding is consistent with logistic regression's significant variables except for Triglyceride.

Similar to logistic regression, the treatment for class imbalance was performed due to the low sensitivity of the model for predicting weight regain. The best predictive model found when we used "ROSE" package to create new synthetic similar instances of weight regain in a train set. Furthermore, we chose the variables according to their Gini index to build the tree. Variables which were the top 10 variables in order of importance were included in the model (see table9 in appendix4). As shown in table 9, time since the operation, preoperative GGT, preoperative ALAT, preoperative BMI and LDL level were among the top five most important variables according to their Gini index value.

After the correcting the class imbalance and choosing the top ten most important variables, the model had accuracy of 64.9% (CI=59.8% - 69.8%), sensitivity of 70.49% and specificity of 63.82% (table10). The tree is presented in figure1, where time since the surgery still is the most important variable to make the classification. At the top, it is the overall probability of weight regain. It shows that 49% of obese patients regain weight and then divide the root node with the time since the patients had the surgery. Going down the tree from the root node will reveal the criteria to reach the terminal node and the predicted outcome. For example, looking at the extreme left branch, we can predict that 98% of patients who had bariatric surgery will not regain weight within 27 months after they had the surgery. On the other hand, looking at the extreme right branches, when patients reach more than 38 months since they had the surgery, those who had preoperative LDL-cholesterol level of ≥2.9mmol and postoperative ALAT ≥19U/l, 81% of patients were predicted to have weight regain.

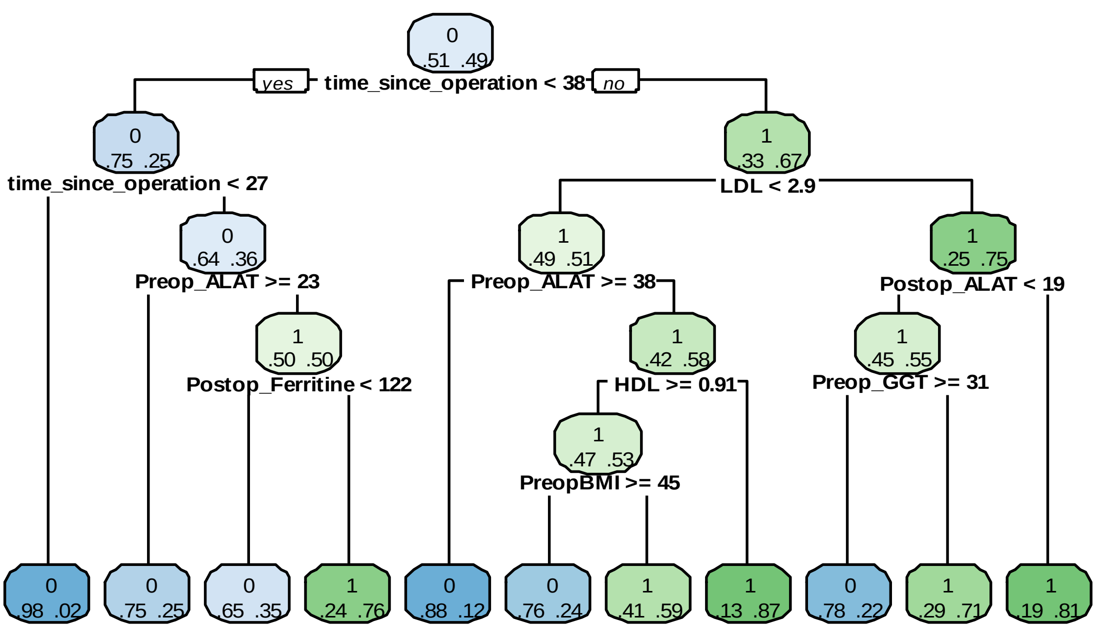

Figure1. Optimized decision tree with cp=0.01, minsplit=50

3.4. Evaluation of the Models

Figure 2 shows the performance of the two models by calculating the AUC metrics in the ROC curve. The diagonal line in the curve indicates a useless model, where the points of sensitivity equal to 1-specificity. The top left corner of the curve indicates sensitivity and specificity of 100%, which is a perfect model. The performance of the models is better if the ROC curve is getting closer to the top left corner of the square. In the figure, the ROC curve of the decision tree is slightly closer to the left corner than logistic regression as evidenced by the AUC of 73%.

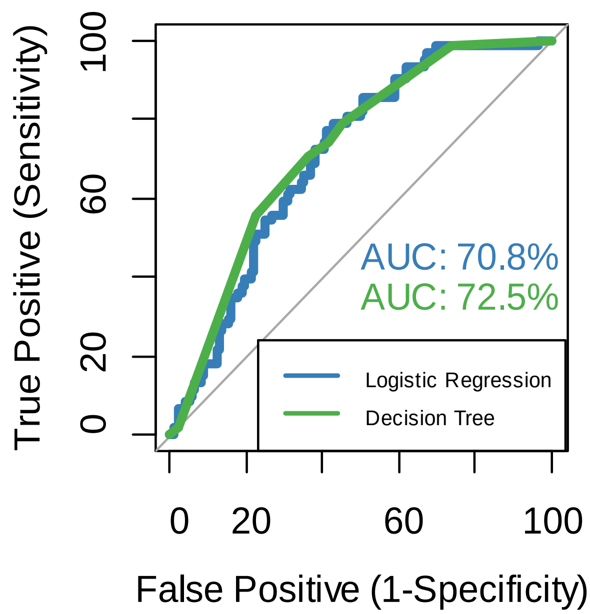

Figure2. AUC-ROC curve metrics for logistic regression and decision tree

Chapter 4. DISCUSSION

In this study, we aimed to uncover the preoperative and postoperative factors that contribute for the occurrence of weight regain, following the three commonly performed bariatric surgeries at ZGT hospital: RYGB, Sleeve gastrectomy and Mini gastric bypass. Our multivariate logistic regression model demonstrated that patient with weight regain had shown a significant relationship with higher preoperative LDL-cholesterol and the long time since they had the surgery. Additionally, obese patients who had a greater preoperative BMI or had mini gastric bypass surgery were associated with a lower chance of regaining weight. Similarly, decision tree revealed that time since the operation, preoperative LDL and BMI values were among the most important variables for predicting the weight regain group. On the question of performance of the models, this study found that decision tree had a slightly better performance in predicting weight regain over logistic regression. This discussion section of this paper presents the findings of the research in detail, focusing on the three common predictors of weight regain addressed by both logistic regression and decision tree models.

The prevalence of WR differs in different studies, depending on the criteria they used to define WR, ranging from 7.5% to 86.5%[7]. In this study, 15.8% of patients had WR after including patients who had experienced optimal and suboptimal %EWL within two years. Similar finding was reported in the trajectory modeling study by Keith et.al with 20.8% prevalence in 589 patients[12]. A study by Shantavasinkul et.al had also shown a comparable prevalence of 17.8%[1] by only involving patients who had optimal %EWL of at least 50%. Despite the different methods used for including patients, the prevalence among these studies were almost comparable with this study of 15.8%.

In this study, a higher level of LDL-cholesterol (hypercholesterolemia) stood out as a significant predictor of weight regain. It is particularly interesting to find that higher LDL level was the only independent predictor to weight regain from other lipid measurements (HDL, total cholesterol and triglyceride). LDL is commonly known as bad cholesterol and its high level is positively associated with risk of being obese and other metabolic disorders due to the delayed clearance of cholesterols, thereby increased the concentration of other plasma lipoproteins such as Triglyceride[32]. Hypercholesterolemia is mainly caused by sedentary lifestyle habits and unhealthy eating behaviors. The interrelation of genetic, psychological, behavioral and environmental factors as explanatory for the occurrence of obesity is a complex process[33, 12]. However, for the occurrence of weight regain who had bariatric surgeries may be explained by that the existence or recurrence of hypercholesterolemia due to the continuation of unhealthy lifestyle in the postoperative period. Furthermore, studies hardly investigate the effect of preoperative plasma lipid profiles on weight regain. It is common practice to generalize abnormal profiles in umbrella term as dyslipidemia without assessing which lipid type is a contributor for dyslipidemia. In our univariate analysis, patients diagnosed with dyslipidemia were associated with weight regain (*P* =0.027, OR= 2.15, 95%CI: 1.15-4.49).

Consistent with studies, there were some studies that have shown a preoperative diagnosis of hyperlipidemia as a risk factor for the occurrence of weight regain[22, 34]. A recent work by Keith et.al (2017) has carried out group based trajectory modeling on 586 bariatric patients over 10 years and found that dyslipidemia, from other comorbidities, was the only significant predictor for weight regain[22-]. In view of all that has been mentioned so far, one might think that it is common to find obese patients with an abnormal level of lipid profiles. However, our result can serve as a metabolic profile explanation why dyslipidemia related with weight regain, given the emphasis to the higher preoperative LDL level as a predictor to weight regain after experiencing weight loss through bariatric surgeries. Future prospective studies should give emphasis to the lipid profile measurements of patients after the surgery to provide better insights on the trends of the measurements and the possible behavioral and lifestyle factors associated with weight regain.

Another main finding in our multivariate analysis was the significant association between a longer time since the surgery and weight regain (OR=1.06, 95%CI=1.04-1.08). For every one month increment after having the surgery is associated with 1.06 times the odds of weight regain. Similarly, in our decision tree, time since the surgery was the most important variable for making the split, by appearing as a root node in the tree. This finding is consistent with previous studies that were done in patients who had RYGB and SG with a follow up of at least 2 years postoperatively[15, 35]. There are plenty of postoperative clarifications given for postoperative time, including healthy lifestyle noncompliance of patients such as lack of physical exercise[7], and poor diet quality[35, 26]. Poor diet quality is characterized by consumption of high glycemic index diet, snacks, fats and low intake of fiber diet. It is also related to the operative factors and adaptations to the anatomical and physiological changes such as the dilation of gastric the pouch and low energy expenditure[36], occurring over the passage of time[11]. Moreover, adherence to follow up or higher frequency of visits to dietician has shown a counter effect to weight regain after bariatric surgery through the encouragement to participate in healthy and behavioral interventions[26, 33, 37]. As a result, patients who have inadequate engagement with health professionals during postoperative will most likely to regain weight due to the above mentioned factors.

In our multivariate analysis, one of the intriguing findings was the association of lower preoperative BMI with weight regain (OR=0.99, 95%CI: 0.95-1.02). In contrary to plenty of studies that revealed the association of greater preoperative BMI with weight regained group[5, 38,39], this study has shown for every 1kg/m^2 decrease in preoperative BMI the odds of weight regain were 0.99 times the odds of those with BMI 1kg/m^2 lower. There is no straight forward explanation for this variable due to the no difference in the mean value of preoperative BMI among the two groups. Therefore, it is not possible to provide clinical interpretability based on the multivariate logistic regression. However, the possible clinical meaningful explanation for this variable to have an association with weight regain is portrayed in the decision tree. A BMI > 45 kg/m^2 is used as a cutoff to classify patients as weight regain after observing the preoperative LDL, HDL and ALAT level 38 months after the surgery. This finding is consistent with that of Baig et.al (2019) who compared three different definitions of weight regain in SG, RYGB and mini gastric bypass patients. The study found that those patients with preoperative of BMI >50 kg/m^2 experienced a lower weight regain using a definition similar to this study[39]. These results may be explained by the amount of weight loss achieved postoperatively. Cruz et.al (2018) had shown higher preoperative BMI is related to a greater percentage loss of excess weight[5]. It is expected for patients who had a higher BMI to seek help during a preoperative time than those who have lower BMI level. Moreover, higher BMI patients had a higher chance of suffering from obesity related comorbidities. So that it is possible that these patients had more likely to have exposure to the management of obesity and try to engage themselves in a healthy lifestyle. Therefore, they probably would have a better knowledge of how to control their body weight than those who have a lower BMI level. It is possible, therefore, that those with greater preoperative BMI try to maintain their greater excess weight loss by following a healthy lifestyle as they have previous exposure to the management of obesity. Unfortunately, this is only speculative explanation given the retrospective nature of the study.

Surprisingly, patients who diagnosed or had sign and symptoms of depressions are associated with no regaining of weight (*P*=0.017, OR=0.64, 95%CI: 0.44-0.92) in univariate analysis. As the *P* value is almost close to our significance level, we included it in our multivariate analysis and having depression turned out to be an independent variable for weight maintenance with OR=0.63, 95%CI:0.42-0.94. On our decision tree, depression was not among the important variables. Hence, there is no easy way to explain this association. Less is understood about the impact of preoperative diagnosis of depression as an independent factor in weight loss outcomes after having bariatric surgeries. Most studies focus on the postoperative psychiatric disorders in relation to the quality of life as predictive to understand bariatric surgery outcomes[2, 33]. Rutledge et.al assessed the total number of psychiatric disorders as predictors of weight regain/weight loss and found that patients with more number of psychiatric disorders are more likely to have weight regain that those who do not have a history of psychiatric disorder[40]. But Rutledge et.al measured the indicators collectively rather than examining the disorders individually. Another study by Yanos et.al on 97 patients who had RYGB had shown a significant relationship of weight regain with postoperative nocturnal eating, depression and problematic alcohol use. Hence, our study goes in contrary to the above mentioned studies. This is probably due to our definition of depression used during the data collection process from EMR. In addition to those who had a confirmed diagnosis of depression and/or they had been taking antipsychotic/anxiolytic medications, patients who had a higher score on depression scale on the psychiatric evaluation forms (BDI-II, SCL-90, and NPV-2) were included as they had depression. The definition used in this study was successful as it was able to identify patients who had the symptoms of the depression. However, it might overestimate the number of patients who were eligible to be diagnosed as depression because the instruments rating scale are not meant to substitute the clinical diagnosis of depression made through interview. It is important to bear in mind the possible bias in patient's responses to those questionnaires as well. Even though this finding is new, future studies on psychological disorders are highly recommended to confirm the relationship of preoperative depression with weight regain.

Decision tree findings' of the predictors were consistent with logistic regressions. Time since the operation, level of LDL and preoperative BMI were found to be predictors to weight regain in both models. The test accuracy of the decision tree, after optimization through correcting the imbalanced train set and choosing the most important variables, exhibited better performance in predicting weight regain. On the other hand, the sensitivity metric of optimized logistic regression was 72% which is better than 70% of the decision tree (table7, appedix3). In order to decide the overall performance of the models to this classification problem of the research, ROC curve is an important evaluation metric. The AUC-ROC curve of the decision tree revealed a slight advantage in classifying patients with weight regain than logistic regression. In addition to the better AUC value, decision tree able us to portray various predictors of weight regain due to its capability to handle nonlinear relationships between the variables. The graphical output of the decision tree makes the model to be amicable to health professionals, as it is easy to understand and explain the decisions using the cut points. Moreover, decision tree offers different techniques of ensemble models such as random forest and bagging in order to improve the overall predictive power of the model including the sensitivity and specificity. Future researches regarding bariatric surgeries should apply decision trees to better understand the complex and poorly understood the occurrence of weight regain. While logistic regression remains to be one of the best predictive models in the field of medicine, we encourage the application of decision tree in comparison with logistic regression where possible for the above reasons.

3.2. Limitations

There are several limitations in this study. One of the limitations is the retrospective design of the study which is prone to lack of retrieving the complete data of patient's records. The larger number of missing data was present in our study which resulted in the possibility of introducing bias while using different imputation techniques. Imputation techniques might also affect the predictive power of models. Moreover, this study doesn't acknowledge the variability in surgical outcomes from the three procedures. It is also possible to have differences in the techniques used for the operation depending on the surgeon's preference. Another limitation was the relatively homogeneous population (>75% females and white representation), which hampers the generalizability of this study to other population. Our first intention to examine postoperative variables such as the behavioral and psychological indicators and laboratory measurements were not possible, due to the occurrence of high missing values in extracted data using CTcue.

3.3. Strength

To our knowledge, this is the first research which tried to predict the occurrence of weight regain. And it is also the first time to use two models in order to understand the complex and possible predictors of weight regain after bariatric surgeries. As it is a retrospective research, it is prone to have missing data. As a result, we have used all possible ways to collect comprehensive data by combining CTcue application and SQL. The statistical analysis for making a prediction using the two models increases the strength of this study in terms of finding the possible predictors to weight regain. Lastly, the comparison between the two models for better accuracy forges the good predictability of weight regain.

3.4. Recommendations

Understanding factors contributing to long-term weight-loss maintenance in the post-bariatric surgery setting is vital in order for clinicians to provide patients with tools necessary to achieve long-term weight success. This study has shown that those who had higher preoperative LDL-cholesterol were most likely to regain weight after bariatric surgeries. This result warrants the importance of individualized attention for these patients during the postoperative period by providing pharmacological treatments and behavioral counseling. Future prospective researches are needed to confirm these findings and should focus on the modifiable behavioral and lifestyle characteristics of the patients as this research did not discern those risk factors, which will add in the process of uncovering the predictors of long term weight regain following bariatric surgeries.

We have used one definition of weight regain to find the predictors of weight regain due to the shortage of time to compare different definitions of weight regain in assessing the predictors. We preferred the definition based on other literature which compared the various definitions with respect to their predictive power and fitness to the model. The application of this definition in this study can serve as a startup for consistency in the definition of WR for future studies and clinical practices. But, it is also worthwhile to investigate the different definitions of weight regain to weight loss outcomes and their variability in terms of finding the association of weight regain with various predictors which will stress the importance of standardizing the definition of weight regain in clinical practice.

Another interesting finding of this study was the association of weight regain with SG and RYGB in univariate analysis. Even if the multivariate logistic regression and decision tree have shown no association, plenty of studies have mentioned the association of weight regain with those types of surgeries. Future studies should focus on assessing the different type of bariatric procedures specifically in order to determine the predictors and the long term outcomes.

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Chapter 6. APPENDICES

6.1. Appendix1. Sampling of the patients using CTcue

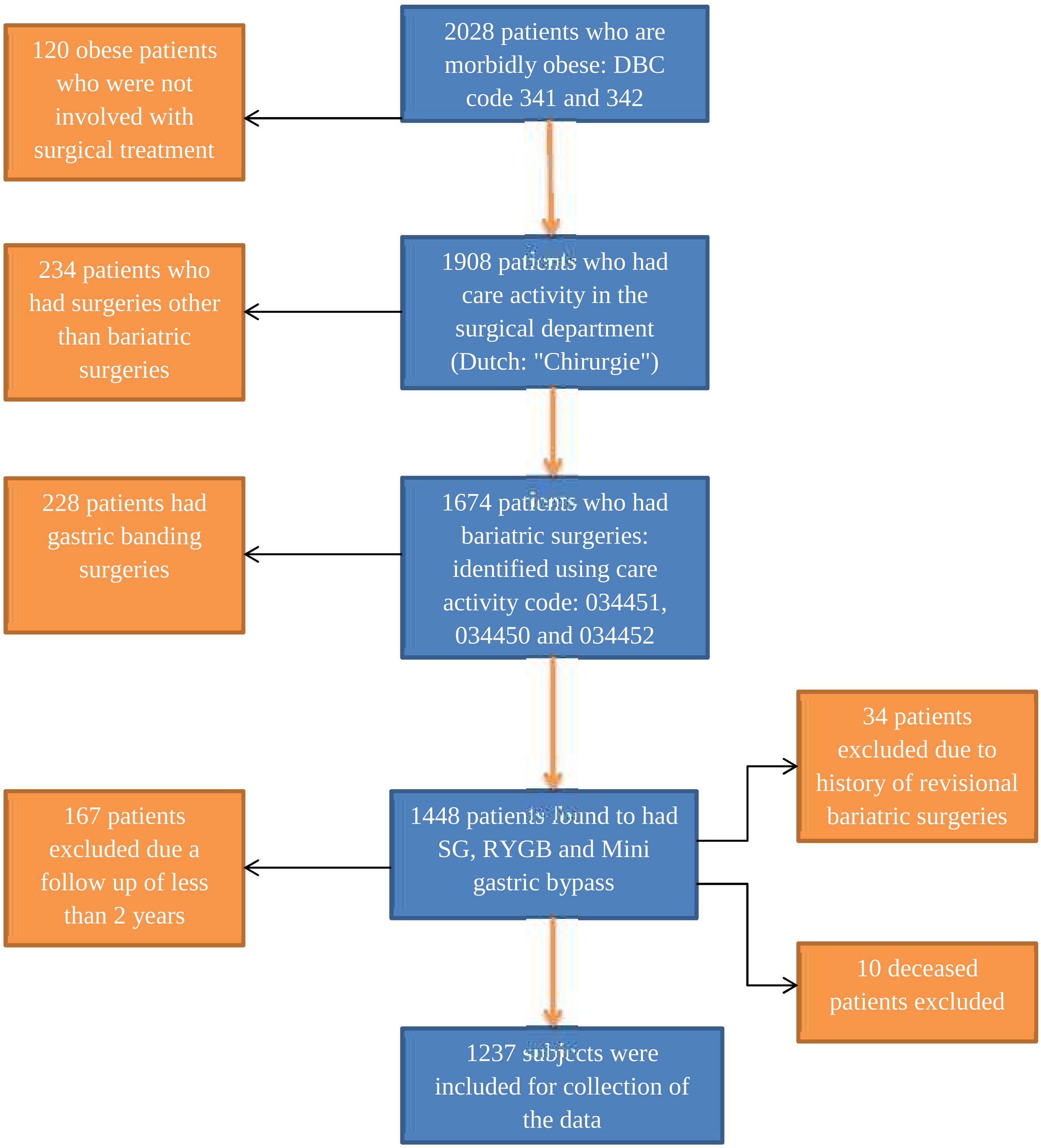

Figure3. Patient flow chart using CTcue in the study

6.2. Appendix2. Number of Missing Values in the combined dataset

Table5. The number and percentage of missing values in each variables of the combined dataset

Variables	No. of NA's	% of NA's	Data Type
Postop LDL	968	78.25	numeric
Postop HDL	968	78.25	numeric
Postop Triglyceride	968	78.25	numeric
Postop Diabetes	597	48.26	factor
Preop Depression	593	47.94	factor
Postop Hypertension	406	32.82	factor
Smoking History	354	28.62	factor
Alcohol History	351	28.38	factor
Postop ALAT	287	23.2	numeric
Postop Ferritine	216	17.46	numeric
Recent Weight	191	15.44	numeric
Recent weight date	190	15.36	Date
Time since operation	190	15.36	numeric
Nadir Weight	74	5.98	numeric
Nadir weight date	61	4.93	Date
Preop LDL	60	4.85	numeric
Preop Diabetes	53	4.28	factor
Preop ALAT	47	3.8	numeric
Preop GGT	45	3.64	numeric
Preop Triglyceride	45	3.64	numeric
Preop Hypertension	44	3.56	factor
Preop TSH	39	3.15	numeric
Preop HDL	38	3.07	numeric
Preop Total cholesterol	36	2.91	numeric
Preop Dyslipidemia	34	2.75	factor
Height	29	2.34	numeric
Marital	19	1.54	factor
Preop Weight	8	0.65	numeric

6.3. Appendix3. Predictive Metrics of Logistic Regression

Table6. Confusion Matrices of Logistic Regression

Logistic regression without correcting the class imbalance		
Predicted	Actual value	
	0	1
0	302	58
1	2	4
Logistic regression correcting the class imbalance (undersampling method)		
Predicted	Actual value	
	0	1
0	182	17
1	122	44

Table7. Output of logistic regression before and after correcting the class imbalance

	Logistic regression without correcting the class imbalance	**Logistic regression correcting the class imbalance (undersampling method)**
Accuracy (95% CI)	83.6% (79.4% - 87.2%)	61.9% (56.7% - 66.9%)
Sensitivity	0.06452	0.7213
Specificity	0.99342	0.5987
Positive predictive value	0.66667	0.2651
Negative predictive value	0.83889	0.9146
Prevalence	0.16940	0.1671
Detection rate	0.01093	0.1205
Detection prevalence	0.01639	0.4548
Balanced accuracy	0.52897	0.66
AUC	67.3	70.8

6.4. Appendix 4. Predictive Metrics of Decision Tree

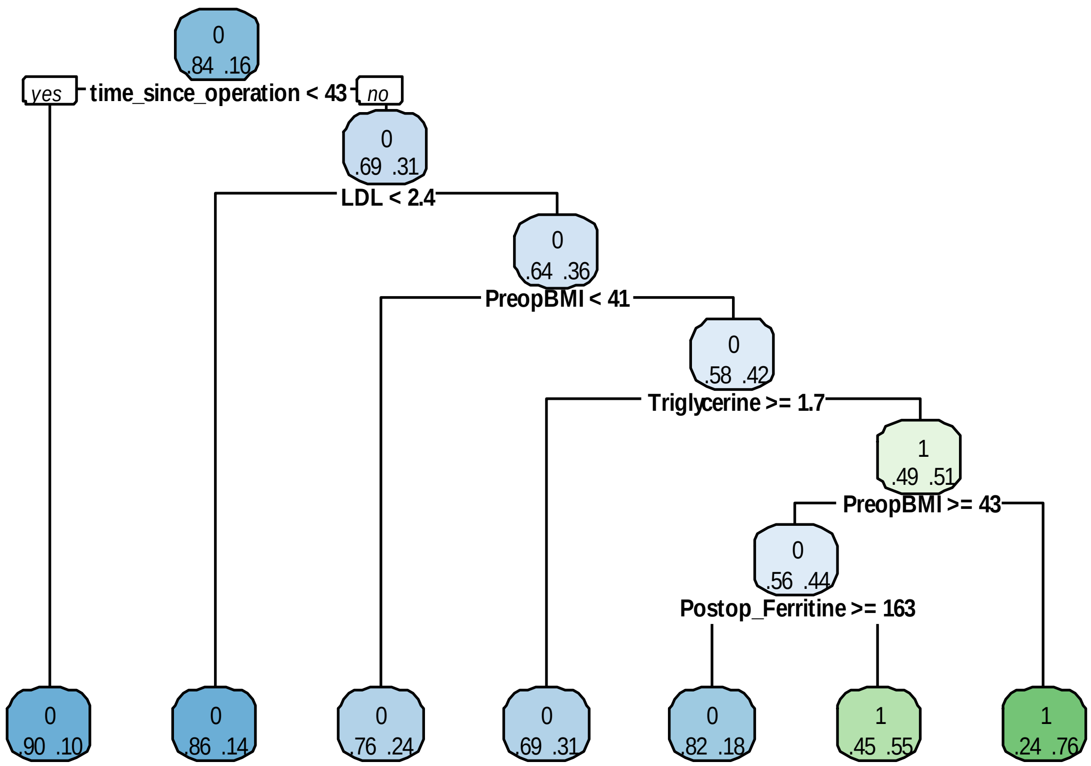

Figure4. Pruned decision tree using CP=0.01 and min.split =50 without correcting the class imbalance

Table8. Confusion Matrices of Decision Tree

Logistic regression without correcting the class imbalance		
Predicted	Actual value	
	0	1
0	291	45
1	18	9
Logistic regression correcting the class imbalance (undersampling method)		
Predicted	Actual value	
	0	1
0	194	18
1	110	43

Table9. Variable importance according to the Gini index of calculation

Rank	Variables	Gini index
1.	Time since operation	92.7947435
2.	Preop ALAT	34.7201341
3.	Preop GGT	34.4637400
4.	Preop BMI	31.3175889
5.	Preop LDL	29.2601098
6.	Postop ALAT	27.2313812
7.	Height	22.1381955
8.	Postop Ferritine	20.3167969
9.	Preop HDL	19.1699712
10.	Operation name	16.6852869
11.	Triglyceride	15.2637689
12.	Preop Total cholesterol	11.4211107
13.	Age	7.6786431
14.	Marital Status	5.8044299
15.	Preop TSH	4.8102099
16.	Smoking History	3.9045875
17.	Depression	3.2447368
18.	Preop dyslipidemia	3.0779898
19.	Preop Diabetes	2.1939255
20.	Patient Gender	2.1354583
21.	Alcohol History	0.9637262

Table10. Output of Decision tree before and after correcting the class imbalance

	Decision Tree without correcting the class imbalance	Decision Tree correcting the class imbalance (ROSE method)
Accuracy (95% CI)	82.6% (78.4% - 86.4%)	64.9% (59.8% - 69.8%)
Sensitivity	0.16667	0.7049
Specificity	0.94175	0.6382
Positive predictive value	0.33333	0.2810
Negative predictive value	0.86607	0.9151
Prevalence	0.14876	0.1671
Detection rate	0.02479	0.1178
Detection prevalence	0.07438	0.4192
Balanced accuracy	0.55421	0.6715
AUC	67.7	72.6