Development and validation of a model to predict cessation of antihyperglycemic medication after laparoscopic bariatric surgery among patients with type 2 diabetes

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Introduction

Laparoscopic bariatric surgery (BxS, also known as 'metabolic surgery'), including laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB), can lead to significant weight loss and improvements in obesity-related comorbidities among obese persons.[1]

In 2016, the American Diabetes Association and other international diabetes organizations published a joint statement in which metabolic surgery was recommended for the treatment type 2 diabetes mellitus (T2DM) in patients with class III obesity (body mass index BMI ≥40 kg/m2) and in those with class II obesity (BMI 35.0–39.9 kg/m^{2}) when hyperglycemia is inadequately controlled by lifestyle and optimal medical therapy.[2] However, treatment response to BxS is not homogenous across patients, and therefore uncertainty remains regarding which specific patients with T2DM may benefit the most among those who are surgically-eligible.
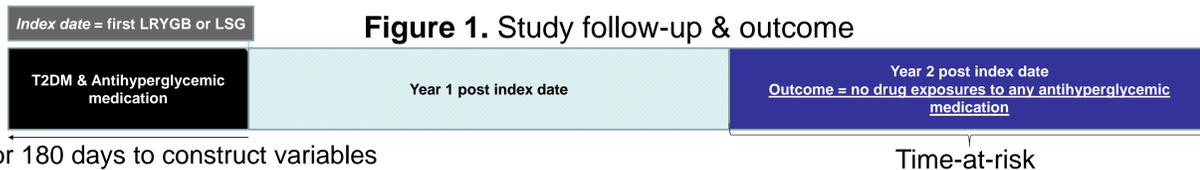
Objective

To develop and validate a model to predict complete antihyperglycemic medication cessation (proxy for T2DM remission) between 1-2 years after BxS in patients with treated T2DM.

Methods

Data Sources: The model was trained in the Truven Health MarketScan Commercial Database (CCAE) and externally validated in the Optum Extended Date of Death Database (OPTUM).

Target Population: The target population comprised patients meeting all following criteria: underwent BxS between 2007-01-01 and 2013-10-01 (first=index); aged ≥18 at index; continuous observation of 180d before (baseline) to 730d after index; ≥1 baseline condition occurrence of T2DM; and ≥1 baseline drug exposure for antihyperglycemic medication.

Outcome: The outcome was defined as no drug exposure for antihyperglycemic medication from 365-730 days after BxS; Figure 1.

Figure 1. Study follow-up & outcome

Index date = first LRYGB or LSG

| T2DM & Antihyperglycemic medication | Year 1 post index date | Year 2 post index date
Outcome = no drug exposures to any antihyperglycemic medication |

Prior 180 days to construct variables

Time-at-risk

Statistical Analysis and Covariates: Using ATLAS and the OHDSI patient-level prediction software, a regularized logistic regression model was used to select the ultimate set of model variables from among the following candidates: demographics; baseline Diabetes Complications Severity Index; baseline SNOMED condition occurrences; baseline drug exposures mapped to ingredient level; LRYGB at index (custom concept); LSG at index (custom concept); prior primary adjustable gastric banding (custom concept); prior adjustable gastric banding revision (custom concept); baseline SNOMED measurements and procedures. All baseline variables used the patients' history recorded in the 180 days prior to index (including index date). A 75%/25% split of the CCAE sample was used for model training/testing; 100% of the OPTUM sample was used for model external validation.

Results

The study included 13,088 and 3,136 patients from CCAE and OPTUM, respectively. Figure 2 displays antihyperglycemic medication rates by database..

Truven Commercial
(N = 12,389)
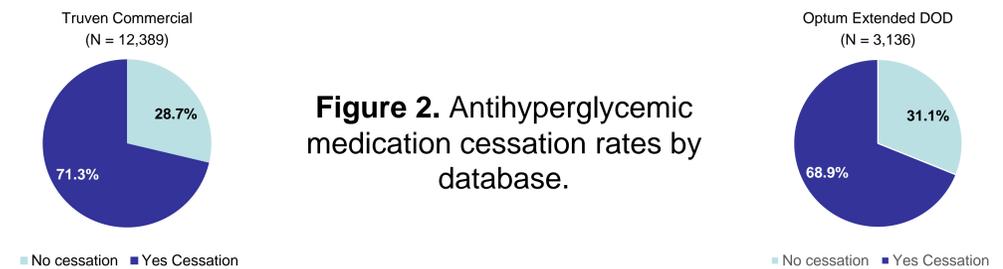
Figure 2. Antihyperglycemic medication cessation rates by database.

Optum Extended DOD
(N = 3,136)

The final model possessed good internal discriminative accuracy (area under the curve **[AUC]=0.76** in CCAE test set with N=3,272) and transportability (**external AUC=0.74** in OPTUM external validation set with N= 3,136); Figure 3.

Figure 3. CCAE test set calibration plot (left panel) & receiver operating characteristic plots (middle panel: CCAE, test set; right panel: OPTUM, external validation set)
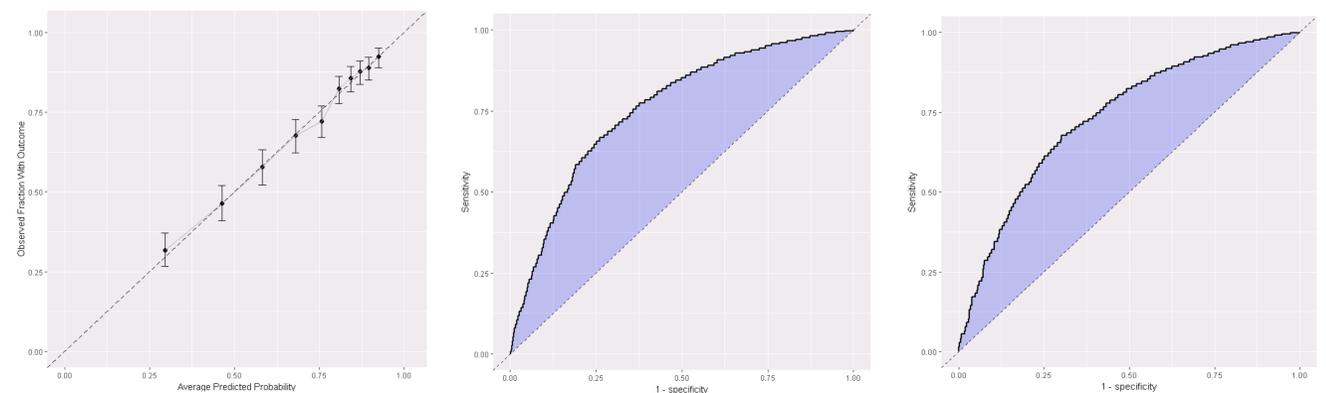
Limitations

Cessation of antihyperglycemic medication is not a validated proxy of T2DM remission. Due to potential technological barriers, this model is currently not ideal for use as a clinical decision support tool. The optimal predicted probability threshold for selection of candidates for BxS is unknown and depends on the expected benefits and costs of the procedures within the target population, an area in need of further research.

Conclusion

We developed and externally-validated a model which performed well in the prediction of complete antihyperglycemic medication cessation between 1-2 years after BxS in patients with treated T2DM. Further dissemination, evaluation, and refinement of this model across the ODHSI network is warranted.

1. Rubino F, Nathan DM, Eckel RH, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: A joint statement by international diabetes organizations. Diabetes Care. 2016;39:861-77.
2. Chang S-H, Stoll CRT, Song J, Varela JE, Eagon CJ, Colditz GA. Bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. JAMA surgery. 2014;149:275-287.

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