Trends in prescriptions of cardio-protective diabetic agents after coronary artery bypass grafting among US Veterans

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SUPPLEMENTARY APPENDIX

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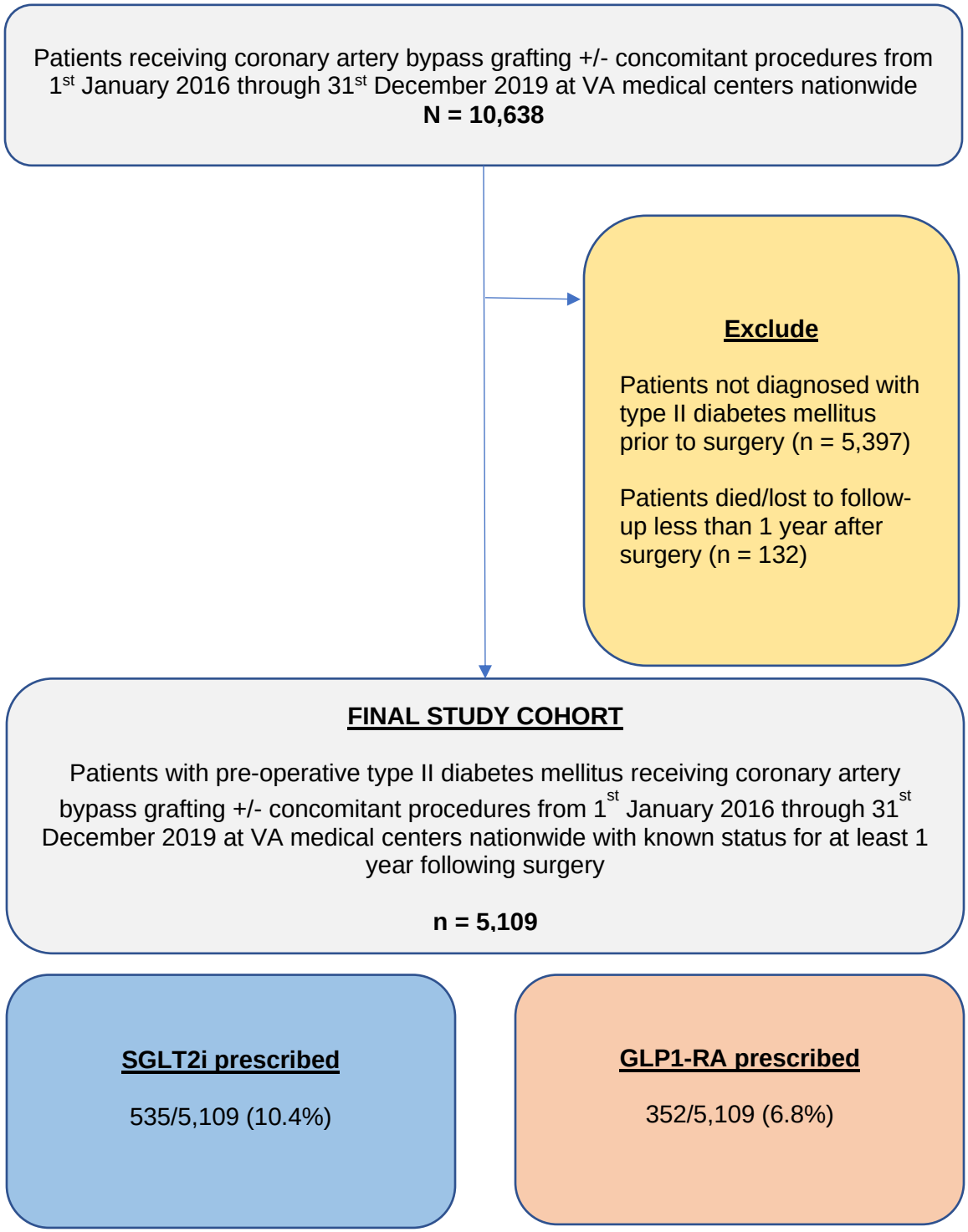
Abbreviations

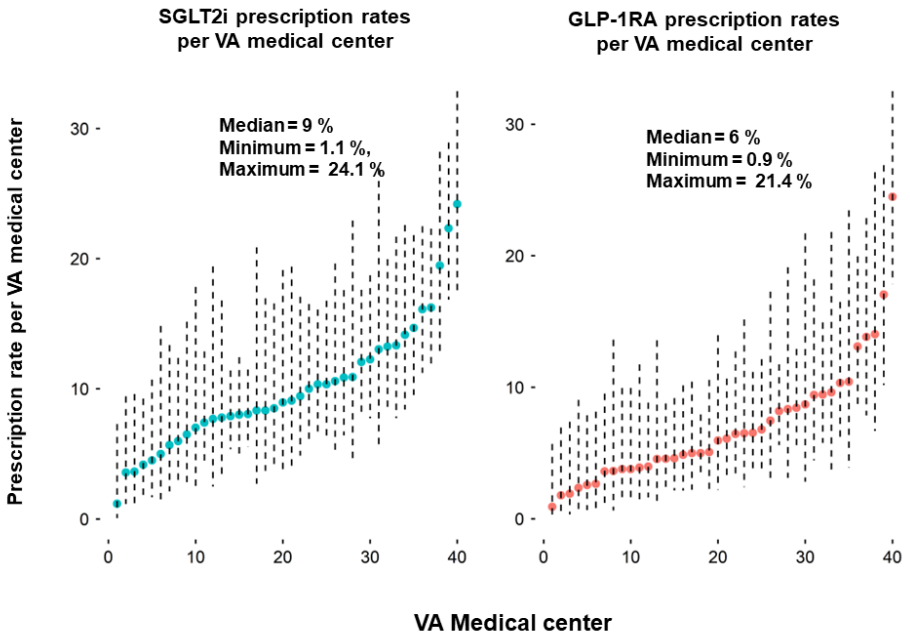
ACC	American College of Cardiology
AHA	American Heart Association
CPT	Common procedure terminology
GLP1-RA	Glucagon like peptide 1 receptor agonist
HbA1c	Glycosylated Hemoglobin
HFrEF	Heart failure with reduction ejection fraction
ICD	International classification of diseases
LVEF	Left ventricular ejection fraction
SGLT2i	Sodium glucose L-type 2 cotransporter inhibitor
VA	Department of Veteran Health affairs

Figure S1. Cohort selection flowchart



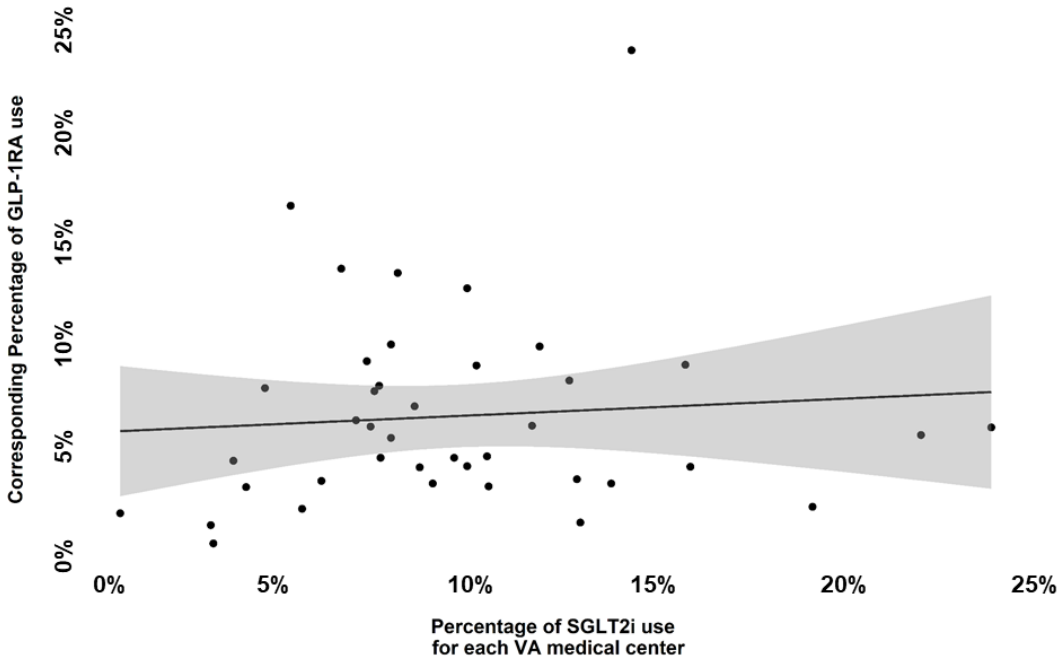
This flowchart describes the process of cohort selection for our study.

Figure S2. Variation in SGLT2i and GLP-1RA prescription rates among VA medical centers



This plot demonstrates the overall SGLT2i and GLP-1RA prescription rate for each VA medical center. As observed in both these graphs, there is wide variation in prescription rates between medical centers.

Figure S3. Correlation between overall SGLT2i / GLP-1RA prescription rates at VA medical centers



This scatterplot demonstrates the overall percentage of SGLT2i use in each VA medical center and its corresponding overall GLP-1RA use. In the whole cohort, the median SGLT2i prescription rate / per VA medical center was 9.02 (IQR: 7.3, 12.45) and the median GLP1-RA prescription rate / per VA medical center was 6.02 (3.68, 8.87). As the fitted line demonstrates we observed a very weak correlation between these estimates (correlation coefficient = 0.08, 95%CI -0.23, 0.38).

Table S1. Covariate Definitions used in our study.

Covariate	Definition used for our study
Type 2 Diabetes Mellitus	The presence of the ICD 10 code (E11x) in at least 1 inpatient or 2 outpatient visits prior to surgery.
Heart failure	Defined as any outpatient visits with the following ICD10 codes as primary/secondary diagnoses codes in the covariate assessment window or as secondary diagnoses codes at the index visit: 'I09.81%' 'I11.0%' 'I13.0%' 'I13.2%' 'I50.1%' 'I50.20%' 'I50.21%' 'I50.22%' 'I50.23%' 'I50.30%' 'I50.31%' 'I50.32%' 'I50.33%' 'I50.40%' 'I50.41%' 'I50.42%' 'I50.43%' 'I50.810%' 'I50.811%' 'I50.812%' 'I50.813%' 'I50.814%' 'I50.82%' 'I50.83%' 'I50.84%' 'I50.89%' 'I50.9%
Heart failure with a reduced ejection fraction (HFrEF)	Patients with a diagnosis of heart failure and a baseline preoperative left ventricular ejection fraction < 45% were classified as HFrEF
Chronic kidney disease	Defined as a baseline preoperative eGFR < 60 ml/min/m^2. Each patient's serum creatinine value (most recent value prior to surgery) was available and the CKD-EPI creatinine equation was used to calculate the estimated glomerular filtration rate (eGFR).
Peripheral arterial disease	These covariates are directly available from the VASQIP (VA surgical quality initiative project) database
Cerebrovascular disease	
Pre-operative left ventricular systolic function	The preoperative left ventricular systolic function was obtained from the VASQIP database. The most recent value prior to the surgery is recorded in VASQIP. A surface echocardiogram is routinely performed as part of the pre-operative evaluation for all patients prior to CABG.
Race and ethnicity	These are self-reported at the time of the admission for surgery
Neighborhood deprivation index (NDI)	The neighborhood deprivation index, measured on a continuous scale from 0 (least deprived) to 1 (most deprived), is derived using the following 6 census-tract measures: fraction of the population below the poverty level, median household income, fraction of the population with at least a high-school

	education, fraction of the population without health insurance, fraction of the population receiving public assistance income, and fraction of vacant houses in that zip code. Each patient's zip code at the time of admission for surgery was obtained and linked to the published CDI[1]
Zip code derived median household income	The median household income was obtained from the American Community Survey 5-year estimates[2]

[1] *The Development of a Standardized Neighborhood Deprivation Index - PMC (nih.gov)*

[2] *American Community Survey (ACS) (census.gov)*

Table S2. Baseline characteristics of our study cohort.

Baseline Characteristics	Whole Cohort (n = 5109)	Patients receiving SGLT2i prescriptions (n = 535)	Patients receiving GLP-1RA prescriptions (n = 352)
Age *	68 (63, 71)	66 (61,70)	68 (62, 71)
Age group			
< 50 years	106 (2)	13 (2.4)	9 (2.5)
- 50 – 60	811 (15.9)	120 (22.4)	68 (19.3)
- 61 – 70	2700 (52.8)	276 (51.5)	186 (52.8)
- 71 – 80	1383 (27.1)	125 (23.5)	88 (25.2)
- > 80 years	109 (2.2)	1 (0.2)	1 (0.2)
Female sex	83 (1.6)	9 (1.7)	10 (2.8)
Race			
- White	3974 (77.8)	413 (77.2)	283 (80.4)
- Black	638 (12.5)	63 (11.8)	31 (8.8)
- Others	497 (9.7)	59 (11)	38 (10.8)
Hispanic Ethnicity	591 (11.6)	72 (13.5)	34 (9.6)
Area Deprivation index *	0.38 (0.31, 0.44)	0.38 (0.30, 0.43)	0.38 (0.31, 0.44)
Median household income (zip code derived) *	$51,036 ($42,225, $63,727)	$53,001 ($43,915, $63,727)	$52,507 ($43,158, $65,629)
Body mass index	31 (27.61, 35)	32.10 (28.35, 35.83)	32.99 (29.63, 37.28)
Obese (BMI > 30 kg/in^2)	2936 (57.5)	348 (65)	255 (72.4)
Chronic kidney disease	1973 (38.6)	162 (30.3)	144 (40.9)
Heart failure	1319 (25.8)	137 (25.6)	93 (26.4)
HFrEF	463 (9)	45 (8.4)	25 (7.1)
Chronic obstructive pulmonary disease	1454 (28.5)	126 (23.6)	101 (28.7)
Peripheral arterial disease	1426 (27.9)	118 (22.1)	92 (26.1)
Cerebrovascular disease	348 (6.8)	31 (5.8)	14 (4)
Poly-vascular disease	1648 (32.3)	134 (25)	101 (28.7)
Atrial fibrillation	1217 (23.8)	116 (21.7)	78 (22.1)
Prior myocardial infarction	2840 (48.5)	256 (47.8)	163 (46.3)
Multi-vessel coronary artery disease /Left main disease	3306 (64.7)	294 (57.8)	185 (55.6)
Preoperative LV systolic function			
LVEF $\geq$ 0.55	2977 (58.2)	319 (60.7)	223 (64.4)
0.45 – 0.54	957 (18.7)	110 (20.9)	71 (20.5)
0.40 – 0.44	340 (6.6)	31 (5.9)	20 (5.7)

0.35 – 0.39	279 (5.4)	26 (4.9)	11 (3.1)
≤ 0.35	431 (8.4)	39 (7.6)	21 (6.3)
Pre-operative HbA1c (%) *	7.5 (6.7, 8.4)	8.2 (7.4, 9.0)	8.0 (7.4, 8.8)
Baseline Anti-diabetes therapy			
Metformin	3189 (62.4)	410 (76.6)	241 (68.5)
Insulin	2794 (54.6)	352 (65.8)	298 (84.6)
Sulphonylureas	1541 (30.6)	195 (36.4)	91 (25.8)
DPP4i	423 (8.2)	88 (16.4)	27 (5.9)

This table presents the baseline characteristics prior to surgery for our study cohort and patients receiving SGLT2i or GLP1-RA prescriptions during the study period.

Missing data: LVEF (125, 2.4%), HbA1c (472, 9.2%), Area deprivation index (123, 2.4%), Median household income (123, 2.4%)
Abbreviations; HFrEF – heart failure with reduced ejection fraction. LVEF – left ventricular ejection fraction,
All values reported as counts(percentage) except those starred which are reported as the median (interquartile range)

Table S3. Regression model to evaluate SGLT2i / GLP-1RA use:

	SGLT2i prescription		GLP-1RA prescription	
Covariate	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Age (for every 10-year increase) *	0.75 (0.66, 0.85)	< 0.001	0.83 (0.71, 0.97)	0.02
Female Sex **	0.85 (0.39, 1.65)	0.66	1.79 (0.85, 3.39)	0.09
Race (Ref: Black)				
-White	1.09 (0.81, 1.47)	0.55	1.64 (1.11, 2.51)	0.01
-Others	1.13 (0.76, 1.68)	0.52	1.78 (1.06, 3.01)	0.02
Hispanic ethnicity	1.28 (0.94, 1.72)	0.10	0.80 (0.52, 1.18)	0.29
Neighborhood Deprivation index (for every 0.1 increase)	1.19 (0.98, 1.44)	0.07	1.07 (0.84, 1.35)	0.55
Median household income (for every $5,000 increase)	1.08 (1.03, 1.13)	< 0.001	1.03 (0.97, 1.09)	0.29
Chronic Kidney Disease	0.72 (0.58, 0.88)	< 0.001	1.13 (0.90, 1.42)	0.27
Heart Failure	1.10 (0.85, 1.40)	0.42	1.19 (0.88, 1.57)	0.23
HFrEF	0.86 (0.59, 1.27)	0.62	0.71 (0.43, 1.13)	0.68
Peripheral Arterial Disease	0.75 (0.60, 0.94)	0.01	0.93 (0.72, 1.20)	0.61
Cerebrovascular Disease	0.90 (0.60, 1.30)	0.59	0.59 (0.32, 0.99)	0.06
Obesity	1.39 (1.15, 1.69)	< 0.001	1.91 (1.50, 2.46)	< 0.001

We fit two separate multivariable generalized logistic regression models to study the association between baseline characteristics and the use of SGLT2i or GLP-1RA within 1 year after coronary artery bypass grafting. Models were fit using the complete case analysis method.

Abbreviations: HFrEF – heart failure with reduced ejection fraction; Both models include a covariate for hospital identifier

Table S4. Quarterly prescription rates for SGLT2i and GLP-1RA

Time - period	Total CABG patients per Quarter	New SGLT2**i** prescriptions	SGLT2i prescription rates per Quarter	New GLP-1RA prescriptions	GLP-1RA prescription rates per Quarter
2016Q1	357	6	1.68 (0.81, 3.81)	3	0.84 (0.22, 2.64)
2016Q2	367	10	2.72 (1.39, 5.11)	6	1.63 (0.67, 3.7)
2016Q3	336	7	2.08 (0.92, 4.43)	7	2.08 (0.92, 4.43)
2016Q4	289	9	3.11 (1.53, 6.03)	8	2.77 (1.29, 5.59)
2017Q1	337	16	4.75 (2.83, 7.75)	19	5.64 (3.52, 8.81)
2017Q2	352	15	4.26 (2.49, 7.08)	16	4.55 (2.71, 7.43)
2017Q3	370	21	5.68 (3.63, 8.68)	18	4.86 (2.99, 7.72)
2017Q4	303	24	7.92 (5.25, 11.71)	20	6.6 (4.18, 10.17)
2018Q1	288	17	5.9 (3.58, 9.46)	22	7.64 (4.96, 11.4)
2018.Q2	323	53	16.41 (12.63, 21.01)	24	7.43 (4.92, 11)
2018Q3	288	27	9.38 (6.38, 13.49)	20	6.94 (4.4, 10.69)
2018Q4	283	53	18.73 (14.45, 23.87)	40	14.13 (10.4, 18.87)
2019Q1	348	58	16.67 (12.99, 21.1)	40	11.49 (8.43, 15.43)
2019Q2	321	75	23.36 (18.92, 28.46)	40	12.46 (9.15, 16.7)
2019Q3	290	59	20.34 (15.96, 25.54)	40	13.79 (10.15, 18.43)
2019Q4	257	85	33.07 (27.42, 39.24)	29	11.28 (7.81, 15.96)

This table presents the quarterly prescription rates for SGLT2i and GLP-1RA in our study.