Use of GLP-1 Receptor Agonists (GLP1a) and/or SGLT-2 Inhibitors (SGLT2i) in Populations with NASH or at Risk of NASH in US Clinical Practice

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1. BACKGROUND AND AIM

Studies have demonstrated some success with GLP-1 receptor agonists (GLP-1) in histological resolution of NASH without worsening of fibrosis and success with SGLT-2 inhibitors (SGLT-2) in reduction of body weight, ALT, and FIB-4 compared with baseline values.

Here, we examined data from diabetic and non-diabetic patients with, or at risk of, NASH to understand utilization of these therapies in clinical practice.

2. METHODS

Data were obtained from a national proprietary EMR database containing demographic, medication, lab, diagnosis, and procedure information from academic, hospital, and community care centers in the US.

Study sample was limited to adult patients with ICD-based NAFLD or NASH diagnoses or with a risk profile (RISK) of Age >50 + ALT >30 U/L + [BMI >30 or Type II diabetes] and without viral hepatitis or evidence of alcohol abuse. Index date was assigned at the first calculable FIB4 between July 2015 to June 2017 and for which >1 year history and >2 years follow-up or to death was available.

Baseline labs and treatment were limited to entries 12 months prior to index up to 3 months after index, but closest to index.

3. RESULTS

Of 30 million adult patients in the database, 81,108 met all study criteria with 22% (17,582) NAFLD (without NASH), 1% (914) NASH, and 77% (62,612) RISK (without NAFLD or NASH) [FIGURE 1].

At index, 50% (40,194/81,095) were male, 80% (65,121/81,108) white, 73% obese (44,190/60,882), 43% (34,730/81,108) diabetic, 11% (9,210/81,108) with FIB-4 ≥2.67, mean (SD) age of the sample was 61.9 (10.8) [TABLE 1].

NASH patients were more likely to be diabetic than NAFLD and RISK, NAFLD were less likely to be diabetic than NASH and RISK (p<.001 both).

Baseline use of SGLT-2 and GLP-1 inhibitors was low among all patients (2% and 3% respectively), though higher in the diabetic subset (4% and 7%) compared to non-diabetics (<1%) (p<.001). Use of SGLT-2, GLP-1 or both was statistically higher in diabetic NAFLD vs. diabetic RISK (p<0.001), while there was no difference in non-diabetics.

Among 105 non-diabetics on SGLT-2 at index, 54% received canagliflozin, 41% dapagliflozin, and 35% empagliflozin. Among 188 non-diabetics on GLP-1 at index, 64% received liraglutide, 30% dulaglutide, 22% exenatide.

Non-diabetic patients receiving SGLT-2 and/or GLP-1 (n=279) differed from those not on these therapies (n=46,099) in age (mean 57.0 v. 60.5 not treated, p<.001), Charlson Comorbidity Index (0.9 v. 1.7 not treated, p<.001), BMI (33.6 v. 32.2 not treated, p<.001), proportion of AST>30 (43% v. 36% not treated, p=0.014), blood glucose ≥1.1 g/dl (66% v. 27% not treated, p<.001), HbA1c ≥5.6 (91% v. 72% not treated, p<.001), triglycerides ≥150 mg/L (35% v. 25% NT, p<.001), LDL cholesterol ≥100 (22% v. 33% not treated, p<.001), eGFR ≥60<90 (44% v. 52% not treated, p=0.016), and eGFR ≥90 (41% vs. 31%, p=.001).

4. SUMMARY

Despite evidence suggesting histologic liver improvements with GLP-1 receptor agonists and/or SGLT-2 inhibitors in patients with NASH or risk of NASH, use of these therapies is low overall and <1% in non-diabetic patients.

Use in non-diabetic patients is more common in those who are younger with fewer comorbidities and with lab measures more aligned with diabetic patients (e.g. high BMI, blood glucose, HbA1c, triglycerides).

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FIGURE 1 DISPOSITION OF THE STUDY PATIENTS

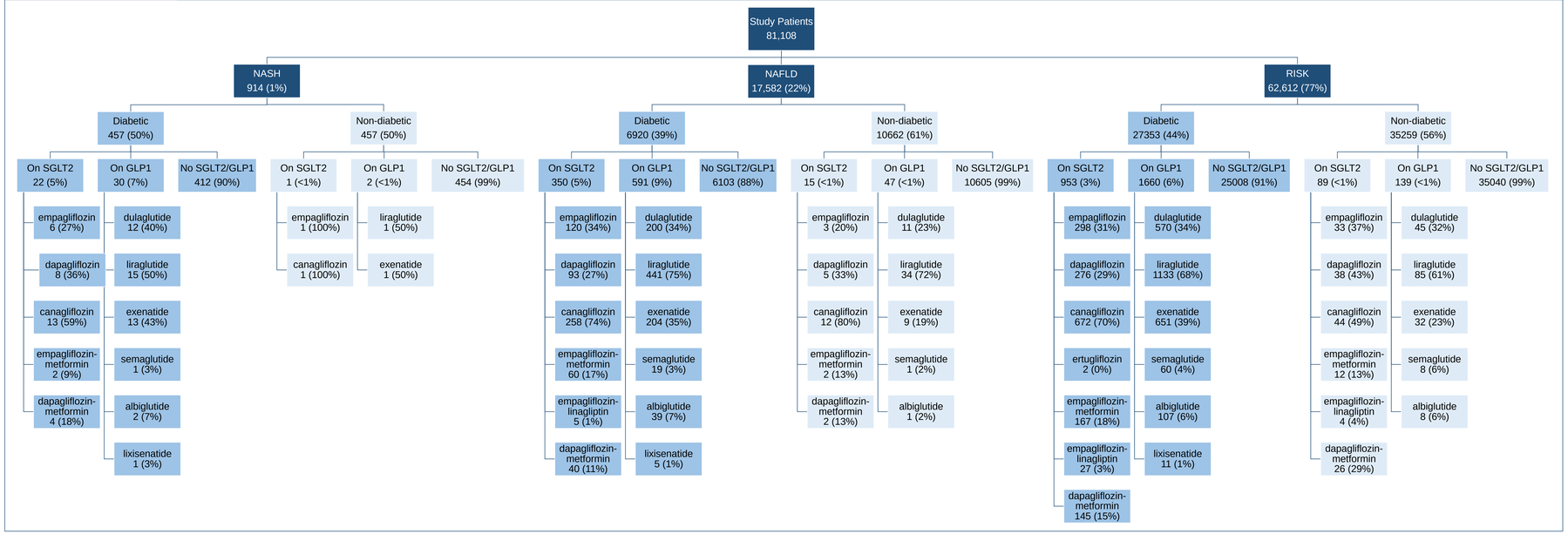

TABLE 1 BASELINE CHARACTERISTICS

Mean (SD) or no. (%) Significant differences (p<0.05) are shown in bold		All Patients N=81,108	NASH n= 914	NAFLD n= 17,582	RISK n= 62,612	Total Non-diabetic n=46,378	Non-diabetics NOT on SGLT2 or GLP1 N=46,099	Non-diabetics on SLT2 or GLP1 N=279	Total Diabetic n= 34,730
Age		61.9 (10.8) n=81108	56.5 (13.6) n=914	56 (14.3) n=17582	63.6 (8.9) n=62612	60.5 (11.1) n=46378	**60.5 (11.1) n=46099**	**57 (9.9) n=279**	63.8 (10.2) n=34730
Follow-up, months		32 (4.7) n=60882	32.7 (10.6) n=914	32.9 (9.8) n=17582	35.4 (9.5) n=62612	34.5 (9.3) n=46378	34.5 (9.3) n=46099	34.4 (8) n=279	35.2 (10) n=34730
Pre index history, months		34.8 (9.6) n=81108	69.8 (55.7) n=914	81.3 (57.8) n=17582	78.7 (56.8) n=62612	78.2 (56.1) n=46378	**78.2 (56.2) n=46099**	**69.1 (50.4) n=279**	80.6 (58.2) n=34730
Charlson Comorbidity Index		79.2 (57) n=81108	3.3 (2.7) n=914	3.4 (2.8) n=17582	2.4 (2.4) n=62612	1.7 (2.1) n=46378	**1.7 (2.1) n=46099**	**0.9 (1.5) n=279**	3.8 (2.6) n=34730
Race	**White**	65121 (80%)	765 (84%)	13752 (78%)	50604 (81%)	38872 (84%)	38638 (84%)	234 (84%)	26249 (76%)
	African American	10934 (13%)	58 (6%)	2455 (14%)	8421 (13%)	5003 (11%)	4976 (11%)	27 (10%)	5931 (17%)
	Other	1580 (2%)	29 (3%)	455 (3%)	1096 (2%)	672 (1%)	670 (1%)	2 (1%)	908 (3%)
	Unknown	3473 (4%)	62 (7%)	920 (5%)	2491 (4%)	1831 (4%)	1815 (4%)	16 (6%)	1642 (5%)
Gender	**Female**	40901 (50%)	582 (64%)	10726 (61%)	29593 (47%)	23464 (51%)	23308 (51%)	156 (56%)	17437 (50%)
	Male	40194 (50%)	332 (36%)	6852 (39%)	33010 (53%)	22907 (49%)	22784 (49%)	123 (44%)	17287 (50%)
FIB-4	**<1.3**	42443 (52%)	349 (38%)	10002 (57%)	32092 (51%)	25694 (55%)	25527 (55%)	167 (60%)	16749 (48%)
	>=1.3<2.67	29455 (36%)	282 (31%)	5473 (31%)	23700 (38%)	15915 (34%)	15827 (34%)	88 (32%)	13540 (39%)
	>=2.67	9210 (11%)	283 (31%)	2107 (12%)	6820 (11%)	4769 (10%)	4745 (10%)	24 (9%)	4441 (13%)
Body Mass Index (BMI)	**Underweight**	427 (1%)	1 (0%)	209 (2%)	217 (0%)	224 (1%)	223 (1%)	1 (1%)	203 (1%)
	Normal	4317 (7%)	59 (9%)	1834 (14%)	2424 (5%)	2098 (6%)	2092 (6%)	6 (4%)	2219 (9%)
	Overweight	11948 (20%)	179 (27%)	3329 (26%)	8440 (18%)	5909 (16%)	5887 (16%)	22 (14%)	6039 (25%)
	Obese	44190 (73%)	423 (64%)	7332 (58%)	36435 (77%)	28159 (77%)	28026 (77%)	133 (82%)	16031 (65%)
High Blood Glucose ≥1.1		36589 (46%)	461 (52%)	7414 (43%)	28714 (47%)	12328 (27%)	**12149 (27%)**	**179 (66%)**	24261 (71%)
eGFR	**<15**	1501 (2%)	19 (2%)	289 (2%)	1193 (2%)	475 (1%)	475 (1%)	0 (0%)	1026 (3%)
	>=15<30	2126 (3%)	34 (4%)	349 (2%)	1743 (3%)	683 (1%)	680 (1%)	3 (1%)	1443 (4%)
	>=30<60	14875 (19%)	145 (16%)	2620 (15%)	12110 (20%)	6647 (15%)	6609 (15%)	38 (14%)	8228 (24%)
	>=60<90	38612 (48%)	342 (38%)	7289 (42%)	30981 (50%)	23585 (52%)	**23462 (52%)**	**123 (44%)**	15027 (44%)
	>=90	23071 (29%)	353 (40%)	6763 (39%)	15955 (26%)	14301 (31%)	**14188 (31%)**	**113 (41%)**	8770 (25%)
High HbA1c (≥5.6)		38683 (87%)	392 (78%)	7471 (82%)	30820 (88%)	10981 (72%)	**10806 (72%)**	**175 (91%)**	27702 (95%)
DCC MELD score>14		6695 (8%)	113 (12%)	1313 (7%)	5269 (8%)	2871 (6%)	2858 (6%)	13 (5%)	3824 (11%)
High Triglycerides (≥150)		24483 (30%)	235 (26%)	5112 (29%)	19136 (31%)	11739 (25%)	**11641 (25%)**	**98 (35%)**	12744 (37%)
Low Platelets (<150)		8311 (10%)	275 (30%)	1998 (11%)	6038 (10%)	4325 (9%)	4304 (9%)	21 (8%)	3986 (12%)
High LDL-cholesterol (≥100)		22917 (28%)	213 (23%)	4851 (28%)	17853 (29%)	15103 (33%)	**15042 (33%)**	**61 (22%)**	7814 (22%)

eGFR=estimated glomerular filtration rate; HbA1c =Hemoglobin A1c; DCC=decompensated cirrhosis; MELD=Model for end-stage liver disease

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