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Increasing Use of SGLT2-Inhibitors in Heart Failure with Reduced Ejection Fraction

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Abstract

Introduction

ESC (European Society of Cardiology) guidelines advise all patients diagnosed with heart failure with reduced ejection fraction (HFrEF) should be prescribed an SGLT2-inhibitor. We conducted an audit of patients attending the local consultant-lead heart failure clinic to assess adherence to this guideline. This was a re-audit of an initial audit done in 2020.

Methods

The intervention since the previous audit consisted of widespread education on the role of SGLT2-inhibitors in HFrEF. Also, information leaflets advising on guidelines were placed in all outpatient heart failure rooms. We analysed data using the electronic medical record, including clinic letters, echocardiography reports, and laboratory results, to assess the number of patient appropriately prescribed SGLT2-inhibitors.

Results

35 of the 53 patients (66%) included in this dataset had HFrEF. Of these, 32 (91.4%) patients were prescribed an SGLT2-inhibitor. One patient did not tolerate an SGLT2-inhibitor. This demonstrates improvement in SGLT2-inhibitor prescribing, as the initial audit found only 4.6% of patients were prescribed an SGLT2-inhibitor.

Discussion

This re-audit represents a clear improvement in local adherence to guideline-directed heart failure therapy. We will aim to continue this high level of adherence in future.

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Introduction

SGLT2-inhibitors have become an important component in the long-term management of heart failure with reduced ejection fraction (HFrEF). ESC guidelines now advise all patients with a diagnosis of HFrEF should be started on either empagliflozin or dapagliflozin[1]. This is a class I recommendation, indicating a good evidence base and general support for their use.

Our initial audit found that only 6 of the 129 patients included were taking and SGLT2-inhibitor. The initial audit had been based on the DAPA-HF study so criteria for starting an SGLT2-inhibitor were more strict that current ESC guidelines. This complicated the introduction of SGLT2-inhibitors, as our population included more asymptomatic patients, patients with low NT-proBNP levels, and patients with CKD IV-V. For the current audit, we compared local practices to the updated ESC guidelines.

As these are relatively new medications, with a recently introduced guideline recommendation, they may not yet have been initiated in appropriate patients. Locally, many patients were not prescribed SGLT2-inhibitors in our initial audit, even when their use would have been indicated for glycaemic control. This was felt to be due to lack of awareness of their role in HFrEF, with or without a concurrent diagnosis of diabetes, and general lack of familiarity in their use. Since our initial audit, there has been a large amount of publications in medical literature about the evidence base for SGLT2-inhibitor use in our target population. In addition to this, the intervention since the previous audit consisted of widespread education on the role of SGLT-2 inhibitors in heart failure with reduced ejection fraction.

Methods

As with the initial audit, this re-audit retrospectively reviewed all patients with HF attending the specialist-led heart failure clinic at GUH between 13th September and 4th October 2022. The audit was approved by the GUH Clinical Audit Committee.

We retrospectively analysed data collected from the outpatient heart failure clinic using the electronic medical record. Medical notes from the hospital database, EVOLVE and CVWeb, were used to obtain demographic, clinical, biochemical, and medication data. We accessed clinic letters, medical history, echocardiography reports, and laboratory results to assess the number of patients prescribed SGLT2-inhibitors and whether appropriate patients were started on SGLT2-inhibitors, as advised by ESC guidelines.

To correspond with the initial audit, and to include appropriate detail on our population sample, we collected data on multiple factors. We included data on age, sex, ejection fraction,

NYHA class, blood pressure in clinic, eGFR, heart failure aetiology, comorbities (specifically hypertension, atrial fibrillation, and diabetes diagnosis), and heart failure hospitalisation within the last year. We included data on prescribed heart failure medications, specifically whether patients were on SGLT2-inhibitors, ACE-inhibitors, angiotensin-II receptor blockers, beta-blockers, mineralocorticoid antagonists, or angiotensin receptor neprilysin inhibitors. We also included data on whether patients had devices in-situ, specifically implantable cardioverter-defibrillators or cardiac resynchronisation therapy devices. We also included medications prescribed for glycaemic control.

The initial audit used the DAPA-HF inclusion criteria. DAPA-HF only included patients with NYHA class II–IV, and an LVEF ≤40% despite optimal medical therapy. Patients were also required to have an elevated plasma NT-proBNP and an eGFR ≥30 mL/min/1.73 m^2. ESC guidelines now state 'Unless contraindicated or not tolerated, dapagliflozin or empagliflozin are recommended for all patients with HFrEF already treated with an ACE-I/ARNI, a beta-blocker, and an MRA, regardless of whether they have diabetes or not.' This simplified the data collection process, as patients were classified as either HFrEF or heart failure with preserved ejection fraction (HFpEF), then either prescribed an SGLT2-inhibitor or not within the HFrEF subgroup. This was then analysed using Microsoft Excel. As with the initial audit, we compared our data to the DAPA-HF trial.

Results

Table 1 summarises the baseline clinical data, compared to that of the formative DAPA-HF study. Of particular note is that only 39.6% of the patients in our study had an ischemic cardiomyopathy in comparison to 56% in the DAPA-HF study. The 53 patients in our study represented a more elderly cohort compared to the DAPA-HF and EMPEROR-Reduced study populations. Only 10/53 (18.9%) of our HFrEF patients were eligible for SGLT-2i therapy based on the DAPA-HF inclusion criteria. This is primarily due to the higher than expected percentage of patients in our cohort who were NYHA class I (34.0%) compared to none in the DAPA HF study, and the higher rate of patients with a diagnosis of Atrial Fibrillation/Flutter (54.7%) compared to the DAPA HF study population (40%). 12/53 (22.6%) had severe CKD with an eGFR <30 ml/min/1.73m^2.

Table 1: Base line characteristics and co-morbidities

	Local Data (n=53)	**DAPA-HF (n=4744)**
Mean Age (Years)	70.64 ±(13.02)	66
Male (%)	81.1	77
T2DM (%)	41.5	45
NYHA Class (%)		
• **NYHA I**	34.0	None

• **NYHA II**	39.6	68
• **NYHA III**	20.8	32
• **NYHA IV**	5.7	1
Mean Left Ventricular Ejection Fraction (%)	33.26 ± (14.142)	31
HFrEF (n)	35	4744
Mean Systolic BP (mmHg)	126.26±(18.52)	122
Median NT-proBNP (pg/mL)	3385.57±(5011.33)	1437
Mean eGFR (ml/min/1.73m²)	50.62±(24.23)	66
Ischemic Aetiology (%)	39.6	56
HF Hospitalization within 1 year (%)	37.7	47
Hypertension (%)	47.2	74
Atrial Fibrillation/Flutter %	54.7	40

Of the 53 patients included in this dataset, 35 (66%) had HFrEF. Within this group, 32 (91.4%) patients were prescribed an SGLT2-inhibitor – either dapagliflozin or empagliflozin. An additional one patient did not tolerate an SGLT2-inhibitor. Of note, 34% of this cohort were classified as NYHA-I, so would not have been included in the trials which demonstrated the benefit of SGLT2-inhibitors in heart failure.

Table 2: Treatment

	Local Data (n=53)	DAPA-HF (n=4744)
SGLT2i	36 (67.9%)	N/A
Diuretic	41 (77.4%)	4411 (93%)
ACEI	16 (30.2%)	2656 (56%)
ARB	19 (35.8%)	1328 (28%)
ACEI/ARB/ARNI	40 (75.5%)	4435 (93.5%)
Beta-Blocker	47 (88.7%)	4554 (96%)
MRA	23 (43.4%)	3368 (71%)

ICD	8 (15.1%)	1233 (26%)
CRT	3 (5.7%)	332 (7%)
Diabetes Medication (n=22)		
Metformin	13 (59%)	
Sulphonylurea	1 (4.5%)	
DPP4 Inhibitor	7 (31.8%)	
GLP-1 Agonist	3 (13.6%)	
Insulin	7 (31.8%)	
SGLT-21	17 (77.3%)	

In total, we found that 36 (67.9%) patients were prescribed an SGLT2-inhibitor, including patients with HFpEF. As SGLT2-inhibitors did not have an ESC guideline recommendation for patients with HFpEF at the time of this study, this was likely for alternative indications. There were 22/53 (41.5%) patients with T2DM the majority of which (17 patients; 77.3%) were already on SGLT2-inhibitor. It is notable that only 75.5% of our sample were prescribed an ACE-i/ARB/ARNI. Much of this may be accounted for by the inclusion of patients with HFpEF, who made up 33% of our sample. Table 2 summarises the rates of medical therapies in this cohort.

The methods used to increase drug prescribing were centred around increased awareness of drug indications and communication to patients about their benefits. Information leaflets were placed in clinic rooms as a reminder to staff on the indication for SGLT2i. Doctor-patient relationship was fundamental for patient support for starting a new medication. Effective communication has been associated with improved medication adherence[2]. For each patient, the benefits of SGLT2i drugs were explained to appropriate patients by the consultant. This included an explanation of the development of SGLT2i, their use in multiple conditions, and the research supporting their use. Patient uptake of these drugs was higher than anticipated given the pre-existing pill-burden and overall lower symptomatology of this cohort.
This may not be replicated in other cohorts as clinics can rarely afford the necessary time to facilitate consultant-directed medication education for individual patients.

Discussion

As the initial audit found that 4.6% of patients were prescribed an SGLT2-inhibitor, this re-audit represents a clear improvement in local adherence to guideline-directed heart failure therapy. We will aim to continue this high level of adherence in future. This audit could be repeated in future to ensure ongoing compliance with current guidelines. We would anticipate that the improvements seen with this re-audit would be continued, given increased awareness of ESC guidelines.

This study found much improved prescribing rates compared to rates during our initial audit. While some of this can be attributed to ESC guidelines or greater coverage and awareness of SGLTi, we believe the measures taken after our initial audit contributed to the higher uptake. Specifically, placing a reminder of SGLT2i indications in each clinic room likely encouraged consideration of these newer drugs in addition to older heart failure medications. Additionally the time taken to educate patients on their condition and potential benefits of adding these medications. These results would have been less likely without this time expenditure and healthy doctor-patient relationship.

Increased prescribing of SGLT2-inhibitors should translate to improved outcomes for patients similar to this cohort. Future audits may investigate the use of SGLT2-inhibitors in patients with HFpEF. This is following the results of EMPEROR-Preserved[3] and DELIVER[4] trials, which showed benefits in patients with HFpEF.

Since completion of this study, the ESC released a focused update to their heart failure management guideline which advises on use of SGLT2-inhibitors for HFpEF[5]. This is Class I recommendation with an A-level of evidence. We will endeavour to adhere to these recommendations and include such patients in future audits.

Declarations of Conflicts of Interest:
None declared.

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References:

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. European heart journal. 2021 Sep 21;42(36):3599-726.

2. Zolnierek KB, DiMatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. Medical care. 2009 Aug 1;47(8):826-34. DOI: 10.1097/MLR.0b013e31819a5acc

3. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M, et al. Empagliflozin in heart failure with a preserved ejection fraction. New England Journal of Medicine. 2021 Oct 14;385(16):1451-61. DOI: 10.1056/NEJMoa2107038

4. Solomon SD, McMurray JJ, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. New England Journal of Medicine. 2022 Sep 22;387(12):1089-98. DOI: 10.1056/NEJMoa2206286

5. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2023 Oct 1;44(37):3627-39. DOI: 10.1093/eurheartj/ehad613