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ORIGINAL ARTICLE

SGLT2 inhibitor therapy for transthyretin amyloid cardiomyopathy: early tolerance and clinical response to dapagliflozin

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Abstract

Aims Sodium-glucose cotransporter 2 inhibitors (SGLT2i) improve clinical outcomes in heart failure patients with reduced and preserved left ventricular ejection fraction (LVEF), but have not yet been investigated in transthyretin amyloid cardiomyopathy (ATTR-CM). This study aimed to evaluate tolerability, clinical outcomes, and changes in NT-proBNP levels and glomerular filtration rate (GFR) in ATTR-CM patients treated with dapagliflozin.

Methods and results Patients with stable, tafamidis-treated ATTR-CM were retrospectively evaluated at the initiation of dapagliflozin and 3 months thereafter. Tafamidis-treated ATTR-CM patients without SGLT2i served as a reference cohort. Overall, SLGT2i therapy was initiated in 34 patients. Seventeen patients with stable disease on tafamidis, who were subsequently started on dapagliflozin, were included in the analysis. Patients selected for SGLT2i presented with signs of advanced disease, evidenced by higher Gillmore disease stage (stage ≥2: 53% vs. 27.5%; $P = 0.041$), baseline median NT-proBNP [median (IQR) 2668 pg/mL (1314–3451) vs. 1424 (810–2059); $P = 0.038$] and loop diuretic demand (76.5% vs. 45% of patients; $P = 0.044$), and lower LVEF (46.6 ± 12.9 vs. 53.7 ± 8.7%; $P = 0.019$) and GFR (51.8 ± 16.5 vs. 68.5 ± 18.6 mL/min; P = 0.037) compared with the reference cohort. At 3-month follow-up, a numerical decrease in NT-proBNP levels was observed in 13/17 (76.5%) patients in the dapagliflozin (−190 pg/mL, IQR: −1,028–71, $P = 0.557$) and 27/40 (67.5%) of patients in the control cohort (−115 pg/mL, IQR: −357–105, $P = 0.551$). Other disease parameters remained stable and no adverse events occurred.

Conclusions In tafamidis-treated ATTR-CM patients, initiation of dapagliflozin was well tolerated. The efficacy of SGLT2i therapy in patients with ATTR-CM needs to be studied in randomized controlled trials.

Keywords Cardiac amyloidosis; Transthyretin; Cardiomyopathy; Tafamidis; Dapagliflozin

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Background

Awareness and improved diagnostics have led to a steady increase in patients diagnosed with transthyretin amyloid cardiomyopathy (ATTR-CM) in recent years.[1,2] If locally available, TTR-stabilizing therapy with tafamidis has been established as standard of care in eligible patients, successfully delaying disease progression, reducing heart failure hospitalizations (HFH) and all-cause mortality.[3] Despite disease-modifying treatment, ATTR-CM continues to progress, evidenced by continually worsening exercise capacity, quality of life, and increasing NT-proBNP levels over time.[3,4] With increasing HFH due to ATTR-CM,[5] the optimal medical therapy for these patients remains unclear. Preliminary evidence from registry data questions whether a role for traditional heart failure therapies—RAAS inhibitors, beta-blockers, and mineralocorticoid receptor antagonists—exists and whether their effectiveness may differ at various stages of ATTR-CM,[6] as left ventricular ejection fraction (LVEF) is initially preserved, before declining with progressive disease.

The most recent drug class added to the heart failure therapy portfolio, sodium-glucose cotransporter 2 inhibitors

(SGLT2i), improves clinical outcomes in HF patients with reduced (HFrEF) and preserved left ventricular ejection fraction (HFpEF), but SGLT2i have thus far not been evaluated in tafamidis-treated ATTR-CM patients, despite their intriguing efficacy and safety profile.[7] SGLT2i successfully reduce HFH and cardiovascular mortality in HFrEF (LVEF <40%) and HFH in HFpEF. Contrary to traditional heart failure therapy, SGLT2i may not adversely affect haemodynamics in ATTR-CM. They neither reduce heart rate and thereby potentially cardiac output in a restrictive cardiomyopathy such as ATTR-CM, nor significantly affect blood pressure, issues encountered with beta-blockers and RAAS inhibition. Within view of their well-established safety profile, these characteristics suggest that SGLT2i may be uniquely suitable for ATTR-CM patients.

In this context, we retrospectively assessed short-term tolerability and effects of the SGLT2i dapagliflozin on ATTR-CM disease stage, required diuretic dosage, kidney function, and NT-proBNP levels in a selected group of tafamidis-treated ATTR-CM patients.

Methods

Study design

Consecutive patients referred to the Cardiac Amyloidosis Clinic at the Department of Cardiology, Bern University Hospital, Inselspital, Bern, Switzerland, and diagnosed with ATTR-CM between June 2019 and December 2021 were prospectively enrolled in the Bern Amyloidosis Registry (B-CARE) (KEK: 2021-00135; NCT04776824) after acquisition of informed consent. After exclusion of AL amyloidosis by serum gel electrophoresis and immunofixation, diagnosis of ATTR-CM was made based on myocardial tracer uptake (Perugini Grade II or III) in a technetium-99-DPD scintigraphy or on the presence of TTR amyloid deposits in biopsy specimen. Genetic testing was performed in 56 of 57 patients included in the final analysis (98.2%). If biopsy specimen were assessed from extracardiac locations, cardiac imaging (echocardiography or cardiac magnetic resonance imaging) suggestive of cardiac amyloidosis was required for the diagnosis. If patients qualified (details see below), tafamidis treatment was initiated. The decision to prescribe or withhold SLGT2i was made at the treating physician's discretion.

Amyloidosis disease stage,[8] weight, cardiac rhythm, medication, NT-proBNP, GFR, and HbA1c levels were assessed at scheduled clinic visits 3 months prior to, at the time of, and 3 months after initiation of therapy with dapagliflozin. For clinical endpoints and potential side effects previously described for dapagliflozin, electronic patient records were additionally searched. ATTR-CM patients treated with tafamidis, but not SGLT2i, served as reference cohort. The design of the study was approved by the local ethics committee. The study was conducted in accordance with the Declaration of Helsinki.

Inclusion criteria

Inclusion criteria for the current analysis were (i) an established treatment with tafamidis without pre-existing SGLT2i intake and (ii) stable ATTR-CM in the 4 weeks prior to SGLT2i initiation, defined as exclusion of heart failure-related hospitalizations, new-onset atrial arrhythmias or need of a >50% increase in diuretic dose during the 4 weeks preceding SGLT2i initiation.

Qualification for tafamidis therapy in Switzerland is based on the ATTR-ACT study[3] (NYHA I–II, prior HFH or requirement for diuretic, NT-proBNP >600 pg/mL, GFR > 25 mL/min/1.73 m^2, 6-min walk test >100 m, life expectancy >2 years).

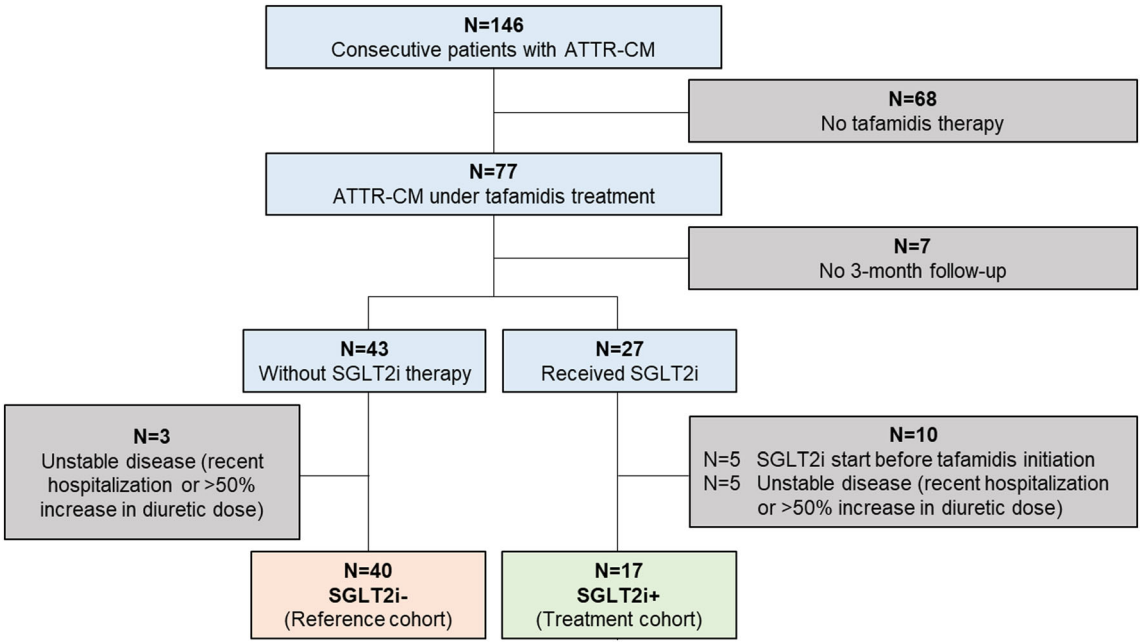
Patient selection

Of 146 patients diagnosed with ATTR-CM between June 2019 and December 2021, 77 were started on transthyretin-stabilizing therapy with tafamidis (*Figure 1*). We identified 34 patients with concomitant SGLT2i therapy (34/76 patients, 44.7%). Dapagliflozin was prescribed at a standard dose of 10 mg/day for all patients. Three-month follow-up including renal and cardiac biomarkers was available for 27 of the 34 patients (79.4%); five of these 27 patients were excluded from the main analysis, as dapagliflozin had been prescribed prior to tafamidis therapy, and five additional patients as the dapagliflozin was prescribed during or shortly after a worsening heart failure episode (*Figure S1*), for which either a hospitalization or transient increase of loop diuretic dose >50% was required. In the reference cohort without SGLT2i, three of 43 (6.98%) patients were excluded from the analysis due to a recent HFH. Seventeen patients were included in the final tafamidis–dapagliflozin cohort, whereas 40 patients treated with tafamidis, but not a SGLT2i, served as the reference cohort.

Follow-up and clinical endpoints

The Swiss health regulatory agency [Bundesamt für Gesundheit (BAG)] mandates yearly follow-up at an amyloidosis reference centre for patients treated with tafamidis. Yet, intervals for follow-ups and examinations performed at each follow-up vary, depending in part on whether patients are exclusively seen at Bern University Hospital or additionally by their resident cardiologist. At Bern University Hospital, 3-monthly follow-up including clinical and laboratory assessment is performed for newly diagnosed patients; this interval

Figure 1 Study CONSORT flow chart.



may be extended for patients with stable disease at the discretion of the treating physician.

Clinical adverse events included death, worsening heart failure episodes requiring either hospitalization or an increase in diuretic dosage of >50% and acute kidney failure, defined according to the current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[9] Furthermore, the prevalence of atrial fibrillation was assessed. To assess safety and tolerability, the incidence of known adverse events associated with SGLT2i use, including genitourinary infections, diabetic ketoacidosis, bone fractures, amputations, and orthostatic hypotension, was assessed.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA). Results are presented as mean ± standard deviation or as frequencies and percentage whenever appropriate. Non-normally distributed variables were provided as median and interquartile range (IQR). Continuous data were compared using a Mann–Whitney *U* test and categorical data using a chi-squared test or Fisher's exact test. For the analysis of changes over time, one-way repeated measures analyses of variance (ANOVAs) with the within-subject factor time (baseline vs. 3 months) were conducted. Binary logistic regression was used to identify predictors of a decline in NT-proBNP after 3 months and to provide the corresponding odds ratio and 95% confidence interval (CI). The two-tailed significance level was set at $\alpha < 0.05$.

Results

Baseline characteristics

Mean patient age was 79.8 ± 4 years (n = 17; 100% male) in the dapagliflozin -treated patients and 78.9 ± 5.8 years in the reference cohort (n = 40; 95% male) (see *Table 1*). Dapagliflozin was started a mean 291 days after initiation of tafamidis therapy, preferentially in patients with signs of advanced ATTR-CM. LVEF was significantly lower (46.6% ± 12.9 vs. 53.4% ± 8.7; P = 0.019), and HFrEF was more common in the dapagliflozin group [5 (29.4%) vs. 2 (5%), P = 0.02]. Lower GFR (51.8 ± 16.5 vs. 68.5 ± 18.6 mL/min; P = 0.037) and higher baseline median NT-proBNP in the dapagliflozin cohort [2668 (1314–3451) vs. 1424 (810–2059) pg/mL; P = 0.038] were reflected in a higher proportion of patients presenting with Gillmore stage ≥II [9 (53%) vs. 11 (27.5%), P = 0.041, see *Figure 2*], and the prevalence of atrial fibrillation was significantly higher [7 (41.2%) vs. 8 (20%), P = 0.043] (*Table 1*) in the treatment group. Whereas loop diuretic dose was similar between the dapagliflozin and control cohort (8.1 ± 7 vs. 5.5 ± 9.2 mg, P = 0.305), more dapagliflozin-treated patients

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Table 1 Clinical characteristics at baseline

	SGLT-2+	SGLT-2−	*P* value
n	17	40	N/A
Patient characteristics			
Gender (male) *n (%)*	17 (100)	38 (95)	0.489
Age [years] *mean ± SD*	79.8 ± 4	78.9 ± 5.8	0.576
TTR genetic testing			
Performed	17 (100)	39 (97.5)	N/A
wt-TTR	15 (88.2)	38 (97.4)	N/A
h-TTR	2 (11.8)	1 (2.6)	N/A
Medication *n* (%)			
Beta-blocker	7 (41.2)	17 (42.5)	0.790
MRA	11 (64.7)	8 (20.0)	**0.001**
RAAS blockage			
ACE-I	2 (11.8)	5 (12.5)	0.999
ARB	7 (41.2)	17 (42.5)	0.926
ARNI	2 (11.8)	0	0.085
Loop diuretic	13 (76.5)	18 (45.0)	**0.044**
Gillmore stage			
Gillmore Stage I	8 (47.1)	29 (72.5)	0.041 (Stage I vs. ≥2)
Gillmore Stage II	7 (41.2)	7 (17.5)	
Gillmore Stage III	2 (11.8)	4 (10.0)	
Biomarkers			
NTproBNP [pg/mL]	2668 (1314–3451)	1424 (810–2059)	**0.038**
GFR [mL/min] *mean ± SD*	51.8 ± 16.5	68.5 ± 18.6	**0.037**
<30 mL/min *n (% of available)*	2 (11.8)	2 (5)	0.575
HbA1c *mean ± SD*	6.18 ± 0.7	5.7 ± 0.57	**0.011**
Above 6.5% *n (% of available)*	5 (29.4)	1 (2.5)	**0.015**
Medical history *n (%)*			
Diabetes mellitus	5 (29.4)	2 (6.3)	**0.041**
Atrial fibrillation	7 (41.2)	8 (20)	**0.043**
LVEF [%] *mean ± SD*	46.6 ± 12.9	53.7 ± 8.7	**0.019**
Below cut-off 40% *n (% of available)*	5 (29.4)	2 (5)	**0.020**

required loop diuretics [13 (76.5%) vs. 18 (45%), *P* = 0.044] and concomitant mineralocorticoid receptor antagonist therapy [11 (64.7%) vs. 8 (20%); *P* = 0.001]. Beta-blocker and RAAS inhibitor usage was not significantly different between the groups.

Clinical outcomes at 3 months

Over the short study period, heart failure-associated adverse events (worsening heart failure episodes, death) were not observed, and neither were new-onset arrhythmias. Atrial fibrillation was equally seen in 7/17 (41.2%) patients in the dapagliflozin cohort at baseline and at 3 months. Dapagliflozin was well tolerated; side effects previously associated with SGLT2i, such as urinary tract or genital yeast infections, ketoacidosis, or orthostatic hypotension, were not observed in our ATTR-CM cohort.

ATTR Gillmore disease staging indicated stable disease in both dapagliflozin-treated patients and the control cohort (compared with baseline *P* = 0.723 and *P* = 0.545, respectively; *Table 2*, *Figure 2*). Weight (75.8 ± 11.4 kg at baseline compared with 75.3 ± 10.7 kg at 3 months), diuretic use, GFR, and HbA1c also remained stable 3 months after initiation of dapagliflozin (*Table 2*).

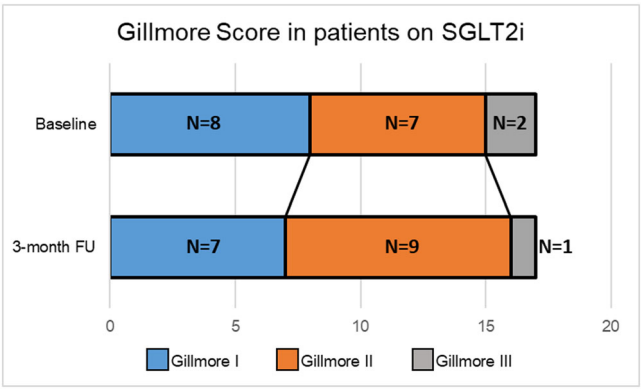
Evolution of NT-proBNP levels

Prior to initiation of dapagliflozin, a median NT-proBNP increase of 67 pg/mL (IQR −14 to 220) was seen in the treatment cohort. The median decline in NT-proBNP levels of −190 pg/mL (IQR −1028 to +71, *P* = 0.557) at the 3-month follow-up, corresponding to a median change of −12.4% was non-significant (*P* = 0.557) (*Table 3*, *Figure 3*). After starting of dapagliflozin, decreased NT-proBNP levels were observed in 13 of the 17 patients (76.5%), and this was equally seen in HFpEF [75.0%; −1375 pg/mL (IQR −3740 to 63.5)] and HFrEF patients [80.0%; −163 pg/mL (IQR − 375 to 71)]. In the reference cohort, a non-significant decline in NT-proBNP was also observed [*n* = 40, −115 pg/mL (IQR −1028 to +71, *P* = 0.551)]. Time*Group interaction was non-significant for an association with dapagliflozin use (*Figure 3*). A binary logistic regression model did not identify any predictors that were associated with a decline in NT-proBNP levels in patients treated with dapagliflozin (*Table 4*).

Discussion

In the present analysis, we describe the short-term tolerability, clinical outcomes, and cardiorenal biomarker response to

Figure 2 Gillmore scores were calculated to assess ATTR-CM disease stage in patient treated with (A) or without (B) SGLT2i. Stage I is defined as NT-proBNP ≤ 3000 ng/L and GFR ≥ 45 mL/min, and Stage III as NT-proBNP > 3000 ng/L and GFR < 45 mL/min; the remaining patients are classified as Stage II. Disease stage remained stable in both groups during the short follow-up of 3 months (P = 0.723 for SGLT2i and P = 0.545 for control cohort).



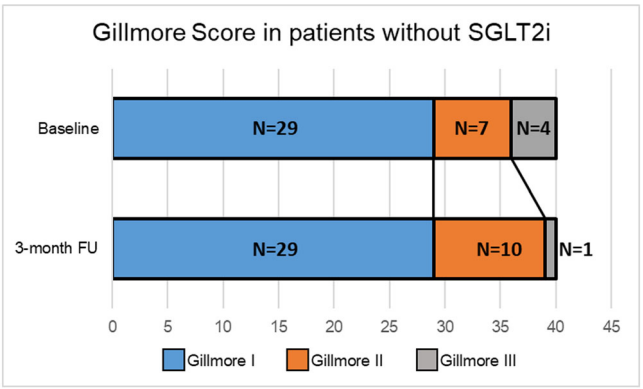


Table 2 Evolution of clinical characteristics stratified by SGLT2i intake

	SGLT-2+			SGLT-2−		
	Baseline	3-month follow-up	*P* value vs. baseline	Baseline	3-month follow-up	*P* value vs. baseline
n	17	17		40	40	N/A
Gillmore stage						
Gillmore Stage I	8 (47.1)	7 (41.2)	0.723	29 (72.5)	29 (72.5)	0.545
Gillmore Stage II	7 (41.2)	9 (52.9)		7 (17.5)	10 (25.0)	
Gillmore Stage III	2 (11.8)	1 (5.9)		4 (10.0)	1 (2.5)	
Loop diuretic *n (%)*	13 (76.5)	11 (64.7)	0.688	18 (45.0)	N/A	N/A
Diuretic dose *mean ± SD*	8.1 ± 7.0	8.2 ± 8.8	0.906	5.5 ± 9.2	N/A	N/A
Weight [kg]	75.9 ± 11.0	75.4 ± 10.7	0.418			
Biomarkers						
GFR [mL/min] *mean ± SD*	51.8 ± 16.5	53.6 ± 15.2	0.220	68.5 ± 18.6	61.3 ± 17.2	0.185
<30 mL/min *n (% of available)*	2 (11.8)	1 (5.9)	0.500	2 (5)	2 (5)	0.999
HbA1c *mean ± SD*	6.18 ± 0.7	5.98 ± 0.48	0.733	5.7 ± 0.57	5.68 ± 0.55	0.360
Above 6.5% *n (% of available)*	5 (29.4)	1 (5.9)	0.111	1 (2.5)	2 (5.0)	0.557

the SGLT2 inhibitor dapagliflozin in tafamidis-treated ATTR-CM patients for the first time. Adverse events were not observed during the 3-month observational period. Disease stage, renal function, weight, and diuretic use remained stable in our cohort, and dapagliflozin was tolerated well in ATTR-CM patients with stable disease.

Epidemiological data show a steady increase in patients diagnosed and admitted with ATTR-CM in recent years.[5] As the

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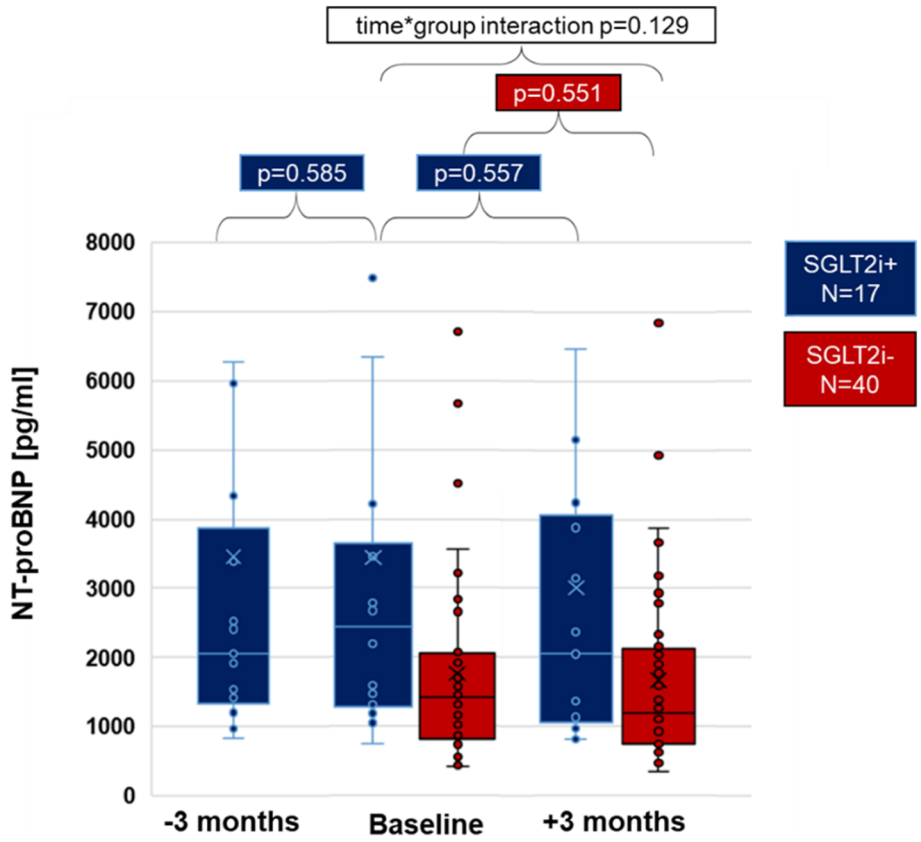
Table 3 Evolution of NT-proBNP levels

		Prior baseline	Baseline	FU1
Time from baseline *median* [days]		−100 (86–112)		+94 (88–102)
SGLT2i+	NT-proBNP [pg/mL]	2058 (1427–3864)	2670 (1353–4026)	2017 (1089–4361)
	Delta to baseline	67 (−141–220)		−190 (−1028 to +71)
	% change vs. baseline	2.0 (−11.2–16.2)		−12.4 (−18.7 to +9.6)
	P value vs. baseline	0.852		0.557
SGLT2−	NT-proBNP [pg/mL]		1424 (810–2059)	1196 (744–2130)
	Delta to baseline			−115 (−357 to +105)
	% change vs. baseline			−12.6 (−22.6–14.3)
	P value vs. baseline			0.551

Figure 3 Change in NT-proBNP in ATTR-CM patients treated with (blue) or without (red) SGLT2i. SGLT2i therapy was started at the baseline visit.



safety and tolerability of traditional heart failure medications have been questioned for ATTR-CM patients, SGLT2i present a promising alternative. Safety and efficacy of these drugs have been established in large randomized controlled trials, and dapagliflozin was tolerated well in our small pilot study. Besides reducing HFH in heart failure patients across all ranges of LVEF,[10,11] benefit for ATTR-CM may additionally derive from reducing the incidence of atrial fibrillation[12] and beneficial effects on myocardial remodelling, such as reductions of extracellular volume and left ventricular mass index.[13]

As it has previously been shown that beneficial effects on clinical outcomes associated with heart failure therapies, including SGLT2i, may be predicted by a decrease in NT-proBNP levels in traditional heart failure cohorts,[14,15] we decided to explore the short-term effects dapagliflozin initiation has on NT-proBNP levels in ATTR-CM. The use of NT-proBNP as a surrogate is challenging in these patients, as even with transthyretin-stabilizing therapy, NT-proBNP increases with disease progression, and a particularly high variability is observed in patients during episodes of atrial fibrillation (we have seen up to sixfold increases in patients

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Table 4 Binary logistic regression model: univariate association with a decline in NT-proBNP from baseline to 3 months in patients with SGLT2i intake

	Odds ratio (95% CI)	*P* value
Demographics		
Age [years]	1.01 (95% CI 0.760–1.343)	0.943
Medical history *n (%)*		
Atrial fibrillation	0.600 (95% CI 0.053–6.795)	0.680
LVEF [%]	0.957 (95% CI 0.871–1.050)	0.350
<40%	0.889 (95% CI 0.064–12.252)	0.930
Medication		
Beta-blocker	1.750 (95% CI 0.173–17.68)	0.635
MRA	1.452 (95% CI 0.434–4.859)	0.545
RAAS blockage	1.714 (95% CI 0.131–22.51)	0.682
Loop diuretic	1.376 (95% CI 0.135–9.715)	0.562
Biomarkers		
GFR [mL/min]	0.953 (95% CI 0.880–1.031)	0.231
<30 mL/min	0.826 (95% CI 0.190–5.22)	0.716
HbA1c [%]	0.504 (95% CI 0.079–3.209)	0.469
>6.5%	0.741 (95% CI 0.015–6.512)	0.616

during AF episodes in our clinic, unpublished data) or suboptimal cardiac pacing. We therefore limited our exploratory analysis to ATTR-CM patients with stable disease. The short-term response with declining NT-proBNP levels seen in 13 of 17 patients, both in patients with HFpEF and HFrEF, seems encouraging, yet this was not statistically significant, and the small sample size coupled with NT-proBNP variability seen in our cohort precluded identification of any trend. Furthermore, a non-significant decrease was also seen in the reference cohort, even though comparability may be limited, with these patients presenting at an earlier disease stage. Five patients in whom dapagliflozin was started prior to tafamidis were excluded from the main analysis, as a decline in NT-proBNP has been described 6–12 weeks after starting tafamidis therapy.[4] Inclusion of these five patients in the analysis did not change the results (see *Table S1*, *Figure S1*), dapagliflozin was well tolerated, adverse events were not recorded, and similar response rates to NT-proBNP were observed when either looking at these five patients separately or including them in the main analysis.

Limitations

Limitations include the small sample size, the unblinded and retrospective single-centre analysis, and the selection bias introduced prospectively when prescribing SGLT2i preferentially to patients with progressive disease and retrospectively by the limitations of NT-proBNP measurements in this patient population. As follow-up is often shared between the amyloidosis reference centre and resident cardiologists, and follow-up intervals may vary, 3-month follow-up data were not available for all patients after initiation of SGLT2i therapy. Whereas the SGLT2i-naïve cohort provides a reference, these patients differ significantly from the SGLT2i treatment group limiting comparability. ATTR-CM is overwhelmingly diagnosed in men, which is reflected in our cohort; by chance, the SGLT2i-treated group included only men. Testing the efficacy of SGLT2i in ATTR-CM and whether SGLT2i may differentially affect ATTR-CM patients at early and late disease stages was beyond the scope of this small pilot study.

Conclusions

In this retrospective pilot study, initiation of SGLT2i therapy with dapagliflozin in patients with ATTR-CM was well tolerated. Larger, randomized controlled studies are needed to assess the effect of SGLT2i therapy on long-term morbidity and mortality in ATTR-CM patients.

Conflict of interest

Dr Windecker reported institutional research and educational grants from Abbott, Amgen, AstraZeneca, Bristol Myers Squibb, Bayer, Biotronik, Boston Scientific, Cardinal Health, Cardiovalve, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Johnson & Johnson, Medicure, Medtronic, Novartis, Polares, OrPha Suisse, Pfizer, Regeneron, Sanofi-Aventis, Sinomed, Terumo, and V-Wave outside the submitted work; reported serving as unpaid advisory board member and/or unpaid member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, AstraZeneca, Bayer, Bristol Myers Squibb, Boston Scientific, Biotronik, Cardiovalve, Edwards Lifesciences, Janssen, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, V-Wave and Xeltis; and reported being a member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration. Dr Stortecky reported research grants to the institution from Edwards Lifesciences, Medtronic, Boston Scientific, and Abbott, as well as personal fees from Boston Scientific, Teleflex, and BTG. Dr Pilgrim reports research grants to the institution from Biotronik, Boston Scientific, and Edwards Lifesciences; speaker fees from Biotronik and Boston Scientific; clinical event committee for study sponsored by HighLifeSAS; and travel reimbursement from Medira; proctoring for Medtronic. Dr Gräni receives funding from the Swiss National Science Foundation, InnoSuisse, Center of Artificial Intelligence UniBern, and GAMBIT Foundation. All other authors report no conflicts of interest.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Evolution of NT-proBNP and weight after initiation of SGLT2i therapy.

Figure S1. Change in NT-proBNP in ATTR-CM patients treated with (blue) or without (red) SGLT2i. SGLT2i-therapy was started at the baseline visit.

Compared to Table 3 in the main manuscript, 5 additional patients started on SGLT2i *prior to* tafamidis were included in the analysis. For SGLT2i+, n = 22, and for SGLT2−, n = 40.

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