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Adjunctive empagliflozin therapy in endocrine-driven heart failure with preserved ejection fraction after thyroid cancer surgery

O. M. Didushko, M. V. Bielinskyi, A. S. Herashchenko, N. B. Nyshchuk-Oliinyk, O. O. Tkachuk-Hryhorchuk, A. Y. Pavliskyi

Ivano-Frankivsk National Medical University

Differentiated thyroid cancer (DTC) is one of the fastest-growing malignancies worldwide, with excellent disease-specific survival but a substantial burden of long-term treatment-related morbidity. Recent population-based studies and meta-analyses show that survivors of DTC have an increased incidence of cardiovascular (CV) events and CV mortality compared with the general population, and that CV disease is now a leading cause of non-cancer death in this group. Total thyroidectomy followed by chronic levothyroxine therapy and, in many patients, varying degrees of thyroid-stimulating hormone (TSH) suppression or hypothyroidism, is the standard of care for intermediate- and high-risk disease. These iatrogenic alterations in thyroid status are increasingly recognized as an important determinant of cardiometabolic risk in DTC survivors, particularly in those with additional CV risk factors [1].

Thyroid hormones have profound effects on cardiac structure and function. Hypothyroidism promotes bradycardia, increased systemic vascular resistance, impaired left ventricular (LV) relaxation and prolonged isovolumic relaxation time, changes that collectively favor a phenotype of diastolic dysfunction with preserved ejection fraction. The concept of «hypothyroid cardiomyopathy» reflects this pattern like heart failure with preserved ejection fraction (HFpEF), in which symptoms and biomarker elevation coexist with normal LV systolic function [2]. Contemporary data indicate that both overt and subclinical hypothyroidism associate with impaired endothelial function, measured as reduced brachial artery flow-mediated dilation (FMD), increased carotid intima-media thickness and an adverse lipid and inflammatory profile [3]. In a recent study of patients with HFpEF, subclinical hypothyroidism was associated with lower FMD and a higher rate of major adverse CV events, suggesting that thyroid dysfunction may amplify the endothelial and myocardial abnormalities that characterize HFpEF [4].

Heart failure with preserved ejection fraction is now understood as a systemic, comorbidity-driven syndrome in which microvascular inflammation, endothelial dysfunction and myocardial fibrosis play central roles [5]. Diagnostic and prognostic evaluation of HFpEF relies heavily on biomarkers of myocardial stretch, among which the N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) is the most widely validated. Recent reviews emphasize that NT-proBNP not only supports the diagnosis of HFpEF and distinguishes it from non-cardiac dyspnea, but also carries independent prognostic information across

Дідушко Оксана Миколаївна, д. мед. н., проф. кафедри ендокринології. E-mail: odidushko@ifnmu.edu.ua. ORCID: http://orcid.org/0000-0002-7140-1595; **Бєлінський Микита Вадимович,** доктор філософії з медицини, асистент кафедри терапії, сімейної та невідкладної медицини післядипломної освіти. E-mail: mbelinskiy@ifnmu.edu.ua. ORCID: http://orcid.org/0000-0001-5013-3838; **Геращенко Андрій Сергійович,** доктор філософії з медицини, асистент кафедри терапії, сімейної та невідкладної медицини післядипломної освіти. ORCID: http://orcid.org/0000-0003-4090-7320; **Нищук-Олійник Наталія Богданівна,** доктор філософії з медицини, асистент кафедри терапії, сімейної та невідкладної медицини післядипломної освіти. ORCID: http://orcid.org/0000-0002-4338-6121; **Ткачук-Григорчук Олеся Олегівна,** к. мед. н., асистент каф. загальної та судинної хірургії. E-mail: tkolesia@bigmir.net. ORCID: http://orcid.org/0009-0000-5022-4238; **Павліський Андрій Ярославович,** асистент кафедри терапії, сімейної та невідкладної медицини післядипломної освіти. E-mail: apavliskyy@ifnmu.edu.ua. ORCID: http://orcid.org/0009-0008-0195-3205

the spectrum of preserved and mildly reduced EF [6]. In patients with additional endocrine or metabolic comorbidities such as hypothyroidism or type 2 diabetes, elevated NT-proBNP may thus capture the combined burden of cardiac loading conditions, subclinical myocardial injury and neurohormonal activation [7].

Objective. To evaluate the effect of adding empagliflozin to standard beta-blocker and angiotensin-converting enzyme inhibitor therapy on left ventricular diastolic function, endothelial function and galectin-3 levels in post-thyroidectomy thyroid cancer patients with hypothyroid cardiomyopathy and preserved ejection fraction.

MATERIALS AND METHODS

A total of 61 patients fulfilled eligibility criteria and were included in the analysis: 27 in group 1 (standard therapy) and 34 in group 2 (standard therapy plus empagliflozin). All patients received standard heart failure therapy appropriate for HFpEF and underlying risk factors, including beta-blockers and angiotensin-converting enzyme inhibitors (ACE-I), titrated according to current clinical practice and tolerated doses. Group 1 received standard therapy only. Group 2 received standard therapy plus empagliflozin at a dose of 10 mg once daily, initiated at baseline (day 0) and continued throughout the 6-month observation period, provided no safety issues or intolerance occurred. Concomitant medications such as statins, antiplatelet agents and diuretics were prescribed as clinically indicated and kept as stable as possible during the study. Levothyroxine dosing was adjusted by the treating endocrinologist according to routine practice to maintain target TSH ranges appropriate for thyroid cancer survivors; changes in dose and thyroid function tests were recorded.

Each patient was evaluated at three predefined time points: baseline (day 0, before initiation of empagliflozin in group 2), 1-month visit (± 7 days) and 6-month visit (± 14 days). At each visit, clinical assessment, blood pressure and heart rate measurement, routine laboratory tests, NT-proBNP, galectin-3, transthoracic echocardiography and brachial artery FMD were performed according to standardized protocols. Transthoracic echocardiography was performed using a Siemens NX3 Elite ultrasound system with a phased-array transducer by an experienced radiologist blinded to group allocation. Standard parasternal long- and short-axis and apical (2- and 4-chamber) views were acquired. LVEF was calculated using the biplane Simpson method. Diastolic function was assessed according to current guideline-based parameters. For each parameter, the average of three cardiac cycles in sinus rhythm was used. The same operator performed follow-up examinations, and machine settings were kept constant to minimize inter-study variability.

Endothelial function was evaluated by brachial artery FMD using high-resolution vascular ultrasound. Patients were examined in the morning after at least 8 hours of fasting and abstinence from caffeine, nicotine and vasoactive medications when possible. All FMD examinations were performed by the same trained sonographer using the same equipment and analysis protocol.

Venous blood samples were obtained in the morning after an overnight fast at each study visit. Routine hematology and biochemistry (including renal and liver function, fasting glucose and lipid profile) were measured by standard automated methods in the hospital laboratory. Serum NT-proBNP concentrations were measured using an electrochemiluminescence immunoassay according to the manufacturer's instructions. Serum galectin-3 levels were determined by a commercially available enzyme-linked immunosorbent assay (ELISA). For biomarker analyses, samples were centrifuged within 30 minutes of collection and stored at –70 °C until batch analysis to minimize inter-assay variability. Thyroid function tests (TSH, free thyroxine [FT4]) were performed at baseline and as required for clinical management; results closest to each study visit were recorded.

All statistical analyses were performed using IBM SPSS Statistics (version 26.0). Continuous variables were checked for normality (Shapiro–Wilk test) and are presented as mean ± standard deviation or median (interquartile range), as appropriate; categorical variables are presented as counts and percentages. Baseline differences between groups were assessed using the Student's t-test or Mann–Whitney U test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. Longitudinal changes and between-group differences over time were analyzed using two-way repeated-measures ANOVA for normally distributed variables. For key outcomes (E/e', FMD, NT-proBNP, galectin-3), linear mixed-effects models with random intercepts were additionally constructed, including time, treatment group and their interaction as fixed effects with adjustment for major confounders. No formal a priori sample size calculation was performed; the sample size was determined by the number of eligible patients during the study period. A two-sided p value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics were well balanced between the two treatment groups (Table 1). Patients were predominantly middle-aged women with overweight/obese body mass index (BMI) and a high prevalence of arterial hypertension, dyslipidemia and type 2 diabetes mellitus, without statistically significant differences in comorbidities. Papillary thyroid carcinoma represented the main histological type, and early (I—II) and advanced (III—IV) stages were distributed similarly between groups. Time since thyroidectomy, thyroid function parameters (TSH, free T4, free T3) and weight-adjusted L-thyroxine dose did not differ. By design, all patients had elevated NT-proBNP at baseline, and mean NT-proBNP levels were comparable between groups, confirming similar hemodynamic and neurohormonal status at study entry.

Table 1

Baseline clinical and biochemical characteristics of the study population

Parameter	Standard therapy (n = 27)	Standard + empagliflozin (n = 34)
Age, years	57.8 ± 10.2	56.9 ± 9.8
Females	21 (77.8 %)	27 (79.4 %)
Body mass index, kg/m^2	29.4 ± 4.1	29.7 ± 4.3
Arterial hypertension	22 (81.5 %)	27 (79.4 %)
Type 2 diabetes mellitus	7 (25.9 %)	9 (26.5 %)
Dyslipidemia	18 (66.7 %)	23 (67.6 %)
Coronary artery disease	6 (22.2 %)	7 (20.6 %)
Paroxysmal atrial fibrillation	4 (14.8 %)	6 (17.6 %)
Papillary carcinoma	23 (85.2 %)	28 (82.4 %)
Follicular carcinoma	3 (11.1 %)	4 (11.8 %)
Other histology	1 (3.7 %)	2 (5.9 %)
Thyroid cancer stage I—II	17 (63.0 %)	20 (58.8 %)
Thyroid cancer stage III—IV	10 (37.0 %)	14 (41.2 %)
Time since thyroidectomy, years	4.8 ± 3.1	4.5 ± 2.9
TSH, mIU/L	0.36 ± 0.24	0.39 ± 0.27
Free T4, pmol/L	19.2 ± 2.3	19.0 ± 2.1
Free T3, pmol/L	4.2 ± 0.6	4.1 ± 0.5
L-thyroxine dose		
μg/day	150 ± 25	152 ± 27
μg/kg/day	1.90 ± 0.32	1.92 ± 0.35
NT-proBNP, pg/mL	634 ± 188	646 ± 201

Note. All $p > 0.05$.

At baseline, both groups demonstrated a diastolic profile compatible with HFpEF-like dysfunction (E/e = 15, low e′ velocities and enlarged left atrium). Over 6 months, E/e′ declined significantly in both groups ($p_{time} < 0.001$), but the reduction was more pronounced with empagliflozin (Group 1 : 15.2 → 13.8; Group 2 : 15.4 → 11.9). The significant time × group interaction ($p < 0.001$) indicates a steeper improvement in LV filling pressures in the empagliflozin group.

Similarly, the E/A ratio increased toward a more favorable pattern of LV relaxation, with a modest rise in the standard-therapy group and a more marked shift in the empagliflozin group (0.81 → 1.01; $p_{time \times group} = 0.008$). Tissue Doppler indices improved in both groups but more so with empagliflozin: septal e′ increased from 5.3 ± 1.1 to 6.7 ± 1.3 cm/s and lateral e′ from 6.2 ± 1.3 to 7.8 ± 1.4 cm/s, with significant time × group interactions for both. LA volume index decreased in both groups, but the reduction was greater in Group 2 (–5.9 mL/m^2 vs –1.8 mL/m^2 over 6 months; $p_{time \times group} = 0.004$), suggesting more robust reverse atrial remodeling.

Endothelial function, assessed by brachial FMD, improved over time in the whole cohort ($p_{time} < 0.001$). In Group 1, FMD increased modestly from 4.1 ± 1.3 % to 5.0 ± 1.5 %, whereas in the empagliflozin group it improved from 4.0 ± 1.3 % to 7.1 ± 1.8 %, with a highly significant time × group effect ($p < 0.001$), indicating a substantially more favorable trajectory of endothelial function with the addition of empagliflozin.

Baseline galectin-3 levels were elevated in both groups (~21 ng/mL). Over 6 months, galectin-3 decreased slightly in the standard-therapy group (21.3 ± 4.9 → 19.8 ± 4.4 ng/mL), but declined much more in Group 2 (21.6 ± 5.1 → 16.2 ± 3.8 ng/mL). The overall effect of time was significant ($p = 0.03$), and the time × group interaction was highly significant ($p < 0.001$), supporting a stronger attenuation of profibrotic/inflammatory activity with empagliflozin (Table 2).

Mixed-effects modelling confirmed the unadjusted findings and quantified the independent effect of empagliflozin over time (Table 3).

For E/e′, time was associated with a modest overall decrease ($\beta = –0.42$ per visit, $p < 0.001$), while the significant negative time × treatment interaction ($\beta = –0.79$; $p < 0.001$) indicated a substantially steeper decline in E/e′ in the empagliflozin group. This effect remained robust after adjustment for age, sex and baseline NT-proBNP, implying that empagliflozin independently contributed to the improvement in LV filling pressures.

Table 2

Dynamics of echocardiographic diastolic parameters, flow-mediated dilation and galectin-3 over 6 months

Parameter	Group	Baseline	1 month	6 months	p_{time}	$p_{time \times group}$
E/e′	1	15.2 ± 2.8	14.4 ± 2.6	13.8 ± 2.5	< 0.001	< 0.001
	2	15.4 ± 3.0	13.6 ± 2.4	11.9 ± 2.1		
E/A	1	0.82 ± 0.19	0.86 ± 0.18	0.89 ± 0.17	0.004	0.008
	2	0.81 ± 0.18	0.93 ± 0.17	1.01 ± 0.19		
e′ septal, cm/s	1	5.4 ± 1.0	5.7 ± 1.1	5.9 ± 1.1	0.01	0.003
	2	5.3 ± 1.1	6.1 ± 1.2	6.7 ± 1.3		
e′ lateral, cm/s	1	6.3 ± 1.2	6.6 ± 1.3	6.8 ± 1.2	0.02	0.002
	2	6.2 ± 1.3	7.1 ± 1.4	7.8 ± 1.4		
LA volume index, mL/m^2	1	41.6 ± 6.8	40.7 ± 6.4	39.8 ± 6.1	0.01	0.004
	2	42.1 ± 7.0	39.1 ± 6.1	36.2 ± 5.6		
FMD, %	1	4.1 ± 1.3	4.6 ± 1.4	5.0 ± 1.5	< 0.001	< 0.001
	2	4.0 ± 1.3	5.5 ± 1.5	7.1 ± 1.8		
Galectin-3, ng/mL	1	21.3 ± 4.9	20.7 ± 4.7	19.8 ± 4.4	0.03	< 0.001
	2	21.6 ± 5.1	18.9 ± 4.2	16.2 ± 3.8		

In the FMD model, both time ($\beta = +0.21$; $p = 0.001$) and the time × treatment interaction ($\beta = +0.65$; $p < 0.001$) were significant, demonstrating that endothelial function improved over the study period in the entire cohort but markedly more in patients receiving empagliflozin. The positive interaction persisted after correcting for age, sex and BMI, suggesting that the endothelial benefit of empagliflozin was not simply due to differences in baseline cardiovascular risk.

For galectin-3, time ($\beta = -0.32$; $p = 0.006$) and the interaction term ($\beta = -1.05$; $p < 0.001$) were both significant, indicating an overall decline in galectin-3 with a much greater reduction in the empagliflozin group. Even after adjustment for age, sex and baseline NT-proBNP, empagliflozin remained strongly associated with a steeper decrease in galectin-3, supporting a potential antifibrotic/anti-inflammatory effect.

In the NT-proBNP model, natriuretic peptide levels decreased over time ($\beta = -28$ pg/mL per visit, $p < 0.001$) with an additional significant reduction in the empagliflozin group (time × treatment $\beta = -46$ pg/mL, $p < 0.001$). Lower baseline eGFR was associated with higher NT-proBNP, as expected, but did not eliminate the treatment effect.

Overall, the mixed-effects analyses show that, beyond standard beta-blocker and ACE-inhibitor therapy, empagliflozin was independently associated with more favorable longitudinal trajectories of diastolic function (E/e′), endothelial function (FMD), fibrosis/inflammation (galectin-3) and neurohormonal activation (NT-proBNP) in post-thyroidectomy patients with hypothyroid cardiomyopathy and preserved ejection fraction.

DISCUSSION

Beyond natriuretic peptides, there is growing interest in fibrosis-related biomarkers that reflect the structural remodeling underlying HFpEF. Galectin-3, a β-galactoside-binding lectin secreted by activated macrophages and fibroblasts, has emerged as a key mediator and biomarker of myocardial fibrosis, inflammation and adverse ventricular remodeling [8]. Several recent studies and meta-analyses have demonstrated that elevated galectin-3 is associated with the presence of HFpEF, worse functional status and increased risk of hospitalization and mortality, often independent of natriuretic peptide levels. Importantly, galectin-3 concentrations also appear to be relevant in patient groups with preserved systolic function but high CV risk, suggesting a potential role in phenotyping and risk stratification of patients with hypothyroid-related cardiomyopathy [9].

Endothelial dysfunction is another key mechanism linking thyroid status, HFpEF and CV outcomes. Experimental and clinical data indicate that hypothyroidism is associated with reduced nitric oxide bioavailability, increased oxidative stress and impaired endothelium-dependent vasodilation. Recent work in subclinical

Table 3

Linear mixed-effects models for longitudinal changes in E/e′, FMD, galectin-3 and NT-proBNP

Fixed effect	β (95 % CI)	p
E/e′		
Time (per visit)	–0.42 (–0.61 ... –0.23)	< 0.001
Treatment group (empagliflozin)	+0.11 (–0.58 ... +0.80)	0.76
Time × treatment interaction	–0.79 (–1.06 ... –0.52)	< 0.001
Age (per year)	+0.03 (+0.00 ... +0.06)	0.04
Female sex	+0.28 (–0.51 ... +1.07)	0.49
Baseline NT-proBNP (per 100 pg/mL)	+0.15 (+0.04 ... +0.26)	0.008
FMD		
Time (per visit)	+0.21 (+0.09 ... +0.33)	0.001
Treatment group (empagliflozin)	–0.02 (–0.54 ... +0.49)	0.93
Time × treatment interaction	+0.65 (+0.47 ... +0.83)	< 0.001
Age (per year)	–0.04 (–0.06 ... –0.02)	< 0.001
Female sex	+0.39 (–0.08 ... +0.86)	0.10
Baseline BMI (per kg/m^2)	–0.03 (–0.07 ... +0.01)	0.15
Galectin-3		
Time (per visit)	–0.32 (–0.55 ... –0.09)	0.006
Treatment group (empagliflozin)	+0.24 (–0.98 ... +1.46)	0.70
Time × treatment interaction	–1.05 (–1.42 ... –0.68)	< 0.001
Age (per year)	+0.06 (+0.01 ... +0.11)	0.02
Female sex	+0.91 (–0.18 ... +2.00)	0.10
Baseline NT-proBNP (per 100 pg/mL)	+0.18 (+0.03 ... +0.33)	0.02
NT-proBNP		
Time (per visit)	–28 (–43 ... –13)	< 0.001
Treatment group (empagliflozin)	+5 (–71 ... +81)	0.90
Time × treatment interaction	–46 (–70 ... –22)	< 0.001
Age (per year)	+3 (+0.1 ... +5.9)	0.04
Female sex	+19 (–49 ... +87)	0.58
Baseline eGFR (per 10 mL/min/1.73 m^2)	–12 (–22 ... –2)	0.02

hypothyroidism has shown that even modest elevations in TSH are associated with lower FMD and adverse changes in vascular biomarkers, supporting the concept that thyroid hormone deficiency contributes directly to vascular dysfunction. In HFpEF populations, impaired FMD has been identified as an independent predictor of adverse outcomes, and endothelial dysfunction is increasingly viewed as a therapeutic target rather than merely a marker of risk [10]. However, the interplay between hypothyroid status after thyroidectomy, HFpEF-like manifestations, and non-invasive measures of endothelial function such as FMD remains poorly characterized in thyroid cancer survivors.

Sodium-glucose cotransporter-2 (SGLT2) inhibitors have transformed the management of heart failure. In the EMPEROR-Preserved trial, empagliflozin significantly reduced the composite of CV death or hospitalization for heart failure in patients with HFpEF (LVEF > 40 %) irrespective of diabetes status, establishing SGLT2 inhibition as a disease-modifying therapy across the EF spectrum [11]. Subsequent analyses and translational studies have suggested that the benefits of empagliflozin extend beyond osmotic diuresis and glycemic control, encompassing favorable effects on myocardial energetics, LV diastolic function, ventricular–arterial coupling and renal hemodynamics. Preclinical and early clinical investigations indicate that empagliflozin can attenuate myocardial inflammation and fibrosis, improve cardiomyocyte stiffness and enhance endothelial function in HFpEF m empagliflozin has been reported to improve LV dia odels. In particular, stolic parameters and markers of vascular stiffness in patients with HFpEF and type 2 diabetes, suggesting a potential role in modulating both myocardial and vascular components of diastolic dysfunction.

Despite these advances, there is a striking paucity of data regarding the use of SGLT2 inhibitors in thyroid cancer survivors with hypothyroid cardiomyopathy. Recent work in disease-free athyreotic patients with DTC has documented an unfavorable CV risk profile, including increased arterial stiffness and subclinical myocardial dysfunction, in spite of apparently adequate oncologic control. Systematic reviews highlight that DTC survivors, especially those exposed to long-term TSH suppression or fluctuating thyroid hormone levels, carry higher risks of atrial fibrillation and CV mortality than matched controls [12]. However, few studies have focused specifically on patients who already manifest a HFpEF-like phenotype with elevated NT-proBNP and preserved LVEF, and virtually none have examined whether adjunctive empagliflozin therapy can

favorably modify diastolic function, endothelial function and fibrosis-related biomarkers in this context.

Galectin-3 and FMD are attractive mechanistic and surrogate endpoints in this population. Galectin-3 captures the fibrotic and inflammatory component of hypothyroid-related cardiac remodeling, while FMD reflects systemic endothelial health, which may be chronically perturbed by both thyroid hormone deficiency and the pro-inflammatory milieu associated with cancer and its treatment. Evaluating the dynamics of these markers in parallel with NT-proBNP and detailed echocardiographic measures of LV diastolic function may provide novel insights into the pathophysiology of hypothyroid cardiomyopathy after thyroidectomy and into the pleiotropic actions of empagliflozin in a non-diabetic, endocrine-driven HFpEF phenotype.

Therefore, the present study has shown of the benefits of adding empagliflozin to standard heart failure therapy (beta-blockers and ACE inhibitors) in post-thyroidectomy thyroid cancer patients with hypothyroid cardiomyopathy and preserved systolic function. Taken together, our results underscore (i) the elevated cardiometabolic risk among thyroid cancer survivors after total thyroidectomy, (ii) the central roles of diastolic dysfunction, endothelial impairment and fibrosis in hypothyroid-related HFpEF, and (iii) the potential of SGLT2 inhibition with empagliflozin to favorably influence these mechanisms.

CONCLUSIONS

In post-thyroidectomy thyroid cancer patients with hypothyroid cardiomyopathy and preserved ejection fraction, addition of empagliflozin to standard beta-blocker and ACE-inhibitor therapy was associated with greater improvement in left ventricular diastolic function, endothelial function and galectin-3 levels, together with a more pronounced reduction in NT-proBNP, compared with standard therapy alone. These findings support the potential role of empagliflozin as a cardio- and vasculoprotective strategy in endocrine-driven HFpEF phenotypes and provide a rationale for larger randomized trials in this high-risk population of thyroid cancer survivors.

Conflicts of interest: none.

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ABSTRACT

Survivors of differentiated thyroid cancer after total thyroidectomy form a growing population with increased long-term cardiovascular risk related to chronic thyroid hormone imbalance and lifelong L-thyroxine replacement. In this setting, hypothyroid cardiomyopathy with preserved left ventricular ejection fraction is associated with elevated N-terminal fragment of pro-B-type natriuretic pept ide (NT-proBNP), diastolic dysfunction, atrial remodeling and endothelial impairment. Data on disease-modifying treatment for this endocrine-driven heart failure with preserved ejection fraction (HFpEF)-like phenotype remain limited.

Objective — to assess the effect of adding empagliflozin to standard beta-blocker and angiotensin-converting enzyme inhibitor therapy on left ventricular diastolic function, endothelial function and galectin-3 levels in post-thyroidectomy thyroid cancer patients with hypothyroid cardiomyopathy and preserved ejection fraction.

Materials and methods. This prospective controlled study included 61 adults (57,2 ± 7,3 years, 48 female, 23 male) after total thyroidectomy for thyroid cancer with heart failure symptoms, elevated NT-proBNP and left ventricular ejection fraction ≥ 50 %. Patients received either standard therapy or standard therapy plus empagliflozin 10 mg/day for 6 months.

Results. Baseline clinical characteristics, thyroid status, L-thyroxine dose and NT-proBNP levels were comparable between groups. Standard therapy alone produced only modest improvement in diastolic indices, flow-mediated dilation (FMD), galectin-3 and NT-proBNP. In contrast, empagliflozin was associated with greater reductions in E/e′, larger increases in e′ velocities, a more pronounced decrease in left atrial volume index, stronger improvement in FMD, and greater declines in galectin-3 and NT-proBNP. In multivariable linear mixed-effects models, time × treatment interactions for E/e′ FMD, galectin-3 and NT-proBNP remained significant. Empagliflozin was well tolerated, with no serious drug-related adverse events.

Conclusions. In post-thyroidectomy thyroid cancer patients with hypothyroid cardiomyopathy and preserved ejection fraction, empagliflozin added to standard therapy was associated with greater improvement in diastolic and endothelial function and with larger reductions in galectin-3 and NT-proBNP than standard treatment alone. These findings support its potential cardio- and vasculoprotective role in endocrine-driven HFpEF phenotypes and justify larger randomized trials.

Keywords: hypothyroidism, hypothyroid cardiomyopathy, differentiated thyroid cancer, SGLT2 inhibitors, heart failure with preserved ejection fraction, endothelial function, galectin-3.

РЕЗЮМЕ

Емпагліфлозин як доповнення до стандартної терапії ендокринно зумовленої серцевої недостатності зі збереженою фракцією викиду після хірургічного лікування раку щитоподібної залози

О. М. Дідушко, М. В. Бєлінський, А. С. Геращенко, Н. Б. Нищук-Олійник, О. О. Ткачук-Григорчук, А. Я. Павліський

Івано-Франківський національний медичний університет

Пацієнти з диференційованим раком щитоподібної залози після тотальної тиреоїдектомії належать до групи з підвищеним довгостроковим серцево-судинним ризиком через порушення тиреоїдного гомеостазу та довічною замісною терапією левотироксином. За цих умов гіпотиреоїдна кардіоміопатія зі збереженою фракцією викиду супроводжується підвищенням рівня N-кінцевого фрагмента попередника мозкового натрійуретичного пептиду (NT-proBNP), діастолічною дисфункцією, ремоделюванням передсердь та ендотеліальною дисфункцією. Дані щодо ефективної хворобомодифікаційної терапії цього ендокринно зумовленого фенотипу обмежені.

Мета роботи — оцінити вплив додавання емпагліфлозину до стандартної терапії β-адреноблокаторами та інгібіторами ангіотензинперетворювального ферменту на діастолічну функцію лівого шлуночка, ендотеліальну функцію та рівень галектину-3 у пацієнтів після тиреоїдектомії з приводу раку щитоподібної залози з гіпотиреоїдною кардіоміопатією та збереженою фракцією викиду.

Матеріали та методи. У проспективне контрольоване дослідження було залучено 61 пацієнта (48 жінок, 23 чоловіки, середній вік — (57,2 ± 7,3) року) після тотальної тиреоїдектомії з приводу раку щитоподібної залози з наявністю симптомів серцевої недостатності, підвищеним рівняем NT-proBNP і фракцією викиду лівого шлуночка ≥ 50 %. Пацієнтів розподілили на дві групи: перша отримувала стандартну терапію, друга — стандартну терапію в поєднанні з емпагліфлозином у дозі 10 мг/добу впродовж 6 міс.

Результати. До початку лікування групи були порівнянними за клінічними характеристиками, тиреоїдним профілем, дозою L-тироксину та рівнем NT-proBNP. На тлі стандартної терапії спостерігали лише помірне поліпшення діастолічних показників, потік-опосередкованої дилатації, рівня галектину-3 і NT-proBNP. Додавання емпагліфлозину супроводжувалося виразнішим зниженням E/e′, більшим підвищенням швидкостей e′, вірогідним зменшенням індексу об'єму лівого передсердя, виразнішим поліпшенням потік-опосередкованої дилатації, а також із більшим зниженням рівня галектину-3 та NT-proBNP. У змішаних багатофакторних моделях взаємодія «час × лікування» для E/e′ потік-опосередкованої дилатації, галектину-3 і NT-proBNP залишалася статистично значущою. Емпагліфлозин добре переносився, серйозних побічних реакцій не виявлено.

Висновки. Після тиреоїдектомії з приводу раку щитоподібної залози з гіпотиреоїдною кардіоміопатією та збереженою фракцією викиду додавання емпагліфлозину до стандартної терапії асоціювалося з виразнішим поліпшенням діастолічної та ендотеліальної функції, а також із більшим зниженням рівнів галектину-3 і NT-proBNP порівняно зі стандартним лікуванням. Отримані результати підтверджують потенційну кардіопротекторну та васкулопротекторну роль емпагліфлозину при ендокринно зумовлених фенотипах серцевої недостатності зі збереженою фракцією викиду і обґрунтовують доцільність проведення більших рандомізованих досліджень.

Ключові слова: гіпотиреоз, гіпотиреоїдна кардіоміопатія, рак щитоподібної залози, інгібітори SGLT2, серцева недостатність, ендотеліальна функція, галектин-3.

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