Prevalencija i kardiovaskularni ishodi kod dijabetičke kardiomiopatije u egipatskih bolesnika s dijabetesom tipa 2: presječna multicentrična studija u bolničkom okružju

Prevalence and Cardiovascular Outcomes of Diabetic Cardiomyopathy in an Egyptian Type II Diabetic Patient Population: A Cross-sectional Hospital-based Multicenter Study

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SAŽETAK: *Cilj:* Proveli smo multicentričnu studiju kako bismo odredili prevalenciju i kardiovaskularne ishode kod dijabetičke kardiomiopatije (DCM) u bolesnika s dijabetesom tipa 2.

Metode: U istraživanje je bilo uključeno dvjesto ispitanika s dijabetesom tipa 2 (DM). Isključeni su ispitanici s koronarnom bolesti srca (CAD), valvularnom bolesti srca ili anamnestičkim podatcima o zlouporabi droga ili alkohola. Nakon anamnestičkih podataka utvrđeni su indeks tjelesne mase, učestalost pušenja, dislipidemije, DM-a, uporaba lijekova te su provedeni procjena dijagnostičkih kriterija zatajivanja srca (HF) prema Framinghamskoj studiji, klinički pregled, 12-kanalni elektrokardiogram u mirovanju, transtorakalna ehokardiografija te jedna od laboratorijskih varijabli: HbA1c, nasumične ili natašte izmjerene vrijednost glukoze u krvi ili rezultat dvosatnog testa oralne podnošljivosti glukoze.

Rezultati: Prevalencija u usporedbi s odsutnošću DCM-a, dijastolička disfunkcija lijeve klijetke (LV) II. i III. stupnja, sistolička disfunkcija i hipertrofija u istraživanoj skupini iznosile su, redom: 23,0 % prema 77,0 %, 18,5 %, 5,0 % i 8,0 %. U skupini s DCM-om postojala je značajna razlika u učestalosti dijastoličke disfunkcije LV-a II. i III. stupnja, sistoličke disfunkcije i hipertrofiji u usporedi sa skupinom ispitanika bez DCM-a, s apsolutnim povećanjem rizika u skupini s DCM-om za ta stanja od, redom, 80 %, 22 % i 35 %. Pronađena je i signifikantna razlika u prosječnoj vrijednosti ejekcijske frakcije (EF) između skupina s DCM-om i bez DCM-a. Prosječna EF u skupini s DCM-om bila je za 5,5 % niža nego u skupini bez DCM-a. Zastupljenost HF-a i pretkliničke HF u skupini s DCM-om iznosila je 65 % i 35 %. U skupni s DCM-om prosječna je dob kod HF-a bila 4,1 godinu viša nego prosječna dob za pretklinički HF. Pušenje je bilo izrazito i značajno povezano s HF-om u odnosu prema predkliničkom HF-u u skupni s DCM-om.

Zaključci: DCM je bio zastupljen u egipatskih bolesnika s dijabetesom tipa 2 te se može smatrati primarnom miokardijalnom bolešću koja uzrokuje predispoziciju za HF kod dijabetesa tipa 2.

SUMMARY: *Objective:* A multicenter study to evaluate the prevalence and cardiovascular outcomes of diabetic cardiomyopathy in type II diabetic patients.

Patients and Methods: Two hundred participants with type II diabetes mellitus (DM) were included, while participants with coronary artery disease (CAD), valvular heart disease, or history of alcohol or drug abuse were excluded. Participants were subjected to history taking for age, gender, body mass index, smoking, dyslipidemia, medications, DM, Framingham diagnostic criteria of heart failure (HF), comprehensive clinical examination, 12 leads resting electrocardiogram, transthoracic echocardiography and one of the following laboratory investigations: glycated hemoglobin, random blood sugar, fasting blood sugar, or 2-hour 75-gram oral glucose tolerance test.

Results: The prevalence of diabetic cardiomyopathy versus (vs) no diabetic cardiomyopathy, left ventricular (LV) diastolic dysfunction grade II and III, systolic dysfunction, and hypertrophy in the study population was 23.0% vs 77.0%, 18.5%, 5.0%, and 8.0%, respectively. There was a highly significant difference between LV diastolic dysfunction grade II and III, systolic dysfunction, and hypertrophy in the diabetic cardiomyopathy group vs no diabetic cardiomyopathy group, with an absolute risk increase of 80%, 22%, and 35% in the diabetic cardiomyopathy group, respectively. There was a highly significant difference between the mean ejection fraction (EF) in the diabetic cardiomyopathy group vs the no diabetic cardiomyopathy group. The mean EF for the diabetic cardiomyopathy group was 5.5% lower than the mean EF for the no diabetic cardiomyopathy group. The prevalence of HF and pre-clinical HF in the diabetic cardiomyopathy group was 65% and 35%, respectively. The mean age for HF was 4.1 years older than the mean age for pre-clinical HF in the diabetic cardiomyopathy group. Smoking was significantly and strongly associated with HF vs pre-clinical HF in the diabetic cardiomyopathy group.

Conclusions: Diabetic cardiomyopathy was prevalent in an Egyptian type II diabetic patient population and could be considered a primary myocardial disease predisposing to HF in type II DM.

KLJUČNE RIJEČI: diabetes mellitus, dijabetička kardiomiopatija, dijastolička disfunkcija lijeve klijetke, sistolička disfunkcija lijeve klijetke.

KEYWORDS: diabetes mellitius, diabetic cardiomyopathy, left ventricular diastolic dysfunction, left ventricular systolic dysfunction.

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Uvod

Diabetes mellitus (DM) predstavlja značajan uzročnik pobola i smrtnosti u cijelome svijetu.[1] DM tipa 1 obilježava gubitak mase beta-stanica i smanjeno lučenje inzulina u gušterači, uz prosječnu životnu dob kada nastaje bolest od 7 do 15 godina. S druge strane, dijabetes tipa 2 obilježava disfunkcija beta-stanica i inzulinska rezistencija, s prosječnom dobi nastupanja bolesti od 45 do 65 godina.[2] Prema Američkom društvu za dijabetes, razina HbA1c ≥6,5 %, nasumično izmjerena glukoza u krvi (GUK) od 11,1 mmol/L, vrijednosti GUK-a natašte ≥7 mmol/L ili dvosatni test tolerancije na glukozu s oralnom dozom od 75 grama s rezultatom od 11,1 mmol/L dijagnostički su kriteriji za dijagnozu DM-a.[3] U bolesnika s DM-om česte su makrovaskularne komplikacije poput cerebrovaskularne bolesti, koronarne bolesti srca (CAD) i periferne arterijske bolesti te mikrovaskularne komplikacije poput nefropatije, neuropatije i retinopatije. Dijabetičari imaju veći rizik od nastajanja CAD-a i zatajivanja srca (HF) u usporedbi s bolesnicima koji nemaju DM. Finsko populacijsko istraživanje koje su proveli Haffner *i sur.* pokazalo je da bolesnici s dijabetesom tipa 2 imaju veći rizik od infarkta miokarda. Kohortna populacijska studija provedena u Reykjaviku, istraživanja SOLVD i registri utvrdili su da je DM neovisni čimbenik rizika za HF, kao i neovisni prediktor pobola i smrtnosti u HF-u.[4-6] Dijabetička kardiomiopatija (DCM) jest remodeliranje, fibroza i stvrdnjavanje miokarda uzrokovana DM-om u bolesnika koji nemaju prisutne kardiovaskularne čimbenike rizika, kao što su CAD, arterijska hipertenzija i valvularna bolest srca.[7] U 2005. Fang *i sur.* utvrdili su prevalenciju DCM-a od 27 % u kohorti od 120 bolesnika s DM-om tipa 2 bez poznate bolesti srca ili hipertrofije lijeve klijetke (LV).[8] Istraživanja o prevalenciji i kardiovaskularnim ishodima kod DCM-a u bolesnika s DM-om dosad su većinom provođena u Sjevernoj Americi ili Europi. Cilj je ovog istraživanja bio istražiti prevalenciju i kardiovaskularne ishode za DCM u egipatskoj populaciji bolesnika s dijabetesom tipa 2.

Bolesnici i metode

DIZAJN ISTRAŽIVANJA

Proveli smo jednogodišnju, presječnu, multicentričnu studiju u jednoj skupini ispitanika u četirima kardiološkim centrima u četirima tercijarnim bolnicama smještenima u guvernoratima Cairo, Giza i El Fayum u Egiptu. Dizajn istraživanja dobio je odobrenje etičkog odbora, a svi su sudionici potpisali informirani pristanak.

SUDIONICI ISTRAŽIVANJA

U istraživanje smo uključili 200 bolesnika iz četiriju bolnice u jednoj državi tijekom 2018. i 2019. godine. Sudionici su bili bolesnici upućeni na kardiološke odjele Policijske bolnice Agouza, Nacionalnog instituta za srce, Sveučilišne bolnice u Kairu i Sveučilišne bolnice u Fayumu, koje su sve smještene u Egiptu. Nakon uzimanja anamneze i demografskih podataka utvrđeni su indeks tjelesne mase (BMI), učestalost pušenja, dislipidemije, DM, CAD-a i primjene farmakološke terapije, provedeni su procjena dijagnostičkih kriterija zatajivanja srca (HF) prema Framinghamskoj studiji te klinički pregled, 12-kanalni elektrokardiogramu u mirovanju, transtorakalna ehokardiografija (TTE) te jedna od sljedećih laboratorijskih varijabli: razina HbA1c, nasumično izmjereni GUK, vrijednost GUK-a natašte ili rezultat dvosatnog testa oralne podnošljivo-

Introduction

Diabetes mellitus (DM) is a major cause of morbidity and mortality worldwide.[1] Type I DM is characterized by loss of β cell mass and reduced pancreatic insulin secretion with an average age of onset of 7-15 years. Conversely, type II is characterized by β cell dysfunction and peripheral insulin resistance with an average age of onset of 45-65 years.[2] As per the American Diabetes Association, glycated hemoglobin (HbA1c) levels ≥6.5%, random blood sugar levels 11.1 mmol/L, fasting blood sugar levels ≥7 mmol/L, or 2-hour, 75-gram oral glucose tolerance test reading 11.1 mmol/L is diagnostic of DM.[3] Macrovascular complications such as cerebrovascular disease, coronary artery disease (CAD), and peripheral vascular disease, and microvascular complications such as nephropathy, neuropathy, and retinopathy are common in patients with DM. Patients with DM have a higher risk of developing CAD and heart failure (HF) compared with non-diabetic patients. A Finnish population-based study by Haffner *et al.* showed that type II diabetic patients have a significant high risk of myocardial infarction. The Reykjavik population-based cohort study and Studies of Left Ventricular Dysfunction (SOLVD) trials and registry showed DM to be an independent risk factor for HF and an independent predictor of morbidity and mortality in HF, respectively.[4-6] Diabetic cardiomyopathy is DM-induced myocardial remodeling, fibrosis, and stiffness in the absence of cardiovascular risk factors as CAD, hypertension, and valvular heart disease.[7] In 2005, Fang *et al.* demonstrated a 27% prevalence of diabetic cardiomyopathy in a cohort of 120 type II diabetic patients without known cardiac disease or left ventricular (LV) hypertrophy.[8] Studies on the prevalence and cardiovascular outcomes of diabetic cardiomyopathy in patients with DM are mainly North American or European. The aim of this study was to explore the prevalence and cardiovascular outcomes of diabetic cardiomyopathy in an Egyptian type II diabetic patient population.

Patients and Methods

STUDY DESIGN

Single group study conducted at four cardiac centers in four tertiary care hospitals located in Cairo, Giza and El Fayoum governerates in Egypt. The study design was approved by the ethics committee, and all participants signed written informed consents.

STUDY PARTICIPANTS

We recruited 200 patients from four hospitals in one country in 2018 and 2019. Study participants were patients referred to the Cardiology Departments at Agouza Police Hospital, National Heart Institute, Cairo University Hospital, and Fayoum University Hospital, Egypt. They were subjected to history taking and data collection for age, gender, body mass index (BMI), smoking, dyslipidemia, medications, DM, CAD, Framingham diagnostic criteria of HF, comprehensive clinical examination, 12-leads resting electrocardiogram, transthoracic echocardiography (TTE), one of the following laboratory investigations: HbA1c level, random blood sugar level, fasting blood sugar level, or 2-hour, 75-gram oral glucose tolerance test, and one of the following medical imaging investigations: cardiac catheterization and coronary angiography, computerized tomography coronary angiography, thallium stress myocardial

sti glukoze. Bolesnici su također bili podvrgnuti oslikavanju primjenom jedne od sljedećih metoda: kateterizacija srca i koronarna angiografija, MSCT koronarografija, perfuzijska scintigrafija miokarda talijem, dobutaminska stresna ehokardiografija ili MR angiografija srca. Pregledani su bolesnici uključeni u istraživanje ako su imali DM tipa 2. Bolesnici s CAD-om, arterijskom hipertenzijom, prirođenom bolesti srca, cerebrovaskularnim bolestima, valvularnom bolesti srca, ugrađenim elektrostimulatorom ili defibrilatorom, zlouporabom alkohola, amfetamina ili steroida i/ili primanjem kemoterapije ili radioterapije isključeni su iz istraživanja.

POSTUPAK ISTRAŽIVANJA

Dvjesto je bolesnika uključeno u istraživanje i konsekutivno dodano u jednu skupinu. Učinjen je TTE kako bi se otkrila prisutnost DCM-a. U ovom je istraživanju DCM definirana kao prisutnost svih sljedećih kriterija: prisutnost DM-a tipa 2, promjene na srcu u obliku disfunkcije ili hipertrofije LV-a i odsutnost drugih uzročnika kardiomiopatije. Podatci prikupljeni ehokardiografijom uključivali su omjer brzina E i A-vala mitralnog protoka, omjer E/E' uporabom tkivnog doplera, ejekcijska frakcija (EF) prema modificiranoj Simpsonovoj metodi i masa LV-a indeksirana prema tjelesnoj površini (LVMi) s pomoću dvodimenzionalne (2D) ehokardiografije.

Granične vrijednosti za E/A i E/E' bile su 0,75 i 10,0, granična vrijednost za EF bila je 50 % ili granična vrijednost LVMi od 125 g/m^2 za muškarce ili 110 g/m^2 za žene iskorištene su da bi se ispitanike svrstalo u dvije kategorije. Bolesnike s E/A >0,75 i E/E' ≥10, EF <50% ili LVMi od 125 g/m^2 za muškarce ili 110 g/m^2 za žene klasificirali smo kao ispitanike s DCM-om, dok su oni s E/A ≤0,75 i E/E' <10, EF ≥50 % ili LVMi ≤125 g/m^2 za muškarce i ≤110 g/m^2 za žene bili klasificirani kao ispitanici bez DCM-a.

ISHODI

Istraživanje je evaluiralo prevalenciju i kardiovaskularne ishode za DCM u egipatskoj populaciji bolesnika s dijabetesom tipa 2.

STATISTIČKA ANALIZA

Podatci prikupljeni ehokardiografskim pregledom bili su kodirani te zatim analizirani s pomoću programa *Statistical Package for the Social Sciences* (SPSS®) verzije 25. Kvantitativni su podatci izraženi kao prosjek i standardne devijacije, dok su kvalitativne varijable izražene kao srednje vrijednosti i rasponi. Parametrijski distribuirane varijable uspoređivane su neovisnim t-testom, dok su neparametrijski distribuirane varijable uspoređivane Mann-Whitneyjevim testom. Kvalitativne su varijable uspoređivane s pomoću Hi-kvadrat testa ili Fisherova egzaktnog testa.[9,10] Interval pouzdanosti bio je 95 %, a prihvatljiva granica pogreške 5 %. Svaka usporedba smatrana statistički značajnom imala je *P*-vrijednost od *P* <0,05, a vrijednost od *P* <0,01 smatrala se izrazito značajnom. Krajnja analiza podataka obavljena je prema planu ispitivanja.

Rezultati

U istraživanje je uključeno 200 ispitanika. Muški je spol bio dominantan (71 % ispitanika).

DIJABETIČKA KARDIOMIOPATIJA

Među 200 sudionika u istraživanju (57 žena i 143 muškarca; prosječna dob 51 ± 7,02 godina), prevalencija dijastoličke

perfusion imaging, dobutamine stress echocardiography, or cardiac magnetic resonance angiography. Screened participants were enrolled if they had type II DM. Screened participants with CAD, hypertension, congenital heart disease, cerebrovascular disease, valvular heart disease, pacemaker or defibrillator implantation, alcohol, amphetamine or anabolic steroids drug abuse, and/or cancer chemotherapy or radiotherapy were excluded from the study.

STUDY PROCEDURES

Two hundred participants were enrolled, consecutively assigned to a single group, and underwent TTE to detect diabetic cardiomyopathy. In our study, we defined diabetic cardiomyopathy by all of the following criteria: presence of type II diabetes mellitus, myocardial abnormalities in the form of LV dysfunction or hypertrophy, and absence of other causes of cardiomyopathy. Data documented with TTE included ratio of early diastolic mitral inflow velocity (E wave) to late diastolic mitral inflow velocity (A wave) (E/A) by transmitral flow, ratio of E wave to early diastolic mitral annulus velocity (E' wave) (E/E') by tissue Doppler imaging, ejection fraction (EF) by modified Simpson's method, and LV mass indexed to body surface area (LVMi) by 2-dimensional (2D) echocardiography.

E/A and E/E' cut-off values of 0.75 and 10.0, EF cut-off value of 50%, or LVMi cut-off value of 125 g/m^2 for men or 110 g/m^2 for women were used to categorize participants into 2 categories. Participants with E/A >0.75 and E/E' ≥10, EF <50%, or LVMi >125 g/m^2 for men or >110 g/m^2 for women were classified as diabetic cardiomyopathy participants, while participants with E/A ≤0.75 and E/E' <10, EF ≥50%, or LVMi ≤125 g/m^2 for men or ≤110 g/m^2 for women were classified as no diabetic cardiomyopathy participants.

END POINTS

The study evaluated the prevalence and cardiovascular outcomes of diabetic cardiomyopathy in an Egyptian type II diabetic patient population.

STATISTICAL ANALYSIS

The echocardiographic assessment data were coded, and the data were analysed with the Statistical Package for the Social Sciences software (SPSS®) version 25. Quantitative data was expressed as means and standard deviations, while qualitative data was expressed as medians and ranges. Parametrically and non-parametrically distributed quantitative variables were compared with the Independent t-test and Mann-Whitney test, respectively. Qualitative variables were compared with the Chi-square test or Fisher exact test.[9,10] The confidence interval and accepted margin of error were set to 95% and 5%, respectively. Any comparison considered statistically significant was at *P*<0.05 or less, while *P*<0.01 was considered highly significant. Final data analysis was as per protocol analysis.

Results

We recruited 200 patients in the study. There was male gender predominance in the study (71% were men).

DIABETIC CARDIOMYOPATHY

Among the 200 participants studied (57 women and 143 men; mean age was 51 ± 7.02 years), the prevalence of LV diastolic

disfunkcije LV-a II. ili III. stupnja (E/A >0,75 i E/E' ≥10) bila je 18,5 %, zastupljenost sistoličke disfunkcije LV-a (EF <50 %) bila je 5,0 %, a zastupljenost hipertrofije LV-a (LVMi >125 g/m^2 za muškarce ili >110 g/m^2 za žene) bila je 8,0 %, dok je učestalost za skupinu s DCM-om i skupinu bez DCM-a bila 23 % i 77 % (**slika 1**). Prosječna dob u skupini s DCM-om bila je 7,8 godina viša od prosječne dobi u skupini bez DCM-a (*P* = 0,008), a prosječni BMI za skupinu s DCM-om bio je 1,6 kg/m^2 viši nego u skupini bez DCM-a (*P* = 0,010). Postojale su značajne razlike među dvjema grupama glede prisutnosti dislipidemije $X^2(1)$ = 5,860, *P* = 0,015, *V* = 0,171), trajanja DM-a (t(198) = −3,440, *P* = 0,0007), i vrijednosti HbA1c (t(198) = −9,415, *P* = <0,0001) (**tablica 1**). Pronađena je i izrazito značajna statistička razlika između prosječne EF u skupini s DCM-om u usporedbi sa skupinom bez DCM-a (t(198) = −4,963, *P* = <0,0001). Prosječna EF u skupini s DCM-om bila je za 5,5% niža nego u skupini bez DCM-a. Pronađena je i izrazito statistički značajna povezanost između DCM-a i II. i III. stupnja dijastoličke disfunkcije LK ($X^2(1)$ = 151,987, *P* = <0,0001, *V* = 0,872), izrazito značajna povezanost između DCM-a i sistoličke disfunkcije LV-a ($X^2(1)$ =

dysfunction grade II or III (E/A >0.75 and E/E' ≥10), LV systolic dysfunction (EF <50%), and LV hypertrophy (LVMi >125 g/m^2 for men or >110 g/m^2 for women) in the study population was 18.5%, 5.0%, and 8.0%, and the percentages of the diabetic cardiomyopathy vs no diabetic cardiomyopathy participants were 23% vs 77%, respectively (**Figure 1**). The mean age for the diabetic cardiomyopathy group was 7.8 years older than the average age for the no diabetic cardiomyopathy group (*P* = 0.008), and the mean BMI for the diabetic cardiomyopathy group was 1.6 kg/m^2 higher than the mean BMI for the no diabetic cardiomyopathy group (*P* = 0.010), respectively. Dyslipidemia ($X^2(1)$ = 5.860, *P* = 0.015, *V* = 0.171), duration of DM (t(198) = -3.440, *P* = 0.0007), and HbA1c (t(198) = -9.415, *P* = <0.0001) were significantly different between both groups (**Table 1**). There was a highly significant statistical difference between the mean EF in the diabetic cardiomyopathy group vs no diabetic cardiomyopathy group (t(198) = -4.963, *P* = <0.0001). The mean EF for the diabetic cardiomyopathy group was 5.5% lower than the mean EF for the no diabetic cardiomyopathy group. There was a highly significant strong association between diabetic

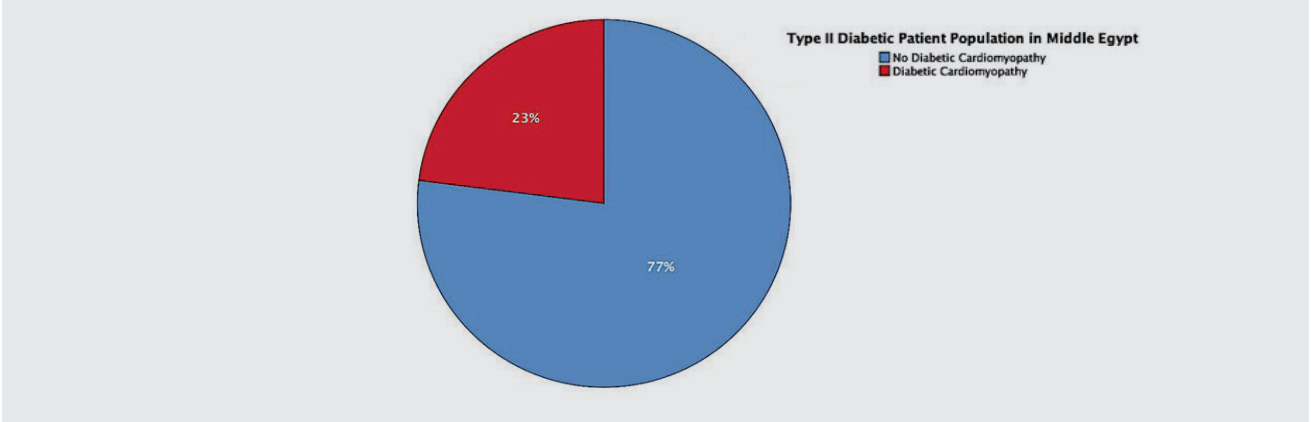

FIGURE 1. Prevalence of diabetic cardiomyopathy.

TABLE 1. Comparison between diabetic cardiomyopathy and no diabetic cardiomyopathy groups in an Egyptian type II diabetic patient population regarding the risk factors.

		No diabetic cardiomyopathy	Diabetic cardiomyopathy	Independent t-test	P value
		No: 154	No: 46		
Duration of Diabetes Mellitus	Mean ± SD	8.14 ± 3.93 years	10.52 ± 4.70 years	-3.440	0.0007
	Range	1 – 16 years	3 – 21 years		
HbA1c	Mean ± SD	7.57% ± 1.01%	9.32% ± 1.37%	-9.415	<0.0001
	Range	6% – 10.5%	7% – 11.6%		
		No Diabetic cardiomyopathy	Diabetic cardiomyopathy	Chi-square test	P value
		No: 154	No: 46		
Dyslipidemia	No	102 (66.0%)	39 (85.0%)	5.860	0.015
	Yes	52 (34.0%)	7 (15.0%)		
Smoking	No	65 (42.0%)	17 (37.0%)	0.404	0.525
	Yes	89 (58.0%)	29 (63.0%)		

35,240, *P* = <0,0001, *V* = 0,420) te izrazito značajna povezanost između DCM-a i hipertrofije LV-a (X^2(1) = 58,223, *P* = <0,0001, *V* = 0,540), s povećanjem apsolutnog rizika u skupni s DCM od 80 %, 22 % i 35 % (**slika 2**).

cardiomyopathy and LV diastolic dysfunction grade II and III (X^2(1) = 151.987, *P* = <0.0001, *V* = 0.872), a highly significant moderate association between diabetic cardiomyopathy and LV systolic dysfunction (X^2(1) = 35.240, *P* = <0.0001, *V* = 0.420), and a highly significant strong association between diabetic cardiomyopathy and LV hypertrophy (X^2(1) = 58.223, *P* = <0.0001, *V* = 0.540), with an absolute risk increase of 80%, 22%, and 35% in the diabetic cardiomyopathy group, respectively (**Figure 2**).

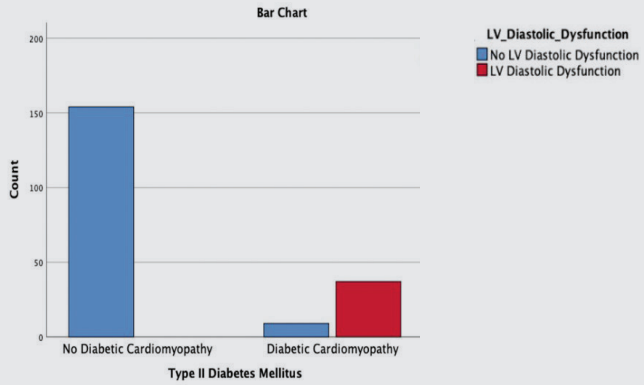

FIGURE 2. Comparison between diabetic cardiomyopathy and no diabetic cardiomyopathy groups regarding the rates of left ventricular diastolic dysfunction grade II and III.

ZATAJIVANJE SRCA

Prevalencija HF-a (gdje su nalazi ehokardiografije odgovarali dijagnostičkim DCM, a klinički su nalazi odgovarali Framinghamovim dijagnostičkim kriterijima HF-a) i pretkliničkog HF-a (nalazi ehokardiografije odgovarali su dijagnostičkim kriterijima DCM-a, ali klinički nalazi nisu odgovarali Framinghamovim dijagnostičkim kriterijima HF-a) bila je 65 % u skupini s DCM-om i 35 % u skupini bez DCM-a. Postojala je izrazito značajna povezanost između DCM-a i HF-a (X^2 (1) = 118,159, *P* = <0,0001, *V* = 0,769) (**slika 3**). Prosječna dob za HF bila je 4,1 godinu viša nego prosječna dob za pretkliničko HF u skupini s DCM-om (58,1 prema 54 godine za pretkliničko HF)

HEART FAILURE

The prevalence of HF (where the echocardiographic findings met the diagnostic criteria of diabetic cardiomyopathy and the clinical findings met the Framingham diagnostic criteria of heart failure) and pre-clinical HF (where the echocardiographic findings met the diagnostic criteria of diabetic cardiomyopathy but the clinical findings did not meet the Framingham diagnostic criteria of heart failure) in the diabetic cardiomyopathy group was 65% and 35%, respectively. There was a highly significant strong association between diabetic cardiomyopathy and HF (X^2 (1) = 118.159, *P* = <0.0001, *V* = 0.769) (**Figure 3**). The mean age for HF was 4.1 years older

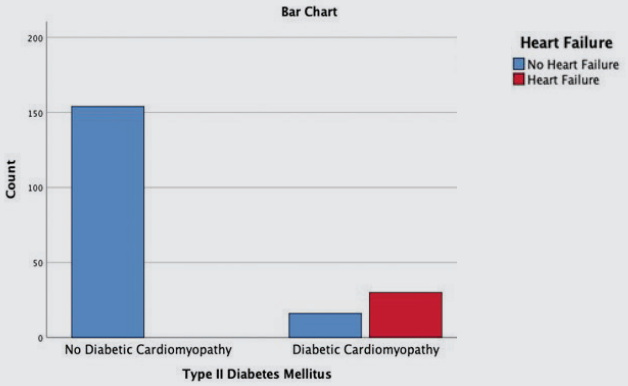

FIGURE 3. Comparison between diabetic cardiomyopathy and no diabetic cardiomyopathy groups regarding the rates of heart failure.

(*P* = 0,033). Pušenje je bio značajno i snažno povezano s HF-om u skupini s DCM-om (X^2 (1) = 41,851, *P* = <0,0001, *V* = 0,954) (**slika 4**). Pušači u skupini s DCM-om imali su 20 % veći rizik od HF-a (relativni rizik = 1,17, 95% interval pouzdanosti (95% CI): 0,7352 do 1,8696). S druge strane, postojala i povezanost između dislipidemije i HF-a u skupini s DCM-om koja nije bila statistički značajna (X^2 (1) = 4,403, *P* = 0,078, *V* = 0,309).

than the mean age for pre-clinical HF in the diabetic cardiomyopathy group (58.1 vs 54 years for the preclinical HF) (*P* = 0.033). Smoking was significantly and strongly associated with HF in the diabetic cardiomyopathy group (X^2 (1) = 41.851, *P* = <0.0001, *V* = 0.954) **(Figure 4)**. Smokers in the diabetic cardiomyopathy group had 20% increased risk for HF (RR= 1.17, 95 CI: 0.7352 to 1.8696). In contrast, there was a non-significant association between dyslipidemia and HF in the diabetic cardiomyopathy group (X^2 (1) = 4.403, *P* = 0.078, *V* = 0.309).

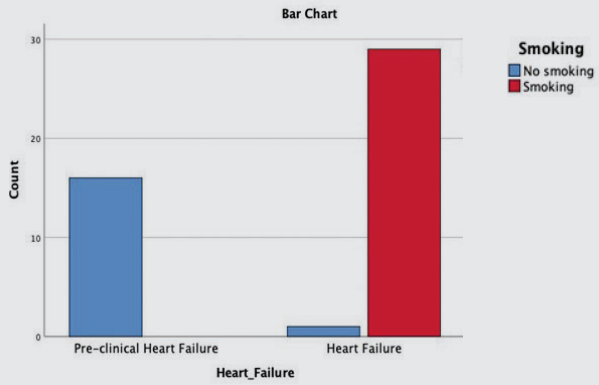

FIGURE 4. Comparison between heart failure and pre-clinical heart failure in the diabetic cardiomyopathy groups regarding the rates of smoking.

Rasprava

Strukturne promjene u miokardu smatraju se najvjerojatnijim mehanizmom razvoja disfunkcije LV-a u bolesnika s DCM-om. Istraživanja parova koje su proveli Bertoni *i sur.* pronašla je značajnu povezanost između DM-a i DCM-a (OR = 1,58, 95 % CI: 1,55 – 1,62), nakon prilagodbe za arterijsku hipertenziju, spol, rasu i srednju vrijednost dohotka.[11] Retrospektivna kohortna studija objavljena 2010. godine pokazala je značajnu povezanost dijastoličke disfunkcije LV-a s naknadnim HF-om u dijabetičara nakon prilagodbe za dob, spol, BMI, arterijsku hipertenziju, CAD, EF, volumen lijeve pretklijetke, vrijeme deceleracije, LVMi i relativnu debljinu stijenke.[12] Dandamudi *i sur.* proveli su presječnu studiju koja je istraživala rizik od razvijanja disfunkcije LV-a u bolesnika s DCM-om. Pronašli su značajnu zastupljenost DCM-a od 16,9 % u dijabetičkih pacijenata u okrugu Olmsted. Zastupljenost dijastoličke disfunkcije LV-a u bolesnika s DCM-om bila je 54,4 %, dok je zastupljenost sistoličke disfunkcije LV-a u tih ispitanika bila 7,3 %. Dijabetička je kardiomiopatija gotovo podvostručila rizik od disfunkcije LV-a, dijastoličke disfunkcije LV-a i sistoličke disfunkcije LV-a nakon prilagodbe za dob i spol.[13] Rezultati ove presječne studije u skladu su s rezultatima koje su predočili Dandamudi *i sur.* te smo pokazali visoku zastupljenost DCM-a u egipatskoj populaciji dijabetičara tipa 2. Također smo pokazali i značajnu snažnu povezanost između DCM-a i II. i III. stupnja dijastoličke disfunkcije LV te hipertrofije LV, značajnu povezanost između DCM i sistoličke disfunkcije LV-a, visoku zastupljenost HF-a u bolesnika s DCM-om te značajnu snažnu povezanost između pušenja i HF-a u bolesnika s DCM-om.

Discussion

Structural alterations of the myocardium have been suggested as probable mechanisms for LV dysfunction in patients with diabetic cardiomyopathy. A nationwide case-control study by Bertoni *et al.* demonstrated a significant association between DM and diabetic cardiomyopathy (OR = 1.58, 95% CI: 1.55-1.62), after adjustment for hypertension, gender, race, and median income.[11] A retrospective cohort study published in 2010 demonstrated a significant association of LV diastolic dysfunction with subsequent HF in diabetic patients after adjustment for age, gender, BMI, hypertension, CAD, EF, left atrial volume, deceleration time, LVMi and relative wall thickness.[12] Dandamudi *et al.* cross-sectional study investigated the risk of developing LV dysfunction in patients with diabetic cardiomyopathy. They found a significant 16.9% prevalence of diabetic cardiomyopathy in the Olmsted County community diabetic patient population. The prevalence of LV diastolic and systolic dysfunction in patients with diabetic cardiomyopathy was 54.4% and 7.3%, respectively. Diabetic cardiomyopathy nearly doubled the risk of LV dysfunction, diastolic dysfunction, and systolic dysfunction after adjustment for age and gender.[13] Our cross-sectional study results were consistent with the results of the Dandamudi *et al.*, and we demonstrated high prevalence of diabetic cardiomyopathy in an Egyptian type II diabetic patient population. In addition, we demonstrated significantly strong associations between diabetic cardiomyopathy and LV diastolic dysfunction grade II and III and LV hypertrophy, significant association between diabetic cardiomyopathy and LV systolic dysfunction, high

U ovoj studiji nisu nedostajali nikakvi podatci, što je omogućilo dobru analizu prema planu ispitivanja; istraživači koji su analizirali i navodili rezultate procjene na temelju TTE-a nisu bili upoznati s laboratorijskim rezultatima. Koliko nam je poznato, ehokardiografska obilježja DCM-a nisu dosad istraživana u egipatskoj populaciji dijabetičara tipa 2.

Ovo je istraživanje imalo neka ograničenja koja treba navesti. Proveli smo multicentričnu studiju s malenim uzorkom. S obzirom na to da je bila riječ o presječnoj studiji, nismo mogli istražiti kronološki odnos između ishoda procjene primjenom TTE-a i vremenskoga slijeda HF-a u bolesnika s DCM-om. Novije tehnike, kao što je metoda stope deformacije, *speckle tracking* oslikavanje i 3D ehokardiografija omogućuju točniju procjenu debljine i funkcije stijenke LV-a u usporedbi s transmitralnim protokom, tkivnim doplerom, modificiranom Simpsonovom metodom i 2D ehokardiografijom.

Zaključci

Dijabetička je kardiomiopatija bila zastupljena u egipatskoj populaciji pacijenata s dijabetesom tipa 2, značajno i snažno povezana s II. i III. stupnjem dijastoličke disfunkcije LV-a i hipertrofijom LV-a te značajno povezana sa sistoličkom disfunkcijom LV-a, a može se smatrati primarnom bolesti miokarda koja uzrokuje predispoziciju za HF. Bolesnici s DCM-om koji su pušači time rizik od nastupa HF-a povećavaju za 20%, što je rezultat koji potiče na daljnje istraživanje o toj temi.

prevalence of HF in the diabetic cardiomyopathy patients, and a significantly strong association between smoking and HF in patients with diabetic cardiomyopathy.

Our study did not have missing data, allowing robust per protocol analysis; the investigators who analysed and reported the TTE assessment outcomes were blinded to the laboratory results; and, to the best of our knowledge, the echocardiographic features of diabetic cardiomyopathy in the Egyptian type II diabetic patients had not been previously studied.

The study has some limitations that need to be acknowledged. It was a multicentered study with a small sample size. Being a cross-sectional study, did not allow us to investigate the chronological relationship between the TTE assessment outcomes and the HF timeline in patients with diabetic cardiomyopathy. Newer techniques such as the strain rate method, speckle tracking image, and 3D echocardiography are more accurate for evaluation of the LV wall function and thickness compared to transmitral flow, tissue Doppler imaging, modified Simpson's method, and 2D echocardiography.

Conclusions

Diabetic cardiomyopathy was prevalent in an Egyptian type II diabetic patient population, significantly and strongly associated with LV diastolic dysfunction grade II and III and LV hypertrophy, significantly associated with LV systolic dysfunction, and could be considered a primary myocardial disease predisposing to HF. Patients with diabetic cardiomyopathy who smoke increase their risk of developing HF by 20%, an observation which warrants further research.

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Disclosures
The authors have no conflicts to disclose.

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