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

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 ispitanih s dijabetesom tipa 2 (DM). Isključeni su ispitanci s koronarnom bolesti srca (CAD), valvularnom bolesti srca ili anamnestičkim podacima o zloupotrebi 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 Framinghamovoj studiji, klinički pregled, 12-kanalni elektrokardiogram u mirovanju, transtorakalna ekoangiografija te jedna od laboratorijskih varijabli: HbA1Cs, nusumične ili natašte izmjere vrijednosti glukoze u krvi ili rezultat dvosatnog testa oralne podnožljivosti glukoze.

Rezultati: Prevalencija u usporedbi s odsutnošću DCM-a, dijastolička disfunkcija lijeve klijetke (LV), sistolička disfunkcija i hipertrofija u istraživanoj skupini iznosile su, redom: 23,0 % prema 77,0 %, 18,5 % i 8,0 %. U skupini s DCM-om postojala je značajna razlika u učestalosti dijastoličke disfunkcije i hipertrofije u usporedi sa skupinom ispitanih bez DCM-a, s apsolutnim povećanjem rizika u skupini s DCM-om za stanja od, redom, 80, %, 22, % i 35, %. Pronađena je i signifikantna razlika u prosječnoj vrijednosti ejeckih frakcija (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 prekliničke HF-a u skupini s DCM-om iznosila je 65 % i 35 %. U skupini s DCM-om prosječna dob kod HF-a bila je 41 godinu viša nego prosječna dob za preklinički HF. Pušenje je bilo izrazito i značajno povezano s HF-u u odnosu prema predkliničkom HF-u u skupini s DCM-a.

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, transtoracic 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 85%, 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 41 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.

KLIJUĆNE RIJEČI: diabetes mellitus, dijabetesi, kardiomiopatija, dijastolička disfunkcija, sistolička disfunkcija, dijabetesi.

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

CITATION: Cardiol Croat. 2021;16(7-8):239-45. | https://doi.org/10.15836/ccar2021.239

TO CITE THIS ARTICLE: Ebeid HM, Elkhashab KA, Hussain ZA, Mohammad MSS. Prevalence and Cardiovascular Outcomes of Diabetic Cardiomyopathy in an Egyptian Type II Diabetic Patient Population: A Cross-sectional Hospital-based Multicenter Study. Cardiol Croat. 2021;16(7-8):239-45. | https://doi.org/10.15836/ccar2021.239

TO LINK TO THIS ARTICLE: https://doi.org/10.15836/ccar2021.239
Prevalence and Cardiovascular Outcomes of Diabetic Cardiomyopathy in an Egyptian Type II Diabetic Patient Population: A Cross-sectional Hospital-based Multicenter Study

**Uvod**

Diabetes mellitus (DM) predstavlja značajan uzročnik pobola i smrtnosti u cijelom svijetu. DM tipa 1 obilježava gubitak mase beta-stanica i smanjeno učinkovanje inzulina u gušterači, uz prosječnu životnu doba kada nastaje bolest od 7 do 15 godina. S druge strane, dijabetes tipa 2 obilježava disfunkcija beta-stanica i inzulinomske rezistencije, s prosječnim dobi nastupanja bolesti od 45 do 65 godina. Prema Američkom društvu za dijabetes, razina HbA1c ≥6.5 %, nasumično izmjerenja glukoze u krvi (GUK) od 11,1 mmol/L, vrijednosti GUK-a natašte ≥7 mmol/L ili dvostatne test tolerance na gluksu u oralom dozom od 75 grama s rezultatom od 11,1 mmol/L dijagnostički su kriteriji za dijagnozu DM-a. 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. Dijabetsičari imaju veći rizik od nastajanja CAD-a i zatavanja 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 utvrdi­rizik 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. Dijabetička kardiom­opatija (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 važvalarna bolest srca. U 2006. 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). 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 jednodijagnošću, prosječnu, multicentričnu studiju u jednoj skupini ispitanika u četirima kardioškim centrima u četirima terciarnim bolnicama smeštenima u guvernerata Cairo, Giza i El Fayyum u Egyptu. Dizajn istraživanja dobio je odobrećen etičkog odbora, a svi su sudionici potpisali informatan pristanak.

**SUDIONICI Istraživanja**

U istraživanje smo uključili 200 bolesnika iz četiri 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 Cairo i Sveučilišne bolnice u Fayoumu, koje su sve smeštena u Egyptu. 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 zatavanja srca (HF) prema Framinghamskoj studiji te klinički pregled, 12-kanalni elektrokardiogram u mirovanju, transtorakalna echokardiografija (TTE) te jedna od sljedećih laboratorijskih varijabli: razina HbA1c, nasumično izmjereni GUK, vrijednost GUK-a natašte ili rezultat dvosatnog testa oralne podnošljivo-
Analiza podataka obavljena je prema planu ispitivanja.

Istraživanje je evaluiralo prevalenciju i kardiovaskularne ishemične dijabetes miokardne u EBDM.

Podatci prikupljeni echokardiografskom pregledom uključivali su omjer brzina E i A va-

vrijednost od E/A ≤0,75 i E/E′ <10, EF ≥50%, ili LVMi ≤125 g/m2 za muškarce ili 110 g/m2

sve bolesnike uključene u istraživanje, a statistički značajna je bila P-vrijednost od

P<0,01 smatrala se izrazito značajnom. Krajnja

Krajnja

interval pouzdanosti bio je 95%

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 hypertension, 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/m² for men or 110 g/m² 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/m² for men or >110 g/m² 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/m² for men or ≤110 g/m² 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. 

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

...disfunction grade II or III (E/A >0.75 and E/E′ ≥10), LV systolic dysfunction (EF <50%), and LV hypertrophy (LVMi >125 g/m² for men or >110 g/m² 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/m² higher than the mean BMI for the no diabetic cardiomyopathy group (P = 0.010). Dyslipidemia (Χ²(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 strong association between diabetic...
ZATAJIVANJE SRCA
Prevalence of HF-a (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 ($\chi^2(1) = 118.159, P < 0.0001, V = 0.769$) (Figure 3). The mean age for HF was 4.1 years older than the mean age for pre-clinical HF in the diabetic cardiomyopathy group (58.1 years for HF and 54 years for pre-clinical 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 ($\chi^2(1) = 118.159, P < 0.0001, V = 0.769$) (Figure 3). The mean age for HF was 4.1 years older than the mean age for pre-clinical HF in the diabetic cardiomyopathy group (58.1 years for HF and 54 years for pre-clinical HF).
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 \( (X^2 (1) = 41.85, P = <0.0001, V = 0.954) \) (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 \( (X^2 (1) = 4.4, P = 0.078, V = 0.309) \).

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.\(^1\)\(^1\) 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.\(^1\)^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.\(^1\)^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 podaci, što je omogućilo dobru analizu prema planu ispitivanja; istraživači koji su analizirali i navodili rezultate procjene na temelju TTE-a nisu bili upoznati s laboratorijским rezultatima. Koliko nam je poznato, ehokardiografska obilježja DCM-a nisu dosad istraživana u egipatskoj populaciji dijabetesa tipa 2.

Ovo je istraživanje imalo neka ograničenja koja treba navedi. Proveli smo multicentričnu studiju s mašenim uzorkom. Odbrijali smo dobro analizu prema planu ispitivanja; istraživači koji su analizirali i navodili rezultate procjene na temelju 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 ehokardiografia omogućuju točniju procjenu debljine i funkcije stijenke LV-a u usporedbi s transmuralnim protokom, tkivnim doplerom, modificiranom Simpsonovom metodom i 2D ehokardiografijom.

Zaključci

Dijabetes je kardiomiopatija bila zastupljena u egipatskoj populaciji pacijenata s diabetom tipa 2, značajno i snažno povezana s II. i III. stupnjem dijastolike disfunkcije LV-a i hipertrofijom LV-a te značajno povezana sa sindromom dihne i funkcije stijenke LV-a, a može se smatrati primarnom bolesti miokorda 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.