Relationship Between Left Atrial Strain and Malnutrition Scores in Diabetic Patients

Flora Özkalaycı[1], Ali Karagöz[2], Işıl Kutlutürk Karagöz[3], Süleyman Çağan Efe[2], Erdem Türkyılmaz[2], İbrahim Halil Tanboğa[4], Cihangir Kaymaz[2]

[1] Department of Cardiology, Hisar Intercontinental Hospital, Istanbul, Turkey
[2] Department of Cardiology, Kartal Kosuyolu High Specialization Training and Research Hospital, Istanbul, Turkey
[3] Department of Ophtalmology, Umraniye Training and Research Hospital, Istanbul, Turkey
[4] Department of Cardiology, Faculty of Medicine, University of Nisantasi, Istanbul, Turkey

ABSTRACT

Introduction: Malnutrition is a serious public health problem that is associated with adverse outcomes in a broad range of disease including cardiovascular disease and diabetes mellitus. Malnutrition is demonstrated to be accompanying to several disease, yet there is a lack of evidence on the impact of malnutrition on cardiac functions in patients with diabetic patients with diabetic retinopathy. Herewith our primary goal was to evaluate the relation between any degree malnutrition with left atrial strain in relevant patient group.

Patients and Methods: Patients with diabetes mellitus with retinopathy, who were referred to the outpatient cardiology clinic were assessed. Those who had sinus rhythm, had no findings of significant valvular heart disease or coronary artery disease underwent to 2-dimensional speckle tracking echocardiography and assessed for malnutrition in their prior examinations were included to the study. Hundred and seventy patients met the inclusion criteria. Malnutrition scores such as Controlling Nutritional Status score (CONUT), nutritional risk index (NRI) and The Prognostic Nutritional Index score (PNI) index were used to evaluate nutrition condition of the patients.

Results: Thirty percent of all diabetic patients were demonstrated to have malnutrition according to the CONUT score. Left atrial conduit strain was demonstrated to decrease [ß: -7.5 (CI 95%, -10.7, -4.3 p< 0.001)], Left atrial reservoir strain was demonstrated to increase [ß: 2.48 (CI 95%,0.83-4.13 p< 0.03)] and Left atrial contractile strain was demonstrated to decrease [ß: -4.21 (CI 95%, -2.21, -6.01 p< 0.001)] in the presence of any degree malnutrition.

Conclusion: In this study we have demonstrated that malnutrition is an important entity in patients with diabetes mellitus and has a significant impact on left atrial strain.

Key Words: CONUT score; diabetes mellitus; left atrial strain.

Diyabetik Hastalarda Sol Atriyal Strain ile Malnütrisyon Skorlarının İlişkisi

ÖZ

Giriş: Malnütrisyon, kardiyovasküler hastalık ve diabetes mellitus dahil olmak üzere birçok hastalıkta olumsuz sonlanımlarla ilişkili ciddi bir halk sağlığı sorunudur. Malnütrisyonun çeşitli hastalıklara eşlik ettiği önceki çalışmalarda gösterilmiştir. Öte yandan malnütrisyonun, diyabetik retinopatinin eşlik ettiği diyabetik hastaların kalp fonksiyonlarına etkisi konusunda yeterli kanıt bulunmamaktadır. Çalışmamızda bu hasta grubunda malnütrisyon varlığı ile kardiyak fonksiyonlar arasındaki ilişkinin sol atriyal strain analizi ile değerlendirilmesi amaçlanmıştır.

Hastalar ve Yöntem: Tarafımıza sevk edilen diyabetik retinopati tanısı almış diyabetik hastaların verileri geriye dönük incelendi. Sinüs ritmi olan, ciddi kapak hastalığı ve koroner arter hastalığı bulgusu olmayan, konvansiyonel ekokardiyografiyle birlikte strain analizi yapılmış ve önceki muayenelerinde malnütrisyon açısından değerlendirilmiş olan hastalar çalışmaya alındı. Yüz yetmiş hasta dahil edilme kriterlerini karşıladı. Hastaların beslenme durumlarını değerlendirmek için CONUT skoru, NRI ve PNI gibi malnütrisyon skorları kullanıldı.

Bulgular: CONUT skoruna göre, tüm diyabetik hastaların %30'unun malnütrisyona sahip olduğu gösterilmiştir. Sol atriyal kondüit strain değerinin malnütrisyon ile azaldığı gösterilmiştir [ß: -7.5 (CI %95, -10.7, -4.3 p< 0.001)], sol atriyal rezervuar strain değerinin malnütrisyon ile arttığı gösterilmiştir [ß: 2.48 (CI %95 0.83-4.13 p< 0.03)] ve sol atriyal kontraktil strain değerinin malnütrisyon ile azaldığı gösterilmiştir [ß: -4.21 (CI %95, -2.21, -6.01 p< 0.001)].

Sonuç: Bu çalışmada, malnütrisyonun diyabetik hastalarda sol atriyal strain üzerine etkisi gösterilmiştir.

Anahtar Kelimeler: COUNT skoru; diabetes mellitus; sol atriyal strain.

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Correspondence

Flora Özkalaycı

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INTRODUCTION

Diabetes mellitus (DM) is a growing health problem all around the world, the global DM prevalence in 2019 is 463 million, rising to 578 million by 2030[1]. Diabetes mellitus is associated with both microvascular and macrovascular complications, resulting in end-organ damage. Microvascular and macrovascular complications are associated with poor diagnosis and indicative for a longer period to hyperglycaemia and impaired glycaemic control[2]. Cardiovascular disease is counted in macrovascular complications while diabetic retinopathy is counted in microvascular complications. Those patients already diagnosed with microvascular complications of DM are candidates for macrovascular complications as well[3,4]. Cardiovascular disease (CVD) is demonstrated to be the leading cause of morbidity and mortality in patients with DM[5]. Several mechanisms are identified to explain the pathophysiology of cardiovascular disease progression in patients with DM. Hypertension (HT), obesity, dyslipidaemia is seen both in DM and CVD. These risk factors are also associated with CVD, regardless of DM presence[6]. Diabetes mellitus may directly or indirectly effect cardiac functions. For example, DM may lead to diabetic cardiomyopathy without any evidence of coronary atherosclerosis or may accelerate coronary artery disease and may result with ischemic heart disease. Therefore, via direct or indirect pathways diabetic patients are at increased risk of cardiovascular adverse events. Similar risk factors for CVD are seen frequently in diabetic patients[5,7,8].

Malnutrition is demonstrated to be accompanying to DM in several studies. There is still lack of evidence on the impact of malnutrition on cardiac functions in patients with DM of whom are already diagnosed with a microvascular complication. Malnutrition is known to be a serious public health problem that is associated with worse outcomes in a broad range of disease including DM[9].

Although evaluation of left atrial (LA) function is not applied to most of our clinical practice, this technique is getting more and more important regarding its's prognostic implications. In several studies LA size and function were demonstrated to be associated with increased cardiovascular risk and worse prognosis[10-15].

Herewith we aimed to evaluate the influence of any degree malnutrition on cardiac functions by comparing patients' atrial functions assessed by LA strain analysis.

PATIENTS and METHODS

This is a single centre retrospective observational study conducted by ophthalmology and cardiology departments. Diabetic patients who were investigated for malnutrition and referred to ophthalmology and cardiology policlinics between 2012-2016 were investigated. Among these patients, those who were diagnosed with DR were enrolled to the study. Patients' medical history, ECG, non-invasive/invasive test results, physical examination findings, blood test results were obtained from the electronical health records of the hospital.

Those who had sinus rhythm, had no evidence of coronary artery disease (established by non-invasive and/or invasive techniques) and underwent 2-dimensional speckle tracking echocardiography were enrolled to the study. Patients with known coronary artery disease, or those in whom ischemia was demonstrated by non-invasive methods were excluded from the study. Additionally, patients with moderate and severe mitral valve regurgitation and mitral stenosis were also excluded. Those patients without LA strain analysis were excluded. Hundred and seventy patients met the inclusion criteria and were enrolled to the study. Echocardiography reports were obtained from the medical records of each patient. Results of LA strain analysis, 2D and doppler echocardiography were obtained from the electronic data base of the hospital. GE Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5-MHz transducer was utilised for echocardiographic evaluation of the patients. Doppler echocardiography was performed. Chamber diameters, wall thickness, LA volume, left ventricular ejection fraction, were assessed according to the recommendations of EACVI[16]. Apical four and two chamber views were obtained using conventional 2D gray-scale echocardiography in terms of analysing LA strain. The frame rate was adjusted between 60 and 80 frames/s and patients were told to hold their breaths while recording the images. Three consecutive cardiac cycles were recorded and averaged. The data were analysed using EchoPAC (GE Vingmed Ultrasound AS). We defined the endocardial border manually. The tracing procedure was done automatically by the software[16-19]. A strain image is demonstrated in Figure 1.

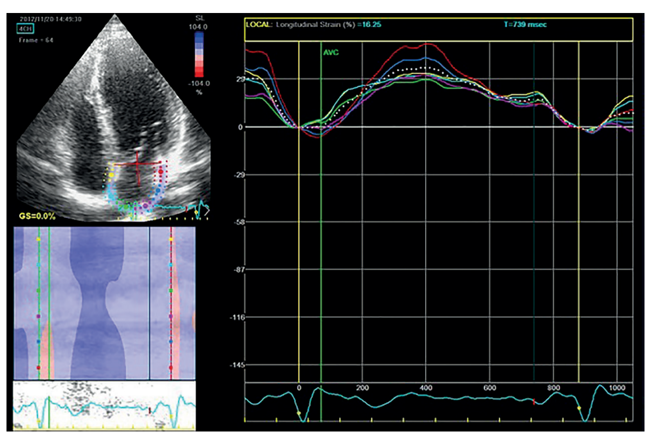

Figure 1. An example of strain image.

Malnutrition was evaluated by using three indices: Controlling Nutritional Status score (CONUT), nutritional risk index (NRI) and The Prognostic Nutritional Index score (PNI) index[20-22]. The CONUT score was calculated by using albumin (g/dL), total cholesterol (mmol/L), total lymphocyte count. A score of 0 to 1 is accepted normal; scores of 2 to 4 indicate mild, 5 to 8 indicate moderate and 9 to 12 indicate severe malnutrition. We defined those patients who have a CONUT score of ≥ 2 as patients with "any-degree malnutrition". The NRI was calculated by the following formula 1,489 x serum albumin (g/L) +41.7 [current body weight (kg)/usual body weight (kg)]. Severe nutritional risk was identified as NRI < 83.5, moderate risk was identified as 83.5 ≤ NRI < 97.5, mild risk was identified as 97.5 ≤ NRI < 100. NRI ≥ 100 is considered no nutritional risk. The PNI score was calculated by the following formula 10 x serum albumin (g/dL) +0.005 x total lymphocyte count (mm^3). In PNR scoring system there is no mild category. A PNR score higher than 38 is considered to be normal, 35 to 38 is moderate, less than 35 is severe. CONUT score was the instrument that was used in our regression analysis.

Statistical Analysis

Continuous data was presented as median and interquartile ranges. Categorical data was defined as frequency and percentage. For the continuous data group comparisons, we used Mann-Whitney U test. Pearson Chi-Square or Fisher exact test was used for categoric data comparison. To determine independent predictors for dependent (LA strain parameters function) variable, univariable (Crude) and multivariable (adjusted) logistic regression analysis were used. For correlation analysis between continuous variables Spearman test was used.

Outcome variables: Left atrial strain parameters (contractile, reservoir and conduit function).

Statistical modelling: Multivariable logistic regression models were used. The analyses were based on non-missing data. Predictors (confounders) of multivariable were selected according to a literature consensus opinion by an expert group of physicians. Age, BMI, LVEF, gender, LAVI, SBP, HBA1c and malnutrition indices were included to the model[23-25]. For all statistical analyses, statistical significance was defined as $p < 0.05$. Statistical analyses were performed by using R 4.02 software (Vienna, Austria) with "desctool", "rms", "ggplot" packages.

We have demonstrated the association between LA conduit and body mass index in added variable plot and also heterogeneity between malnourished and non-malnourished patients (according to CONUT score) for predicting LA conduit function (Figure 2). In scatter plot we have also assessed the association between LA conduit function and CONUT (continuous scale) (Figure 3).

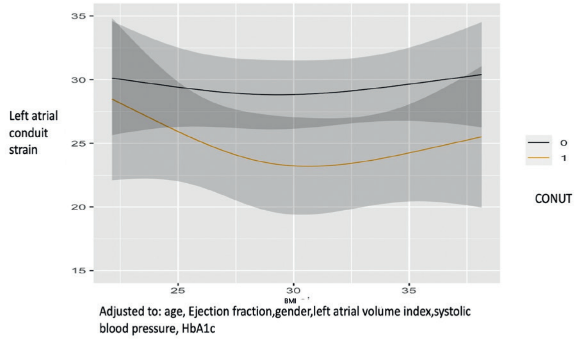

Figure 2. Association between LA conduit and BMI.

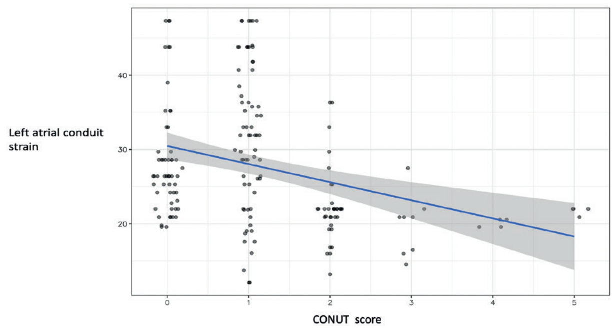

Figure 3. Association between LA conduit function and CONUT score.

RESULTS

Hundred and seventy diabetic patients were enrolled to the study. Basal characteristics of the patient according to the presence of any degree malnutrition calculated by CONUT are given in Table 1. The median value of HBA1c in the any-degree malnourished group was 8 (IQR= 6.85-8.89) while it was 8.2 (IQR= 7.2-10.1) in the non-malnourished. Fifty-one (30%) patients had malnutrition of any degree according to the CONUT score. Median age in patients with any degree malnutrition was 57 (IQR= 53-62.5), while 54 (IQR= 47-60) in non-malnourished group. Hypertension was present in 26 (50.9%) patients in malnourished group, while 80 (67%) of non-malnourished group. Forty-one percent of the patients in the any-degree malnourished group was female, while 64.7% in the non-malnourished group. Body mass index of two groups were similar (p= 0.86). Left atrial strain was analysed in terms of LA reservoir, conduit and contractile functions. Left atrial strain revealed as 14 (IQR= 11.9-18.6), 22 (IQR= 20.2-24.7), 8 (IQR= 3.5-10) for reservoir, conduit, and contractile function respectively for the patients with any-degree malnutrition, while 13 (IQR= 11-17.3), 28.6 (IQR= 24.2-35.5), 15.6 (IQR= 9.35-22.3) respectively for those without any-degree malnutrition (p= 0.25, p< 0.001, p< 0.001 respectively). Median value of albumin was 4.3 (IQR= 3.9-4.7) in the group with any degree malnutrition while 4.4 (IQR= 4.3-4.7) in the non-malnourished group. More detailed information on general characteristics of

Table 1. Basal characteristics of diabetic patients according to their nutrition condition

	Malnutrition (-) (n= 119)	Malnutrition (+) (n= 51)	p value
Age	54 (47-60)	57 (53-62.5)	0.048*
Gender (female) (n, %)	77 (64.7)	21 (41.2)	0.007*
Smoke (n, %)	28 (23.5)	22 (43.1)	0.02*
HT (n, %)	80 (67)	26 (50.9)	0.06
Retinopathy (n, %)	84 (70.6)	32 (62.7)	0.41
BMI	28.7 (26.7-31.6)	28.4 (26.4-32.1)	0.86
Systolic blood pressure	140 (126-152)	130 (126-140)	0.048*
Total cholesterol (g/dL)	209 (174-249)	156 (139-173)	< 0.001*
Creatinine (g/dL)	0.80 (0.70-0.95)	0.98 (0.70-1.30)	0.004*
Albumin (g/dL)	4.4 (4.3-4.7)	4.3 (3.9-4.7)	0.008*
Triglyceride	171 (136-252)	124 (112-154)	< 0.001*
LDL	113 (90.4-146)	83 (73-101)	< 0.001*
Lymphocyte count (mm^3)	2 (1.71-2.48)	1.51 (1.21-1.59)	< 0.001*
Neutrophil (mm^3)	4.61 (3.85-5.77)	3.81 (3.46-4.97)	0.005*
HbA1c	8.2 (7.2-10.1)	8 (6.85-8.89)	0.03*
TSH	1.3 (1-1.9)	1.1 (0.78-2)	0.32
WBC	7.56 (6.52-8.86)	6.06 (5.53-7.59)	< 0.001*
PLT	278 (245-346)	257 (236-285)	0.01*
HB	13.1 (12.3-13.8)	12.8 (11-14.3)	0.42
hsCRP	0.37 (0.20-0.85)	0.31 (0.12-0.52)	0.08
Heart rate	81 (72-91)	80 (74-86)	0.04*
LVEF (by simpson method)	55 (51.5-58.3)	54 (50.5-59.7)	0.57
Septum	1.1 (1.0-1.15)	1.1 (1-1.20)	0.14
LVEDD	4.5 (4.20-4.80)	4.85 (4.60-5.20)	< 0.001*
LVESD	2.8 (2.54-3.10)	3.30 (2.70-3.40)	0.001*
TAPSE	2.2 (2-2.35)	2.3 (2.10-2.70)	0.003*
E/e’	9.2 (7.27-10.6)	8.75 (7.28-10.6)	0.93
Basal circumferenceal strain	-18.5 (-21.1, -15)	-17.5 (-19.4, -15)	0.055*
Apical circumferenceal strain	-27.6 (-34, -23)	-26.3 (-29.3, -22)	0.13
LV twist	19 (14.9-24)	18.5 (16-24.6)	0.49
GLS	-18.6 (-19.9, -16.9)	-17.9 (-20.3, -15.4)	0.31
LAVI	42 (31.3-48.9)	51.7 (43.1-68.8)	< 0.001*
LA strain reservoir	13 (11-17.3)	14 (11.9-18.6)	0.25
LA strain conduit	28.6 (24.2-35.5)	22 (20.2-24.7)	< 0.001
LA strain contractile	15.6 (9.35-22.3)	8 (3.5-10)	< 0.001
LA strain rate S	1.2 (1-1.5)	1.2 (1-1.5)	0.55
LA strain rate E	-0.8 (-1.4, -0.5)	-0.9 (-1.3, -0.6)	0.65
LA strain rate A	-1.6 (-1.9, -1.3)	-1.45 (-1.88, -1)	0.15

* Statistically significance, p< 0.05.

HT: Hypertension, BMI: Body mass index, HBA1c: Haemoglobin A1c, TSH: Thyroid stimulant hormone, PLT: Platelet, hsCRP: High sensitivity C reactive protein, WBC: White blood cell count, HB: Haemoglobin, LVEF: Left ventricle ejection fraction, LVEDD: Left ventricle end diastolic diameter, LVESD: Left ventricle end diastolic diameter, TAPSE: Tricuspid annular plane systolic excursion, LAVI: Left atrial volume index, LV: Left ventricle, LA: Left atrium, GLS: Global longitudinal strain, Malnutrition: Assessed according to CONUT score.

Table 2. Malnutrition parameters in all over patients

Variables	Total sample
CONUT (continious)	1 (0-2)
CONUT (categoric) (n, %)	51 (30)
NRI (continious)	107 (106-112)
NRI (categoric) (n, %)	16 (9.4)
PNI (continious)	54.8 (51.3-57.2)
PNI (categoric) (n, %)	2 (1.17)

CONUT: Controlling nutritional status score, NRI: Nutritional risk index, PNI: Prognostic nutritional index.

Table 3. Multivariable logistic regression, model-1, model-2 and model-3. Model performance measurements

Variables	Beta coeff and CI	p value
Model-1 (LA-conduit)		
CONUT (any degree)	-7.5(-10.7, -4.3)	< 0.001
Model-2 (LA-reservoir)		
CONUT (any degree)	2.48 (0.83, 4.13)	< 0.03
Model-3 (LA-contractile)		
CONUT (any degree)	-4.21 (-2.21, -6.01)	< 0.001

Data are given in Odds-Ratio (95%CI). Multivariable lineer regression analyses was used all 3 models adjusted for age, BMI, LVEF, gender, LAVI, SBP, HBA1c. CI: Confidence interval, LA: Left atrium, CONUT: Controlling nutritional status score.

patients is given in Table 1. Status of malnutrition parameters among all patients are given in Table 2.

In multivariable logistic regression analysis, LA conduit strain was demonstrated to decrease in the presence of any degree malnutrition [ß: -7.5 (CI 95%, -10.7, -4.3 p< 0.001)], LA reservoir strain was demonstrated to increase [ß: 2.48 (CI 95%, 0.83-4.13 p< 0.03)] and LA contractile strain was demonstrated to decrease [ß: -4.21(CI 95%, -2.21, -6.01 p< 0.001)] (Table 3).

DISCUSSION

Malnutrition is a serious public health problem that is associated with adverse outcomes in a broad range of disease including cardiovascular disease and DM[26-30].

Previously, several studies have emphasised on the impact of malnutrition on cardiac disease, yet the impact of malnutrition on LA strain has not been investigated comprehensively for DM accompanied by microvascular complications[27-32].

In this study we have shown the possible unfavourable effects of malnutrition on cardiac functions via LA strain analysis which is a simple, reproducible and angle independent technique. Taking into consideration that malnutrition is a preventable risk factor, it is important to evaluate these patients for nutrition status. By improving nutrition status, we may also improve the prognosis of our patients.

Although recent studies have demonstrated its' value in predicting the cardiovascular adverse events, evaluation of LA functions has not reached its rightful place in clinical practice. Left atrial functions could be summarised in 3 sections: 1st reservoir function 2-conduit function and 3-contractile function[33,34]. In a study by Karagoz A et al. the longitudinal, circumferential, and rotational myocardial mechanics were demonstrated to be impaired in diabetic patients comparing to non-diabetics[35]. Herewith we have demonstrated a similar relation between any-degree malnutrition and cardiac functions assessed by LA strain analysis. Nutrition status is a growing public health issue, yet it is still ignored in our clinical practice[9,26]. Recently Roubin et al.[26] demonstrated that malnutrition was associated with worse outcomes in patients with acute coronary syndrome. In our study we have demonstrated that malnutrition is associated with decreased conduit and contractile strain values which are indicative for cardiac adverse events.

The decrease in LA conduit and contractile strain in malnourished patients may be attributed to the deficiency of proteins for maintaining the functions of myocardium[36]. Another reason may be the alterations in inflammatory state due to malnutrition. Given that chronic inflammation is associated with cardiac fibrosis, the inflammatory alterations in malnourished patients may explain the changes in myocardial functions[37,40].

There are several tools to assess nutritional status. In our study we used three tools and among these CONUT score was able to determine nutrition status more detailed comparing with PNI, NRI similar with the results of Roubin et al.[26] CONUT score is a simple reproducible method that can be applied to our clinical practice easily. Evaluating diabetic patients for malnutrition may help the clinician identify the patients who are more prone to develop cardiac adverse events. Considering that malnutrition is a preventable risk factor and easy to diagnose, it is important to evaluate diabetic patients for nutrition status. Accordingly, it is crucial to encourage the patients for developing right dietary habits and appropriate lifestyle changes.

LIMITATIONS

The retrospective design and small sample size are the main limitations of our study. There are still gaps in standardization of the of methodology for LA strain software algorithms. Finally, there may be unmeasured confounder which are not included in our regression model.

CONCLUSION

In this study we have demonstrated that malnutrition is an important entity in diabetic patients with DR, regarding its' relationship with LA strain which is an indicator for cardiac adverse events. Yet further studies with a prospective design and larger sample size are needed to establish the impact of malnutrition on cardiac functions.

Ethics Committee Approval: This study was approved by Kartal Kosuyolu High Specialization Training and Research Hospital Ethics Committee (5, Date: 12.12.2019).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - CK; Analysis/Interpretation - AK, IK; Data Collection - SE; Writing - FÖ; Critical Revision - FÖ, AK; Statistical Analysis - İT, AK; Overall Responsibility - FÖ; Final Approval - All of Authors.

Conflict of Interest: The authors have no conflicts of interest to declare.

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