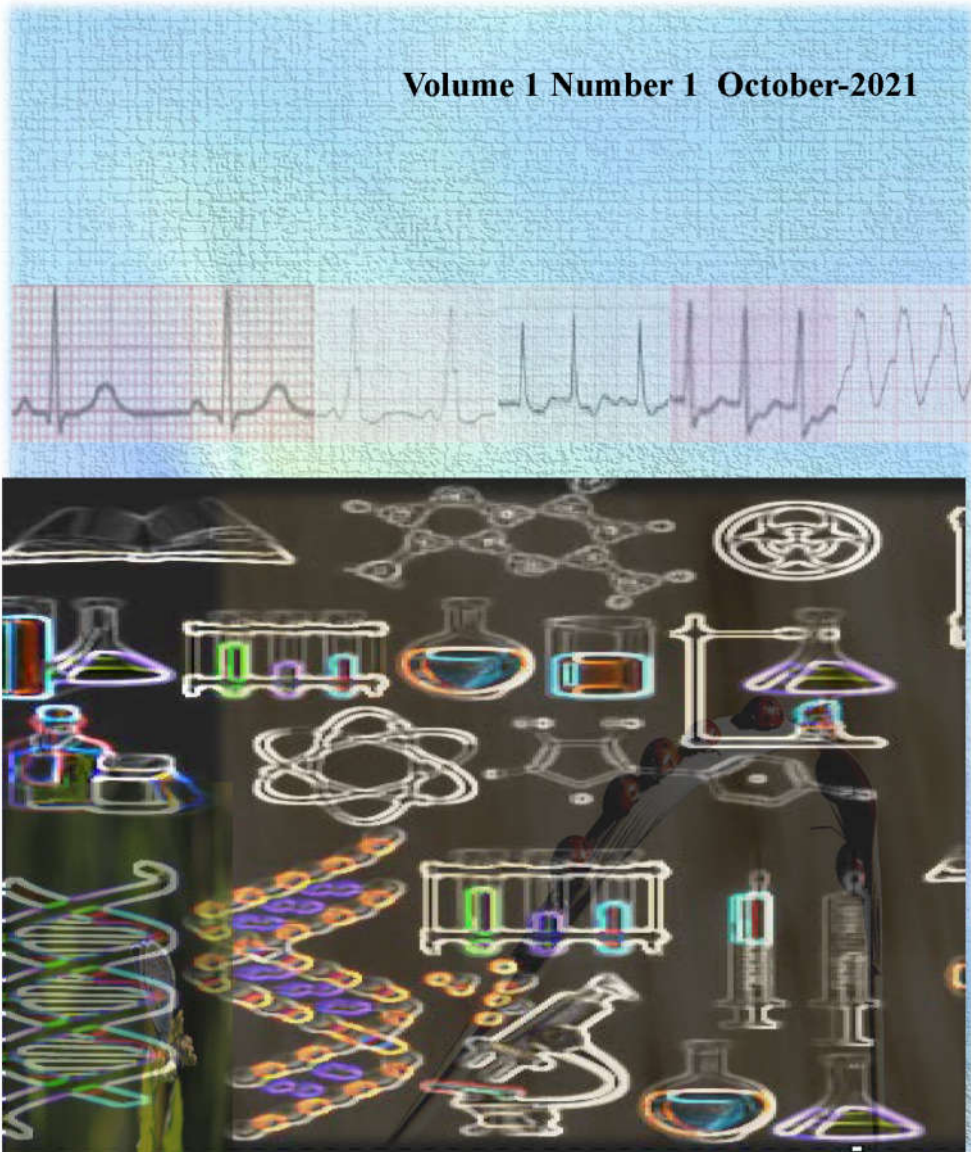


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**Web article:** Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. *Am J Nurs* [serial on the Internet] 2002 [cited 12 Aug 2002]. Available from: [www.nursingworld.org/AJN/2002/june/wawatch.htm](http://www.nursingworld.org/AJN/2002/june/wawatch.htm)

**Website;** Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 July 2002]. Available from: [www.cancer-pain.org](http://www.cancer-pain.org)

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## The Role of Gender in Heart Diseases

Kalp Hastalıklarında Cinsiyetin Rolü

Dr. Songül Usalp<sup>1</sup>

<sup>1</sup>Sancaktepe Şehit Profesör Doktor İlhan Varank Eğitim Araştırma Hastanesi, Kardiyoloji Bölümü, İstanbul

Corresponding Author : Dr. Songül USALP

Sancaktepe Şehit Profesör Doktor İlhan  
Varank Eğitim Araştırma Hastanesi,  
Kardiyoloji Bölümü, İstanbul.  
e-mail: : dr.songulusalp@hotmail.com  
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### Abstract

**Background:** In our study, we aimed to investigate the course and frequency of cardiovascular diseases in female and men and whether there is a change in their cardiac functions in the follow-up of these patients.

**Material and Method:** The files of the patients who applied to the cardiology outpatient clinic of our hospital due to various heart conditions were analyzed retrospectively, the patients' coronary angiography, heart surgeries, first and follow-up echocardiographic findings were compared to between two groups as male and female.

**Results:** Two hundred and seventy female (mean age 63.8 years) and 271 male (mean age 62.4 years) patients were included in the study. The rate of coronary artery disease (CAD), heart failure, degenerative mitral valve disease (MVD) and serum creatinine levels were higher in men ( $p<0.05$ ). There was no difference between the two groups in terms of diabetes mellitus, chronic obstructive pulmonary disease, dialysis treatment, cerebrovascular diseases, hypertrophic cardiomyopathy, and pacemaker implantation ( $p>0.05$ ). Hypertension, rheumatic MVD, Takotsubo Cardiomyopathy were more common in female than in man ( $p<0.05$ ). In the clinical course of both female and men, a significant decrease in left ventricle ejection fraction (LVEF) and a significant increase in systolic pulmonary artery pressure (SPAP) were observed ( $p<0.001$ ). The age was found an independent risk factor for both genders ( $p<0.05$ ).

**Conclusion:** CAD, degenerative MVD and heart failure were higher in men, rheumatic MVD and Takotsubo cardiomyopathy were higher in female. LVEF was relatively protected in female, but follow-up both genders it was observed that LVEF significant decreased and SPAP increased.

**Key words:** heart disease, gender, echocardiography

### Öz

**Amaç:** Çalışmamızda, kardiyovasküler hastalıkların kadın ve erkeklerdeki seyrini, sıklığını, bu hastaların takiplerinde kalp fonksiyonlarında değişiklik olup olmadığını araştırmayı hedefledik.

**Materiyal ve metod:** Hastanemiz kardiyoloji polikliniğine çeşitli kalp rahatsızlıkları nedeniyle başvuran hastaların dosyaları geriye dönük tarandı, erkek ve kadın olarak iki gruba ayrılan hastaların koroner anjiyografileri, geçirmiş oldukları kalp ameliyatları, başvuru ve sonrasındaki ekokardiyografik bulguları karşılaştırıldı.

**Bulgular:** Çalışmaya 270 bayan (ortalama yaş 63.8 yıl) ve 271 erkek (ortalama yaş 62.4 yıl) hasta alındı. Koroner arter hastalığı (KAH), kalp yetersizliği, dejeneratif mitral kapak hastalığı (MKH) oranı ve serum kreatinin düzeyleri erkeklerde fazlaydı ( $p<0.05$ ). Diyabetes mellitus, kronik obstrüktif akciğer hastalığı, diyaliz tedavisi, serebrovasküler hastalıklar, hipertrofik kardiyomyopati, kalp pili uygulaması açısından her iki grup arasında fark yoktu ( $p>0.05$ ). Kadınlarda hipertansiyon, Takotsubo kardiyomyopatisi, romatizmal MKH erkeklere göre sıklı. Hem kadınların hem erkeklerin takiplerinde sol ventrikül ejeksiyon fraksiyonunda (SVEF) belirgin düşme ve sistolik pulmoner arter basıncında (SPAB) anlamlı artış izlendi ( $p<0.001$ ). Her iki cinsiyette yaş, önemli bağımsız bir risk faktörü olarak bulundu ( $p<0.05$ ).

**Sonuç:** Erkeklerde KAH, dejeneratif MKH ve kalp yetersizliği, kadınlarda ise romatizmal MKH ve Takotsubo kardiyomyopatisi daha fazlaydı. SVEF nispeten kadınlarda korunmuştu, fakat, her iki cinsiyette de takipte, hem SVEF'de düşme, hem SPAB da artış olmaktaydı. Yaş her iki cinsiyette KAH için bağımsız prediktif risk faktörü idi.

**Anahtar kelimeler:** Kalp hastalıkları, cinsiyet, ekokardiyografi



## Introduction

Heart diseases progress differently in men and female due to genetic structure, the effect of hormones, the interaction of psychosocial and environmental factors, eating habits and behavioral differences (1,2). Although the age at which female suffer from heart diseases is 10 years later compared to men, in recent years, female have come to be diagnosed with heart diseases at an early age (1). Although mortality and morbidity rates seem to be close to each other, since ischemic etiology is at the forefront in men, the effect is stronger; ischemic heart diseases in female are more uncertain, and the diagnosis can be missed (2). Less use of health services by female and delayed diagnosis have given rise to the increase in cardiovascular mortality in female in recent years (3). Hormones secreted in female of childbearing age are known to protect against atherosclerosis thanks to their positive effects on the vascular endothelium and sympathetic system (4). Female who benefits from the beneficial effects of estrogen in the period before menopause, unfortunately, do not enjoy this benefit even if they take hormone replacement therapy after menopause (4). Cardiovascular mortality rate in female exceeds that of men especially after the age of 65. Apart from ischemic heart diseases, the involvement of valvular heart diseases can be different in men and female. While mitral valve prolapse is common in female, aortic stenosis due to congenital bicuspid aortic valve is 3 times more common in men (5). One of the most significant differences between the genders is that female have heart failure with preserved ejection fraction, even at advanced age.

In this study which intended for investigating the distribution of heart diseases by gender, we aimed to reveal the differences between the characteristics of male and female patients that we followed up for various heart problems, together with their echocardiographic measurements.

## Material and Method

The files of the patients who applied to the cardiology clinic of our hospital due to various heart diseases were reviewed retrospectively. All patients' age, previous diseases, biochemical parameters, coronary angiography (CAG) results, coronary artery disease (CAD), coronary artery bypass graft (CABG) results, heart valve surgery [mitral valve replacement (MVR), aortic valve replacement (AVR), tricuspid valve replacement (TVR)] results, heart failure and whether cardiac resynchronization (CRT) treatment was administered in consequence of it, echocardiography results at the first admission to our hospital and

follow-up (within 1-2 years) [left ventricular ejection fraction (LVEF), left and right atrial measurements, systolic pulmonary artery pressures (SPAP)] were recorded (6). The study investigated whether they have co-morbid diseases [hypertension (HT), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), end-stage chronic kidney disease on dialysis (ESRD), cerebrovascular disease (CVD), hypertrophic obstructive cardiomyopathy (HOCM)]. In the center where the study was conducted, the glomerular filtration rate was calculated with the Cockcroft-Gault formula. Coronary angiography reports were examined, and we recorded whether they have and occlusive or non-occlusive coronary artery disease and whether stent implantation was performed. The patients included in the study were divided into two main groups as male and female.

## Statistics

The data obtained from the medical histories of the patients were recorded in the statistical program of SPSS version 20.0 (Statistical Package for Social Sciences, Inc. Chicago, IL, USA). The distribution was expressed as mean  $\pm$  standard deviation (SD) in numerical data with normal distribution, and as percentage (%) in categorical data. Comparisons between the two groups were made using the Students t-test for normally distributed data, and the Chi-square test for categorical variables. Whether the data were suitable for normal distribution was evaluated with the Kolmogorov Smirnov test. Data showing abnormal distribution were expressed as median, min-max values, and Mann Whitney U test was used to compare the two groups. Multivariate logistic regression analyzes were used to identify independent predictors of gender and CAD association. A p value of <0.05 was considered significant in all results.

## Results

270 female (mean age  $63.8 \pm 14.5$  years) and 271 male (mean age  $62.4 \pm 12.6$  years) patients were included in the study, and the mean age of both groups was found to be close to each other ( $p > 0.05$ ). Serum creatinine values were slightly higher in males [ $1.0 (0.5-5.1)$  vs  $0.8 (0.5-2.0)$  mg/dL,  $p < 0.001$ ]. Significantly, CAD [204 (75.2%) vs 67 (24.8%),  $p < 0.001$ ], CABG [90 (33.2%) vs 26 (9.6%),  $p < 0.001$ ], CAG [222 (81.9%) vs 90 (33.3%),  $p < 0.001$ ], stent implantation [117(43.1%) vs 37(13.7%),  $p < 0.001$ ], low LVEF on echocardiography [83 (30.6%) vs 36(13.3%)] were high in men (Table 1).

**Table 1. Comparison of demographic characteristics and comorbidities of female and men**

Variables	Female (n=270)	Men (n=271)	P
Age, years	63.8 $\pm$ 14.5	62.4 $\pm$ 12.6	0.256
Creatinine, mg/dL	0.8 (0.5-2.0)	1.0 (0.5-5.1)	0.001*
GFR ml/dk/1.73 m <sup>2</sup>	79.6 $\pm$ 29.9	83.5 $\pm$ 29.9	0.187
CAD (%)	67 (24.8)	204 (75.2)	0.001
CAG (%)	90 (33.3)	222 (81.9)	0.001
CABG (%)	26 (9.6)	90 (33.2)	0.001
Stent implantation (%)	37 (13.7)	117 (43.1)	0.001
MVR (%)	14 (5.1)	14 (5.1)	0.332
AVR (%)	9 (3.3)	13 (4.7)	0.984
TVR (%)	3 (1.1)	4 (1.4)	0.311°
° HFrEF (%)	36 (13.3)	83 (30.6)	0.003
HFpEF (%)	67 (24.8)	127 (46.8)	0.284
CRT (%)	3 (1.1)	7 (2.5)	0.537°
COPD (%)	15 (5.5)	21 (7.7)	0.936
ESRD (%)	3 (1.1)	4 (1.4)	0.921°
Hypertension (%)	89 (32.9)	100 (36.9)	0.036
Diabetes Mellitus (%)	41 (15.1)	42 (15.4)	0.092
CVD (%)	9 (3.3)	13 (4.7)	0.990
Takotsubo CMP (%)	2 (0.7)	0 (0)	0.022°
HOCM (%)	4 (1.4)	3 (1.1)	0.383°

Aberrations: \*; Mann-Whitney U test, °; Fisher's Exact test, °; Those with an EF value below 50% are expressed. n= number of people, AVR: Aortic valve replacement; CABG: Coronary artery by-pass graft; GFR: Glomerular filtration rate; HOCM: Hypertrophic obstructive cardiomyopathy; CAD: Coronary artery disease; CAG: Coronary angiography; MVR: Mitral valve replacement; CMP: Cardiomyopathy; CRT: Cardiac resynchronization therapy; COPD: Chronic obstructive pulmonary disease; HFrEF: Heart failure with low Ejection Fraction; HFpEF: Heart failure with preserved Ejection Fraction; TVR: Tricuspid valve replacement; ESRD: End-stage chronic renal failure; CVD: Cerebrovascular disease

Considering the co-morbid diseases, the rate of HT in female [89 (32.9%) vs. 100 (36.9%),  $p=0.036$ ] was higher than in men. In echocardiographic examination, LVEF was lower in men at first admission [50 (18-65) vs 56.0 (30-67),  $p < 0.001$ ]; Left ventricular wall motion defect [149 (54.9%) vs 66 (24.3%),  $p < 0.001$ ] was higher. Left ventricular end diastolic diameter (LVEDD) [ $4.9 \pm 0.5$  vs.  $5.2 \pm 0.6$ ,  $p < 0.001$ ], left ventricular end systolic diameter (LVESD) [ $3.4 \pm 0.6$  vs  $3.7$

$\pm 0.7$ ,  $p < 0.001$ ], inter ventricular septum (IVS) thickness [ $1.0 \pm 0.1$  vs  $1.1 \pm 0.2$ ,  $p < 0.001$ ], posterior wall (PW) thickness [ $1.0 \pm 0.1$  vs  $1.1 \pm 0.2$ ,  $p < 0.001$ ] was smaller (Table 2). Rheumatic mitral valve disease was more common in female [(14 (5.1%) vs. 5 (1.8%),  $p = 0.003$ )], while degenerative mitral valve disease was more common in men [(95 (35.1%) vs 168 (61.9%),  $p = 0.005$ ] (Table 2)

**Table 2. Echocardiographic differences in male and female hearts**

Variables	Female (n=270)	Men (n=271)	P
LVEF (%)	56.0 (30-67)	50.0 (18-65)	0.001*
LVEDD cm	$4.9 \pm 0.5$	$5.2 \pm 0.6$	0.001
LVESD cm	$3.4 \pm 0.6$	$3.7 \pm 0.7$	0.001
IVS thickness cm,	$1.0 \pm 0.1$	$1.1 \pm 0.2$	0.001
PW thickness cm	$1.0 \pm 0.1$	$1.1 \pm 0.2$	0.001
RVDD cm	$2.3 \pm 0.4$	$2.4 \pm 0.4$	0.201
LA cm	$4.0 \pm 0.6$	$4.1 \pm 0.6$	0.322
RA cm	$3.7 \pm 0.5$	$3.8 \pm 0.5$	0.074
TAPSE mm	$2.3 \pm 0.4$	$2.2 \pm 0.4$	0.068
SPAP mmHg	30.0 (17-86)	28.5 (20-70)	0.298*
LVWMD (%)	66 (24.3)	149 (54.9)	0.001
<b>Mitral valve disease</b>			
Normal (%)	49 (18.1)	59 (21.7)	0.330
Mitral valve prolapse (%)	7 (2.5)	6 (2.2)	0.344
Rheumatic (%)	14 (5.1)	5 (1.8)	0.003
Degenerative (%)	95 (35.1)	168 (61.9)	0.005
Mechanical (%)	6 (2.2)	4 (1.4)	0.227°
Severe stenosis (%)	4 (1.4)	0 (0)	0.008°
Severe insufficient (%)	15 (5.5)	14 (5.1)	0.242
<b>Aort valve disease</b>			
Normal (%)	56 (20.7)	7 (2.5)	0.517
Aorta valve prolapse (%)	5 (1.8)	3 (1.1)	0.221°
Rheumatic (%)	5 (1.8)	3 (1.1)	0.221°
Degenerative (%)	98 (36.2)	157 (57.9)	0.119
Mechanical (%)	3 (1.1)	5 (1.8)	0.821°
Bicuspid aorta (%)	1 (0.3)	1 (0.4)	0.805°
Severe stenosis (%)	4 (1.4)	4 (1.4)	0.621°
Severe insufficient (%)	1 (0.3)	4 (1.4)	0.306°
<b>Tricuspid valve diseases</b>			
Normal (%)	155 (57.4)	225 (83.0)	0.389
Degenerative (%)	2 (0.7)	4 (1.4)	0.686°

**Aberrations:** \*, Mann-Whitney U test, °, Fisher's Exact test, n=Number of people; LVEF: Left ventricular ejection fraction, LVEDS: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; RVDD: Right ventricular diastolic diameter; IVS: Left ventricular interventricular wall diameter; PW: Left ventricular posterior wall diameter; TAPSE: Tricuspid annular plane systolic excursion; SPAP: Systolic pulmonary artery pressure; LVWMD: Left ventricular wall motion defect.

Significant reductions in LVEF [ $56.0$  (30-67) vs  $54.0$  (25-73),  $p < 0.001$ ], LVEDD [ $4.9 \pm 0.4$  vs  $5.1 \pm 0.5$ ,  $p = 0.003$ ], LVESD [ $3.4 \pm 0.5$  vs  $3.5 \pm 0.7$ ,  $p = 0.046$ ], and increase in left atrial diameter [ $4.2 \pm 0.6$  vs  $4.4 \pm 0.8$ ,  $p = 0.019$ ] and right atrial diameter [ $3.8 \pm 0.5$  vs  $4.0 \pm 0.6$ ,  $p = 0.010$ ] diameters and SPAP values [30 (17-86) vs 37 (20-72),  $p < 0.001$ ] were observed on echocardiograms during follow-up of the female (Table 3). Similar to female, men had a significant decrease in LVEF [50 (18-65) vs. 47 (20-65  $p < 0.001$ ]), although LVEDD [ $5.3 \pm 0.1$  vs  $5.4 \pm 0.6$ ,  $p = 0.013$ ], LVESD [ $3.8 \pm$

$0.6$  vs  $3.9 \pm 0.7$ ,  $p = 0.009$ ], left atrial diameter [ $4.2 \pm 0.7$  vs  $4.3 \pm 0.6$ ,  $p = 0.009$ ], right atrial diameter [ $3.8 \pm 0.6$  vs  $3.9 \pm 0.5$ ,  $p = 0.029$ ] and SPAP [ $30.6 \pm 9.7$  vs  $32.3 \pm 9.0$ ,  $p = 0.035$ ] values were increased (Table 3).

The study investigated independent predictors of coronary artery disease in both men and female using multivariate logistic regression analysis and Chi-Square test. Unfortunately, the study found that, apart from age factor, other factors were not gender-specific independent predictor risk factors [RR: 1.019, 95% CI (0.598-0.904),  $p = 0.011$ ], in males [RR: 1.098, 95% CI (0.280- 0.916),  $p = 0.041$ ] (Table 4).

**Table 4. Independent predictors of coronary artery disease in men and female**

Variables	Female			Men		
	OR	% 95 CI	P	OR	% 95 CI	P
Age	1.019	(0.598-0.904)	0.011	1.098	(0.280-0.916)	0.041
HT	0.705	(0.388-1.280)	0.249	0.885	(0.542-1.444)	0.624
DM	1.431	(0.702-2.918)	0.349	1.480	(0.726-3.017)	0.306
COPD	0.336	(0.074- 1.533)	0.115	1.137	(0.445-2.918)	0.728
CVD	1.164	(0.282-4.799)	0.833	0.468	(0.153-1.426)	0.172
ESRD	0.981	(0.959-1.003)	0.140	0.992	(0.078-4.025)	0.567

**Aberrations:** DM: Diabetes Mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; ESRD: End stage renal disease; CVD: Cerebrovascular diseases

**Table 3. Comparison of the basal and control echocardiograms of the patients**

Female	First	Control	P
LVEF, (%)	56.0 (30-67)	54.0 (25-73)	0.001°
LVDD, cm	4.9 ± 0.4	5.1 ± 0.5	0.003
RVDD, cm	3.4 ± 0.5	3.5 ± 0.7	0.046
IVS thickness, cm	1.0 ± 0.1	1.0 ± 0.2	0.748
PW thickness, cm	1.0 ± 0.1	1.0 ± 0.1	0.122
LA, cm	4.2 ± 0.6	4.4 ± 0.8	0.019
RA, cm	3.8 ± 0.5	4.0 ± 0.6	0.010
SPAP, mmHg	30.0 (17-86)	37 (20-72)	0.001°
TAPSE, mm	2.2 ± 0.4	2.0 ± 0.4	0.221
<b>Men</b>			
LVEF, (%)	50.0 (18-65)	47 (20-65)	0.001°
LVDD, cm	5.3 ± 0.1	5.4 ± 0.6	0.013
RVDD, cm	3.8 ± 0.6	3.9 ± 0.7	0.009
IVS thickness, cm	1.1 ± 0.2	1.1 ± 0.1	0.183
PW thickness, cm	1.0 ± 0.1	1.0 ± 0.1	0.738
LA, cm	4.2 ± 0.7	4.3 ± 0.6	0.009
RA, cm	3.8 ± 0.6	3.9 ± 0.5	0.029
SPAP, mmHg	28.5 (20-70)	32.0 (20-75)	0.001°
TAPSE, mm	2.3 ± 0.6	2.3 ± 0.7	0.481

**Aberrations:** ° Wilcoxon was used. n=Number of people; LVEF: Left ventricular ejection fraction, LVEDS: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; RVDD: Right ventricular diastolic diameter; IVS: Left ventricular interventricular wall diameter; PW: Left ventricular posterior wall diameter; TAPSE: Tricuspid annular plane systolic excursion; SPAP: Systolic pulmonary artery pressure; LVWMD: Left ventricular wall motion defect

### Discussion

In this study, in which we tried to compare the hearts of men and female in many aspects, found that, as expected, ischemic heart diseases, degenerative mitral valve disease, and heart failure with low LVEF are more common in men. In female, hypertension and mitral valve stenosis were common. Age was an important risk factor for CAD in both genders. Unfortunately, at follow-up within 1-2 years, the study observed that the ejection fraction decreased, cardiac diameters increased, and pulmonary artery pressure increased in both men and female.

While ischemic heart diseases are found 3-4 times more frequently in men than in female until the age of 60, female constitute most of these patients after the age of 75. However, in recent years, it is known that younger female suffers from ischemic heart diseases (7). Smoking habits, stressful life, irregular release of hormones due to active working life, early menopause can be considered among the contributing factors. In this study, the rates of CAD, CAG and CABG were higher in men. Also, due to the damaged myocardial tissue, men had lower LVEF rates and larger cardiac cavities. While obstructive coronary artery diseases are more common in men presenting with acute coronary syndrome, non-occlusive or completely normal coronary arteries are found in most female (8). While decision is made for placement of stent or by-pass for most of the men, no action is taken for normal or mild atherosclerotic coronary vessels in female. In our study, the rate of stent implantation and CABG was higher in men than in female.

In recent years, one of the most common causes of non-occlusive coronary artery disease has been thought to be microvascular angina (9). Other conditions that cause acute coronary syndrome in female can be listed as follows; spontaneous coronary artery dissection, vasospastic angina, Takotsubo cardiomyopathy (10,11). However, normal coronary arteries in female should be taken seriously. Because, after the next 5-8 years, the risk for obstructive coronary artery disease for these patients are found to be 2 times higher (12,13).

In the premenopausal period, the rate of hypertension and the cholesterol levels in female are lower than in men. The presence of diabetes (gestational or type 1, type 2 DM) affects cardiovascular outcomes adversely (14).

Unlike these generalizations, the rate of hypertension in female was higher than in men in this study. We attributed this result to the fact that most of our female patients who participated in the study were in the postmenopausal period. In the subgroup analyzes, when we compared the patients under 50 years of age and above, there was no difference between men and female under 50 years of age, while the prevalence of hypertension was more prevalent in female above 50 years of age. In addition, we thought that we achieved such a result due to the high birth rate in our country, salty eating habits and the fact that female are exposed to more stress. Likewise, the rate of DM was the same in both groups and we thought that we achieved such a result because the patients were over a certain age.

Heart failure affects almost 10% of the elderly population and is more common in female (15). Evidence suggesting this fact can be listed as the longer life expectancy in female than in men, the higher incidence of ischemic heart failure in men and therefore a shorter life span, and the higher incidence of heart failure with preserved EF (HFpEF) in female (16).

Dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM) are slightly higher in men than in female (15,16), while Takotsubo cardiomyopathy (TTC) is more common in female (11). Estrogen activates vasodilation by decreasing catecholamine-mediated vasoconstriction and may possibly increase the  $\beta_2$  adrenergic receptor response (4). The decrease in estrogen with advancing age may contribute to increased catecholamine sensitivity, which may contribute to both Takotsubo cardiomyopathy (TCM) and heart failure with HFpEF (4).

In the study, the rate of men with low ejection fraction (HFrEF) was higher, but HFpEF was equal in both groups. The number of female patients diagnosed with TCM was low, but they were more than males, and HCM was found to be equal in both groups. We are of the opinion that the reason for this was that both genders were affected equally, since HCM is more of a genetic disease.

CRT, which is used in the treatment of heart failure, can reduce the progression of heart failure by increasing the quality of life and reducing conduction defects (17). In many studies, it is controversial whether female benefit from this treatment because the number of females included in the study is low and LVEF is higher in female (17,18,19). Since the number

of patients who underwent CRT in this study was few, it is very difficult to express a general opinion on this issue. However, unlike other studies, the rates of CRT administration in both men and female were close to each other in this study. Although aortic stenosis, which is one of the most common valvular heart diseases in adults, seems to be dominant in males, it was found to be similar in both sexes in our study. There was no difference between the two groups in terms of severe aortic regurgitation. Although mitral valve prolapse was more common in female (20), it was the same in both groups in our study. The low number of our patients and the advanced age of the patients may have caused detection of mitral valve prolapse less frequently. While severe mitral regurgitation is similar in both groups, one of the reasons why severe mitral stenosis is more common in female may be that female are more likely to have rheumatic mitral valve disease in childhood.

In our country, one of the largest studies investigating gender differences in heart diseases is the TEKHARF study (21). A total of 1852 men and 1835 female participated in that study. The frequency of CAD in men was 4.1%; the frequency of HT was 1.5; the rate of rheumatic heart diseases was 0.2%; the rate of other diseases was 0.2%; the frequency of CAD was 3.5% in female; the frequency of HT was 2.8%; rheumatic heart diseases 0.7; other heart diseases was 0.3. Also, according to this large-scale study, the presence of DM, systolic blood pressure, and high C-reactive protein were predictors of the most important risk factors for the development of coronary heart diseases in both groups, while smoking and high rates of LDL-cholesterol were independent predictors for CAD only in the male group (21).

In our study, when HT, DM, COPD, LVH, and CRF were evaluated separately in both genders, they were not found to be independent predictors of CAD. Only age was found to be an independent predictor for both genders. The reason for such a different result may be that our age range was not as wide as that in the TEKHARF study, and that already known heart patients were included in the study. Many risk factors (medical history of CAD in the family, stressful personality, inactivity, obesity, pre-diabetes, smoking, cholesterol values, hormonal changes, etc.) for coronary artery disease should be considered together (22).

In this study, unlike other studies conducted so far, the first admission and control echocardiograms of our patients were also available. Thus, data on the course of heart diseases in both genders were obtained.

#### Limitations

The most important limitations were the retrospective nature of this study, the small number of patients, and the inability to follow-up most of the patients.

#### Conclusion

In this study, we tried to present the differences found between male and female hearts in the light of the data in literature. The study found that men are more prone to ischemic heart diseases; heart failure with low LVEF is more common in men; hypertension and rheumatic mitral valve diseases are more common in female. LVEF was relatively preserved in female, but although the genders were different, both groups had a decrease in LVEF and an increase in SPAB over time. Therefore, regardless of gender and co-morbid diseases, the heart was getting tired over time. Heart diseases appear in different roles in men and female. Symptoms in female should not be ignored if they are associated with mood changes, and microvascular angina should be considered in non-occlusive coronary artery diseases. Patients who present with palpitations and shortness of breath should be alert for rheumatic mitral stenosis. In the future, more extensive studies are needed

to determine the risk factors for heart diseases in both genders.

**Conflict of Interest:** The author has no conflicts of interest to declare.

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## Determining University Students' Energy Drink Use Habits

Üniversite Öğrencilerinin Enerji İçeceği Kullanım Alışkanlıklarının Belirlenmesi

Suzan Havlioglu<sup>1</sup>, Mustafa Begenc Tascanov<sup>2</sup>

<sup>1</sup> Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Şanlıurfa, Türkiye

<sup>2</sup> Harran Üniversitesi, Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Şanlıurfa, Türkiye

Corresponding Author : Dr.Öğretim Üyesi, Suzan Havlioglu,

Sağlık Hizmetleri Meslek Yüksekokulu, Harran Üniversitesi, Şanlıurfa, Türkiye

e-mail : suzanhavlioglu@hotmail.com

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### Abstract

**Background:** The use of energy drinks has increased among young people in recent years. While these drinks may initially increase physical and mental performance, they also have many negative effects, such as causing heart rhythm disorders, migraine, anxiety disorders, insomnia, interactions with other drugs, and addiction. This study determined the knowledge of university students about energy drinks and their usage habits.

**Method:** This descriptive study targeted 2400 students studying at the Vocational School of Health Services. No sampling method was used and 435 students agreed to participate in the study.

**Results:** Of the students, 10.8% used energy drinks, 50.6% knew about energy drinks, 30.3% used the internet, and 29.8% thought that they posed a danger to cardiac health. Of the users, 42.6% loved the taste and 54.5% used them because they provided energy.

**Conclusions:** There were significant differences in the students' consumption of energy drinks by gender and smoking status ( $p<0.05$ ). It is necessary to increase the awareness of students about the effects of energy drinks using both through written-visual-social media and in schools.

**Keywords:** University students, energy drink, habit

### Öz

**Amaç:** Son yıllarda genç nüfus arasında artış gösteren enerji içeceklerinin kullanımı, başlangıçta fiziksel ve mental performansı artırabilir ancak kalp ritim bozukluğu, migren, kaygı bozukluğu, uykusuzluk, diğer ilaçlar ile etkileşim ve bağımlılık oluşturma gibi birçok olumsuz etkisi de bulunmaktadır. Bu çalışmanın amacı üniversite öğrencilerinin enerji içecekleri hakkında bilgi düzeylerini ve kullanım alışkanlıklarını belirlemektir.

**Materyal ve Metod:** Tanımlayıcı tipte bir araştırma olarak planlanan çalışmanın evrenini Sağlık Hizmetleri Meslek Yüksekokulunda öğrenim gören 2400 öğrenci oluşturmuştur. Çalışmada örneklem yöntemine gidilmemiş ve evrenin hepsine ulaşılması hedeflenmiştir. Araştırmaya çalışmaya katılmayı kabul eden 435 öğrenci dahil edilmiştir.

**Bulgular:** Öğrencilerin %10,8'inin enerji içeceği kullandığı, %50,6'sının enerji içeceği hakkında bilgisinin olduğu, %30,3'ünün bilgiyi internet aldığı, %42,6'sının tadını sevdiği için, %29,8'inin enerji verdiği için kullandığı ve %54,5'inin kalp sağlığı için tehlike oluşturduğunu düşündükleri tespit edilmiştir.

**Sonuç ve Öneriler:** Öğrencilerin enerji içeceği tüketme durumları ile cinsiyet ve sigara içme durumları arasında istatistiksel olarak anlamlı bir fark saptanmıştır ( $p<0.05$ ). Öğrencilerin enerji içeceği tüketimi ve etkileri konusunda hem yazılı-görsel-sosyal medya aracılığı ile hem de okullarda bilgi ve bilinç düzeyinin artırılması gerekmektedir.

**Anahtar Kelimeler:** Üniversite öğrencileri, enerji içeceği, alışkanlık

## INTRODUCTION

Energy drinks are defined in the Turkish Food Codex Regulation, Energy Drinks Communiqué as follows: "Energy drink refers to a flavored non-alcoholic beverage containing caffeine, taurine, glucuronolactone, inositol, carbohydrates, amino acids, vitamins, minerals and other food and components." (1).

In recent years, consumption of energy drinks has been increasing among the young in our country as well as all over the world. It draws attention as a product preferred by students, athletes and individuals between the ages of 21-35 (2-3).

The positive effect on cognitive and psychomotor functions, the effect of increasing attention in the ability to drive, the effect of reducing fatigue by increasing long-term attention, the widespread views of increasing physical performance, endurance and energy, and also the effect of some study results cause the use of energy drinks to increase (2-5).

Energy drinks have health benefits as well as harms (6). Many studies found that excessive consumption of energy drinks causes heart rhythm disorder, migraine, anxiety disorder, insomnia, interaction with other drugs and causes addiction (7-10). The use of energy drinks can reduce water consumption, resulting in decreased salivation and dental erosion. The decrease in salivary flow accelerates the formation of dental caries with the decrease in the buffering ability of saliva and the increase in dental erosion accordingly. (11)

Although energy drinks vary according to companies, they generally contain caffeine, guarana, glucuronolactone, taurine, ginseng, L-carnitine, sugar and B vitamins (12). It has been reported that substances that have an effect on the sympathetic system, such as caffeine, are associated with undesirable cardiac events (12-13). In addition, the most important effect of caffeine on the gastrointestinal system

is that it increases the acid secretion of the stomach and causes symptoms such as gastritis and reflux (14). The aim of this study is to determine the level of knowledge and usage habits of university students about energy drinks.

## MATERIAL AND METHOD

The study, which was planned as a descriptive study, was carried out in Harran University, Health Services Vocational School between February and March 2020. The target population of the study consists of 2400 students studying at the Health Services Vocational School. The sampling method was not employed in the study, and the study aims to reach the entire target population. 435 students who agreed to participate in the study were included in the study.

An information form created by literature review was used to collect the data. The Information Form consists of 26 questions that include students' socio-demographic data, daily life habits, energy drink usage and energy drink knowledge levels. The data were collected by applying face-to-face interview technique after the students were informed about the study.

In order to conduct the study, permission was obtained from the participants and the Ethics Committee of Harran University, Vocational School of Health Services. SPSS 20.0 package program was used in the evaluation of the data, and descriptive statistics (number, percentage, mean) and chi-square test were performed in the analysis.

## RESULTS

When Table 1 was examined, it was found that the average age of the students was  $20.25 \pm 1.99$ , and 70.1% of them were women. Considering the education levels of the fathers, it was found that 13.5% did not receive any education; when the education levels of the mothers were examined, 48.5% did not receive any education; 48.2% of the students stays in the dormitory, 12% works, and 31.7% have a family income less than their expenditure.

**Table 1. Percentage distribution of university students socio-demographic characteristics**

Variable		
<b>Gender</b>	Male (%)	129 (29.9)
	Female (%)	306 (70.1)
<b>Father's education status</b>	illiterate (%)	24(5.5)
	Literate (%)	35(8.0)
	Primary school (%)	150(34.5)
	Middle School (%)	115 (26.4)
	High school (%)	74 (17.0)
<b>Mother's Educational Status</b>	University (%)	37 (8.5)
	Illiterate (%)	151 (34.7)
	Literate (%)	60(13.8)
	Primary school (%)	131 (30.1)
	Middle School (%)	56(12.9)
<b>Income status</b>	High school (%)	26(6.0)
	University (%)	9 (2.1)
	Income less than expenses (%)	138(31.7)
	Income equal to expenses (%)	260 (59.8)
<b>Working Status</b>	Income more than expenses (%)	37 (8.5)
	Yes (%)	52 (12.0)
	No (%)	383 (88.0)
<b>Shelter</b>	Credit dormitories institution (%)	175 (40.2)
	Private dormitory (%)	35 (8.0)
	home with friends (%)	43 (9.9)
	with family (%)	151 (34.7)
	Alone (%)	8 (1.8)
	Other (%)	23 (5.3)

When Table 2 was examined, it was found that 13.8% of the students smoke, 84.6% consumes coffee, and 75.4% exercises occasionally.

**Table 2. Percentage distribution of university students about their daily living habits**

Smoking	Yes (%)	60 (13.8)
	No (%)	375 (86.2)
Alcohol Use Status	Yes (%)	13 (3)
	No (%)	422 (97)
Coffee Consumption status	Yes(%)	368 (84.6)
	No (%)	64 (14.79)
Do you sport activite?	Everyday (%)	28 (6.4)
	Several times a week (%)	79 (18.2)
	Sometimes (%)	328 (75.4)

When Table 3 is examined, it has been found that 10.8% of the students drink energy drinks; 42.6% of those drink it as they like the taste; 29.8% drink it as it gives energy. It was found that 50.6% of the students had knowledge about energy drinks, 30.3% of them got the information from the internet and 54.5% of them thought that it was dangerous for their heart health.

**Table 3. Energy drink consumption habits of university students and their level of knowledge about energy drinks**

Do you consume energy drinks?	Yes (%)	47 (10.8)
	No (%)	388 (89.2)
Do you know about energy drink?	Yes (%)	220 (50.6)
	No (%)	215 (49.4)
Where did you get the information?	School (%)	9 (5.1)
	Newspaper, television (%)	68(15.6)
	Friend (%)	29 (6.7)
	Internet (%)	132(30.3)
Are energy drinks harmful?	Yes (%)	203(46.7)
	No (%)	24 (5.5)
	No idea (%)	298 (47.8)
What is the effect of energy drink on health?	Dangerous for the heart (%)	237 (54.5)
	Awake(%)	131(30.1)
	Provides energy (%)	189 (43.4)
	Source of vitamins (%)	21(4.8)
	No health benefit (%)	206 (47.4)
What is your reason for consuming energy drinks?	I like the taste (%)	20 (42.6)
	To feel energetic (%)	14 (29.8)
	Because it improves exercise performance (%)	5 (10.6)
	When I need to be sleep deprived (%)	7 (14.9)
	To increase attention (%)	5 (10.6)

When Table 4 was examined, a statistically significant difference was found between the energy drink consumption of the students and their gender and smoking habit (p<0.05).

**Table 4. Comparison of students' use of energy drinks according to their characteristics**

Variables	Energy drink use status				X <sup>2</sup>	p
		Yes	No			
Gender	Male (%)	24 (51.1)	105 (81.4)	11.49	0.001	
	Female (%)	23 (7.5)	282 (92.5)			
Smoking	Yes (%)	15 (25.0)	45 (75.0)	14.55	0.001	
	No (%)	32 (8.5)	343 (91.5)			

**DISCUSSION**

The use of energy drinks has been increasing constantly around the world. This study was conducted to determine the level of knowledge and usage habits of university students about energy drinks.

When education level of the fathers of the students who participated in the study was examined, it was found that

13.5% did not receive education; when education level of the mothers' was examined, 48.5% did not receive any education. The study found that 12% of the students are working and 31.7% of them have a family income less than their expenditures.

The study found that 48.2% of the students participating in the study stay in the dormitory, 34.7% lives with their



families and 9.9% lives at home with their friends. In a study conducted on university students, it was found that 20% of the students stay with their families, 27% in the dormitory, and 30% with friends (15); in another study, it was found that 31% of the students stay with their families, 22% in the dormitory, and 44% at home with friends (16). In this study, it is assumed that the large amount of students living in the dormitory is due to their economic status.

When Table 2 was examined, it was found that 13.8% of the students smoke; 84.6% consumes coffee and 75.4% exercises occasionally. In different studies on students, cigarette consumption varies between 37-48%. (15-16-17). Exercise status also varies between 51-65%. (15-17). It was found that 10.8% of the students participating in the study use energy drinks. In studies conducted on university students in literature, the rates of energy drink usage vary between 17.5% and 55%. (15, 18, 19).

It was found that 10.8% of the students participating in the study use energy drinks. In studies conducted on university students in literature, the rates of energy drink usage vary between 17.5% and 55% (15, 18, 19). It is assumed that these differences are due to the fact that the groups participating in the study have different cultural characteristics, different economic levels and living in different geographical conditions.

It was found that the 30% of the students participating in the study received information and were affected from internet; 6% from friends, and 15% from television-newspaper. In a study, it was found that 32.2% of students consuming energy drinks were influenced by their friends; 27.5% by advertisements, and 40.3% by other sources (17). These results clearly show that students are influenced by the internet and advertisements.

When the students participating in the study were asked about the effects of energy drinks on health, 54% answered that it is dangerous for the heart, 30% answered that they keep awake; 43% answered that they provide energy; 47% answered that they have no health benefits. In a study, 62% of the students stated that energy drinks are dangerous for the heart; 46% stated that they reduce sleep time; 26% stated that they have a negative effect on the kidneys. (15) On the other hand, the most reported side effect was palpitations in another study (20). Consistent with our study, these results show that students know the effects of energy drinks on heart health. In addition, the effects of energy drink on the heart range from simple palpitations to myocardial infarction and sudden cardiac arrest. It exerts a positive inotropic effect on heart function causing an increase in heart rate, cardiac output, contractility, and arterial blood pressure on the heart. In addition, it has been reported to cause myocardial infarction as a result of affecting platelet aggregation and endothelial function in the early period in healthy young adults (21-22).

42.6% of the students who consume energy drinks stated that they like the taste; 29.8% stated that they use it because it gives energy. When different studies conducted on students were examined, it was found that 55% of the students stated that they consume energy drinks because they like the taste (15) while 43% stated that they consume it to

stay awake, 61% to make cocktails with alcohol, and 35% for their taste (16). In addition, 67% of the students indicated insufficient sleep as the most common reason for drinking energy drinks (18), while another study indicates the struggle with fatigue (20). The reasons for using energy drinks differ according to the geography where the students live.

A statistically significant difference was found between the energy drink consumption status of the students and their gender and smoking status. In other studies conducted with students, it was found that male students tend to consume energy drinks more (19-20, 23).

## CONCLUSION

A statistically significant difference was found between the energy drink consumption status of the students and their gender and smoking habit. It is necessary to increase the level of knowledge and awareness of students about energy drink consumption and its effects, both through written-visual-social media and in schools.

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

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## A Case of High Dose Metoprolol Poisoning; Case Report and Literature Review

Yüksek Doz Metoprolol Zehirlenme Vakası; Case Report ve Literatürün Gözden Geçirilmesi

Metin Ocak<sup>1</sup> MD, Halil Çetinkaya<sup>1</sup> MD, Hüseyin Kesim<sup>1</sup> MD

<sup>1</sup>Gazi State Hospital, Emergency Clinic Samsun, Turkey

**Corresponding Author** : Dr. Metin Ocak.

Gazi State Hospital, Emergency Clinic  
Samsun, Turkey.

e-mail: mdmocak@gmail.com

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### Abstract

$\beta$ -Blockers are prescribed by physicians for many medical reasons (hypertension, long-term prophylaxis of angina pectoris, myocardial infarction, stable heart failure treatment, cardiac arrhythmias, etc.). Although cases of  $\beta$ -blocker poisoning have a low rate of 0.9% among all poisoning cases, they have a high mortality rate. Metoprolol, a type of  $\beta$ -blocker, is a selective  $\beta_1$ -adrenoceptor antagonist with sympathomimetic effect. This article aims to present a case who took high-dose metoprolol for suicidal purposes and to examine metoprolol poisoning and its treatment in the light of current literature.

### Öz

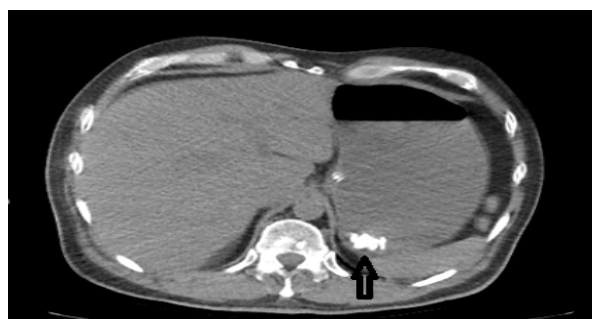
$\beta$  -blokerler hekimler tarafından bir çok tıbbi gerekçe ile reçete edilmektedirler (Hipertansiyon, anjina pektorisin uzun süreli profilaksisi, miyokard infarktüsü, stabil kalp yetmezliği tedavisi, kardiyak aritmiler, v.b.).  $\beta$  -bloker zehirlenmeleri tüm zehirlenmeler içerisinde % 0.9 gibi düşük bir orana sahip olsa da mortalite oranı yüksek seyretmektedirler. Bir  $\beta$  -bloker çeşidi olan metoprolol semptomimetik etkisi olan selektif  $\beta_1$ -adrenoseptör antagonistidir. Bu makalede suisid amaçlı yüksek doz metoprolol alan bir olgunun sunumu ve metoprolol zehirlenmelerinin ve tedavisinin güncel literatür ışığında incelenmesi amaçlanmıştır.

## Introduction

Beta-adreno receptor antagonists, more commonly known as  $\beta$ -blockers, are prescribed by physicians for many medical reasons (hypertension, long-term prophylaxis of angina pectoris, myocardial infarction, stable heart failure treatment, cardiac arrhythmias, etc.) (1). Although cases of  $\beta$ -blocker poisoning have a low rate of 0.9% among all poisoning cases, they have a high mortality rate (2). According to the data of the American Poison Control Center published in 2019,  $\beta$ -blocker poisoning is reported to be in the 7th place among 25 deadly substances (3). In  $\beta$ -blocker poisoning with high lipid solubility; serious central nervous system findings such as seizures, respiratory depression, and coma may be encountered (2). In  $\beta$ -blocker poisoning with high lipid solubility; serious central nervous system findings such as seizures, respiratory depression, and coma may be encountered. In addition, resistant bradycardia-hypotension and shock may occur due to cardiac involvement (2). Metoprolol, a type of  $\beta$ -blocker, is a selective  $\beta_1$ -adrenoceptor antagonist with sympathomimetic effect (4). In addition, it has been reported that metoprolol is the second most commonly prescribed  $\beta$ -blocker after bisoprolol worldwide (5). This article aims to present a case who took high-dose metoprolol for suicidal purposes and to discuss metoprolol poisonings in the light of current literature

## Case Report

The patient, who had a previously known diagnosis of diabetes mellitus, coronary artery disease and schizophrenia, was found unconscious at home by his relatives. The patient was brought to the emergency room by the emergency medical call center (112) teams. In the physical examination findings of the patient; his general condition was poor, he was unconscious, his respiration was superficial, arterial blood pressure: 60/40 mmHg, heart rate: 46/min, and glasgow coma score: 5. Elective endotracheal intubation was applied to the patient to ensure airway safety. Bolus IV fluid therapy, dopamine and nor-epinephrine infusion were administered for blood pressure regulation. In the first anamnesis taken from the relatives of the patient, it was learned that the patient did not have any problems and suddenly became ill. There was no evidence of poisoning in the first anamnesis. In the patient's examinations, the findings were as follows: pH:7.29, PO<sub>2</sub>:52 mmHg, PCO<sub>2</sub>:36.1 mmHg, HCO<sub>3</sub>:17.7 mmol/L, Wbc:11.9  $10^9$ /L, Hgb:13.1 g/dL, plt:120  $10^9$ /L, glucose:319 mg /dL, creatinine: 1.5 mg/dL, Na:128 mmol/L, CRP: 20 mg/L. First degree AV block and bradycardia were detected in the patient's electrocardiography. In the patient's abdominal tomography, a linear well-circumscribed image suggestive of multiple drug capsules was seen in the gastric lumen (**Figure 1**).



**Figure 1.** Drug particles visible in the stomach lumen on the patient's abdominal tomography

Thereupon, the relatives of the patients were informed that there might be drug intoxication and they were asked to look for the drug boxes at home. About 1 hour later, the patient's relative said that the patient may have taken about 40 of his

own medicine, which contains 50 mg of metoprolol. Thereupon, gastric lavage with nasogastric tube and 50 gr activated charcoal were applied to the patient. It was observed that drug particles came from the lavage fluid. Since the arterial blood pressure values of the patient were 60/30 mmHg, the patient was administered 3\*1 mg of atropine. In addition, calcium gluconate 30 ml slow push was applied to the patient. Since there was no response to atropine and calcium treatment, 2\*5 mg glucagon treatment was administered to the patient with an interval of 15 minutes. Since there was no adequate response to this treatment, the patient was started on 5 mg/hour IV infusion therapy. The patient was admitted to the intensive care unit for continued treatment and follow-up. The patient, who did not respond to all supportive treatments in the intensive care unit, was requested to be referred to the upper center for further treatment.

However, the patient whose hemodynamics was unstable could not be referred. Despite all the interventions, the patient died approximately 36 hours after hospitalization.

## Discussion

Blockade of  $\beta$ -receptors results in decreased production of intracellular cyclic adenosine monophosphate (cAMP). As a result, the multiple metabolic and cardiovascular effects of circulating catecholamines are reduced (6). The most important predictive factor in  $\beta$ -blocker toxicity is whether the drug has membrane stabilizing activity. It is known that metoprolol has low membrane stabilizing activity only at high doses (7). It is reported that the therapeutic plasma concentration range of metoprolol in the treatment of cardiovascular diseases is 0.035-0.50 mg/L (8). Metoprolol is metabolized by the liver and excreted by the kidneys. The half-life is 3-7 hours. It has moderate lipid solubility and blocks  $\beta_1$  adrenergic receptors. It is reported that the threshold value is 400 mg in adults and 5mg/kg in children (9). Metoprolol overdose, depending on the dose taken in the clinic, may lead to symptoms such as bradycardia, hypotension, cardiogenic shock, hypoglycemia, hypothermia, seizure, altered consciousness, QT prolongation and QRS enlargement (10). In this case, the dose taken by the patient was not clear due to the unreliability of the anamnesis and the inability to measure the blood metoprolol level in our hospital. Our patient had signs of hypotension, cardiogenic shock, bradycardia, first-degree AV block, and altered consciousness.

Due to its lipophilic properties, the drug crosses the blood-brain barrier in  $\beta$ -blocker poisoning and central nervous system effects may be observed. Therefore, rapid airway management is important in such patients (9). In literature, majority of the publications recommend gastric lavage and the administration of activated charcoal in  $\beta$ -blocker poisoning (11,12). However, cases that died despite gastric lavage and administration of activated charcoal were also reported (13). Removal of drug particles by lavage after high-dose drug intake may have a positive effect on prognosis. However, in this case, it was thought that the lavage procedure limited its possible positive effect. In case of seizures in  $\beta$ -blocker poisoning, the first choice is benzodiazepines. If there is QTc prolongation, magnesium sulfate is given; if QRS widening is present, sodium bicarbonate is given in the treatment (9).

In the treatment of hypotension and shock, IV fluids and ketocalamine and/or high-dose insulin euglycemic treatments are recommended. The mechanism of action of high-dose insulin therapy in  $\beta$ -blocker poisoning is not clear. In the literature, it is unclear whether high-dose euglycemic insulin therapy or ketocalamine therapy is superior. However, case series in which high-dose insulin euglycemic therapy is more effective constitute the majority (1,14,15). In another study, it was reported that the combined use of ketocalamine and high-dose insulin euglycemic therapy is more effective (16). Such patients may also benefit from the treatment of calcium salts (7). In this case, the patient was administered ketocalamine and

calcium therapy, but no adequate response was obtained. The effect of IV glucagon therapy in patients with hypotensive and cardiogenic shock is also unclear when compared to other agents. Glucagon activates adenylate cyclase independently of beta-adrenergic agents and causes an increase in cAMP. increased cAMP: Increases the amount of intracellular calcium required for depolarization by increasing contractility. In a previous study, it was reported that high-dose glucagon treatment increased mean arterial pressure and mean heart rate (17). In another study, it was reported that glucagon therapy was not superior to high-dose insulin euglycemic therapy and lipid emulsion therapy (18). In previous studies on animals studies, it has been reported that IV glucagon treatment increases heart rate but does not have a positive effect on mean arterial pressure, cardiac output and mortality (14,20). In this case, the patient was administered IV glucagon bolus and infusion therapy, but no response was obtained. There are limited publications in the literature supporting the efficacy of atropine therapy in bradycardia for  $\beta$ -blocker poisoning. In a previous case report, it was reported that 0.5 mg of atropine treatment increased heart rate and mean arterial pressure in a 15-year-old female patient who received 500 mg of atenolol (20). In a previous study on animal, it was reported that IV atropine was effective in correcting bradycardia due to propranolol overdose (21). The patient in this presentation was also administered IV atropine treatment, but no response was obtained.

There are many case reports and animal studies investigating the effectiveness of IV lipid emulsion therapy in the treatment of  $\beta$ -blocker poisoning. However, there is no clear evidence supporting the effectiveness of this treatment. In a previous study with 36 patients, 10 patients were given IV lipid emulsion therapy and it was found to be ineffective (22). However, in some case reports, it has been reported that IV lipid emulsion therapy increases heart rate and blood pressure (11,12,23). An experimental study showed that high-dose insulin therapy was more effective than IV lipid emulsion therapy (24). More extensive studies are needed to investigate the efficacy of this treatment.

Since metoprolol is not a water-soluble drug, hemodialysis treatment has no efficacy on it (9). Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) therapy also plays an active role in  $\beta$ -blocker poisoning in cardiogenic shock resistant to all pharmacotherapy. In a previous comparative observational study, V-A ECMO treatment was shown to be effective in eliminating hemodynamic instability (25).

There are case reports reporting that cardiac pacemaker application is also effective to eliminate hemodynamic instability in  $\beta$ -blocker poisoning cases (26).

As a result, treatment of  $\beta$ -blocker poisoning is complex and difficult for physicians. Despite all treatment efforts, mortality is high in such patients. If possible, these patients should be treated and followed up in fully equipped hospitals with toxicology centers. In treatment, catecholamines, vasopressors, fluid therapy, high-dose insulin euglycemic therapy and V-A ECMO applications have a mortality-lowering effect. However, the mortality-reducing effect of glucagon, lipid emulsion therapy, calcium and atropine is not clear (1)

**Conflict of Interest:** None declared

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## **Dramatic Response to Ozone Application: Raynaud's Phenomenon**

### **Ozon Uygulamasına Dramatik Yanıt: Raynaud Fenomeni**

**Onur Öztürk<sup>1,2</sup>, İsmail Şen<sup>2</sup>, Gülşah Bal<sup>1</sup>, Muhammed Emin Göktepe<sup>1</sup>**

<sup>1</sup> Samsun Education and Research Hospital, Clinic of Family Medicine, Samsun, Turkey

<sup>2</sup> Samsun Education and Research Hospital, Traditional and Complementary Medicine Center, Samsun, Turkey

#### **Abstract**

Ozone application is used in medicine with many indications, vascular diseases are one of them. In this case report, the regression of ischemia-related complaints in the finger of a young female patient with Raynaud's Phenomenon after ozone application was mentioned.

**Keywords:** Ozone, Raynaud's phenomenon

#### **Öz**

Ozon uygulamasının birçok endikasyonla tıpta kullanımı söz konusudur, vasküler hastalıklar da bunlardan biridir. Bu vaka sunumunda Raynaud Fenomeni olan genç kadın hastanın ozon uygulaması sonrası parmağındaki iskemi kaynaklı şikayetlerinin gerilemesinden bahsedilmiştir.

**Anahtar kelimeler:** Ozon, Raynaud Fenomeni

#### **Introduction**

Ozone gas which was discovered in 1839 is an inorganic molecule consisting of three oxygen molecules, highly soluble in water and highly oxidant (1). In medical ozone therapy, ozone produced from pure oxygen by a special generator is mixed with the patient's own blood, distilled water or applied to various parts of the body in gaseous form. It is used in medicine with many indications such as dental caries, hypercholesterolemia, ischemia (2).

Raynaud's Phenomenon (RP) is a disorder characterized by cold-induced vasoconstriction in the fingers and toes and progressing with attacks.

Diagnosis is easy when the characteristic skin color change (white, blue-purple or red) that occurs during the occurrence of an attack (3). This case report deals with a patient diagnosed with RP whose complaints was eliminated with ozone application.

#### **Presentation of the case**

A 37-year-old female patient applied to our traditional and complementary medicine center in July 2021 with complaints of coldness, pain, bruising and burning sensation in the left hand that had been present for several months. Her symptoms are triggered by stress

and cold. The general condition was good; she was conscious, oriented, cooperative, and vital signs were within normal limits. There is an ecchymotic image in the 5th phalanx of the left hand (**Figure-1A**).

In her medical history, it is learned that cilostazol 100 mg 2x1 medication was administered with the diagnosis of RP in the cardiovascular surgery clinic that she applied with the same complaints; after a month of treatment, there was some regression in her complaints, then she stopped taking the drug and her complaints recurred a few weeks later. The patient, who was hospitalized this time in the same clinic, left the hospital voluntarily, as her complaints continued. In addition, the patient has been smoking 1 pack of cigarettes a day for 20 years. There is no such characteristic in the medical history of her family.

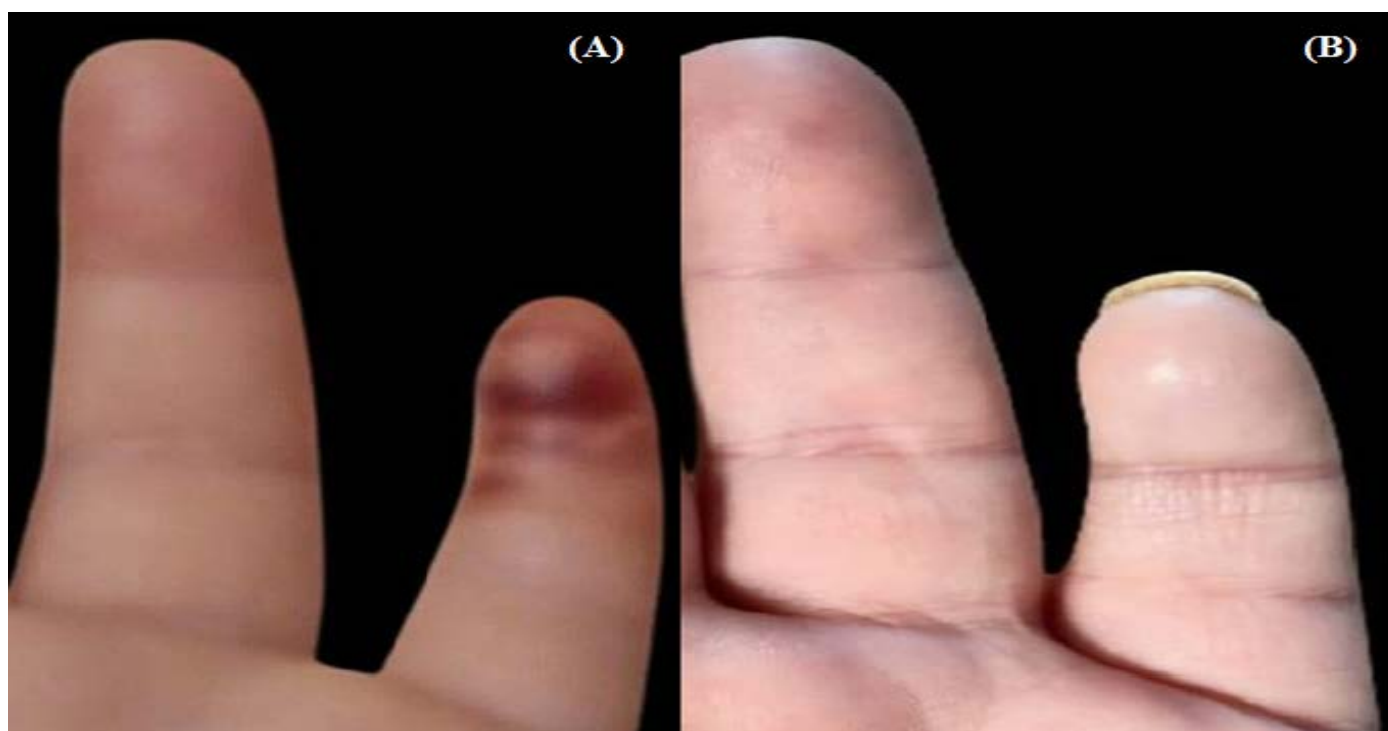
A total of 12 major autohemotherapy (between 20 and 35 gamma) and 4 minor autohemotherapy (30 gamma) sessions of ozone therapy were applied to the patient, 3 days a week, for a month. Intermediate sessions, once a week, were recommended to the patient who was recommended to quit smoking. The patient's pain decreased and her ecchymotic appearance improved (**Figure-1B**).

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**Corresponding Author:** Onur ÖZTÜRK, M.D, Assoc. Prof. Clinic of Family Medicine Head of Traditional and Complementary Medicine Center Samsun Education and Research Hospital, Samsun, Turkey Tel: +90 (554) 7536566

Email: dr.onurozturk@yahoo.com ORCID: 0000-0002-3371-6051

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**Figure -1.** (A) Image before treatment an ecchymotic 5th phalanx of the left hand. (B) Post treatment

### Discussion

Ozone application has properties such as increasing the amount of oxygen in the blood, increasing blood circulation, activating erythrocyte metabolism, restoring tissue oxygenation and cell function (4). Larini et al. revealed that ozone autohemotherapy can activate antioxidant enzymes and scavenge free radicals (5), and various studies have shown that ozone autohemotherapy can be used to treat vascular diseases (6,7).

RP, which is a vascular problem, may respond well to ozone application as it manifests itself with ischemia in the limbs. Considering the literature on this matter, Haug et al. were among the first physicians who applied ozone to a patient with RP and became successful (8). Cook et al. reported that a combined therapy containing ozone may be beneficial in severe

RP (9). The clinical management of our patient will also contribute to the literature in this regard.

RP is more common in women in their thirties (3). The demographic datas of our patient are compatible with the literature. RP is clinically classified as primary and secondary. Primary RP is idiopathic and is the most common form of the disease. Secondary RP may accompany diseases such as autoimmune or cancer, or it may be caused by smoking or the use of certain drugs (3). The fact that our patient did not have a known chronic disease may suggest the diagnosis in favor of primary RP, while being a smoker may increase the severity and frequency of his current complaints.

Ozone application provided significant clinical improvement in the patient's symptoms. Thus, it can be applied as a supportive treatment in patients with RP.

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## **A Rare Cause of Chronic Constipation in The Field of Family Medicine Practice: Dyssynergic Defecation** **Aile Hekimliği Pratiğinde Nadir Rastlanan Bir Kronik Kabızlık Nedeni: Dissinerjik Defekasyon**

**Onur Öztürk<sup>1</sup>, Tuğba Şenel<sup>2</sup>, Muhammed Okuyucu<sup>3</sup>**

<sup>1</sup> Samsun Education and Research Hospital, Clinic of Family Medicine, Samsun, Turkey

<sup>2</sup> Department of Internal Medicine, Division of Gastroenterology, Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey

<sup>3</sup> Department of Internal Medicine, Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey

### **Öz**

Kabızlık seyrek dışkılama, ağrı, sertlik ve zor dışkı geçişi ile sonuçlanabilen bir bozukluktur ve patogenezi çok faktörlüdür. Otuz iki yaşında kadın hasta çocukluktan beri mevcut olan kabızlık şikâyeti ile aile hekimi kliniğine başvurmuştur. Etiyolojik araştırma yapılan hastada kronik kabızlığın nadir nedenlerinden biri olan dissinerjik defekasyon tespit edilmiştir. Kronik kabızlık; risk faktörlerinin ve etyolojik nedenlerinin göz önünde bulundurularak ayrıntılı bir öyküyle değerlendirilmesi gereken bir durumdur.

**Anahtar Kelimeler:** Aile hekimi, kabızlık

### **Abstract**

Constipation is a disorder that can result in infrequent defecation, pain, stiffness and difficult stool passage and pathogenesis is multifactorial. A 32-year-old female patient was admitted to family medicine clinic with the complaint of constipation that has been present since childhood. Dyssynergic defecation, which is one of the rare causes of chronic constipation, was detected in the patient whose etiological investigation was carried out. Chronic constipation is a condition that should be evaluated with a detailed medical history, taking into accounts the risk factors and etiological causes.

**Keywords:** Family practice, constipation

### **Introduction**

Constipation is a disorder that can result in infrequent defecation, pain, stiffness and difficult stool passage. Pathogenesis is multifactorial depending on genetic predisposition, socioeconomic status, low fiber consumption, lack of fluid intake, inactivity, hormonal disorder, side effects of drugs and body anatomy. Appropriate clinical approach is required to evaluate secondary causes such as systemic diseases and drugs (1). After excluding secondary causes of constipation, evaluation should be made for chronic idiopathic constipation, one of the most common gastrointestinal disorders worldwide. Chronic idiopathic constipation is divided into three subtypes as dyssynergic defecation, slow transit constipation, and normal transit constipation, which are problems with rectal defecation (2). In this study, a case having dyssynergic defecation for a long time is discussed.

### **Presentation of the case**

A 32-year-old female patient was admitted to our family medicine clinic in April 2021 with the complaint of constipation that has been present since childhood. The patient had applied to clinicians several times with this complaint and she was administered pinaverium bromide, lactulose and magnesium hydroxide treatments from time to time. Constipation complaints of the patient, who had benefited from medical treatments for a short time, recurred each time. We learned that the patient, who had no known additional

systemic disease and had a normal menstrual cycle, had occasional hemorrhoidal bleeding. In the physical examination of the patient, who did not have any additional findings in the system examination, it was observed that she had mild tenderness in the left lower quadrant upon deep palpation.

In laboratory findings; Hb: 8.9 g/dL, MCV: 64.5 fL, RDW: 19.1 %, PLT: 367 10<sup>3</sup>/uL, iron: 17.7 µg/dL, iron binding capacity: 388 µg/dL, iron saturation: 4.5 %, ferritin: 3.7 ng /mL, TSH: 3.9 µIU/mL, complete urinalysis was found to be normal. Electrocardiography was sinus rhythm and abdominal ultrasonography was normal. Upper and lower endoscopies were requested in terms of etiological investigation for the patient with iron deficiency anemia and oral iron preparation treatment was started. In the total colonoscopy evaluation of the patient whose esophagogastroduodenoscopy evaluation was normal, mild melanosis coli and grade 1 internal hemorrhoids were detected. In the first month of iron treatment, iron parameters were found to be normal and Hb: 13.6 g/dL. Anorectal manometric examination is planned for the etiology of chronic constipation. As a result of the examination; anal sphincter resting pressure is low, pressure increase is sufficient with voluntary contraction of the sphincter, rectoanal inhibitory reflex is normal, there is no sphincter relaxation with straining, and rectal sensitivity is decreased. Accordingly, dyssynergic defecation was considered as the cause of chronic constipation

in the patient, and biofeedback treatment was recommended for constipation. The patient's constipation complaint was eliminated after the treatment.

### Discussion

Chronic constipation is a condition that should be evaluated with a detailed medical history, taking into accounts the risk factors and etiological causes. Since it is encountered with a prevalence of up to 80% in the general population (3), it is frequently encountered in routine family medicine practice and therefore it is important to manage it. Constipation is more common over the age of 65 and it is more common in women, as in our patient (4). Our patient applied to clinicians for constipation complaints at various times and used different medical treatments for short-term benefit, but the complaint recurred each time. This revealed the importance of examining the etiological causes in more detail and planning the appropriate investigations in our patient.

The relationship between constipation and the development of colorectal cancer is controversial, and further investigation is required in the presence of alarm symptoms (5). Since our patient had deep anemia as an alarm symptom, endoscopic examination was required. No cancer was found as a result of endoscopic examinations. The cause of the anemia in the patient was thought to be intermittent hemorrhoidal bleeding due to the effect of chronic constipation, and its treatment was planned.

Anorectal manometer is a diagnostic tool that can show rectal reflexes, sensation, compliance, rectosphincter reflex at rest and during defecation, and helps to recognize dyssynergic defecation, especially as in our patient (6,7). Biofeedback therapy is a behavioral approach that can be used to cure inappropriate contraction of the pelvic floor muscles and external anal sphincter during defecation in patients with defecation dysfunction such as dyssynergic defecation (8,9). It has been found that more than 70% of patients with gastrointestinal disorders were relieved of symptoms with biofeedback therapy (10). Our patient benefited from biofeedback treatment and her constipation complaint was eliminated.

While the causes of chronic constipation, which is difficult to manage in common practice, are being examined, dyssynergic defecation should also be kept in mind, and the

patient should be referred for further investigation.

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