Pansystolic Tricuspid Regurgitation May Be Associated with Patent Foramen Ovale in Healthy Young Adults

Sağlıklı Genç Erişkinlerde Triküspid Yetersizliği Patent Foramen Ovale ile İlişkili Olabilir

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ABSTRACT Objective: Tricuspid regurgitation is a common finding in healthy subjects. This finding may associate with patent foramen ovale that it is relatively common in the community. No study was found investigating the association between tricuspid regurgitation and patent foramen ovale. The aim of this study was to evaluate the association between tricuspid regurgitation and patent foramen ovale in healthy young subjects. **Material and Methods:** Eighty-eight subjects were included in the study. Subjects who had evidence of cardiovascular or other systemic disease were excluded from the study. Detection of tricuspid regurgitation was performed with color flow Doppler. The tricuspid regurgitation jet length and area were measured using color Doppler images. The tricuspid regurgitation jet peak velocity and duration were measured with continuous wave Doppler modality. Study subjects were divided into two groups according to whether patent foramen ovale was present [PFO (+) group and PFO (-) group]. **Results:** There were 23 subjects in the PFO (+) group and 65 subjects in the PFO (-) group. Tricuspid regurgitation flow was pansystolic in 70% of subjects in the PFO (+) group and 8% of subjects in the PFO (-) group ($p<0.001$). Sensitivity and specificity pansystolic tricuspid regurgitation for detecting patent foramen ovale were 70% and 92% respectively. **Conclusion:** Our data indicate that pansystolic tricuspid regurgitation associated with patent foramen ovale in healthy individuals. Pansystolic tricuspid regurgitation has high specificity and sensitivity for detecting of patent foramen ovale.

Key Words: Foramen ovale, patent; tricuspid valve insufficiency

ÖZET Amaç: Sağlıklı bireylerde triküspid yetersizliği sık rastlanan bir bulgudur. Bu bulgu toplumda göreceli olarak sık görülen patent foramen ovale ile ilişkili olabilir. Patent foramen ovale ve triküspid yetersizliğini araştıran herhangi bir yayına rastlamadık. Çalışmamızın amacı, sağlıklı genç erişkinlerde patent foramen ovale ve triküspid yetersizliği arasındaki ilişkiyi araştırmaktır. **Gereç ve Yöntemler:** Sağlıklı 88 birey çalışmaya alındı. Kardiyovasküler veya başka bir sistemik hastalığı olanlar çalışmaya alınmadı. Triküspid yetersizliği renkli Doppler ekokardiyografi ile saptandı. Triküspid yetersizlik akımının uzunluğu ve alanı renkli Doppler görüntülerden elde edildi. Triküspid yetersizlik akımının zirve hızı ve süresi devamlı Doppler spektral görüntülerden ölçüldü. Çalışma vakaları patent foramen ovale olup olmadığına göre PFO (+) grup ve PFO (-) grup olmak üzere 2 gruba ayrıldı. **Bulgular:** Çalışma kriterlerine uyan 88 vakanın 23'ü PFO (+) grupta ve 65'i PFO (-) grupta idi. Triküspid yetersizlik akımı PFO (+) gruptaki vakaların %70'inde pansistolik iken bu oran PFO (-) grupta %8 idi. Patent foramen ovalenin saptanmasında pansistolik triküspid yetersizliğinin özgüllüğünü %92 ve duyarlılığını %70 olarak bulduk. **Sonuç:** Çalışmamızın bulguları sağlıklı genç erişkinlerde pansistolik triküspid yetersizliğinin patent foramen ovale ile ilişkili olabileceğini göstermektedir.

Anahtar Kelimeler: Oval foramen, patent; triküspid kapak yetersizliği

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Tricuspid regurgitation is a commonly encountered condition in healthy subjects. In various studies, the prevalence of tricuspid regurgitation has been reported to be between 44-100% in normal subjects.[1-4] Tricuspid regurgitation in absence of structural abnormalities of tricuspid leaflets and dilatation of the right ventricle is called "physiological tricuspid regurgitation". This physiological regurgitant flow is a thin central jet and often limited to early systole.

Patent foramen ovale is an opening between the left and right atria during intrauterine life. After birth, as a result of decreased pulmonary vascular resistance, the septum primum is pushed towards to the septum secundum and functional closure occurs. The anatomical closure occurs at the end of the first year of life. But, in some individuals, the closure is incomplete. Echocardiographic and autopsy studies have shown that the closure is incomplete in 25% of the population.[5,6] As a result of this incomplete closure, the foramen ovale remains open in one out of four adults. It has been reported that patent foramen ovale is a strong risk factor for cryptogenic stroke, especially in young adults.[7] In addition, patent foramen ovale is a high-risk situation for paradoxical embolism.[8] Recently, it has been shown that patent foramen ovale is closely related with migraine.[9] Finally, it has been demonstrated that patent foramen ovale is associated with decompression illness.[10]

The standard method for detecting a patent foramen ovale is transesophageal echocardiography using contrast agent (agited saline). This method is semi-invasive, uncomfortable, expensive, and is not available in many clinics.

The aim of the study is to investigate the association between tricuspid regurgitation and patent foramen ovale in healthy young subjects.

MATERIAL AND METHODS

INCLUSION CRITERIA

This was a retrospective, cross-sectional study. Subjects with suspected patent foramen ovale who had been referred to our cardiology clinic for transesophageal echocardiography between April 2014 and August 2015 were evaluated for possible inclusion in the study. Demographic, clinic, echocardiographic and laboratory data were obtained from the files of the subjects.

EXCLUSION CRITERIA

The exclusion criteria consisted of (1) patients who had cardiovascular or other systemic disease (according to the physical examination, transthoracic echocardiography, ECG, and laboratory results), (2) subjects who were used cardiovascular drug, alcohol or narcotic drug consumption, cigarette smoke, and obesity (body mass index >36 kg/m^2), (3) subjects who were younger than 18 or older than 40 years.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Transesophageal echocardiography was done with a multiplane transesophageal echocardiography probe. Ten ml of agitated saline solution was used as a contrast agent. Agitated saline injection via antecubital vein with standardized Valsalva maneuver was used for detection of patent foramen ovale. Patent foramen ovale was considered present if at least 3 bubbles were seen in the left atrium within 3 cardiac beats after complete right atrial opacification. Study subjects were divided into two groups according to whether patent foramen ovale was present [PFO (+) group and PFO (-) group].

Systolic pulmonary artery pressure was estimated from the peak systolic velocity of the tricuspid regurgitation obtained with continuous-wave Doppler using the modified Bernoulli equation and adding the estimated right atrial pressure (5 mmHg in all subjects).

STATISTICAL ANALYSIS

SPSS for Windows version 20.0 (SPSS Inc., Chicago, IL), a statistical package program, was used for statistical analysis. Normally distributed continuous data were expressed as mean±standard deviation; non-normally distributed continuous variables were presented as median (minimum-maximum). Categorical data were expressed as numbers with percentages. We used the Student t test for normally distributed continuous variables

and the Mann-Whitney-U test for non-normally distributed continuous variables. Categorical data were compared using the χ^2 test. A p value less than 0.05 was accepted as statistically significant. Study protocol was approved by institutional ethics committee.

RESULTS

DEMOGRAPHICS

Eighty-eight subjects who met the study criteria were enrolled in the study. Our study group were consisted 32 men (36%) and 56 women (64%). Sixty six subjects (78%) had tricuspid regurgitation and there were 22 subjects (25%) who did not have tricuspid regurgitation. There were 23 subjects in the PFO (+) group and 65 subjects in the PFO (-) group. Forty-two of subjects (65%) were female in the PFO (-) group and 14 subjects (61%) in the PFO (+) group. The gender was similar in the two groups (p=0.75). The age (mean± standard deviation) was 28.1± 6.4 years in the PFO (-) group and 31± 8 years in the PFO (+) group (p=0.08). Body mass index and body surface area were similar in the two groups (p=0.384 and p=0.50, respectively). Demographic characteristics of the groups were shown in Table 1.

TRICUSPID REGURGITANT JET CHARACTERISTICS

The tricuspid regurgitation jet length (cm) was 1.35±0.23 in the PFO (-) group, whereas it was 1.84±0.3 in the PFO (+) group. The tricuspid regurgitation jet length was significantly higher in the PFO (+) group (p=0.019). In the PFO (+) group, the tricuspid regurgitation jet peak velocity (cm/s) was statistically significant higher (237±20 versus 191±25, p<0.001). Tricuspid regurgitant jet area (cm^2) was 1.23±0.42 in the PFO (-) group and 1.98±0.6 in the PFO (+) group. Tricuspid regurgitant jet area was statistically different between the groups (p<0.001). A regurgitant jet that limited early systole was present in 38 of the subjects in the PFO (-) group, while 22 subjects had not regurgitant flow in this group. Thus, there were 60 subjects without pansystolic tricuspid regurgitation in the PFO (-) group. A pansystolic regurgitant jet was detected in 5 of the 60 subjects (8%) in the PFO (-) group. On the other hand, pansystolic regurgitant jet was present in 16 (70%) of the subjects in the PFO (+) group. Only seven subjects (30%) had a regurgitant jet that limited early systole in the PFO (+) group. Finally, pansystolic regurgitant jet was present in 5 subjects (8%) of PFO (-) group, while16 subjects (70%) had pansystolic regurgitant flow in the PFO (+) group. The frequency of pansystolic regurgitant flow was significantly higher in the PFO (+) group (p<0.001). Examples of pansystolic and early systolic TR were presented in Figure 1 and 2 (respectively). The tricuspid regurgitant flow characteristics of the groups were shown in Table 2. Sensitivity and specificity of pansystolic tricuspid regurgitant flow for detection of patent foramen ovale were 70%, and 92%, respectively. Systolic pulmonary artery pressure was significantly higher in the PFO (+) group (p<0.001).

DISCUSSION

Tricuspid regurgitation is a frequently encountered finding in healthy subjects. The frequency has been reported as 44 % to 100% in several older studies.[1-4] In a recent study, it has been found that tricuspid regurgitation prevalence is 73% in healthy population.[11] The large differences between studies may be related to operators or echocardiography instruments. Also, in none of these stu-

TABLE 1: Demographics.

Variable\Group	PFO (-) Group (n=65)	PFO (+) Group (n=23)	P
Age, years (mean±SD)	28.1±6.4	31±8	0.08
Female, n (%)	42 (65)	14 (61)	0.75
BMI, kilogram/m^2 (mean±SD)	23.3±1.85	23.84±1.76	0.348
BSA, m^2 (mean±SD)	1.65±0.1	1.68±0.2	0.50

SD: Standard deviation; BMI: Body mass index; BSA: Body surface area PFO: Patent foramen ovale, SD:Standard deviation.

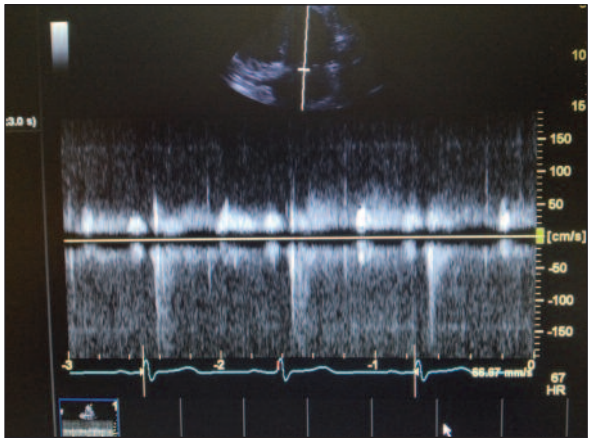

FIGURE 1: An example of early systolic tricuspid regurgitation.
CW: Doppler spectral image.

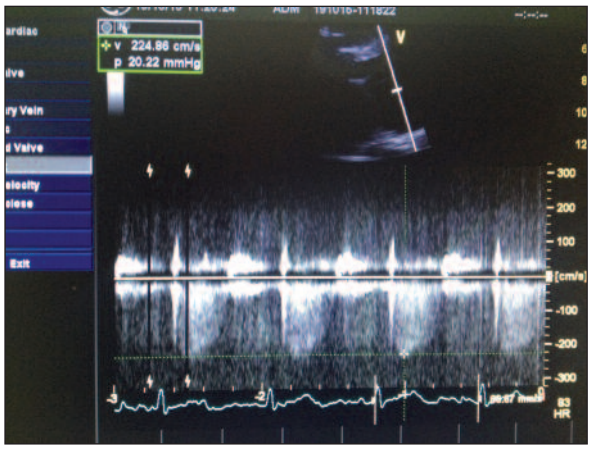

FIGURE 2: An example of pansystolic tricuspid regurgitation.
CW: Doppler spectral image.

dies, patent foramen ovale was not exclusion criteria. It is reasonable that some subjects with patent foramen ovale may be included to the studies. Because of this, some individuals with tricuspid regurgitation may have patent foramen ovale. We aim at providing clarity to this issue in the present study.

It has been shown that color flow mapping has high sensitivity and specificity in detection of mild tricuspid regurgitation.[12] We also used color flow imaging for detection of tricuspid regurgitation. Recently, it has been demonstrated that there are important changes in right ventricular diameters and volumes and tricuspid regurgitation flow characteristics during respiratory cycles.[13] In order to eliminate the effects of breathing, all measurements were made on records at the end expiration in present study.

Pathological tricuspid regurgitation was not exactly defined. In a study, it has been shown that normal tricuspid regurgitation jet length is not enlarged more than 1 cm from leaflet.[14] In another study, it has been reported that tricuspid regurgitation may be as large as 4 cm in subjects without cardiovascular disease.[15] In our present study, regurgitant jet length was not more than 2 cm in all study subjects. In addition, tricuspid regurgitation was central and thin in both groups. These findings have shown that tricuspid regurgitant flow was within physiological limits in the study group. There is significant difference in terms of tricuspid regurgitation jet length between groups. The tricuspid regurgitation jet area was higher in the PFO (+) group. However, there was no significant difference between groups. Tricuspid regurgitant flow peak velocity (with continuous wave Doppler) was

TABLE 2: Tricuspid regurgitant flow characteristics.

Variable\Group	PFO (-) Group (n=65)	PFO (+) Group (n=23)	P
sPAP, mmHg (mean±SD)	20.3±3.6	28±3.7	<0.001
TRJL, cm (mean±SD)	1.35±0.23	1.84±0.30	0.019
TRJPV, cm/s (mean±SD)	191±25	237±20	<0.001
TRJA, cm^2 (mean±SD)	1.23±0.42	1.98±0.60	<0.001
TR, n (%)	43 (66)	23 (100)	<0.001
TR limited to early systole or no TR, n (%)	60 (92)	7 (30)	<0.001
Pansystolic TR	5 (8)	16 (70)	<0.001

sPAP: Systolic pulmonary artery pressure; SD: Standard deviation; TRJL: Tricuspid regurgitant jet length; TRJPV: Tricuspid Regurgitant jet peak velocity; TRJA: Tricuspid regurgitant jet area; TR: Tricuspid regurgitation.

normal acceptable limits in the study population. However, it was statistically higher in the group with patent foramen ovale. In addition, estimated Systolic pulmonary artery pressure was found statistically higher in the PFO (+) group.

It has been reported that physiological tricuspid regurgitation flow is not pansystolic; it is limited to early systole.[16] In our study, regurgitant flow was limited to early systole in most subjects without patent foramen ovale (92%), whereas the ratio was 30% in subjects with patent foramen ovale. Most of the subjects in the PFO (+) group had pansystolic tricuspid regurgitation flow (70%). Moreover, we showed that tricuspid regurgitation that continued throughout entire systole (pansystolic tricuspid regurgitation) had a high sensitivity (70%) and high specificity (92%) for patent foramen ovale in healthy young adults.

These findings indicate that the tricuspid regurgitant volume is greater in subjects with patent foramen ovale compared with subjects without patent foramen ovale. Potential mechanisms were not elucidated in present study. However, it could be speculated that left-to-right shunt causes overcirculation in the pulmonary vascular bed in subject with patent foramen ovale (as in patients with atrial septal defect). Thus, overcirculation in the pulmonary vascular bed causes increased tricuspid regurgitant volume (probably increasing pulmonary vascular resistance). In our study, estimated systolic pulmonary artery pressure was higher in the PFO (+) group.

CONCLUSION

Our study results show that pansystolic tricuspid regurgitation in healthy young adults could be associated with patent foramen ovale. Pansystolic tricuspid regurgitation in healthy young adults has high specificity and sensitivity for the detection of subjects with patent foramen ovale.

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