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ORIGINAL PAPER

Frequency of fragmented QRS in patient with psoriasis vulgaris without cardiovascular disease

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Abstract Myocardial fibrosis causes the fragmentation of QRS complexes on electrocardiogram. We hypothesized that the frequency of fragmented QRS (fQRS) could be more common in patients with psoriasis vulgaris than in healthy control subjects. In this prospective study, 100 patients with psoriasis vulgaris who did not have any cardiovascular disease were compared with 50 healthy volunteers in control group. The Psoriasis Area Severity Index (PASI) was used for expressing the severity of psoriasis. Patients with psoriasis were categorized according to presence of fQRS in ECG [fQRS (+) group and fQRS (−) group]. Patients with psoriasis had higher frequency of fQRS, higher levels of C reactive protein (CRP) and sedimentation rate (ESR) than the control group ($n = 49$, 49 % vs. $n = 3$, 6 %, $p < 0.001$; 9.91 ± 17.86 vs. 3.59 ± 0.79 mg/dL, $p = 0.014$; 17.37 ± 17.40 vs. 5.66 ± 5.22 mm/h, $p < 0.001$, respectively). Within the patient group there was no statistically significant difference between fQRS (+) and fQRS (−) subgroups with regards to sex, disease duration, CRP, ESR, medications and PASI score. It was suggested that presence of fQRS in ECG may be related with myocardial fibrosis in patients with psoriasis who do not have cardiovascular disease. For this reason, in our opinion, fQRS could be used as a predictive marker for myocardial fibrosis in patients with psoriasis.

Keywords ECG · Fragmented QRS · Myocardial fibrosis · Psoriasis

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Introduction

Psoriasis is a relapsing inflammatory disease characterized by white scaly patches on top of erythematous papules and plaques that have well-defined borders; the disease is observed in the rates of 1–3 % in different populations [16]. In recent years, it has been stated that psoriasis is an immune-mediated inflammatory disease, and that patients with psoriasis are also subject to systemic effects of the inflammation [3]. Cardiovascular comorbidities of the disease have been known for a long time; nearly 37 years ago it was reported that occlusive vascular diseases were more frequent and cardiovascular mortality was higher in psoriasis patients [21]. In addition, even if there is not classical cardiovascular risk factors and cormorbidities of the disease, studies suggest the disease itself constitutes a risk [1, 2, 15, 18].

Although myocardial fibrosis is very important clinically, there is no simple non-invasive technique to detect it directly [11]. Presence of fQRS in ECG may be of significance for this reason. Because, fQRS is a depolarization disorder indicating delay in the impulse caused by the fibrotic tissue in myocardium and it can be detected easily from the routine ECG recording. Fibrotic tissue increases the distance that electrical impulse must travel, and slows the speed of the impulse, which results in non-homogenous ventricular activation. This situation causes dentation in QRS complex in the ECG [10, 13]. Michael and colleagues

demonstrated that fQRS without pathological Q-waves on ECGs signified remote myocardial infarction [22]. Moreover, based on cardiac magnetic resonance imaging (CMR) and myocardial single-photon emission computed tomography (SPECT) studies, it has been shown that fQRS on ECGs signifies myocardial fibrosis [6, 8, 20].

In this study, patients with psoriasis vulgaris who do not have cardiovascular risk factors were compared with healthy control group who had similar demographic properties. It was assumed that frequency of fQRS would be higher in psoriasis patients compared to the control group.

Patients and methods

Study population

Study group was selected prospectively and randomly from the patients with psoriasis vulgaris who have been followed up in dermatology polyclinic of our hospital. The study group was composed of classic plaque-type psoriasis vulgaris patients who met the exclusion criteria and did not have comedication and comorbidity. Atypical forms of psoriasis (Erythrodermic, pustular etc.) and patients with psoriatic arthritis were excluded from the study. The Psoriasis Area Severity Index (PASI) was used to express severity of psoriasis. Patients with psoriasis were categorized according to presence of fQRS in ECG [fQRS (+) group and fQRS (−) group]. Control group was randomly selected from voluntary hospital personnel who met the inclusion criteria. In addition, attention was given to make the control group similar to study group with regard to demographic properties. Routine biochemistry and hematology tests were carried out in study and control groups. To rule out cardiac diseases, exercise stress testing and echocardiographic examination were performed on both study and control groups. The following exclusion criteria were applied both to study and control groups: metabolic disease, chronic systemic inflammatory disease, coronary artery disease, hypertension, diabetes mellitus, cardiomyopathy, heart valve disease, atrial fibrillation, AV block, cardiovascular drug use, morbid obesity, smoking, dyslipidemia, malignancy, renal insufficiency, liver disease, typical left bundle block or right bundle block on ECG (QRS duration > 120 ms) and incomplete right bundle block (QRS duration < 120 ms and RSR′ patterns in V1–2 precordial leads).

ECG criteria for fQRS

In the presence of normal QRS duration (QRS duration < 120 ms), fQRS was defined as the presence of an additional R wave (R′), or notching of the R′ or S′, or the presence of fragmentation (more than oneR′) in 2 contiguous leads corresponding to the territory of a major coronary artery. All ECGs were analyzed by two independent experienced cardiologists blinded to the study.

Statistical analyses

Normally distributed continuous data were expressed as mean ± standard deviation (SD); non-normally distributed continuous variables were presented as medians and interquartile ranges (IQRs). Categorical data were expressed as frequencies and percentages. Continuous data were expressed as mean ± SD. We used the χ^2 test to test for differences in categorical factors between fQRS (+) and fQRS (−) patients. We used Student's t test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed continuous variables. A multivariate logistic regression model was implemented to determine relation among selected variables and fQRS. Power analysis was performed to fQRS. Statistical analyses were carried out using SPSS-18.0/Windows® (SPSS Inc., Chicago, IL, USA) package software. $p < 0.05$ value was accepted as statistically significant.

All patients provided their written informed consent for participation in the present study, which complied with all of the principles of the Declaration of Helsinki. This study was approved by the Medical Ethical Committees of the University of Gaziosmanpasa, Tokat, Turkey (Approval number: 83116987-176/15-KAEK-018, March 03, 2015).

Results

One hundred patients with psoriasis vulgaris who did not have any cardiovascular disease [Gender (Male) (*n*/%), 50 (50); Age (years), mean ± SD, 40.61 ± 14.92] and 50 healthy individuals in control group [Gender (Male) (*n*/%), 25 (50); Age (years), mean ± SD, 45.08 ± 8.64] were included in the study. There was no statistically significant difference regarding age, sex, body mass index, systolic blood pressure, diastolic blood pressure and heart rate between study and control groups (Table 1). C reactive protein (CRP) levels and sedimentation rates (ESR) were higher in psoriasis patients compared to control group (9.91 ± 17.86 vs. 3.59 ± 0.79 mg/dl, $p = 0.014$; 17.37 ± 17.40 vs. 5.66 ± 5.22 mm/h, $p < 0.001$, respectively).

fQRS was significantly more frequent in psoriasis patients compared to control group ($n = 49$, 49 %; $n = 3$, 6 %, $p < 0.001$, respectively). Within the patient group there was no statistically significant difference between fQRS (+) and fQRS (−) subgroups with regards to sex,

Table 1 Clinical characteristics of the study population at the time of examination

	Study group ($n = 100$)	Control group ($n = 50$)	p
fQRS, *n* (%)	49 (49)	3 (6)	**<0.001**
Age (years), mean ± SD	40.61 ± 14.92	45.08 ± 8.64	ns
Gender (M), *n* (%)	50 (50)	25 (50)	ns
BMI (kg/m^2), mean ± SD	27.15 ± 5.32	27.47 ± 4.13	ns
SBP (mmHg), mean ± SD	117.25 ± 88.94	118 ± 9.63	ns
DBP(mmHg), mean ± SD	73.45 ± 7.61	74.7 ± 7.17	ns
HR (bpm), mean ± SD	71.35 ± 11.24	70.68 ± 11.56	ns
ESR (mm/h), mean ± SD	17.37 ± 17.40	5.66 ± 5.22	**<0.001**
CRP (mg/dl), mean ± SD	9.91 ± 17.86	3.59 ± 0.79	**0.014**
FBG (mg/dl), mean ± SD	92.89 ± 11.67	96.30 ± 10.80	ns
LDL-C (mg/dl), mean ± SD	123.58 ± 40.69	124.82 ± 30.00	ns
HDL-C (mg/dl), mean ± SD	47.78 ± 14.27	51.79 ± 12.67	ns
TC (mg/dl), mean ± SD	186.02 ± 43.73	191.84 ± 31.95	ns
TG (mg/dl) mean ± SD	145.89 ± 84.32	142.76 ± 78.64	ns

CRP C reactive protein, *DBP* diastolic blood pressure, *ESR* erythrocyte sedimentation rate, *FBG* fasting blood glucose, *fQRS* fragmented QRS, *HDL-C* high-density lipoprotein cholesterol, *HR* heart rate, *LDL-C* low-density lipoprotein cholesterol, *ns* not significant, *SBP* systolic blood pressure, *SD* standard deviation, *PASI* Psoriasis Area Severity Index, *TC* total cholesterol, *TG* triglycerides

Table 2 Clinical and demographic characteristics of patients in the fQRS(+) and fQRS(−) subgroups

	fQRS (+) ($n = 49$)	fQRS (−) ($n = 51$)	Odds ratio (95 % CI)	p^*
Age, years, mean ± SD	44.63 ± 14.60	36.74 ± 14.32	1.05 (1.01–1.10)	**0.021**
Gender, male, *n* (%)	23 (46)	27 (54)	0.40 (0.11–1.47)	ns
Gender, female, *n* (%)	26 (52)	24 (48)		
Duration of disease, years, mean ± SD	11.03 ± 9.55	11.55 ± 10.17	0.98 (0.92–1.05)	ns
PASI, mean ± SD	13.34 ± 11.88	14.09 ± 11.64	0.98 (0.93–1.03)	ns
CRP (mg/dl), mean ± SD	11.14 ± 23.69	8.63 ± 8.30	0.99 (0.91–1.08)	ns
ESR (mm/h), mean ± SD	18 ± 15.14	16.77 ± 19.46	0.97 (0.92–1.03)	ns
Medications				
Initial treatment, *n* (%)	5 (62.5)	3 (37.5)	1.05 (0.30–3.59)	ns
Only topical treatment, *n* (%)	23 (46.9)	26 (53.1)		
Systemic therapy, *n* (%)				
Phototherapy	6 (60)	4 (40)		
Methotrexate	1 (25)	3 (75)		
Cyclosporine	0	1 (100)		
Acitretin	2 (40)	3 (60)		
Biological	1 (50)	1 (50)		
Combination therapy	11 (52)	10 (48)		
Total	21 (48.8)	22 (51.2)		

fQRS fragmented QRS, *SD* standart deviation, *PASI* Psoriasis Area Severity Index, *CRP* C reactive protein, *CI* confidence interval, *ESR* sedimentation, *ns* not significant

* Multivariate logistic regression analysis

disease duration, CRP, ESR, medications and PASI score (Table 2). However, age of the patient was found to be statistically significant [Odds ratio (95 % CI) 1.05 (1.01–1.10), $p = 0.021$].

Power analysis for fQRS is found 99 %.

Discussion

Comorbidities accompanying psoriasis such as obesity, hypertension, diabetes mellitus, metabolic syndrome and hyperlipidemia contribute in development of

atherosclerosis in psoriasis patients. Additionally, higher smoking rates compared to general population, and administered systemic treatments might also have contributions in this respect [5, 14, 23]. Augustin et al. determined incidence of general comorbidity twice as high in psoriasis patients younger than 20 years old when compared to those without psoriasis [4]. Additionally, they found higher incidences of hyperlipidemia, obesity, and hypertension even in patients with juvenile psoriasis [4].

However, there are also studies showing that the disease itself alone presents a risk even if there are no cardiovascular risk factors and comorbidities of the disease in psoriasis patients [1, 2, 15, 18]. Ahlehoff et al. reported that psoriasis is a risk factor for cardiovascular disease independent of age, sex, comorbidities of the disease, administered systemic treatments, and socioeconomical status. Additionally they found this risk was higher in young age, severe disease and presence of psoriatic arthritis [1]. Armstrong et al. determined that cardiovascular disease risk was 1.5 fold higher in patients with severe psoriasis when compared to mild and moderate psoriasis [2]. Gelfand et al. reported psoriasis was a risk factor by itself for development of myocardial infarction (MI), after following up their patients for average of 5.4 years. In addition, Alehoff et al. found that MI risk was greater especially in younger psoriasis patients and those who have severe psoriasis [15]. In another study; Kaye et al. determined both MI and vascular disease risks were greater in psoriasis patients [18].

Etiopathogenesis of psoriasis is not very clear. However, marked inflammation and especially cytokines from T helper 1 cells have a role in pathogenesis [16]. Similarly, there is T helper 1 and T helper 17 activation and T regulatory cell inhibition in atherosclerosis [3, 26]. Additionally, it is known that cytokines that cause endothelial dysfunction such as TNF-α, IL-6 and IL-2 are released into systemic circulation in psoriasis. Endothelial dysfunction is a major component of atherosclerosis. Sun et al. showed contribution of TNF-α in myocardial fibrosis development in their experimental study [25]. These common pathogenetic mechanisms explain why cardiovascular events and psoriasis coexist [3, 25, 26].

Although myocardial fibrosis is clinically very important, there is no simple non-invasive technique to detect it directly [11]. For this reason, presence of fQRS on ECG may be of significance. fQRS is a depolarization sign that is easily detectable on ECG recording, which indicates delay in the impulse caused by the fibrotic tissue in myocardium. In individuals who have coronary artery disease or who are suspected to have coronary artery disease, fQRS that is detected on superficial ECG has been shown to be associated with myocardial scar. Moreover, it has been reported that presence of fQRS is more sensitive and has higher negative predictive value than Q wave for detection of scar tissue [8]. Additionally, fQRS has been shown to be related with myocardial fibrosis in studies based on CMR and SPECT examinations [6, 8, 13, 20, 22]. In addition, in autopsies of patients who had MI and LV aneurysm, there were histopathological findings that were consistent with possible mechanism of fQRS [12, 13]. Das et al. determined all-caused mortality and cardiac event rate (MI, cardiac death, and need for revascularization) were significantly higher in patients who had fQRS on their ECG compared to those who did not [9].

fQRS frequency has been reported to be higher in some pathologies involving chronic systemic inflammation [17, 19, 24]. Inanır et al. found more fQRS presence in ankylosing spondylitis patients than control group [17]. Kadi et al. reported the frequency of fQRS higher in patients with rheumatoid arthritis compared to patients with fibromyalgia [19]. In another study, frequency of fQRS has been found higher in Behcet's disease compared to healthy control group [24]. As far as we know, our study is the first to report the relation between fQRS and psoriasis. In our study, frequency of fQRS on ECG were higher in psoriasis patients compared to control group in a statistically significant ratio ($p < 0.001$). Çetin et al. determined there was a relation between CRP levels and fQRS in patients with stable angina pectoris [7]. Sayın et al. found higher levels of CRP in fQRS(+) patients with Behcet's disease [24]. In our study, levels of CRP and ESR were higher in psoriasis patients compared to control group ($p = 0.014$, $p < 0.001$, respectively). However, within the patient group there was no statistically significant difference between fQRS (+) and fQRS (−) subgroups with regards to CRP, ESR, sex, disease duration, medications and PASI score (Table 2). This result might indicate the parameters do not reflect the level of exposure to chronic systemic inflammation in psoriasis patients. That is because psoriasis has a course with remissions and relapses, while the parameters are more related with the clinical condition at the time of examination.

Study limitations

Many limitations could be brought about in this study. But one important limitation is that presence of myocardial fibrosis was not demonstrated with detailed examinations like CMR imaging.

Conclusion

We found frequency of fQRS significantly higher in psoriasis patients compared to control group that had similar demographic properties. It was suggested that presence of

fQRS in psoriasis patients who do not have cardiovascular disease may be related with myocardial fibrosis and reflect asymptomatic myocardial involvement. Therefore, we think fQRS could be used as a predictive marker for myocardial fibrosis in psoriasis patients.

As far as we know, this is the first study to report association between fQRS and psoriasis. Therefore, we state there should be more detailed research to confirm these findings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Ahlehoff O, Gislason GH, Charlot M, Jørgensen CH, Lindhardsen J, Olesen JB, Abildstrøm SZ, Skov L, Torp-Pedersen C, Hansen PR (2011) Psoriasis is associated with clinically significant cardiovascular risk: a Danish nationwide cohort study. J Intern Med 270:147–157
2. Armstrong AW, Schupp C, Bebo B (2012) Psoriasis comorbidities: results from the National Psoriasis Foundation surveys 2003–2011. Dermatology 225:121–126
3. Atakan N, Dogan S (2012) Psoriasis, a systemic disease. Turk J Dermatol 6:119–122
4. Augustin M, Glaeske G, Radtke MA, Christophers E, Reich K, Schäfer I (2010) Epidemiology and comorbidity of psoriasis in children. Br J Dermatol 162:633–636
5. Balci DD, Balci A, Karazincir S, Ucar E, Iyigun U, Yalcin F, Seyfeli E, Inandi T, Egilmez E (2009) Increased carotid artery intima-media thickness and impaired endothelial function in psoriasis. J Eur Acad Dermatol Venereol 23:1–6
6. Basaran Y, Tigen K, Karaahmet T, Isiklar I, Cevik C, Gurel E, Dundar C, Pala S, Mahmutyazicioglu K, Basaran O (2011) Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. Echocardiography 28:62–68
7. Cetin M, Kocaman SA, Canga A, Durakoglugil ME, Erdogan T, Satiroglu O, Kiris T, Ugurlu Y, Cicek Y, Bostan M (2012) The independent relationship between systemic inflammation and fragmented QRS complexes in patients with stable angina pectoris. Kardiol Pol 70:668–675
8. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J (2006) Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation 113:2495–2501
9. Das MK, Saha C, El Masry H, Peng J, Dandamudi G, Mahenthiran J, McHenry P, Zipes DP (2007) Fragmented QRS on a 12-lead ECG: a predictor of mortality and cardiac events in patients with coronary artery disease. Heart Rhythm 4:1385–1392
10. Das MK, Zipes DP (2009) Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm 6:8–14
11. de Jong S, van Veen TA, van Rijen HV, de Bakker JM (2011) Fibrosis and cardiac arrhythmias. J Cardiovasc Pharmacol 57:630–638
12. Friedman BM, Dunn MI (1995) Postinfarction ventricular aneurysms. Clin Cardiol 18:505–511
13. Gardner PI, Ursell PC, Fenoglio JJ Jr, Wit AL (1985) Electrophysiologic and anatomic basis for fractionated electrograms recorded from healed myocardial infarcts. Circulation 72:596–611
14. Gelfand JM, Mehta NN, Langan SM (2011) Psoriasis and cardiovascular risk: strength in numbers, part II. J Invest Dermatol 131:1007–1010
15. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB (2006) Risk of myocardial infarction in patients with psoriasis. JAMA 296:1735–1741
16. Gisondi P, Ferrazzi A, Girolomoni G (2010) Metabolic comorbidities and psoriasis. Acta Dermatovenerol Croat 18:297–304
17. Inanir A, Ceyhan K, Okan S, Kadi H (2013) Frequency of fragmented QRS in ankylosing spondylitis: a prospective controlled study. Z Rheumatol 72:468–473
18. Kaye JA, Li L, Jick SS (2008) Incidence of risk factors for myocardial infarction and other vascular diseases in patients with psoriasis. Br J Dermatol 159:895–902
19. Kadi H, Inanir A, Habiboglu A, Ceyhan K, Koc F, Çelik A, Onalan O, Arslan S (2012) Frequency of fragmented QRS on ECG is increased in patients with rheumatoid arthritis without cardiovascular disease: a pilot study. Mod Rheumatol 22:238–242
20. Mahenthiran J, Khan BR, Sawada SG, Das MK (2007) Fragmented QRS complexes not typical of a bundle branch block: a marker of greater myocardial perfusion tomography abnormalities in coronary artery disease. J Nucl Cardiol 14:347–353
21. McDonald CJ, Calabresi P (1978) Psoriasis and occlusive vascular disease. Br J Dermatol 99:469–475
22. Michael M, El Masry H, Khan BR, Das MK (2007) Electrocardiographic signs of remote myocardial infarction. Prog Cardiovasc Dis 50:198–208
23. Naldi L, Mercuri SR (2010) Epidemiology of comorbidities in psoriasis. Dermatol Ther 23:114–118
24. Sayin MR, Akpinar I, Gursoy YC, Kiran S, Gudul NE, Karabag T, Koca R, Aydin M (2013) Assessment of QRS duration and presence of fragmented QRS in patients with Behçet's disease. Coron Artery Dis 24:398–403
25. Sun M, Chen M, Dawood F, Zurawska U, Li JY, Parker T, Kassiri Z, Kirshenbaum LA, Arnold M, Khokha R, Liu PP (2007) Tumor necrosis factor-alpha mediates cardiac remodeling and ventricular dysfunction after pressure overload state. Circulation 115:1398–1407
26. Xiao J, Chen LH, Tu YT, Deng XH, Tao J (2009) Prevalence of myocardial infarction in patients with psoriasis in central China. J Eur Acad Dermatol Venereol 23:1311–1315