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ORIGINAL PAPER

# Epicardial fat thickness is ıncreased and associated with disease severity in hidradenitis suppurativa

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## Abstract

Previous studies showed an association between various dermatological diseases and epicardial fat thickness (EFT). However, EFT, which has been accepted as a cardiometabolic risk factor in recent years, has not been studied in the context of hidradenitis suppurativa (HS). Therefore, we aimed to determine whether EFT is increased in HS patients, and whether EFT is associated with disease severity. Forty adult patients with HS and 100 age- and sex-matched controls were included. Patients with diabetes mellitus, cardiovascular diseases, chronic renal or hepatic diseases, or other inflammatory conditions were excluded. The EFT was measured by transthoracic echocardiography. Disease severity was assessed by Hurley stage, and stage III patients have been described as having severe disease. High-sensitivity C-reactive protein (hs-CRP) and EFT were significantly higher in HS patients compared to controls. There were positive correlations between EFT and the duration of the disease, hs-CRP, and Hurley stage. The EFT was proportionally increased in HS patients with increasing disease severity; the largest EFT was found in Hurley stage 3 patients ($7.34 \pm 2.30$ mm), followed by Hurley stage 2 patients ($6.12 \pm 1.82$ mm), and Hurley stage 1 patients ($4.83 \pm 0.98$ mm). Multivariate analysis showed that male gender, hs-CRP, body mass index, and EFT $\geq 5.9$ mm were independent predictors of severe disease. The EFT is increased in HS, and it is an independent predictor of disease severity in adult patients with HS.

**Keywords** Epicardial fat thickness · Hidradenitis suppurativa

## Introduction

Previous studies have suggested that hidradenitis suppurativa (HS) is not only a cutaneous disease, as the patients with HS have a higher risk of stroke and cardiovascular adverse events compared with controls, but also a systemic disease [1–3]. The pathophysiology of HS has not been well elucidated, but current evidence supports the association between HS and obesity [4], insulin resistance [5], hyperlipidemia [6], and metabolic syndrome [7]. Several studies also showed that obese HS patients have more severe disease and more joint problems than patients with lower body mass indexes [8].

Epicardial adipose tissue is a fat depot on the surface of the myocardium surrounding the coronary arteries [9]. However, it is not only fat tissue, but also produces several inflammatory and atherogenic cytokines [10]. Epicardial fat thickness (EFT) has been shown to be associated with coronary artery disease, insulin resistance, and metabolic syndrome [11]. These results motivated the physicians to investigate the association between EFT and chronic inflammatory skin diseases. Although EFT has been investigated in patients with lichen planus [12], psoriasis [13], and rosacea [14], there has been no study investigating EFT in HS patients. Therefore, we aimed to examine the association between EFT and HS, and also aimed to identify the relation between the severity of the disease and EFT in HS.

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## Methods

### Study patients

A total of 40 patients with HS and 100 age- and gender-matched controls were enrolled in the present study from June to September 2019. All consecutive adult (aged ≥ 18 years) HS patients admitted to our dermatology outpatient and emergency clinic were prospectively included during the study period. However, patients with any acute illness, diabetes mellitus, and with a history of chonic renal or hepatic insufficiency, cardiovascular, coronary, cerebrovascular, chronic inflammatory or connective tissue diseases, pregnant women, and patients with poor echocardiographic imaging were not included in the patient or control groups in our study. The control group consisted of age- and gender-matched subjects admitted to the dermatology outpatient clinic during the study period due to skin disorders other than HS. Our study protocol was approved by the Muğla University ethics committee, and informed consent was obtained from all subjects. The study population included 40 consecutive patients with HS and 100 subjects as controls.

### Data collection

The demographic characteristics and clinical features, including age, smoking habits, gender, height, weight, and body mass index, were recorded. Routine biochemical measurements including fasting blood glucose, albumin, electrolytes, creatinine, high-sensitivity C-reactive protein (hs-CRP), and lipid profile were obtained at admission.

Information about disease-specific characteristics such as duration of the disease and the number of involved areas was also obtained from HS patients. The severity of HS was assessed by the Hurley staging [15], and stage III patients were defined as having severe HS.

### Epicardial fat thickness measurement

A single experienced cardiologist who was blinded to the subjects' data performed transthoracic echocardiography in all HS patients and in control group using a Philips EPIQ system (Koninklijke Philips N.V.; Best, The Netherlands). The EFT was identified as the echo-free space between the epicardial layers and it was measured on the free wall of the right ventricle from the parasternal long-axis and short-axis views at the enddiastole [16] (Fig. 1).

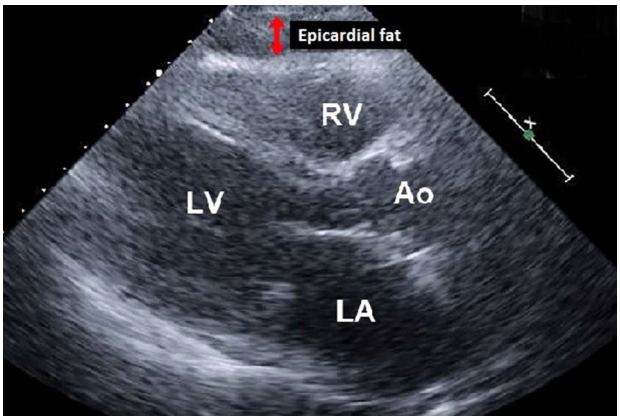


**Fig. 1** Echocardiography in the parasternal long-axis view of a 36-year-old male with HS showed an EFT of 7.1 mm. *Ao* aorta; *LA* left atrium; *LV* left ventricle; *RV* right ventricle

### Statistical analysis

All analyses were performed using SPSS Statistics version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Quantitative variables were compared by the Student *t* test or Mann–Whitney *U* tests, and qualitative variables were compared by the Pearson $^2$ test or Fisher exact tests. Pearson and Spearman's analyses were used to find out the correlation of EFT with other factors in patients with HS. To identify the independent predictors of ''severe disease'', univariate and multivariate linear regression analyses were performed. An optimal cutoff value of EFT for the detection of ''severe disease'' was determined by receiver operating characteristics (ROC) analysis.

## Results

Forty patients with HS (mean age 41.7 ± 10.6 years; 47.5% female) and 100 controls (mean age 42.2 ± 11.3 years; 47% female) were enrolled in the study (Fig. 2). Comparison of demographic, clinical, laboratory characteristics, and EFTs of patients with HS and control subjects is presented in Table 1. No differences were found between HS and age- and gender- matched controls in terms of body mass index, lipid profile, or serum glucose levels. However, the hs-CRP (2.12 ± 1.86 vs. 1.32 ± 0.85 mg/L, respectively; $p < 0.001$) and EFT (6.8 ± 1.2 vs. 4.9 ± 0.7 mm, respectively; $p = 0.001$) were significantly increased in patients with HS compared with the controls.

The disease-specific characteristics of HS patients are presented in Table 1. The mean duration of HS was 12.1 ± 8.3 years, and mean age of onset was

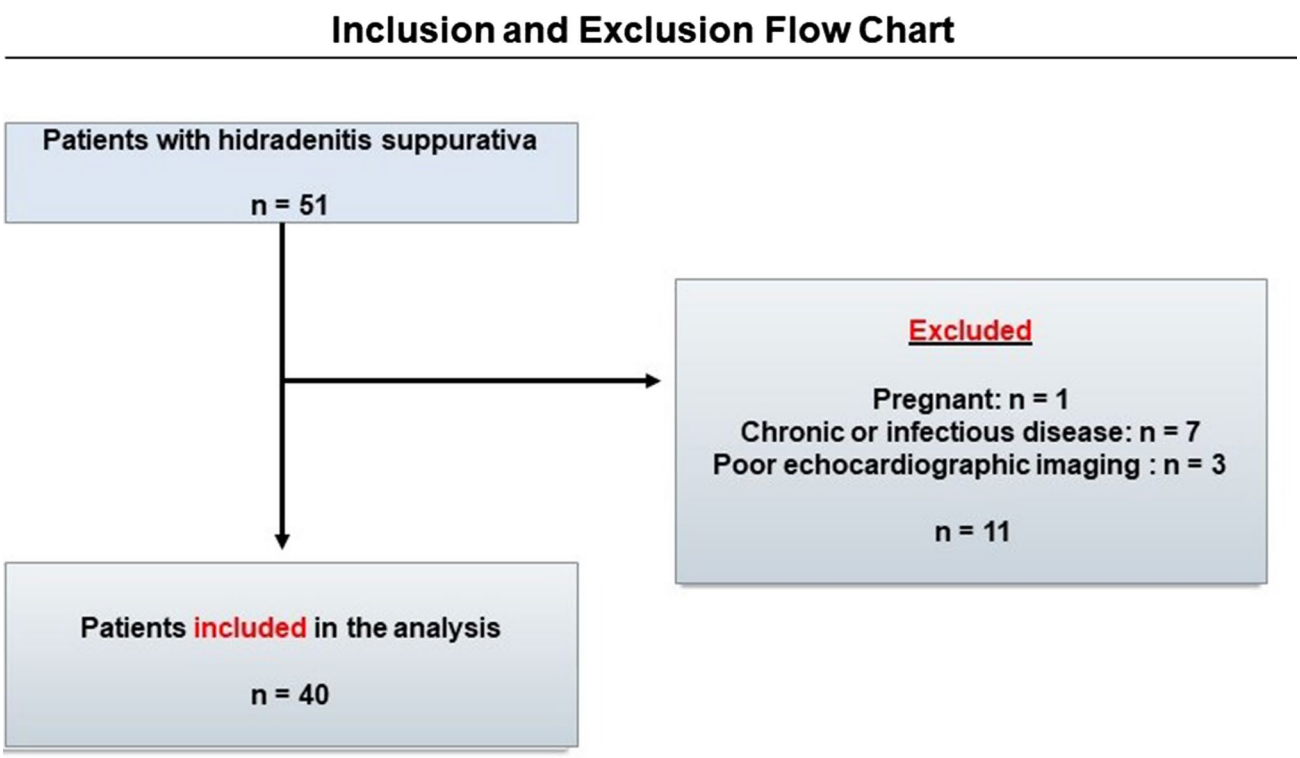


**Fig. 2** Flowchart of the study population who met inclusion/exclusion criteria

21.6 ± 9.4 years. The mean number of affected sites was 4.1 ± 1.9, and the most commonly involved sites were groin and axilla. Of the study population, the proportion of the patients with severe disease was 27.5% according to the Hurley staging.

### Correlation between EFT and other parameters

There were no significant correlations between EFT and age, smoking, or lipid profile. However, there was a positive correlation between EFT and Hurley stage (correlation coefficient ($r$) = 0.432, $p$ = 0.001), hs-CRP ($r$ = 0.471, $p$ = 0.001), and disease duration ($r$ = 0.365, $p$ = 0.032) (Table 2).

### Association of EFT with disease severity

The EFT increased significantly with increase in disease severity; the largest EFT was found in Hurley stage 3 patients (7.34 ± 2.30 mm), followed by Hurley stage 2 patients (6.12 ± 1.82 mm), and Hurley stage 1 patients (4.83 ± 0.98 mm) (Fig. 3).

### Predictors of severe disease

Multivariate and ROC analyses were performed to identify the predictors of Hurley stage III HS patients (Table 3). The ROC analysis revealed that the optimal cutoff EFT value to predict severe HS was 5.9 mm (AUC = 0.877; 95% CI 0.815–0.923; $p$ < 0.001). Multivariate analysis showed that male gender (OR 2.562; 95 CI 0.756–5.261; $p$ = 0.015), hs-CRP (OR 1.345; 95 CI 1.113–1.721–5.261; $p$ = 0.001), body mass index (OR 1.251; 95 CI 0.899–3.242; $p$ = 0.031), and EFT ≥ 5.9 mm (OR 1.876; 95 CI 1.369–3.01; $p$ = 0.018) were independent predictors of severe disease (Table 3).

## Discussion

The main findings of this preliminary study are as follows: [1] HS patients had a greater EFT than those without HS [2]. Increased EFT positively correlated with the duration of the disease and Hurley stage, and [3] EFT ≥ 5.9 mm independently predicted a higher severity of HS.

Increased risk for cardiovascular diseases has been demonstrated in various dermatological diseases in recent decades [17]. Although the underlying mechanism remains not completely understood, chronic inflammation is thought to provide a connection between these two distinct entities [17]. However, the linkage and association between dermatological and cardiovascular diseases are often investigated in patients with psoriasis [18]. On the other hand, HS patients are known to have a high prevalence of overlapping

**Table 1** Comparison of hidradenitis suppurativa (HS) patients and control subjects

| | HS ($n=40$) | Control ($n=100$) | $P$ value |
|---|---|---|---|
| Female | 19 (47.5) | 47 (47) | 0.769 |
| Age (years) | 41.7 ± 10.6 | 42.2 ± 11.3 | 0.425 |
| Weight, m | 1.67 ± 0.2 | 1.66 ± 0.1 | 0.965 |
| Height, kg | 80.5 ± 16.9 | 78.8 ± 15.9 | 0.096 |
| Body mass index, kg/m$^2$ | 27.3 ± 6.2 | 27.8 ± 5.9 | 0.125 |
| Current smoking | 14 (35.0) | 34 (34.0) | 0.844 |
| Laboratory findings | | | |
| Creatinine (mg/dL) | 0.90 ± 0.32 | 0.91 ± 0.30 | 0.741 |
| Hs-CRP (mg/L) | 2.12 ± 1.86 | 1.32 ± 0.85 | < 0.001 |
| Hemoglobin (g/dL) | 12.8 ± 3.6 | 12.7 ± 2.9 | 0.562 |
| LDL cholesterol (mg/dL) | 129.2 ± 32.4 | 127.2 ± 27.9 | 0.254 |
| HDL cholesterol (mg/dL) | 47.2 ± 11.9 | 48.3 ± 12.5 | 0.366 |
| Triglycerides (mg/dL) | 129.3 ± 80.3 | 125.9 ± 81.2 | 0.101 |
| Total cholesterol (mg/dL) | 182.4 ± 35.4 | 179.9 ± 35.6 | 0.069 |
| Fasting glucose (mg/dL) | 90.2 ± 10.6 | 89.7 ± 9.9 | 0.112 |
| Epicardial fat thickness (mm) | 6.8 ± 1.2 | 4.9 ± 0.7 | 0.001 |
| Age at onset | 21.6 ± 9.4 | | |
| Duration of the disease (years) | 12.1 ± 8.3 | | |
| Hurley stage | | | |
| I | 4 (10) | | |
| II | 25 (62.5) | | |
| III | 11 (27.5) | | |
| Number of affected sites | 4.1 ± 1.9 | | |

Values are presented as number (%), or mean ± standard deviation

*HS* hidradenitis suppurativa, *Hs-CRP* high-sensitivity C-reactive protein, *HDL* high-density lipoprotein; LDL: Low-density lipoprotein

conditions with cardiovascular diseases such as hyperlipidemia, insulin resistance, diabetes, and metabolic syndrome, making these patients more susceptible to atherosclerosis [2]. Moreover, Egeberg and colleagues demonstrated that the risk of cardiovascular mortality was higher in patients with HS compared with the risk in those with psoriasis [19]. Therefore, the early prediction of severe disease and optimal management of high-risk patients in HS may prevent late-onset cardiovascular complications.

Obesity is one of the most important modifiable risk factors for cardiovascular diseases such as coronary artery disease, heart failure, and atrial fibrillation. Although body mass index, waist, circumference, and other measures are useful indications of general adiposity, recent interest has focused on EFT as it plays a significant role in the development of cardiovascular diseases through secreting several inflammatory cytokines [20]. Different studies conducted during the last few years have demonstrated that EFT is also associated with the presence and severity of different chronic inflammatory skin diseases [12–14]. Ertem et al. enrolled 54 patients with lichen planus, and 50 control subjects [12]. Like the results we found in patients with HS, they found positive correlations between EFT and duration of lichen planus, and hs-CRP levels. Bacaksız and colleagues included 115 adult patients with psoriasis and 60 healthy individuals [13]. They found that EFT and hs-CRP were significantly higher in the psoriasis group than in the control group. The EFT was correlated with body mass index, waist circumference, hs-CRP levels, and psoriasis severity index [13]. Belli et al. enrolled 40 patients with rosacea and 40 control subjects to investigate EFT in rosacea [14]. Rosacea patients had significantly higher EFT than controls, and EFT was independently associated with another marker of atherosclerosis;

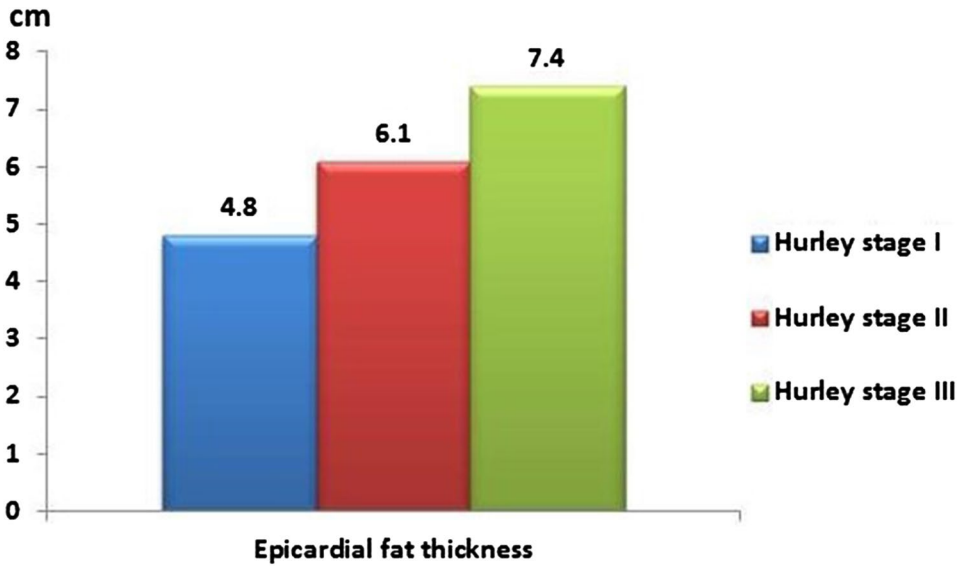


**Fig. 3** Changes in epicardial EFT according to the severity of the disease. ($p=0.013$ for Hurley stage I vs. stage II, $p=0.001$ for Hurley stage II vs. stage III, and $p<0.001$ for Hurley stage I vs. stage III)

**Table 2** Pearson correlation analysis between epicardial fat thickness and other confounding variables in patients with hidradenitis suppurativa

| | Correlation coefficient (r) | *p* value |
|---|---|---|
| Smoking | 0.098 | 0.201 |
| Age | 0.080 | 0.358 |
| Creatinine (mg/dL) | 0.096 | 0.420 |
| Hs-CRP (mg/dL) | 0.471 | 0.001 |
| Disease duration | 0.365 | 0.032 |
| Hurley stage | 0.432 | 0.001 |
| Total cholesterol | 0.086 | 0.562 |

*Hs-CRP* high-sensitivity C-reactive protein

**Table 3** Multivariate regression analysis for the prediction of severe disease (Hurley stage III)

| | Odds ratio | 95% CI | *P* value |
|---|---|---|---|
| Gender (male) | 2.562 | 0.756–5.261 | 0.015 |
| Age (per 1 year) | 1.015 | 0.743–1.485 | 0.764 |
| High-sensitivity C-reactive protein | 1.345 | 1.113–1.721 | 0.001 |
| Disease duration | 1.012 | 0.975–1.124 | 0.356 |
| Epicardial fat thickness ≥ 5.9 mm | 1.876 | 1.369–3.081 | 0.018 |
| Body mass index | 1.251 | 0.899–3.242 | 0.031 |

*Hs-CRP* high-sensitivity C-reactive protein

carotid intima–media thickness [14]. The results of these three studies were in line with our findings that the EFT is increased and associated with the severity of the chronic inflammatory skin diseases. Although our and others studies could not determine the causality due to the case–control, and cross-sectional design of the studies, we postulate that persistent inflammation may be the reason for the increased EFT in HS. The association between duration of the disease and EFT supports our hypothesis, as the longer duration of HS causes higher cumulative effect of inflammation. Whatever the reason, our study showed that EFT was increased and associated with the duration and severity of the disease in HS.

The EFT can be easily and non-invasively measured by echocardiography, and it may have the potential to be a marker of subclinical cardiovascular diseases and a predictor of severity of the disease in patients with HS. Therefore, increased EFT may guide the patient's cardiovascular risk in HS. It remains, however, unknown whether a reduction in the amount of EFT could reduce the risk of cardiovascular diseases in patients with HS or treatment of HS reduces the thickness of epicardial adipose tissue.

## Limitations

The results of our study may not be applicable to all patients due to strict inclusion criteria and the small sample size of the study. This is a cross-sectional study, and the prognostic value of serial changes in EFT could not be assessed. We did not use magnetic resonance imaging, which is the gold standard method in assessing EFT.

## Conclusions

Although the pathological background of increased EFT in HS is not known, this study is the first to demonstrate that EFT is increased in HS patients, and it is associated with the severity and the duration of the disease. Further large volume prospective studies are warranted to examine the EFT in HS and to investigate whether increased EFT has prognostic importance in HS.

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