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Impact of Inflammatory Bowel Disease on Pulmonary Hemodynamics and Right Ventricular Function: The Role of Pulmonary Pulse Transit Time in Assessing Pulmonary Stiffness and Right Ventricular Function

İnflamatuvar Bağırsak Hastalığının Pulmoner Hemodinami ve Sağ Ventrikül Fonksiyonu Üzerine Etkisi: Pulmoner Pulse Transit Time'ın Pulmoner Stiffness ve Sağ Ventrikül Fonksiyonunun Değerlendirilmesindeki Rolü

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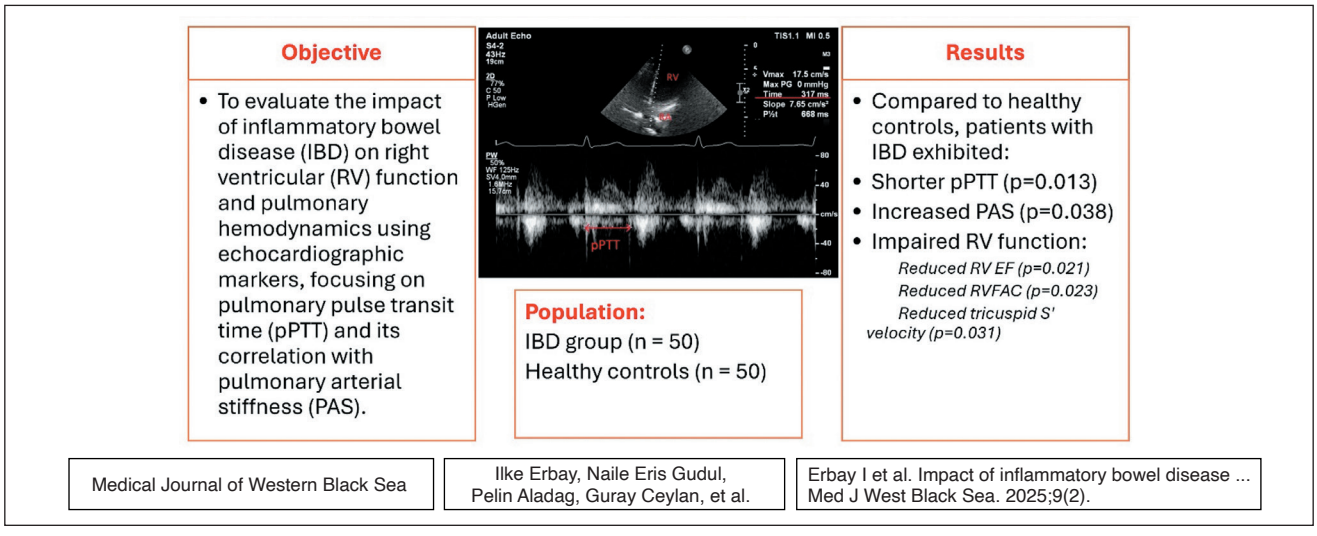
GRAPHICAL ABSTRACT



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ABSTRACT

Aim: Inflammatory bowel disease (IBD) is a chronic disease with systemic implications, including cardiovascular effects. The aim of this study was to investigate the impact of IBD on right ventricular (RV) function and pulmonary hemodynamics, focusing on the relationship between pulmonary pulse transit time (pPTT) and other echocardiographic markers.

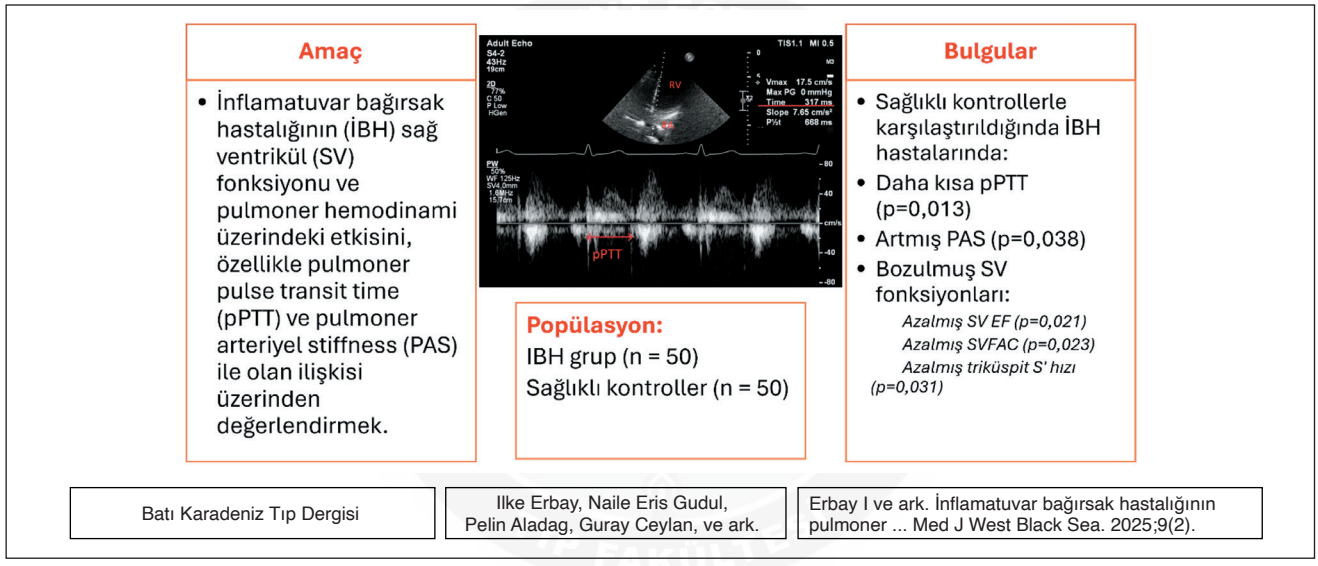
Material and Methods: Fifty IBD patients and 50 matched healthy controls underwent echocardiographic evaluation to assess RV function, including parameters such as RV myocardial performance index (RVMPI), RV ejection fraction (RV EF) and tricuspid annular plane systolic excursion (TAPSE). Pulmonary hemodynamics were assessed by pPTT and pulmonary arterial stiffness (PAS). Statistical analyses explored the associations between IBD and these echocardiographic parameters.

Results: No differences in systolic pulmonary artery pressure (sPAP) or TAPSE were observed between the groups. PAS was increased and pPTT was shortened in IBD patients compared to controls. pPTT correlated with PAS, IBD duration, RV EF, RV fractional area change (RVFAC), TAPSE, tricuspid S', RVMPI and C-reactive protein (CRP). pPTT was an independent predictor of PAS ($p < 0.001$).

Conclusion: IBD patients show impaired RV function and increased pulmonary stiffness. pPTT may serve as a practical marker for early detection of pulmonary vascular changes in IBD, replacing PAS for hemodynamic assessment.

Keywords: Inflammatory bowel disease; right ventricular function; pulmonary pulse transit time; pulmonary arterial stiffness

GRAFİKSEL ÖZET



ÖZ

Amaç: İnflamatuvar bağırsak hastalığı (İBH), sistemik etkileri olan kronik bir hastalık olup kardiyovasküler sistemi de etkileyebilmektedir. Bu çalışmada, İBH'nin sağ ventrikül (SV) fonksiyonları ve pulmoner hemodinami üzerindeki etkileri araştırılmış; özellikle pulmoner pulse transit time (pPTT) ile diğer ekokardiyografik göstergeler arasındaki ilişki incelenmiştir.

Gereç ve Yöntemler: Çalışmaya 50 İBH hastası ile yaş ve cinsiyet açısından eşleştirilmiş 50 sağlıklı kontrol birey dahil edildi. Tüm katılımcılarda ekokardiyografi ile SV fonksiyonları değerlendirildi. Bu kapsamda SV miyokardiyal performans indeksi (SVMPI), SV ejeksiyon fraksiyonu (SV EF) ve triküspit anüler düzlem sistolik ekskursiyonu (TAPSE) gibi parametreler analiz edildi. Pulmoner hemodinamik değerlendirme ise pPTT ve pulmoner arteriyel stiffness (PAS) ölçümleri ile yapıldı. İBH ile bu ekokardiyografik parametreler arasındaki ilişkiler istatistiksel olarak incelendi.

Bulgular: Gruplar arasında sistolik pulmoner arter basıncı (sPAP) ve TAPSE açısından anlamlı fark bulunmazken, İBH hastalarında PAS düzeyleri belirgin şekilde artmış, pPTT süreleri ise anlamlı olarak kısalmıştı. pPTT; PAS, İBH süresi, SV EF, SV fraksiyonel alan değişimi (SVFAC), TAPSE, triküspit S', SVMPI ve C-reaktif protein (CRP) ile anlamlı korelasyon gösterdi. Ayrıca, pPTT'nin PAS üzerinde bağımsız bir belirleyici olduğu saptandı ($p < 0,001$).

Sonuç: İBH hastalarında sağ ventrikül fonksiyonlarında bozulma ve pulmoner damar sertliğinde artış gözlenmektedir. pPTT, pulmoner vasküler değişikliklerin erken tanısında pratik ve erişilebilir bir belirteç olarak PAS'ın yerini alabilecek potansiyele sahiptir.

Anahtar Sözcükler: İnflamatuvar bağırsak hastalığı, sağ ventrikül fonksiyonu, pulmoner pulse transit time, pulmoner arteriyel stiffness

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a progressive disease defined by increased pulmonary arterial pressure and pulmonary vascular resistance, which can lead to right ventricular (RV) failure and early mortality (1). Inflammation is a critical factor in the pathogenesis of PAH and there is growing evidence that chronic inflammatory conditions, including autoimmune diseases (2) and chronic infections such as Human Immunodeficiency Virus (HIV) (3), may significantly contribute to the development of PAH.

Inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory diseases of the small and large intestine (4) and are characterised by elevated levels of cytokines and chemokines throughout the body (5). Extraintestinal symptoms are commonly reported due to chronic inflammation caused by IBD (6, 7), one of which is pulmonary involvement (8). Various bronchopulmonary findings, including bronchiectasis, inflammatory small airway disease, parenchymal lung disease and vascular disease, have been described in case reports (9-12).

Investigations into the direct relationship between IBD, pulmonary hemodynamics, and RV function are limited. Studies suggest that pulmonary disease is a significant risk factor for the development of PAH (13). The higher prevalence of respiratory disease in patients with IBD compared with the general population suggests a possible link between pulmonary hemodynamic disturbances and IBD (14). Early detection of changes in pulmonary hemodynamics may improve the timely diagnosis of RV dysfunction and thus improve the prognosis of IBD.

Transthoracic echocardiography is an easily accessible and non-invasive diagnostic tool for the assessment of pulmonary hemodynamics. Recent studies have shown that early hemodynamic changes in the pulmonary artery can be detected by measuring the time it takes for the pulse pressure wave to travel from the pulmonary valve to the left atrium (LA) (15). This interval, known as pulmonary pulse transit time (pPTT), can be measured using echocardiography and is considered a valuable marker of pulmonary hemodynamics and vascular changes in PAH (15).

In the current literature, there are no studies investigating RV functions and pulmonary artery hemodynamics in IBD patients. The aim of this study was to investigate the impact of IBD on RV function and pulmonary artery hemodynamics, focusing on the relationship between pPTT and other echocardiographic markers of RV function.

MATERIALS and METHODS

Study Patients

In this cross-sectional observational study, fifty IBD patients (CD or UC) over 18 years of age without cardiac symptoms such as shortness of breath or chest pain were enrolled from the gastroenterology outpatient clinic between January 2023 and July 2024, along with fifty age- and sex-matched healthy IBD (-) controls. Informed consent was obtained from all participants prior to their inclusion in the study. Patients with known coronary artery disease, heart failure (left ventricular [LV] ejection fraction [EF] less than 50%), moderate to severe valvular heart disease, history of arrhythmia, congenital heart disease, moderate to severe pulmonary disease, active infection, pregnancy, malignancy, diabetes mellitus, hypertension, thyroid disease, renal failure, flare-up phase of IBD, and with suboptimal echocardiographic image quality were excluded from the study.

Demographic and clinical history was obtained from all patients and controls. On the day of the echocardiographic evaluation, biochemical blood tests and erythrocyte sedimentation rate (ESR) tests were performed in the laboratory and the results were recorded. All IBD patients had available bilateral chest X-rays in the hospital record system, which showed no evidence of pulmonary parenchymal pathology, pleural effusion, or increased cardiothoracic index.

Echocardiographic Assessment

Echocardiography was performed with patients in the standard left lateral decubitus position using a commercially available Philips EPIQ 7 ultrasound machine (Philips Healthcare, Amsterdam, The Netherlands) with an X5-1 three-dimensional (3D) transthoracic probe (Philips Healthcare, Amsterdam, The Netherlands). Investigators were blinded. Pulmonary vein flow was assessed by pulse wave (PW) Doppler of the right superior pulmonary vein from the apical four-chamber view according to the guidelines of the American Society of Echocardiography (16). All Doppler recordings were performed at a sweep speed of 100 mm/sec, with continuous electrocardiogram (ECG) overlaid for accurate synchronization (16). pPTT was defined as the time interval between the R-wave on the ECG and the peak velocity of late systolic pulmonary vein flow (R-PVs2 interval) (Figure 1). This measurement was calculated as the average of two separate PW Doppler measurements taken during the same examination.

Conventional two-dimensional echocardiography, Doppler and tissue Doppler imaging were used to measure the following parameters: LA diameter, left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), interventricular septal thickness (IVS), posterior wall thickness, right atrial (RA) diameter, right atrial area

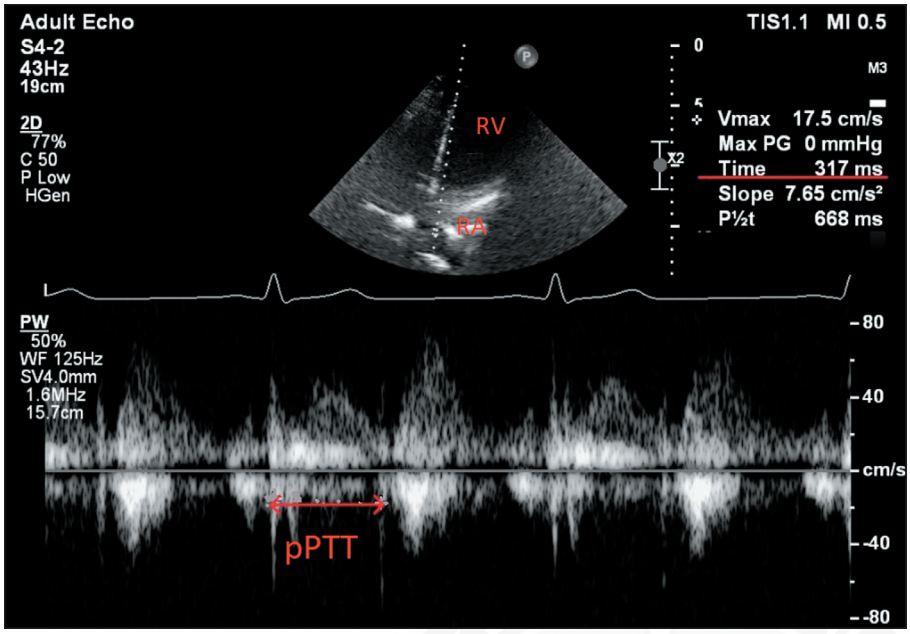


Figure 1: Pulmonary vein flow PW Doppler recordings showing pulmonary pulse transit time (pPTT), identified as the time interval between the peak of the ECG R-wave and the corresponding peak late systolic pulmonary vein flow velocity. RA, right atrium; RV, right ventricle

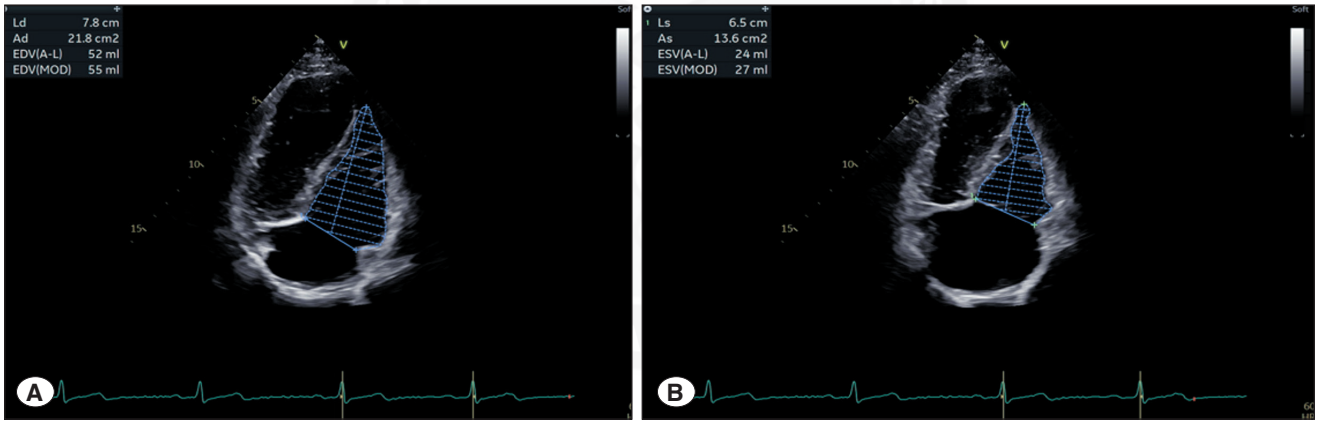


Figure 2: Three-dimensional (3D) echocardiographic assessment of right ventricular end- diastolic and end- systolic volumes (EDV and ESV) using model-based optimisation of dynamic imaging (MOD) **(A,B).**

(RAA) and right ventricular fractional area change (RVFAC). Systolic pulmonary artery pressure (sPAP) was estimated using Bernoulli's equation derived from measurements of tricuspid regurgitation.

To evaluate RV systolic function, measurements were made using M-mode and tissue Doppler techniques to assess tricuspid annular plane systolic excursion (TAPSE) and tricuspid lateral annular systolic velocity (tricuspid S'). RV myocardial performance index (RVMPI) was also measured using the pulsed Doppler method calculated as follows:

[Tricuspid valve closure to opening time (ms) – RV ejection time (ms)] / RV ejection time (ms)] (17).

RV end-diastolic volume (RVEDV) and end-systolic volume (RVESV) measurements were performed by imaging the RV over multiple cardiac cycles to create a comprehensive 3D reconstruction of the ventricular chamber using model-based optimisation of dynamic imaging (MOD) for improved accuracy (Figure 2). RV EF was then calculated using the formula: (RVEDV-RVESV)/RVEDV×100% (17). Pulmonary acceleration time (PAT) and maximal frequency shift (MFS) were measured from Doppler flow traces obtained in the parasternal short-axis view using PW Doppler ultrasound of the pulmonary artery, approximately 10-15 mm below the pulmonary valve annulus. Pulmonary artery stiffness (PAS) was calculated as the ratio of MFS to PAT.

Four subjects in whom Doppler measurements of right upper pulmonary vein flow could not be obtained, and three subjects with ambiguous separation between the S2 and D waves of pulmonary vein flow were excluded from the study.

Statistical Analysis

Normality of the data was assessed using the Kolmogorov-Smirnov test. Variables were presented as percentages (%) and means with standard deviations for normally distributed data, and medians with interquartile ranges for non-normally distributed data. Categorical variables were analysed using the chi-squared test to compare IBD patients and controls. Independent samples t-tests or Mann-Whitney U tests were used for group comparisons of continuous variables, as appropriate. Spearman correlation analysis was also performed to assess the relationships between pPTT and various echocardiographic and laboratory parameters. Two separate linear regression models using the enter method were developed to identify the determinants of pPTT and PAS. Univariate linear regression analyses were conducted to evaluate the relationship between each independent variable and the dependent variables (pPTT and PAS), with statistically significant variables being included in the final multivariate regression models. All data processing and statistical analyses were performed with SPSS version 26.0 (SPSS Inc., Chicago, IL). A two-tailed p-value < 0.05 was considered statistically significant.

A post-hoc power analysis was conducted using G*Power software (version 3.1). Based on the observed effect size (Cohen's d = 0.51) for the difference in pPTT between IBD patients and controls, the achieved statistical power was 0.71 at a significance level of $\alpha = 0.05$.

RESULTS

Clinical and Demographic Characteristics

Table 1 presents the demographic and clinical characteristics of the study population. Male participants comprised 44.0% of the IBD group and 38.0% of the control group, with no significant difference ($p = 0.542$). The mean age was 41.0 ± 11.4 years in the IBD group and 40.3 ± 10.2 years in the control group. There was no significant difference in age between the groups ($p = 0.775$). Also, there were no significant differences in body mass index (BMI) ($p = 0.990$) and smoking status ($p = 0.523$) between the groups. The inflammatory markers C-reactive protein (CRP) and ESR were significantly higher in the IBD group ($p < 0.001$, $p = 0.030$, respectively).

Echocardiographic Assessment

Echocardiographic images and parameters are shown in Table 2. There were no significant differences between the IBD patients and the control group in terms of LVEDD ($p = 0.941$), LVESD ($p = 0.654$), LV EF ($p = 0.179$), LA diameter ($p = 0.896$), IVS ($p = 0.827$), pulmonary artery diameter ($p = 0.344$) and sPAP ($p = 0.439$). Compared to the control group, the IBD group showed significantly higher values for RA diameter ($p = 0.023$), RAA (p = 0.007), RVMPI ($p < 0.001$) and PAS ($p = 0.038$). Significant reductions were observed in RV EF ($p = 0.021$), tricuspid S' ($p = 0.031$), RVFAC ($p = 0.023$), and pPTT ($p = 0.013$) in the IBD group, whereas no significant change was found in TAPSE ($p = 0.213$).

Table 1. Demographic, clinical and inflammatory marker characteristics of IBD patients and controls

Variables	IBD (n=50)	Control (n=50)	*p*-value
Age, years (SD)	41.0 ± 11.4	40.3 ± 10.2	0.775
Male, n (%)	22 (44.0)	19 (38.0)	0.542
Heart rate (beats/min)	73.3 ± 8.8	72.1 ± 7.0	0.461
BMI (kg/m^2)	25.2 ± 5.8	25.2 ± 5.7	0.990
Smoking, n (%)	15 (30.0)	18 (36.0)	0.523
IBD duration, years (median)	7.5 (3.0–14.8)	–	–
Crohn's disease, n (%)	26 (52.0)	–	–
Ulcerative colitis, n (%)	24 (48.0)	–	–
5-Aminosalicylic acid, n (%)	27 (54.0)	–	–
Azathioprine, n (%)	22 (44.0)	–	–
TNF-alpha blocker, n (%)	10 (20.0)	–	–
Inflammatory markers			
CRP (mg/L)	27.3 (17.4–52.3)	11.5 (7.1–18.1)	<0.001
ESR	13.5 ± 8.3	10.4 ± 5.7	0.030

BMI, body mass index; **CRP,** C-reactive protein; **ESR,** erythrocyte sedimentation rate; **IBD,** inflammatory bowel disease; **SD,** standard deviation; **TNF,** tumor necrosis factor

Table 2. Echocardiographic analysis of IBD and control group

Variable	IBD (n=50)	Control (n=50)	*p*-value
LVEF (%)	63.5 (60.0–65.0)	65.0 (62.0–65.0)	0.179
LV end diastolic diameter (mm)	45.6 ± 4.1	45.7 ± 2.8	0.941
LV end systolic diameter (mm)	30.9 ± 5.9	30.4 ± 4.6	0.654
LA diameter (mm)	33.4 ± 3.6	33.3 ± 3.1	0.896
IVS (mm)	9.4 (8.0–10.3)	10.0 (9.0–10.0)	0.827
Posterior wall (mm)	9.0 (8.0–10.0)	9.0 (8.9–10.0)	0.509
Pulmonary artery diameter (mm)	17.9 ± 1.3	18.2 ± 2.0	0.344
sPAP (mmHg)	25.9 ± 4.5	25.3 ± 3.7	0.439
RA diameter (mm)	32.0 ± 3.4	30.4 ± 3.6	0.023
RA area (cm^2)	13.9 ± 2.2	12.7 ± 2.2	0.007
RV diameter (mm)	32.8 ± 3.2	31.4 ± 3.1	0.032
RVEDV (mL)	71.6 ± 8.9	70.1 ± 9.3	0.405
RVESV (mL)	34.8 ± 6.2	32.7 ± 6.0	0.090
RV EF (%)	51.4 ± 4.8	53.5 ± 4.1	0.021
Tricuspid S' (m/s)	15.1 ± 1.9	16.0 ± 1.9	0.031
TAPSE (mm)	21.9 ± 2.7	22.6 ± 2.9	0.213
RVFAC (%)	45.5 ± 6.0	48.1 ± 4.9	0.023
pPTT (ms)	190.3 ± 37.1	207.4 ± 30.3	0.013
PAS (kHz/s)	19.1 ± 2.5	17.9 ± 3.0	0.038
RVMPI	0.43 ± 0.1	0.35 ± 0.1	<0.001

IBD, inflammatory bowel disease; **IVS,** inter-ventricular septal thickness; **LA,** left atrium; **LV,** left ventricle; **LVEF,** left ventricular ejection fraction; **PAS,** pulmonary artery stiffness; **pPTT,** pulmonary pulse transit time; **RA,** right atrium; **RV,** right ventricle; **RVEDV,** right ventricular end-diastolic volume; **RV EF,** right ventricular ejection fraction; **RVESV,** right ventricular end-systolic volume; **RVFAC,** right ventricular fractional area change; **RVMPI,** right ventricular myocardial performance index; **sPAP,** systolic pulmonary artery pressure; **TAPSE,** tricuspid annular plane systolic excursion; **Tricuspid S,** tricuspid lateral annular systolic velocity.

Table 3. Correlation analysis between pPTT and other echocardiographic and clinical parameters

	pPTT	
	R	*p*-value
PAS	-0.517	<0.001
IBD duration	-0.459	0.001
RV EF	0.430	<0.001
RVFAC	0.429	<0.001
TAPSE	0.343	<0.001
Tricuspid S'	0.336	0.001
RVMPI	-0.250	0.012
CRP	-0.429	<0.001

CRP, C-reactive protein; **IBD,** inflammatory bowel disease; **PAS,** pulmonary artery stiffness; **pPTT,** pulmonary pulse transit time; **RV EF,** right ventricular ejection fraction; **RVFAC,** right ventricular fractional area change; **RVMPI,** right ventricular myocardial performance index; **TAPSE,** tricuspid annular plane systolic excursion; **Tricuspid S,** tricuspid lateral annular systolic velocity.

A significant correlation was observed between pPTT and PAS (r = -0.517), moderate correlations with RVFAC (r = 0.429) and RV EF (r = 0.430) ($p < 0.001$ for all) (Table 3). The first multivariate regression analysis was performed to predict pPTT and identified age ($p = 0.012$), PAS ($p < 0.001$), RVFAC ($p = 0.019$), and CRP ($p = 0.007$) as independent predictors of pPTT (Table 4). The second multivariate regression analysis was performed to predict PAS and identified only pPTT ($p < 0.001$) as an independent predictor of PAS (Table 5).

DISCUSSION

This study showed that pPTT was shorter in IBD patients than in healthy controls. pPTT correlated with several parameters, including PAS, duration of IBD, RV EF, RVFAC, TAPSE, tricuspid S', RVMPI and CRP. Even in the absence of PAH, IBD patients showed impaired RV function as indicated by lower tricuspid S', RVFAC and RV EF values compared to controls. Furthermore, multivariate regression analysis identified pPTT as an independent predictor of PAS.

Table 4. Regression analysis for predictors of pPTT

	Coefficient	Standard error	*p*-value	*95% Confidence interval*
Male (ref. female)	15.122	6.871	0.030	1.486 – 28.758
Age	-1.586	0.284	<0.001	-2.149 to -1.002
PAS	-6.364	1.064	<0.001	-8.475 to -4.253
sPAP	-2.509	0.817	0.003	-4.131 to -0.888
Tricuspid S'	6.053	1.716	0.001	2.648 – 9.459
RVFAC	2.655	0.565	<0.001	1.534 – 3.776
TAPSE	4.226	1.171	<0.001	1.903 – 6.550
IBD (ref. no)	-17.140	6.770	0.013	-30.575 to -3.705
IBD duration	-2.096	0.585	0.001	-3.275 to -0.917
CRP	-0.624	0.133	<0.001	-0.887 to -0.361
Multivariate Regression Analysis for pPTT*				
Age	-0.918	0.359	0.012	-1.631 to -0.205
PAS	-4.371	1.048	<0.001	-6.452 to -2.290
RVFAC	1.591	0.666	0.019	0.267 – 2.915
CRP	-0.363	0.131	0.007	-0.624 to -0.103

R^2:0.491, **Durbin-Watson:** 1.871, F<0.001
*** Model variables:** sex, age, PAS, sPAP, tricuspid S', IBD, RVFAC, CRP
CRP, C-reactive protein; **IBD,** inflammatory bowel disease; **PAS,** pulmonary artery stiffness; **pPTT,** pulmonary pulse transit time; **RVFAC,** right ventricular fractional area change; **sPAP,** systolic pulmonary artery pressure; **TAPSE,** tricuspid annular plane systolic excursion; **Tricuspid S,** tricuspid lateral annular systolic velocity.

Table 5. Regression analysis for predictors of PAS

	Coefficient	Standard error	*p*-value	*95% Confidence interval*
Male (ref. female)	-1.143	0.560	0.044	-2.225 to -0.032
Age	0.095	0.025	<0.001	0.046 – 0.144
pPTT	-0.042	0.007	<0.001	-0.056 to -0.028
sPAP	0.178	0.067	0.009	0.045 – 0.312
Tricuspid S'	-0.506	0.139	<0.001	-0.782 to -0.231
RVFAC	-0.098	0.050	0.052	-0.197 to -0.001
TAPSE	-0.324	0.096	0.001	-0.541 to -0.133
IBD (ref. no)	1.170	0.555	0.038	0.068 – 2.272
IBD duration	0.091	0.042	0.035	0.007 – 0.176
CRP	0.027	0.012	0.020	0.004 – 0.050
Multivariate Regression Analysis for PAS*				
pPTT	-0.033	0.089	<0.001	-0.051 to -0.016

R^2:0.318, **Durbin-Watson:** 1.648, F<0.001
*** Model variables:** sex, age, pPTT, sPAP, tricuspid S', IBD, CRP
CRP, C-reactive protein; **IBD,** inflammatory bowel disease; **PAS,** pulmonary artery stiffness; **pPTT,** pulmonary pulse transit time; **RVFAC,** right ventricular fractional area change; **sPAP,** systolic pulmonary artery pressure; **TAPSE,** tricuspid annular plane systolic excursion; **Tricuspid S,** tricuspid lateral annular systolic velocity.

This is the first study to show that RV function is impaired in IBD patients compared to healthy controls. IBD is characterized by inappropriate immune-mediated intestinal and systemic inflammatory activity (18). Although extraintestinal manifestations are more common in the joints, eyes and skin, pulmonary involvement has recently become increasingly important (19). Subclinical pulmonary involvement is more prevalent than overt respiratory symptoms in IBD patients. In particular, it has been reported that 42% of IBD patients without respiratory symptoms have abnormal lung

function tests, compared with only 3% of healthy controls (20). These changes persist even when the disease is in remission (20). Persistent airway inflammation in IBD patients can lead to airway narrowing in some locations, potentially resulting in conditions such as bronchiectasis or bronchiolitis obliterans. In fact, chronic bronchitis or bronchiectasis is common in IBD patients presenting with respiratory symptoms (21). Pulmonary parenchymal involvement could be associated with IBD itself, but also be induced by medications (e.g. mesalazine, sulfasalazine, methotrexate) (21, 22). This increases the importance of investigating the impact of IBD on pulmonary vascular status and thus on right heart function.

RV failure is more prevalent in patients with PAH associated with chronic inflammatory diseases such as systemic sclerosis (23). IBD is also known to induce chronic inflammation, which may contribute to a number of systemic effects and complications (24). Inflammatory activation is likely to play a pivotal role in the pathogenesis of impaired pulmonary vascular bed through mechanisms such as endothelial dysfunction (25, 26). In our study, the IBD group had impaired RV function, as evidenced by reduced tricuspid S', RVFAC and RV EF, as well as elevated CRP and ESR levels, compared with the control group. RV function may be subtly impaired in IBD, potentially mediated by chronic systemic inflammation.

Recent evidence suggests that inflammatory activation plays a significant role in the pathogenesis of adverse RV remodelling and dysfunction (27). In the context of chronic inflammatory processes, increased PAS leads to the progression of RV dysfunction (27). Echocardiography is an important screening tool to measure RV function and pulmonary vascular stiffness. Recent studies have introduced a new non-invasive technique to assess the hemodynamics of the pulmonary circulation. This technique calculates the pPTT by measuring the interval between ventricular electrical activity on the ECG and when the PW reaches the pulmonary vein using Doppler echocardiography (28). The R-wave on the ECG and the peak late systolic flow velocity in the pulmonary vein determined by PW Doppler are used to calculate the pPTT. Pulse transit time (PTT) reflects the time the pulse pressure wave travels from one arterial region to another. As arterial stiffness increases, pulse wave velocity (PWV) increases, leading to a shortening of the PTT (29). A study by Wibmer et al. showed that the time taken for the pulse pressure wave to travel from the pulmonary valve to the LA may be a marker of PAH and vascular stiffness (30). They also showed that pPTT, estimated non-invasively using Doppler techniques, was significantly lower in PAH patients than controls, with PAS having a more significant effect on pPTT.

In a study involving HIV-positive patients, pPTT was identified as a potential marker for pulmonary vascular disease, even when sPAP levels were within normal ranges, compared to healthy controls (31). A similar finding was seen in systemic connective tissue diseases characterised by chronic inflammation, where a reduction in pPTT was noted (32). The researchers in this study hypothesised that early pathophysiological changes in pulmonary vascular structures could be associated with shorter pPTT values, as the patient group had higher mean RVMPI values (32).

In the present study, there was no significant difference in sPAP measurements between the two groups. However, some RV function parameters such as RVFAC, tricuspid S' and RVMPI, which assesses both systolic and diastolic function of the RV, were impaired in IBD patients without PAH. pPTT was also significantly shorter in the IBD group than in the controls and was significantly correlated with PAS, IBD duration, RV EF, RVFAC, tricuspid S', RVMPI and CRP. pPTT and PAS were identified as independent predictors in both multivariate linear regression analysis models, suggesting that these parameters could serve as equivalent tools for assessing pulmonary hemodynamics. As pPTT can be easily calculated using PW Doppler, it could be a more practical alternative to PAS in the assessment of pulmonary vascular function.

TAPSE primarily assesses the longitudinal function of the RV, providing valuable insight into its performance (33). However, RVFAC, which reflects both longitudinal and transverse RV motion, may provide a more comprehensive assessment of RV function (34). In the present study, TAPSE values were within the normal range in the IBD and control groups, with no significant difference. However, although RVFAC and tricuspid S' were also within normal limits, they were significantly lower in the IBD group. In addition, RVFAC, tricuspid S' and RV EF showed a positive correlation with pPTT, suggesting that PAS may contribute to RV dysfunction even in the absence of overt PAH. This study indicates that RV function may be impaired in IBD patients compared to controls, even in the absence of clinical and echocardiographic evidence of PAH. The results suggest that in patients with IBD, pPTT may be a sensitive marker reflecting early changes in pulmonary hemodynamics and RV dysfunction, and changes may be detectable by shorter pPTT values before they become clinically apparent. Therefore, incorporating pPTT into routine echocardiographic screening of IBD patients may help detect early cardiopulmonary involvement, even in the absence of overt symptoms.

Limitations

The main limitations of this study include its single-centre design and relatively small sample size. Although chest X-rays were available for all IBD patients, the use of high-resolution computed tomography and pulmonary function tests would have provided a more comprehensive assessment of

pulmonary involvement in IBD and potentially strengthened our study results. Another limitation is the absence of an a priori power analysis. However, a post-hoc analysis based on the primary variable (pPTT) demonstrated a statistical power of 0.71 (Cohen's d = 0.51), which is considered acceptable in exploratory studies. Importantly, this study focused on a specific patient population (IBD) and evaluated a novel echocardiographic parameter (pPTT) that has not been previously investigated in this context, thereby providing valuable preliminary data despite the moderate sample size. The absence of cardiac magnetic resonance imaging (MRI) or RV strain analysis is another limitation, as these techniques could have offered further insight into subclinical RV dysfunction in IBD patients.

Conclusion

This study demonstrates that patients with IBD may exhibit subclinical RV dysfunction and increased pulmonary stiffness despite the absence of overt pulmonary hypertension. pPTT, which showed strong associations with multiple RV function parameters, may serve as a practical and non-invasive marker for early pulmonary vascular changes in this population.

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Author Contributions

Ilke Erbay: Writing – original draft, Resources, Conceptualization, Project administration, Data curation. **Naile Eris Gudul:** Writing – original draft, Methodology, Investigation, Validation. **Pelin Aladag:** Writing – review & editing. **Guray Ceylan:** Data curation. **Selim Aydemir:** Resources, Writing – review & editing, Data curation. **Ahmet Avci:** Formal analysis, Supervision, Writing – review & editing, Resources, Data curation.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ethical Approval

The study was designed by the principles of the Declaration of Helsinki and the principles of Good Clinical Practice and did not violate the ethical rules of research involving human subjects. All participants provided their informed consent to participate in the study. Approval for the study was obtained from the Bioethics Committee of Zonguldak Bülent Ecevit University (No. 2024/13).

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