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Prognostic Implications of Baseline and New-Onset Fragmented QRS Complex in Patients Undergoing Transcatheter Aortic Valve Implantation

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ABSTRACT

Fragmented QRS complex (fQRS), which can be easily detected by electrocardiography (ECG), is an indicator of myocardial fibrosis and has adverse prognostic impact in cardiovascular diseases. The aim of this study was to investigate the effect of the presence of both pre- and post-operative fQRS on short- and long-term prognosis in patients undergoing transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS).

Data of 615 patients who underwent TAVI from different risk categories in a single-center were retrospectively screened and 289 patients were included after exclusion criteria. The presence of fQRS was recorded on pre- and postoperative ECGs and the effect of the fQRS on in-hospital and 2-year all-cause mortality was investigated.

fQRS was detected in 85 (29.4%) patients before TAVI and also 24 (11.8%) patients had new-onset fQRS after TAVI. The presence of preop fQRS was found to be an independent predictor of in-hospital mortality. Postop fQRS, moderate or severe paravalvular aortic regurgitation and high systolic pulmonary artery pressure were associated with long-term mortality. In addition, patients with preop fQRS were more likely to need permanent pacemaker implantation after TAVI (14.1% vs. 2.9%).

fQRS, which can be considered an indicator of subclinical left ventricular dysfunction due to myocardial fibrosis, is associated with decreased short- and long-term survival in patients undergoing TAVI. The presence of preop fQRS and postop new-onset fQRS is associated with a 3.8- and 3.2-fold increased cumulative mortality risk, respectively, at 24-month follow-up compared to patients without fQRS.

Keywords: Fragmented QRS complex, aortic stenosis, transcatheter aortic valve implantation, long-term outcomes, electrocardiogram.

Introduction

Severe aortic stenosis (AS) is among the most prevalent valvular heart diseases in the elderly population and constitutes a major cause of cardiovascular morbidity and mortality in this demographic (1). The advent of transcatheter aortic valve implantation (TAVI) has revolutionized the management of high-risk AS patients, offering an effective and safe interventional treatment particularly beneficial for individuals over the age of 75 (2). To optimize outcomes in candidates for TAVI, it is imperative to identify clinical, laboratory, and imaging findings with prognostic significance, enabling accurate patient selection and precise risk stratification (3).

The fragmented QRS complex (fQRS) is an electrocardiographic (ECG) marker characterized by various RSR' patterns within the QRS complex (duration <120 msec) that does not present with a typical bundle branch block morphology. This marker, detected in at least two contiguous leads corresponding to a coronary artery territory, signifies myocardial scar or fibrosis, reflecting delayed ventricular depolarization (4). fQRS is readily identifiable on a standard 12-lead surface ECG and has been associated with significant prognostic implications across a spectrum of cardiovascular diseases (5-7). As an indicator of ventricular depolarization defects, fQRS is

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recognized as a potential predictor of malignant ventricular arrhythmias and sudden cardiac death in patients with coronary artery disease or structural heart disease (8-10). Moreover, the presence of fQRS has been linked to adverse clinical outcomes and increased mortality in both ischemic and non-ischemic cardiomyopathy patients (11,12). Recent studies have also suggested a correlation between fQRS and increased rates of rehospitalization and cardiovascular mortality in patients with heart failure with preserved ejection fraction (HFpEF) (13).

In the pathogenesis of severe AS, chronic elevation of left ventricular (LV) pressure due to valvular-level LV outflow obstruction precipitates progressive hypertrophy and myocardial fibrosis within the LV myocardium. These structural changes ultimately result in LV diastolic dysfunction, mitral regurgitation, pulmonary hypertension, and a reduction in left ventricular ejection fraction (LVEF) as the disease advances (14). The detection of myocardial fibrosis and its implications for clinical outcomes have been well documented, yet the role of fQRS in severe AS, particularly in patients undergoing TAVI, remains underexplored. Although numerous studies have elucidated the clinical significance of the fQRS in various cardiovascular conditions, there is a paucity of literature addressing its relevance in patients with severe AS and in specific subgroups treated with TAVI. This study aimed to determine the incidence of fQRS in preprocedural ECGs and investigate the emergence of new-onset fQRS following TAVI in patients with symptomatic severe AS. Additionally, the study evaluated the impact of fQRS presence on in-hospital and two-year long-term prognosis.

Materials and Methods

Study Population: The data of 615 symptomatic patients with severe AS who underwent TAVI across different risk categories at a tertiary center were retrospectively analyzed. Following strict exclusion criteria, 289 patients were included in the final analysis. The flowchart of the study is presented in Figure 1. Clinical and demographic characteristics of all patients, whose diagnosis of severe AS was confirmed by transthoracic echocardiography (TTE) within one week prior to the procedure, were recorded. Postoperative echocardiographic data were collected from TTE measurements taken during the first month of follow-up after discharge. All TTE data were obtained according to current guidelines and meticulously transferred to the dataset (Vivid E9, GE, Milwaukee, USA) (15). Follow-up data for the first two years post-discharge were evaluated for patients who survived the in-hospital period following a successful TAVI procedure.

Definition of Fragmented QRS Complex: All patients underwent a resting standard 12-lead surface ECG (filter range 0.5-150 Hz, 25 mm/s, 10 mm/mV) within one week prior to TAVI. Additionally, another ECG was performed during the in-hospital period after the procedure. All ECGs were interpreted by two independent cardiologists according to guideline recommendations, and the data were recorded (16). fQRS was defined in this study by the presence of various RSR' patterns (QRS <120 msec) with or without an initial Q wave, which included an additional R wave (R') or notching of the R wave or S wave, or the presence of more than one R' (fragmentation) without typical right or left bundle-branch block in two contiguous leads corresponding to a major coronary artery territory. The coronary artery regions were classified as anterior (leads V1–V5), inferior (leads II, III, and aVF), and lateral (leads V6, I, and aVL). The QRS duration was determined by the longest QRS in any lead (17).

Procedural Characteristics for TAVI: Preprocedural risk assessment for TAVI was performed using the Society of Thoracic Surgeons (STS) risk scoring system (18). TAVI procedures was performed by experienced interventional cardiologists using either self-expanding or balloon-expandable transcatheter valves via a transfemoral approach under general anesthesia or deep sedation. Hemostasis at the femoral artery access site was achieved using a dedicated device (Perclose ProGlide™ device; Abbott Vascular, CA, USA). Periprocedural and long-term outcomes and complications associated with TAVI were documented according to the Valve Academic Research Consortium (VARC-3) criteria (20).

Primary Endpoints: The primary endpoint of the study was in-hospital mortality in the patients undergoing TAVI. The secondary endpoint was all-cause mortality during the first two years of follow-up after discharge.

Data Collection and Ethics: Clinical data for the in-hospital period and the two-year long-term follow-up were recorded using the hospital's digital archive and the Ministry of Health's Electronic Database. Written informed consent was obtained from all patients prior to the

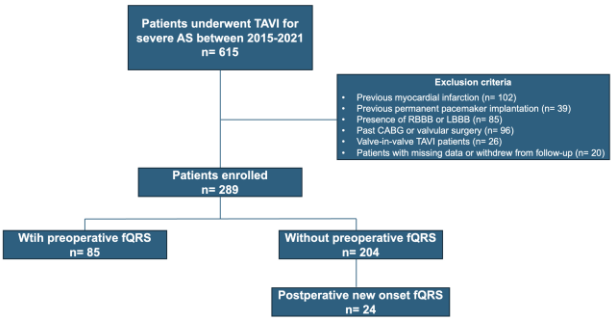

Fig.1. Flow-chart of the study. (AS, aortic stenosis, CABG, coronary artery bypass graft, fQRS, fragmented QRS complex, LBBB, left bundle branch block, RBBB, right bundle branch block, TAVI, transcatheter aortic valve implantation.)

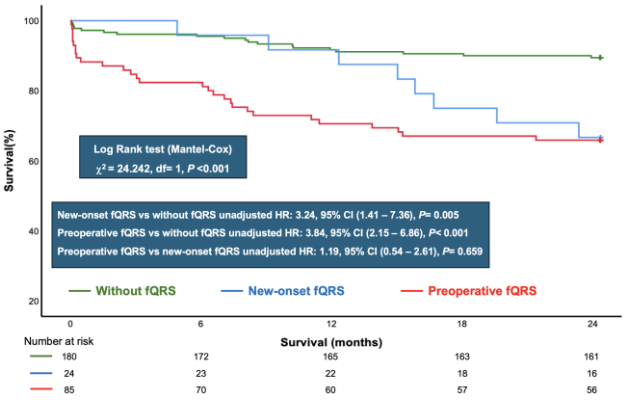

Fig. 2. Kaplan-Meier survival curves for the 24-month follow-up period were generated for patients without fQRS, those with preoperative fQRS, and those with new-onset postoperative fQRS.

intervention. The study was approved by the ethics committee of Istanbul Medipol University (Approval Date: 22.05.2024, no: 2024/535) and conducted in full accordance with the Declaration of Helsinki.

Statistical Analyses: The normality of the distribution of continuous variables in the dataset was evaluated using the Kolmogorov-Smirnov test and histogram analysis. Normally distributed parameters are expressed as mean ± standard deviation, while non-normally distributed parameters are expressed as median and interquartile range (25th-75th percentiles). Categorical variables are presented as absolute numbers (n) and percentages (%). The study population was divided into two groups based on the presence of preoperative fQRS. Continuous and categorical variables, both normally and non-normally distributed, were compared between the two groups using independent t-tests, Mann-Whitney U tests, and Pearson's $\chi 2$ or Fisher's exact tests, respectively. Statistical significance was set at a two-tailed p-value of <0.05. According to the two-tailed independent samples t-test analysis using the G-power program with 95% confidence (1-α), 80% test power (1-β) and d=0.5 effect size, the minimum number of samples required in each group was 64 and the total number of samples was 128. The power of this study, which included 289 patients, was >95% (G-power version 3.1, Dusseldorf, Germany). To investigate the variables associated with in-hospital mortality, univariate binary logistic regression analysis was initially performed to calculate the odds ratios (OR) and 95% confidence intervals (CI). Subsequently, a multivariate binary logistic regression model was constructed by including clinically significant parameters that showed statistical significance in the univariate analysis to identify independent predictors. The variables determining the risk of mortality during the two-year follow-up in patients who survived the in-hospital period were identified using Cox regression analysis and hazard ratios (HR) with 95% CIs were calculated. Univariate analysis was performed, followed by multivariate Cox regression analysis of statistically significant parameters. Kaplan-Meier survival curves, generated using the log-rank method, were used to estimate two-year survival among the patient groups with baseline fQRS, new-onset postoperative fQRS, and no fQRS. All statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corp., NY, USA).

Results

Evaluation of Patient Characteristics: The characteristics of the 289 patients included in the study (mean age 78.4 ± 8.7 years, n=167 [57.8%] female) were compared based on the presence of preoperative fQRS, as shown in Table 1. The group with preoperative fQRS was older and had higher STS scores and lower glomerular filtration rates (GFR). No significant differences were observed between the two groups in terms of sex or other comorbidities. In the TTE assessments, the fQRS group had a lower mean LVEF and a higher systolic pulmonary artery pressure (sPAP). In addition, this group had higher rates of moderate or severe mitral and tricuspid regurgitation. Other TTE findings and procedural characteristics were similar between the two groups.

In-Hospital and Long-Term Outcomes: Firstly, the in-hospital mortality rate was higher in the preoperative fQRS group (15.3% vs. 3.4%, p=0.001). Additionally, the overall mortality rate

Table 1: Comparison of the Study Population In Terms of the Presence of Fragmented QRS (fQRS) Before TAVI

	Without fQRS (n= 204, 70.6%)	With fQRS (n= 85, 29.4%)	Overall population (n= 289)	P value
Age, years	77.8±8.8	80±8.1	78.4±8.7	0.048 [a]
Gender, female	115 (56.4%)	52 (61.2%)	167 (57.8%)	0.451 [b]
BMI, kg/m²	27.3±4.6	26.6±3.9	27.1±4.4	0.222 [a]
STS score	7 (5 – 9.7)	9 (7 – 12)	8 (6 – 10)	0.001 [c]
Hypertension	178 (87.3%)	71 (83.5%)	249 (86.2%)	0.403 [b]
Diabetes mellitus	58 (28.4%)	29 (34.1%)	87 (30.1%)	0.337 [b]
Atrial fibrillation	71 (34.8%)	31 (36.5%)	102 (35.3%)	0.787 [b]
COPD	78 (38.2%)	34 (40%)	112 (38.8%)	0.779 [b]
Previous CVE	10 (4.9%)	5 (5.9%)	15 (5.2%)	0.732 [b]
GFR, mL/min/1.73 m²	76 (57.1 – 88.1)	64 (45 – 82.8)	73 (52.9 – 87.9)	0.005 [c]
LVEF, %	56.3±8.4	49.4±11.9	54.3±10.1	0.001 [a]
LA diameter, cm	4.2±0.6	4.3±0.6	4.3±0.6	0.121 [a]
Peak trans-aortic gradient, mmHg	76.7±18.3	77.9±21.4	77.1±19.3	0.644 [a]
Mean trans-aortic gradient, mmHg	49.6±11.7	50.1±14.7	49.7±12.7	0.371 [a]
Aortic valve area, m²	0.71±0.15	0.71±0.15	0.71±0.15	0.504 [a]
Moderate or severe AR	33 (16.2%)	16 (18.8%)	49 (17%)	0.585 [b]
Moderate or severe MR	41 (20.1%)	28 (32.9%)	69 (23.9%)	0.021 [b]
Moderate or severe TR	42 (20.6%)	36 (42.4%)	78 (27%)	0.001 [b]
sPAP, mmHg	40.7±9.9	48.1±12.1	42.8±11.1	0.001 [a]
General Aneshesia	33 (16.2%)	20 (23.5%)	53 (18.3%)	0.141 [b]
Self-expanding THV	128 (62.7%)	48 (56.5%)	176 (60.9%)	0.319 [b]
THV Size, mm	26 (26 – 29)	27 (26 – 29)	26 (26 – 29)	0.711 [c]
THV implantation Success	201 (98.5%)	82 (96.5%)	283 (97.9%)	0.263 [b]
Sheat size, F	16 (14 – 18)	16 (14 – 18)	16 (14 – 18)	0.977 [c]
Predilatation	58 (28.4%)	26 (30.6%)	84 (29.1%)	0.713 [b]
Postdilatation	56 (27.5%)	22 (25.9%)	78 (27%)	0.784 [b]
Hospitalisation, days	4 (3 – 6)	4 (3 – 7)	4 (3 – 6)	0.231 [c]
Hemoglobin, g/dL	11.5±1.6	11.3±1.8	11.4±1.6	0.342 [a]
Hematocrite, %	34.2±4.4	34.2±5.3	34.2±4.7	0.754 [a]
Creatinine, mg/dL	0.9 (0.7 – 1.2)	1.1 (0.8 – 1.3)	1 (0.8 – 1.2)	0.011 [c]

[a] Independent t-test, [b] Pearson's $\chi 2$ test, [c] Mann-Whitney U test.

AR, aortic regurgitation, BMI, body mass index, COPD, chronic obstructive pulmonary disease, CVE, cerebrovascular event, F, french, GFR, glomerular filtration rate, LA, left atrium, LVEF, left ventricle ejection fraction, MR, mitral regurgitation, n, number, sPAP, systolic pulmonary artery pressure , STS, Society of Thoracic Surgeons, TAVI, transcatheter aortic valve implantation, THV, transcatheter heart valve, TR, tricuspid regurgitation.

Table 2: In-hospital and Long-Term Outcomes of The Study Population Regarding The Preoprocedural Presence of Fragmented QRS (fQRS)

	Without fQRS (n= 204, 70.6%)	With fQRS (n= 85, 29.4%)	Overall population (n= 289)	*P* value
In-hospital mortality	7 (3.4%)	13 (15.3%)	20 (6.9%)	0.001 [b]
Mortality during follow-up	20 (9.8%)	16 (18.8%)	36 (12.5%)	0.034 [b]
Overall 2-year mortality	27 (13.2%)	29 (34.1%)	56 (19.4%)	0.001 [b]
Postoperative LVEF, %	57.2±8.1	50.5±11.7	55.3±9.7	0.001 [a]
Postoperative sPAP, mmHg	37.9±9.6	41.9±11.9	39±10.4	0.009 [a]
Moderate or severe PVAR	13 (6.5%)	6 (8.1%)	19 (7%)	0.649 [b]
New onset fQRS	24 (11.8%)	-	-	-
Permanent pacemaker implantation	6 (2.9%)	12 (14.1%)	18 (6.2%)	0.001 [b]
Major bleeding	26 (12.7%)	15 (17.6%)	41 (14.2%)	0.276 [b]
Minor bleeding	33 (16.2%)	12 (14.1%)	45 (15.6%)	0.660 [b]
Major vascular complication	15 (7.4%)	9 (10.6%)	24 (8.3%)	0.364 [b]
Minor vascular complication	24 (11.8%)	8 (9.4%)	32 (11.1%)	0.561 [b]
Acute kidney injury	18 (8.8%)	11 (12.9%)	29 (10%)	0.288 [b]
Periprocedural MI	1 (0.5%)	1 (1.2%)	2 (0.7%)	0.521 [b]
Periprocedural stroke	3 (1.5%)	5 (5.9%)	8 (2.8%)	0.051 [b]
Cardiac tamponade	4 (2%)	3 (3.5%)	7 (2.4%)	0.423 [b]
Need for urgent surgery	6 (2.9%)	2 (2.4%)	8 (2.8%)	0.781 [b]

[a] Independent t-test, [b] Pearson's $\chi 2$ test,
LVEF, left ventricle ejection fraction, MI, myocardial infarction, n, number, PVAR, paravalvular aortic regurgitation, sPAP, systolic pulmonary artery pressure.

during the two-year follow-up period for patients who survived the in-hospital phase was significantly higher in this group (18.8% vs. 9.8%, p=0.034). Second, patients with preoperative fQRS had a higher incidence of permanent pacemaker implantation (PPI) (14.1% vs. 2.9%, p=0.001). Another significant finding was that 24 of 204 patients (11.8%) who initially did not have fQRS developed new-onset fQRS post-TAVI. When comparing TTE data collected at the one-month follow-up, postoperative mean LVEF and sPAP values were worse in the preoperative fQRS group, although rates of moderate or severe paravalvular aortic regurgitation (PVAR) were similar. Finally, the frequency of major or minor bleeding, vascular complications, and other periprocedural in-hospital adverse events did not differ between the two groups (Table 2).

Predictors of In-Hospital Mortality: Univariate logistic regression analysis revealed that body mass index (BMI), baseline sPAP, preoperative fQRS, STS score, and chronic obstructive pulmonary disease (COPD) were associated with in-hospital mortality in the current cohort. Multivariate analysis, including these variables, revealed that preoperative fQRS (adjusted OR: 3.65, 95% CI [1.26–10.57], p=0.017), STS score (adjusted OR: 1.16, 95% CI [1.02–1.32], p=0.023), and COPD (adjusted OR: 3.95, 95% CI [1.38–11.31], p=0.011) were independent predictors of in-hospital mortality (Table 3).

Predictors of Long-Term Mortality: Age, GFR, postoperative sPAP, postoperative LVEF, moderate or severe PVAR, and postoperative fQRS were identified as variables associated with all-cause mortality during the two-year follow-up in patients who survived the in-hospital period. According to the multivariate Cox regression analysis, postoperative sPAP (adjusted HR: 1.04, 95% CI [1.02–1.07], p=0.001), moderate or severe PVAR (adjusted HR: 3.75, 95% CI [1.55–9.05], p=0.003), and the presence of postoperative fQRS (adjusted HR: 2.49, 95% CI [1.19–5.23], p=0.015) were independent predictors of long-term mortality.

Kaplan-Meier survival curves for the 24-month follow-up period were generated for patients without fQRS, those with preoperative fQRS, and those with new-onset postoperative fQRS (Figure 2). The survival rates were lower in both the

Table 3: Univariate and Multivariate Logistic Regression Analyses For In-Hospital Mortality

Variable	In Hospital Mortality			
	Univariate		Multivariate	
	Unadjusted OR (95%CI)	P value	Adjusted OR (95% CI)	P value
BMI, kg/m²	0.86 (0.75 – 0.97)	0.018	0.86 (0.75 – 1.01)	0.051
Baseline sPAP, mmHg	1.05 (1.01 – 1.09)	0.008	1.02 (0.97 – 1.06)	0.361
Preop fQRS	5.08 (1.95 – 13.24)	0.001	3.65 (1.26 – 10.57)	0.017
STS score	1.21 (1.07 – 1.35)	0.001	1.16 (1.02 – 1.32)	0.023
COPD	4.07 (1.51 – 10.93)	0.005	3.95 (1.38 – 11.31)	0.011

BMI, body mass index, CI, confidence interval, COPD, chronic obstructive pulmonary disease, fQRS, fragmented QRS complex, OR, odds ratio, sPAP, systolic pulmonary artery pressure, STS, Society of Thoracic Surgeons

Table 4: Cox Regression Analyses Among In-Hospital Survivors For Mortality During 2-Year Follow-Up

Variable	Follow-up Mortality			
	Univariate		Multivariate	
	Unadjusted HR (95%CI)	P value	Adjusted HR (95% CI)	P value
Age, years	1.05 (1.01 – 1.09)	0.036	1.03 (0.98 – 1.08)	0.188
GFR, mL/min/1.73 m²	0.98 (0.97 – 0.99)	0.021	0.99 (0.98 – 1.01)	0.732
Postoperative sPAP, mmHg	1.06 (1.03 – 1.08)	0.001	1.04 (1.02 – 1.07)	0.001
Postoperative LVEF, %	0.95 (0.92 – 0.98)	0.002	0.97 (0.93 – 1.01)	0.092
Moderate or severe PVAR	3.85 (1.68 – 8.81)	0.001	3.75 (1.55 – 9.05)	0.003
Postoperative fQRS	3.97 (1.98 – 7.95)	0.001	2.49 (1.19 – 5.23)	0.015

preoperative and new-onset fQRS groups than in patients without fQRS, whereas the survival probabilities were similar between the preoperative and new-onset fQRS groups.

Discussion

The fQRS, an ECG marker of myocardial fibrosis resulting from ventricular depolarization defects, has been established as a prognostic indicator for various cardiovascular diseases. This study demonstrated that the fQRS is also a significant predictor of both in-hospital and long-term mortality in patients undergoing TAVI for severe AS. Additionally, the emergence of new-onset fQRS post-TAVI was found to have an impact on long-term mortality. However, no significant difference in survival was observed between patients with preoperative fQRS and those with new-onset fQRS post-TAVI. Another notable finding of this study was the higher incidence of PPI in patients with preoperative fQRS.

fQRS is frequently identified as an incidental finding on ECGs, representing a minor ventricular depolarization defect. In an evaluation of ECGs from a general population of 10.904 individuals, the prevalence of fQRS was observed to be 19.7%, with distribution rates of 15.7%, 2.9%, and 0.8% in the inferior, anterior, and lateral leads, respectively. fQRS has not been associated with increased mortality in individuals without known cardiovascular diseases. However, lateral fQRS is associated with an increased risk of all-cause, cardiac, and arrhythmic mortality in individuals with documented cardiac disease (20). Another study in a healthy population found that the presence of fQRS was associated with reduced LV global strain (21). The prognostic value of fQRS has been extensively documented in various structural heart diseases, especially coronary artery disease and hypertrophic cardiomyopathy. However, its significance in patients with severe AS remains underexplored. Initially, the incidence of fQRS in a specific cohort of severe AS patients was reported to be 46% (22). Subsequent studies have shown that fQRS is related to the severity of AS and LV hypertrophy, potentially serving as a

better indicator than traditional LV hypertrophy criteria (23).

The first study investigating the prognostic value of the fQRS in patients with severe AS undergoing TAVI was reported by Ay et al. In this retrospective study of 117 patients, 36 (30.7%) had preoperative fQRS, and this group had higher rates of both in-hospital and long-term mortality (24). Another study with 116 patients reported an fQRS incidence of 37.9%. In a median follow-up of 319 days, fQRS presence was found to be an independent predictor of mortality along with a history of stroke and baseline creatinine levels (25). In our cohort, the preoperative fQRS rate was similarly observed to be 29.4%. Preoperative fQRS, high STS scores, and the presence of COPD were found to influence in-hospital mortality. Unlike other studies in the literature, our study also evaluated ECGs post-TAVI, identifying new-onset fQRS in 24 patients (11.8%) who initially had normal QRS complexes. The long-term prognosis of patients surviving the in-hospital period was assessed based on the postoperative ECG and TTE findings. Postoperative sPAP, moderate or severe PVAR, and postoperative fQRS were identified as independent predictors of long-term mortality. Furthermore, patients with new-onset fQRS had a cumulative 3.24-fold increased risk of long-term mortality compared with those without fQRS. This is the first study to present the prognostic significance of new-onset QRS fragmentation post-TAVI. It also stands out because of its large patient population and long follow-up period.

Beyond the prognostic impact of the fQRS on survival in TAVI patients, its perioperative arrhythmogenic effects have also been minimally explored. In a study of 124 patients using only self-expanding transcatheter valves, higher rates of new-onset left bundle branch block and PPI requirement post-TAVI were observed in patients with preoperative fQRS. Additionally, fQRS in the anterior leads was shown to be a predictor of postoperative rhythm disturbances (26). Similarly, in our series, the incidence of high-degree atrioventricular block requiring postoperative PPI was significantly higher in the preoperative fQRS group than in those without fQRS (14.1% vs. 2.9%).

In the pathogenesis of severe AS, increased intracavitary pressure leads to endomyocardial fibrosis in the LV myocardium, independent of ischemia. This accumulation of myocardial fibrosis has been corroborated by preoperative cardiac magnetic resonance (CMR) imaging (27). Additionally, a positive correlation has been reported between the degree of histopathological myocardial fibrosis and both LV end-diastolic diameter and LV mass, while a negative correlation exists with LVEF (28). Extracellular volume load measured by CT has also been shown to have prognostic significance in patients undergoing TAVI (29). In patients undergoing surgical valve replacement for severe AS, a high degree of myocardial fibrosis identified through biopsy has been associated with reduced 10-year survival (30).

In light of these recent findings, it is beneficial to utilize advanced diagnostic tools such as CMR and cardiac CT, which allow for the evaluation of subclinical LV remodeling and myocardial fibrosis, in addition to basic echocardiographic and clinical predictors, for prognosis determination in patients planned for TAVI due to severe AS (31). Despite the prognostic importance of myocardial fibrosis in TAVI patients demonstrated by CMR and CT studies, the high cost, limited accessibility, and requirement for experienced specialized staff for interpretation restrict their widespread use. Therefore, identifying myocardial fibrosis indirectly through fQRS on a conventional ECG can be a simple, easy, and inexpensive alternative tool for prognosis in this patient group. However, for this method to be more widely used and to enhance its diagnostic power, extensive large-scale studies, particularly those investigating correlations with modern imaging techniques, are needed.

fQRS, which is easily detectable as a ventricular depolarization defect on a standard 12-lead ECG, is an indicator of subclinical myocardial fibrosis. Both preoperative and postoperative fQRS negatively impact short-term and two-year long-term survival in patients undergoing TAVI for symptomatic severe AS.

Study Limitations: The main limitation of this study was its retrospective design, which was conducted at a single center with a relatively small sample size. The investigation of preoperative ECGs for fQRS was conducted with great care in all patients, but patients with fQRS were not categorized based on the territories of the coronary arteries. As a result, the prognostic differences of the fQRS in various derivation regions could not be explored. Additionally, patients with pre- or postoperative fQRS did not undergo further examinations, such as rhythm Holter monitoring or electrophysiological studies, to investigate arrhythmias. The lack of additional

imaging modalities to confirm myocardial fibrosis represents another limitation.

Ethics Approval Statement: The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Istanbul Medipol University (Approval Date: 22.05.2024, No:2024/535).

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Availability of data and materials: The authors confirm that the data supporting the findings of this study are available within the article.

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